EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

7 November 2014
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Human Medicines Evaluation

EMA workshop on the investigation of subgroups in confirmatory clinical trials

Programme

7 November 2014
European Medicines Agency, London, United Kingdom

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Background

The investigation of subgroups in confirmatory clinical trials

The Guideline On The Investigation Of Subgroups In Confirmatory Clinical Trials is intended to provide assessors in European regulatory agencies with guidance on assessment of subgroup analyses and findings in confirmatory clinical trials. It is of particular interest how these considerations for assessment impact on the planning of the clinical trial and hence the document should also be useful to clinical trial sponsors and to assessors engaged in providing Scientific Advice. This guidance document describes principles and does not dictate any particular practical solutions in respect of statistical methodology for estimating or testing the treatment effect in subgroups of the trial population.

A differentiation is made between investigation of a subgroup as part of the confirmatory testing strategy and investigation of subgroups in a more exploratory manner. Whilst a number of the considerations outlined in this document will apply to the former, this is principally a problem related to multiple-testing because the trial seeks to test hypotheses relating to both the subgroup and the full trial population. Recommendations regarding pre-planned approaches for decision making in a confirmatory testing strategy based on subgroups are not discussed here. The guiding principles and examples for multiple-testing procedures that control the overall false positive rate are described in the respective guidance (Points to Consider on multiplicity issues in clinical trials).

Objectives of the workshop

- Discuss the role of subgroup analyses and subgroup findings in clinical trials submitted for marketing authorisation.
- Receive input on the positions outlined in the draft EMA guideline from experts and stakeholders.
- Provide an open forum for discussions of subgroup issues in the planning and at the assessment stage of phase III clinical trials.

Scientific Organising Committee

David Wright (Chair), Medicines and Healthcare Products Regulatory Agency, UK; **Robert Hemmings**, Medicines and Healthcare Products Regulatory Agency, UK; **Armin Koch**, Hannover Medical School, Germany; **Frank Pétavy**, **Andrew Thomson**, **Marisa Papaluca**, European Medicines Agency, UK.

Programme details

Friday, 7 November 2014

08:15 Registration

08:45 Opening statement

Marisa Papaluca, European Medicines Agency, UK

09:00 Session 1: Setting the Scene

Chair: Frank Pétavy, European Medicines Agency, UK

Clinical, Non-Statistical Perspective on Subgroup Analyses

Jens Heisterberg, Health and Medicines Authority, Denmark (15')

Rationale for Issuing the Guideline and Main Points

Robert Hemmings, Medicines and Healthcare products Regulatory Agency, UK (15')

Key Comments from the Public Consultation and the Regulatory Challenge

Armin Koch, Hannover Medical University, Germany (15')

The PMDA Perspective

Yuki Ando, MHLW/Pharmaceuticals and Medical Devices Agency, Japan (15')

Comments from the FDA Working Group on Subgroup Analyses

Estelle Russek-Cohen, Food and Drug Administration, USA (15')

Discussion (15')

10:30 Coffee break

11:00 Session 2: Stakeholders' Reactions on the Guideline I

Chair: David Jonathan Wright, Medicines and Healthcare products Regulatory Agency, UK

Subgroup Analyses in Confirmatory Trials – EFPIA perspectives

Albert Radlmaier and Christine Fletcher, European Federation of Pharmaceutical Industries and Associations (EFPIA) (30')

Subgroups - The Quest for Enlightenment

Alan Phillips, European Federation of Statisticians in the Pharmaceutical Industry (EFSPI), UK (15')

Discussion about the Proposed Different Levels of Subgroup Analysis
Claudia Schmoor and Frank Langer, German Region of the International Biometric Society (IBS-DR) and German Society for Medical Informatics, Biometry and Epidemiology (GMDS), Germany (15')

Discussion (30')

12:30 Lunch break

13:30 Session 3: Stakeholders' Reactions on the Guideline II

Chair: Andrew Thomson, European Medicines Agency, UK

Subgroup Analysis: trying to get more from less?
Geert Molenberghs, Integrated DEsign and AnaLysis of clinical trials in sample population groups (IDeAl), Belgium (15')

Selection and estimation in exploratory Subgroup Analyses – A proposal
Gerd Rosenkranz, Novartis Pharma AG, Switzerland (15')

Exploratory Subgroup Analysis: post-hoc subgroup identification in clinical trials
Alex Dmitrienko, Quintiles, USA (15')

On the Utility of Subgroup Analyses in Confirmatory Clinical Trials
Brian Millen, Eli Lilly and Company, USA (15')

Discussion (30')

15:00 Coffee Break

15:30 Session 4: Question and Answer Session

Chair: Steven Teerenstra, Medicines Evaluation Board and Radboud University Nijmegen Medical Centre, the Netherlands

Discussion with pre-submitted questions and from the floor

16:45 Session 5: Closing remarks

David Wright, Medicines and Healthcare Products Regulatory Agency, UK

17:00 End of meeting

Conference venue and Secretariat

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