IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Meeting report series

Report of the 2nd Teleconference of the WG on Biotechnology-derived products including cell & gene-based therapies

30 January 2014

Organization

Organized by: Scientific Secretariat
Teleconference

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Agenda

- Issue about the proposal for guidelines for clinical trials (European Union)
- Feedback from TSC
- Review of the list of research projects and clinical trials
- Discussion on the role and position of Pharma and Biotech
- Exon Skipping COST action

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REPORT

Issue about the proposal for guidelines for clinical trials (European Union)

In the 'Proposal for a Regulation of the European Parliament and of the Council on Clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC', the article 31h (p71) states that 'there are scientific grounds for expecting that participation in the clinical trial will produce a direct benefit for the minor concerned outweighing the risks and burdens involved or will produce some ~~direct~~ benefit for the population represented by the minor concerned ~~group of patients is obtained from the clinical trial~~ and will pose only minimal risk to, and will impose minimal burden on, the minor concerned in comparison with the standard treatment of the minor's condition.'

The problem in this article is the definition of minimal risk compared to the current treatment. The phrasing of this article will make it difficult to perform early stage trials in untreatable diseases as there is no way to compare the burden to nothing. The voice of oncology is dominant in this field where there is chemotherapy treatment with high burden.

A lobbying of the European parliament or at the national level should be conducted to change the phrasing of this document under review to allow the comparison to the burden of the disease for untreatable diseases.

This problem will be brought to the attention of the Therapies Scientific Committee (TSC).

Feedback from the TSC

There was no feedback from the TSC as the previous teleconference of this WG was essentially dedicated to the overview of IRDIRC and the WG mandate.

For information, the Interdisciplinary Scientific Committee already provided recommendations that were discussed by the TSC.

Two points coming from the TSC and TSC WGs discussion of interest for this WG are:

- The importance of timely development of pharmacodynamic and the monitoring of biomarkers.
- Necessity of funding to improve the recording of natural history.

Review of the list of research project and clinical trials

The members of the WG wish the listing to be reformatted to increase readability.

- The listing should be sorted by the name of the disease.
- Information to be included:
    - Name of the disease
    - PI name

- Country
- Funding body
- Title

- The listing should be separated in 3 tables: Cell therapy/Gene therapy/ Animal

This optimization of the listing will help to define the gaps and opportunities, to provide comments and suggestions to the Scientific Committee.

Comment from the WG: As ongoing projects are underexposed in the community, it would be useful to publish the list of projects on a public website to help researcher to get in touch.
Notes from the Scientific Secretariat: This will be a publication as an Orphanet Report Series.

Discussion on the role and position of Pharma and Biotech

There is a disconnection between small biotech and pharmaceutics companies, which sometimes have diverse goals, particularly in regard to the number of participants in clinical trials where it is easier for pharmaceutics companies than biotech to include enough participants for statistical purpose.

However, regulatory agencies are aware of the specificity of rare diseases and are open to discussion with applicants to accept larger type 1 error for clinical trials with small populations to avoid false negative. There are guidelines for clinical trials with small population to explain the position of EMA.
On the contrary, increasing the number of participants in clinical trials for statistical purpose can induce false negative as the trial may be not restricted to the appropriate population.

The level of education from regulatory agencies is essential to the development of therapies for rare diseases.

Exon Skipping COST action

Although this COST action (http://exonskipping.eu) is specific to Duchenne disease, some points are relevant to this WG in general and for the development of therapies for rare diseases:

- Timely development of (PD and Effect-Monitoring) biomarkers and natural history to avoid this needs to be done when undertaking trials. i.e., improving TRIAL-READINESS
- Make cross-connection between different diseases based on *technologies*. Eg. viral manufacturing, reproducible protein detection, etc. as these are done in many projects
- Educational exchange: Developers to regulatory agencies on generic and specific issues in RD and from regulators to make developers aware of key issues in an early stage.

NB: This now already happens occasionally, like the meeting at the FDA in January 2014, but may be repeated at regular intervals as we learn more, and issues broaden on one hand and converge on the other.

WG Deliverables

- Send the new listings for gap and opportunity analysis