SSC Subcommittee Project/Collaborative Project

NAME OF PROJECT: *Gene Therapy Working Group*

Subcommittee: **FVIII / IX & RBD**

- Person responsible (Co-Chairs / Principal Investigators): **Alok Srivastava (India) / Barry J. Byrne (USA)**
- Members: Anneliese Hilger (EMA, PEI Germany), Wilson Bryan / FDA rep (USA) [TBC], Thierry VandenDriessche (Belgium), Glenn Pierce (USA)
- Design: ***Establish an expert group to address issues related to clinical trials for gene therapy for hemophilia by review of literature and through discussions with all stakeholders to arrive at consensus for options for study design and conduct aimed at establishing norms for efficient and harmonized approach to product development.***
- Aim/Objective/Rationale (Needs assessment / Reason)

  1.To identify issues that are important considerations in gene therapy clinical trials for hemophilia including preclinical data essential for proceeding to clinical trials.

  2.To define principles and criteria for patient selection including those related to assessment of pre-existing immune response including assay development and standardization.

  3.To define the quality parameters which need to be specified for gene therapy products to be used in clinical trials and to address the standardization of these products.

  4.To define the outcomes (clinical & laboratory endpoints) which need to be documented to determine success of gene therapy clinical trials in hemophilia – safety and efficacy criteria and to address the issue of inter-patient variation.

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

  Data will be collected from the published literature through a systematic review and by personal communication & survey questionnaires from investigators and sponsors and other stake holders in the field. A consensus will be arrived with due process to address the above mentioned issues. The aim will be to standardize where there is adequate data and provide guidance, where there is less data, on the approach to these issues in clinical trials of gene therapy for hemophilia.

- Study population (Inclusion, exclusion, eligibility) (patient population; recruitment of participating institutions/physicians and subjects; minimum number needed; expected number, follow-up period): ***Data will be used from completed and on-going gene therapy studies in hemophilia to provide guidance statements***

- Expected timeline:

- ***Project stage/set up: 1-2 months***
- ***Launch: 2-3 months***
- ***Duration: 1 year***
- ***Finalization/analysis: 3 months***
- ***Reporting: 3 months***

- Expected outcomes (ie. publications):
  - Publication type (***SSC Communication***, Guidance document or original article): **Guidance document**

- Description of project set/up and management, needed infrastructure and resources (summary): **As mentioned above, the expert group will work by reviewing the literature, getting opinions. This will be done by emails and web conferences supplemented with in person meetings at conferences of common interest, if possible.**

- Possible references: latest reviews:

Pierce GF, Ragni MV, van den Berg HM, Weill A, O'Mahony B, Skinner MW, Pipe SW. Establishing the appropriate primary endpoint in haemophilia gene therapy pivotal studies. Haemophilia. 2017 Sep;23(5):643-644. doi: 10.1111/hae.13313. Epub 2017 Aug 17. No abstract available. PMID: 28833947

VandenDriessche T, Chuah MK. Hemophilia Gene Therapy: Ready for Prime Time? Hum Gene Ther. 2017 Nov;28(11):1013-1023. doi: 10.1089/hum.2017.116. Epub 2017 Aug 3. PMID: 28793786

Arruda VR, Doshi BS, Samelson-Jones BJ. Novel approaches to hemophilia therapy: successes and challenges. Blood. 2017 Oct 10. pii: blood-2017-08-742312. doi: 10.1182/blood-2017-08-742312. [Epub ahead of print]