

## Meeting report series

### Report of the 4th Therapies Scientific Committee Meeting

24 January 2014

#### Organization

Organized by: Scientific Secretariat

#### Participants

Yann Le Cam, Paris, France (Chair)  
Dr Adam Heathfield, Sandwich, UK  
Dr Maria Mavris, Paris, France  
Dr Elizabeth McNeil, Bethesda, USA  
Dr Luigi Naldini, Milan, Italy  
Dr Glen Nuckolls, Bethesda, USA  
Dr Asla Pitkänen, Kuopio, Finland  
Dr Karin Rademaker, Utrecht, the Netherlands  
Dr Robert Schaub, Waltham, USA  
Prof Josep Torrent I Farnell, Barcelona, Spain  
Prof Gert-Jan Van Ommen, Leiden, the Netherlands

Dr Barbara Cagniard, Scientific Secretariat  
Dr Virginie Hivert, Scientific Secretariat  
Ms Sandra Peixoto, Scientific Secretariat

#### Apologies

Dr Giles Campion, Leiden, the Netherlands  
Dr Fulvio Mavilio, Evry, France  
Dr John McKew, Bethesda, USA  
Dr Marc Walton, Silver Spring, USA  
Dr Ellen Welch, South Plainfield, USA

## **Agenda**

1. Review of the WG inputs and feedback to the WGs
2. Review of ISC recommendations to the Exec Com
3. Main policies recommendations from the TSC to the Executive Committee: including and beyond the WGs inputs
4. Scientific program for IRDiRC conference in Shenzhen

## REPORT

### 1. Review of the WG inputs and feedback to the WGs

At the time of the 3<sup>rd</sup> TSC teleconference, several sessions of the WGs have already taken place:

- 2 sessions for the WG on Biomarkers for disease progression and therapy response
- 2 sessions for the WG on Orphan drug-development and regulatory processes
- 1 session for the WG on Biotechnology-derived products including cell- & gene-based therapies
- 1 session for the WG on Chemically-derived products including repurposing

#### **WG on Orphan drug-development and regulatory processes**

During the first teleconference, the general mandate and the specific tasks have been reviewed, and members of the WG provided feedbacks on the specific tasks for this WG by email after the teleconference. Dr Anne Parisier and Dr Jordi Llinares agreed to be co-chairs. This WG has an issue of attendance with a very small turnout in the two sessions, the second one having been cancelled by lack of participants. There is a need to motivate the members.

#### **WG on Biotechnology-derived products including cell- & gene-based therapies**

One teleconference already took place and a second one was scheduled on 30<sup>th</sup> of January. Within this WG, it appeared that under the COST action, an inventory of activities related to biotechnological products has already been made and does not need to be duplicated but rather to be spread around. It was also pointed that a representative from EMA and FDA would be important in this WG to get the view of the regulatory field.

#### **WG on Chemically-derived products including repurposing**

Two co-chairs have been elected: Dr Ramaiah Muthyala and Dr Fred Marin. Members reviewed the general mandate and the specific tasks and mentioned several analyses they are interested in. The Scientific Secretariat will look at the feasibility -not only technical feasibility- of these requests and those from other WGs to determine which analyses can be performed by the Scientific Secretariat and which analyses should be included in the recommendations.

Topics discussed by the WG:

- ▶ The main focus of this WG is to explore the mechanisms to be put in place to detect the drugs that are available for therapeutic development and how they are linked to clinical conditions.

- ▶ A second topic concerns the products that have been developed within the framework of the main funders (like for EU, FP6, FP7 and E-Rare) but never reached the market. It was highly recommended to involve also the NCAT, NIH in the discussion.
- ▶ It was recommended to make best use of the annual reports which are submitted to EMA and FDA for orphan designated products to identify the difficulties of development and reasons of failure. The recommendations will address issues of methodology, issues of lack of natural history or financial issues for SMEs.
- ▶ The last analysis involves clusters of compounds based from the one already designated in EU or US or not yet designated but already gone through scientific advice. The recommendations could be shaped as guidelines for development of clinical trials for these clusters of products or for identification of unmet medical needs.

### **WG on Biomarkers for disease progression and therapy response**

Prof Alessandra Ferlini has been elected as the chair of this WG. The first point was to define the scope of the forthcoming discussions which will focus on the conversion of biomarkers discovered in academic settings into clinical endpoints of use for clinical research purpose. It was agreed to concentrate on biochemical biomarkers, with a clear identified function.

The main topics discussed were:

- ▶ Analysis of the field of interest: The WG requested the list of research projects and clinical trials related to biomarkers and natural history. Some data have already been extracted from the clinicaltrials.gov website and from the Orphanet database. The idea of the WG is to contact all or some of the project leaders of those projects in order to perform a survey on the kind of biomarkers they are working on.
- ▶ A set of criteria was also prepared to be associated to the recommendations to research funding agencies.
- ▶ Discovery of new biomarkers and the necessity to develop circulating biomarkers (plasma, urine, etc.).
- ▶ Need of standardized assay for biomarkers.
- ▶ Regulatory aspects of the use of biomarkers to accelerate drug development process. There has been a good feedback from the representative of the FDA stating it was easier to include biomarkers in the early phase of development but much more difficult at the level of clinical trials.

The attendance to this WG is quite good. However, the WG is only composed of seven members and it could be extended by inviting 2 or 3 additional people.

The TSC mentioned that it was important that the WG on Biomarkers gives feedback such as specific advice or conceptual steps to the Therapies Committee because the field is complex.

Emphasis has been put on the fact that currently many fields are trying to harmonize data collected in different labs in different part of the world and that there were some initiatives to streamline common data elements such as the initiative of NINDS (<http://www.ninds.nih.gov/>). In the field of RD, each disease is an entry but generating a template that could be translated from a disease to another which would

include common data elements is a critical issue to resolve. This issue of common data elements for harmonization was only discussed in the ISC WG on Registries and Natural History.

### **Summary for the TSC follow-up**

- ▶ There is a need to add some new members to the WG on Biomarkers and WG on Chemically – derived products
- ▶ There is an issue of attendance to some WGs. Participants need to be motivated.
- ▶ There is a recurrent issue of attendance from EMA/FDA people but there is a huge need for regulators to be involved in the discussions so it would have to be handled at the top of the hierarchy.
- ▶ Keeping in mind that the gap analysis is of course valuable for strategy purpose, but as sometimes gaps and opportunities may not correspond, it is also important to look at the opportunities, especially those existing from a disease to another.

## **2. Review of ISC recommendations to the Exec Com**

The participants of the TSC have reviewed the recommendations issued by the ISC. Some of these recommendations may also be mentioned in the recommendations from the TSC. For example, It could be emphasized that:

- ▶ Funding bodies should consider natural history studies of rare diseases to be of high importance for the development of products as well as the assessment of data once they have been submitted to the regulatory bodies.
- ▶ Modeling in vitro and vivo should be improved.
- ▶ Interoperability of data and common data elements should be supported.
- ▶ A common unique identifier is probably an interesting point.
- ▶ Multinational clinical trials, pharmacoeconomic studies as well as studies on paediatric populations require more attention.

To summarize, the recommendations to be issued by the TSC will be based on the input from the WGs, discussions within the TSC and reference to the ISC recommendations which are of particular relevance for the R&D process. However the idea is to have a rather limited number of concrete recommendations that can be implemented with a short-term leverage effect on the development of therapies.

For example, in practice assessing the quality of biobanks is under the scope of BBMRI which proposed common standards for biobanks and the standards for common diseases are valuable also for rare diseases.

Natural history studies, particularly with regards to quality of life, are needed for regulatory purposes, to define/redefine, when necessary, the read-out for therapeutic success to be consistent with patients' expectations.

In order to make recommendations with a potential for implementation, it is necessary to support existing structures such as NCAT for repurposing or the IMI initiatives for development of products and clinical studies. Similarly, the ERA-NET E-RARE and the EU infrastructures (EATRIS, ELIXIR, BBMRI, ECRIN, etc.) are aligning their objectives to those of the IRDiRC Consortium.

### **3. Main policies recommendations from the TSC to the Executive Committee: including and beyond the WGs inputs**

The policy recommendations from the TSC will be developed in 4-5 pages summarizing the recommendations towards IRDiRC and towards the members of the Consortium with key priorities and criteria for funding decisions. The outcomes of the TSC discussion, the input from the WGs and additional elements from the discussion on ISC and DSC recommendations will be gathered and then circulated to the members of the TSC for comments or further development.

A new draft will then be prepared for discussion during the face-to-face meeting of the TSC on 19 March, in Paris, France. The final version will be submitted to the Executive Committee in May in Berlin.

The TSC members unable to attend the face-to-face meeting are invited to give their input on the document by e-mail before the session.

The Scientific Secretariat will prepare in parallel a summary of the requests for analysis coming from the WGs, the specific topics drafted in the briefing document and the lists of projects with specific search identifiers requested by the different WGs and that have already been prepared by the Scientific Secretariat, to be circulated to the TSC members. The Scientific Secretariat mentioned that those files already provided include raw data only.

The next step is to detect the requests that seem to be of higher importance and more refined in terms of search identifiers for the TSC, the feasibility in terms of gap and opportunities analysis, the needs of additional resources and whether they could be converted as recommendations for funding.

### **4. Scientific program for IRDiRC conference in Shenzhen**

A member of the TSC has to be appointed as to liaise with the other Committees for the preparation of the scientific content of the Shenzhen conference. The work will be done mostly by teleconference but may include a travel to China (with expenses covered by the Scientific Secretariat).