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Pharmacodynamic Activity of MEDI1873, a Glucocorticoid-Induced Tumor Necrosis Factor Family-Related Protein (GITR) Agonist Molecule, Administered Intravenously to Patients with Advanced Solid Tumors

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Presenter Disclosure Information

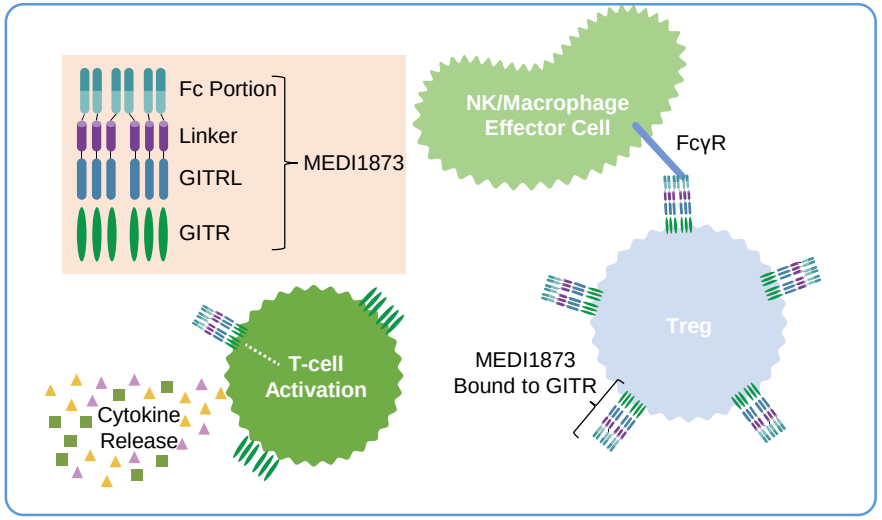
Nick Durham

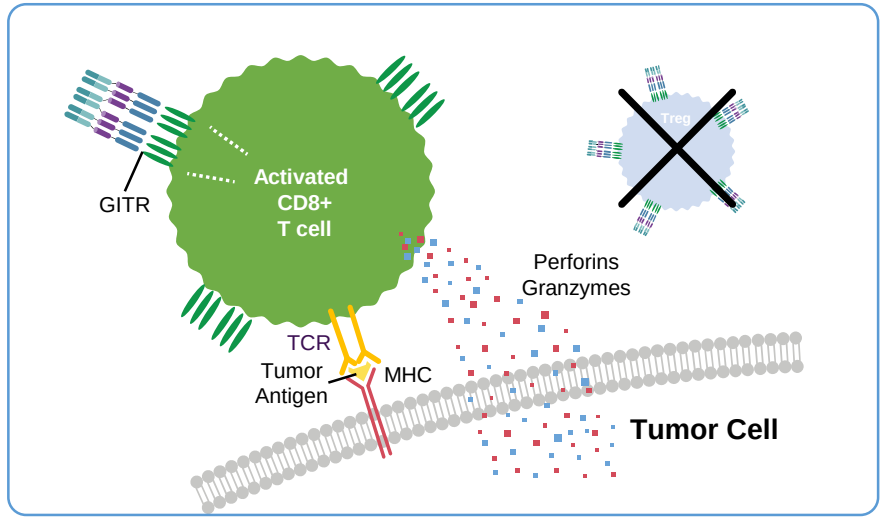
The following relationships exist related to this presentation:

MedImmune, Salary, Employee

Background

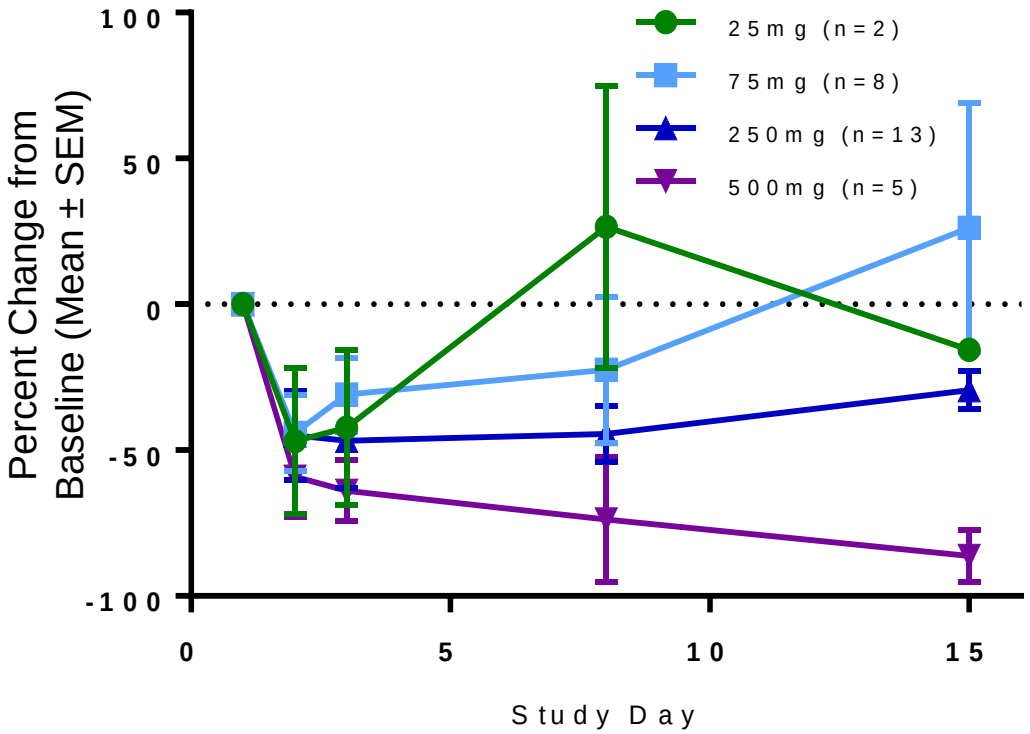
- MEDI1873 is a novel GITR-ligand/IgG1 agonist fusion protein that binds to GITR activating effector T cells and depleting Tregs.
- In a Phase 1, first-time-in-human, dose-escalation study in patients with advanced solid tumors (NCT02583165), MEDI1873 showed an acceptable safety profile.[6]
- Secondary objectives of the study included MEDI1873 pharmacokinetics (PK), pharmacodynamics (PD) and immunogenicity.



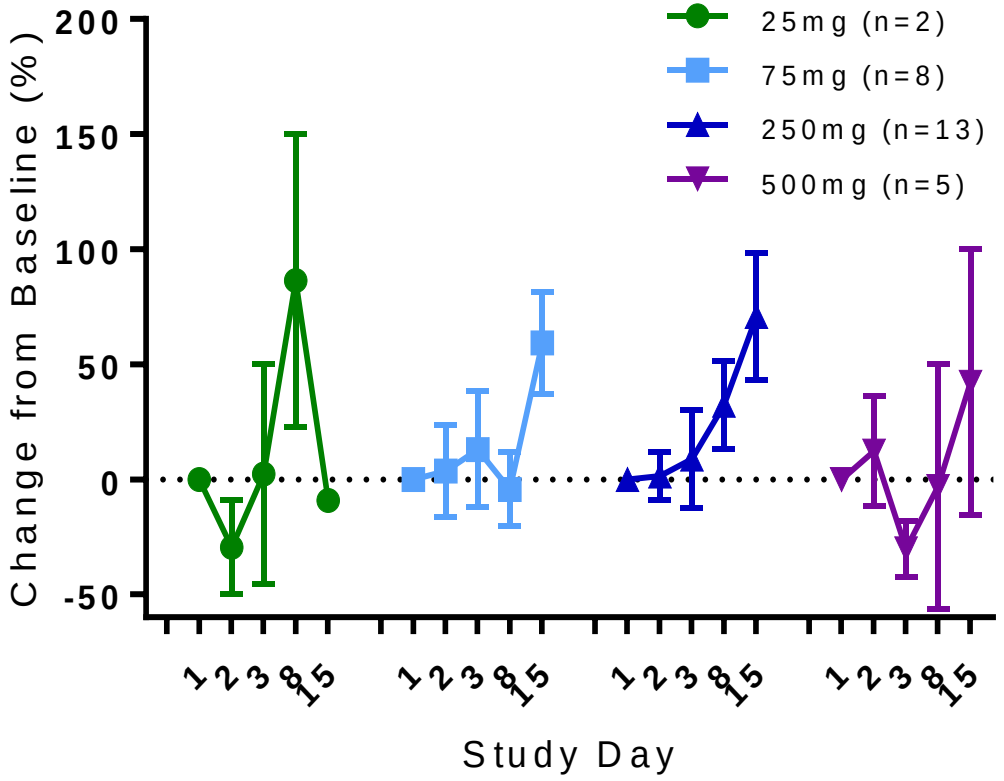


GITR Engagement Drives T-cell Proliferation

Changes from baseline in peripheral GITR+ CD4+ cells

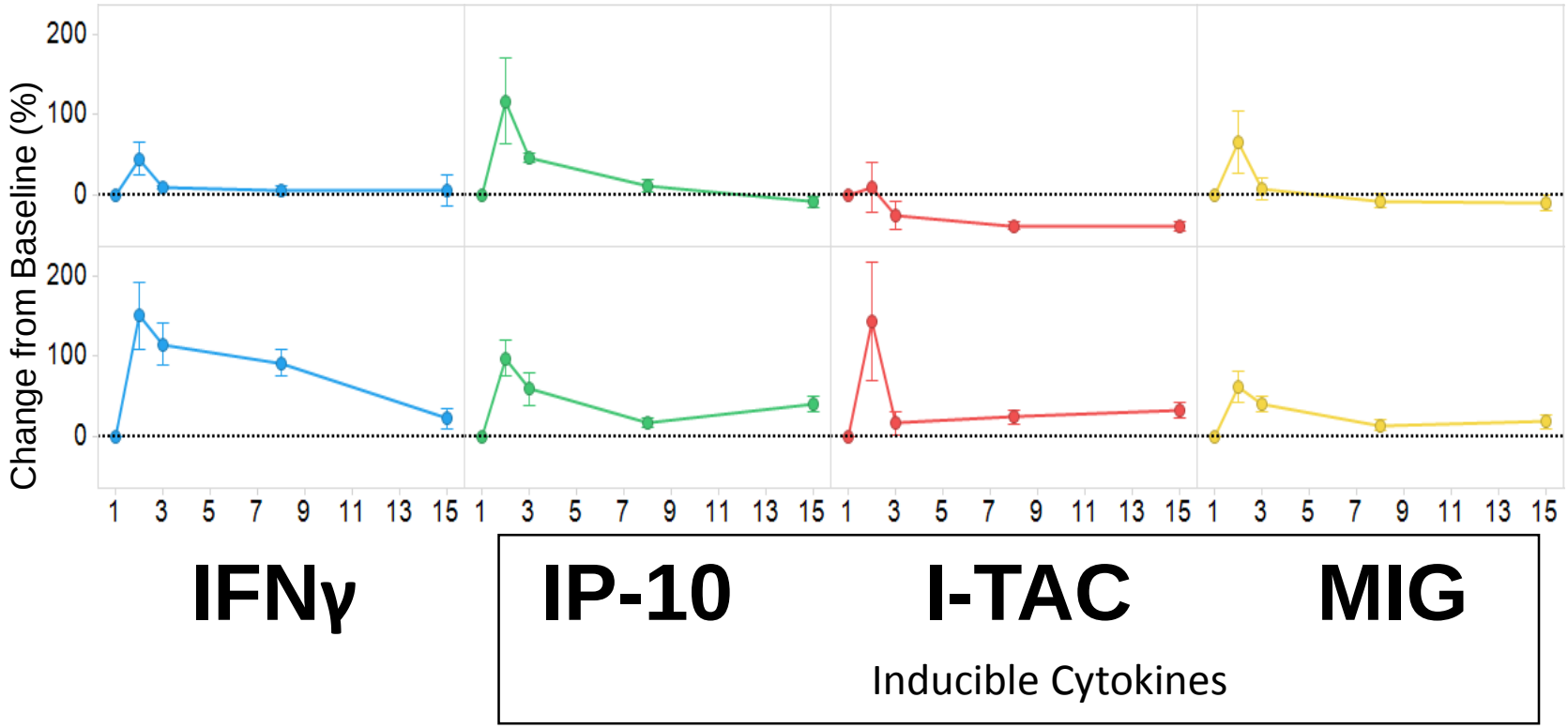


Changes from baseline in Ki-67 on peripheral CD4+ T cells



CD4+ memory T cells expressed 5-fold higher levels of GITR than CD8+ memory T cells

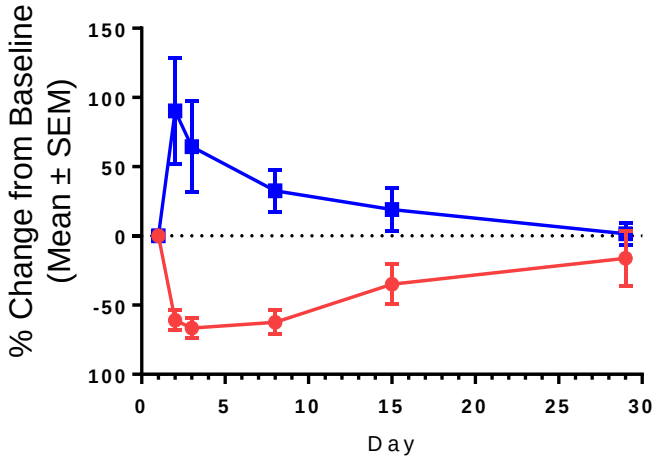
MEDI1873 Increases Peripheral IFNγ and Inducible Cytokines



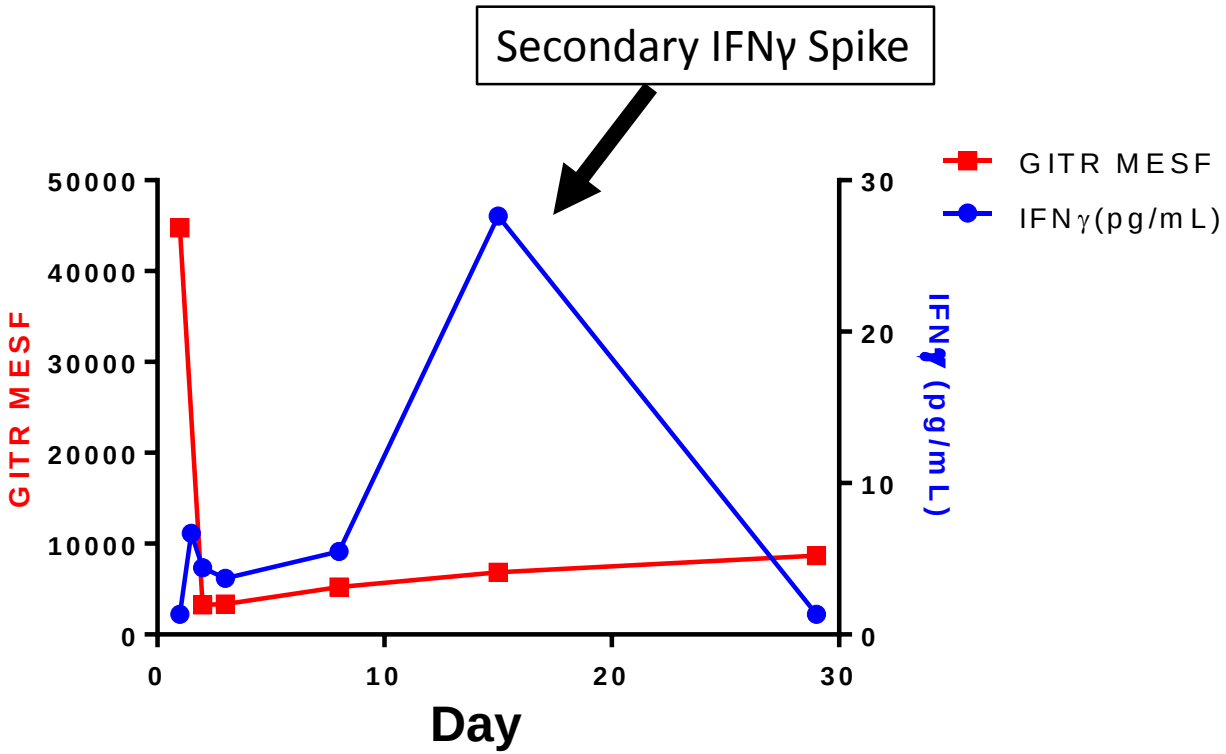
≤ 25 mg MEDI1873

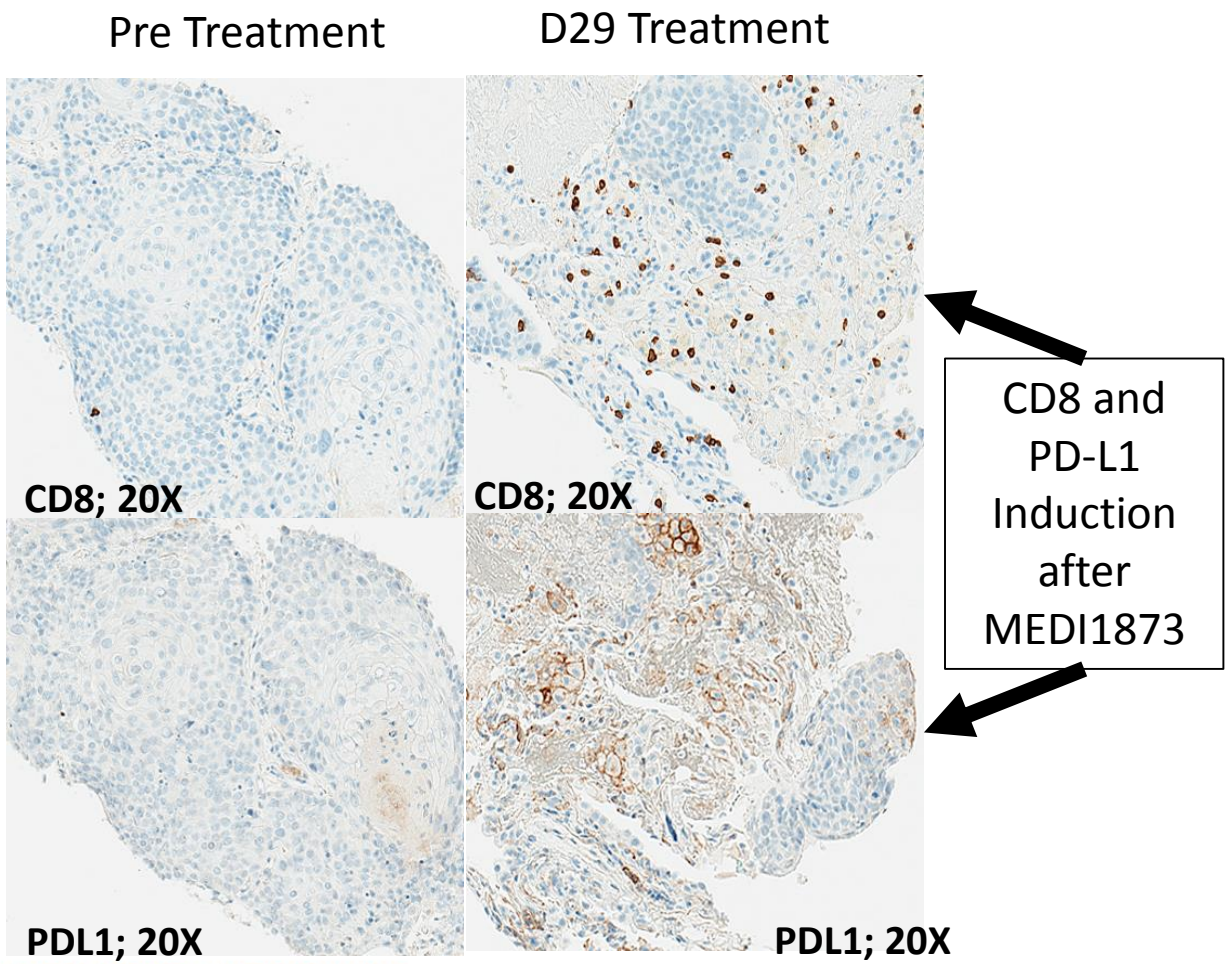
≥ 75 mg MEDI1873

Percent Change from Baseline in IFNγ and GITR



Patient with Highest Basal GITR Levels Shows Increased Peripheral and Tumoral Immune Activation





Conclusions

- MEDI1873 engages GITR on circulating memory T cells, and the duration of its activity is dose-correlated. This interaction induces robust PD effects as demonstrated by:
  - Elevations in peripheral IFNγ, IP-10, I-TAC, and MIG on Days 2 and 3 after the first dose
  - Elevations in peripheral Ki-67+ CD4+ T cells
  - Decreases in intratumoral GITR+ FOXP3+ cells (data on poster)
- These PD effects are consistent with the compound's mechanism of action and may be enhanced in patients with high baseline GITR expression. This information is critical for selecting dose and schedule.

Acknowledgments

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