General Considerations

- Older people in many cases constitute the main users of a drug, not a special population.
- Older adults are underrepresented in clinical trials (relative to disease prevalence) but the situation seems to be improving.
- Following ICH E7 Q&A, a representative number of patients should be studied pre-authorisation.
- Data should be presented for the entire age spectrum
- But it is not only a matter of numbers, it is a matter of asking the right questions and setting up a strategic plan – use Scientific Advice!

General Considerations (2)

- There is a learning curve to gather data and modulate risk
- Clinician often acts as gatekeeper in recruitment, and determines a selection bias by recruiting only some of the eligible patients
- Population PK or specific PK study including the very elderly should be performed and will help informed prescription
- M&S is powerful to identify patients at risk (efficacy and/or safety)

Endpoints - Considerations

- Depending on frailty/disability the desirable outcome and treatment decisions might be different
- Functional endpoints might be more relevant in certain cases (GEG input)
- This may have HTA implications
- Discuss in Scientific advice or parallel HTA/SA
- Do we need to change the endpoints or the way we evaluate them?

Increasing recruitment - Considerations

- Strategies and interventions to improve participation at level of ethic committees, recruitment process and trial conduct have been presented
  - Communication & Logistics
  - Make use of existing networks
  - Feed back the results
  - age exclusion should be justified,
  - commonly prescribed co-medication in this population should be allowed;
  - multimorbid patients should be allowed;
  - trial sponsor should provide support measures to encourage recruitment;
  - CT outcome measures should be relevant to old people.

Frailty and Older-old patients- Considerations

- Consensus on Frailty definition and evaluation tools is needed (input from geriatric expert group GEG suggests SPPB)
- More effort is needed to recruit patients 75+ in clinical trials: EFPIA survey shows preferred option is same clinical trial. Separate trial might be needed.
- Accurate reflection of data in patients >75 years is important
- EFPIA: comorbid patients should be in same Phase 3, However there is indication that a separate trial might be have better results in terms of recruitment
- Data expected in the MAA, postmarketing will depend on target population- condition in RMP/Annex 2
- Sarcopenia is a worthwhile clinical endpoint *per se* (frailty is predictor of clinical outcomes + global societal benefit)
- Heterogeneity can be in some measure allowed and analysed in clinical trial design both pre and post authorisation

Product information – Considerations

- No good information is possible if there are no good data
- Sometimes there is good information but not reflected
- Channels of information are important- both to patient and prescriber
- Better focus on Package leaflet
- Specific measures are needed particularly as the older group is non homogeneous Better explain how to take medicine/increase compliance/PK and PD changes/concomitant medication
- Consolidate in a comprehensive section?
- information to Nurses should be allowed (?)

Formulations and Adherence – Considerations

- Inappropriate formulations are conductive to low adherence and Safety and Efficacy problems
- Multimorbidity/ dose reduction/ visual and mobility impairment needs to be considered when designing formulations
- Issue probably more complex than paediatric due to variability in older population)
- Protocols to evaluate the ability of patients to manage medication could be considered
- QWP might take conclusions of workshop as starting points for a consultation on possible guideline on formulations (possible Q&A document)
- Medication errors is an area where PRAC might seek QWP input
- A Q&A on adherence aspects pertaining to Q/MI/PhV could be developed

Conclusions: how to strengthen pharmacovigilance

- Risk management – based on the risk profile – plan to fill knowledge gaps through post-authorisation studies; targeted risk minimisation
- Collection of data – optimise all possible data sources – facilitate reporting of suspected side effects, patient reporting; drug utilisation; electronic health records
- Detecting new safety issues – huge potential to better use spontaneously reported adverse reactions: drug-drug and drug-disease interactions; focus on off-label use, medication errors, event clusters (e.g. falls dizziness);

Conclusions: how to strengthen pharmacovigilance 2

- Evaluation of safety issues – always consider the elderly
- Benefit risk evaluation – dedicated consideration of elderly population; specific patient values placed on benefits and risks
- Regulatory action – consider targeted action
- Communications – meet the information needs of the elderly; support decision-making; target communication and risk minimisation

Conclusions: opportunities to move forward

- **New pharmacovigilance legislation** – current consultations; dedicated new guidance; new tools (e.g. patient reporting)
- **Regulatory sciences** – methods for collecting data, signal detection, bias and confounding in observational studies, novel clinical trial design, biomarkers
- **Resources**: Research funding (IMI, Framework Programme etc); Accessing data; funding studies; expert staff; involving patients

Conclusion

- We can further strengthen the protection and promotion of the health of the elderly, through a focus on the elderly in all aspects of regulation
- ..and in partnership with all stakeholders

Next steps (1)

- Report in one year on strategy impact as compared to baseline
- CHMP will continue to consider older population in assessment
- Reporting of results in regulatory documents will need to be improved
- When drafted or revised, CHMP will consider strengthening existing disease specific guidelines, with particular regard to older-old, comorbidities, frailty

Next steps (2)

- Pharmacovigilance activities, based in particular on new legislative tools
- QWP might take conclusions of workshop as starting points for a consultation on possible Q&A on formulations
- Frailty: need to agree on scale(s) for regulatory purpose
- Internal EMA Processes to consider age-appropriateness of formulations, packaging are being developed (both in SA and MAA