

## Meeting report series

### Report of the 2nd Teleconference of the WG on Biomarkers for Disease Progression and Therapy Response

9 January 2014

#### Organization

Organized by: Scientific Secretariat

Hosted by: GoToMeeting

#### Participants

Dr Anne Bechet, Leiden, Netherlands

Dr Gillian Butler-Browne, Paris, France

Dr Giles Campion, Leiden, Netherlands (member of the TSC)

Prof Alessandra Ferlini, Ferrara, Italy

Dr Marc Walton, Silver Spring, USA

Dr Sophie Höhn, Scientific Secretariat

Dr Sandra Peixoto, Scientific Secretariat

#### Apologies

Dr Marlene Haffner, Rockville, USA

Dr Spiros Vamvakas, London, UK

Dr David Wishart, Edmonton, Canada

## REPORT

The aim of the teleconference was to decide:

- ▶ How are we going to decide on particular diseases or projects to focus on?
- ▶ How to facilitate the development and use of biomarkers in clinical trials to help to expedite the development process?

### Topics of discussion

#### Analyse of the field of interest

One goal is to enlarge the dialogue among all projects linked to rare diseases and biomarkers. This would necessitate an inventory of the projects and their purpose to have an overview of what is done. The dialogues should be facilitated:

- ▶ Between research projects
- ▶ Between research projects close to clinical trials with regulatory authorities to accelerate procedures with authorities

It was proposed to prepare a form to be circulated among all the project leaders to see what they are doing with biomarkers.

The Scientific Secretariat provided lists of research projects and clinical trials related to biomarkers. However, some of the files present raw data with multiples entries for the same projects that are difficult to read. The members of the WG would prefer to work with a single file merging the different lists, including the list extracted from Cordis. The information for each project should include at least the title of the project, the name and email address of the principal investigator.

The members of the WG agreed to use their experience with muscle dystrophies to find bottlenecks.

#### Standardization of assay

The need for biomarkers is critical. However, troubles are:

- ▶ Researchers only have small amount of materials providing from small isolated population
  - ▶ Different researchers use different methods and it is difficult to compare or understand other people's results.
- ⇒ There is a need for standardized assay, reliable, robust and reproducible, to be qualified by the regulatory agencies.

For example, the standardization of the dystrophin, a biomarker for Duchenne Muscular Dystrophy, is difficult as it is challenging to standardize the biopsy. There is an important inter-individual and intra-individual variation. The level of dystrophin depends on the size of the biopsy, the mass muscle and the quality of the muscle (content of fatty tissue).

## Discovery of new biomarkers

Exploratory biomarkers are a topic of interest:

- ▶ Numerous projects involve the discovery of new biomarkers, correlated to muscle functions (muscle remodelling, muscle signalling, etc.). However, data are often obtained from a small population. Large cohorts are necessary to identify and validate biomarkers. It is essential to find a way to put together patients from US and Europe to help the identification of biomarkers to be of use in clinical trials (a meeting on that topic is scheduled at the end of January).
- ▶ Developing circulating biomarkers (plasma, urine, etc.) could compensate for the difficulty of standardizing biopsies for dystrophin.
- ▶ Combining biomarkers with functional assay in early stage of drug development is an approach that may help to register drugs faster than conventional approach.

## Regulatory aspect of the use of biomarkers to accelerating drug development process

EMA and FDA recognize the importance of biomarkers in clinical trials.

The use of biomarkers to accelerate the development process is very feasible and appropriate for some portion of the development process. For example, the use of biomarkers as a proof of concept is helpful in early development. However, using biomarkers as a surrogate end-point is a difficult proposition for regulatory agencies. In efficacy trials, it is necessary to show that the biomarker is adequately useful, in what circumstances and what diseases. The implication is thus very disease-specific.

- ⇒ Discussion with regulatory agency should start very early in the planning stage of clinical trials. However, the problem is complex and an individual researcher is often not going to create a coherent volume of information that is sufficient to really advance the field.

## Involvement of the entire community

The WG agreed that the involvement of the entire community (researchers, industries, patients association, funding agencies, etc.) would be beneficial to solve the issues and to define how each stakeholder can participate.

## Review of the document entitled ‘Biomarkers criteria proposal’

The document summarises criteria that would be useful for selecting biomarkers. Members of the WG are in agreement with the general concepts presented in the document, but feel that some wording should be adjusted.

- ▶ Slide 5: the phrasing ‘direct pharmacologic effect’ is open to misinterpretation, i.e., ‘immediate cellular response to the drug binding to target’, instead of the ‘primary pathophysiological pathway between the drug and clinical outcome’.
- ▶ Slide 6: ‘preferably linear’: linearity is better but it is mostly important to have an understanding of the quantitative relationship between biomarkers and the clinical response.

## Other comments

The WG could include representative from the hereditary cancers, renal diseases and liver diseases fields as they have a lot of experience with biomarkers.

## Main deliverables

- ▶ Summarize the main topics discussed in meeting schedule at the end of January
- ▶ Preparation of a template form (to be circulated to project leaders)
- ▶ Modification of the document 'Biomarkers criteria proposal'
- ▶ The Scientific Secretariat will sent a new list of projects
- ▶ The Scientific Secretariat will sent a Doodle to organise the next teleconference at the end of February