Design and implement an adaptive confirmatory trial in Japanese patients with palmoplantar pustulosis

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More and more literature can be found describing how to overcome the design and implementation challenges of adaptive designs in the drug approval process. However, most of the adaptive trials were conducted in Western Europe or USA for Phase II or Phase II/III and case studies in the field of non-oncology tailored to pivotal adaptive trials used for Japan approval consideration remain unavailable or rare. This presentation elaborates on our statistical experience with designing and implementing a Phase III adaptive confirmatory trial with sample size re-estimation and futility analysis in Japanese patients with palmoplantar pustulosis [1].

After describing the background information, we give insights in what should be considered at the design stage of this adaptive study: design alternatives, the reasoning for choosing the adaptive design, statistical analysis method, and operational risks. Then we share our key implementation experience from 2 aspects: regulatory agency interaction and setting up a Japan domestic data monitoring committee (DMC). Statistical simulations played a crucial role at the planning stage of our development program and some simulation results used to evaluate the proposed trial design are also presented.

Final analysis results of this study successfully demonstrated the effectiveness of our drug and based on the interim analysis results, it was recommended to continue the study without sample size adjustment. We discuss results versus design assumptions and advantages from the conduct of the study with the adaptive design approach. Huge cost savings have been gained and development time has been reduced compared to the option with one conservative fixed design. Several limitations of our study are also pointed out in the last section part of the article.

[1] **Trial registration:** ClinicalTrials.gov identifier: NCT02641730.