# Efficacy, safety and PKPD of 23ME-00610, a first-in-class anti-CD200R1 antibody, in patients with tumor mutational burden-high (TMB-H) or microsatellite instability-high (MSI-H) cancers: Results from an expansion cohort

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## BACKGROUND

### Genetic Signature

- CD200R1 was identified as a promising immuno-oncology (IO) target from the 23andMe database [1]. Pleiotropic causal variants with opposing effect on risks for cancer and immune diseases, referred to as an IO signature, were observed for 3 critical components of the CD200R1 pathway, including CD200R1, its sole ligand CD200, and the downstream signaling protein DOK2.

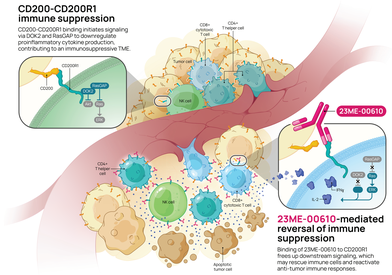
### CD200R1

- CD200R1 is expressed on immune cells and binds to CD200, its only known ligand in humans, downregulating proinflammatory cytokines by activated T and myeloid cells and/or hindering immune cell infiltration into tumors, and promoting an immunosuppressive microenvironment in human cancers, where CD200 is highly expressed[2-9] **(Figure 1)**.

### 23ME-00610

- 23ME-00610 is a first-in-class IgG1 antibody that binds CD200R1 with high affinity (KD < 0.1 nM) and inhibits immunosuppressive signaling, leading to restoration of T cell activity and killing of CD200-expressing tumor cells in preclinical studies [1] **(Figure 1).**
- 23ME-00610 is currently in the Phase 2a portion of a Phase 1/2a clinical trial in participants with advanced solid malignancies (NCT05199272) **(Figure 2)**. Based on data from the first N=28 patients, 23ME-00610 demonstrated excellent safety and tolerability, a favorable PK profile supporting Q3W dosing, full target engagement with peripheral saturation at doses ≥ 60 mg, and pharmacodynamic evidence of activity, including on-target immune-related AEs, a > 50% stable disease rate, and emerging evidence of clinical activity in neuroendocrine, renal and ovarian cancer[10,11].

Figure 1: 23ME-00610 ('610), a Fully Humanized, Effectorless IgG1, Inhibits Immunosuppressive CD200/R1 Signaling via High Affinity Binding to CD200R1




Abbreviations: Akt: protein kinase B; CD: cluster of differentiation; DOK: docking protein; ERK: extracellular signal-regulated kinase; IFN: interferon; IL: interleukin; NK: natural killer; RasGAP: Ras-specific GTPase-activating proteins; TME: tumor microenvironment

## METHODS

Figure 2: Phase 1/2 Study Design in Patients with Locally Advanced or Metastatic Solid Malignancies

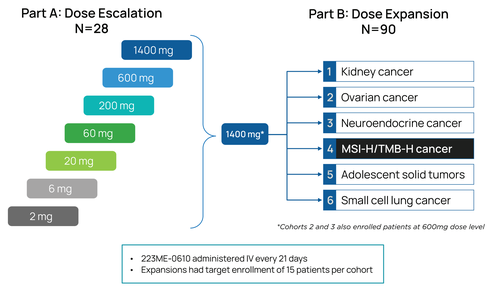
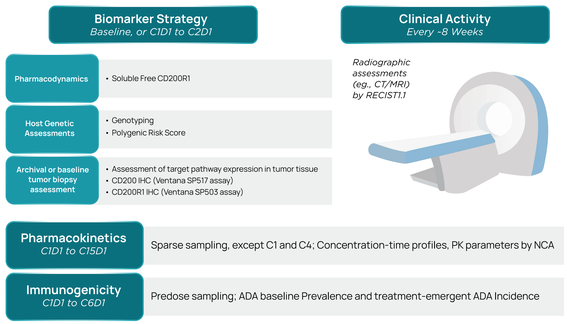



Figure 3: Schedule of Assessments




## RESULTS

Table 1: Patient Demographics and Disease Characteristics

| Characteristic | N = 13 |
|---|---|
| Age, median years (range) | 60 (36-79) |
| Sex, n (%) | |
| Male | 6 (46%) |
| Female | 7 (54%) |
| Race, n (%) | |
| White | 9 (69%) |
| Black | 2 (15%) |
| Other/unknown | 2 (15%) |
| Ethnicity, n (%) | |
| Hispanic or Latino | 1 (8%) |
| Not Hispanic or Latino | 11 (85%) |
| Unknown | 1 (8%) |
| Geographic Region, n (%) | |
| USA | 11 (85%) |
| Canada | 2 (15%) |
| ECOG, n (%) | |
| 0 | 1 (8%) |
| 1 | 12 (92%) |
| Years since Initial Diagnosis, median (range) | 3.0 (1.4-13.2) |
| Prior Lines of Treatment, median (range) | 5 (3-11) |

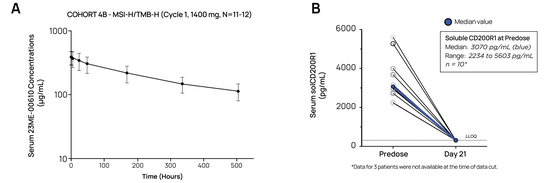
| Characteristic | N = 13 |
|---|---|
| Prior Systemic Cancer Therapy, n (%) | |
| Anti-PD/PD-L1 | 11 (85%) |
| Anti-VEGF | 5 (38%) |
| Anti-CTLA4 | 1 (8%) |
| Anti-TIGIT | 1 (8%) |
| Microsatellite or TMB status, n (%) | |
| MSI-High | 5 (38.5%) |
| Not MSI-High (Stable or Low) | 5 (38.5%) |
| TMB-High | 11 (84.6%) |
| TMB Status Unknown | 1 (7.7%) |
| TMB-Median (range), n=11 | 18.3 (10-66) |
| Primary tumor location, n (%) | |
| Colorectal | 6 (46%) |
| Endometrial | 2 (15%) |
| Cervical | 1 (8%) |
| Breast (HR+/HER2+) | 1 (8%) |
| Head and neck | 1 (8%) |
| Skin | 1 (8%) |
| Unknown primary | 1 (8%) |

### Safety Assessment

- All patients reported adverse events in the TMB-H / MSI-H cancer cohort, of which, 9 patients (69%) reported adverse events related to study treatment.
- Related AEs reported in more than two patients in this cohort included: fatigue (n=4), headache (n=2), and nausea (n=2), with other adverse events generally similar across the entire study.
- 1 of 13 patients had 2 related irAEs (grade 1 nausea and grade 2 hypothyroidism).
- Across the entire study, two SAEs were reported as related by the investigators, including a grade 3 deep vein thrombosis (DVT) and grade 3 diarrhea.

## RESULTS (continued)

Figure 4: 23ME-00610 Excellent PK and Full Target Engagement at 1400 mg Q3W




- PK of 23ME-00610 is generally similar in dose escalation and dose expansion cohorts
- A dose of 1400 mg achieves prespecified PK target at trough > EC90 in tumor
- Apparent median Cycle 1 half life of ~13-15 days supports Q3W or better dosing
- Minimal treatment-emergent ADA; ADA does not appear to meaningfully affect PK
- Complete saturation of free sCD200R1 by C2D1 observed in all evaluable patients

Figure 5. Response and Duration of Treatment (Swimmer's Plot)

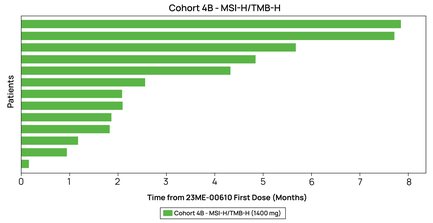



Table 2. Response and Duration of Treatment

| Best Overall Response | n (%) |
|---|---|
| Complete Response (CR)[1] | 0 (0.0) |
| Partial Response (PR) | 0 (0.0) |
| Stable Disease (SD) | 4 (30.8) |
| Progressive Disease (PD) | 7 (53.8) |
| Not Evaluable (NE) | 2 (15.4) |
| Disease Control Rate (DCR) | 4 (30.8) |

1. Complete response, partial response, table disease and progressive disease as defined by RECIST 1.1 criteria

Figure 6. Maximum RECIST Change vs. CD200 Expression vs. Prior Therapy

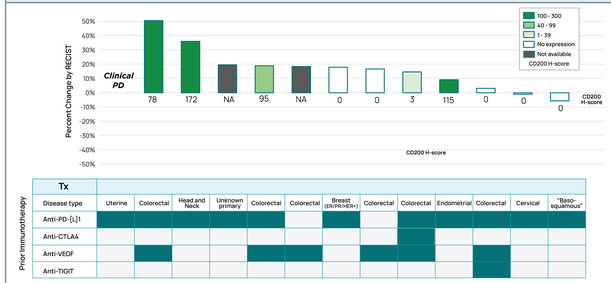
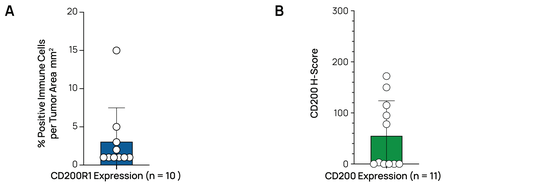
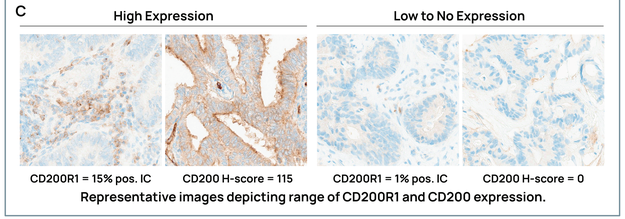



Figure 7: Tumor Expression of CD200R1 Pathway Components




- Mean 3.1%, st. dev 4.4%. 11 patients had archival tumor material available for CD200R1 IHC staining; however, 1 sample was not evaluable.
- The H-score captures both the intensity and the proportion of CD200 tumor cell expression and comprises values between 0 and 300. Mean H-score was 55.7, st. dev. 68. 2 patients did not have evaluable archival tissue for IHC staining.




Representative images depicting range of CD200R1 and CD200 expression.

## CONCLUSIONS

- 23ME-00610 continues to show an acceptable safety and tolerability profile, full peripheral target engagement, and PK that supports Q3W dosing, though limited anti-tumor activity as monotherapy in a small cohort of participants with TMB-H/MSI-H tumors.
- Related AEs were generally grade 1 or 2 in severity.
- Related irAEs occurred in 1 patient, were grade 1 and 2 in severity, and manageable in nature.
- No grade 4 AEs or AEs that led to death or discontinuation occurred.
- 1400 mg results in full peripheral saturation with limited ADA with no apparent impact on exposure or safety.

## REFERENCES

1. Fenaux J, et al. *Oncoimmunology*. 2023;12(1):2217737. 2. Mihrshahi R, et al. *J Immunol*. 2009;183(8):4879-4886; 3. Timmerman LM, et al. *PLoS One*. 2021;16(3):e0244770; 4. Misstear K, et al. *J Virol*. 2012;86(11):6246-6257; 5. Salek-Ardakani S, et al. *Eur J Immunol*. 2019;49(9):1380-1390; 6. Choueiry F, et al. *J Immunother Cancer*. 2020;8:e000189; 7. Moreaux J, et al. *Biochem Biophys Res Commun*. 2008;366:117-122; 8. Vathiotis IA, et al. *Cancers (Basel)*. 2021;13:1024; 9. Love JE et al. *Am J Clin Pathol*. 2017;148:236-242; 10. Rasco DW, et al. *J Clin Oncol*. 2024;42 (suppl 16): abstr 4129; 11. Khaki AR, et al. *J Clin Oncol*. 2024;42(suppl 16): abstr 5575.

## DISCLOSURES

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