Aging Population - A Challenge In Drug Development Today

Demographic Changes & Increasing Importance

Why Elderly?

There is an unmet medical need for safe and effective drugs in geriatric patients (2,3) resulting in an important opportunity for pharma companies. Currently up to 10% of the population in developed countries is 75 years or older, and about one quarter of these is at least 85 years old (1,2). Higher age is associated with an exponentially increasing number of drugs taken. However, geriatric patients can respond differently than younger patients to drug therapy in a number of ways, and such differences can be more pronounced in patients 75 years and older (2,3,4). The geriatric population has age-related physiological changes that can affect both the pharmacokinetics and pharmacodynamics of drugs. Recently, the implications for development of drugs for elderly has been addressed by both, FDA and EMA (4,5).

High age is related to a decreased kidney function (6), which is a key physiological factor influencing drug effects in the elderly population. Furthermore geriatric patients are more prone to adverse drug effects, given the higher rate of comorbidities and concomitant therapies. Adverse events can be more severe, or less compensated for than in younger patients. Not all potential differences in the geriatric population can be predicted from non-geriatric populations or simply extrapolated taking into account age-related impairment of renal function. Therefore, to assess the benefit/risk balance of a drug that will be used in the geriatric population, these patients should be appropriately represented in clinical trials. Data should be presented for various age groups to assess the consistency of the treatment effect and safety profile in these patients (4). Demonstrated efficacy and safety in eldery population are key success factors of drugs today.

Challenges

The major challenges of clinical trials in geriatric individuals pertain to recruitment, safety, regulatory approvals, and clinical conduct. The high frequency of diseases and number of medications, a decreased tolerability for adverse drug effects, and an increasing incidence of frailty and cognitive impairment raise concerns in potential participants, treating physicians, Ethics Committees and authorities. Furthermore, there is a general reluctance of suitable elderly to engage in clinical drug trials and standard recruitment tools fail. Established special recruitment networks, a close collaboration with the treating physicians and external experts, proper documentation of health status, including adequate assessment of renal function (4), and a highly flexible organisational structure are key success factors for a fast and successful clinical trial conduct.

Additionally the right social and economic setting is the key factor: Both life expectancy and health system organisation support the conduct of such studies in Germany.

References:

1. Destatis, 2014: Bevölkerung und Erwerbstätigkeit (Zensusdaten 10.04.2014).
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3. Sera LC et al. Pharmacokinetics and pharmacodynamic changes associated with aging and implications for drug therapy. Clin Geriatr Med. 2012 May;28(2):273-86.
4. FDA, CDER, CBER: Guidance for Industry. E7 Studies in Support of Special Populations: Geriatrics. Questions and Answers/February 2012
5. EMA geriatric medicines strategy. EMA/ CHMP/137793/2011

CRS Clinical Research Services

CRS - Your Partner In Elderly (≥75 Years) And Very Elderly (≥85 Years) Populations

Case Study

Recently a sponsor of CRS requested a trial to assess the pharmacokinetic changes of a drug under renal impaired functions. CRS is working in this field for many years. During further discussions with the authorities, they requested to provide clinical data of elderly and very elderly due to the therapeutic area and the applicable population. The sponsor decided to integrate further elderly populations into the trial design. CRS developed a strategy based on its long experience in the recruitment of special populations including trial design aspects as well as special referral networks, treating physicians and an adapted advertisement strategy for the target population.

Strategy & Outcome:

- In close communication with the EC special safety assessments for geriatric participants were integrated
- Trial design was adapted to minimise the risk for the most vulnerable population
- For very elderly subjects (≥85 years) a stable background illness was allowed
- Strict standardisation & coordinated recruiting management by involving only three CRS CPUs
- Trouble free clinical conduct in 14 months (FSI to LSO)
- Sponsor was very pleased by the recruitment rate, especially by the recruitment of 24 very elderly subjects ≥85 years within 14 months

Top Recruitment By CRS

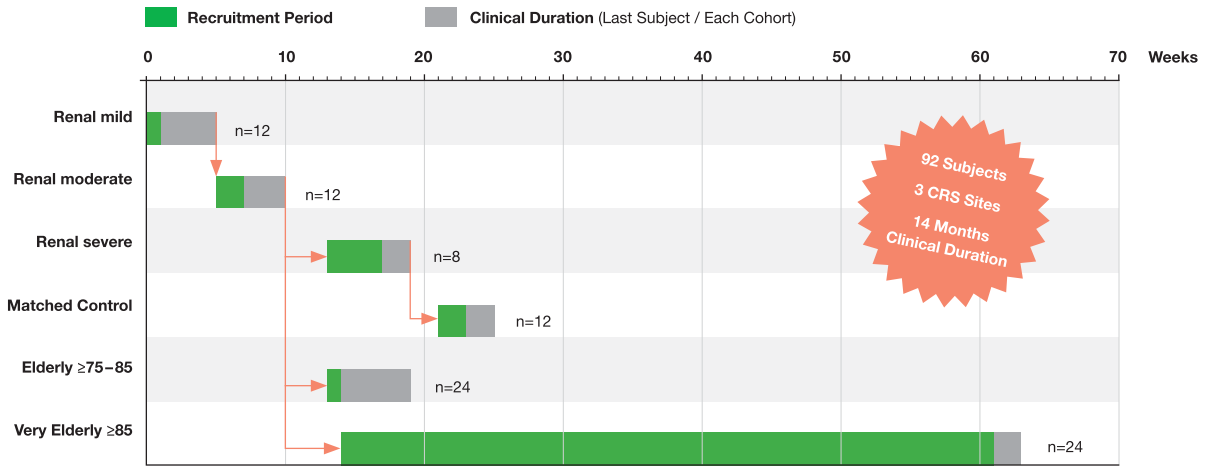

Figure: Illustration of the recruitment duration in a case study with staggered enrollment: Cohorts of severe renal patients and elderly ≥75 years were enrolled only after completion of the moderate renal cohorts.

About CRS

CRS is among the top recruiters worldwide for renal insufficiency patients and preferred partner by both big pharma and small biotech companies. Since the early 90s, CRS has realised more than 120 trials in patients with renal impairment and runs around 8 trials per year.

The successful conduct of the trials and the availability of suitable patients is based on three decades of experience of Dr. Atef Halabi, internist and medical director of CRS-Kiel, and on a reliable referral network of university clinics as well as external dialysis centres and specialists.

Most renal impairment trials are being realised in a monocentre approach at the CPU in Kiel. In case of large sample sizes or rare patient populations, further CRS CPUs in Germany may be involved. This approach enables fast trial conduct in a single regulatory environment and in a highly standardised in-house fashion at CRS.

Reference:

6. Schaeffner ES, Ebert N, Delanaye P, Frei U, Gaedeke J, Jakob O, Kuhlmann MK, Schuchardt M, Tölle M, Ziebig R, van der Giet M, Martus P. Two novel equations to estimate kidney function in persons aged 70 years or older. Ann Intern Med. 2012 Oct 2;157(7):471-81.

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