

A PHASE 1 DOSE ESCALATION AND EXPANSION STUDY OF THE ANTI-CD200R1 ANTIBODY 23ME-00610 IN PATIENTS WITH ADVANCED SOLID MALIGNANCIES

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Background 23ME-00610 is a first-in-class, fully humanized monoclonal antibody that inhibits the CD200R1 immune checkpoint, a promising immuno-oncology target identified by the 23andMe genetic database.¹ 23ME-00610 binds with high affinity ($K_D < 0.1$ nM) to CD200R1 on immune cells and has been shown to block immunosuppressive signaling and enhance T cell-mediated killing of tumor cells that express its only known ligand in humans, CD200, in preclinical studies.² We hypothesize that blocking CD200R1 with 23ME-00610 will reverse immune cell tolerance in the microenvironment of tumors that are reliant on the CD200R1 pathway, leading to immune-mediated disease control.

Methods The safety and preliminary antitumor activity of 23ME-00610 is being evaluated in a Phase 1 dose escalation and expansion study in adults with locally advanced unresectable, or metastatic solid malignancies who have progressed on standard therapies with an ECOG score of 0 or 1; adolescents at least 12 years, weighing at least 40 kg with a Lansky play scale score of at least 50 will be included in the expansion phase. The primary objectives in the dose escalation phase are determination of the maximum tolerated dose (MTD)/recommended phase 2 dose (RP2D), and safety and tolerability, measured by the incidence and severity of dose-limiting toxicities, treatment-emergent adverse events (AEs) and withdrawals due to AEs. Secondary objectives include pharmacokinetics, immunogenicity, and preliminary antitumor activity of 23ME-00610. The monotherapy activity of 23ME-00610 will be evaluated in indication-specific expansion cohorts (N~15/cohort), which include clear cell renal cell carcinoma; epithelial ovarian, fallopian tube or primary peritoneal carcinoma; neuroendocrine cancer; and microsatellite instability-high (MSI-H) or tumor mutational burden-high (TMB-H) cancers that have progressed on standard therapies. A cohort of adolescents with locally advanced unresectable, or metastatic solid malignancies will also be enrolled. These indications were selected based on the expression of CD200R1 and its ligand, CD200, T cell markers, and immune characteristics that may increase likelihood of response to CD200R1 inhibition. The primary objective of the expansion phase is objective response rate (ORR) based on RECIST 1.1. The pharmacodynamic profile of 23ME-00610, including markers of CD200R1 engagement, will be evaluated. Germline genotypic information collected from participants will be used to correlate genetic variants and polygenic risk scores with safety and efficacy outcomes. The statistical analyses will primarily be descriptive. Participants reflecting the characteristics for the indication-specific cohorts with regards to age, sex, race, and ethnicity, including those from the Black, Latinx/Hispanic and Indigenous communities, will be prioritized for enrollment.

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Trial Registration www.clinicaltrials.gov; NCT05199272

REFERENCES

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2. Fenaux J, Huang Y, Melero C, Chung W, Lee S, Ayupova D, Poggio M, Glatt D, Yi Z, Lay C, Schmidt M, Majeed SR, Fuh G, Chen A, and Kumar S. 23ME-00610 is a first-in-class monoclonal antibody that targets the CD200R1 immune checkpoint to enhance T cell-mediated antitumor activity. AACR Annual Meeting 2022.

Ethics Approval The study obtained approval from the following ethics committees/institutional review boards (approval IDs are in parentheses): Advarra IRB (Pro00062976), Salus IRB (START2021.35), MD Anderson OHRP IRB (2021-0888), Oregon Health & Science University IRB (STUDY00023966) and Ontario Cancer Research Ethics Board (3953). All study participants must provide informed consent prior to taking part in the study.

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