Focal characterization of OR502, an anti-LILRB2 antibody that rescues innate and adaptive immune responses from LILRB2 mediated immunosuppression

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Background: The selective use of monoclonal immune checkpoint receptor antibodies 

OR502 demonstrates specific binding to LILRB2 and blocks LILRB2-FC binding to HLA-G

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OR502 does not bend to other LILRA/B family members

OR502 is required for anti-PD-1 efficacy in M2c-exhausted T cell culture assay

OR502 pharmacokinetic profile and in vivo anti-tumor activity of parental antibody

Abstract #498

1. LILRB2 promotes immunosuppression and blockade drives anti-tumor activity

2. OR502 demonstrates specific binding to LILRB2 and blocks LILRB2-FC binding to HLA-G

3. OR502 does not bind to other LILRB family members

4. OR502 boosts LPS-induced IFN-γ secretion by PBMC

5. OR502 relieves CD8+ T cells from M2c macrophage-mediated immunosuppression

6. Combination with OR502 is required for anti-PD-1 efficacy in M2c-exhausted T cell culture assay

7. OR502 pharmacokinetic profile and in vivo anti-tumor activity of parental antibody

RESULTS

4000 0 1000 2000 3000 4000 5000 Antibody [µg/mL] IFN-γ [pg/mL] Isotype OR502

0 10 20 30 40 0 20 40 60 80 100 Antibody [µg/mL] CD11b (gMFI) on CD66b+ CD15+ PMNs (%) Isotype OR502

OR502 demonstrates specific binding to LILRB2 and blocks LILRB2-FC binding to HLA-G

A) Binding to HEK293T, LILRB2
B) Receptor Occupancy on myeloid cells
C) Blocking of LILRB2 binding to HLA-G

OR502 relieves CD8+ T cells from M2c macrophage-mediated immunosuppression

A) Autoimmune T cell lines were incubated with OR502 or Isotype at 500 ng/mL and IFN-γ production was assayed.
B) Data represent the mean ± SEM of triplicates in a representative experiment of 2.

Combination with OR502 is required for anti-PD-1 efficacy in M2c-exhausted T cell culture assay

A) M2c macrophages were cultured with OR502 or Isotype at 100 ng/mL for 10 days and cytokine production was assayed.
B) Data represent the mean ± SEM of triplicates in a representative experiment of 2.

OR502 pharmacokinetic profile and in vivo anti-tumor activity of parental antibody

A) SC mice were treated with OR502 or Isotype at 0.1 mg/kg and SHC2 tumor burden was measured.
B) Data represent the mean ± SEM of triplicates in a representative experiment of 3.

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