

The number of included older people in recent pre-approval trials



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Background

- Older people have often been excluded from pre-approval trials
- The regulatory ICH E7 guideline requires a minimal number of older subjects for trials:
 - Regarding diseases primarily related to aging: >50% of database 65+.
 - Regarding diseases not typical for, but present in old age: >100 subjects 65+.

Objective

To analyze the number of older people in trials of recently authorized drugs indicated for diseases regularly present in old age.

Methods

Included medicines:

- Authorized by the European Medicines Agency between 2008 and 2011.
- Chosen indications - diseases primarily related to aging:
 - prevention of venous thromboembolism after replacement arthroplasty: dabigatran, rivaroxaban;
 - Osteoporosis: bazedoxifene, lasofoxifene, denosumab;
 - Atrial fibrillation: dronedarone, vernakalant;
- Diseases present in old age:
 - Diabetes mellitus type II: liraglutide, saxagliptin;
 - Depression: agomelatine;
 - Bipolar disorder: asenapine maleate;
 - Epilepsy: eslicarbazepine

Methods ctd.

- Data sources:
 - European public assessment report (EPAR);
 - WHO Trials Registry;
 - Published trials.

Outcome measures:

- The number of randomized subjects and
- The number of those aged 65+ and 75+.
- Trial characteristics
- Of all phase II and III trials identified in the EPAR.

Results

One-hundred and fourteen (114) phase II and phase III trials were included. The number of people aged 65+ and 75+ was available in 29% and 35% of the 114 included trials, respectively.

Characteristic	Overall values (n=114)
Design and setting	
Single centre, n (%)	3 (2.6)
Multicentre, n (%)	88 (77.2)
Single country, n (%)	11 (9.6)
More than one country, n (%)	74 (64.9)
Number of countries, median (range)	6 (1–37)
Trial location	
European Union ^a (EU)	29 (25.4)
European Union and North America ^b (NA)	30 (26.3)
NA ^c	20 (17.5)
Other countries (neither EU nor NA)	2 (1.8)
Start date trial, n (%)	
2000–2002	16 (14.0)
2003–2005	40 (35.1)
2006–2008	20 (17.5)

Table 1. Trial characteristics

Approved therapeutic indication	Number of randomised participants		
	Overall, n	Aged 65+, n (%)	Aged 75+, n (%)
Overall	78,617	19,678 (25.0)	7,938 (10.0)
Characteristically associated with aging (n = 7)	56,200	18,483 (32.9)	7,857 (14.0)
Prevention venous thromboembolism	23,777	12,598 (53.0)	3,150 (13.2)
Osteoporosis	23,465	1,365 (5.8)	2,471 (10.5)
Atrial fibrillation	8,958	4,520 (50.5)	2,236 (25.0)
Present in older people (n = 5)	22,417	1,195 (5.3)	81 (0.4)
Type 2 diabetes mellitus	10,883	996 (9.2)	55 (0.5)
Depressive disorder	4,614	136 (2.9)	26 (0.6)
Bipolar disorder	5,496	49 (0.9)	0 (0)
Epilepsy	1,424	14 (1.0)	0 (0)

Table 2. The number and proportion of participants aged 65 years and 75 years and older

Results ctd.

In trials for diseases characteristically related to aging (n=7) (Table 2):

- 32.9% of the randomized participants were aged 65+ (median 1365; range 0–6750);
- 14.0% were aged 75+ (median 331; range 0–2471).

In trials for indications present in old age (n=5):

- 5.3% were aged 65+ (median 12; range 0–206);
- 0.4% were aged 75+ (median 0; range 0–36).

Conclusions

This study on the number of older subjects in clinical trials shows that in trials for indications primarily related to aging, almost half of the randomized subjects is 65+. In trials for indications not specific for, but present in old age, the number and especially the proportion of older subjects is very limited.

Conflicts of interest

No conflicts of interest declared.

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