EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 July 2022
EMA/665019/2022
Stakeholders & Communication Division

Pilot on early dialogue with patient organisations for orphan marketing authorisation applications: Outcome Report

1. Background/rationale

A range of methodologies have been tested and established to capture patients' perspectives throughout the medicine's lifecycle at EMA and the added value has been well demonstrated over time. Patients' involvement is continually monitored with regular analyses on where potential improvements or enhancements can be made.

One area where it was felt a gap existed was the early stages of the evaluation of marketing authorisation applications (MAA) where requests for patient input generally come at a late stage of the evaluation (e.g. Scientific Advisory Group (SAG)/Ad-hoc expert meetings and oral explanations). We explored how current practices could be enhanced to avoid any missed opportunities for early interaction and proposed a pilot study to reach out to patient organisations at the start of marketing authorisation assessments. This would complement other engagement methodologies and facilitate any further interactions as the procedures progress.

The proposal was also supported by both the CHMP work plan: 'Incorporate additional and regular processes to capture and include patients' views and preferences in benefit/risk evaluations' and EMA's Regulatory Science Strategy recommendations: 'Enhance methods to systematically incorporate patient data in regulatory decision-making'.

2. Pilot phase

The pilot phase was initially planned for a period of one year to assess the feasibility and value of the proposal. It was later extended by another five months to ensure a substantial number of cases.

Methodology

- New marketing authorisation applications with orphan status identified on a monthly basis.
- (Co-)Rapporteurs and EMA product lead informed that EMA will reach out to relevant patient organisations, via EMA's network of eligible patient/consumer organisations.
- Relevant patient organisations contacted by EMA Public and Stakeholders Engagement Department, using template 'letter' (See Annex 1). The template gives medicine name and indication and invites patient organisation to share information on aspects likely to be useful for the evaluation, e.g. quality of life, treatment options, unmet medical needs and preferences for

new treatments; no specific questions are asked, although (Co-)Rapporteurs have the option to ask specific questions in the previous step.

- Organisations were given 3-4 weeks to respond (at least 6 weeks prior to D80 assessment report (AR)).
- Once received, information from patients was shared with (Co-)Rapporteurs and EMA product lead. The applicant was also sent a copy for transparency purposes.
- (Co-)Rapporteurs decided if the information received provided added value, was useful for assessing the dossier, and whether it merited being included in AR.
- To assess contribution and value of patient input received during pilot, short online questionnaire sent to (Co-) Rapporteurs for feedback (see Annex 2).

3. Outcome results

The pilot ran from January 2021 to May 2022 (17 months) and included **37 products**.

The information received from the patient organisations was varied and included: individual testimonies, survey results, websites, and links to articles. The length ranged from a few paragraphs to several pages. Some examples of information received:

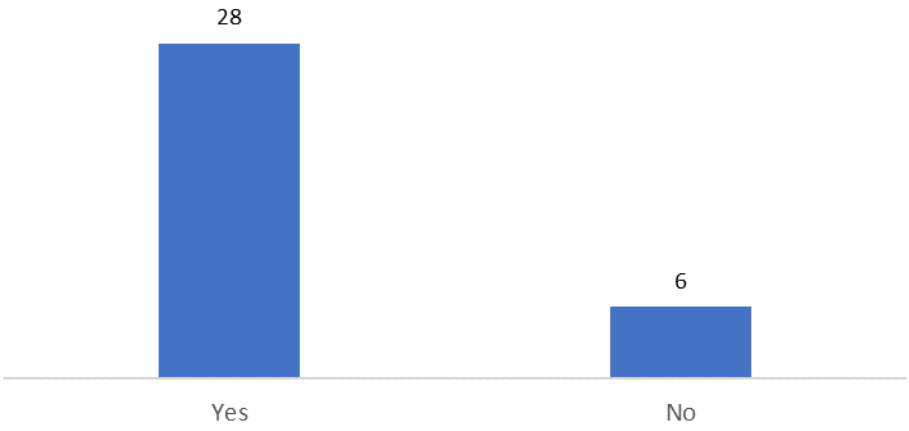
Parents often reluctant to accept an aggressive treatment when they see their child suffering with side effects	Among 17 patients surveyed, pain and fatigue are the most frequent symptoms	A treatment-naive patient is ready to accept more side effects than a patient switching between products
Quality of life affects so many aspects of daily life	Patients often use off-label medicines	Crises and complications can turn their lives upside down at any time - fear of the onset of a crisis is the patients obsession

A questionnaire was sent to all (Co)-Rapporteurs following receipt of patient information.

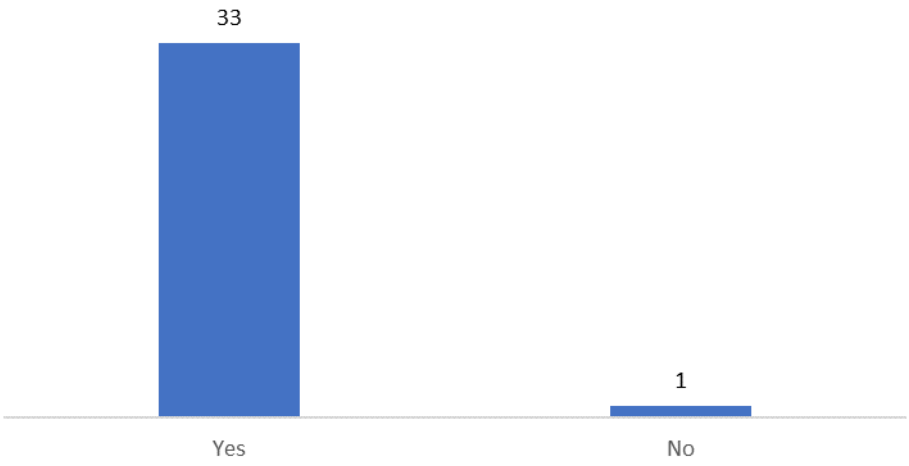
34 responses were received (46%), and analysis of these responses is the basis for this outcome report.

The cumulative results for each question are shown in the graphs below:

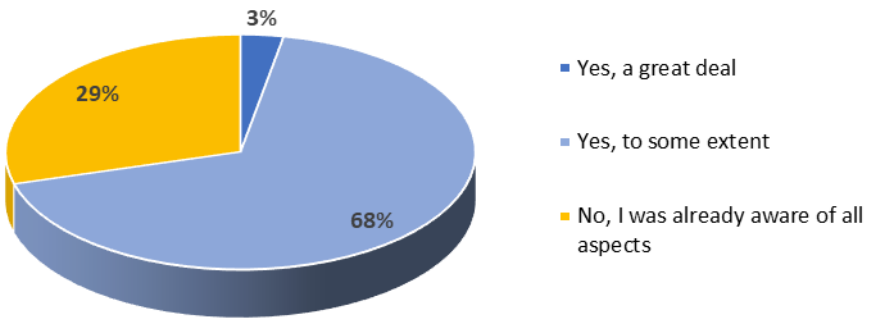
1. Did you receive the information from the patient organisation in sufficient time for it to be able to contribute to your initial assessment of the medicine?



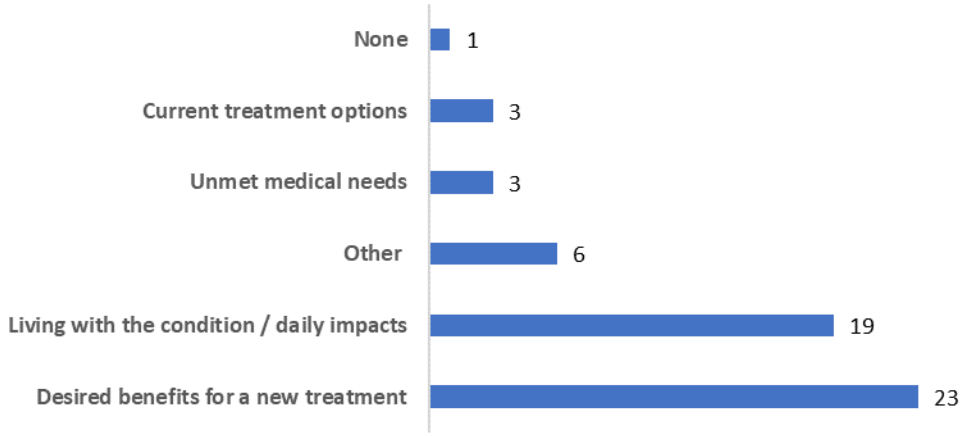
2. Was the information received in a format that was easy to read and understand?



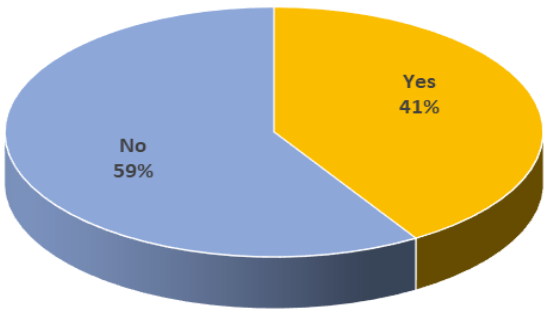
3. Did the information from the patient organisation highlight aspects that you were not already aware of?



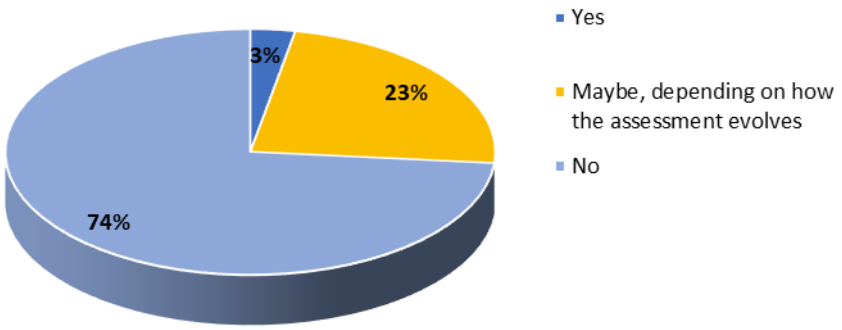
4. Which aspect(s) of the patient information were most useful / insightful?



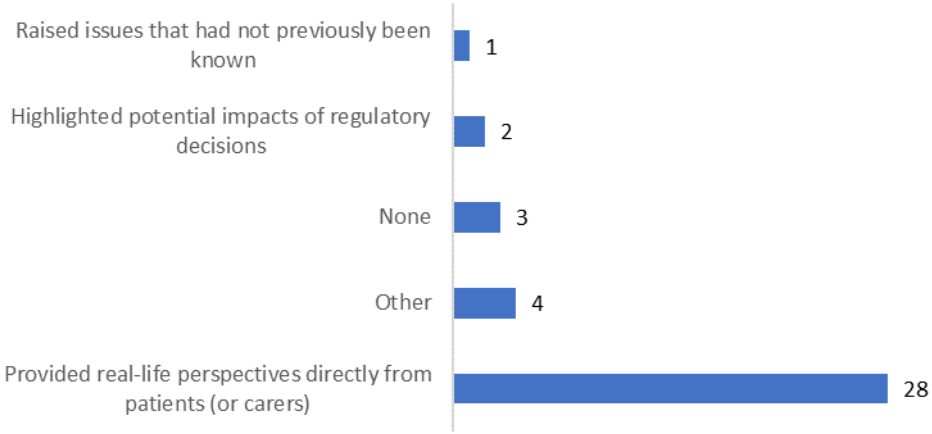
5. Did any of the patient information contribute to the development / content of first assessment report?



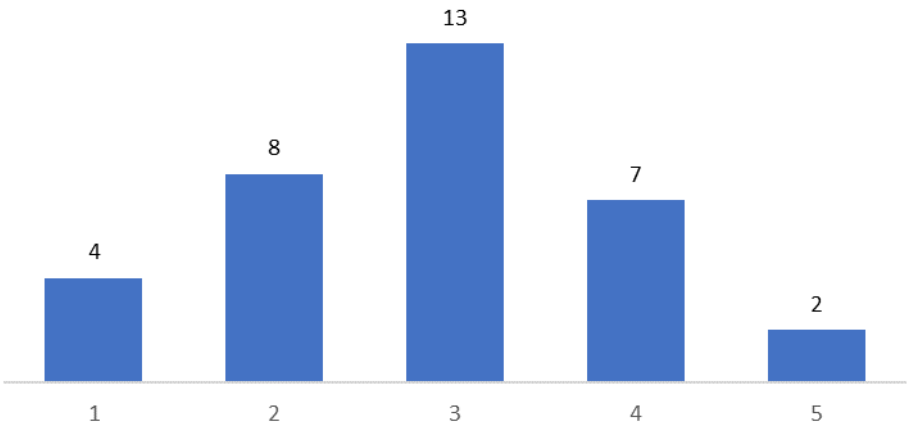
6. Are you likely to request further clarifications or input from the patient organisations?



7. What was the added value of the information received from the patient organisation (if any)?



8. Overall, on a scale of 1 to 5, how useful did you find the information received from the patient organisation (5 being highest)



Summary of responses from (Co-)Rapporteurs:

Analysis of the responses revealed the following:

Most respondents (82%) confirmed they received the information from the patient organisation in sufficient time to contribute to their initial assessment of the medicine. Regarding the six where this was not the case, reasons include that some emails sent to (Co-)Rapporteurs were missed and also that a few patient organisations submitted the information after the deadline.

The majority confirmed the information received was in a format that was easy to read and understand and 68% felt that the information from the patient organisation highlighted aspects they were not already aware of. Respondents cited the following aspects as most useful and insightful: desired benefits for a new treatment, living with the condition and its daily impacts, unmet medical needs and current treatment options (descending order of importance).

Importantly 41% of (Co-)Rapporteurs advised that the patient information contributed to the development of the (D80) assessment report. Interestingly only 23% cited they would be likely to request further clarifications or input from the patient organisations, depending on how the assessment developed.

Many respondents said that it was the real-life perspectives received directly from patients (or carers) that added most value. Finally, when asked how useful they found the information received from the patient organisation overall, on a scale of 1 to 5 (5 being highest), most gave a middle range score of 3, with similar number of responders choosing either 2 / 4, or 1 / 5.

The qualitative feedback was generally very positive; (Co-)Rapporteurs found the patient information to be valuable and insightful, especially on quality of life, daily impact of the disease and treatments and unmet medical needs. They also mentioned other useful aspects such as what are considered important improvements, risks of poor compliance with new formulations, level of acceptable risks, impact of side effects and limitations of current treatment options. These elements provided new information that could help assessors consider and balance between statistical significance and clinical relevance when carrying out the first assessment. It was also highlighted that the information received is not necessarily representative of all patients' views, and that some of the information was too general to be considered during the assessment of the specific medicines proposed indication. All qualitative feedback received is included in Annex 3.

4. Conclusion

The overall feedback received from CHMP (Co-)Rapporteurs involved during the pilot is positive and reflects the usefulness and benefit of reaching out to patient organisations at the start of the assessment of (orphan) marketing authorisation applications. Information from patients provided direct insights, not necessarily known beforehand, which was a useful complement while assessing the marketing authorisation application dossier, and the development of the first assessment report.

The pilot also provided a space to explore the new methodology and amend where needed, for example to ensure emails are not missed, the assessor teams are copied. The (Co-)Rapporteurs were also offered the opportunity to include questions in the template letter in case they would like to ask specific aspects.

It is also important to note that there was a variability in terms of the quality and quantity of the patient information received, often depending on the availability of patients, which is not evident for orphan conditions.

5. Way forward

The results of the pilot were presented to all CHMP members during their plenary meeting in July 2022 where further positive feedback was received.

It was proposed and agreed to continue to reach out to relevant organisations at the start of new MAAs for orphans as a regular procedure, and to explore including new indications for products where no therapies currently exist. Furthermore, we will also explore reaching out to healthcare professionals at the same time in a similar manner.

The patient information can also continue to be shared with the CAT members for their information.

Work will be undertaken to define the best way to reflect this input systematically in the assessment report, paying due consideration to any possible improvement to the CHMP AR template.

This is an important milestone in providing an additional methodology to capture and integrate patient experience data within medicines assessments at EMA and avoid missed opportunities to include their voice from the beginning of new MAA evaluations. It establishes early dialogue, which can be continued as needed, depending how assessment progresses.

ANNEX 1

Template letter to patient organisations

Date
Public and Stakeholders Engagement Department
Stakeholders and Communication Division

CHMP early contact with patient and consumer organisations.

EMA engages with patients and their representatives at multiple stages of its activities and the added value of including their perspectives in the evaluation of medicines has been well demonstrated. They are currently involved at various timepoints during the medicines' lifecycle, and we believe this can be further enhanced by establishing contact with relevant patient organisations at the start of the assessment of new medicines.

The CHMP provides recommendations on the approval and use of medicines in Europe. Its key task is to assess all the scientific data when a company applies for a marketing authorisation. It decides whether a proposed medicine is made to the proper standards, works well and has benefits in treating the illness that outweigh the risks of side effects ('positive benefit-risk'). The CHMP then issues a positive or negative recommendation and the final decision is issued by the European Commission.

Reaching out to patient organisations when medicines are in active development will enable CHMP members to fully appreciate patients' experience and concerns about their conditions. This will help the CHMP understand aspects that are important for patients, such as quality of life, treatment options, unmet medical needs and what benefits they would hope for in new treatments. Early contact can also guide CHMP on when to seek more in-depth interactions with patients or carers.

The CHMP has started its assessment of ***product name*** (***INN***) intended for the treatment of ***condition*** and is inviting ***organisation*** to share patients' perspectives on behalf of its patient/carer members. See below for details.

We would appreciate your feedback by ***date*** 2022.

Your views will be shared with the CHMP (and any other relevant committee) and anonymously with the pharmaceutical company who has submitted the marketing authorisation application (personal names will be removed).

For any questions, please don't hesitate to contact Nathalie Bere (nathalie.bere@ema.europa.eu).

PATIENT / CARER EXPERIENCE OF:

condition

Please include below any aspects that are of particular importance to patients/carers, such as quality of life, standard treatments and how acceptable they are, therapeutic/unmet medical needs, what benefits they would hope for in new medicines as well as what level of side effects they would consider acceptable.

- Highlight if there are large differences between groups of patients/carers about these aspects or if these views are generally similar across the condition.
- Please also mention any aspects about the condition or its treatments that you feel are not well-understood or not sufficiently considered.
- Please include anything else you feel is important for EMA to know. Try to keep your main points to 1-2 pages, if necessary, include more details in an appendix.

Please do not include any individual patients contact details or health data.

☐ Tick here to confirm you give consent for EMA to share your views with third parties, as applicable.

RESPONSE:

ANNEX 2

Questionnaire to (Co)-Rapporteurs

CHMP pilot 2021

Fields marked with * are mandatory.

Purpose of questionnaire

The aim of this survey is to gather feedback during the CHMP pilot project related to early contact with relevant patient organisations at the start of new MAA for orphan medicines.

Your input will help assess the value of the contributions received and the overall process.

Thank you for your time.

Product information

* 1. Product name / INN:

* 2. MAA start date:

Practical elements

* 3. Did you receive the information from the patient organisation in sufficient time for it to be able to contribute to your initial assessment of the medicine?

- ○ Yes
- ○ No

* 4. Was the information received in a format that was easy to read and understand?

- ☐ Yes
- ☐ No

If no to either of the above questions, please provide additional information

Patient information

* 6. Did the information from the patient organisation highlight aspects that you were not already aware of?

- ○ Yes, a great deal
- ○ Yes, to some extent
- ○ No, I was already aware of all aspects

* 7. Which aspect(s) of the patient information were most useful / insightful?

- ☐ Living with the condition / daily impacts
- ☐ Current treatment options
- ☐ Unmet medical needs
- ☐ Desired benefits for a new treatment
- ☐ Other (please explain below)
- ☐ None

* 8. Did any of the patient information contribute to the development / content of first assessment report?

- ○ Yes
- ○ No

* 9. Are you likely to request further clarifications or input from the patient organisations?

- ○ Yes
- ○ Maybe, depending on how the assessment evolves
- ○ No

Please, explain your choice

* 10. What was the added value of the information received from the patient organisation (if any)?

- ☐ Raised issues that had not previously been known
- ☐ Provided real-life perspectives directly from patients (or carers)
- ☐ Highlighted potential impacts of regulatory decisions
- ☐ None

☐ Other

If other, please describe

11. Overall, on a scale of 1 to 5, how useful did you find the information received from the patient organisation (5 being highest)

Any other comments or suggestions?

Thank you very much for taking the time to complete this questionnaire. At the end of the pilot phase, we will present the overall results.

ANNEX 3
Qualitative feedback received within questionnaires

- Input from the patient organizations concerns valuable background information.
- Daily impact, current treatment options and desired benefits for new treatment were very useful to gain insight on the disease and its consequences.
- It became clear that for some patients' treatment burden is not at all an issue given the benefits, while other patients would rather wait for treatment till disease deteriorates further, considering the burden of the administration which is not compatible with daily life. The patients' need/wish for treatment depends on the severity of the disease but also on the personal lifestyle in case of less severe cases (waiting for a more severe stage or hoping to stabilise the condition rather than waiting)
- Possibly in further assessment rounds the patient's information may be more useful for final decision making.
- Depending on the applicant's response further information from patient organisation may be requested.
- Sometimes it can be unclear to assessors how important improvements in certain disease parameters are. What seems to us to be of less important can make a significant difference to patients in their daily functioning. That input will always be appreciated.
- It is of interest to get a general opinion of the patients' situation and their expectations. For this product, the patients' comments were quite few and of a general nature. The patient input confirmed our knowledge.
- The input from patients' organisations might be useful with regard to adding some more knowledge surrounding living with the condition and potential desired benefits of a new treatment. However, the benefit/risk balance decision will in the end be based purely on the strength of the scientific evidence.
- The information from the patient representative more resembled a textbook on the disease, rather than a personal view of a patient, or a caregiver of a patient. All information contained could be found in scientific literature with almost similar content.
- Constraints of the new, proposed formulation were discussed from the patients' perspective, including the risk of poor compliance. This was very helpful.
- The information received was very general and already part of the assessor's knowledge of the disease. It would be helpful if the input would be more targeted to the current dossier instead of generalized views.
- According to the patient information, the key aspect of further therapy options is the safety profile of the drug, and especially the long-term safety.
- The part about reimbursement and access to drugs in other EU countries I was not familiar with. The most important message was the high unmet medical need.
- Are parents prepared to accept any treatment--no matter what the side effects are--that may increase overall survival? This seems not to be the case according to the received information.
- The application involves a very specific situation of metastasis - the comments were all geared towards the early phase of treatment and not relevant to the application under review.

- The most useful aspect of the patient information was the patient perspective on side effects. In particular that many side effects classified as grade 1-2 and non-severe, nausea, vomiting, diarrhoea etc, could still be very impactful on quality of life and should not be underestimated.
- The patient information is valuable regarding the strong impact of the disease in daily life and the limitations of the current treatment options, clearly indicating an unmet medical need.
- The information collected did not present a patient perspective on the possible contribution in disease management of the claimed clinical effect of the product itself, therefore, the input received was too general to be directly taken into account in the benefit/risk assessment of this particular product.
- The RB balance is uncertain to date and advice from patients' organizations could be of value if any critical consideration remains, mainly regarding the QoL and treatment expected compliance.
- At this moment 3 on the scale; however, depending how the procedure evolves, the patient information may become more useful in further assessment rounds and the number on the scale may change.
- We would like to express our gratitude and support the further involvement of patients, especially as counsellors, in the decision-making process about potential new therapeutic options. Assessors must consider and balance between statistical significance and clinical relevance. Often, we cannot see things from the patient's point of view. Potential new drugs, in addition to their primary therapeutic roles, should be able to meet the expectations of those to whom they are intended and improve their quality of life.
- One of the organisations focussed on bringing forward positive effects of the product in question experienced in clinical trials by individuals. This kind of input, although highly understandable, is considered less helpful.
- We were not very sure how to implement the information received from the patient representatives. In principle, the structured discussion on the impact on patients' lives is valuable, although it is difficult to assess if their experience is likely to be shared by the majority of patients. It was noted that one of the two patients had previously refused standard of care - their experience is of course also of interest but may not fully represent those who accept such treatment.
- I personally consider patients' input extremely important for providing new information which even health professionals may not be aware of. Thank you for all your work, very helpful and very much appreciated.
- It remains important that patients' views are included in the assessments.
- The input from the patient community provides valuable information to assessors on what they should focus their attention on while assessing the documentation for the medicine under evaluation as well as when writing the assessment report.
- I would have liked some more information on the patients' acceptability of safety issues such as risk of hospital admissions, treatment-related deaths and/or severe safety issues that are chronic and may require treatment.
- Information seems to be based on individual interviews and it is difficult to understand if the parents selected for interviews are representative. The patients (children) views were absent (for obvious reasons, perhaps?)
- Information about patients' quality of life and daily impact of disease and treatments was considered most valuable. It was very interesting to receive individual patient perspectives, although it was difficult to draw one conclusion based on multiple individual perspectives that were not always in agreement. Patients' benefit risk

evaluations were difficult to interpret. This since with regulatory decision making, the conduct of the trial must be taken into account, which might have consequences for the actual benefit of treatment in clinical practice.

- It is regrettable that the information was not received on time to be considered in the first assessment. This would have been clearly helpful to better consider the QoL of the concerned patients.
- Considering that this is a rare disease with no curative treatment, patient opinion was consistent with the medical need. Nevertheless, it is always interesting to have patient point of view.