

A PHASE 1B/2 STUDY OF A NOVEL ANTI-CTLA-4 NEOBODY™ ADG116 MONOTHERAPY AND IN COMBINATION WITH TORIPALIMAB (TORI; ANTI-PD-1 ANTIBODY) IN PATIENTS WITH ADVANCED/METASTATIC SOLID TUMORS

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Background The anti-CTLA-4 immuno-oncology therapy (IO) is limited in clinical efficacy due to its on-target toxicities. ADG116 is a fully human IgG1 monoclonal antibody that targets a unique and highly conserved epitope of CTLA-4. ADG116 enables a controlled T cell activation via partial CD80/86 ligand blockade and promotes strong Treg depletion in the tumor microenvironment via enhanced ADCC. In pre-clinical studies, ADG116 has been shown to be more potent and better tolerated than ipilimumab. We believe ADG116 can offer a better therapeutic window for this class of molecules, especially when combined with anti-PD-1 therapies.

Methods ADG116 monotherapy [10 dose levels from 0.003 to 15 mg/kg (mpk)] and ADG116 (3 or 6 mpk) plus Tori (240 mg) combination therapy were administered Q3W intravenously. The primary endpoints are safety and tolerability; the secondary endpoints are PK, ORR per RECIST 1.1, and PFS.

Results As of July 14, 2022, 45 patients (pts) were treated with ADG116 monotherapy, among which 3, 4, 6, 18, and 3 pts received 1, 3, 6, 10, and 15 mpk dose, respectively. The median age was 62; 62% received ≥ 3 prior lines of therapies, and 31% progressed after prior IO therapies. Only 1 DLT [Grade (G) 4 hyperglycemia] was observed (10 mpk), and MTD was not reached. Only 3 pts showed G3 or above treatment-related AEs (TRAEs); common TRAEs ($>10\%$) consisted of diarrhea, pruritis, and fatigue. Disease control rate is 35% across doses of ≥ 1 mg/kg (range 30-80%). An initial partial response was observed from a patient with Kaposi's sarcoma (15 mpk). Dose expansion is ongoing at 10 mpk.

Nine pts received ADG116/Tori combination therapy. The median age was 59; 11% received > 3 prior lines of therapies, and none had prior IO therapies. At 6 mpk ADG116/Tori, two pts developed DLTs (2/3; G3 myocarditis & G3 diarrhea). At 3 mpk ADG116/Tori, 1 DLT (1/6, G3 diarrhea) was observed, and five pts are still on treatment (2-5 cycles). One pt with recurrent platinum-refractory HNSCC has a confirmed complete response (CR) and is still on the study (cycle 5). Detailed safety and efficacy data from this study will be reported.

Conclusions ADG116 monotherapy has cleared multiple dose levels including 15 mpk, a dose higher than any reported anti-CTLA-4 class agents in the repeat dose setting. ADG116 (3 mpk)/Tori (240mg) Q3W continuous dosing showed a manageable safety profile and encouraging efficacy including CR, supporting its further clinical evaluation.

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Trial Registration Clinical trial identification: NCT04501276

Ethics Approval The study obtained ethics approvals from the following Ethics Committee(s)/Institutional Review Board(s), the number/ID of the approval(s),

1. Macquarie University HREC; ID: 520-2166-4335-513
2. National Health Group Central IRB; ID: 2021/00824
3. Bellberry HREC; ID: 2020-04-397-AA
4. Salus IRB; ID: IORG0005674
5. CHAMG IRB; ID: 2021-10-064-001-HE001
6. Yonsei University Health System IRB; ID: 2021-2495-002/4-2021-1454
7. Samsung Medical Center IRB; ID: 2021-09-053-001
8. WCG IRB; ID: 2021-4916

All participants of this clinical study gave informed consent before taking part.

Consent Written informed consent was obtained from patients for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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