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138P Improved efficacy response attributed to diagnostic selection – Interim results of the phase 1 experience from ALKA-372-001

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Background: The ALKA-371-001 phase 1 trial was implemented to assess safety and dosing in patients with advanced solid tumors and treated with entrectnib, which targets the tyrosine kinases encoded by NTRK1, NTRK2, NTRK3, ROS1, and ALK. Being a targeted therapy, a subset of patients were enrolled based on the local assessment of gene rearrangements in the NTRK1, ROS1 or ALK genes, by FISH or IHC, during dose escalation and expansion. Retrospectively, a subset of phase 1 patient specimens were submitted for central laboratory testing using RNA based next generation sequencing (NGS) to determine status of gene rearrangements (n = 33) of those, 23 were treated at, or above, the recommended phase 2 dose. Together, these clinical responses were correlated with diagnostic detection of a gene rearrangement to assess prediction of outcome based on patient selection.

Methods: Two primary hospital centers performed FISH or IHC for the assessment of gene rearrangements and applied consensus scoring. These results were used for patient enrollment and treated as the reference standard. For central testing, an anchored multiplex PCR NGS of sample RNA was used to assess gene rearrangements. Tumor response was determined using RECIST criteria. Statistical analyses to test correlation with outcomes was performed.

Results: For patients with results from both local testing and central confirmation testing (n = 33), there is strong negative agreement (100%) yet poor positive agreement (ALK 62.5%, ROS1 40%, NTRK 0%). However, when results are correlated for n = 23 study patients with the overall response rate (PR or CR), the use of central NGS testing provides a significant ORR of 66.7% (CI: 30%, 90%) vs local testing 41.7% (CI: 19%, 68%).

Conclusions: The current response data of the ALKA-371-001 trial demonstrates that the use of high sensitivity NGS testing is significantly predictive of overall response rate in the targeted patient population. Indicating that the predictive methods used centrally must be readily deployable to local testing laboratories to find patients beyond the clinical trial setting. The early identification of appropriate diagnostic testing at the phase 1 level improves the chances for effective trial outcomes and treatment of patients.

Clinical trial identification: ALKA-371-001, Phase 1 (EudraCT Number: 2012-000148-88)

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