Fallzahlschätzung	STA/01 Version 0x

Änderungen gegenüber der letzten Fassung:

1 Zweck und Ziel

In order to restrict the probability that the trial shows a negative result while actual the treatments are active (consumer's risk, type-II-error) to an acceptable level (e.g. 10 or 20%, this means to avoid weak' studies with significant results only by chance), to avoid unnecessary high sample sizes and to check if assumptions and objectives harmonise and can be shown in a study with practical sample size a statistical sample size calculation is obligatory.

2 Anwendungsbereich

In general the sample size for a study should be determined by means of a correct statistical sample size calculation prior to begin of the clinical phase and du ring the protocol development. Only in case of sequential designs the total sample size is calculated or re-calculated after treatment of a fixed number of patients.

3 Beschreibung

The study protocol therefore has to pre-specify the sample size. For phase I studies there can be a well-founded motivation to state a sample size without any statistical sample size calculation while for most phase III and pharmacokinetic equivalence trials a statistical sample size determination is necessary.

Sample size calculation is based on the primary parameter which is specified in the protocol. The primary objective leads to the null hypothesis for which the sample size should be calculated.

Sample size calculation is based on assumptions about mean, variance and correlation or incidence or number of events of primary parameters within a population. In addition, the biostatistician needs information what clinical difference one may wish to detect (in case of tests for difference) respectively information about the maximum tolerable difference one will admit that two treatments still be considered as equivalent (in case of equivalence trials).

This information will be drawn out of results of trials with comparable design, treatments and study parameters. The clinical relevant difference has

to be worked out in close connection with the project manager medical advisors and the sponsor.

lf no such information is available, formal statistical sample size calculation is not possible. This should be clearly stated in the protocol. In most such

cases (early phase I studies, phase 2/3 studies with new indication, safety studies) a pre-defined sample size is stated without a statistical sample size calculation.

lf all necessary information is collected (means, standard error, correlation, relative frequency, significance level, power etc.) the biostatistician can perform the estimation.

Sample size estimation is made by means of N and NSurv by IDV©. In case of metrical and nominal data the program N is used, in case of time-to-event data the program NSurv is used. Both programs use state-of-the-art procedures to estimate a correct sample size if the assumptions made a-priori are correct.

4 Dokumentation

The output of the software programs N and NSurv which includes sample size estimations and statistical power calculations will be stored in the subdirectory 'xxx\smplsize' were 'xxx' denotes the study number. No further restrictions to filenames are given.

A hard copy of the output of sample size calculation will be stored in the study file. The biostatistician will incorporate the sample size calculation in the specific chapter of the study protocol.

5 Ressourcen

5.1 Zeitbedarf

5.2 Software

software programs N and NSurv von IDV

6 Risiken

7 Zuständigkeiten

8 Hinweise und Anmerkungen

9 Mitgeltende Unterlagen

9.1 Literatur, Vorschriften

9.2 Begriffe

10 Anlagen

Freigabevermerk

Fahrdorf, den Autor