23 February 2018

Monsieur le Président de la République Française
Palais de l'Elysée
55 Rue du Faubourg Saint-Honoré
75008 Paris
France

Re: Lysiane Pakter – French baby with a rare disease

> If a newborn French baby suffering from a rare disease, immobilized in an intensive care unit and connected to a ventilator machine, doesn't have the right to obtain a highly specialised, medically proven and cost-effective treatment for her rare disease in another EU Member State – then who in France does have the right to obtain cross-border medical care?

Dear President Macron,

My partner and I are writing to you to **urgently** request your intervention in a matter involving our baby, Lysiane, who suffers from a rare disease, Pierre Robin Sequence, and our continuing struggle to obtain an S2, L'Assurance Maladie's administrative approval, for a highly specialised, medically proven and cost-effective treatment, the "TPP" treatment in Germany, for her rare disease. **Our intervention request is for your assistance obtaining this S2, which we were wrongfully denied**.

France's Reference Centre for this rare disease confirmed that the TPP treatment is not available in France, but that it is available in fellow EU Member State, Germany. Nevertheless, L'Assurance Maladie rejected our request for this treatment, and denied us the S2. In spite of our efforts, L'Assurance Maladie continues to maintain its unfounded rejection; this is why we have finally decided to make this heartfelt appeal to you. We as parents want this administrative ordeal with L'Assurance Maladie to finally be resolved, so that we can focus our energy where it belongs: on our baby Lysiane, who suffers from a rare disease.

L'Assurance Maladie's rejection of our request for this highly specialised rare disease treatment violates the 2011/24/EU Directive on Cross-border Healthcare, Regulation (EC) No 883/2004 on Social Security Systems, and the fundamental principle of the freedom to provide and receive services under Article 56 of the Treaty on the Functioning of the European Union. It infringes upon the EU's four fundamental freedoms – the free movement of goods, services, people and capital; it undermines a key EU policy objective at the heart of the European project – the effort to create a single EU market; and it cannot possibly be justified as "necessary and proportionate" on any public policy grounds. We have a growing list of individuals and international organizations who have carefully analysed our case, and who openly agree with our position. Attached please find several letters of support, beginning on page 4. Our allies include:

1. the European Commission's SOLVIT network, which agrees with our legal position, Case Number 2569/17/DE;

2. the Member of Parliament representing our district in France, Mr. Bruno Bonnell, of the Assemblée Nationale; Mr. Bonnell is an active defender of patients' rights, and people with disabilities; he is supporting us in our appeal;
3. EURORDIS, the largest rare disease patient organization in the EU; EURORDIS has pledged to accompany us in court, all the way up to the European Court of Justice; EURORDIS has sent a formal letter of support to L'Assurance Maladie;
4. a Member of European Parliament, Ms. Françoise Grossetête, who has extensive experience working with the 2011/24/EU Directive on Cross-border Healthcare; Ms. Grossetête has sent a formal letter of support to France's Minister of Health, Ms. Agnès Buzyn;
5. the European Patients' Forum, the largest patient advocacy umbrella organization in the EU, and a key stakeholder in the drafting of the 2011 Directive; the European Patients' Forum has sent a formal letter of support directly to you, President Macron;
6. an international network of law professors who specialise in EU cross-border healthcare and social security law, who agree that L'Assurance Maladie's rejection was unfounded.

As we explain in this document, the treatment which is used in France to treat our baby's rare disease, Pierre Robin Sequence, consists of keeping the baby in a hospital, attached to a ventilator machine. Since ventilation assistance generally requires long term hospitalisation, the French treatment creates colossal healthcare costs, and it uses up precious space in neonatal intensive care units. Germany's highly specialised TPP treatment, on the other hand, is medically proven to resolve the upper airway obstruction associated with this rare disease. The TPP treatment liberates the baby from the ventilator machine without surgery, and without long term hospitalization, making it a cost-effective medical breakthrough in the treatment of this rare disease.

Thus, not only does the French treatment have the disadvantage of keeping the baby attached to a ventilator machine, substantially reducing mobility, and quality of life – but in addition to this, it doesn't even make financial sense. For L'Assurance Maladie in France to deliberately obstruct a French baby's access to the medically proven German treatment, which dramatically improves the baby's ability to breathe, and quality of life – *and which reduces healthcare costs, by eliminating the need for long term hospitalisation* – is as irrational as refusing to adopt email, and stubbornly insisting on using expensive and cumbersome fax machines instead.

Since the lives and suffering of newborn babies is at stake, L'Assurance Maladie's rejection doesn't just defy logic; it is also unconscionable. No ethical doctor or civil servant should force a newborn baby suffering from a rare disease to endure long term intensive care, with all of the burdens this entails, when fellow doctors in the EU Member State just next door have successfully developed a cost-effective medical treatment to safely get the baby off of the ventilator machine, and home to her parents, where the baby belongs. Doctors should not play God; they should facilitate patient access to care, not obstruct patient access to care. A patient's rights should take priority over a physician's ego.

L'Assurance Maladie's unfounded rejection is particularly inappropriate now, with Brexit. The cohesion of the EU has become a central issue; each Member State should solemnly respect its obligations vis-à-vis EU law. "Europe is crossing an important milestone," as you have said. Now is not the time for a leading Member State like France to act as if EU law

should apply to other Member States, but not to her. Intentional obstruction, market interference, and non-cooperation is not at all how the EU community is supposed to operate.

Furthermore you have expressed your wish to "totally integrate" the French and German markets, and "restore a strong trust between France and Germany." L'Assurance Maladie's senseless refusal to authorise French babies to receive this breakthrough treatment in Germany casts doubt upon France's commitment to this goal. If France is unwilling to cooperate with Germany to reduce the suffering of newborn French babies who are struggling to breathe, then France will have a very hard time cooperating with Germany on major international projects which are actually divisive and complex.

This case raises an issue of wider principle which matters to all French citizens, and which affects their daily lives: if a newborn French baby suffering from a rare disease, immobilized in an intensive care unit and connected to a ventilator machine, doesn't have the right to obtain a highly specialised, medically proven and cost-effective treatment for her rare disease in another EU Member State – then who in France does have the right to obtain cross-border medical care?

Mr. President, this document, with its extensive evidence, and letters of support, make it clear that L'Assurance Maladie's rejection was unfounded. My partner and I urgently request your assistance obtaining Lysiane's S2, which L'Assurance Maladie illegally and senselessly denied. We hope to hear from you very soon. Thank you.

Sincerely,

Philippe Pakter and [redacted] – the parents of Lysiane
2 rue Gérard Maire
69100 Villeurbanne
France

Contents

Monsieur le Président de la République
Palais de l'Elysée
55 rue du Faubourg Saint-Honoré
75008 Paris

Brussels, 16 January 2018

Dear President Macron,

Subject: Access to healthcare in France – breach of EU law

We are writing to you on behalf of the European Patients' Forum (EPF), an umbrella organisation representing 74 patient organisations across the EU, to ask for your support in the case of Lysiane Pakter, 9 months old, represented by her parents Mr Philippe Pakter and Ms [redacted], to have her right to access cross-border-border healthcare recognised by the Caisse Primaire d'Assurance Maladie (CPAM) in Lyon.

Equitable access to healthcare is a core patients' right and has been one of EPF's main priorities since the foundation of our organisation. It was in the context of our work on Directive 2011/24/EU on patients' rights in cross-border healthcare that we came in contact with Mr Pakter and Ms [redacted]. They have given an excellent overview of the shocking situation they have been faced with after their daughter was diagnosed with the rare Pierre Robin syndrome.[1]

Their dispute with CPAM comes down to the following. CPAM rejected the transfer of Lysiane to Tübingen University Hospital in Germany, arguing that the French treatment – which involves connecting the new-born baby to a ventilator machine, and keeping her in an intensive care unit for long-term hospitalisation – is "the same or equally effective" as the highly specialised TPP treatment offered in Tübingen. The latter not only removes the baby's upper airway obstruction but at the same time also corrects its underlying anatomical cause, glossoptosis, without surgery and without long-term hospitalisation. To argue that these treatments are the same, or equally effective, is a surprising claim to say the least. What is even more surprising is the consistent refusal of CPAM to review their assessment, despite the institutional support that Mr Pakter and Ms [redacted] have received.

[1] Please see: http://avantetapres.com/

We need not repeat the legal and medical analysis of their situation, based on the EU Directive and its transposition into French law, which has been comprehensibly provided by a letter from EPF's member organisation EURORDIS – Rare Disease Europe dated 17 November 2017 and addressed to CPAM. From this analysis it is clear that the right to access care has been breached, and that the assessment of CPAM is not only contrary to the provisions of the EU Directive and the implementing French law, but also to the general spirit of the Directive and the benefits that the sharing of expertise between Member States can have. Especially in the area of rare diseases, this is, of course, of utmost importance.

SOLVIT, a network of national administrations that aims at finding rapid and pragmatic solutions for problems encountered by citizens when EU law is not applied correctly by national authorities, agrees with the legal assessment of Mr Pakter and Ms [redacted] and is trying to help them overcome the unnecessary obstacles they are facing.

A prominent Member of the European Parliament, Ms Françoise Grossetête, has also voiced her support to Mr Pakter and Ms [redacted]. In her letter of 18 December 2017 to the French Minister of Social Affairs, Health and Women's Rights, she urges CPAM to accept their claim and to have their rights recognised under the Directive. Having been the European Parliament's rapporteur for this legislation, Ms Grossetête has a thorough understanding of the legislation and the rights it grants to citizens.

We wish to add our voice to the above and ask for your kind support in putting an end to this unnecessary struggle of Lysiane's parents to access quality treatment for their daughter, based on an unfounded denial of patient's rights that violates both EU and French law.

Sincerely,

Nicola Bedlington
EPF Secretary General

Marco Greco
EPF President

Annexed:

1) Eurordis letter of 17 November 2017
2) Letter of Françoise Grossetête of 18 December 2017

Unofficial translation; original French text is included after this translation.

Brussels, 18 December 2017

Françoise GROSSETÊTE
Member of European Parliament
Vice-President of the PPE Group
European Parliament
Rue Wiertz, B-1047
Brussels

Ms. Agnès BUZYN
Minister
Ministry of Social Affairs, Health, and Women's Rights
14, avenue Duquesne
75350 Paris 07 SP
France

Dear Ms. Minister,

I wish with this letter to alert you to the very urgent case of Lysiane Pakter, born on 29 March 2017, and diagnosed with a rare disease called Pierre Robin Sequence. To treat this pathology, Lysiane should receive a highly specialized treatment, which the Orphanet Reference Centre for this rare disease confirmed is only available in Germany.

In accordance with the Directive 2011/24/EU on the application of patients' rights in cross-border healthcare, Lysiane's parents, Mr. Pakter and Ms. [redacted], applied, as properly required, for prior authorization for this care, via the S2 form.

Unfortunately, their application was rejected by the Caisse Primaire d'Assurance Maladie (CPAM) of Lyon; the parents found themselves running up against the administration's lack of knowledge of the applicable rules and procedures of cross-border healthcare. At this point, the case is still undergoing an internal administrative review by CPAM.

Viewing CPAM's decision as a violation of European law, the parents referred the matter to the SOLVIT network (Case No. 2569/17/DE), which acknowledged that in this case, CPAM's refusal to provide prior authorization was contrary to the laws in force.

While these procedures are underway, and in the face of the emergency, Lysiane was transferred to Germany without waiting for CPAM's decision, because to correct the problem, the treatment should begin as early as possible.

Faced with this unacceptable situation, and sensitive to the distress of this family, I appeal to you for your support and assistance in calling upon the appropriate department in the Social

Unofficial translation; original French text is included after this translation.

Security administration to move this issue forward, and ensure the correct application of the Directive 2011/24/EU on Patients' Rights in Cross-border Healthcare.

Thanking you in advance for your attention to this request, I remain at your disposal, and I ask you to please accept, Ms. Minister, the assurance of my highest consideration.

I am counting on you.

Françoise GROSSETÊTE

Parlement européen

Françoise Grossetête

Députée européenne
Vice-Présidente du Groupe PPE

Ref : 20171812/RP

Bruxelles, le 18 décembre 2017

Madame la Ministre,

Je souhaite par cette lettre vous alerter sur le cas très urgent de Lysiane Pakter, née le 29 mars 2017 et diagnostiquée avec un cas de maladie rare appelée Séquence de Pierre Robin. Pour traiter cette pathologie, Lysiane doit recevoir un traitement hautement spécialisé, dont le Centre de Référence Orphanet pour cette maladie rare a confirmé qu'il n'était disponible qu'en Allemagne.

Au regard de la Directive 2011/24/UE relative à l'application des droits des patients en matière de soins de santé transfrontaliers, les parents de Lysiane, M. Pakter et Mme [redacted], ont donc tenté d'obtenir comme il se doit une autorisation préalable pour ces soins, via le formulaire S2.

Malheureusement, cette demande a été rejetée par la Caisse Primaire d'Assurance Maladie (CPAM) de Lyon, les parents se heurtant à la méconnaissance des procédures et des textes existants en matière de soins de santé transfrontaliers de la part de l'administration. À ce stade, l'affaire est toujours en cours de révision administrative interne par la CPAM.

Estimant que la décision de la CPAM viole le droit européen, les parents ont saisi le réseau SOLVIT (numéro de dossier 2569/17/DE), qui a reconnu que le refus d'autorisation préalable en l'espèce était contraire aux textes en vigueur.

B-1047 Bruxelles - ASP 13E154 - Tél. +32 2 28-45952
F-67070 Strasbourg - LOW T10049 - Tél. +33 3 881-75952
francoise.grossetete@ep.europa.eu

Pendant que ces procédures suivent leur cours, et face à l'urgence, Lysiane a dû être transférée en Allemagne sans attendre le retour de la CPAM, car le traitement permettant de corriger le problème doit être réalisé le plus tôt possible.

Face à cette situation inacceptable, et sensible à la détresse de cette famille, j'en appelle à votre soutien et à votre aide afin de saisir les services compétents de la Sécurité Sociale pour faire avancer ce dossier et assurer la bonne application de la Directive 2011/24/UE concernant les droits des patients en matière de soins de santé transfrontaliers.

Vous remerciant par avance de l'attention que vous voudrez bien accorder à cette demande, je reste à votre entière disposition et vous prie d'agréer, Madame la Ministre, l'assurance de ma très haute considération.

Je compte sur vous

Françoise GROSSETÊTE

Madame Agnès BUZYN
Ministre
Ministère des Affaires sociales, de la Santé et des Droits des femmes
14, avenue Duquesne
75350 Paris 07 SP
FRANCE

Unofficial translation; original French text is included after this translation.

François Houÿez
EURORDIS
Plateforme Maladies Rares
96 rue Didot
F-75014 Paris
+331 56 53 52 18

Mr. Nicolas Revel

General Director
Caisse Nationale d'Assurance Maladie
50, avenue du Professeur André Lemierre
75986 Paris Cedex 20

Subject: Access to healthcare in another Member State - child Lysiane Pakter

Dear Mr. General Director,

EURORDIS, the European Organization for Rare Diseases, defends the rights of patients to access healthcare in other Member States of the European Union and the European Economic Area, among other activities.

In this capacity, EURORDIS supports Lysiane Pakter's parents, in the face of L'Assurance Maladie's refusal of their request for planned healthcare in Germany.

During the debates which took place in the European Parliament prior to the adoption of Directive 2011/24/EU of 9 March 2011 on the application of patients' rights in cross-border healthcare, EURORDIS advocated for the adoption of the Directive, based on the limitations we identified in Regulation 883/2004 and the S2 Form.

The vagueness of Regulation 883/2004 in certain situations led the European Court of Justice (the ECJ) to issue a number of legal decisions, for example the ECJ's judgment in case 157/99, 12/07/2001, the Geraets-Smits case. This substantial body of ECJ jurisprudence led the European authorities to fill the legal vacuum, by adopting Directive 2011/24/EU.

In no case should the national transposition of the Directive constitute a regression, when viewed in relation to the case law of the ECJ. In the Geraets-Smits case, the ECJ states that:

- Prior authorization can not be refused if the treatment is sufficiently tested and validated by international medical science, and
- Prior authorization can be refused when the same or equally effective treatment for the patient can be obtained without undue delay from an institution which has entered into an

agreement with the health insurance fund to which the insured person belongs (absence of medical necessity)

Transposition of the Directive into French law

The Public Health Code, Article R160-2, as amended by Decree No. 2017-736 of 3 May 2017, Art. 1, states that:

II. The authorization can not be refused when the following conditions are met:

1° Coverage of the medical treatment sought is provided for by the French regulations;

2° The treatment sought is appropriate based on the patient's state of health;

3° The same or equally effective treatment can not be obtained in France within a medically acceptable timeframe, taking into account the patient's current state of health, and the probable course of the patient's condition.

In the matter of Lysiane

Regarding point 1°: medical treatments involving surgical techniques (mandibular distraction osteogenesis, mandibular traction, tracheostomy, insertion of a nasopharyngeal tube…) to treat Pierre Robin sequence are provided for by France's healthcare provisions. The community has arranged for babies born with this medical syndrome to be treated. One technique, labioglossopexy, involves the sewing of the tip of the baby's tongue to the baby's lower lip; it has a high rate of failure, due to the tearing of the baby's tongue or the baby's lip. If this type of treatment is covered by the French regulations then a non-surgical alternative method such as the Tübingen Palatal Plate with velar extension (the TPP), which is not disabling, and which, in a word, is not barbaric, is just as worthy of being covered.

Regarding point 2°: the medical studies listed in this letter's annex confirm the greater effectiveness of the TPP treatment proposed in Germany.

Regarding point 3°: the baby should be fitted with the TPP device shortly after birth, a time period too brief to allow the French healthcare system to learn the technique, without exposing the baby to a loss of chance.

The treatment proposed in Germany (the Tübingen Palatal Plate with velar extension, the TPP) is indicated for treating feeding and breathing difficulties in the context of Pierre Robin sequence, but this is the only thing it has in common with the treatments proposed in France. The treatments offered in France are not the same: neither mechanical ventilation assistance, with all the limitations it imposes on the young child's movement, nor complex and painful surgical interventions. Thus Lysiane was hospitalized in France for 5 consecutive weeks in an intensive care ward, with no scheduled release date, except for the eventual possibility of home hospitalization, with mechanical ventilation assistance.

Furthermore, the treatments offered in France appear less effective than the TPP treatment; the authors of the prospective study (No. 1 in the annex) conclude: "This prospective longitudinal cohort study confirms the effectiveness of the [Tübingen Palatal Plate] in

improving upper airway obstruction and weight gain in infants admitted with (mostly isolated) RS."

Finally, this TPP device has been tested by multiple teams, and a third of babies born with Pierre Robin sequence in Germany already benefit from this treatment (see the selection of medical studies listed in the annex).

If the opinion of French experts is that it would be advisable to carry out a comparative controlled study before deciding to cover this treatment, then we must rebut the idea of a direct comparison; this is simply no longer ethically possible. Comparative data involving historical studies do however already allow this treatment to be compared with other treatments (indirect comparison).

The authors of the study cited above ("Multicenter study on the effectiveness of the pre-epiglottic baton plate for airway obstruction and feeding problems in Robin sequence", Poets et al., Orphanet Journal of Rare Diseases, 2017, 12:46) point this out; the measurement of weight gain achieved with the different treatment techniques makes it possible to compare their relative effectiveness.

On this basis the TPP treatment is at least as effective as the other methods, or more effective. In any case in terms of the baby's comfort, and quality of life, and safety too, the TPP treatment is superior.

Furthermore, clinical equipoise is no longer present, at least in Germany, where doctors and parents are informed about the different techniques which are available for treating this rare disease. No doctor would be willing to carry out a randomized clinical trial in which the treatment to be administered to each baby is randomly selected. Based on current knowledge of the various treatments, they are already convinced of the overall superiority of the TPP technique. Parents would refuse it as well.

"Clearly, a controlled study design would have been preferable. This, however, was impossible in participating centers, as there was no longer equipoise among team members. However, we tried everything possible to minimize other potential sources of bias and thus consider our results valid against a background of studies performed in patients with rare conditions."

What EURORDIS advocates in general

Regarding the transposition of Directive 2011/24/EU by Member States, EURORDIS has advocated the following principles:

- Effectiveness: the measures taken by Member States must be of a nature to assist citizens in their efforts, and healthcare administrations must put themselves at the service of citizens and help them exercise their rights
- Proportionality: the Directive imposes limits on the prior authorization system, restricting it to what is necessary and proportionate to the objective to be achieved; it may not constitute a means of arbitrary discrimination or an unjustified obstacle to the free movement of patients, in accordance with Article 8.1
- Justice: the system of prior authorization must allow the applicant to submit his application and to lodge an appeal if his application has been refused, and the

administration must inquire with experts who are familiar with the disease before authorizing or rejecting the patient's application for healthcare abroad

In the interest of French citizens, EURORDIS asks you to respect these principles. The Directive was adopted precisely to allow patients to access the most effective treatment available in the European Union, even if that treatment is not available in their Member State of affiliation.

According to experts who treat children suffering from Pierre Robin sequence: "If the functional difficulties are managed effectively during the first year of life, the prognosis is favorable. Feeding and breathing difficulties, as well as glossoptosis, improve in the first 2 years of life; mandibular growth corrects retrognathism in 3 to 6 years. The cleft palate can be closed surgically before 9 months. The neurological prognosis of these children is thus good."

EURORDIS invites you to urgently consider the case of this baby and others in the same situation in order to facilitate their right to access quality care. Failure to do so could result in a loss of chance, with significant long term impact throughout their entire lives.

With sincere compliments, please kindly accept, Sir, the expression of my most profound respect.

François Houÿez, Director of Access to Care
francois.houyez@eurordis.org

EURORDIS
17 November 2017

CC: Ms. Emmanuelle Lafoux, General Director, Caisse Primaire d'Assurance Maladie de Lyon

Unofficial translation; original French text is included after this translation.

Annex

1. **Multicenter study on the effectiveness of the pre-epiglottic baton plate for airway obstruction and feeding problems in Robin sequence.**

   Poets CF, Maas C, Buchenau W, Arand J, Vierzig A, Braumann B, Müller-Hagedorn S. In Orphanet J Rare Dis. 2017 Mar 9;12(1):46. doi: 10.1186/s13023-017-0602-8.

2. **Functional treatment of airway obstruction and feeding problems in infants with Robin sequence.**

   Buchenau W, Wenzel S, Bacher M, Müller-Hagedorn S, Arand J, Poets CF in Arch Dis Child Fetal Neonatal Ed. 2017 Mar;102(2):F142-F146. doi: 10.1136/archdischild- 2016-311407. Epub 2016 Jul 19.

3. **Initial treatment and early weight gain of children with Robin Sequence in Germany: a prospective epidemiological study.**

   Maas C, Poets CF in Arch Dis Child Fetal Neonatal Ed. 2014 Nov;99(6):F491-4. doi: 10.1136/archdischild-2014-306472. Epub 2014 Aug 27.

4. **Airway and feeding problems in infants with Fairbairn-Robin triad deformities.**

   du Plessis SM, van den Berg HJ, Bütow KW, Hoogendijk CF. Curationis 2013;36(1):E1-9.

5. **The influence of the Tübingen soft palate plate and early cleft closure on the nasopharyngeal airway for the management of airway obstruction in an infant with Pierre Robin sequence: A case report.**

   Gerzanic L1, Feichtinger M, Kärcher H in Int J Surg Case Rep. 2012;3(12):608-10. doi: 10.1016/j.ijscr.2012.08.011. Epub 2012 Aug 31.

François Houÿez

EURORDIS
Plateforme Maladies Rares
96 rue Didot
F-75014 Paris
+331 56 53 52 18

M. Nicolas Revel

Directeur Général
Caisse Nationale d'Assurance Maladie
50, avenue du Professeur André Lemierre
75986 Paris Cedex 20

Objet : Accès aux soins dans un autre Etat Membre – Enfant Lysiane Pakter

Monsieur le Directeur Général,

EURORDIS, l'Organisation Européenne des Maladies Rares, défend les droits des malades en ce qui concerne l'accès aux soins dans un autre Etat Membre de l'Union Européenne et de l'Espace Economique Européen, entre autres activités.

A ce titre, EURORDIS soutient les démarches des parents de Lysiane Pakter face au refus de l'Assurance Maladie de leur demande de soins médicaux programmés en Allemagne.

Lors des débats au Parlement européen pour l'adoption de la Directive 2011/24/UE du 9 mars 2011 relative à l'application des droits des malades en matière de soins de santé transfrontaliers, EURORDIS a défendu l'adoption de la Directive du fait des limites du Règlement 883/2004 et du formulaire S2 que nous avions identifiées.

L'imprécision du Règlement 883/2004 dans certaines situations a conduit la Cour de Justice Européenne à faire jurisprudence à plusieurs reprises, par exemple dans son arrêt 157/99, 12/07/2001 Geraets- Smits. Cette jurisprudence abondante a conduit les autorités européennes à combler le vide juridique en adoptant la Directive 2011/24/UE.

En aucun cas la transposition nationale de la Directive ne doit représenter une régression du droit par rapport à la jurisprudence de la Cour. Dans l'arrêt Geraets-Smits, la CJUE stipule que :

- L'autorisation préalable ne peut pas être refusée si le traitement est suffisamment éprouvé et validé par la science médicale internationale et

- L'autorisation préalable peut être refusée lorsqu'un traitement identique ou présentant le même degré d'efficacité pour le patient peut être obtenu en temps opportun auprès d'un établissement ayant conclu une convention avec la caisse de maladie dont relève l'assuré (absence de nécessité médicale)

La transposition de la Directive dans le droit français

Dans le Code de Santé Publique, l'article R160-2 modifié par Décret n°2017-736 du 3 mai 2017 - art. 1stipule que :

II.- L'autorisation ne peut être refusée lorsque les conditions suivantes sont réunies :

1° La prise en charge des soins envisagés est prévue par la réglementation française ;

2° Ces soins sont appropriés à l'état de santé du patient ;

3° Un traitement identique ou présentant le même degré d'efficacité ne peut pas être obtenu en France dans un délai acceptable sur le plan médical, compte tenu de l'état de santé actuel du patient et de l'évolution probable de son affection.

Au sujet de Lysiane

En ce qui concerne le point 1° : les soins utilisant des techniques chirurgicales (ostéogénèse par distraction de la mâchoire, étirement de la mâchoire, trachéostomie, pose d'un tube nasopharyngé…) pour traiter le syndrome de Pierre Robin sont prévus par la réglementation française. La collectivité a pris les dispositions pour que les enfants naissant avec ce syndrome soient traités. Une technique, la labioglossopexie consiste à coudre l'extrémité de la langue du bébé sur la lèvre inférieure, avec un taux d'échec élevé, dû à la déchirure de la langue ou de la lèvre. Si ce type de soin est prévue par la réglementation française, alors une méthode alternative non chirurgicale, non invalidante et en un mot non barbare, comme la plaque de palais de Tübingen avec extension vélaire mérite tout autant de l'être.

En ce qui concerne le point 2° : les travaux listés en annexe attestent d'une plus grande efficacité de la Plaque de Palais proposée en Allemagne.

En ce qui concerne le point 3° : la Plaque de Palais doit être implantée dans des délais très brefs après la naissance, délais qui ne permettent pas au système de soins français d'acquérir cette technique sans exposer l'enfant à une perte de chance.

Le traitement proposé en Allemagne (Plaque de Palais de Tübingen avec extension vélaire) est indiqué pour traiter les troubles de la déglutition et de la ventilation au cours du syndrome de Pierre Robin, mais c'est le seul point commun avec les traitements proposés en France. Ceux-ci ne sont pas identiques : ventilation mécanique externe avec toutes les limitations des mouvements que cela impose à un très jeune enfant, ou intervention chirurgicale complexe et douloureuse. Ainsi, Lysiane était hospitalisée en France 5 semaines consécutives en soins intensifs, sans aucune sortie envisagée ou bien en hospitalisation à domicile avec ventilation assistée.

Outre plus, les soins dispensés en France semblent moins efficaces que la Plaque de Palais : les auteurs de l'étude prospective (1) concluent : « Cette étude de cohorte longitudinale et prospective confirme l'efficacité de la Plaque de Palais pour l'amélioration de l'obstruction des voies aériennes supérieures et la prise de poids chez des enfants hospitalisés pour le syndrome de Pierre Robin ».

Enfin ce traitement par implant a été testé par différentes équipes, et un tiers des enfants naissant avec le syndrome de Pierre Robin en Allemagne en bénéficient déjà (voir sélection d'articles scientifique en annexe).

Si l'avis d'experts français est qu'il convient de mener des essais comparatifs contrôlés avant toute décision de prise en charge, nous tenons à réfuter l'idée d'une comparaison directe. Cela n'est tout simplement plus éthiquement possible. Les données de comparaison avec contrôles historiques permettent de comparer les méthodes (comparaison indirecte).

Les auteurs de l'étude citée (Multicenter study on the effectiveness of the pre-epiglottic baton plate for airway obstruction and feeding problems in Robin sequence. Poets et al. Orphanet Journal of Rare Diseases (2017) 12:46)) l'expliquent: la mesure du gain de poids avec les différentes méthodes permet de comparer leur efficacité relative.

Sur cette base, la méthode TPP est au moins aussi efficace que les autres, voire meilleure. Et en tous cas, en termes de confort pour l'enfant, de qualité de vie, de sécurité aussi, elle leur est supérieure.
Aussi, l'équipoise n'est plus réalisée, en tous cas en Allemagne, où médecins et parents sont informés des différentes techniques disponibles. Aucun médecin ne souhaitera conduire un essai clinique randomisé avec affectation par tirage au sort de la méthode à utiliser pour chaque enfant. L'état des connaissances en la matière ne le permet plus, car ils sont déjà convaincus de la supériorité globale de la méthode TPP. Les parents le refuseraient également.

"*Clearly, a controlled study design would have been preferable. This, however, was impossible in participating centres, as there was no longer equipoise among team members. (However, we tried everything possible to minimize other potential sources of bias and thus consider our results valid against a background of studies performed in patients with rare conditions.)*"

Ce que préconise EURORDIS dans le cas général

En ce qui concerne la transposition de la Directive 2011/24/UE par les Etats Membres, EURORDIS a préconisé les principes suivants :

- Efficacité : les mesures prises par les Etats-Membres doivent être de nature à aider les citoyens dans leurs démarches, et les administrations sanitaires doivent se mettre au service des citoyens pour faciliter l'accès à leur droit
- Proportionnalité : la Directive encadre le régime d'autorisation préalable en le limitant à ce qui est nécessaire et proportionné à l'objectif poursuivi et ne peut

constituer un moyen de discrimination arbitraire ni une entrave injustifiée à la libre circulation des patients conformément à son article 8.1

- Justice : le régime d'autorisation préalable doit permettre au demandeur d'exposer sa demande, d'introduire un recours si refus, et l'administration doit s'enquérir auprès d'experts connaissant la maladie en question avant d'autoriser ou non le malade à recourir à des soins à l'étranger

Dans l'intérêt des citoyens français, EURORDIS vous demande de suivre ces principes. La Directive a été adoptée précisément afin de permettre à des malades d'accéder aux soins les plus efficaces proposés dans l'Union Européenne, même si ces soins ne sont pas disponibles dans leur Etat Membre d'affiliation.

Selon les experts traitant les enfants atteints de la séquence de Pierre Robin : « Si les troubles fonctionnels sont bien compensés pendant la première année de vie, l'évolution est favorable. Les troubles alimentaires et respiratoires, ainsi que la glossoptose, s'améliorent au cours des 2 premières années de vie, la croissance mandibulaire corrige le rétrognathisme en 3 à 6 ans. La fente palatine peut être fermée chirurgicalement avant 9 mois. Le pronostic neurologique de ces enfants est alors bon ».

EURORDIS vous invite à considérer d'urgence la situation de cet enfant et des autres dans le même cas afin de faciliter leur droit d'accéder à des soins de qualité. A défaut, cela risquerait d'entraîner une perte de chances avec un retentissement considérable tout au long de leur vie.

Avec mes respectueux hommages, je vous prie d'agréer, Monsieur l'expression de ma considération la plus distinguée.

François Houÿez, Directeur de l'Accès aux Soins
francois.houyez@eurordis.org

EURORDIS
17 Novembre 2017

Copie: Mme Emmanuelle Lafoux, Directrice Générale, Caisse Primaire d'Assurance Maladie de Lyon

Annexe

1. **Multicenter study on the effectiveness of the pre-epiglottic baton plate for airway obstruction and feeding problems in Robin sequence.**

   Poets CF, Maas C, Buchenau W, Arand J, Vierzig A, Braumann B, Müller-Hagedorn S. In Orphanet J Rare Dis. 2017 Mar 9;12(1):46. doi: 10.1186/s13023-017-0602-8.

2. **Functional treatment of airway obstruction and feeding problems in infants with Robin sequence.**

   Buchenau W, Wenzel S, Bacher M, Müller-Hagedorn S, Arand J, Poets CF in Arch Dis Child Fetal Neonatal Ed. 2017 Mar;102(2):F142-F146. doi: 10.1136/archdischild-2016-311407. Epub 2016 Jul 19.

3. **Initial treatment and early weight gain of children with Robin Sequence in Germany: a prospective epidemiological study.**

   Maas C, Poets CF in Arch Dis Child Fetal Neonatal Ed. 2014 Nov;99(6):F491-4. doi: 10.1136/archdischild-2014-306472. Epub 2014 Aug 27.

4. **Airway and feeding problems in infants with Fairbairn-Robin triad deformities.**

   du Plessis SM, van den Berg HJ, Bütow KW, Hoogendijk CF. Curationis 2013;36(1):E1-9.

5. **The influence of the Tübingen soft palate plate and early cleft closure on the nasopharyngeal airway for the management of airway obstruction in an infant with Pierre Robin sequence: A case report.**

   Gerzanic L1, Feichtinger M, Kärcher H in Int J Surg Case Rep. 2012;3(12):608-10. doi: 10.1016/j.ijscr.2012.08.011. Epub 2012 Aug 31.

Summary of Dispute

I, Mr. Jean-Philippe Pakter, a Dutch citizen, and my partner, Ms. [redacted], a French citizen, are the parents and legal guardians of Lysiane Pakter, born on 29 March 2017 in Lyon, France. At birth Lysiane was diagnosed with Pierre Robin Sequence, a rare disease affecting approximately 1 baby in 10,000. This rare disease is associated with upper airway obstruction, respiratory difficulties and feeding difficulties, and is potentially life-threatening. Lysiane suffered a dangerous, difficult birth. She was intubated, and rushed to the Neonatal Resuscitation unit, where she spent six straight days. When her condition stabilized she was transferred to the Intensive Care unit. Within less than a week, Lysiane had to be put back onto a ventilator machine, due to continuing respiratory difficulties. She remained in Intensive Care, connected to a ventilator machine, with no scheduled release date.

After exhaustive research, we as parents identified a highly specialised and medically proven technique to effectively treat Lysiane's rare disease. This treatment, the TPP treatment, is not available in France, or anywhere else in Europe, except for one single country: Germany. The TPP treatment was developed at the Tübingen University Hospital, which the EU's Orphanet database officially recognizes as a Centre of Expertise for this rare disease. The TPP treatment is not a new, unproven, experimental treatment. More than 10 years' worth of peer reviewed medical studies have definitively proven that the TPP treatment is a safe and effective treatment for babies suffering from Pierre Robin Sequence, including:

"Treatment of infants with Syndromic Robin sequence with modified palatal plates: a minimally invasive treatment option"; "Multicenter study on the effectiveness of the pre-epiglottic baton plate for airway obstruction and feeding problems in Robin sequence"; "Initial treatment and early weight gain of children with Robin Sequence in Germany: a prospective epidemiological study"; "Functional treatment of airway obstruction and feeding problems in infants with Robin sequence"; "Treatment of Upper Airway Obstruction and Feeding Problems in Robin-Like Phenotype"; "An Oral Appliance With Velar Extension for Treatment of Obstructive Sleep Apnea in Infants With Pierre Robin Sequence", and more.

The TPP treatment is the only Pierre Robin Sequence medical treatment available today which removes the baby's upper airway obstruction, and which at the same time also corrects its underlying anatomical cause, glossoptosis, without surgery, and without long term hospitalization. No other Pierre Robin Sequence treatment does this. This German dento-facial orthopaedic treatment represents a medical breakthrough, and was developed in the EU.

We submitted an application to L'Assurance Maladie requesting prior approval for this highly specialised, medically proven and cost-effective treatment, the TPP treatment, for Lysiane's rare disease. L'Assurance Maladie rejected our request for the TPP treatment, on 19 May 2017. The basis of the rejection was that "the same treatment or an equally effective treatment can be obtained in France without undue delay."

The "same treatment" is not available in France. This fact was verified in writing by the director of France's Reference Centre for this rare disease, Pierre Robin Sequence. Does France offer an "equally effective" treatment? The treatment France proposes is "Continuous Positive Airway Pressure" (CPAP), a form of ventilation assistance. CPAP requires the baby

to be connected to a ventilator machine. The baby must remain connected to this ventilator machine whenever the baby sleeps, both at night and during the day, and long-term hospitalization is generally required.

Medically speaking, the CPAP treatment offered in France is not "equally effective" as the TPP treatment offered in Germany; the TPP treatment is superior to the CPAP treatment in numerous fundamental ways. CPAP does not resolve the baby's core, underlying problem – upper airway obstruction. This is why Lysiane, after a month in the French Intensive Care unit, continued to face breathing difficulties, which the video on this webpage painfully illustrates: http://avantetapres.com/
Our baby's breathing difficulties, and the unnecessary suffering caused by these breathing difficulties, were safely, successfully, and immediately eliminated with the TPP treatment – without risk, and without surgery. No objective and impartial medical comparison can reasonably conclude that CPAP, which requires the baby to be connected to a ventilator machine, and the TPP treatment, which achieves crucial medical objectives that CPAP cannot and does not achieve, are "the same or equally effective".

Article 13 ("Rare Diseases") of the 2011 Directive sets out "the possibilities offered by Regulation (EC) No 883/2004 for referral of patients with rare diseases to other Member States even for diagnosis and treatments which are not available in the Member State of affiliation." By email, CLEISS, the national contact point for France under the 2011 Directive, confirmed for us that the 2011 Directive grants EU citizens suffering from a rare disease the right to obtain a highly specialised treatment in another Member State, if it is <u>not</u> available in their Member State of affiliation.

L'Assurance Maladie's refusal to grant prior authorisation for the highly specialised and medically proven TPP treatment for our baby's rare disease violates the 2011 Directive, Regulation (EC) No 883, and the fundamental principle of the freedom to provide and receive services under Article 56 of the Treaty on the Functioning of the European Union. It represents the kind of arbitrary, irrational, and unreasonable exercise of national discretion which the European Court of Justice has repeatedly struck down. It cannot be justified on any public policy grounds, and was neither necessary nor proportionate. We request your urgent assistance, President Macron, reversing this unfounded rejection.

Background Information

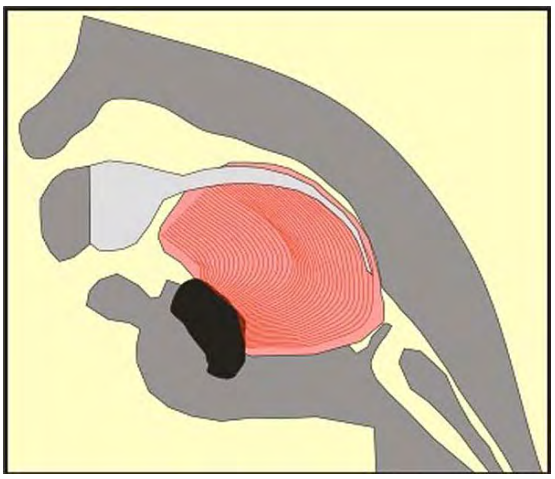
Pierre Robin Sequence, a rare disease

As a result of Pierre Robin Sequence, our child's rare disease, Lysiane suffers from three orofacial deformities:

1. micrognathia: an undersized and underdeveloped lower jaw, and retrognathia: the abnormal rear positioning of her lower jaw toward the posterior;
2. glossoptosis: the abnormal backward retraction and verticalized positioning of her tongue toward the rear of her throat, obstructing her pharynx and blocking her airway;
3. a cleft soft palate, connected to the presence of her tongue in a retracted and verticalized position toward the rear of her throat during prenatal development.

In informal language, micrognathia means that the baby has a very small lower jaw and chin; retrognathia resembles a severe "overbite". A cleft soft palate means that there is a small hole in the soft, rear roof of the mouth. However, the second technical term, glossoptosis, is more difficult to visualize. Since glossoptosis is the deformity which generally poses the most serious threat to the Pierre Robin Sequence baby's health and development, it is worth providing the following illustration.

Normally, the tongue lays down flat, horizontally, on the floor of the mouth. When a baby suffers from glossoptosis, the tongue remains bunched up, in the back of the mouth, and it is raised up, almost vertically. In the image below, the large pink/red object is the baby's tongue.



By looking at the illustration above, one can see why this is an extremely dangerous position for the tongue to be in. In this position, the baby's pharynx (upper airway) is almost completely obstructed. When a baby with Pierre Robin Sequence is struggling to breathe, you don't just see the look of panic on the baby's face; you can also hear the sound of the baby's tongue obstructing the baby's upper airway, as the baby fights to get air down, or to get milk down.

The medical files from Lyon indicate a dangerous and difficult birth, with an Apgar score of 1 / 4 / 8 / 8. An Apgar score of "0" indicates apparent death; Lysiane was born with an Apgar score of just "1", on a scale of 1 to 10. Initial emergency resuscitation efforts included manual ventilation assistance; this failed, so in her 3rd minute of life, Lysiane received a

laryngeal mask. In her 29th minute of life, Lysiane was intubated – a tube was placed into her mouth and through her airway, and connected to a ventilator machine, which pushed air into her lungs. She was then rushed to the Neonatal Resuscitation unit ("Réanimation Néonatale"), which provides Croix-Rousse's highest possible level of urgent care, for newborns in the most precarious conditions of health. According to the French medical record ("Résumé de Séjour") Lysiane suffered from respiratory distress as a result of inhalation of clear amniotic fluid, as well as upper airway obstruction caused by Pierre Robin Sequence ("ILAC + obstructive sur séquence de Pierre Robin").

On her second day of life Lysiane was extubated. After 6 days in the Neonatal Resuscitation unit, Lysiane's condition was stabilized. She was then transferred from the Neonatal Resuscitation unit, to the Intensive Care unit ("Soins Intensifs").

In the Intensive Care unit, treatment of her upper airway obstruction and respiratory difficulties consisted of prone positioning – Lysiane was placed on her stomach to sleep. Prone (stomach) sleeping is a practice which is strongly discouraged for healthy babies, because numerous medical studies have demonstrated a five to ten times increase in the risk of Sudden Infant Death Syndrome when babies are placed on their stomach to sleep. In the Intensive Care unit, we were told that the purpose of stomach sleeping for a child suffering from Pierre Robin Sequence is that when the baby is sleeping on her stomach, her face is pointing down; this causes her tongue to fall forward in her mouth, and thus out of the way of her throat. With the tongue falling forward in the mouth, and out of the way of the throat, the baby's Pierre Robin Sequence upper airway obstruction is temporarily relieved. Lysiane's prone sleeping was monitored by medical equipment, presumably intended to limit the dangers of Sudden Infant Death Syndrome.

In spite of prone (stomach) positioning, Lysiane continued to face both breathing difficulties and feeding difficulties. The medical record indicates that Lysiane suffered from respiratory fatigue, signs of struggle, hypercapnia – abnormally high levels of carbon dioxide in the blood – and desaturation – abnormally low levels of oxygen in the blood ("fatigue respiratoire avec signes de lutte et hypercapnie"; "désaturations avec signes de lutte"). As a result, after less than one week in the Intensive Care unit, Lysiane had to be put back onto a ventilator machine, due to her continuing respiratory difficulties. Lysiane was connected by tubes to a machine providing high flow ventilation assistance. This ventilator machine helped her to breathe, and ensured sufficient levels of oxygen, thus preventing the risk of brain damage caused by repeated episodes of oxygen desaturation.

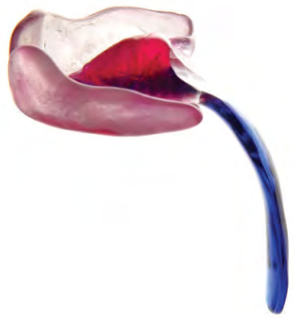
Lysiane never came home. She was born in Croix-Rousse hospital, and she remained in Croix-Rousse hospital, in the Intensive Care unit, where she was receiving high flow ventilation assistance – with no scheduled date of release. This continued until we, Lysiane's parents, finally decided to take our baby's life and health into our own hands, and transferred her from France, to Germany. In Germany, Lysiane received a highly specialised medical treatment, the TPP treatment, for her rare disease, Pierre Robin Sequence, at the Universitätsklinikum (The Tübingen University Hospital) in Tübingen, Germany, on 2 May 2017.

The TPP treatment which we wanted – an introduction to the TPP treatment

As Lysiane's parents we wanted Lysiane to receive a specific medical treatment for her rare disease: the TPP treatment. The TPP treatment is the only Pierre Robin Sequence medical treatment available today which removes the baby's upper airway obstruction, and which at

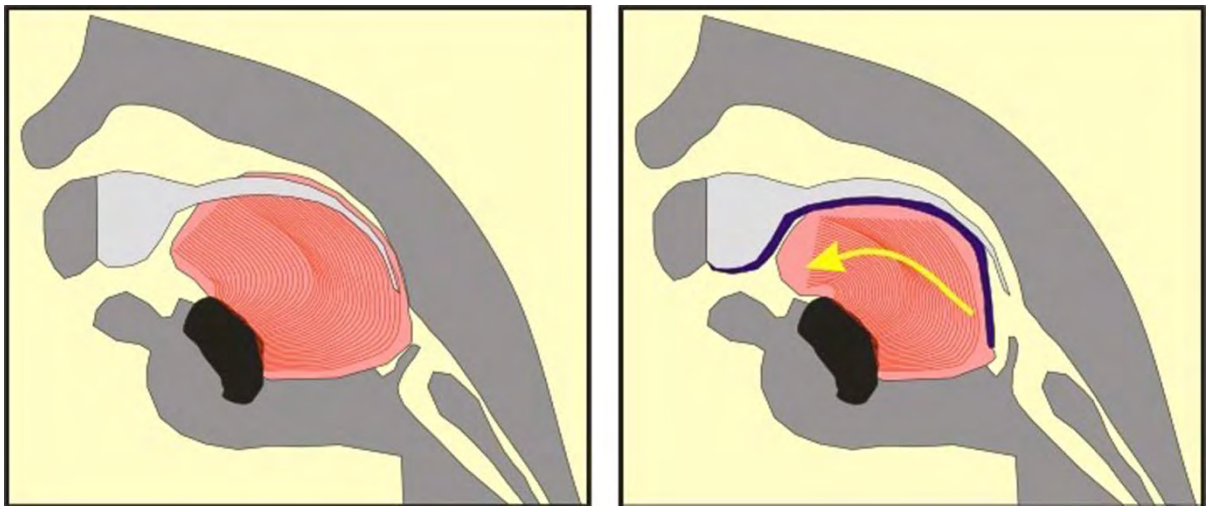
the same time also corrects its underlying anatomical cause – glossoptosis – without any surgery whatsoever. This fact, that the TPP treatment removes the baby's upper airway obstruction, and corrects its underlying anatomical cause, glossoptosis, renders the TPP treatment fundamentally different from the ventilation assistance Lysiane received during the first five weeks of her life.

Here is a photo showing an example of the TPP device:



Below is an illustration showing how the TPP works. The large pink/red object is the baby's tongue. In the cross-section image on the left, the Pierre Robin Sequence patient has no TPP device; the abnormal rear position of the tongue blocks the upper airway, creating potentially life-threatening breathing and eating difficulties. In the illustration on the right, the TPP device is in place; it is represented by a dark blue line. The dark blue line begins at the upper alveolar ridges (where the upper front teeth will eventually grow), continues along the upper palate, covers the cleft in the palate, and then extends down. In the image on the right, toward the right side, we can see this downward dipping dark blue line extension pushing the base of the tongue left, toward the front of the mouth. By shifting the tongue forward, the TPP device instantly liberates the throat – without any invasive surgery.

On the left, without the TPP device; on the right, with the TPP device



The TPP treatment is a medical innovation which was developed at the Tübingen University Hospital's Department of Orthodontics in Tübingen, Germany. It is provided through the Interdisciplinary Centre for Craniofacial Malformations, a centre which encompasses multiple departments in the hospital: The Department of Orthodontics, The Department of

Craniofacial Surgery, and The Department of Neonatology. The Chairman of The Interdisciplinary Centre for Craniofacial Malformations is Professor Dr. Christian Poets. Dr. Poets is also the Coordinator of Tübingen University Hospital's highly specialised Pierre Robin Sequence knowledge centre, a knowledge centre which is officially recognized by the Orphanet database as being a Centre of Expertise for Pierre Robin Sequence. We, as parents of a child suffering from Pierre Robin Sequence, carefully read several TPP medical studies published by Dr. Poets and his colleagues. We then made contact with Dr. Poets directly, in order to learn more about the TPP treatment.

Requesting the TPP treatment: our efforts with Dr. Abadie, and other doctors

According to the 2011/24/EU Directive on the application of patients' rights in cross-border healthcare, an EU citizen seeking planned cross-border healthcare involving hospitalisation should apply for and receive prior authorisation from his or her "Member State of affiliation" (i.e. the country in which the patient lives), before the patient obtains the cross-border treatment. If the patient is suffering from a rare disease, a recognized expert on the rare disease must provide the patient with a medical certificate which confirms the efficacy of the proposed cross-border treatment, and which confirms the non-availability of the proposed treatment in the patient's Member State of affiliation. Thus, as part of the application procedure, a patient suffering from a rare disease must begin the process by consulting one of these recognized experts, at a Centre of Expertise for the rare disease.

Article 13(a) in the 2011 Directive formally names the EU's Orphanet database as an official directory listing of all of Europe's Centres of Expertise for each rare disease.

The Orphanet database makes no reference to any Centre of Expertise for the rare disease, Pierre Robin Sequence, in Lyon. This fact can be confirmed by visiting the following page on the Orphanet website, which lists no Centre of Expertise in Lyon:
http://tinyurl.com/pierre-robin-europe

Because there is no Centre of Expertise specialised in the rare disease of Pierre Robin Sequence in Lyon, we contacted the main Centre of Expertise for Pierre Robin Sequence for all of France. Orphanet identifies this main Centre of Expertise for all of France as France's "Reference Centre"; this Reference Centre is based in Paris, and is located at Necker Hospital. The following link to the Orphanet website confirms that Orphanet identifies the Pierre Robin Centre at Necker Hospital in Paris as being the Reference Centre for all of France for Pierre Robin Sequence:
http://tinyurl.com/pierre-robin-paris

The Reference Centre at Necker Hospital is managed by Dr. Véronique Abadie.

On 7 April 2017 we sent Dr. Abadie an e-mail in which we asked her (1) whether the TPP treatment is available in France, and (2) if the TPP treatment is not available in France, whether she would write us the medical certificate we needed in order to submit our application to L'Assurance Maladie to receive this cross-border healthcare in Germany. This 7 April email we sent to Dr. Abadie was both detailed and clear, and left no room for misunderstanding:

> "Therefore, we would like to ask you:
>
> 1. Is the 'Tübingen Palatal Plate (TPP)' device available in France?

2. If the 'Tübingen Palatal Plate (TPP)' device is not available in France, would it be possible to provide us with a letter of reference, so that our child can receive the TPP at the Tübingen University Hospital. This letter will allow us to make a request to the French Department of Social Security, for financial support of the treatment. If the financial support is not total, we are able to cover the difference. According to Professor Poets, his department has already treated children from other European countries, such as Austria and Hungary, so they already have a procedure in place for admitting patients from the European Union. We would be pleased to put you in direct contact with Professor Poets, in order to exchange information on the transfer procedure."

French original:
"De ce fait, nous souhaiterions vous demander:

1. Si l'appareil 'Tübingen Palatal Plate (TPP)' est disponible en France?

2. Si l'appareil 'Tübingen Palatal Plate (TPP)' n'est pas disponible en France, serait-il possible de nous fournir une lettre de référence afin que notre enfant puisse recevoir le TPP à l'hôpital universitaire de Tübingen. Cette lettre nous permettra de faire une demande particulière à la sécurité sociale pour un support financier de prise en charge. Bien que si ce support financier n'est pas total, nous sommes en mesure de couvrir la différence. D'après le Professeur Poets, son département a déjà traité des enfants d'autres pays européens comme l'Autriche et la Hongrie, donc il existe une procédure pour admettre des patients membres de l'Union Européenne. Nous serions heureux de pouvoir vous mettre en relation directement avec le Professeur Poets afin d'échanger amplement sur la procédure de transfert."

On Monday 10 April 2017, we discussed by telephone the health of our child, Lysiane, with Dr. Abadie. Dr. Abadie explained that she knows Dr. Poets in Tübingen, and she knows his work. Regarding the TPP treatment, Dr. Abadie told us:

"I know this technique and I know Professor Poets. It's a technique which works. It works, it's undisputable."

French original:
"Je connais cette technique et je connais le Professor Poets. C'est une technique qui marche – ça marche, c'est indiscutable."

Dr. Abadie also confirmed that this medical device, the TPP, is not available in France, England, or in the United States of America. The TPP device is a medical device custom made for each particular patient by a team of German medical professionals using highly specialised healthcare technology, which requires a particular concentration of expertise, located only in Germany. Dr. Abadie explained to us:

"The TPP treatment is not a generalized treatment. It's very local, it's done only in Germany. You have to go to Germany for this treatment."

French original:
"Le TPP n'est pas un traitement généralisé. C'est très local, c'est fait qu'en Allemagne. Il faut aller en Allemagne pour ce traitement."

Toward the end of this April 10 phone call, we asked Dr. Abadie if she could help us in getting this treatment. She told us that "you have complete freedom" ("vous avez toute la liberté"). Hearing this from Dr. Abadie, the head of France's Reference Centre for Pierre Robin Sequence, was extremely reassuring to us as parents. It was reassuring because she was the top Pierre Robin Sequence expert in all of France, and she had not only confirmed the medical effectiveness of the TPP treatment with total certainty, but she even knew Dr. Poets. Also, it was reassuring because our child was suffering from a rare disease, which strikes only one baby in approximately 10,000 babies. This rare disease requires highly specialised knowledge and expertise – but experts are few and far between, and Orphanet identified no Centre of Expertise for this rare disease in Lyon, where Lysiane was being treated. Thus we told Dr. Abadie how grateful we were to speak with her.

We specifically told Dr. Abadie during this 10 April phone call that Orphanet does not identify a Pierre Robin Sequence Centre of Expertise in Lyon, where we were based. Dr. Abadie assured us that this would not be a problem; she then asked us who was in charge of the neonatology department where Lysiane was being hospitalized. We told Dr. Abadie that the director of our hospital's neonatology department was a doctor named Dr. Picaud. She said that she would contact Dr. Picaud.

The above describes our initial, reassuring contact with Dr. Abadie.

Unfortunately, our subsequent efforts with Dr. Abadie proved to be remarkably different. Regarding the medically proven TPP treatment, she had assured us that "you have complete freedom" ("vous avez toute la liberté"). It would take us weeks to learn that what she was really saying was, "You can do whatever you want to do, or in any case you can *try* to do whatever you want to do, but don't think for a second that you're going to get a single bit of help from me." In total, we asked for Dr. Abadie's assistance obtaining the TPP treatment five separate times:

1. in the April 7 email, described above;
2. during the April 10 telephone call, described above;
3. in an email my partner and I sent her the evening we returned from a trip we took to Tübingen, to visit Dr. Poets and learn more about the TPP treatment (she never responded);
4. in another e-mail, which contained a detailed proposal we wrote to submit with our S2 application for L'Assurance Maladie, requesting the TPP treatment (she never responded);
5. In a paper letter which we sent to her at the Necker Hospital in Paris, using certified mail ("une lettre recommandée avec avis de réception").

Dr. Abadie knew that Orphanet identified no Centre of Expertise in Lyon, so we would not be able to obtain the medical certificate we needed for our S2 application from our local physicians; thus she knew we relied totally and completely on her.

Therefore Dr. Abadie, by ignoring our request for the medical certificate, and by eventually ignoring all of our emails altogether, effectively prevented us from even submitting our application to L'Assurance Maladie in the first place. If Dr. Abadie had told us on 10 April, when we spoke with her by telephone, "I will not give you the medical certificate which you are seeking", then we never would have dedicated three weeks to pursuing her in search of the certificate. Instead, we would have known that waiting for a medical certificate from Dr. Abadie would be a hopeless waste of time. This would have allowed us to proceed with other plans.

Ultimately, the only way we succeeded in getting Dr. Abadie to write anything at all was by sending her a paper letter from the Post Office using official, certified mail. This is regrettable. Dr. Abadie is the director of the Pierre Robin Reference Centre for France, at Necker Hospital, which is funded by the French government. The Pierre Robin Reference Centre at Necker Hospital includes, in its mission statement, "Facilitation of patients' access to care" ("Facilitation de l'accès aux soins des patients"). As parents of a baby suffering from a rare disease, it should not have been necessary for us to resort to certified mail in order to finally elicit a response from Dr. Abadie regarding our request for an S2 medical certificate.

Furthermore, during our 10 April phone call, Dr. Abadie had assured us that she would be in touch with Dr. Picaud, the director of neonatology at our local hospital in Lyon. We believed that this meant that she was going to instruct Dr. Picaud to facilitate the transfer of Lysiane from his neonatal department in Lyon, to the hospital in Tübingen, to obtain the medically proven TPP treatment which we were seeking. However, at a meeting we had with Dr. Picaud on Friday 21 April 2017, Dr. Picaud stated very clearly that he could not write us the medical certificate which we needed for our S2 application; Dr. Picaud specifically told us that only Dr. Abadie could do this.

In addition to the five separate times we asked Dr. Abadie for her help, we also pleaded with our local physicians in Lyon to help us. We expressed our strong interest in the medically proven TPP treatment for Lysiane's rare disease:

- Monday 3 April, when we met with Dr. Hays;
- Tuesday 4 April, during a meeting with the surgeon, Dr. Gleizal;
- Wednesday 5 April, during a meeting with Dr. Mory Thomas;
- Wednesday, 5 April, in an e-mail we sent to Dr. Franco;
- Thursday 6 April, during a meeting with Dr. Ragouilliaux;
- Friday 7 April, when we sent a second e-mail to Dr. Franco;
- Friday 7 April, during a meeting with Dr. Mory Thomas;
- Tuesday 12 April, during a meeting with Dr. Gleizal and Dr. Mory Thomas;
- Friday 14 April, in another discussion with Dr. Mory Thomas.

On Tuesday 18 April we travelled to Tübingen Germany in order to meet with Dr. Poets and his colleagues in person, visit their department, and learn more about the TPP treatment. We saw the TPP medical device first hand being worn by a three-week old baby, born on 28 March, the day before Lysiane. This baby had Pierre Robin Sequence, but she was not sleeping in the dangerous prone (stomach) position; instead she was sleeping on her back, just like any normal baby, and yet she had absolutely no problems breathing whatsoever. It was astonishing for us to see this, because for babies suffering from Pierre Robin Sequence, breathing tends to be at its absolute worst when the baby is on her back. This baby was being discharged from the hospital the same day we arrived. We met the baby's parents, a couple

which had come from Austria so that their baby could benefit from the TPP treatment. This visit brought us a great deal more information, and left us deeply impressed. In addition, Dr. Poets assured us that he was ready to provide the TPP treatment to Lysiane.

When we returned from this trip to Tübingen, back to France, we had a series of meetings with Dr. Picaud, starting with the meeting described above on April 21. After Dr. Picaud informed us that he could not write the medical certificate which we needed for our S2 application, and that only Dr. Abadie could do this, we decided to try one last time with Dr. Abadie, this time by certified mail.

We finally gave up on receiving any support for our S2 application from Dr. Abadie in Paris, or from anyone in Lyon. We began organizing the transfer of Lysiane from Lyon to Tübingen on our own, using money which we had to borrow from family. We set a departure date – the morning of Tuesday 2 May, since Monday 1 May was a national holiday (May Day). Dr. Abadie knew that we were departing to Tübingen on Tuesday 2 May, because although she was disregarding our request for the S2 medical certificate, she was, during this same time period, in regular contact with Dr. Picaud. It was then that she finally sent us a response to the paper letter we had sent her by certified mail.

In fact, Dr. Abadie's response did not include a medical certificate. Instead, she wrote a simple email, and delivered this email on Friday 28 April at 4:20 pm, less than one hour before the long May Day weekend was about to begin. In her email, Dr. Abadie did finally confirm, in writing, that the TPP treatment is effective; she also confirmed that it is only available in Germany. She added, however, that:

> "In France we have an effective alternative strategy for the treatment of upper airway obstruction, as is shown in our publications: *Continuous Positive Airway Pressure for Upper Airway Obstruction in Infants with Pierre Robin Sequence*. Amaddeo A, Abadie V, Chalouhi C, Kadlub N, Frapin A, Lapillonne A, Leboulanger N, Garabédian EN, Picard A, Fauroux B. Plast Reconstr Surg. 2016 Feb; 137(2):609-12."
>
> French original:
> "Nous avons en France une stratégie alternative efficace sur le traitement de l'obstruction ventilatoire, comme en témoigne également nos publications, *Continuous Positive Airway Pressure for Upper Airway Obstruction in Infants with Pierre Robin Sequence*. Amaddeo A, Abadie V, Chalouhi C, Kadlub N, Frapin A, Lapillonne A, Leboulanger N, Garabédian EN, Picard A, Fauroux B. Plast Reconstr Surg. 2016 Feb; 137(2):609-12."

This email from Dr. Abadie, France's leading expert on Pierre Robin Sequence, suggesting that Continuous Positive Airway Pressure (CPAP) is equally effective as the TPP treatment, forms the basis upon which L'Assurance Maladie rejected our S2 application.

Also, by sending us her message on Friday at 4:20pm, Dr. Abadie guaranteed that there was no possible way we would be able to submit our S2 application to the L'Assurance Maladie office before our departure to Tübingen on Tuesday morning. The L'Assurance Maladie office, a government office, would of course be closed on Saturday – but it would also be closed on Monday, May Day, a public holiday. Thus we would have to depart to Tübingen

before L'Assurance Maladie would even receive our S2 application, thereby further reducing our prospects for S2 application approval.

L'Assurance Maladie has a maximum of 2 weeks to respond to an S2 application. However, that 2-week clock doesn't begin ticking until they receive the patient's S2 request. We had asked Dr. Abadie in writing for the medical certificate on 7 April 2017. The only reason we were postponing the submission of our S2 application was because we were waiting to receive a response from her. She finally sent her written response, an email, *without* the medical certificate, on Friday 28 April, a full three weeks later. At any point during this three week period, Dr. Abadie could have either prepared the medical certificate, or, alternatively, informed us honestly and directly that under no circumstances was she going to give us the medical certificate we needed. By making us wait three full weeks for her Friday 28 April email, Dr. Abadie prevented us from even submitting our application to L'Assurance Maladie in the first place.

In the context of this particular rare disease, three weeks is a very long time. For babies suffering from Pierre Robin Sequence, it is generally during the first few months of the baby's life that the baby's upper airway obstruction is most severe. Upper airway obstruction has many harmful effects. To begin with, it increases the "work of breathing" – the energy which the baby needs to dedicate to simply getting in enough air. This increased "work of breathing" can be thought of in the following way. If someone were forced to breathe all day and all night through a thin and narrow straw, they might be able to do it, and live. However, being forced to breathe through that thin and narrow straw would greatly increase the person's "work of breathing". It would put significant stress on the person's heart, lungs, circulatory system, and nervous system too, since the upper airway obstruction would cause discomfort, anxiety, and even occasional panic. It was a torture for us to watch our newborn baby daughter Lysiane struggling to breathe in this way.

Also, upper airway obstruction may lead to hypoxia – oxygen deprivation – and hypercapnia – excess carbon dioxide, also called hypercarbia… and hypoxia and hypercapnia cause brain damage. A medical study on Pierre Robin Sequence, "*Mandibular distraction osteogenesis for neonates with Pierre Robin sequence and airway obstruction*", explains that:

> "Intensive management of the airway is mandatory in patients with moderate to severe airway obstruction in order to prevent episodes of hypoxia and hypercarbia, which can lead to significant cognitive impairment."

When Lysiane was born, she was not able to breathe at all – she had to be rushed to the Neonatal Resuscitation unit ("Réanimation Néonatale"), to receive the highest possible level of urgent care. Also, Lysiane's medical report from Croix-Rousse Hospital confirms that in the weeks that followed her birth, Lysiane suffered from both hypoxia *and* hypercapnia:

> "oxygen desaturation [hypoxia] with signs of struggle"
>
> French original:
>
> "désaturations avec signes de lutte"

> "respiratory fatigue with signs of struggle and hypercapnia"
>
> French original:
>
> "fatigue respiratoire avec signes de lutte et hypercapnie"

We knew that for Lysiane, these first few months were critical; they would have long term consequences for her entire life. We also knew that for the TPP treatment itself, time was critical. The TPP treatment is composed of two main stages of care. During the first stage, the baby spends approximately 2 to 3 weeks in the hospital. During this time, a custom made TPP device is created for the baby, and the baby starts wearing this TPP device in her mouth; the baby is closely monitored. After this 2 to 3 week period is over, the baby is discharged from the hospital; the baby goes home with the parents, and lives life like any normal baby – no ventilation machines or any other breathing equipment. During the second stage, at home, the baby simply wears the TPP device in her mouth. Depending upon the baby's condition, the baby wears the TPP device in her mouth from 3 to 5 months. Once a day, the parents remove the TPP device for cleaning, which is done using a normal toothbrush, the way one would clean a set of dentures. Then, at the end of this second stage, the TPP treatment is over; the TPP device has done its work, and the baby never has to wear the TPP device in her mouth ever again.

The key thing is that this two-stage process: the 2 to 3 weeks of hospitalisation, and then wearing the TPP device for 3 to 5 months – should all be completed *before* the baby's teeth start to come in. A baby's teeth start to come in when the baby is approximately 6 months old. Once the teeth start to come in, the TPP device would need constant adjustments, to adapt to the baby's changing dental anatomy – and this would be impractical. Thus, if one waits too long, one can reach a point where, practically speaking, it is too late to choose the TPP treatment. In order for a baby suffering from Pierre Robin Sequence to enjoy the full potential of the TPP's medically proven benefits, the baby should begin the TPP treatment as soon after birth as possible. Time was really important – and yet we had to wait three full weeks to receive an email from Dr. Abadie.

Although Dr. Abadie had not written us the medical certificate we had requested, we had no choice but to print out Dr. Abadie's email, combine it with the other documents we had prepared, and send L'Assurance Maladie our S2 application requesting cross-border healthcare for our child's rare disease, on Tuesday 2 May, because the post office was closed on Monday 1 May.

Respiratory difficulties up until our departure to Germany

In our application to L'Assurance Maladie requesting an S2 for the TPP treatment in Germany, we submitted a standard dossier, but we also published and shared, with L'Assurance Maladie, a video of our daughter Lysiane, struggling to breathe, in the French hospital. The video we presented to L'Assurance Maladie can be found here:
http://avantetapres.com/

The video clearly demonstrates that after weeks of ventilation assistance, under 24/7 Intensive Care in Lyon, Lysiane continued to face respiratory difficulties. The video, "Lysiane – Pierre Robin Sequence – respiratory difficulties", was created on Friday 28 April, four days before our departure to Tübingen. In the video you can see Lysiane and hear her, fighting to breathe. The video makes it clear that ventilation assistance does not remove the baby's upper airway obstruction, or correct the underlying anatomical problem, the glossoptosis.

In addition to these clinically visible signs of upper airway obstruction and breathing difficulty, a polysomnography examination indicated that Lysiane suffered from a moderate syndrome of obstructive hypopneas. This sleep study was performed in Lyon at Hôpital

Femme Mère Enfant on 26 April 2017. The polysomnography results indicate that when Lysiane was placed to sleep on her back – the natural sleeping position – and when she was disconnected from the breathing machine – the "l'index d'apnées-hypopnées obstructives" – the IAHO – was 6.5/hour, with an increase during REM sleep (18.2/hour), and sleep efficiency reduced by fragmented sleep (index of arousals plus micro-arousals, 28.4/hour). In children, an IAHO greater than 1.5/hour confirms a diagnosis of Obstructive Sleep Apnea; the question then becomes one of which treatment to employ.

On Friday 28 April, the doctor who helped carry out the polysomnography, Dr. Mainguy, explained that if Lysiane were to remain in France, then she would recommend an increase in the flow of Lysiane's ventilator machine to 6 l/min. Other than that, neither Dr. Mainguy, nor any of the doctors in the Intensive Care unit where Lysiane was being treated, could give us any indication of an end date to Lysiane's continuing 24/7 hospitalisation. The only hope we as parents could hold onto was the possibility of "l'hospitalisation à domicile", or HAD, which is simply home hospitalization. This would require us to bring the entire ventilator machine and associated equipment home with us. Lysiane would have to be connected by tubes and a face mask to this ventilator machine whenever she slept, which included night time sleep, but also daytime naps, and therefore almost constantly. Taking her outside in a stroller to the park would be out of the question.

After nearly five weeks of nonstop 24/7 hospitalization in the Intensive Care unit in Lyon, we desperately wanted to finally get our baby out of the hospital so that we as a family could finally be together, like any normal family. At the same time, we did not want to bring the hospital and its equipment home with us, and turn our home into an intensive care unit. With the TPP treatment, long term hospitalization would be completely unnecessary.

Departure to Tübingen for the TPP treatment

On 2 May 2017 we transferred Lysiane from the Croix-Rousse Hospital in Lyon, to the University Hospital of Tübingen in Germany, to receive the TPP treatment. **In spite of the fact that the TPP treatment has been regularly utilized in Germany for over 10 years, and its effectiveness has been medically proven in numerous peer reviewed medical studies, we believe that our child, Lysiane, is the first French baby to ever receive the TPP treatment.** We will discuss this remarkable fact in the "Legal Analysis" section which appears later in this document.

Notification of L'Assurance Maladie's refusal

L'Assurance Maladie refused our request for authorisation for cross-border medical care for the rare disease of our child, Lysiane. The letter from L'Assurance Maladie, which is attached, states the following:

> "… the medical evaluation department has determined that:
> the same treatment or an equally effective treatment can be obtained in France without undue delay. On this basis, we inform you that the medical care can be provided in France within the required time period."
>
> French original:
> "… le service du contrôle médical a estimé:
> qu'un traitement identique ou présentant le même degré d'efficacité peut être obtenu en temps opportun en France. A ce titre, nous vous indiquons que ces soins peuvent être dispensés en France dans le délai requis."

Medical Analysis

The medical basis of L'Assurance Maladie's rejection

The statement explaining the medical basis of L'Assurance Maladie's rejection declares that "*the same treatment or an equally effective treatment can be obtained in France without undue delay*".

Is "the same treatment" available in France?

Concerning the first scenario, "the same treatment": in the email from Dr. Abadie, dated 28 April 2017, Dr. Abadie, the top Pierre Robin Sequence expert in France, admits that:

> "Currently, this technique can only be carried out by this German team because it is based on the custom manufacture of an orthosis which has to be set up, monitored and changed by the experienced team."
>
> French original:
> "Cette technique n'est actuellement réalisable que par cette équipe allemande car elle repose sur la fabrication sur mesure d'une orthèse qui doit être mise en place, surveillée et changée par l'équipe qui en a l'expérience."

As confirmed by Dr. Abadie in writing, the TPP treatment is not available in France.

Furthermore, on Monday 10 April 2017, we discussed our child Lysiane's health with Dr. Abadie by telephone. Dr. Abadie explained that she knows Dr. Poets in Tübingen, and she knows his work. Concerning the TPP treatment, Dr. Abadie told us, "I know this technique, and I know Professor Poets. It's a technique which works. It works, it's undisputable." Dr. Abadie also confirmed that this medical device, the TPP, is not available in France, in England, or in the United States of America. The TPP device is a medical device custom made for each particular patient by a team of German medical professionals using highly specialised health technology, which requires a particular concentration of expertise, based in Germany. Dr. Abadie explained to us: "The TPP treatment is not a generalized treatment. It's very local, it's done only in Germany. You have to go to Germany for this treatment."

Once again, the TPP treatment is not available in France, and no treatment identical to the TPP treatment is available in France.

Is there "an equally effective treatment" in France?

The "same treatment" is not available in France; this is a straightforward fact. Does France offer an "equally effective treatment"? Various invasive surgical techniques are available in France for treating babies with Pierre Robin Sequence. One example of these invasive surgical techniques is mandibular distraction osteogenesis. Mandibular distraction osteogenesis essentially involves fracturing the baby's lower jaw, and then surgically enlarging the lower jaw using a series of metal rods and screws – all in an effort to reduce the baby's upper airway obstruction.

Another invasive surgical technique which France offers to treat babies suffering from Pierre Robin Sequence is labioglossopexy. This surgical procedure involves sewing the end of the baby's tongue to the baby's lower lip; the idea is that by sewing the baby's tongue down, it will prevent the baby's tongue from moving up and blocking the baby's upper airway, or

from moving at all. Labioglossopexy – sewing a baby's tongue to the baby's lip – is a hideous procedure; it resembles something from the Middle Ages, not medicine from the 21st century. Furthermore it often fails to do its job; either the flesh of the baby's tongue rips, or the flesh of the baby's lip rips, creating flesh wounds and possible infection – and allowing the baby's tongue to return to its dangerous vertical position (glossoptosis), where it obstructs the upper airway.

We believe that if France's doctors informed French mothers and French fathers that there was a safe and effective alternative to these painful and invasive and potentially risky surgical procedures – if they were told that an oral device, the TPP device, has been medically proven to consistently and successfully eliminate the baby's upper airway obstruction, without any surgical intervention whatsoever – then at least some of these French families would forego the surgery, and opt instead for the TPP treatment.

In her email dated 28 April 2017 for L'Assurance Maladie, concerning the treatments France offers for babies suffering from Pierre Robin Sequence, Dr. Abadie avoids any mention of these or other surgical techniques which are offered in France. Instead she indicates that France's strategy for treating babies with Pierre Robin Sequence is to attach these babies to ventilator machines:

> "In France we have an effective alternative strategy for the treatment of upper airway obstruction, as is shown in our publications: *Continuous Positive Airway Pressure for Upper Airway Obstruction in Infants with Pierre Robin Sequence.*"

Is it true that when compared to the TPP treatment, France's ventilation assistance – attaching the baby to a ventilator machine – is "equally effective"?

- The TPP treatment, by unblocking the baby's throat, corrects the underlying anatomical problem, Pierre Robin Sequence's upper airway obstruction; this allows the baby to breathe naturally and independently, on her own. Ventilation assistance, on the other hand, simply forces air down the baby's blocked airway; the baby's airway, however, **remains obstructed**, and when the baby is disconnected from the ventilator machine, the breathing difficulties return. Here is Lysiane, struggling to breathe, when she was momentarily disconnected from the ventilator machine, after a month of nonstop 24/7 hospitalization in France, where she was receiving ventilation assistance: http://avantetapres.com/
- The TPP treatment requires no external equipment; instead the TPP is a small oral device which is worn inside of the baby's mouth. Ventilation assistance, on the other hand, requires cumbersome hospital equipment, including a ventilator machine, tubes, a facial mask, and electrical cables; this ventilation equipment **radically limits the mobility** of both the baby and the parents, since the baby has to be attached to the ventilator machine whenever the baby sleeps, both night and day.
- The TPP treatment generally requires 2 to 3 weeks in the hospital; the baby is then discharged from the hospital, and goes home to join the parents. Ventilation assistance generally requires **long term hospitalization**, which can last for several months, half a year, or longer. The need for long term hospitalization, which ventilation assistance generally requires, has several major disadvantages:
    - long term hospitalization comes at a **tremendous financial cost**, in any healthcare system, regardless of how that healthcare system is managed;

    - long term hospitalization exposes the baby to **bacterial pathogens** in the hospital, which can worsen the baby's existing health problems; and
    - long term hospitalization creates a **painful, unnatural, and unhealthy separation** between the baby and the parents, and interferes with the bonding process which is crucial for the baby's healthy development.
- The TPP treatment, by correctly repositioning the baby's tongue forward, and flat in the mouth, successfully places it in the correct and natural position for nursing; this helps to trigger the baby's natural and inborn sucking and swallowing instincts. Bottle feeding is thus dramatically improved, because the TPP ensures that the baby's tongue is, by default, in the correct nursing position. This has been proven in peer reviewed medical studies; the TPP treatment substantially improves and facilitates the feeding process in infants suffering from Pierre Robin Sequence. Ventilation assistance, on the other hand, does **nothing to improve or facilitate feeding**.
- The TPP treatment, by repositioning the tongue toward the front of the mouth, causes the baby's tongue to press against the baby's lower alveolar ridge. There is medical evidence suggesting that this gentle pressure of the baby's tongue, pressing against her lower alveolar ridge, naturally induces mandibular catch-up growth, thereby reducing the jaw deformities associated with Pierre Robin Sequence, safely and non-surgically. CPAP, on the other hand, has been shown to create a clinically significant risk of actually **causing facial deformities** in young children, due to the constant pressure the ventilation mask exerts on the growing facial structures of these children. Dr. Brigitte Fauroux, a member of France's Pierre Robin Reference Centre at Necker Hospital in Paris, published a study here in France showing that 68% of the children observed, who received ventilation assistance, suffered from facial deformities, including global facial flattening and maxillary retrusion.

No objective and impartial medical comparison can reasonably conclude that CPAP, which requires the baby to be connected to a ventilator machine, and the TPP treatment, which achieves crucial medical objectives that CPAP cannot and does not achieve, are "the same or equally effective".

Below we will provide further details on the points raised above.

<u>Equipment, and patient mobility</u>

In the S2 application we submitted to L'Assurance Maladie, we included a letter from Dr. Christian Poets. In this letter, Dr. Poets explained the following:

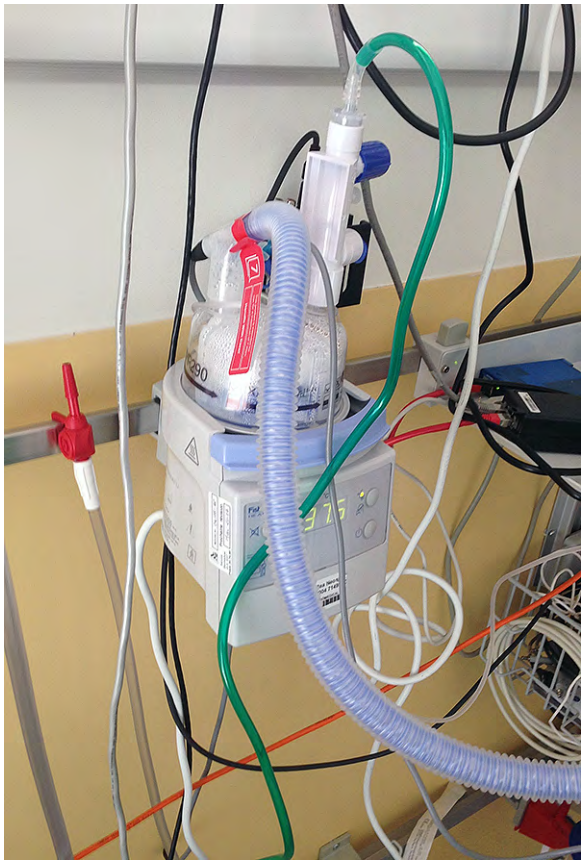
> "…ventilation comes with several challenges, including the fact that this intervention must be applied almost continuously in (young) infants, as these sleep for most of the day, which substantially reduces the patient's mobility. In contrast, the TPP, which is placed inside of the baby's mouth, eliminates the need for any cumbersome external equipment and thus allows parents to move their baby around freely and, most importantly, also at home."

The issue which Dr. Poets is addressing above relates to patient mobility. Ventilation support has to be applied when the baby sleeps – but a baby sleeps most of the day, and most of the night. Thus, a baby receiving ventilation support needs to be connected to the external ventilation equipment almost 24 hours a day. This makes it very difficult for parents to move the baby from one room to another, to take the baby to medical appointments, and so on. The following two images illustrate this difference in the equipment required for ventilation

support, as opposed to the TPP treatment, and the effect this required equipment has on the mobility of children and parents:

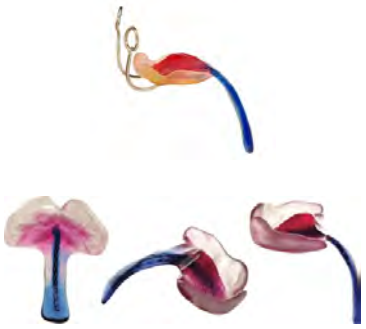
Equipment, and its effect on patient mobility

Ventilation assistance



Ventilation equipment; the various air tubes and electrical wires are part of the ventilation equipment. The baby has to be connected to this equipment each time the baby sleeps, which is the majority of the time.

TPP treatment



The small objects above are examples of the TPP device, which is worn inside of the baby's mouth.

This small oral device is all the equipment our child needs to unblock her upper airway obstruction and allow her to breathe naturally and freely, on her own.

There is no need for any external equipment whatsoever, no need for any electrical wires, and no need to remain stationary, anchored to a ventilator unit, and connected to tubes in a hospital's intensive care unit.

Long term hospitalization

In the same letter from Dr. Poets, he added the following:

> "...ventilation typically requires a long-term hospital stay, which greatly increases the cost of treatment and carries additional risks, particularly contact with pathogenic bacteria (hospital-acquired, i.e. nosocomial, infections). In the present case, the patient, Lysiane Pakter, has already been under constant hospitalization for over 4 weeks. Unfortunately, she continues to require both, ventilation and critical nutritional support. The TPP treatment, on the other hand, requires a hospitalization period which averages two to three weeks; the patient is then discharged home to rejoin his/her parents, who have been trained in handling and maintaining the TPP device on their own."

Long term hospitalisation is a critical issue. Not only does long term hospitalisation come at a tremendous financial cost, and not only does it expose the baby to bacterial pathogens, but long term hospitalisation also creates a painful, unnatural, and unhealthy separation between the baby, and the baby's parents. As Lysiane's parents, we were traumatized by the terrifying circumstances of Lysiane's dangerous birth, and the discovery that she had a rare disease, and the fact that she had to spend 6 straight days in the Neonatal Resuscitation unit, receiving the highest level of urgent medical care. However, we were further devastated that after Lysiane left the Neonatal Resuscitation unit, the long term hospitalization continued, in the Intensive Care unit – week after week after week after week.

We could not move into the hospital and live with Lysiane in the Intensive Care unit; all we could do was visit her every day. However, every night we had to leave the hospital, and go home without her. This was not good for Lysiane, and it was not good for us, the parents.

Furthermore there was no endpoint in sight; there was no scheduled release date, no estimate from any of the doctors, as to when we would be able to finally bring Lysiane, our newborn baby, home.

On the other hand, in Tübingen, in Germany, after only one week of the TPP treatment, we were able to put Lysiane in a stroller, leave the hospital, and take our baby out into the open air for a walk in the park. With the French treatment, putting Lysiane into a stroller and taking her to the park would have been an impossible dream.

On 21 May 2017, after less than three weeks of the TPP treatment, we were completely discharged from the German hospital. We took Lysiane, our baby, home. We did not need to bring a ventilator machine, air tubes or face masks. From the German hospital's discharge report:

> "After the TPP's modifications were complete we carried out a repeat sleep study which revealed an MOAI < 1. Clinical signs of upper airway obstruction were eliminated... With regard to her respiratory difficulties, treatment has allowed Lysiane to achieve total independence from ventilation assistance."

The following two images illustrate this important difference: the need for long-term hospitalization, in the case of ventilation assistance – and freedom to leave the hospital, in the case of the TPP treatment.

Long term hospitalisation

Ventilation assistance

Above, in France, with ventilation support; five consecutive weeks at the hospital, without ever leaving once, and no release date in sight.

TPP treatment

Our daughter Lysiane was fitted with a TPP device on 4 May 2017. Six days later, on 10 May 2017, we were able to take Lysiane outside in a stroller for a walk in the park. Lysiane did not need any ventilation equipment, only the TPP device in her mouth, which unblocks her airways, and allows her to breathe naturally and independently, on her own.

On 21 May 2017, after less than three weeks of the TPP treatment, we were discharged from the hospital completely. We brought Lysiane, our baby, home. We did not need to bring any ventilator machine, air tubes, or face masks with us.

The palatal plates of Professor Isabelle James in Lyon

The TPP device we sought in Germany is an example of a type of medical device called a palatal plate. This type of treatment – a palatal plate – is available in France, and is covered by L'Assurance Maladie. This is confirmed by Dr. Abadie in her email dated 28 April 2017, in which she wrote:

> "In Lyon, little palatal plates can be proposed by the surgical team of Professor Isabelle James. These palatal plates have no effect on ventilation, but they are able to help some infants to position their tongue during feeding. This technique is not backed by scientific proof, but it exists."
>
> Original text, in French:
> "A Lyon, des petites orthèses palatines peuvent être proposées par l'équipe de chirurgie du Pr Isabelle James. Elles n'ont pas d'effet sur la ventilation mais peuvent aider certains enfants à positionner leur langue pendant la tétée. Cette technique n'a pas fait la preuve scientifique de son efficacité, mais existe."

In describing the palatal plates of Professor Isabelle James, Dr. Abadie's goal was to convince L'Assurance Maladie that there is no need for Lysiane to travel to Germany to obtain the TPP device, because this type of treatment, the palatal plate, is readily available in France as well.

We as parents made contact, in France, with the mother of a French baby suffering from Pierre Robin Sequence. Her baby recently received one of the "little palatal plates… of Professor Isabelle James", which Dr. Abadie is referring to above. The mother told us about the French palatal plate her baby had received, and she sent us photos. This confirmed for us that although the French palatal plates and the German palatal plates both belong to the exact same type of medical treatment, the German palatal plates are, objectively speaking, medically superior to the French palatal plates:

- The French palatal plates do nothing to help Pierre Robin Sequence babies with their potentially life-threatening breathing difficulties; as Dr. Abadie admitted in writing, the French palatal plates have "no effect on ventilation";
- The German palatal plates do successfully resolve the baby's breathing difficulties; by successfully resolving the baby's breathing difficulties, the German palatal plates effectively eliminate the baby's risk of oxygen deprivation, brain damage, and death; in terms of quality of life, the German palatal plates liberate these babies from mechanical breathing machines, and from long-term hospitalisation, and from painful, risky and invasive surgery;
- The French palatal plates lack peer-reviewed medical studies to demonstrate what benefits they offer, and what risks they create; this too is a fact which Dr. Abadie admitted in writing;
- The German palatal plates are backed by, and benefit from, over ten solid years' worth of peer-reviewed medical studies; these peer-reviewed medical studies have not only proven the German plates to be highly effective – they have also proven that the German plates are indeed safe for these babies to use.

Thus, while this type of treatment, the use of palatal plates, is offered in France, and is covered by L'Assurance Maladie, the French palatal plates, and the German palatal plates,

are not “equally effective”. The German palatal plates are, objectively speaking, medically superior to the French palatal plates.

In conclusion, L’Assurance Maladie is indeed willing to authorise this type of medical treatment, the use of palatal plates, to treat French babies suffering from this specific rare disease, Pierre Robin Sequence. However, L’Assurance Maladie will only authorise the use of palatal plates if two conditions are met. The first condition is that the palatal plates must not resolve the upper airway obstruction and breathing difficulties faced by these babies. If the palatal plates do in fact resolve the upper airway obstruction, and potentially life-threatening breathing difficulties, faced by these babies – as the German plates do – then they will not be authorised by L’Assurance Maladie. The second condition to qualify for authorisation by L’Assurance Maladie is that the palatal plates must not be backed by any peer reviewed medical studies. If the palatal plates are in fact backed by peer reviewed medical studies, confirming their safety, and effectiveness – as the German plates are – then they will not be authorised by L’Assurance Maladie.

It appears that for Dr. Abadie and L’Assurance Maladie, it does not matter how effective the palatal plates are, or whether the palatal plates have been medically tested and scientifically proven. What matters is where the palatal plates come from. If they come from France, they must be good, so L’Assurance Maladie is willing to authorise their use. If they come from Germany, then they must be bad, so L’Assurance Maladie will refuse them. By similar logic, the French government has every right to obstruct French citizens from purchasing BMW and Mercedes cars, because here in France we propose Peugeot and Citroën cars – and Peugeot and Citroën cars should be good enough for any French citizen. Based on EU law, it is difficult to believe that L’Assurance Maladie considers such conduct to be acceptable.

From the perspective of patients’ rights, which includes the right to receive the best possible medical treatment – especially a newborn baby suffering from a rare disease – it would be difficult to conjure up a healthcare policy more irrational or more perverse.

Palatal plates in France; palatal plates in Germany

The French palatal plates

In terms of form, these plates do not have any rear extension descending down into the pharynx. In terms of function, these plates do not shift the base of the tongue forward, and do not unblock the upper airway. Dr. Abadie does not mention these important facts in her letter dated 28 April 2017, but she does admit that:

> *"They have no effect on ventilation…"*

Dr. Abadie explains that these palatal plates:

> *"...are able to help some infants to position their tongue during feeding."*

but she admits a lack of scientific proof:

> *"This technique is not backed by scientific proof, but it exists."*

The German palatal plates (the TPP)

The TPP device has a velar extension which descends approximately 2 to 3 centimetres into the pharynx. This velar extension shifts the base of the tongue forward, so that the tongue is in a flat and horizontal position in the baby's mouth. This unblocks the rear of the baby's throat, and instantly frees the upper airways.

Creating a mould of the baby's mouth for the purpose of producing a conventional palatal plate is not overly difficult. The velar extension, on the other hand, makes the manufacture of the TPP device complex. The manufacture of a TPP device requires an interdisciplinary team including neonatologists trained in upper airway nasopharyngeal fibre optic endoscopy. These doctors study the interior of the baby's throat while the baby is wearing the TPP device, to precisely modify and perfect the form, angle and dimensions of the TPP's velar extension, in order to unblock the baby's upper airway.

The TPP treatment, available only in Germany, has been definitively proven in numerous peer reviewed medical studies over more than 10 years. The effectiveness and safety of the TPP device is medically proven.

CPAP: the "equally effective" treatment

In her email dated 28 April 2017 for L'Assurance Maladie, Dr. Abadie wrote that:

> "In France we have an effective alternative strategy for the treatment of upper airway obstruction, as is shown in our publications: *Continuous Positive Airway Pressure for Upper Airway Obstruction in Infants with Pierre Robin Sequence.*"

Also, during our 10 April 2017 telephone call, when Dr. Abadie was comparing the TPP treatment to CPAP, she said that "les résultats sont les mêmes" ("the results are the same").

We as parents were already familiar with ventilation assistance, because Lysiane was receiving ventilation assistance during her hospitalisation in Lyon. She received it shortly after her birth, and she had to be put back on ventilation assistance less than a week after being admitted to the Intensive Care unit, as a result of continuing respiratory difficulties. Thus when we were speaking with Dr. Abadie by telephone on 10 April, we were genuinely surprised that she would characterize the TPP treatment and CPAP as being medically equivalent. The TPP device is a small device which is worn in the mouth. CPAP, on the other hand requires a considerable amount of serious hospital equipment.

Below, a Pierre Robin Sequence baby receiving ventilation assistance through a custom made mask. The mask must be connected by tubes to external equipment, a ventilator machine, which radically limits the baby's mobility.

In addition to the fact that CPAP requires serious hospital equipment, including a mask, tubes and a ventilator machine, the CPAP equipment has to be used whenever the baby sleeps. This was something of a surprise for us. During the phone call, seeking clarification, we asked Dr. Abadie, "so the baby has to wear the CPAP mask at night?" She responded, "*when the baby sleeps*" – in other words, yes, at night, all night, but also during the day – *whenever* the baby is sleeping. This suddenly made it clear to us that ventilation, whether provided in the hospital, or provided through in-home hospitalisation, was far more intrusive than we had originally thought. Ventilation, even for moderate upper airway obstruction, has to be applied "when the baby sleeps" – but our baby, like most babies, doesn't just sleep at night – she also sleeps during the day. This means that with CPAP, we would have to keep Lysiane connected to external CPAP equipment, or have external CPAP equipment available just next to her in case she suddenly takes a nap, almost around the clock, 24 hours a day.

This fact is confirmed in the medical study which Dr. Abadie wrote, and which she referred to in her letter to L'Assurance Maladie – "Continuous Positive Airway Pressure for Upper Airway Obstruction in Infants with Pierre Robin Sequence". This medical study, authored by Dr. Abadie, states the following:

> "Continuous positive airway pressure was used continuously in the severe upper airway obstruction group with the aim of decreasing continuous positive airway pressure use to sleep periods only over a 1 – to 2-week period. *The moderate upper airway obstruction group was treated with noninvasive continuous positive airway pressure during sleep periods only*."

The need to depend on the external CPAP equipment both at night and during the day is a major disadvantage of CPAP, when comparing CPAP with the TPP treatment. However, this is only one of the several major disadvantages of CPAP, when compared with the TPP treatment.

CPAP and facial deformities

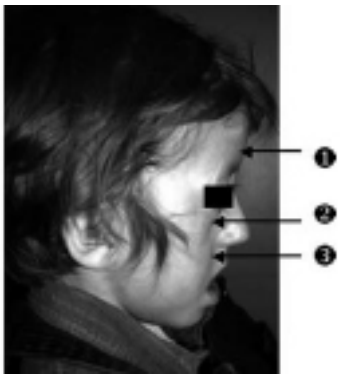
Another major disadvantage of CPAP when compared with the TPP treatment is that CPAP creates a serious danger of "facial side effects" – i.e. physical deformities of the face. This is a risk which Dr. Abadie never mentioned over the telephone during our 10 April conversation, and which she also failed to mention in her email dated 28 April for L'Assurance Maladie. However, the risk of facial side effects when applying CPAP is medically documented. Not only is the risk of facial side effects medically documented, but it is documented in a medical study authored by a doctor who works with Dr. Abadie, Dr. Brigitte Fauroux. What makes this almost incredible is that Dr. Brigitte Fauroux happens to be the major advocate of CPAP for babies with Pierre Robin Sequence at Dr. Abadie's Pierre Robin Reference Centre at Necker Hospital in Paris.

Dr. Fauroux's study is called "Facial side effects during noninvasive positive pressure ventilation in children" (Fauroux B, Lavis JF, Nicot F, et al. *Facial side effects during noninvasive positive pressure ventilation in children*. Intensive Care Med. 2005; 31:965–969). The study states that:

> "In children facial deformity can occur due to the pressure applied by the mask on growing facial structures. The aim of the present study was to evaluate the facial side effects of nasal masks use for NPPV in children."
>
> "**Global facial flattening was observed in 68% of the patients** and concerned the forehead (43%), malar area (38%), and maxilla (28%). One or two anatomical regions were concerned in 37% and 18% of the patients, respectively. A concave face was observed in 12% of the patients."
>
> "**A maxillary retrusion was observed in 37% of the patients**."
>
> "**This observational study underlines the high prevalence of facial side effects of nasal mask use in children**."

Below is evidence from Dr. Fauroux's study, "Facial side effects during noninvasive positive pressure ventilation in children". The photo below shows a child who suffered from severe deformities as a result of receiving NPPV. The child below suffered from flattening of the

forehead (1), flattening of the malar area (2), and flattening of the maxilla (3), all due to the pressure exerted by the ventilation mask on the growing bones of the child's face.



Dr. Fauroux's study points out that the high risks of facial side effects from NPPV was independent of whether the NPPV mask was a commercial mask, or a custom-made mask which was specially designed for babies:

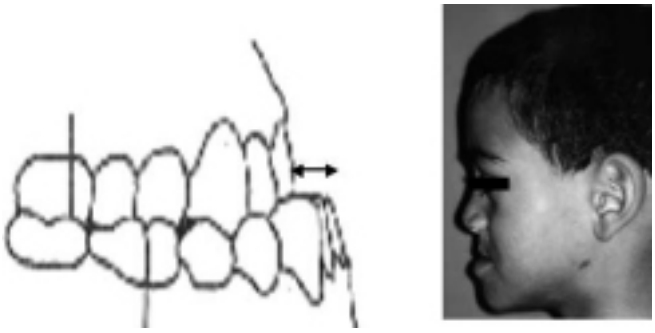
> "Custom-made masks were used in all the patients younger than 6 years of age and in older patients in the case of nontolerance of commercial masks... *Global facial flattening was not related to the type of mask, presumably because both commercial and custom-made masks exert pressure on the same anatomical area."*

In spite of the fact that custom-made masks were used for all patients younger than 6 years old, the very young patients still suffered from a high risk of facial side effects from NPPV. Apparently, the physical deformities caused by the masks were a result of the pressure the masks exerted on the face – and this pressure is necessary to create a proper seal, regardless of which type of mask is being used, custom-made or commercial.

CPAP, Maxillary Retrusion, > 10 hours per day

Global facial flattening was not the only side effect of NPPV; maxillary retrusion was another deformity caused by NPPV. In informal language, maxillary retrusion is a caving in of the upper jaw, where the baby's upper teeth will eventually grow.

Below is more evidence from Dr. Fauroux's study, "Facial side effects during noninvasive positive pressure ventilation in children". The photo below shows a child who suffered from maxillary retrusion, again as a result of receiving NPPV.



For babies like Lysiane, who suffer from Pierre Robin Sequence, maxillary retrusion is a particularly serious concern, for several reasons.

The first reason maxillary retrusion is a serious matter for our daughter, and for any baby with Pierre Robin Sequence, is that Pierre Robin Sequence is already associated with facial deformities, including micrognathia (a small underdeveloped lower jaw) and retrognathia (an abnormal rear positioning of the lower jaw). The last thing such a baby needs is to be exposed to the serious risk of yet another deformity affecting the jaw, maxillary retrusion.

The second reason maxillary retrusion is so serious is that Dr. Fauroux's study showed that maxillary retrusion – which was observed in no less than 37% of their patients – *was not correlated at all with how many months or how many years the mask was used*. Instead, maxillary retrusion was only correlated with the number of hours per day which the mask was worn:

> "A maxillary retrusion was observed in 37% of the patients… *In univariate and multivariate analyses* ***only daily use (>10 h per day) was associated with maxillary retrusion*** *(OR 6.3, 95% CI 1.3–29.3, p=0.02)… maxillary retrusion was associated with a daily NPPV use exceeding 10 h per day."*

As Dr. Abadie explained, babies suffering from Pierre Robin Sequence would receive NPPV/CPAP "when the baby sleeps". Babies certainly sleep more than "10 h per day". This means that our daughter, who already suffers from midface hypoplasia facial deformities, retrognathia and micrognathia, would, with NPPV, also be exposed to a high risk of further deformities, both global facial flattening, and maxillary retrusion. Furthermore, she would be exposed to this high risk of further facial deformities even if she only wore the NPPV mask for a few weeks. This is because, as Dr. Fauroux's study showed, maxillary retrusion was the result of using the mask for ">10 h per day" – not how many weeks or months or years the NPPV treatment was applied.

This is a very important point which bears repeating: according to Dr. Fauroux's study, the serious risk of maxillary retrusion is triggered not by months and months of use, but by usage which exceeds 10 hours per day. Pierre Robin Sequence babies suffering from moderate or severe upper airway obstruction would need to wear the mask whenever they sleep, which is definitely more than 10 hours per day.

In the study, Dr. Fauroux presents ideas for preventing the facial deformities caused by NPPV. However, her proposed solutions are themselves quite alarming:

> "A decrease in the mask pressure and a reduction in the daily NPPV use could present a preventative measure of these side effects."

Thus, to reduce the risk of facial deformities caused by NPPV, the patient should simply receive less NPPV per day. How can a baby who is suffering from Pierre Robin Sequence, and who is supposed to wear the mask "*when the baby sleeps*", as Dr. Abadie explained, cut back on the daily use of the NPPV mask? Should parents of a baby suffering from Pierre Robin Sequence prevent their baby from going to sleep, in order to reduce the high risk of facial deformities caused by CPAP? No answer is given to this troubling question.

And what happens when the NPPV treatment has indeed actually caused physical deformities – global facial flattening and/or maxillary retrusion – in a given patient? Once again, Dr.

Fauroux proposes the same "solution" which she proposed for prevention: simply reduce the daily use of the NPPV treatment:

> "Remedial measures for side effects could include a prompt change of the mask in the case of skin injury and the reduction in the daily use of NPPV."

Dr. Fauroux provides the following conclusion:

> **"Conclusions: The prevalence of facial side effects is clinically significant in children using NPPV."**

In proposing CPAP as a treatment which is medically equivalent to the TPP treatment, neither Dr. Abadie, nor anyone in Lyon, ever once mentioned to us the significant risks of physical deformities caused by NPPV, risks which are documented by Dr. Fauroux herself.

Dr. Abadie's CPAP study

In the letter from Dr. Abadie dated 28 April 2017, Dr. Abadie presents ventilation as being medically equivalent to the TPP treatment. In support of her position, she cites the following study, authored by herself, Dr. Fauroux, and other colleagues: "Continuous Positive Airway Pressure for Upper Airway Obstruction in Infants with Pierre Robin Sequence." This study states that:

> "Duration of noninvasive continuous positive airway pressure ranged from 4 weeks to more than 4 months, showing that noninvasive continuous positive airway pressure is necessary only during a critical window of a maximum of 6 months in most patients."

There are several comments worth making about the above statement.

First of all, this statement does not provide a very clear understanding of what the range of treatment actually was, since the upper end of the range remains undefined: "from 4 weeks *to more than 4 months*".

Also, the study appears to draw conclusions based on the evaluation of only 9 patients who actually received ventilatory support:

> "In conclusion, during a 1-year period, 44 neonates with Pierre Robin Sequence were evaluated in our reference center before the age of 1 month; seven patients (16 percent) were seen as outpatients and 37 (84 percent) were seen as inpatients. Four patients (9 percent) required a tracheotomy *and nine (20 percent) were successfully managed by noninvasive continuous positive airway pressure*, with the remaining 31 patients (70 percent) having no significant upper airway obstruction and being managed by prone positioning."

This relatively small sample size of 9 patients who actually received CPAP makes it doubtful whether this study provides sufficient evidence that CPAP is medically equivalent to the far better documented and more carefully studied TPP treatment.

Furthermore, of the 9 patients in Dr. Abadie's study who actually received CPAP, Table 1 indicates that 3 of them are "Still on CPAP". Does this mean that on the date the study was submitted for publication, 3 of the 9 patients who were receiving CPAP were still in fact

receiving CPAP, and had already received more than 4 months of CPAP? This might explain the ambiguous date range, "from 4 weeks *to more than 4 months*"; nevertheless the issue of CPAP treatment duration remains unclear.

Thus the "Continuous Positive Airway Pressure" study uses an ambiguous set of treatment duration data, from a relatively small sample size of 9 patients, to support the following statement:

> "…noninvasive continuous positive airway pressure is necessary only during a critical window of a maximum of 6 months in most patients."

This statement above concerning the maximum 6 month duration period for the typical CPAP treatment is used as the building block of a very important medical conclusion. The medical conclusion is important because it concerns the serious risk that CPAP will cause Pierre Robin Sequence babies to suffer from physical deformities of the face. The conclusion is as follows:

> "This relatively short period restricts the potential side effects of long-term noninvasive continuous positive airway pressure such as facial flattening and maxillary retrusion."

Thus, according to the "Continuous Positive Airway Pressure" study which Dr. Abadie presented to L'Assurance Maladie, the risk that CPAP will cause Pierre Robin Sequence babies to suffer from the physical facial deformity, maxillary retrusion, can be restricted, because the typical Pierre Robin Sequence baby will only need to receive CPAP for a maximum period of 6 months.

This important medical conclusion makes reference to footnote 10. Footnote 10 is a citation containing Dr. Fauroux's "Facial side effects during noninvasive positive pressure ventilation in children" medical study, which was discussed above. **The glaring problem is that Dr. Fauroux's "Facial side effects" study not only doesn't support this important medical conclusion, but in fact, Dr. Fauroux's "Facial side effects" study directly contradicts it. Dr. Fauroux's "Facial side effects" study makes it very clear that the serious risk of maxillary retrusion – 37% of the patients in her study suffered from it – can NOT be restricted by limiting the duration of treatment. In the "Facial side effects" study, maxillary retrusion was not correlated at all with how many months or how many years the mask was used. Instead, maxillary retrusion was *only* correlated with the number of hours per day which the mask was worn. According to Dr. Fauroux's study, the serious risk of maxillary retrusion was triggered when the baby received the ventilation treatment for more than 10 hours per day.** Once again, this comes directly from Dr. Fauroux's "Facial side effects study":

> "A maxillary retrusion was observed in 37% of the patients… *In univariate and multivariate analyses* ***only daily use (>10 h per day) was associated with maxillary retrusion*** *(OR 6.3, 95% CI 1.3–29.3, p=0.02)… maxillary retrusion was associated with a daily NPPV use exceeding 10 h per day."*

According to Dr. Fauroux's "Facial side effects" study, a CPAP mask will not cause a baby to suffer from maxillary retrusion because the baby is wearing the mask for 3 months 6 months or 1 year, but rather because the baby is wearing the CPAP mask for many hours

each day. That constant pressure of the CPAP mask on the baby's face, and on the soft bones of her skull, for 10 hours or more hours each day, is what triggers the risk of maxillary retrusion. As Dr. Abadie told us by telephone, CPAP would be applied "when the baby sleeps", which is certainly more than 10 hours per day. The point is that according to Dr. Fauroux's "Facial side effects" study, the serious risk of maxillary retrusion can NOT be eliminated by simply capping the treatment period to "a maximum of 6 months". The serious risk of maxillary retrusion is triggered when the mask is worn for more than 10 hours a day, even if the treatment period is only a matter of weeks or a few short months.

It is difficult to believe but it is true. To support her claim that CPAP and the TPP treatment are medically equivalent, Dr. Abadie presented L'Assurance Maladie with the "Continuous Positive Airway Pressure" study. This study contains a serious medical conclusion, which minimizes an important health risk – of CPAP causing a physical facial deformity, maxillary retrusion, a deformity of the jaw, in babies already suffering from jaw deformities (retrognathia and micrognathia). In minimizing this important health risk, Dr. Abadie's study cites Dr. Fauroux's study… but Dr. Fauroux's study, which is cited, clearly indicates the opposite.

Did Dr. Abadie, the lead author of "Continuous Positive Airway Pressure", not read the "Facial side effects" study? Or did she assume that nobody else would read it?

The "Continuous Positive Airway Pressure" study raises additional concerns. The study begins by stating the following:

> "Noninvasive continuous positive airway pressure has been shown to be an effective treatment for severe upper airway obstruction in Pierre Robin Sequence."

This statement above makes reference to footnote 5. Footnote 5 is a citation to the following medical study:

> Leboulanger N, Picard A, Soupre V, et al. *Physiologic and clinical benefits of noninvasive ventilation in infants with Pierre Robin Sequence*. Pediatrics 2010; 126: e1056–e1063.

When one reads this study above, "Physiologic and clinical benefits of noninvasive ventilation in infants with Pierre Robin Sequence", one finds, once again, that the actual number of patients who received noninvasive respiratory support ("NRS") is again quite small:

> "During the 10-year period, 81 patients with a PRS were treated in our institution. Fifty-four (67%) had an isolated sequence and 27 (33%) had an associated syndrome or malformation. Fifty-one patients (63%) had no or minor respiratory symptoms and were treated with positioning and medical treatment only; 30 patients (37%) had severe respiratory symptoms and required temporary tracheal intubation and positioning (10 patients [12%]), tracheotomy (13 patients [16%]), or *NRS (7 patients [9%])… Breathing patterns, respiratory efforts, and gas exchange were analyzed for 7 infants with a PRS during spontaneous breathing and during NRS."*

Apparently, of the 81 PRS patients observed in the "Physiologic and clinical benefits" study, only 7 received NRS.

Thus, it turns out that the "Continuous Positive Airway Pressure" study is based on the use of CPAP for a total of only 9 patients. This is not a large sample size of patients. Therefore, the "Continuous Positive Airway Pressure" study cites the "Physiologic and clinical benefits" study for support. However, the "Physiologic and clinical benefits" study is itself based on only 7 patients who received NRS. This is quite disturbing.

From a salesman one expects a hard sell; a physician however is supposed to present substantial medical evidence, as well as full and honest disclosure of any accompanying health risks. The "Continuous Positive Airway Pressure" study which Dr. Abadie wrote, and which she shared with L'Assurance Maladie, contains neither.

Once again, unless one takes the time to carefully read these CPAP studies, one might incorrectly assume that the "Continuous Positive Airway Pressure" study and the "Physiologic and clinical benefits" study together provide definitive and generalizable conclusions on the efficacy and even safety of providing NRS/CPAP to children suffering from Pierre Robin Sequence. However, they do not. The TPP treatment, on the other hand, rests upon a solid foundation of medical evidence, including peer reviewed medical studies which observed not 9 patients or 7 patients but *literally hundreds of patients, spanning over a decade*. These were babies whose Pierre Robin Sequence was successfully and safely treated with the TPP technique, requiring hospitalization periods typically ranging in the weeks, not months. These peer reviewed TPP medical studies include:

"Treatment of infants with Syndromic Robin sequence with modified palatal plates: a minimally invasive treatment option"; "Multicenter study on the effectiveness of the pre-epiglottic baton plate for airway obstruction and feeding problems in Robin sequence"; "Initial treatment and early weight gain of children with Robin Sequence in Germany: a prospective epidemiological study"; "Functional treatment of airway obstruction and feeding problems in infants with Robin sequence"; "Treatment of Upper Airway Obstruction and Feeding Problems in Robin-Like Phenotype"; "An Oral Appliance With Velar Extension for Treatment of Obstructive Sleep Apnea in Infants With Pierre Robin Sequence"; and more.

In our S2 application we provided L'Assurance Maladie with hard colour copies of 4 of the abovementioned TPP medical studies. We understand that L'Assurance Maladie is very busy, but did they read any of these studies we sent them?

Yet another issue raised by these studies is that the "Physiologic and clinical benefits" study makes it very clear that the typical duration of NRS treatment is *much longer* than the "Continuous Positive Airway Pressure" study suggests. The "Continuous Positive Airway Pressure" study states that *"...noninvasive continuous positive airway pressure is necessary only during a critical window of a maximum of 6 months in most patients."* However, the "Physiologic and clinical benefits of noninvasive ventilation" study, which the "Continuous Positive Airway Pressure" cites, states that: *"All of the patients could be discharged successfully from the hospital with NRS. The mean duration of NRS was 16.7 +/ – 12.2 months."* Table 1 of the "Physiologic and clinical benefits" study confirms this fact, that the typical duration of NRS treatment was far greater than the "maximum of 6 months in most patients" which the "Continuous Positive Airway Pressure" study sets out.

Specifically, the "Physiologic and clinical benefits of noninvasive ventilation", in Table 1, indicates that the treatment periods for the 7 patients were, respectively: 7 months, 10

months, 13 months, 13 months, 16 months, 27 months, and 39 months. Importantly, these are periods of NRS treatment in which the mask was worn for *many* hours during each 24 hour period. As the "Physiologic and clinical benefits" study indicates, "Within 2 weeks, NRS was required only during night time sleep and daytime naps." Thus, the mask was worn "when the baby sleeps", which is well over 10 hours per day, *and* the total duration of treatment was quite long. Based on Dr. Fauroux's, "Facial side effects", study, all of these children were therefore exposed to the high risk of facial deformities, both global facial flattening, and maxillary retrusion.

Dr. Abadie completely ignores these known risks of facial side effects when informing L'Assurance Maladie that the TPP treatment, and CPAP, are medically equivalent. The TPP treatment has never been shown to produce any risks of any facial side effects or any other physical deformities in any babies. On the contrary, there is medical evidence which suggests that the TPP treatment, by shifting the tongue into a forward position, actually promotes mandibular catch-up growth.

Thus, CPAP creates a high risk of causing additional facial deformities in Pierre Robin Sequence babies who are already suffering from physical deformities of the face, micrognathia and retrognathia. The TPP treatment, on the other hand, offers the possibility of reducing the baby's existing deformities, micrognathia and retrognathia, by naturally promoting mandibular catch-up growth during a high growth period in the patient's life.

Prone (stomach) sleeping

For babies suffering from Pierre Robin Sequence in France, the most common treatment appears to consist of "positioning" – placing the baby in a prone (stomach) sleeping position. This is illustrated in both the "Continuous Positive Airway Pressure" study, as well as in the "Physiologic and clinical benefits" study. In the "Physiologic and clinical benefits" study, it appears that 75% of the patients were treated with positioning, or some combination of positioning and other strategies (63% "were treated with positioning and medical treatment only"; an additional 12% "required temporary tracheal intubation and positioning"). In the "Continuous Positive Airway Pressure" study, 70% of the Pierre Robin Sequence babies were "managed by prone positioning" alone.

In Lyon, Lysiane was "treated with positioning". However, this treatment proved inadequate. From the moment of Lysiane's birth, we as parents were in the Intensive Care unit every single day, spending time with Lysiane. Lysiane was placed on her stomach to sleep, and due to her breathing difficulties, she was also frequently placed on her stomach even when she was awake.

In spite of this treatment by prone (stomach) positioning, we continued to see Lysiane not only struggling to breathe, but also desaturating, time and time again. We knew that Lysiane was desaturating because the monitoring equipment which Lysiane was connected to would flash red lights, and sound urgent alarms. This was a regular event, and since we as parents knew that these repeated episodes of hypoxemia were putting Lysiane at risk of brain damage, these desaturation events were horrifying.

The failure of "positioning" to resolve Lysiane's breathing difficulties led the doctors in Lyon to combine "positioning" with an additional treatment strategy, ventilation assistance. The medical report ("RESUME DE SEJOUR") prepared by Lysiane's attending neonatologist, Dr. Nathalie Mory Thomas, indicates that high-flow nasal cannula ventilation was applied:

"as a result respiratory fatigue with signs of struggle and hypercapnia" [abnormally high levels of carbon dioxide in the blood]

Original text, in French:
"sur fatigue respiratoire avec signes de lutte et hypercapnie"

However, even after the doctors put Lysiane on the high-flow nasal cannula, the prone (stomach) positioning continued; prone positioning was used in conjunction with ventilation. Below, Lysiane receiving ventilation assistance (high-flow nasal cannula), and also placed in a prone sleeping position:

Ventilation assistance combined with prone (stomach) sleeping position:

Prone (stomach) sleeping is something that we as parents were always deeply uncomfortable with. During the prenatal period, we had made numerous trips to the hospital for standard checkups and medical ultrasound examinations. In all of the different waiting rooms we sat in, during all of these numerous prenatal appointments, we always saw this same sign, posted in each of the waiting rooms:

What this poster says, in English, is:

> "Even if everything in this room looks perfect… a baby sleeping on her stomach runs a mortal risk. Do not make this mistake! Your baby should ALWAYS sleep on her back."

Having seen these posters, and having heard about Sudden Infant Death Syndrome ("SIDS"), we as parents were highly uncomfortable with the idea of our child Lysiane sleeping on her stomach. We read medical studies which made it very clear that prone (stomach) sleeping substantially increases the risk of SIDS, anywhere from five times, to as much as 13 times [R G Carpenter, L M Irgens, et. al. *Sudden unexplained infant death in 20 regions in Europe: case control study*. The Lancet 2004: 363: 185-191, showing that prone sleeping increased the risk of SIDS 13 times; Table 2, "Prevalence of multivariately significant potential risk factors for SIDS in cases and controls", indicates that the Risk factor, "Prone vs supine", produced a Multivariate OR (95% CI) of 13·1 (8·51–20·2)].

In spite of these known risks, Lysiane was attached to monitors, and placed on her stomach to sleep. We were told that the purpose of stomach sleeping for a child suffering from Pierre Robin Sequence is that with stomach sleeping, the baby's face is pointing down; this causes the baby's tongue to fall forward in her mouth, and thus out of the way of her throat. With the tongue falling forward in the mouth, and out of the way of the throat, the baby's upper airway obstruction is temporarily relieved.

Although this stomach sleeping was done with monitoring, we as parents still couldn't help but think of this situation as a kind of medical schizophrenia. The same medical establishment which was issuing dire warnings concerning stomach sleeping, was now telling us that we should accept the risks, and place our baby to sleep on her stomach – but to not worry, because everything was going to be OK.

Imagine for a moment traveling in a strange and distant land. You and your travel guide come before a field. The field is enclosed by a barbed wire fence, and is marked with a huge sign, warning you that the field ahead is a deadly minefield. The sign explains that if you walk through this minefield, you will be exposing yourself to the grave risk of sudden death. "Don't worry", your guide tells you – "I've got this trustworthy mine detector over here. This mine detector is going to detect all the mines in this minefield. Trust me, you don't need to worry about a thing; we're going to be completely safe."

What would you do? Would you cross this minefield? Would you knowingly expose yourself to the grave risk of sudden death?

Wouldn't it make more sense to simply walk around the minefield, and avoid the risk altogether?

Now for a moment imagine that it's not your life which is at stake. Instead, it's the life of your baby child – that is, your guide is not telling *you* to walk through the treacherous minefield – rather, your guide is telling you to send *your baby* through that minefield, all alone. Your job is to just stand there quietly, and watch.

This is what it was like for us, as parents, to stand there for weeks and weeks and weeks on end, while the doctors knowingly exposed our child to the substantially increased risk of SIDS, by placing her in a prone (stomach) sleeping position.

We as parents strongly believe that the proven dangers of prone sleeping are so great that prone sleeping should only be prescribed if it is absolutely necessary – i.e., when there is no alternative treatment available which would allow our child to avoid the SIDS minefield altogether.

The TPP treatment achieves this goal. The TPP treatment corrects the underlying problem, Pierre Robin Sequence's upper airway obstruction, in both the prone (stomach) sleeping position, as well as in the supine (back) sleeping position. Thus, with the TPP treatment, the baby never has to sleep in the prone sleeping position again.

A rare disease requires a particular concentration of expertise

Lysiane, who suffers from a rare disease, is a patient "with a medical condition requiring a particular concentration of expertise in medical domains where expertise is rare" (the 2011 Directive, Article 12). Regarding rare diseases, the 2011 Directive, Article 13(a), names Orphanet, a database, to provide information about each rare disease, and to identify the Centres of Expertise in Europe for each rare disease. When looking up the Pierre Robin Sequence rare disease on Orphanet, one finds the following:

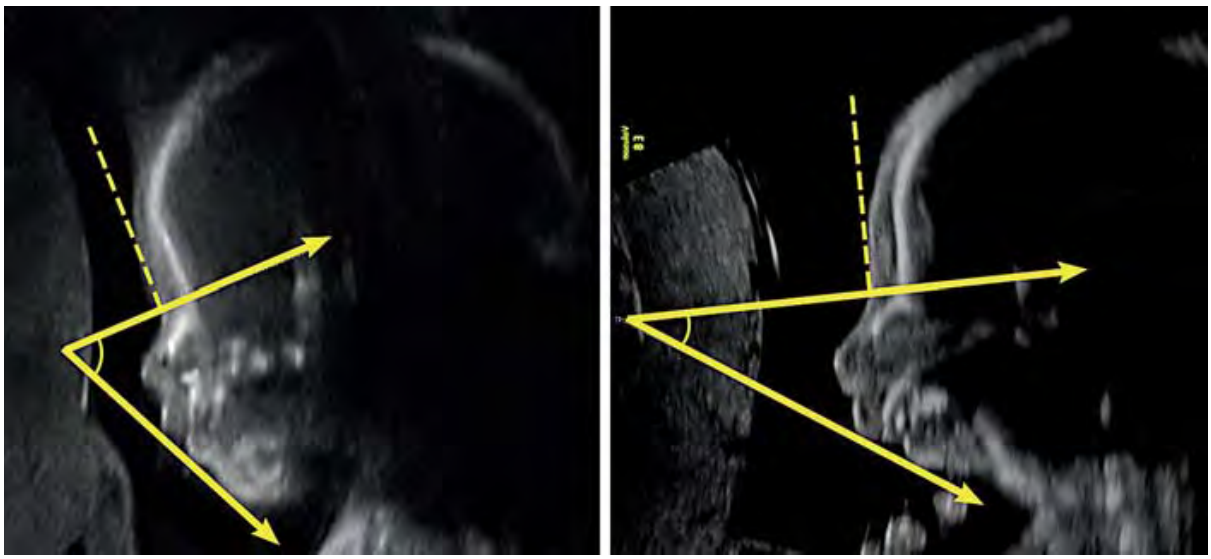
> "Prenatal diagnosis is possible if the retrognathism is detected at ultrasound. An excess of amniotic fluid is a good diagnostic indicator.

Expert reviewer(s): Pr Véronique ABADIE – Last update: March 2006"

Found here: http://tinyurl.com/pierre-robin-orphanet

We did have a prenatal ultrasound, in fact several of them – and our prenatal ultrasounds *did* indicate that our child suffered from retrognathia.

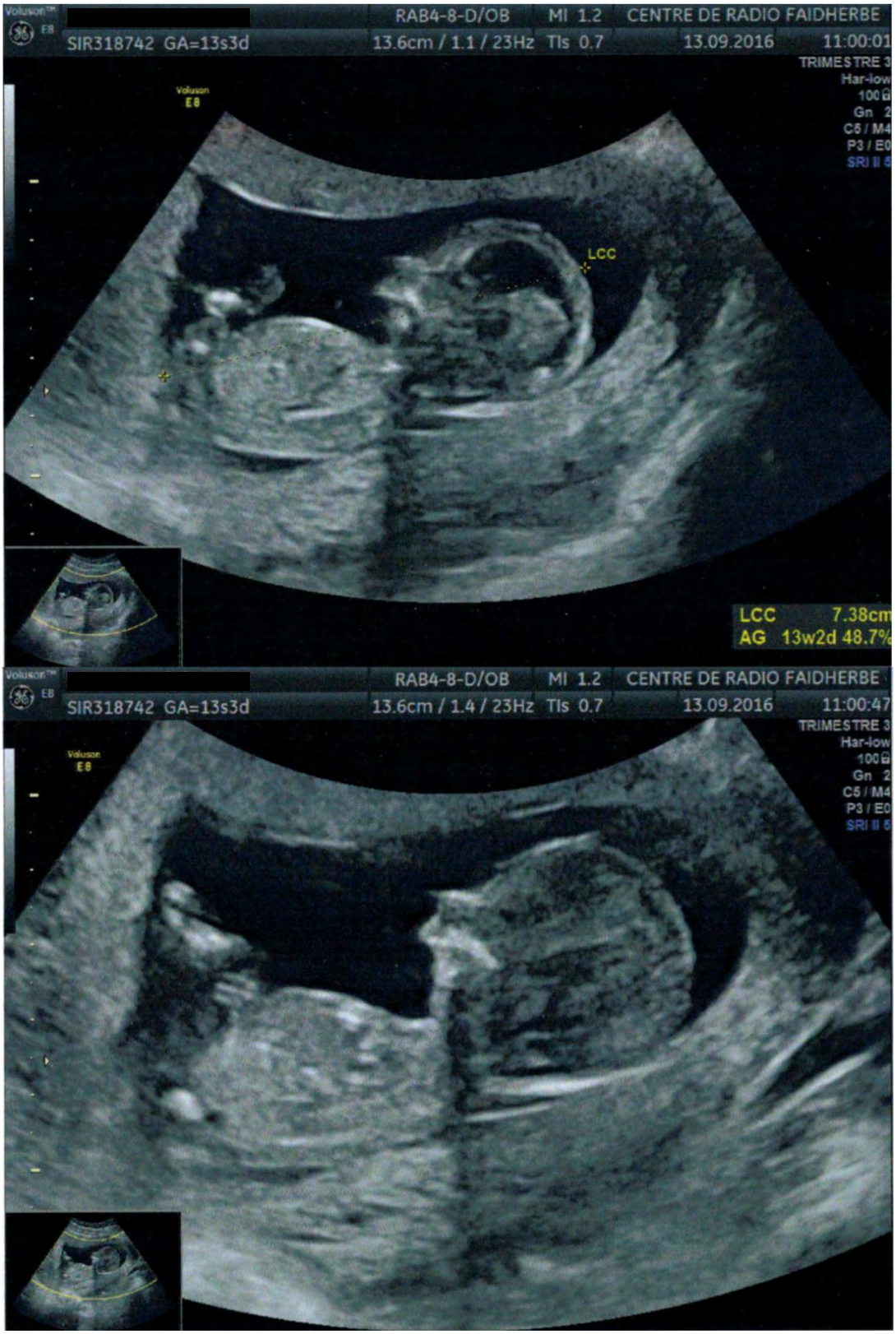
First, an illustration from the medical study, "Prenatal Identification of Pierre Robin Sequence". Below are two ultrasound images. The ultrasound image to the left shows a normal foetal facial profile. The ultrasound image to the right shows the foetal profile of a baby with Pierre Robin Sequence, suffering from retrognathia and micrognathia.



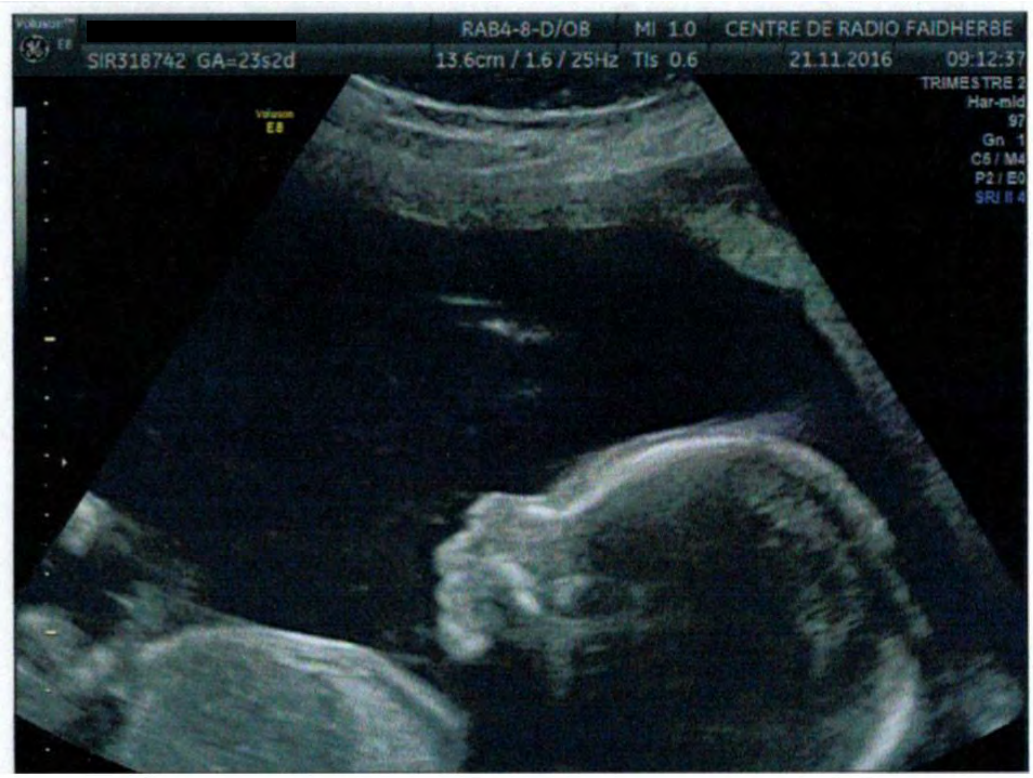
[Kaufman, Matthew G; Cassady, Christopher I; Hyman, Charles H; Lee, Wesley; Watcha, Mehernoor F; Hippard, Helena K; Olutoye, Olutoyin A; Khechoyan, David Y; Monson, Laura A; Buchanan, Edward P. *Prenatal Identification of Pierre Robin Sequence: A Review of the Literature and Look towards the Future*. Fetal Diagnosis and Therapy 2016; 39: 81-9.]

What follows are actual prenatal ultrasound images of Lysiane showing retrognathia, and indicating Pierre Robin Sequence – critical warning signs which were all overlooked.

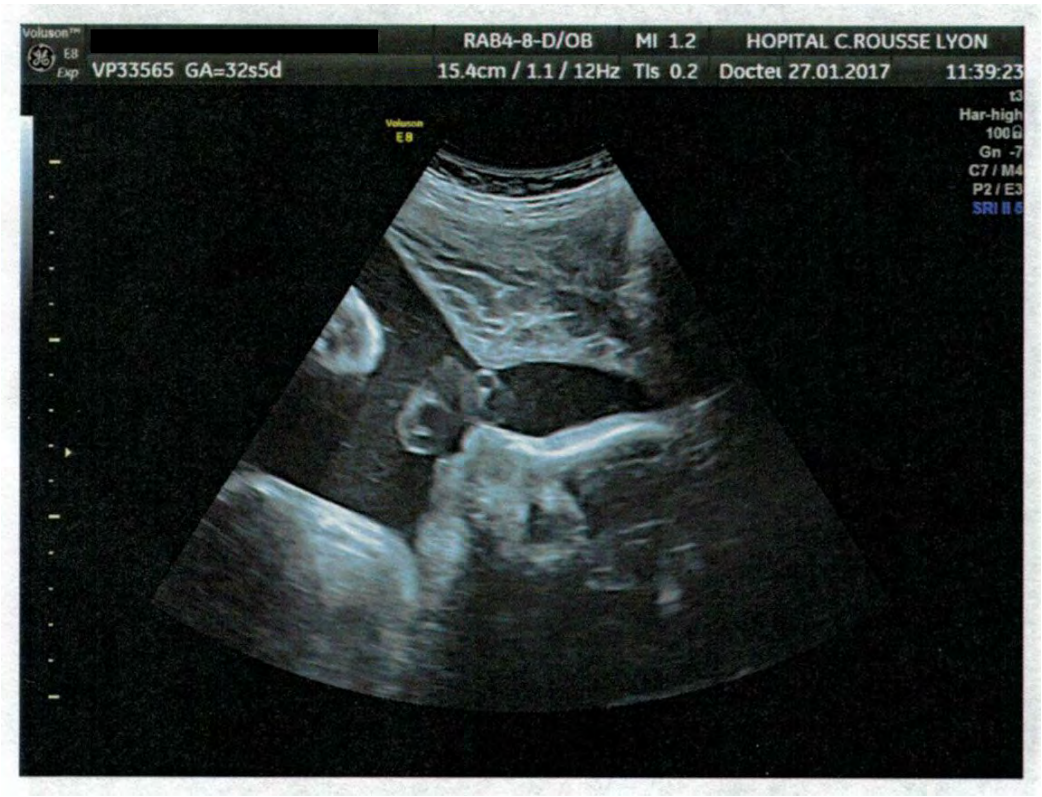
13 September 2016 ultrasound, Paris:



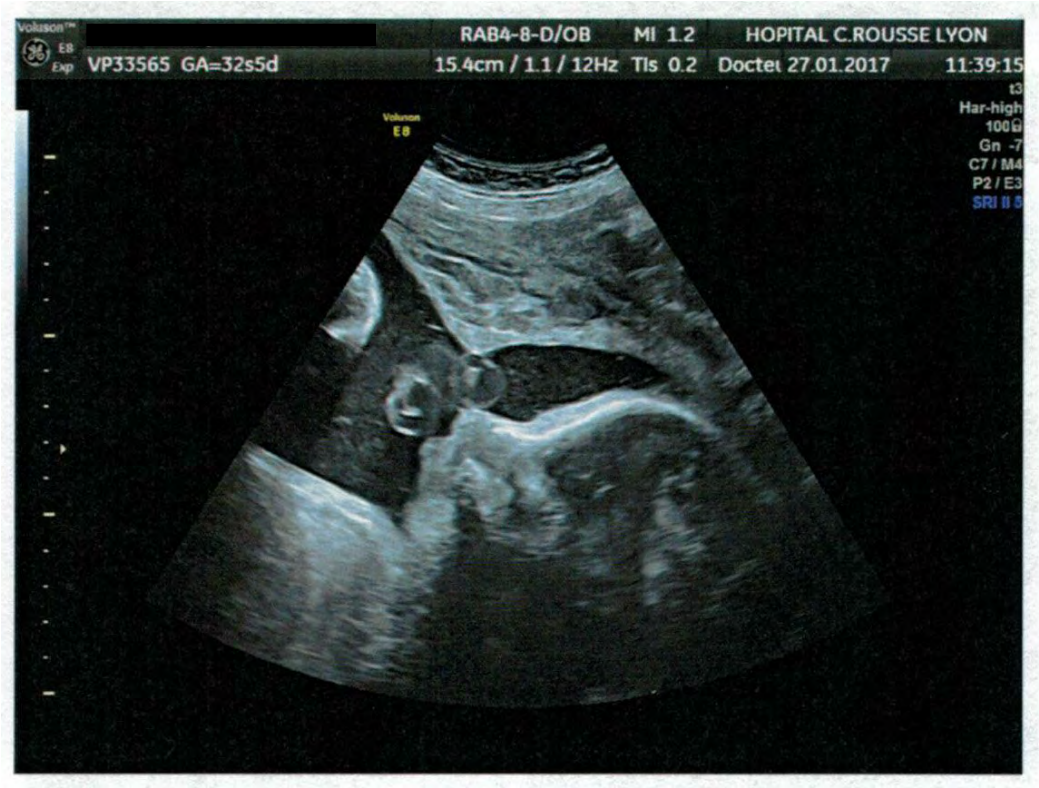
21 November 2016 ultrasound, Paris:

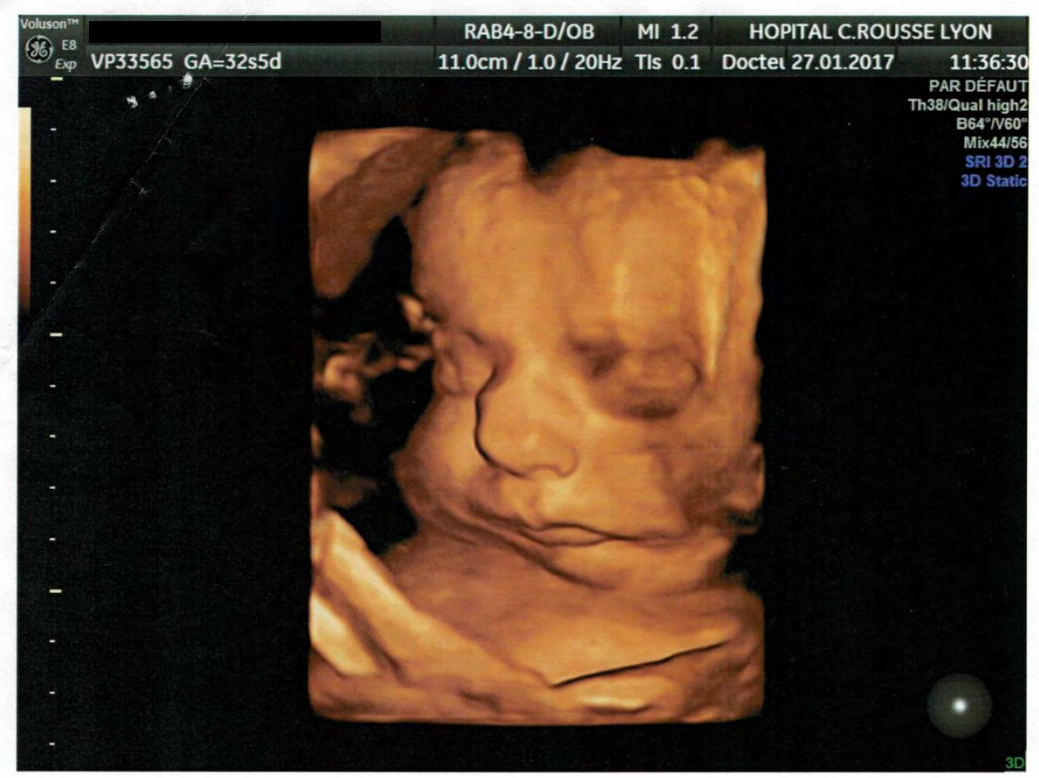


27 January 2017 ultrasound, Lyon:



27 January 2017 ultrasound, Lyon:





In addition to the ultrasound images showing retrognathia, *there was also a second entire set of warning signs, an excess of amniotic fluid, which as Orphanet explains is "a good diagnostic indicator" of Pierre Robin Sequence*. During the pregnancy, an excess of amniotic fluid was observed. This excess of amniotic fluid was specifically noted in multiple echographie (ultrasound) reports, including the echographies performed on:

- 18 January ("croissance au 50°P MAIS EXCES DE LIQUIDE AMNIOTIQUE INDEX 22");
- 27 January ("Le liquide amniotique est augmenté avec excès de LA. Index du liquide amniotique: Plus grande citerne 62,0 cm, Index LA: 21,2 cm."); and
- 14 February ("Le liquide amniotique est augmenté avec excès de LA. Index du liquide amniotique: Plus grande citerne 6,2 cm [sic], Index LA: 19,3… Conclusion: Persistance de l'excès de LA, pas des autres signes d'appel échographique").

In addition to being noted in several echographie reports, this excess of amniotic fluid was discussed several times during [redacted]'s prenatal examinations. As a result, [redacted] was ordered to cancel a planned trip, remain at home, and limit her movements to an absolute minimum.

Thus, in Lyon, two critical sets of warning signs indicating that Lysiane had Pierre Robin Sequence were overlooked. This failure in Lyon to identify two critical warning signs pointing to Pierre Robin Sequence had consequences at birth.

The medical file from Lyon indicates that one minute after birth, Lysiane's Apgar's score was 1. The next Apgar figure was still critical: it was 4. The question is, what happened during this important initial interval? The summary that was prepared by the hospital in Lyon, for the German hospital, indicates the following:

> "Initial treatment:
> Resuscitation: Aspiration: pharyngeal. VAM: for 3 minutes
> Intubation: at 29 minutes of life. Tube: number 3.5. Tube length: 11cm.
> Immediate postnatal development:
> 14h11: treatment by the midwives… Call for JM Labaune in the face of difficulties providing ventilation, attempt to place oropharyngeal cannula/Guedel by midwives. Failure.
> 14:14: arrival Dr. JM Labaune: Pierre Robin Sequence. Placement of laryngeal mask. Poor adaptation despite laryngeal mask: intubation tube number 4."
>
> > Original text, in French:
> > "Prise en charge initiale :
> > Réanimation : Aspiration : pharyngée. VAM : pendant 3 minutes
> > Intubation : à 29 minutes de vie. Sonde : numéro 3,5. Repère Sonde : 11cm.
> > Evolution postnatale immédiate :
> > 14h11 : prise en charge par les sages-femmes…Appel JM Labaune devant difficultés d'efficacité de la ventilation essai de pose de canule de Mayo par SF. Echec.
> > 14h14 : arrivée Dr JM Labaune : Séquence de Pierre Robin. Pose masque laryngé. Mauvaise adaptation malgré masque laryngé : intubation sonde no 4."

What the above suggests is that at birth, Lysiane was not breathing. According to the medical report ("RESUME DE SEJOUR") prepared by Lysiane's attending neonatologist, Dr. Nathalie Mory Thomas, at birth Lysiane suffered from respiratory distress as a result of an inhalation of clear amniotic fluid, and obstruction caused by Pierre Robin Sequence:

> "ILAC [Inhalation de Liquid Amniotique Clair] + obstruction from Pierre Robin Sequence"
>
> Original text, in French:
> "ILAC + obstructive sur séquence de Pierre Robin"

More important however are the actions which were carried out: three critical minutes were devoted to the application of "VAM", which probably refers to manual ventilation assistance of some kind. This did not work, so a doctor was called in. The reason this is important is that it is difficult to provide ventilation assistance to a baby with Pierre Robin Sequence, due to the baby's very specific anatomical defects. Lysiane suffers from micrognathia, the incomplete development of her lower jaw, and retrognathia, the abnormal positioning of her lower jaw to the posterior. In informal language, micrognathia means that the baby has a very small lower jaw and a small chin, while retrognathia resembles a severe overbite. With these anatomical defects, medical instruments that work on a face with normal facial anatomy will fail, because the lack of a chin makes it difficult or impossible to create a seal on the face using a standard facial mask.

If the hospital in Lyon had been able to recognize the two warning signs of Pierre Robin Sequence – the ultrasound images which showed that Lysiane had retrognathia, and the excess amniotic fluid – then the hospital could have anticipated a difficult birth, the birth of a baby with Pierre Robin Sequence. Instead of spending three valuable minutes trying to apply VAM, they could have gone directly to the laryngeal mask and intubation, knowing in advance that the anatomical defects of the baby would make ventilation difficult or impossible using the standard tools and procedures. The birth of Lysiane illustrates why it is so important for a patient with a rare disease to receive treatment from caregivers who have highly specialised knowledge about the rare disease.

According to Orphanet:

> Isolated Pierre-Robin sequence (without any other associated malformation) occurs in about 50% of cases… In one half [the other half] of the cases, Pierre-Robin sequence occurs as part of a complex malformation syndrome.
>
> Found here: http://tinyurl.com/pierre-robin-orphanet

Since about half of all patients with Pierre Robin Sequence also suffer from another associated condition, physicians attending to a patient with Pierre Robin Sequence must be vigilant to check for signs of the other associated conditions. The medical condition that is most often associated with Pierre Robin Sequence is a condition known as Stickler's Syndrome, which is a genetic disease affecting connective tissue.

During a meeting which took place on 7 April 2017 we discussed our concerns with the neonatologist in charge of Lysiane's care. We raised the issue of associated conditions. We were surprised when the neonatal physician asked us, "like what?" We assumed that she

would know the conditions most frequently associated with Pierre Robin Sequence, and that she would explain these associated conditions to us. [redacted] said, "for example, Stickler's Syndrome." The doctor looked at us, and asked [redacted] to repeat it. "I do not know that," said the doctor. She turned to the medical student sitting next to her; the medical student did not know either. The medical student literally went to her computer, did a Google search for Stickler Syndrome, and read aloud what was on the web page. The doctor then looked at us, and admitted, "I do not know Stickler's Syndrome." We were stupefied.

If the doctor treating our daughter doesn't even know what she should be looking for, how is she ever going to find it? Once again, this proves the point that a patient with a rare disease requires "a particular concentration of expertise in medical domains where expertise is rare" (the 2011 Directive, Article 12).

<u>The TPP treatment: a step forward in the treatment of this rare disease</u>

Dr. Brigitte Fauroux, from the Pediatric Noninvasive Ventilation and Sleep Unit of Necker Hospital in Paris, is an expert in the use of ventilation. Regarding ventilation, Dr. Fauroux has written that:

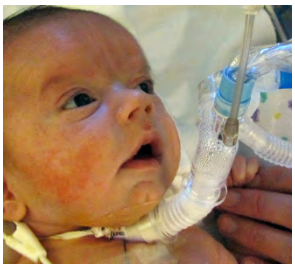
> "The better comfort of this noninvasive technique [ventilation], as compared with a tracheostomy, is likely to translate into a better quality of life, not only for the patients but also for their families."

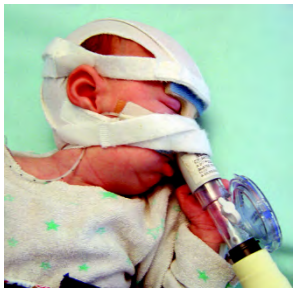
One can draw at least two significant conclusions from Dr. Fauroux's noteworthy remark on ventilation. The first is that all things being equal, a noninvasive technique (ventilation) is preferable to an invasive technique (tracheostomy).

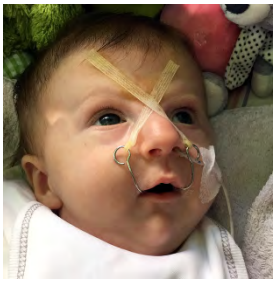
The second lesson is that quality of life – for patients, and for the families of patients – is a critical issue to take into account when choosing a medical treatment. This principle is even more important in the context of a rare disease. Patients should take quality of life into account, the families of patients should take quality of life into account, and doctors themselves should take quality of life into account, when they recommend possible treatment options. If we, as parents of a child suffering from Pierre Robin Sequence, were forced to choose between tracheostomy and ventilation, we would absolutely choose ventilation; in fact we would prefer ventilation over any surgical intervention, if we had a choice in the matter. At the same time, we believe that numerous peer reviewed medical studies have definitively proven, over more than a decade, that the TPP treatment represents the next big step forward in the treatment of Pierre Robin Sequence. When one honestly compares the tiny and portable TPP device, with the ventilation equipment and tubes and extended medical supervision required for ventilation, then it becomes very easy to extend Professor Fauroux's logic to the TPP treatment; ***the better comfort of the TPP device, as compared with ventilation, is likely to translate into a better quality of life, not only for the patients, but also for their families.***

The evolution of treatments for Pierre Robin Sequence

Tracheotomy → CPAP → TPP treatment







Although the effectiveness of the TPP treatment has been medically proven for over ten years, and represents a major step forward in the treatment of this rare disease, Pierre Robin Sequence, we believe that Lysiane, our daughter, is the first French baby to ever receive this proven treatment. This is surprising, considering that France is a country of 65 million people. Also, France is one of the richest countries in the entire EU, and can afford to support its citizens in obtaining cross-border healthcare, especially the relatively few French citizens suffering from a rare disease. Finally, France and Germany are next door neighbours. Why then have babies in France never been transferred to Germany for the proven TPP treatment, when babies from Austria, Hungary, the Czech Republic and other EU Member States have been transferred to Germany – and even babies from as far away as Russia have been transferred to Germany to receive the TPP treatment?

Also: if the effectiveness of the TPP treatment has been medically proven for more than 10 years, then why isn't the TPP treatment available in France? In particular, why isn't the TPP treatment being offered at the Pierre Robin Reference Centre in Paris? The policy of the Pierre Robin Reference Centre is that ventilation is just as effective as the TPP treatment, and therefore there is no need for France to adopt the TPP treatment. Imagine if the French Minister of Information Technology prevented the adoption of e-mail in France, based on the argument that people in France do not need e-mail – they can continue using fax machines instead. The problem is that this type of attitude can have very serious consequences in the realm of human health. When discussing treatments for a rare disease, the refusal to adopt medically proven innovations can subject patients – including innocent newborn babies – to physical harm, suffering, and even death.

In all fairness, there exists no medical or legal obligation for the physicians at the Pierre Robin Reference Centre in Paris to learn the TPP treatment, and offer it to Pierre Robin Sequence patients in France. The 2011 Directive, on the other hand, does indeed create obligations; it obliges all EU Member States, including France, to respect an EU citizen's right to choose the best medical treatment possible, particularly in the context of a rare disease – *"even for diagnosis and treatments which are not available in the Member State of affiliation"* (the 2011 Directive, Article 13, "Rare diseases"). If the Pierre Robin Reference Centre in Paris wishes to intentionally disregard the TPP treatment for Pierre Robin Sequence babies in France, it may do so – but it cannot at the same time obstruct French babies from leaving France, and receiving this medically proven rare disease treatment where it is available, in another EU Member State.

Legal Analysis

The 2011 Directive – highly specialised treatments for rare diseases

Legally speaking, the "*same or equally effective treatment*" medical standard which L'Assurance Maladie applied to Lysiane's S2 application, and which they used as the basis for refusing to authorise the TPP treatment, appears nowhere in the 2011 Directive. Rather, this standard is derived from cases which were decided in the European Court of Justice. These were cases in which EU citizens were seeking, or had received, cross-border healthcare in another EU Member State, outside of their Member State of affiliation. The cases generally involved EU citizens who had travelled to another EU Member State in order to obtain conventional medical care, for common medical conditions. One case involved an individual who had purchased eyeglasses in another Member State, and was denied reimbursement back in his home state. Another patient had travelled to another EU Member State to receive dental care. In one case, a patient had arthritis of the hip – and in another dispute, a woman was suffering from pain in her right wrist.

Occasionally, EU citizens were denied authorisation, or refused reimbursement, for experimental, medically unproven treatments; one patient wished to travel to another EU Member State in order to receive "psychosomatic pain treatment".

In none of these European Court of Justice cases was the patient seeking a medically proven treatment for a *rare* disease – and certainly none of the claimants happened to be a newborn baby suffering from a rare disease, attached to a ventilator machine in a neonatal intensive care unit. There is a reason such a case has never reached the European Court of Justice. The Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare "aims to establish rules for facilitating access to safe and high-quality cross-border healthcare". It explains that:

> "…the vast majority of patients in the Union receive healthcare in their own country and prefer to do so. However, in certain circumstances patients may seek some forms of healthcare in another Member State. Examples include highly specialised care…"

Patients suffering from a rare disease are exactly the kinds of patients who typically require highly specialised cross-border care. For rare disease patients, cross-border healthcare is not a mere question of personal preferences, nor is it a means of exploring the possibilities or testing the boundaries of Regulation 883 and EU law. Rather, it represents an urgent attempt to obtain a life-changing and possibly life-saving treatment for their rare disease. Often, the highly specialised treatments they seek are only available in certain limited locations, geographically distinct knowledge centres, which serve as "centres of expertise" for their rare disease. Due to the seriousness of their rare disease, and a lack of local expertise, rare disease patients are ready to travel to those highly specialised knowledge centres, wherever they happen to be.

Based on the 2011 Directive's recognition of the special needs of these rare disease patients, Article 13 ("Rare Diseases") of the 2011 Directive specifically sets out "the possibilities offered by Regulation (EC) No 883/2004 for referral of patients with rare diseases to other Member States <u>even for diagnosis and treatments which are not available in the Member State of affiliation</u>."

While the 2011 Directive revolves around the notion of patient choice, nowhere is this privilege – the right to choose a highly specialised treatment in another EU Member State – emphasized more strongly or more clearly than in Article 13, "Rare Diseases".

CLEISS, the national contact point for France under the 2011 Directive, confirms the special margin of choice which the 2011 Directive grants to EU citizens suffering from a rare disease:

> "Medical care and reimbursement
>
> Patients diagnosed with or suspected of having a rare disease have the right to access health care in another Member State of the European Union or the European Economic Area (Iceland, Liechtenstein and Norway) within the framework of Regulations No 883/04 and No 987/09, even if the diagnosis and/or treatment in question is not available in the patient's State of affiliation."
>
> Found here: https://www.cleiss.fr/particuliers/venir/soins/ue/maladies-rares.html

Our daughter Lysiane was born with a rare disease; she is a patient "with a medical condition requiring a particular concentration of expertise in medical domains where expertise is rare" (the 2011 Directive, Article 12). Based on this, Lysiane is legally guaranteed a broader margin for selecting appropriate specialised treatment, for her rare disease.

In the context of a rare disease, the question is not the availability in France of existing treatments; in the context of a rare disease, the issue is Lysiane's legally guaranteed right to choose a highly specialised and medically proven treatment which is *not* available in France. This is the whole point of the 2011 Directive's Article 13.

<u>The Four Fundamental Freedoms of the EU</u>

The laws and rights involved in this dispute go beyond the 2011 Directive; they arise out of the central purpose of the EU itself. At the core of the European project is the effort to create a single EU market. The EU's four fundamental freedoms – the free movement of goods, services, people and capital – provide the foundation for this single market.

In joined cases 286/82 and 26/83, Luisi et Carbone, the European Court of Justice specifically confirmed that the fundamental EU freedom, the freedom to provide services, also includes the freedom to *receive* services:

> "…the freedom to provide services includes the freedom, for the recipients of services, to go to another member state in order to receive a service there, without being obstructed by restrictions…"

In the same set of joined cases, the European Court of Justice also declared that:

> "persons receiving medical treatment… are to be regarded as recipients of services."

In addition to the European Court of Justice's case law, the 2011 Directive itself reminds Member States that healthcare services are covered by the fundamental freedom to provide and to receive services in the EU:

> "As confirmed by the Court of Justice, neither its special nature nor the way in which it is organised or financed removes healthcare from the ambit of the fundamental principle of the freedom to provide services."

Thus, based on the fundamental freedom to provide and to receive services, which is enshrined in the Treaty on the Functioning of the European Union, Article 56 – and as confirmed repeatedly by the European Court of Justice in multiple decisions which are binding on all EU Member States – EU citizens enjoy a fundamental legal right to receive services, including medical services, in other EU Member States, without facing arbitrary, unjustified, undue obstruction.

The four fundamental freedoms hold a very special place in EU law. Peter Altmaier, a German Minister, and Angela Merkel's top adviser in the Brexit negotiations, recently explained it the following way:

> "These four fundamental freedoms are at the heart of the single market… That means that any country that would like to participate in the single market, basically has to accept the single market as it exists."

Accepting the single market as it exists means fully respecting the four fundamental freedoms, of every EU citizen.

Because the four fundamental freedoms are so critical for achieving the single EU market, the four fundamental freedoms are treated, legally, as a kind of red line. When an EU Member State is brought before the European Court of Justice for obstructing one of the four fundamental freedoms, the Court subjects the Member State's actions to strict legal scrutiny. The EU Member State has to explain to the European Court of Justice exactly how and why the EU Member State's obstruction was objectively justified. The EU Member State also has to demonstrate, convincingly, that when the EU Member State obstructed one of the four fundamental freedoms, that the EU Member State did not exceed what was objectively necessary to achieve a certain, specific goal. The goal cannot be any vague, random goal, chosen at whim; the goal has to be a specific, *legitimate* goal. The Member State will even be required to convince the Court that the Member State could not have achieved that same, important, legitimate goal, using less restrictive measures.

In brief, when an EU Member State obstructs one of the EU's four fundamental freedoms, the EU Member State will have a great deal of explaining to do.

Large bureaucracies tend to dislike when constraints are placed upon their power and their discretion. This principle is universal, and it holds true when dealing with the social security systems of the various EU Member States. On several occasions, EU social security systems brought before the European Court of Justice have attempted, unsuccessfully, to justify their obstructive behaviour, using the following argument: "each EU Member State is responsible for organising its own social security system; how we carry out that responsibility is our business, and our business alone."

For EU citizens, it is very fortunate that this argument does not work. Every single EU Member State, in managing its social security system, must manage it in conformity with EU law. This means that the social security system's decisions cannot violate EU law, and in

particular, they cannot violate the EU's four fundamental freedoms. This was articulated very clearly by the European Court of Justice in the Watts case, Case C-372/04:

> "Whilst… it is for the legislation of each Member State to determine the conditions in which social security benefits are granted, when exercising that power Member States must comply with Community law, in particular the provisions on the freedom to provide services… Those provisions prohibit the Member States from introducing or maintaining unjustified restrictions on the exercise of that freedom in the healthcare sector."

EU Member State social security systems are not free to simply do whatever they want with their power; they must exercise their power in accordance with EU law. Once again, as explained by the European Court of Justice:

> "It is settled case-law that a system of prior authorisation cannot legitimise discretionary decisions taken by the national authorities which are liable to negate the effectiveness of provisions of Community law, in particular those relating to a fundamental freedom such as that at issue in the main proceedings".

EU Member State social security systems must, at all times, comply with, answer to, and respect, EU law, especially the four fundamental freedoms.

The 2011 Directive, Article 8, reminds Member States of the inviolability of the EU's four fundamental freedoms. Article 8 also reminds them of the legally binding nature of the Court's decisions regarding cross-border healthcare, by using the same phrases and terms which the Court itself used when deciding these cases:

> "…individual decisions of refusal to grant prior authorisation, shall be restricted to what is necessary and proportionate to the objective to be achieved, and may not constitute a means of arbitrary discrimination or an unjustified obstacle to the free movement of patients."

In the case of our daughter Lysiane, the treatment which is used in France to treat our baby's rare disease consists of keeping the baby in a hospital, attached to a ventilator machine. Lysiane was stuck in a French intensive care unit for five straight weeks, with no release date in sight. Since ventilation assistance generally requires long term hospitalisation, the French treatment creates colossal healthcare costs. Germany's highly specialised TPP treatment, on the other hand, is medically proven to resolve the upper airway obstruction associated with this rare disease, and instantly liberate the baby from the ventilator machine – thereby safely and effectively eliminating the need for long term hospitalization. This makes the TPP treatment a cost-effective medical breakthrough in the treatment of this rare disease.

Based on these facts, and considering the law, what crucial objective was L'Assurance Maladie trying to achieve when it refused Lysiane's request for the TPP treatment? The goal L'Assurance Maladie was trying to achieve has to be legitimate; therefore, L'Assurance Maladie cannot say, "our objective was to waste money; forcing Lysiane to remain connected to a ventilator machine in France, and endure expensive long term hospitalisation, was necessary and proportionate for achieving our objective, to waste money."

Once again, the goal has to be legitimate; since the goal has to be legitimate, L'Assurance Maladie cannot say, "our objective was to use up excess space in France's neonatal intensive care units, expose Lysiane to the unnecessary risk of hospital borne illnesses, and separate Lysiane from her parents for as long as possible. Forcing Lysiane to remain connected to a ventilator machine in the neonatal intensive care unit was necessary and proportionate for achieving our objective, to use up excess space in France's neonatal intensive care units, expose Lysiane to the unnecessary risk of hospital borne illnesses, and separate Lysiane from her parents for as long as possible." By putting into words the actual consequences which L'Assurance Maladie's position entails, it becomes clear how irrational it was for L'Assurance Maladie to refuse Lysiane's S2 application for the TPP treatment.

L'Assurance Maladie's irrational rejection of Lysiane's request to obtain the highly specialised, medically proven and cost-effective TPP treatment for her rare disease is a clear example of the type of unjustified obstacle to the fundamental freedom to provide and receive services, and the free movement of patients, which the Treaty on the Functioning of the European Union forbids, and which the 2011 Directive forbids, and which the European Court of Justice, in case after case dating back many years, has militated so strongly against.

Indirect discriminatory effect

In order to achieve a single EU market, state actors in the EU are prohibited from engaging in market interference. If, hypothetically speaking, the UK government, seeking to steer UK consumers to drink more domestically produced English beer, rather than imported French wine, suddenly imposed a high import tax on all wine entering the UK – this, in practice, would produce what EU law specialists call an "indirect discriminatory effect". The tax on imported wine, even though it does not single out French producers, would unfairly prejudice French vineyards, because French wine would suddenly increase in price relative to domestically produced English beer. This type of market interference, even though it is subtle, and indirect, is illegal in the EU.

For at least 5 years now, the Pierre Robin Reference Centre at Necker Hospital in Paris has been maintaining a wall between Pierre Robin Sequence patients in France, and qualified healthcare providers in Germany. This policy does not explicitly target German providers of medical devices, or German providers of healthcare services. However, in practice, the policy has an indirect discriminatory effect upon them. The policy, and its indirect discriminatory effect, can be demonstrated by presenting the Pierre Robin Reference Centre in Paris with the following questions:

- Over the past 5 years, a number of French babies have been diagnosed with Pierre Robin Sequence. How many times were the parents of these babies informed that the TPP treatment was a safe and medically proven treatment option for their baby's rare disease, and that it can be obtained in multiple treatment centres just next door in Germany?
- How many times has the Reference Centre in Paris recommended the medically proven TPP treatment for Pierre Robin Sequence?
- How many times has the Pierre Robin Reference Centre prepared a medical certificate in support of a French patient's S2 application to receive the TPP treatment in Germany?
- How many French patients suffering from the Pierre Robin Sequence have received the TPP treatment in Germany?

The answers to all of these questions – zero, or close to zero, over a period of more than 5 years – will demonstrate that a pattern exists which can only be the result of a deliberate policy. The goal of this policy is to restrict French patients' access to the TPP medical device – a good – and to restrict French patients' access to Pierre Robin Sequence healthcare treatment in Germany – a service. This policy not only turns the spirit of European cooperation upside down, to the detriment of a particularly vulnerable population – babies suffering from a rare disease – but due to its verifiable, indirect discriminatory effect, it also violates Article 34 of the Treaty on the Functioning of the European Union.

This policy also raises broader questions which transcend EU law: the question of basic medical ethics, and the physician's obligation to obtain informed consent, as explained in the following section.

Dr. Veronique Abadie and The Pierre Robin Reference Centre in Paris

Dr. Veronique Abadie, the director of France's Reference Centre for the rare disease, Pierre Robin Sequence, refused to provide us with the medical certificate we needed for Lysiane's S2 application to receive the TPP treatment in Germany. Instead of providing us with a medical certificate, Dr. Abadie wrote a letter suggesting that the same or equally effective treatment is available in France. Dr. Abadie is the director of France's Reference Centre for the rare disease, Pierre Robin Sequence. This means that in France, her medical opinion regarding this rare disease is definitive. Therefore, one cannot be surprised that after L'Assurance Maladie received Dr. Abadie's letter, L'Assurance Maladie rejected Lysiane's S2 application.

In Germany, Dr. Christian F. Poets is the Chairman of The Interdisciplinary Centre for Craniofacial Malformations at Tübingen University Hospital. It was at this Centre in Tübingen University Hospital that our daughter Lysiane received the TPP treatment which resolved her upper airway obstruction, liberated her from the ventilator machine, got her out of the intensive care unit, and changed her life. Dr. Poets was in charge of Lysiane's medical care when Lysiane received the TPP treatment in Tübingen. Dr. Poets was genuinely surprised that L'Assurance Maladie rejected Lysiane's S2 application. He was surprised because his Centre in Tübingen has provided the TPP treatment to patients from various other EU Member States, and those patients from various other EU Member States had always received their S2 documents from their respective EU Member State governments without any problems whatsoever.

Dr. Poets in Tübingen, and Dr. Abadie in Paris, are professional colleagues; they have known one another for years. Dr. Poets and Dr. Abadie address one another on a first name basis: "Christian", and "Veronique". On 7 May 2017, a conference was held in Toronto Canada. The subject of the conference was the rare disease, Pierre Robin Sequence. Experts on Pierre Robin Sequence came from all over the world to attend the conference, and to discuss treatment strategies: https://robin-sequence.com/

Dr. Poets and Dr. Abadie both attended this 7 May 2017 conference in Toronto. During the conference, Dr. Poets and Dr. Abadie spoke with one another. Dr. Poets asked Dr. Abadie why she would not support Lysiane's S2 application.

Dr. Abadie told Dr. Poets that if she did, the result would then be that other French patients suffering from Pierre Robin Sequence would also go to Germany for treatment, instead of going to her.

President Macron: as Lysiane's father, there are many strong words I could use right now to describe this situation in general, and Dr. Abadie's conduct in particular. However, I will refrain from doing so. What I think, and how I feel, is ultimately far less important than the full and open investigation which this situation calls for, and the actions your government takes as a result of this full and open investigation.

We as parents saw first-hand the dramatic advantages of Germany's TPP treatment over France's conventional treatment, ventilator machines, *because our daughter Lysiane received both treatments*. Thus we understand Dr. Abadie's concern that the Reference Centre which she directs at Necker Hospital could in the future lose some French patients to Germany, since the Reference Centre at Necker Hospital does not offer the TPP treatment. However, Dr. Abadie's wish to protect the client base of the Reference Center at Necker Hospital is not an acceptable justification for obstructing Lysiane's S2 application.

Dr. Abadie's conduct raises several disturbing issues, including the following. First of all, Dr. Abadie is the director of an EU recognized Orphanet Reference Centre for the rare disease, Pierre Robin Sequence. The EU's European reference networks, *"especially for rare diseases"*, are supposed to *"help realise the potential of European cooperation regarding highly specialised healthcare for patients and for healthcare systems by exploiting innovations in medical science and health technologies"* (the 2011 Directive, Article 12). The safety and effectiveness of the highly specialised and innovative TPP treatment has been definitively proven in peer-reviewed medical studies dating back over ten years – but throughout all of France, a country of 65 million people, our daughter Lysiane may be the first French baby to ever receive this breakthrough German treatment. This is striking – but Dr. Abadie's explanation to Dr. Poets at the 2017 Pierre Robin Sequence conference in Toronto explains why. Dr. Abadie's intentional obstruction and non-cooperation completely defeats the purpose of the 2011 Directive's European reference networks. If Dr. Abadie is unwilling to help realise the potential of European cooperation regarding highly specialised healthcare for rare diseases by exploiting innovations in medical science and health technologies – such as the TPP treatment – then she should not be directing a European Reference Centre.

Second of all, by obstructing French babies from obtaining the highly specialised TPP treatment in Germany, the Pierre Robin Reference Centre at Necker Hospital, under the leadership of Dr. Abadie, not only violated EU law through intentional market interference, and illegitimate obstruction of the EU's four fundamental freedoms; the Pierre Robin Reference Centre at Necker Hospital also violated its own mission statement. The mission statement of the Pierre Robin Reference Centre at Necker Hospital includes "Facilitation of patients' access to care" ("Facilitation de l'accès aux soins des patients"). Any definition of "care" must in any case include all highly effective and medically proven devices and techniques, even if they were not developed by Dr. Abadie and her team of physicians in Paris, but rather by her colleagues and counterparts in Germany. According to her Reference Centre's mission statement, Dr. Abadie should be *facilitating* patients' access to care. If Dr. Abadie believes it is acceptable to *obstruct* patients' access to care – specifically, to a safe, highly effective and medically proven treatment for a rare disease – then once again, she should not be directing the Pierre Robin Reference Centre at Necker Hospital.

Third of all, and most important, Dr. Abadie's wish to protect the client base of the Reference Center at Necker Hospital, as indicated by her discussion with Dr. Poets at

the Pierre Robin Sequence conference in Toronto on 7 May 2017, is not an acceptable justification for obstructing Lysiane's access to a safe and medically proven treatment for Lysiane's rare disease. No doctor should place professional interests above the health interests of patients. Such conduct raises serious questions of basic medical ethics.

What makes this even more disturbing is that this question concerning basic medical ethics may very well be part of a broader, systematic pattern. As we have already indicated earlier in this document's "Background Information" section, we spoke with Dr. Abadie by telephone regarding our daughter Lysiane's health, and the TPP treatment, on Monday 10 April 2017. During this telephone call, Dr. Abadie confirmed that she knows Dr. Poets in Tübingen, and she knows his work. Regarding the TPP treatment, Dr. Abadie told us:

> *"I know this technique and I know Professor Poets. It's a technique which works. It works, it's undisputable."*
>
> French original:
> "Je connais cette technique et je connais le Professor Poets. C'est une technique qui marche – ça marche, c'est indiscutable."

Before we ever contacted Dr. Abadie, we, Lysiane's parents, were desperate to find the best possible medical treatment for our daughter's rare disease. After exhaustive research, which we carried out on our own, we located several medical studies providing details of the TPP treatment. For us as parents – not doctors, but parents – the TPP treatment was extremely promising news. Learning about the TPP treatment gave us hope for our baby, who was struggling to breathe, and who suffered repeated instances of oxygen desaturation in the French hospital. *For Dr. Abadie, on the other hand, the TPP treatment was not news at all; Dr. Abadie has known about the TPP treatment for years*. She knows the head physician leading the German medical team which administers the TPP treatment in Tübingen, she reads their medical studies, and she knows very well that the medical effectiveness of the TPP treatment is "indisputable".

Dr. Abadie *also* knows that the treatment she has been proposing for French babies in France – connecting the baby to a ventilator machine with a CPAP mask – is a treatment associated with real medical risks. A newborn baby wearing a CPAP mask is exposed to the serious and known risk of facial deformities. As explained earlier, in the Medical Analysis, Dr. Brigitte Fauroux, a colleague of Dr. Abadie at the Pierre Robin Reference Centre at Necker Hospital in Paris, studied the risks of ventilation masks, and the facial deformities caused by these masks. Dr. Fauroux's peer reviewed medical study indicates that the serious risk of maxillary retrusion is triggered not by months and months of the baby wearing the ventilation mask, but from the baby wearing the mask for more than 10 hours per day, *for any period of time* – months, weeks, possibly even days.

This leads to the question: were French parents informed of the serious risk that these CPAP ventilation masks could cause their baby to suffer from facial deformities? If French parents were not clearly informed about the known risks of facial deformities, then how can those French parents possibly have provided informed consent for their baby to receive this particular treatment? For a parent's consent to qualify as *informed consent*, the physicians would first need to explain to the parents all of the relevant and material facts associated with the proposed treatment, including the benefits, the risks, and the alternatives.

The French parents who gave consent for their baby to receive one of the French palatal plates which Dr. Abadie described in her letter to L'Assurance Maladie – were those French parents informed that the French palatal plate which their baby was receiving had "no effect on ventilation", as Dr. Abadie admitted in writing? Were those French parents informed that the French palatal plates lacked peer-reviewed medical studies to demonstrate what benefits they could offer, and what risks they might create? Were those French parents informed that just next door, in Germany, *this exact same type of treatment, a palatal plate*, is used to treat babies suffering from Pierre Robin Sequence? Were those French parents informed that unlike the French plates, the German palatal plates *do* successfully resolve the potentially life-threatening breathing difficulties faced by these babies? Were they told that unlike the French plates, the German palatal plates are backed by over ten years' worth of peer-reviewed medical studies, which prove that the German plates are not only highly effective, but also safe for babies to use?

As for the French parents who gave consent for their baby to undergo invasive surgery, including mandibular distraction osteogenesis, and even labioglossopexy – sewing the baby's tongue to the baby's lip, a shameful practice which civilised countries should ban – were those French parents informed of less invasive alternative treatments? Were those French parents informed that the TPP treatment in Germany might allow their baby to avoid these painful, invasive, and risky surgical procedures altogether, and yet still fully resolve their baby's breathing difficulties, safely, and effectively?

Regarding risks: the Pierre Robin Reference Centre at Necker Hospital in Paris cannot claim that they did not know about the risks of ventilation masks and facial deformities; one of the physicians at this Reference Centre wrote a definitive study on these risks.

Regarding benefits: the Pierre Robin Reference Centre at Necker Hospital in Paris cannot claim that they did not know about the safety and remarkable effectiveness of the TPP treatment in Germany; Dr. Abadie, the director of the Reference Centre, knows Dr. Poets personally, knows his work, and admitted that the medical effectiveness of the TPP treatment is "indisputable."

If French parents of babies suffering from Pierre Robin Sequence were not given sufficient information to form reasoned decisions about the medical treatments which were being recommended and administered to their baby – including all relevant and material facts about the proposed treatment's benefits, risks, and alternatives – then once again, serious questions of medical ethics are raised.

Setting aside EU law, these serious questions of medical ethics warrant a full and open investigation, all by themselves. We ask you, President Macron, to order such an investigation, and we ask you to allow those of us here in France whose children suffer from Pierre Robin Sequence to know the results of the investigation.

Violations of fundamental EU law: justifications and derogations

In 2010, the European Court of Justice issued a ruling in a case concerning a Bulgarian citizen suffering from cancer in his right eye, Case C-173/09. In this dispute, Bulgaria's national healthcare system actually demonstrated that it was capable of successfully treating

the cancer in this patient – however, the treatment proposed by Bulgaria would result in the loss of the patient's eyesight in his right eye.

The patient learned that fellow EU Member State Germany not only offered a medical treatment which would achieve the goal of eliminating his cancer, but that the German treatment would eliminate the cancer in such a way that he would be able to keep his eyesight in his right eye.

The patient asked the Bulgarian national healthcare system for prior authorisation to obtain this medical treatment in Germany; the Bulgarian national healthcare system rejected his request. The matter went before the European Court of Justice.

To Bulgaria's credit, the Bulgarian national healthcare system refrained from presenting the shameless and embarrassing fiction that the proposed treatment in Bulgaria, and the requested treatment in Germany, were "*the same or equally effective*" – even though both treatments would indeed successfully eliminate the patient's cancer. The Bulgarian government was honest enough to admit that the German treatment was superior.

However, the Bulgarian government requested a derogation from Article 56 and from the obligations of EU cross-border healthcare law based, essentially, on a claim of poverty. The Bulgarian government argued that if a sufficient number of Bulgarian patients sought cross-border healthcare treatments in other EU Member States, and if the Bulgarian government had to cover the costs of such cross-border treatments, then it could potentially complicate Bulgaria's ability to engage in healthcare planning, and it might even undermine the financial balance of Bulgaria's entire social security system.

This attempt by Bulgaria to escape the obligations of EU law failed.

The truth is that the dire warnings of a hypothetical exodus of EU patients to other EU Member States, to obtain planned cross-border healthcare, has absolutely no basis in reality, and this is why the European Court of Justice rejected Bulgaria's argument – in spite of the fact that Bulgaria is undoubtedly one of the poorer EU member states.

As the European Commission explained:

> "Patients prefer to receive healthcare in their own country. That is why the demand for cross-border healthcare represents only around 1% of public spending on healthcare, which is currently around €10 billion. This estimate includes cross-border healthcare which patients had not planned in advance (such as emergency care for tourists). *This means that, at present, considerably less of that 1% of the expenditure and movement of patients is for planned cross-border healthcare, like hip and knee operations or cataract surgery*."
>
> Found here: http://europa.eu/rapid/press-release_MEMO-13-918_en.htm

Cross-border healthcare represents approximately 1% of public healthcare spending. This 1% figure includes two distinct components. The first component is planned cross-border healthcare; planned cross-border healthcare is simply healthcare which the patient has planned out in advance. The second component is unplanned cross-border healthcare – for example, when a German skier breaks his leg while skiing in the Austrian Alps, and receives

emergency medical treatment in an Austrian hospital. Since the sum total figure for cross-border healthcare expenditure, i.e. both planned and unplanned added together, amounts to approximately 1% of public healthcare spending, *planned* cross-border healthcare represents just a fraction of this 1%. And since rare diseases are, by definition, rare, *planned cross-border healthcare for EU citizens suffering from a rare disease represents literally a fraction of a fraction of 1% of public healthcare spending*. Based on these miniscule figures, L'Assurance Maladie cannot possibly argue that refusing to provide Lysiane with authorisation to receive the TPP treatment in Germany was a necessary and proportionate measure to preserve the financial integrity of the French social security system.

Furthermore, unlike Bulgaria, France is one of the richest countries in the European Union. France's healthcare system is well-funded, and provides its citizens with a balanced medical and hospital service which is open to all. In France there is no immediate shortage of medical resources, nor any structural or prolonged deficiencies in hospital facilities. France faces no problems maintaining treatment capacity, and the viability of France's welfare system is not at risk.

Also, when one calculates the high cost of France's ventilation assistance, which generally requires long-term hospitalization, and compares it to the cost of sending French Pierre Robin Sequence patients to Germany to obtain the TPP treatment – which typically requires two to three weeks of inpatient care – then it becomes clear that prescribing the TPP treatment would substantially *reduce* the expenses incurred by the French national healthcare system.

The European Court of Justice acknowledged Bulgaria's legitimate need to engage in healthcare planning "to control costs and to prevent, as far as possible, any wastage of financial, technical and human resources". However, L'Assurance Maladie, by preventing French patients from obtaining the TPP treatment, and instead forcing them to endure extremely costly long-term hospitalization, is directly violating all of these legitimate planning objectives.

L'Assurance Maladie's rejection of Lysiane's request for a medically proven and cost-effective treatment for her rare disease violates EU law – both primary law and secondary legislation – and represents the kind of arbitrary, irrational, unnecessary and unreasonable exercise of national discretion which the European Court of Justice has repeatedly struck down.

Conclusion

The legally binding Directive 2011/24/EU on the application of patients' rights in cross-border healthcare aims to "foster developments of the diagnosis and treatment of rare diseases", and "to facilitate improvements in diagnosis and the delivery of high-quality, accessible and cost-effective healthcare for all patients with a medical condition requiring a particular concentration of expertise in medical domains where expertise is rare". The TPP represents exactly the type of high-quality cost-effective rare disease treatment which the 2011 Directive describes.

The TPP treatment corrects the underlying anatomical problem, Pierre Robin Sequence's upper airway obstruction, allowing the baby to breathe naturally and independently, on her own – and the TPP treatment achieves this without any surgery. Ventilation assistance on the other hand simply forces air down the baby's blocked airway; the baby's airway, however, remains obstructed, and when the baby is disconnected from the ventilator machine, the breathing difficulties return. Furthermore with the TPP treatment there is no need for any external equipment. CPAP on the other hand does require equipment, a ventilator machine; this radically limits patient mobility, since the baby has to be connected to the ventilator machine almost around the clock. The TPP treatment also eliminates the need for long term hospitalisation, which CPAP generally requires, and which comes at a tremendous financial and human cost.

No objective and impartial medical comparison can reasonably conclude that CPAP, which requires the baby to be connected to a ventilator machine, and the TPP treatment, which achieves crucial medical objectives that CPAP cannot and does not achieve, are "the same or equally effective". Medically, economically, and in terms of quality of life, the TPP treatment provides fundamental advantages over alternative Pierre Robin Sequence treatments, including CPAP. This is why babies from other EU Member States, and even babies coming all the way from Russia, have been transferred to Germany to receive the TPP treatment.

Article 13 ("Rare Diseases") of the 2011 Directive sets out "the possibilities offered by Regulation (EC) No 883/2004 for referral of patients with rare diseases to other Member States even for diagnosis and treatments which are not available in the Member State of affiliation." By email, CLEISS confirmed for us that the 2011 Directive grants EU citizens suffering from a rare disease the right to obtain a highly specialised treatment in another Member State, if it is <u>not</u> available in their Member State of affiliation.

L'Assurance Maladie's refusal to grant prior authorisation for the highly specialised and medically proven TPP treatment for our child's rare disease violates the 2011 Directive, Regulation (EC) No 883, and the fundamental principle of the freedom to provide and receive services under Article 56 of the Treaty on the Functioning of the European Union. It represents the kind of arbitrary, irrational, and unreasonable exercise of national discretion which the European Court of Justice has repeatedly struck down. It cannot be justified on any public policy grounds, and was neither necessary nor proportionate. This unfounded rejection should be reversed.