ESR Researcher Project: Non-technical Summary

"Bias and precision in early phase adaptive studies and its consequences for the decisions about conducting and designing confirmatory studies"

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The project focusses on the studying of phase II adaptive designs and methods for efficacy estimation in such designs, and to investigate the consequences of bias and imprecision of phase II efficacy estimates on the planning of phase III trials. New estimation methods for a class of adaptive phase II designs are being proposed, and approaches for adjusting phase III sample size estimates are being discussed. In addition new basket designs are proposed for oncology phase II trials. The key points regarding the project are:

The study of the performance of different estimation methods proposed in the literature for oncology phase II group-sequential and adaptive designs. This was done via simulation studies, and included the commonly used single-arm designs with binary endpoint.

The proposal of new estimation methods for oncology phase II adaptive designs. This was for two-stage adaptive designs with binary endpoint in which the second stage sample size and decision rules are functions of the number of successes in the first stage.

The analysis of the consequences of using effect estimates from phase II adaptive design, which are often biased and imprecise, on planning phase III sample size and we discussed and proposed adjustment approaches in order to obtain adequately powered phase III trials.

The proposal of new design approaches for phase II basket trials in oncology. These designs are mainly modifications of the existing ones to accommodate new scenarios and assumptions. The scenarios include the one in which it is assumed that the treatment effect expectations are different across the baskets.

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