PHASE II STUDY TO ASSESS THE SAFETY AND EFFICACY OF THE CLEVER-1 ANTIBODY BEXMARILIMAB IN COMBINATION WITH PD-1 BLOCKADE IN PATIENTS WITH ADVANCED SOLID TUMORS – BEXCOMBO

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Background Clever-1 is an immunosuppressive scavenger receptor expressed on tumor associated macrophages1-2. High levels of Clever-1 are associated with poor survival, T-cell exclusion and dysfunction, and immunotherapy resistance3-7. Bexmarilimab (Bex) is a novel humanized anti-CLEVER-1 IgG4-antibody that induces IFN-γ upregulation, which is required for PD-L1 upregulation and response to PD-1 blockade8. Bex is currently evaluated as monotherapy in a phase I/II study (MATINS; NCT03733990) in patients with advanced solid tumors and in combination with standard of care in patients with hematological malignancies (BEXMAB; NCT05428969). Preliminary data show well tolerated safety profile and promising clinical activity with disease control rates up to 40% translating into enhanced survival9. In addition, early analyses suggest that lower levels of proinflammatory cytokines at base line or higher CLEVER-1 expression in tumor can predict for a superior clinical outcome. The BEXCOMBO study will assess the safety and efficacy of Bex in combination with PD-1 blockade in 1st line setting in patients with advanced solid tumors expressing CLEVER-1 and with modest response to PD-1 blockade. It is anticipated that the induction of IFN-γ production by Bex will result in enhanced clinical efficacy from PD-1 blockade in patients lacking pre-existing immune activation.

Methods BEXCOMBO is a single arm multicentre clinical study with an adaptive design (figure 1). The study uses a Simon’s 2-stage design (Stage 1 n=15: Stage 2 n=40 for each indication). Study treatment will be initiated in patients with advanced head and neck squamous cell (HNSCC) with the potential to open patient cohorts with advanced urothelial carcinoma and non-small cell lung cancer (NSCLC) or other indications based on emerging translational and clinical data. Patient selection based upon lower baseline levels of proinflammatory cytokines or higher levels of CLEVER-1 expression will be considered if supported by translational data. Patients will be treated at the Recommended Phase 2 Dose of Bex in combination with standard of care PD1 blockade until progression or unacceptable toxicity. The primary endpoints are objective response rate based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) and duration of response. Key secondary endpoints include time to response by RECIST 1.1, disease control rate, progression-free survival, overall survival, safety and CLEVER-1 and PD-L1 expression levels in tumor biopsy; as well as IFNγ and TNFα levels in serum.

REFERENCES

Ethics Approval This study will be sent to all participating sites review boards and local ethics committees for approval.

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