

Meeting report series

Report of the 5th Therapies Scientific Committee Meeting

IRDiRC, Rare Disease Platform, Paris, France
19th March 2014

Organization

Organized by: Scientific Secretariat

Hosted by: IRDiRC, Rare Disease Platform, Paris, France

Participants

Dr Seng Cheng, Framingham, USA

Prof Gert-Jan Van Omen, Leiden, Netherlands

Dr Karin Rademaker, Utrecht, Netherlands

Dr Adam Heathfield, Sandwich, UK

Mr Yann Le Cam, Paris, France (phone)

Dr Fulvio Malvilio, Evry, France

Dr Elizabeth Mc Neil, Bethesda, USA (GoToMeeting)

Prof Josep Torrent i Farnell, Barcelona, Spain

Dr Maria Mavris, Paris, France

Dr Barbara Cagniard, Scientific Secretariat

Dr Virginie Hivert, Scientific Secretariat

Dr Sophie Höhn, Scientific Secretariat

Apologies

Dr Giles Champion, Leiden, the Netherlands

Dr John McKew, Bethesda, USA

Dr Luigi Naldini, Milan, Italy

Dr Glen Nuckolls, Bethesda, USA

Prof Asla Pitkänen, Joensuu, Finland

Dr Robert Schaub, Waltham, USA

Dr Marc Walton, Silver Spring, USA

Dr Ellen Welsh, South Plainfield, USA

Dr Anne Zajicek, Bethesda, USA

Agenda

19th March 2014, 10:30 – 17:00

1. Introduction

2. Review and next steps for:

- ▶ WG on Biomarkers for disease progression and therapy response
- ▶ WG on Biotechnology-derived products including cell- and gene-based therapies
- ▶ WG on Chemically-derived products including repurposing
- ▶ WG on Orphan drug-development and regulatory processes

3. Feedback from the Scientific Secretariat on analysis requested by TSC and WGs

4. Recommendations of the TSC

5. Shenzhen conference

6. Next meeting – date and location

EXECUTIVE SUMMARY

The third face-to-face meeting of the TSC took place on 19th March 2014 at IRDiRC, Rare Disease Platform, Paris, France. Seven members of the committee were present all day long and two members temporarily joined the meeting by phone or teleconference.

The members of the TSC first reviewed the outcomes from the 4 WGs and discussed the next steps that should be considered in the setting up of their future work plan.

The TSC then reviewed and agreed on the recommendations, in terms of policy and funding, from the TSC to be submitted to the Executive Committee. The main discussion concerned the targeting of funding to products which have been designated as orphan and went through scientific advice/guidance as a way to stimulate a high quality and faster orphan drug development. The TSC members also agreed on a common set of mandatory criteria and flexible shared criteria, addressing both non-clinical and clinical stages.

The TSC member participating in the preparation of the scientific program of the IRDiRC conference to be held in Shenzhen gave an update on the advancement of the program.

It was proposed to hold the next face-to-face meeting of the TSC in North America.



REPORT

Josep Torrent i Farnell welcomed the participants and conveyed the apologies from the chair of the TSC, Yann Le Cam, who was unable to attend the meeting. Members of the TSC introduced themselves, as well as the members of the Scientific Secretariat.

Review of the WGs outcomes and feedback on data analysis

The morning session was devoted to the review of the outcomes from the 4 WGs and the discussion regarding the next steps of their work. For each of the WGs, the representative of the TSC in the WG or a member of the Scientific Secretariat, made a summary of the previous conference calls, questions and achievements. At the same time, the Scientific Secretariat gave a feedback from the data and analysis requested by the WGs and the TSC for each topic.

WG on Biomarkers for disease progression and therapy response

Feedback from WG

The WG on Biomarkers has expressed the willingness to set up a survey in order to identify research projects of interest in the field, possible collaboration between those research projects and clusters of interest in terms of medical domains.

Feedback from the TSC

- ▶ The TSC members agreed that this analysis is important, indeed, the data already compiled by Scientific Secretariat needs to be further evaluated and analyzed in a more detailed and in a deeply manner. The best way to finance it needs to be carefully considered. In this regard, it was discussed that it would be more appropriate that this funding could come directly from IRDiRC funding bodies, rather than from a call for proposals. The funding would serve to hire one information scientist to be attached to the organization of one of the WG members, as to deeply analyze the data that have already been provided from the Scientific Secretariat (all the files have been uploaded onto the private section of the IRDiRC website). A call for proposal could be beneficial but only once the data analysis has been performed in order to narrow down the scope of the call.
- ▶ The WG should propose a timeline in accordance with the analysis proposal. It was suggested that this phase of analysis should not last more than 6 months.
- ▶ The scope of the WG should focus on those orphan conditions for which biomarkers could really speed up the therapy development process but where there are currently no reliable clinical endpoints or outcome measures.

- ▶ As biomarkers could serve as therapeutic readout, but also for diagnosis purpose, a connection of this WG with the DSC is perceived as good.

WG on Biotechnology-derived products including cell- and gene-based therapies

Feedback from WG

The WG on Biotechnology has expressed some concerns regarding the revision of the European Clinical Trials Regulation. They identified an issue with the wording of ‘minimal risk’ and ‘minimal burden’ and the use of a standard of treatment, which is not always available in the field of rare diseases. The WG would like the TSC to alert the Executive Committee of this problem and discuss possible actions.

In terms of recommendations, the most important for the WG is to insist on a timely development of pharmacodynamics and biomarkers and on giving funding for natural history.

Another important point to emphasize is to anticipate the re-analysis of data coming from clinical trials by statistical methods, for example by the pre-determination of subsection(s) of read out when setting up trials which will allow re-analysis afterwards.

The WG on Biotechnology also received lists of projects/trials from the Scientific Secretariat (all the files have been uploaded onto the private section of the IRDiRC website), which they have found very useful to oversee the available information while quite difficult to review from the perspective of the WG.

This WG has also agreed that in the field of interest, the COST action for Duchenne is a very good model for their future work plan, with its three main topics:

- ▶ Trial readiness, linked to biomarkers and natural history
- ▶ Cross-connection between different diseases
- ▶ Dialogue between scientists and regulators with continuous medical education and training from both sides

WG on Chemically-derived products including repurposing

Feedback from WG

This WG identifies two main objectives related to its scope: to find candidates for therapeutic development and to improve the process in relation with these products. They agreed to focus on drugs already registered (as most of the repurposing comes from registered conventional drugs for non rare diseases).

This WG has listed 4 strategies to identify candidates:

- ▶ Rescuing drugs that have failed
- ▶ Buying library of drugs
- ▶ Asking feedback from patient support groups
- ▶ Exploring gene expression profiles

An analysis of the outcomes from the already funded research projects (FP6, FP7, E-Rare, NIH, FDA) could also help to find candidates.

The next step could be to release a list of couples (molecules & disease); the organization interested in moving on would contact the Orphan designated sponsor to harvest the data available and discuss IP whenever required.

Feedback from TSC

- ▶ According to the TSC members, there are new possibilities in the rare disease field, mainly thanks to the NGS techniques. In particular, mechanistic approaches are of interest not only for repurposing or drugs that have failed, but also for drugs that have never been explored. Regarding these mechanistic approaches, NCATS and FDA have a more long-term overall experience.
- ▶ Repurposing in itself is often difficult to apply because even if data on efficacy are available, there is often a lack of information regarding other characteristics of the drug, i.e., dose, etc. Pharmaceuticals companies are often willing to help screening libraries if an assay is available.
- ▶ IRDiRC could serve as an international platform to release a list of proposed molecules and diseases and try to facilitate connection between companies willing to develop drugs and people that own them (academics, patient organizations, etc.), having in mind that intellectual property is also a major issue.
- ▶ As for the WG on Biomarkers, it was suggested to adopt a dynamic process and to allocate some funding to further analyze the outcomes from the already funded research projects (FP6, FP7, E-Rare, NIH, FDA).
- ▶ It has also been emphasized that the analysis of reports submitted to the regulatory Agencies would help to better understand the delay observed between designation and approval in some cases.

In terms of organization, a link between this WG and the WG on Model systems should be created. It was considered beneficial to include a new industry member with direct experience in this area (i.e. an expert from Pfizer is going to be proposed).

WG on Orphan drug-development and regulatory processes

Feedback from WG

This WG focused on several topics, particularly early dialogue, convergence/alignment of therapeutic guidelines, and adaptive clinical trials design.

The WG has also evoked the usefulness of analysis of the report submitted to the regulatory Agencies, as mentioned before.

Feedback from TSC

- ▶ The TSC member participating involved in the WG has the impression that although the representatives of the Agencies are really willing to be involved in the discussions of this WG, they do not always feel comfortable expressing themselves due to their position. The TSC stated that their role is to identify the bottlenecks that come up and propose appropriate ways to solve these hurdles.
- ▶ During the meeting, the concept of “Orphanage” was also mentioned, which has been raised up at the joint workshop between the EMA, FDA and PMDA (Japan) on 10th of March in London, in order to facilitate the development of molecules that have been left aside for different reasons. In particular it was considered adequate that a specific IRDiRC call in this point could be very effective in increasing the transfer of “dormant/silent” designated orphan products to more active sponsors wishing to further develop these compounds.

Review of the document ‘Recommendations of the TSC’, Shenzhen conference and next meeting

Recommendations of the TSC

The document ‘Policy & Funding Recommendations of the IRDiRC Therapies Scientific Committee (TSC)’ was presented by Yann Le Cam (Chair of TSC) who joined the meeting by phone.

The document is based on 6 months of work by the TSC and its 4 WGs. It was prepared by a drafting group composed of Yann Le Cam, Josep Torrent i Farnell (former chair and member of the TSC), Maria Mavris (member of the TSC), Valentina Bottarelli (EURORDIS) and Virginie Hivert (Scientific Secretariat).

The document and comments collected during the first rounds of review were inserted and have all been reviewed by the TSC members as to ensure that content and wording are in line with the outcomes of the TSC and WGs discussions and the maximal leverage effect that is awaited from these recommendations.

The main discussion concerned the targeting of funding to products which have been designated as orphan and went through scientific advice/guidance at EMA or FDA, or ideally at both Agencies, as a way to stimulate better quality development.

The TSC members finally agreed on a common set of mandatory criteria and flexible shared criteria, addressing both non-clinical and clinical stages.

The document has then been reviewed once again by the drafting group after the TSC meeting in order to incorporate all the modifications that have been agreed during the day as to be presented to the Executive Committee on 10th of April. The recommendations from the 3 Scientific Committees will then be merged in one single road map to be adopted by the Executive Committee on 7th May in Berlin.

Shenzhen conference

The Shenzhen conference will take place in November 7-9, 2014. There will be four parallel tracks: Diagnostics / Therapies / Interdisciplinary-Technologies / Educational track. Some speakers have already been chosen. An e-mail will be sent to the TSC members in order for them to suggest some speakers within a week.

Next meeting of the TSC

It was suggested that the next meeting of the TSC will take place in North America, Boston for example, and that the TSC will adopt a recurrent timeline with two face-to-face meeting per year in March and October.