SSC Subcommittee Project/Collaborative Project

Subcommittee: FVIII / IX & RBD

NAME OF TASK FORCE:

Gene Therapy for Hemophilia - Safety and Efficacy Task Force

Person responsible (Co-Chairs / Principal Investigators): **Alok Srivastava (India) / Johnny Mahlangu (South Africa)**

- Members: **Anneliese Hilger (Germany), FDA Rep (USA), John Pasi (UK) , Lindsey George (USA), Margareth Ozelo (Brazil)**

- Design: ***Establish a consensus based list of parameters that should be included in defining the safety and efficacy of AAV based gene therapy for hemophilia.***

- Aim/Objective/Rationale (Needs assessment / Reason)

  AAV based gene therapy is establishing a new paradigm for the treatment of hemophilia that is challenging the concepts of safety and efficacy established for current therapeutic products. Fresh definitions of these parameters, which will be clinically relevant and based on sound scientific principles of outcomes assessment in chronic disorders, are therefore needed in the context of licensure of new products and their continued surveillance.

  1.To review the current standards of outcome measures for hemostasis product registration and surveillance.

  2.To evaluate the applicability of these outcome measures to the assessment of safety and efficacy of gene therapy for hemophilia and identify the deficiencies which need to be covered.

  3.Identify the new outcome measures, if any, which would be more appropriate for the assessment of gene therapy for hemophilia.

  4.Create a rational and practical list of outcome measures based on consensus which would follow the principles of assessment of outcomes of such diseases and will take into account the significance of patient reported outcomes.

- Methodology (Data expected to collect, sample size and statistical analysis):

  1.The existing literature on outcome assessment for product registration and surveillance will be reviewed and its applicability judged for gene therapy.

  2.A survey will be carried out of all stakeholders in outcome assessment of hemophilia through a structured questionnaire to determine the gaps in the field and the possible solutions

  3.Suitable new outcome measures will then be identified to bridge these gaps.

  4.A final list of outcome measures which will address both safety and efficacy aspects will be arrived at by a formal consensus based approach.

Study population (Inclusion, exclusion, eligibility) (patient population; recruitment of participating institutions/physicians and subjects; minimum number needed; expected number, follow-up period):

1.Apart from the survey of all stakeholders, no other new data collection will be attempted in the project.

2.The rest of the work will be done by literature review and discussion as well as Delphi based consensus approach for deciding on a final set of outcomes.

- Expected timeline:
    - ***Project stage/set up/launch: ~2-3 months***
    - ***Duration of consensus data collection: ~6 months***
    - ***Finalization of data: ~2-3 months***
    - ***Analysis & reporting: ~2-3 months***
- Expected outcomes (ie. publications):
    - Publication type (***SSC Communication***, Guidance document or original article): **Guidance document on a standardized set of outcomes that will assess safety and efficacy of gene therapy for hemophilia.**
- Description of project set/up and management, needed infrastructure and resources (summary): **As mentioned above, the expert group will work by reviewing the literature, and communications / meetings with all stake holders. A web based survey will also be conducted to collect the required data and a consensus process will be established for arriving at the final list of outcomes for recommendation. These efforts could also be supplemented with in person meetings at conferences of common interest, if possible.**
- References (if needed)