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, 1 John Powderly, 2 Kristine Shi, 3 Sangmao Zheng, 3 Guizhong Liu, 3 Jin Shang, 3 Nanwei Wang, 3 Wenda Li, 3 Dana Lowe, 4 Michael Chisamore, 3 Peter Luo, 3 Jing 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 dose expansion data are being generated to inform the safety, tolerability, and activity of ADG116 in combination with the anti-PD-1 therapy.

Acknowledgements: We would like to acknowledge the editorial support from Ami Celeste Knoefler

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.