Abstract TPS2686: A phase 1a/1b study to evaluate the safety, tolerability, pharmacokinetics, and anti-tumor activity of IMGS-001 in patients with relapsed or refractory advanced solid tumors.

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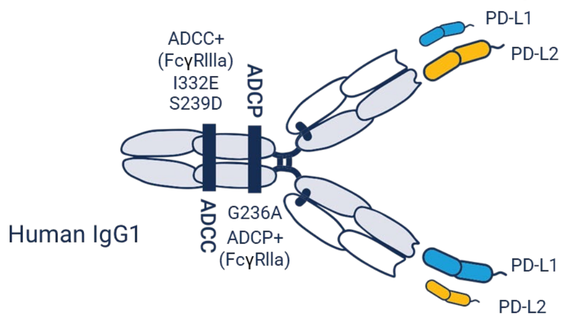
Background

As a significant portion of cancer patients present with "cold" tumors lacking pre-existing immune infiltration and/or significant numbers of mutational neoantigens, these tumors are almost completely resistant to checkpoint blockade and therefore represent a significant unmet medical need.

IMGS-001 is a fully human, dual specific immunoglobulin G1 (IgG1) monoclonal antibody (mAb) that binds both PD-L1 and PD-L2, silencing the entire PD-1 inhibitory circuit, with an engineered fragment crystallizable (Fc) region designed to induce robust antibody-dependent cell-mediated cytotoxicity (ADCC) and phagocytosis (ADCP).

IMGS-001 mediated killing of PD-L1+ and PD-L2+ tumor and stromal cells may reduce the level of multi-modal immune suppression throughout the tumor microenvironment while catalyzing cross presentation of tumor antigens to the adaptive immune system. IMGS-001 also blocks binding of the T cell co-inhibitory receptor PD-1 with its ligands, restoring activation and function to tumor-specific T cells.



IMGS-001 monoclonal antibody: Each antigen binding site is capable of binding either PD-L1 or PD-L2 and blocking their interactions with PD-1. Point mutations within the Fc region enhance the cell-mediated effector function of the antibody.

Methods

A Phase 1a/1b study has been opened to investigate IMGS-001's safety, anti-tumor activity, and pharmacokinetics (PK) in solid tumor patients (Protocol IMGS-001-011; NCT06014502).

Key Patient Eligibility Criteria:

- Histologically confirmed locally advanced, metastatic solid tumors;
  - Phase 1a: Solid tumors
  - Phase 1b: One of 5 select tumor types with prespecified tumor criteria AND confirmed PD-L1+ expression (CPS ≥ 5/TPS ≥ 5%)
- At least one measurable lesion as defined by RECIST 1.1
- ECOG performance status of 0-1
- Progressed after receiving appropriate lines of standard therapy known to potentially confer clinical benefit
  - Phase 1b Colorectal/ Ovarian: Failed SOC chemotherapy/ targeted therapy; PD-1 and PD-L1 naïve
  - Phase 1b Bladder/ TNBC/ Gastric-Esophageal: Failed SOC chemotherapy/ targeted therapy. Failed or intolerant to prior immune checkpoint therapy (e.g., anti-PD-1).

Exploratory Objectives:

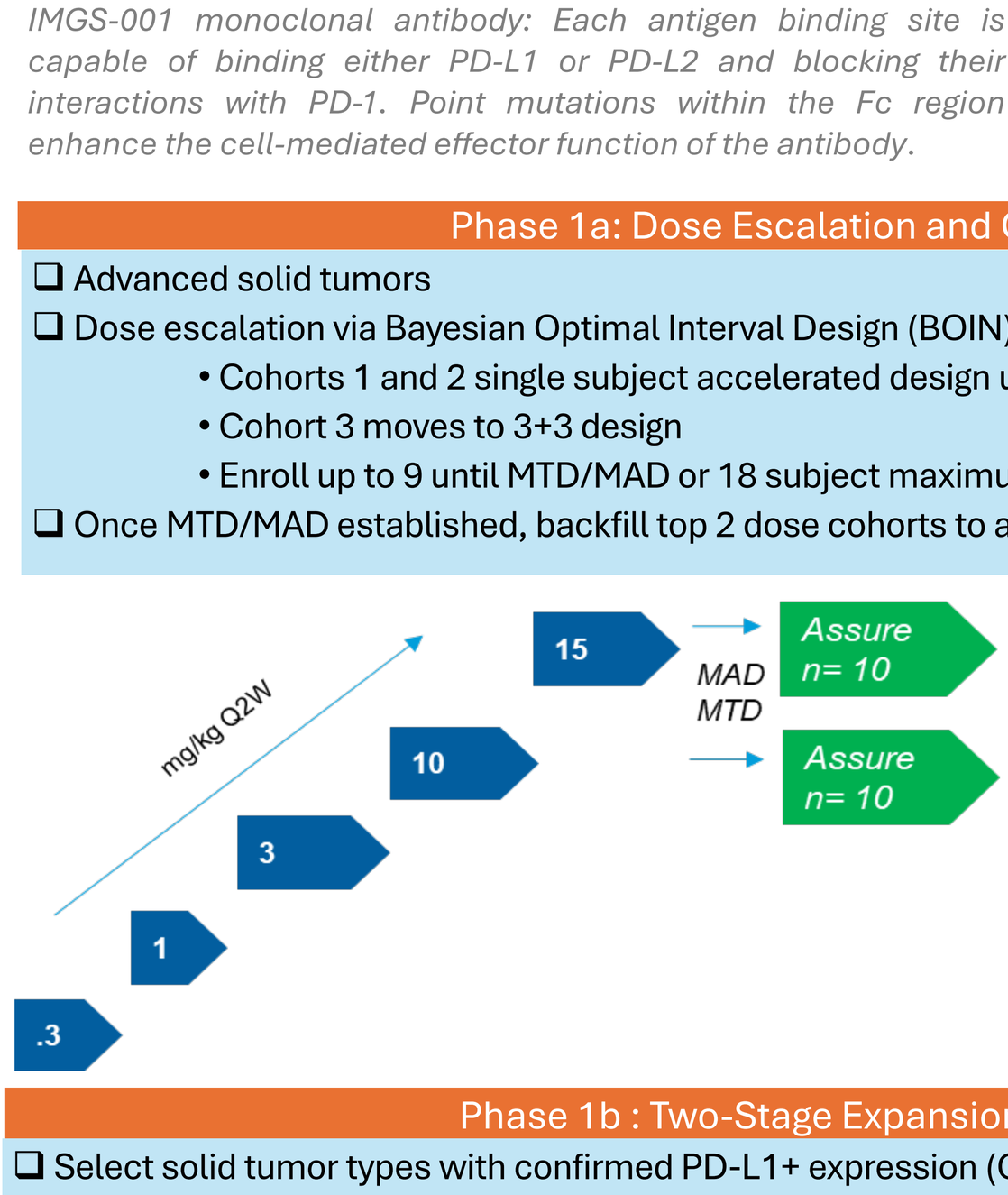
- Evaluate biomarkers of IMGS-001 correlated to treatment response or biological activity in peripheral blood and tumor tissue including expression of PD-L1, PD-L2 and 9p24.1 chromosomal amplification
- Evaluate impact of IMGS-001 on various measures of immune-regulatory effects in peripheral blood and tumor tissue

Study Plan

- Study enrollment: ~25 patients in Ph1a and up to 250 in Ph1b
- The first three cohorts (0.3, 1, and 3 mg/kg) have completed without any DLTs; cohort 4 (10 mg/kg) is actively enrolling
- Approximately 12-15 sites to be activated

Phase 1a: Dose Escalation and Optimization (Approximately 25 subjects)

- ❑ Advanced solid tumors
- ❑ Dose escalation via Bayesian Optimal Interval Design (BOIN) at maximum 18 subjects
  - Cohorts 1 and 2 single subject accelerated design until first Dose Limiting Toxicity (DLT) or Grade 2 adverse event (AE)
  - Cohort 3 moves to 3+3 design
  - Enroll up to 9 until MTD/MAD or 18 subject maximum
- ❑ Once MTD/MAD established, backfill top 2 dose cohorts to assure minimum 10 subjects at each dose (estimated 7-9 added)



Primary Objectives:

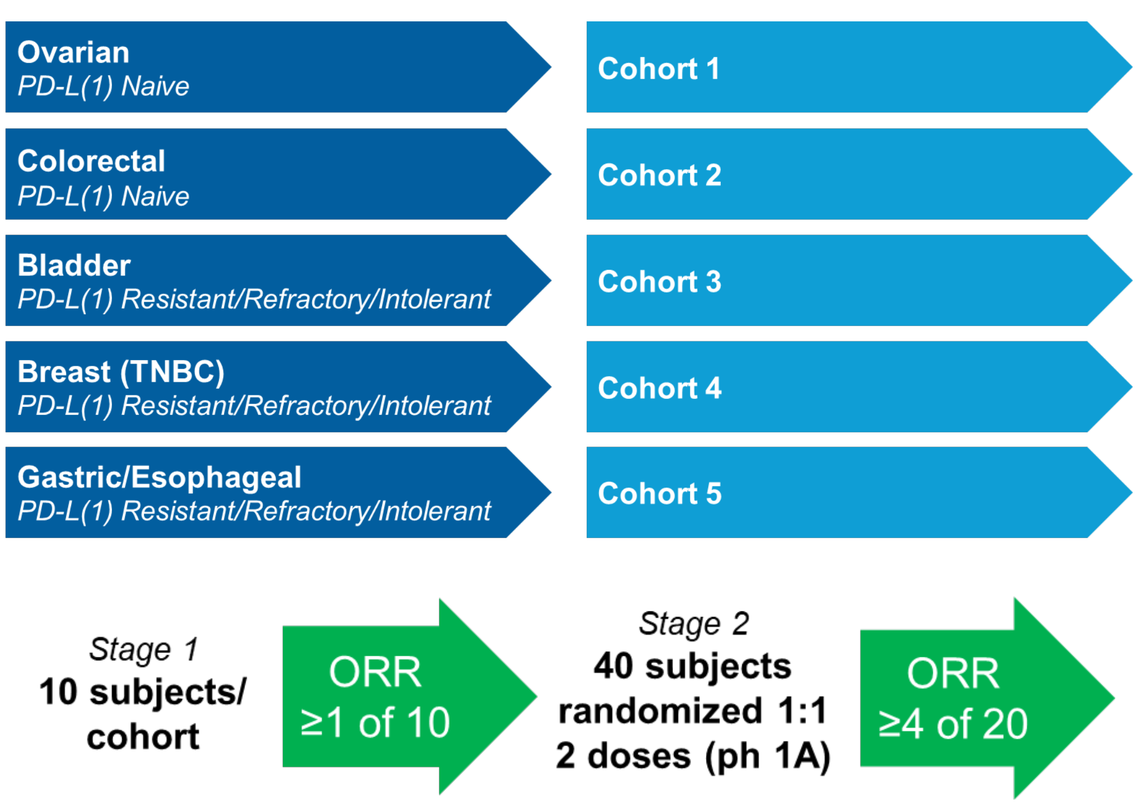
- Safety and tolerability by DLTs and AEs

Secondary Objectives:

- Determine MTD (maximum tolerable dose)
- Assess the pharmacokinetic profile
- Assess potential immunogenicity by anti-drug antibodies
- Assess preliminary anti-tumor activity including objective response rate (ORR) and progression-free survival (PFS)

Phase 1b : Two-Stage Expansion Tumor Cohorts (N=50-250 subjects)

- ❑ Select solid tumor types with confirmed PD-L1+ expression (CPS ≥ 5 or TPS ≥ 5%) per cohort
- ❑ Stage 1 cohorts proceed to Stage 2 if prespecified efficacy criteria are met
- ❑ Stage 2 cohorts are randomized equally between two Phase 1a doses for dose optimization
- ❑ Subjects failed SOC therapy (chemo/ targeted agents); colorectal/ ovarian PD-1/PD-L1 naive



Primary Objectives:

- Define a pharmacologically optimal dose (POD) after evaluating all available pharmacokinetic, pharmacodynamic, target engagement, efficacy, and safety data

Secondary Objectives:

- To evaluate anti-tumor activity (by iRECIST/ RECIST v1.1):
  - objective response rate (ORR)
  - duration of response (DOR)
  - disease control rate (DCR)
  - clinical benefit rate (CBR)
  - progression free survival (PFS)
  - overall survival (OS)
- To assess safety and tolerability by AE frequency/severity
- To assess the PK profile using population-based sampling
- To assess potential immunogenicity by anti-drug antibodies

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