IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Meeting report series

Report of the 2nd teleconference of the Working Group on Orphan drug-development and regulatory processes

28 February 2014

Organization

Organized by: IRDiRC Scientific Secretariat
Teleconference

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Agenda

1) Updates on the Therapies Scientific Committee
2) Early dialogue
3) Aligned therapeutic guidelines
4) Adaptive clinical trial designs
5) Alternatives to animal models
6) Patient focused outcomes

REPORT

Updates on the Therapies Scientific Committee

The Diagnostics Scientific Committee and the Interdisciplinary Scientific Committee have both submitted their recommendations to the Executive Committee. The Therapies Scientific Committee (TSC) still has to do it. A preliminary draft of the TSC recommendations has been realized during a meeting that took place on the 20 February. The draft was based on the feedbacks from all the Working Groups, the discussion of the TSC, and the outcomes from the first IRDiRC meeting in Dublin (15-17 April 2013). This first draft along with a plan of timelines and actions will be distributed to all the members of the TSC and to all the members of the Working Groups of the TSC by 12 March 2014.
On the 19 March 2014, there will be a face-to-face meeting of the TSC in Paris.
The next face-to-face meeting of the Executive Committee will be held in Berlin, on 7-8 May 2014. The recommendations of the three Scientific Committees should be merged into one global document at that stage for adoption by the Executive Committee.

Early dialogue

Health Canada is starting to focus on pediatric trials. They are now getting together some experts to create guidelines for early advice in order to make better choices.

Genethon has already some experience in early dialogue with the European Medicines Agency (EMA) for one of its product in *ex-vivo* gene therapy. This experience has raised many questions. A pediatric investigation plan is ongoing but it was not possible to organize a teleconference with three working groups of the EMA that were necessary to answer all those questions. A more flexible system is necessary for the rare diseases field in order to have more easily teleconferences with working groups of the EMA. Early dialogue is mandatory, but administrative rules may complicate it.

Recommendations for the TSC:

- More regulatory flexibility in the early dialogue procedures for orphan products is needed.
- Proposition of a common document per agency for requests regarding meetings with all committees and working groups.
- Proposition of a common document between agencies if possible (i.e., Food and Drug Administration [FDA] and EMA).
    - There is actually a process to get parallel advice between the EMA and the FDA at the same time.
- Promote the use of a parallel scientific advice.

Aligned therapeutic guidelines

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) would need to have a guideline for development on orphan products. This topic was discussed in Japan in November 2013 but did not appear as a priority. The IRDiRC could eventually put this as a priority in order to obtain more harmonisation between the EMA and the FDA.

Regulators issue guidelines when they have experience about development, but it is not always possible in the case of rare diseases. Instead of a guideline, a procedure could be implemented.
It will always be a challenge to have one set of guidance on rare diseases due to heterogeneity between rare diseases. Nevertheless, it is possible to put together some general principles.
An addendum to the current guidelines regarding the rare diseases field or a new guideline on rare diseases would be necessary.

Recommendations for the TSC

- Emphasize the joint scientific advice between the EMA and the FDA.
- Share drafting procedures between Europe and USA (EMA and FDA) in order to have the same outcomes.

Adaptive clinical trial designs

Flexibility of clinical trial design is common for rare diseases. The quality of the underlying science is mandatory and important. In the rare disease field, there are often not enough patients to have a statistical protocol and a conclusion based on observations can be difficult to achieve. An adaptive clinical trial design should take this into account. In some cases, only one clinical trial can be done during the development.

Recommendations for the TSC

- Agencies should be opened to discussion on adaptive clinical trial designs regarding the type of disease.

Alternatives to animal models

It is recommended to find alternative and validated models which could overcome the limitations of animal models, however some animal models are still needed in some conditions, especially when clinical trials are lacking at the time of designation.

Recommendations for the TSC

- A profound investment and validation in the area of *in vitro* models and biomarkers should be realized.
- Toxicology to obtain marketing authorization needs to be made on animals but proof of concept could be realized on alternative models.

Patients focused / Relevant outcomes

A request for the EMA to update the guidance on patient reported outcomes has been done. As the FDA has been praised on their guidance on patient focused outcomes, the EMA could try to align its guidance with the FDA guidance.

Recommendations for the TSC

- Dialogue and exploration on patient reported outcomes should be welcomed by both agencies in collaboration with patients and experts.

Other recommendations

- Develop further collaborative funding approaches into drug development which could be spearheaded by patient groups or academia, or when pharmaceutical industries might not be interested.
    - At the moment, the only types of funding for these programmes are FP7 or Horizon2020.

Main deliverables

- Revise the current guidance.
- Send a doodle to plan the next teleconference to be held after the TSC meeting.