EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 November 2011
EMA/894153/2011
Human Medicines Development and Evaluation

Expert workshop on subgroup analysis

Programme

18 November 2011
European Medicines Agency, London, United Kingdom

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Background

Regulatory and methodological issues of subgroup analysis

Analysis of subgroups is important in every confirmatory trial to assess internal consistency.

Sometimes subgroup analysis are used with the intention to rescue trials that 'fail' based on the overall population or to try to identify patient groups with the most favourable benefit-risk profile.

Subgroups should be pre-specified in the trial protocol, based on demographic, genomic or disease characteristics (e.g. sub-entities of a disease that are widely recognised within the medical community) but may also materialise based on a need or desire to further explore study results.

Formal statistical methods for investigating the homogeneity of the treatment effect across subgroups do exist and these are used by companies or regulatory bodies to provide re-assurance or to challenge the applicability of overall findings to subgroups.

In addition, simpler (often visual) methods can be helpful in elucidating and displaying results from subgroups. In some dossiers, the investigation of results in subgroups is minimal, perhaps in fear of (possibly false) negative findings that may complicate assessment.

Objectives of the workshop

- To present the scope and content of the proposed guidance document to internal and external experts to receive feedback for further reflection. To discuss the role of subgroups in the assessment of clinical trials, including:
  - Is it important to consider subgroup findings in the assessment of all confirmatory clinical trials? Have all important uses of subgroup analyses (in terms of regulatory assessment) been highlighted in the Concept Paper?
  - When should subgroup findings be incorporated in the assessment? What statistical methodology is available to incorporate findings in the most reliable way?
  - What are the consequences of incorporating subgroup findings in the assessment on the decision making procedure?
- To discuss standards and methods for planning, conducting and reporting 'confirmatory' subgroup analysis as distinct from (exploratory) subgroup analyses to assess internal consistency of study results and as distinct from post-hoc subgroup analyses aiming to rescue a 'failed' trial or improve the expected trade-off of benefits and risks compared to the whole trial population.
- To discuss standards and methods for planning, conducting and reporting 'exploratory' subgroup analysis, including statistical approaches that assist in drawing inferences when multiple subgroup analyses are performed.

Programme details

Friday, 18 November 2011

8.00 Registration

8.30 Opening statement

Marisa Papaluca – Amati, European Medicines Agency, UK

8.40 Session 1: Current guidelines and expectations on subgroup analysis in regulatory decision making

Chair: Bruno Flamion, University of Namur, Belgium

Subgroup analyses in regulatory decision making
Rob Hemmings, Medicines and Healthcare Products Regulatory Agency, UK

Reliably basing conclusions on subgroups in significant and non-significant clinical trials
Armin Koch, Institute for Biometry, Hannover Medical School, Germany

A subgroup or a subpopulation – design and analysis issues in clinical trials
Sue-Jane Wang, Food and Drug Administration**,** USA

Subgroup analysis: a view from an industry statistician
Oliver Keene, GlaxoSmithKline, UK

10.30 Coffee break

11.00 Session 2: 'Confirmatory' conclusions based on subgroups

Chair: Norbert Benda, Federal Institute for Drugs and Medical Devices, Germany

Multiple testing methodology in the context of subgroup analysis
Alex Dmitrienko, Quintiles Innovation, USA

Efficacy claims and subset analyses in phase III: some thoughts and examples
Kevin Carroll, AstraZeneca, UK

Adaptive design strategies to select a subgroup
Nigel Stallard, University of Warwick, UK

Confirmatory subgroup analysis: case studies
Frank Bretz, Novartis Pharma AG, Switzerland

12.30 Lunch break

13.30 Session 3: The role of subgroup analysis in the assessment of clinical trials

Chair: Armin Koch, Institute for Biometry Hannover Medical School, Germany

Perspectives on analysing subgroup effects of clinical trials and their meta-analyses
Kit Roes, Clinical Research University Medical Centre Utrecht, Netherlands

From nasty business to stratified medicine – an HTA perspective
Stefan Lange, Institute for Quality and Efficiency in Health Care, Germany

Use of subgroups to "rescue" a failed trial or improve benefit-risk
Martin King, Abbott Laboratories, USA

Panitumumab: the KRAS story
Christine Fletcher, Amgen, UK

15.00 Coffee break

15.15 Session 4: Plenary discussion and closing remarks

Chair: Bruno Flamion, University of Namur, Belgium

16:30 End of meeting

Conference venue and secretariat

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