SAFETY AND EFFICACY OF YBL-006, A NOVEL ANTI-PD-1 ANTIBODY, IN ADVANCED SOLID TUMORS INCLUDING G3 NET/NEC: RESULTS FROM A PHASE 1/2A STUDY

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Background YBL-006 is a novel human monoclonal antibody against programmed cell death 1 (PD-1). A first-in-human study was conducted to evaluate the safety, the recommended phase 2 dose, and anti-tumor efficacy. We have previously presented interim results, here we present the updated safety and efficacy results based on the data at the end of the study.

Methods A modified 3+3 design was utilized for the dose escalation (cohort A; CA) of 0.5, 2, 5, and 10 mg/kg. In the dose expansion (cohort B; CB), 200 mg every 2 weeks and 300 mg every 3 weeks were administered. Overall response rate (ORR) was evaluated per RECIST v1.1. Adverse events (AEs) were graded according to the CTCAE v5.0. For the exploratory biomarker analysis, tumor-infiltrating lymphocytes (TIL) analysis from H&E slides was conducted using Lunit SCOPE IO (an artificial intelligence-powered whole-slide image analyzer). Tumor mutational burden-high (TMB-H) and microsatellite instability-high (MSI-H) were also evaluated.

Results 10 (CA) and 56 (CB) patients (pts) were included in the safety population and 10 (CA) and 53 (CB) in the efficacy population. In the CA, 1 patient (pemphigus squamous cell carcinoma) experienced complete response (CR); 1 patient (anal squamous cell carcinoma) partial response (PR), and 3 pts stable disease (SD), with ORR 20%, disease control rate (DCR) 50%, and median progression-free survival (PFS) 4.5 months. In the CB, 1 patient (gastric cancer [GC]) experienced CR, 7 pts PR (neuroendocrine tumor/carcinoma [NET/NEC; N=2], GC [N=2], kidney cancer [N=1], nasopharyngeal cancer [N=1] and hurthle cell thyroid carcinoma [N=1]), and 21 pts SD with ORR 15.1%, DCR 54.7%, median duration of response 11.0 months and median PFS 2.8 months. The most reported treatment-related AEs were fatigue (N=3) and pruritus (N=2) in CA; fatigue (N=11), pruritis (N=7), and rash (N=5) in CB. In the overall efficacy population (both CA and CB), 50 pts were evaluated for TIL, and the ORR for the inflamed immune phenotype (IIP) was 38.5% (5/13 pts), which was higher than the Non-IIP (13.5% [5/37 pts]). Two (2/8 pts (25%) with TMB-H (both with GC) had CR and PR, respectively, and they were also MSI-H cases. Among 8 pts with grade 3 NET/NEC, two had PR and they were not MSI-H or TMB-H cases.

Conclusions YBL-006 showed favorable safety profiles. Although the number of enrolled pts was not large, preliminary efficacy data showed similar treatment outcomes compared to currently available anti-PD-1/PD-L1 antibodies. Interestingly, anti-tumor efficacy was also observed in grade 3 NET/NEC.

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Ethics Approval This study obtained ethics approvals at the following ethics/IRB’s:

- Seoul National University Hospital IRB: H-2003-032-1109
- Seoul National University bundang hospital IRB: B-2005/615-402
- Severance Hospital Yonsei University Health System IRB: 4-2021-0912
- Asan Medical Center IRB: 2021-1111
- Samsung medical-center IRB: 2021-06-213
- Macquarie University IRB: S2020631615298
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Participants gave informed consent before taking part.

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