5 November 2010
EMA/696330/2010
Human Medicines Development and Evaluation

Agenda

Expert meeting in familial neurodegenerative disorders

Developing medicinal products for pre-symptomatic carriers: Autosomal dominant Alzheimer's disease and Huntington's disease as models

8 November 2010, 9:00–17:00, Meeting room 2A

Chair: Bruno Flamion (SAWP Chairman)

Co-chairs: Cristina Sampaio (Member of SAWP & CHMP) & Kerstin Westermark (COMP Chairperson)

European Medicines Agency (EMA): Maria Isaac (Scientific Advice), Spiros Vamvakas (Head of Scientific Advice), Jordi Llinares Garcia (Head of Orphan Drugs), Jorge Martinalbo (Scientific Advice), Agnès Saint Raymond (Head of Human Medicines Special Areas)

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Expert meeting in familial neurodegenerative disorders

Developing medicinal products for pre-symptomatic carriers: autosomal dominant Alzheimer's disease (ADAD) and Huntington's disease (HD) as models

The identification of gene mutations that are full determinants of devastating neurodegenerative diseases creates a number of unique stresses in the affected individuals, relevant novel bioethical situations but also a window of opportunity to attempt to delay or stop the pathogenic mechanism of the disease if the right tools to achieve so are developed.

Thus, the scientific communities that study these diseases and with all stakeholders in general, namely the families that are affected by the gene in question are eager to advance the field. There are several important challenges to overcome in order to design relevant clinical trials in these populations. Some of the most important are:

1. The numbers of individual affected worldwide by a given gene are small. Thus we are in realms of the very small population studies where level of uncertainties will always be relatively large.
2. The target diseases in this workshop are diseases with fully determinant genes however, the precise age when the disease becomes manifest is less certain. Thus, the issue of the moment when to include an individual in a trial or when to start treatment is critical.
3. The gene carriers will not have symptoms of the disease until later in the clinical trial, thus the classical endpoints in clinical trials and the classical evaluations of clinical relevance cannot be applied in trials done in individuals who will have only "subtle" manifestations of a disease that is yet to be manifest.

This expert meeting is meant to create a forum of discussion among stakeholders – academics, regulators, industry, and patients – in order to provide a first approximation for the resolution of the issues mentioned. The two diseases chosen for discussion are used as models to illustrate the challenges in pre-symptomatic clinical design studies as there is significant scientific understanding in ADAD and HD. The insights obtained from this discussion might be applicable in other similar circumstances.

Item	Agenda	Time
1	Arrival and registration	8:30
2	***Welcome and introduction*** Maria Isaac, Spiros Vamvakas	9:00
3	***Session 1*** ***Neurodegenerative Familiar Diseases - Common Problems***	9:05
4	**AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE (ADAD)** ***Session 2***	9:25
4.1	***ADAD background genetics/molecular biology and relationship to and implications for sporadic disease***	9:30
4.2	***Rationale for trials in ADAD***	9:40
4.2	***Pre-symptomatic course of ADAD: potential clinical outcomes for trials in ADAD***	9:50
4.3	***Biomarkers potentially applicable to prodromal ADAD***	10:00
4.4	***When, who and how to recruit to trials in ADAD: design of a feasible study?***	10:20
	Coffee break	10:40
4.5	***Introduction to DIAN and trials with DIAN/ADAD participants***	11:00
4.6	***Patient/family's perspective***	11:15
4.7	***Discussion on design regulatory issues***	11:45
4.8	***Industry's perspective***	13:00
4.9	***Ethical issues (placebo), compassionate use, asymptomatic vs. symptomatic***	13:10
	Lunch	13:30
5	**HUNTINGTON'S DISEASE (HD)** ***Session 3***	14:30
5.1	***Concept and rationale for pre-symptomatic treatment trials in HD***	14:30
5.2	***Biomarkers and clinical outcomes potentially applicable to trials for pre-symptomatic patients***	14:50
5.3	***Possible therapeutic trial designs***	15:05
5.4	***What is in the pipeline and how are they being selected to enter human trials?***	15:20
5.5	***Patient/family's perspective***	15:35
5.6	***Is it feasible to conduct pre-symptomatic trials in HD?***	15:50
6	***Discussion on design regulatory issues***	16:05
	End of the meeting	17:00