



## ESR Researcher Project: Non-technical Summary

### “Statistical aspects of animal to human translation”

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The development of diagnostic tests based on biomarkers is increasingly becoming an integral part of clinical development. Especially in the field of oncology, biomarkers are used to develop tests aiming to identify and treat those who are more likely to respond and demonstrate a higher therapeutic benefit.

When using quantitative (sets of) biomarkers, a reliable threshold, or cutoff value, needs to be established to constitute a diagnostic test. This is a critical step in the drug development process, as the patient selection in the subsequent development steps may depend on this value. Moreover, we wanted to include the clinical utility into the selection process to obtain actionable biomarkers that could, in combination, constitute an appropriate diagnostic test.

In early clinical development, the challenge is that often only few data are available to determine a cut-point for biomarkers. Therefore, we investigated the possibility to include external information, for example from previous studies or from the literature, into the estimation process; this would potentially lead to a more precise estimation of the cutoff, and provide more information about the potential uncertainty of this estimation.

We have proposed a statistical method to estimate a cutoff such that the populations below and above the threshold have a pronounced difference in their response rates. Most importantly, we estimate the uncertainty around the estimate of the cutoff and we can utilize possible prior information.

In addition, in the current project we also focused on the development of a method that would simultaneously perform biomarker selection and cutoff estimation by controlling the predictive accuracy of the selected biomarkers. In other words, we aim to select only those biomarkers that relevantly increase the probability of correctly classifying patients with respect to, for example, the response to treatment and therapeutic benefit. We developed a method that combines biomarker selection and cutoff evaluation, leading to sets of biomarkers that can be used to develop a diagnostic test with high clinical utility.