Phase 1 Clinical Research: Should Safety, Drug Exposure and Clinical Efficacy of Diabetes Drugs Be Assessed in Patients or in Healthy Volunteers?

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Based on the dramatically increasing number of patients with diabetes, and the urgent need to find better treatments to effectively battle the diabetes pandemic, the arsenal of drug candidates is growing rapidly. Picking up early indicators about a drug candidate's safety and potential clinical efficacy is highly desirable in order to make the drug development process more effective; in particular, providing robust data much earlier should improve or enable the decision-making about candidates that should be failed early.
Looking into the early phase clinical research toolbox, one sees that the pharmacodynamic (PD) characterization of diabetes compounds has historically been based on a number of different methods, with many of them being applied in different variations.
A question of growing relevance is that of the appropriate target population in which to assess safety, tolerability and efficacy in the early phases of the clinical development process. It appears that adhering to the historical approach of moving from the pre-clinical development into the clinical development with a first-in-human study in healthy volunteers may not necessarily be the most appropriate approach, neither from a safety, tolerability, drug exposure (pharmacokinetics) nor from an efficacy perspective (pharmacodynamics). Based on ethical considerations, the current regulatory environments and on a science-driven, high quality approach to clinical design and clinical execution, it seems appropriate to challenge the current dominant early phase approach. In light of the above, the key regulatory perspectives will be summarized, safety and tolerability considerations will be discussed, and opportunities to include pharmacodynamics (efficacy) profiling into phase 1 clinical research will be presented. Data from studies performed, and methods utilized by the author will be discussed to identify methods that are likely to provide meaningful safety and gluco-metabolic outcome data in early phase clinical research studies.