The safety, pharmacokinetics (PK), pharmacodynamics (PD) and clinical efficacy of uliledlimab (TJ004309), a differentiated CD73 antibody, in combination with atezolizumab in patients with advanced cancer

Francisco Robert, MD1, Estefania E. Dumbrava, MD2, Yan Xing, MD3, Elizabeth Mills, MSN, CRNP1, James Lawrence4, … Xu, MD, PhD5, Yuan Meng, MD6, Linda Lee, PharmD5, Yonggang Zhao, PhD5, Zhengyi Wang, PhD6, Joan Huangrong Shen, MD, PhD6,

METHODS

Study Design

• NCT03835949 is an open label, phase 1 study to evaluate the safety, tolerability, pharmacokinetic and pharmacodynamics of uliledlimab in combination with atezolizumab as a monotherapy (3-week run-in) followed by combination therapy with atezolizumab in patients with solid tumors.

• No dose-limiting toxicity (DLT) was observed and MTD (maximum tolerated dose) was not reached.

• All TRAEs were either Grade 1 or Grade 2.

• The majority of TRAEs occurring first the first infusion, and all were well managed.

RESULTS

Patient Demographics

• Twenty patients with advanced relapsed or refractory solid tumors have been enrolled.

• Among 13 efficacy-evaluable patients dosed ≥ 10 mg/kg, complete response (CR = 1) and partial response (PR = 2) were observed in 3 patients (ORR = 23%), together with 3 stable disease (SD) patients (DCR = 46%).

• The duration on treatment for the 6 patients (CR, PR and SD) ranged from 187 to 485 days. As of April 9, 2021, 3 patients remain on study.

• Two patients with NSCLC dosed at 15 mg/kg QW and 20 mg/kg Q3W achieved PR.

• One patient with sarcoma and the other received prior PD-L1 therapy.

Pharmacokinetics

• Uliledlimab exhibited a linear PK profile at doses ≥ 10 mg/kg, indicating target saturation.

• Effective half-life of 9 days exhibited by population PK modeling supported Q3W dosing interval.

•Confirmed ADA positivity in three patients appears to have no impact on safety or PK.

Pharmacodynamics

• A sustained decrease in free soluble CD73 level was achieved in monotherapy and in combination with atezolizumab in all patients treated with uliledlimab.

• Complete saturation of CD73 receptor occupancy on peripheral CD19+ B cells was reached throughout the dosing period of uliledlimab by QW or Q3W dosing regimen.

• The full saturation was observed in each dose cohort at or above 10 mg/kg.

CONCLUSIONS

• Uliledlimab is safe and well-tolerated up to 20 mg/kg Q3W and 15 mg/kg QW as a monotherapy and in combination therapy with atezolizumab 1200 mg Q3W. No DLT was observed and MTD was not reached.

• Full saturation of circulating and cell-bound CD73 was achieved at doses ≥ 20 mg/kg.

• Linear PK profile was observed at the doses ≥ 10 mg/kg following a single dose.

• The PK profile of uliledlimab supports Q3W dosing.

• There was evidence of clinical activity (1 CR, 2 PR and 3 SD) in both PD-L1+1 treatment naïve and refractory cancer patients, following the treatment with uliledlimab and atezolizumab in this Phase I study.

• Higher tumor CD73 and PD-L1 co-expression was found in all responders compared to that in non-responders, indicating a potential correlation that warrants further investigation.

• Further evaluation of uliledlimab in combination with checkpoint inhibitors in NSCLC and ovarian cancers will be conducted in a separate clinical trial.