The Industry's Views on Geriatric Medicines

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Outline

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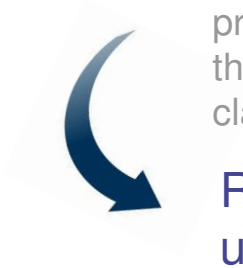
- EFPIA Survey: Overview of collected answers addressing representation of "older patients" in the clinical development programmes
- Evolving our Future Together

Introduction

- In 2006, the European Commission raised the issue of the adequate representation of “elderly patients” in clinical development programmes.

- The scientific opinion of the European Medicine Agency (EMA) was that:
  - **Overall guidance is adequate** (most of the specific guidelines being in coherence with the overarching ICH E7).
  - **Most of the sampled dossiers fulfil** the recommendation to evaluate the investigational product in **at least 100 patients over the age of 65 years**.
  - There was nevertheless **room for improvement** for including in Clinical Trials a more representative sample of the target population: “increasing the number of elderly patients participating in the clinical development programmes, requiring a proportion of the efficacy and safety database, in relation to the indication, and mirroring the target population and considering the minimum requirements for two different age classes: elderly and very elderly”.



Reopening of ICH E7 guideline took place and ended up with a partial update via the E7 Q&As document (endorsed in 2010).

Now, the real life debate is not limited to medicines

- By end of 2010, an increasing number of initiatives/discussions about Ageing/Geriatrics have been fuelled by the European Commission public consultation on the **Pilot European Innovation Partnership on Active and Healthy Ageing,** to which many pharmaceutical industries have responded.

- In February 2011, the EMA published a "**Geriatric Medicines Strategy**".

Europe is paving the way for a different kind of innovation

- Built around **new arising therapeutic needs** of older/ageing citizens and largely centred on prevention of diseases and maintaining function.

- EFPIA welcomes these initiatives and intends to positively contribute to the necessary enlarged debate with all the stakeholders, for a generally productive move in response to major societal and public health changes.

  - **EFPIA Survey:** launched across research-based pharmaceutical industry focusing on today's main topics: demonstration of safety and efficacy (including identification of current gaps), pharmacovigilance activities, adherence and formulations, product information.
  - **TWG: established with the objective to consolidate and develop the identified gaps after today's first collaborative appraisal**

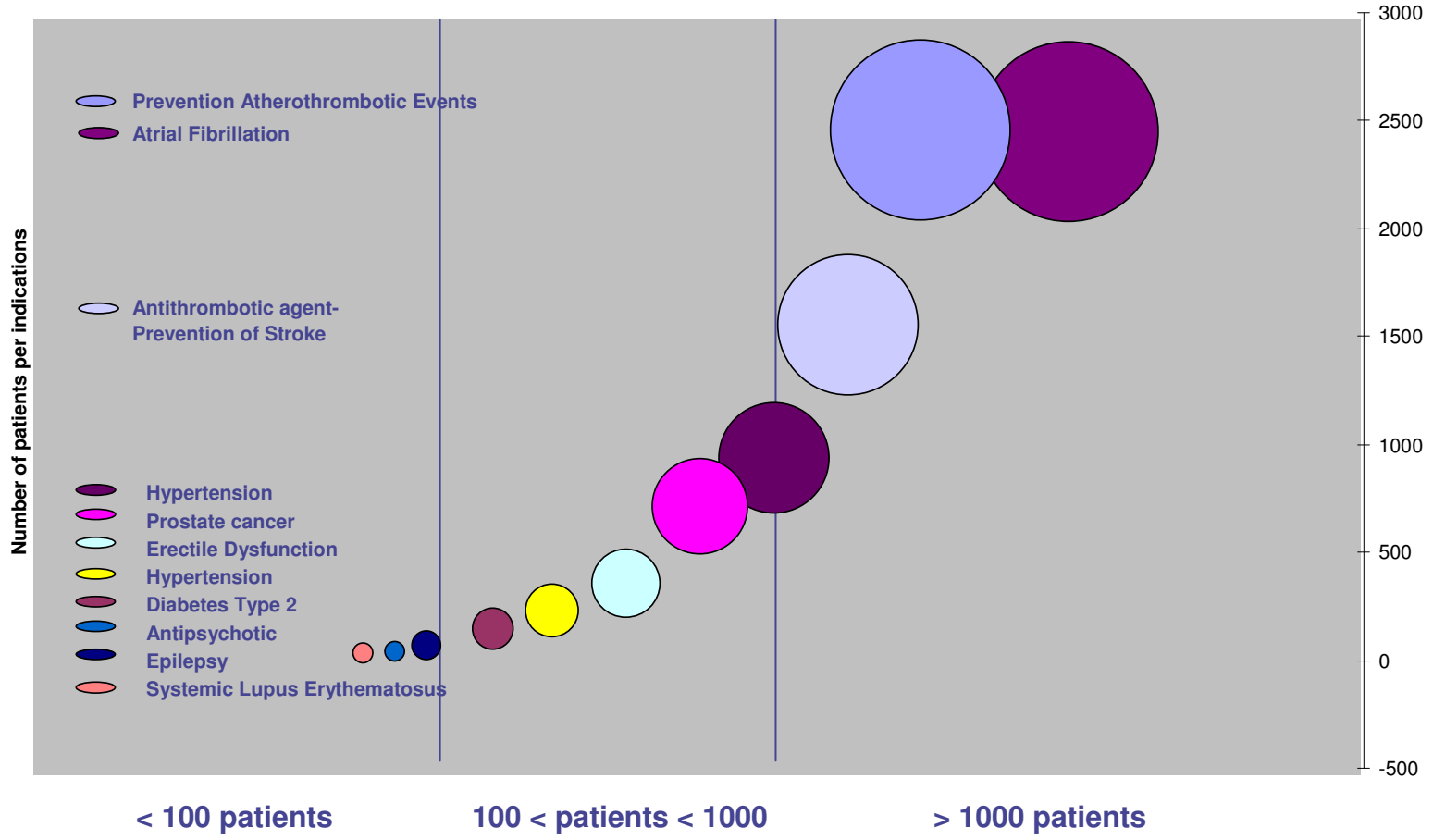
EFPIA Survey on Geriatric Medicines Strategy

- This presentation, based on the answers EFPIA received from 15 Companies, will mostly address the **demonstration of Safety and Efficacy,** starting from **the representation of "older patients"** in the clinical development programmes of new medicinal products.

- The first observation is that in parallel with the ICH E7 updating process and surrounding scientific debate there is a **general positive trend in numbers of older patients included**, as captured by some examples (over last the 3 years) provided by companies within the survey.

- However, when we focus on patients over 75 years, the effort should be continued (even considering that ICH E7 Q&A only came in 2010).

2009-2011 centralised EU applications by indications, documented for patients ≧65 years (source EFPIA Survey Jan 2012)



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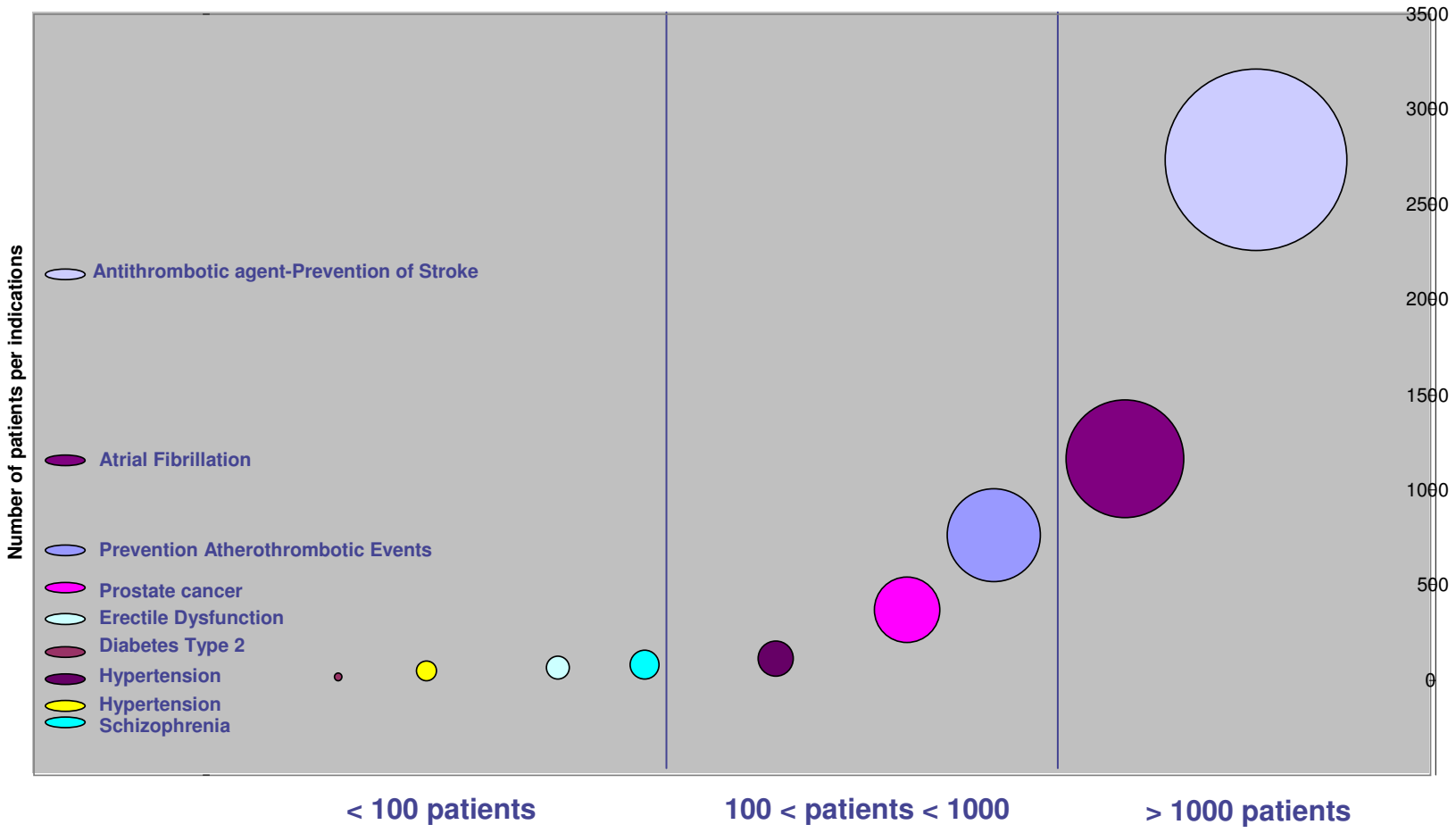


Geriatric Patients: a Heterogeneous Population

- Older Adults without significant morbidities
- Older Adults with significant morbidities and/or functional decline
- Older adults in which certain conditions may assume specific features: e.g. depression, anxiety, apathy, insomnia

- Inclusion would allow for a better understanding of the effect of normal ageing on drug's safety (and efficacy) profile
- Inclusion is likely more appropriate for geriatric-specific indications such as Alzheimer's disease, involuntary weight loss, or sarcopenia
- *Ad hoc* approach

Inclusion of a geriatric patient group may add to the variability of any endpoint potentially resulting in decreased effects, unless the study is adequately powered. 'This may result in a need for larger studies of increased complexity and likely longer drug development timelines', unless alternative approaches are also considered (e.g. collection of data post-authorisation)

Would you be in favour of an **overarching guideline** by the EMA specifying the **practical criteria** to adequately represent geriatric patients and consent adequate evaluation of Benefit/Risk?

- The prevalent opinion is that an overarching guidance should keep a **global scope** to deal with global development and therefore be agreed in the **ICH** (evolving) perimeter, not limited to EU.

- In some cases the geriatric population should be considered as a very specific population with its **own therapeutic needs and benefit/risk**.

  ➲ Industry believes it is appropriate to allow for **flexibility** and consideration of each product development on a case-by-case basis.

And should the guidance be organised per **therapeutic domain/indication**?

- Even if required data to assess the risk-benefit for older patients will **primarily depend on the indication**, both **general** (for medicines normally not intended specifically for geriatrics) and **disease based** guidance (for medicines intended to be used in older patients) is considered useful.

- Consideration needs to be in place particularly for **indications with increased prevalence in the geriatric population**, e.g. CHF, Hypertension….

Are **current guidelines sufficient**? Have you identified a lack of guidance on a **specific area**?

- The level of guidance with respect to older patients per disease area, varies considerably. Regulatory agencies should **promote geriatric expertise sharing and dissemination** more systematically and consistently, and make best use of geriatricians experienced in clinical research**.**
- Guidelines could be considered as sufficient in the most usual cases, but if there is a precise request for data in very old patients, data requirements for the subgroup(s) ≥ 75 years should be better specified.
- Guidance on **adapted study methodology** in older patients might also be appropriate.

  - In particular, consideration of **appropriate functional endpoints** is critical for many trials for improvement of functional capacity.
  - Specifically, the current guidelines are **not sufficient for older patients with co-morbidities, loss of functions, and geriatric syndromes, e.g. sarcopenia**.

Focusing on **patients over 75**: Would you recommend/prefer to test older patients in the **same phase 3 than younger adults**?

- The decision to include geriatric patients in the same or separate phase 3 studies than younger adults will **depend on the disease/indication and other factors** (e.g. some biomarkers may be age related).

- **The overall clinical trial programme should be directed at the relevant patient populations including geriatrics, if appropriate.**

  ➲ The **same phase 3 would generally be the preferred option.**

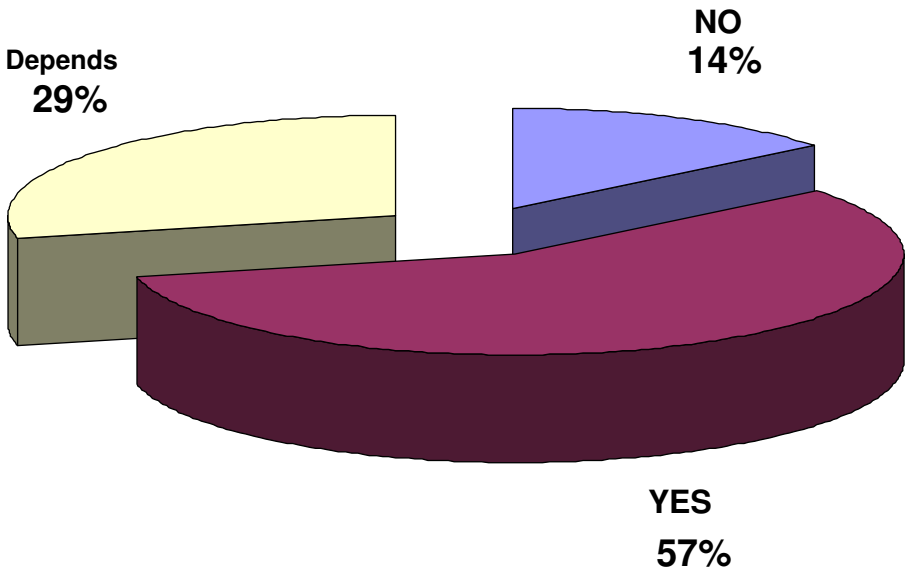
- The choice of a **subgroup** of patients in the same phase 3 trials will be based on:
  - **Logistics** (ability to recruit patients)
  - **Labelling** (so the age group is included)
  - **"Generalisability"/marketing:** Clinicians consider that patients in trials should closely reflect the patients they treat
  - HTA purposes, etc.

- In some cases, it will make more sense to have a completely **separate trial** for the geriatric population, to better deploy adapted methodologies.

Vulnerable geriatric patients with co-morbidities and concomitant therapies: In terms of development costs, **which is the more feasible option?**

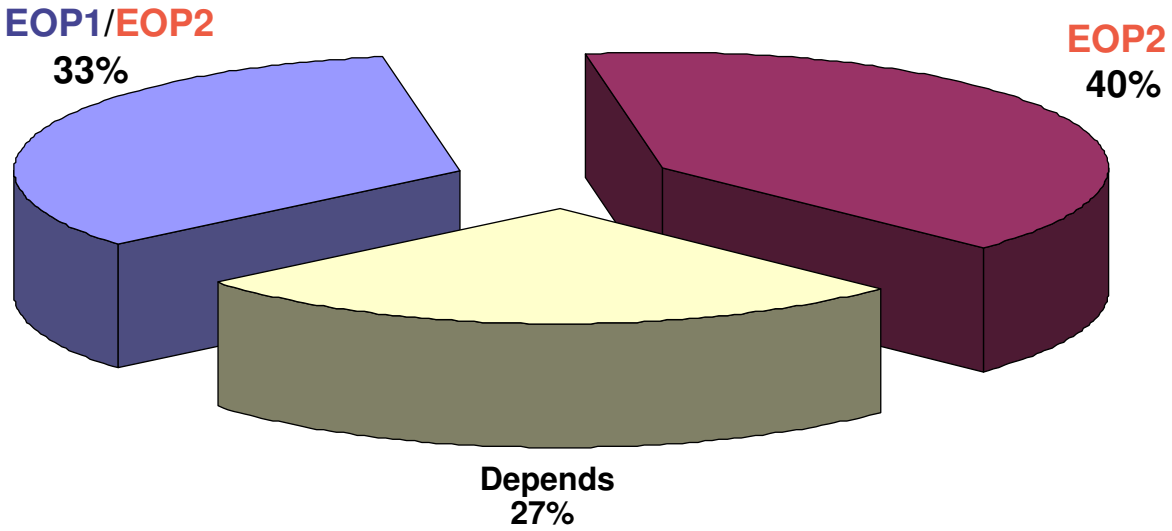
- Simply favouring the inclusion of **older co-morbid patients** in the **general phase 3,** taking the risk of insufficient data or unbalanced results; but **subsequently exploiting these results for HTA?**

  - Could be more efficient to enrol (vulnerable) geriatric patients into the main phase 3 Clinical Trials;
  - This is feasible; the risk of insufficient and/or unbalanced data to be mitigated by **stratification and proper sample sizing of the sub-group;**
  - Additional resources and specific expertise to be taken into account.
  - Alternative options would be:
    - to present comprehensive clinical data in older co-morbid patients as a second step (post-approval).
    - Implement a specific CT targeting labeling specificities**.**



In **which moment** testing regulatory acceptability of our development programme?
Formally? e.g. joint HTA/Scientific Advice

Most of the Companies have clearly indicated they prefer to seek for **scientific advice no later than End of Phase 2**, and **on a voluntary basis**.



Most of the Companies have clearly indicated they prefer to seek for **formal scientific advice**, few would consider systematically joint/parallel SA-HTA discussions.

Some trends from the Survey and EFPIA next steps:

- We observe a general positive trend in the representation of older patients in clinical development programs.
- Development of medicines for the geriatric patients is still on the learning phase, this is a heterogeneous population with diversified and specific therapeutic needs
- Consistent implementation of ICH E7 Q&A should be able to address most of the pending issues; further upgrades should be kept within a global scope
- Engagement of EMA through formal Scientific Advice seems the best path forward, to address the specific needs of geriatric patients, accompanied by regular sharing and dissemination of scientific expertise
- The Survey as a starting point is expected to lead to an EFPIA reflection paper
- There is a clear and shared Industry's commitment to engage in a **collaborative discussion** with Academia, Regulators, HCP, Patients representatives and other Interested parties to better address older/geriatric patients unmet needs.

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