Journal FOR Immunotherapy for Cancer (JITC) – Manuscript:

AdvanTIG-105: a phase I dose escalation study of the anti-TIGIT monoclonal antibody ociperlimab in combination with tislelizumab in patients with advanced solid tumors

Presenter: Dr Kao

Time for recording: 4 mins

Slide 1: Introduction to video abstract

- My name is Dr. Kao and I am a Medical Oncology Senior Staff Specialist at the Chris O'Brien Lifehouse in Sydney, Australia
- On behalf of my co-authors, this video abstract will provide an overview of our manuscript entitled 'AdvanTIG-105: a phase I dose escalation study of the anti-TIGIT monoclonal antibody ociperlimab in combination with tislelizumab in patients with advanced solid tumors'

Slide 2: Background

- There are two compounds of interest in this study; firstly, ociperlimab, which is a novel, humanized Fc-intact monoclonal antibody that binds to T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains, or TIGIT, with high affinity and specificity
- And secondly, tislelizumab, which is a monoclonal antibody targeting the immune checkpoint receptor, PD-1. It is engineered to minimize binding to Fc gamma receptors on macrophages and has shown promising efficacy, with a tolerable safety profile, for the treatment of solid tumors
- The mechanism of action of dual targeting with anti-TIGIT and anti-PD-1 monoclonal antibodies is demonstrated in figure 1 on the slide. Preclinical and clinical studies have shown that this dual targeting of tumors produces synergistic immune cell activation and enhanced antitumor activity
- Therefore, in this phase I study, we investigated the safety/tolerability, pharmacokinetics, and preliminary antitumor activity of ociperlimab plus tislelizumab in patients with advanced solid tumors

Slide 3: Study design

- AdvanTIG-105 is an open-label, multicenter, phase I, first-in-human dose-escalation trial
- The eligibility criteria are shown on the slides
- Eligible patients received one of four escalating doses (from 50 to 900 mg) of ociperlimab intravenously as a single agent on Day 1 of Cycle 1 and intravenous tislelizumab 200 mg on Day 8. If tolerated, patients continued to receive their cohort dose of ociperlimab in combination with tislelizumab 200 mg sequentially on Day 29 and every 3 weeks thereafter until discontinuation
    - Dose escalation for ociperlimab was planned with four dose levels (50 mg, 150 mg, 450 mg, and 900 mg) according to a modified 3+3 design
    - An additional dose level of ociperlimab 1800 mg was also assessed to evaluate whether a higher dose would affect the efficacy and safety of this combination

- In this study, the primary endpoints were safety, determination of the maximum tolerated (or administered) dose, and the recommended phase II dose
- Secondary endpoints are shown on the slide

Slide 4: Safety (all grade and grade ≥3 TEAEs)

- There was a total of 32 patients in the safety analysis set. The safety profile of ociperlimab plus tislelizumab is shown in the table
- Thirty-one patients experienced at least one treatment-emergent adverse event and 20 patients experienced at least one treatment-emergent adverse event of grade 3 or higher.
    - Serious treatment-emergent adverse events occurred in 16 patients
- The bar graph shows the most common treatment-emergent adverse events of all grades and of grade 3 or higher
- There were no treatment-emergent adverse events leading to death

Slide 5: Antitumor activity

- Antitumor activity was assessed in 30 efficacy-evaluable patients, for whom the overall response rate was 10.0%, with a partial response observed in three patients. The disease control rate was 50.0%, including an additional 12 patients with stable disease
- The waterfall plot on the right shows the distribution of responses across the dose cohorts
- The median duration of response across all cohorts was 3.6 months

Slide 6: Conclusions

- In summary, the combination of ociperlimab plus tislelizumab was well tolerated in patients with advanced solid tumors, and preliminary anti-tumor activity was observed with 450 mg, 900 mg, and 1800 mg ociperlimab
- This study established that the recommended phase II dose of ociperlimab is 900 mg plus tislelizumab 200 mg every 3 weeks, and in terms of safety, the types and severity of adverse events observed were consistent with tislelizumab monotherapy; no dose-limiting toxicities were observed
- Given that many patients treated with anti-PD-1 monotherapies do not respond to treatment or experience relapse, multiple phase II/III trials of ociperlimab plus tislelizumab are underway in a range of solid tumors to further investigate the efficacy and safety of this combination
- Thank you for listening