A PHASE 1B/2, OPEN-LABEL, DOSE ESCALATION AND EXPANSION STUDY OF AN ANTI-CTLA-4 NEOBODY™ ADG116 IN COMBINATION WITH PEMBROLIZUMAB (ANTI-PD-1 ANTIBODY) IN PATIENTS WITH ADVANCED/METASTATIC SOLID TUMORS: A PRELIMINARY UPDATE

Anthony Tolcher, 1John Powderly, 2Kristine Shi, 3Songmao Zheng, 3Guizhong Liu, 3Jin Shang, 3Xinwei Wang, 3Wenda Li, 3Dana Lowe, 4Michael Chisamore, 3Peter Luo, 3Jiping Zha*.

1Next Oncology, San Antonio, TX, USA; 2Carolina Biooncology Institute, Huntersville, NC, USA; 3Adagene, San Diego, USA; 4Merck, Kenilworth, NJ, USA.

Background CTLA-4 as an immunotherapeutic target that has been challenged with limited single agent efficacy and high-grade toxicities in the clinic. ADG116 is a fully human anti-CTLA-4 IgG1 monoclonal antibody that targets a unique and a highly conserved epitope of CTLA-4 using the NEObody™ technology platform. ADG116 enables a safer T cell activation via partial CD80/86 ligand blockade and enhances the Treg depletion in the tumor microenvironment via a stronger ADCC. Preclinical studies demonstrated that ADG116 is more potent and better tolerated than ipilimumab. In a Phase 1 dose escalation study, single agent ADG116 has been well-tolerated up to 10 mg/kg when dosed intravenously, once every 3 weeks (Q3W); target lesion size reduction and stable diseases were observed in multiple heavily pre-treated patients including those bearing “cold” tumors. We propose that ADG116 in combination with pembrolizumab may enhance clinical antitumor activity through a simultaneous blockade of the PD-1/PD-L1 and CTLA-4 pathways while still maintaining a favorable safety profile.

Methods This is a Phase 1b/2, open label, multicenter, dose escalation and dose expansion study of ADG116 in combination with pembrolizumab in patients with advanced/metastatic solid tumors. During dose escalation, ADG116 and pembrolizumab are administered intravenously, Q3W. Primary endpoints are safety and tolerability. Secondary endpoints are PK, ORR per RECIST 1.1, and PFS.

Results As of June 30, 2022, 4 patients have been treated by ADG116 (3 mg/kg) + pembrolizumab (200 mg) combination therapy. Patients were 69 (47-74) years-old [median (range)] and have been heavily pre-treated before enrollment: all 4 (100%) had prior chemotherapy, 1 (25%) radiation therapy, 1 (25%) hormonal therapy; 2 (50%) received ≥ 3 prior lines of therapies, but none had been treated with an anti-PD-1/PD-L1, or an anti-CTLA-4 therapy. ADG116 + Pembro combination showed a manageable safety profile with no DLTs. Most common treatment-related adverse events were Grade 1 nausea (50%) and pruritis (50%). One Grade 3 AE (dehydration) was observed after repeated dosing in Cycle 3 (C3D12). Additional safety and efficacy data will be reported.

Conclusions The current safety data supports the regimen of ADG116 (3 mg/kg)+pembrolizumab (200 mg), Q3W for dose expansion, which is a higher dose than that approved for ipilimumab (1 mg/kg) when in combination with nivolumab for several cancer indications. Additional treatment-related adverse events are being generated to inform the safety, tolerability, and activity of ADG116 in combination with pembrolizumab.

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Trial Registration Clinical trial identification NCT04501276

REFERENCE

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. Salus IRB; ID: IORG0005674
2. Advarra IRB; ID: IORG0000635

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.