Safety and antitumor activity of AK104, a bispecific antibody targeting PD-1 and CTLA-4, in patients with mesothelioma which is relapsed or refractory to standard therapies


1 Medical Oncology, Linear Clinical Research, Nedlands, Australia, 2 Medical Oncology, Monash Health, Melbourne, Australia, 3 Medical Oncology, Austin Health, Heidelberg, Australia, 4 Medical Oncology, St Vincent’s Hospital, Sydney, Australia, 5 Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia, 6 Medical Oncology, Icon Cancer Centre, South Brisbane, Australia, 7 Clinical Development, Akeso Biopharma Co. Ltd., Zhongshan, China

Background

Mesothelioma patients (pts) have a poor prognosis with limited treatment options. Platinum/pemetrexed chemotherapy is standard, although a phase 3 trial evaluating nivolumab plus ipilimumab in previously untreated pts with malignant pleural mesothelioma (MPM) recently disclosed statistically significant improvement in overall survival (OS) compared to chemotherapy. Furthermore, dual blockade of PD-1 and CTLA-4 in pts with recurrent MPM can result in improved disease control (DCR at 12 weeks 50%) but are limited by high rates of toxicity (26% Grade 3-4 treatment-related adverse events [TRAE]). Here, we present initial safety and efficacy data for AK104, a bispecific antibody targeting PD-1 and CTLA-4, in mesothelioma pts who have failed prior systemic therapies.

Methods

Pts with mesothelioma relapsed or refractory to at least first line chemotherapy were enrolled in an ongoing phase 1a/1b study of AK104-101 in advanced solid tumors (NCT03261011). Tumor assessments based on RECIST 1.1 were performed once every 2 cycles/8 weeks.

Results

As of 06 May 2020, 18 mesothelioma pts have been enrolled. Tumor assessment data was available for 13 pts enrolled in dose escalation cohorts at 4 mg/kg, 6 mg/kg, 10 mg/kg and 450 mg AK104 Q2W IV (28-day cycles), of which 12 were naïve to prior anti-PD-(L)1 therapy while 1 had prior anti-PD-1 treatment. Confirmed objective response rate (ORR) was 15.4% (2/13; duration of response [DoR]: 3.6+ and 12.9 months) and DCR at 8 weeks was 84.6% (11/13). Tumor shrinkage was observed in 7 pts (53.8%). Progression free survival at 6 months was 64.5%. Duration of stable disease for the pt (6mg/kg Q2W) who had prior anti-PD-1 therapy was 7.2 months. Three out of 18 pts (16.7%) had a Grade 3-4 TRAE (fever, type 1 diabetes mellitus and infusion-related reaction [IRR]); and another 9 subjects experienced Grade 1-2 TRAEs. Most commonly reported TRAEs were rash in 6 pts and IRRs in 5 pts (Grade 1-2 in 4 pts).

Conclusions

The initial results from Study AK104-101 suggest that AK104 is well-tolerated and possesses encouraging antitumor activity against mesothelioma. AK104 for the treatment of mesothelioma should be further evaluated.

Clinical trial identification

NCT03261011.

Legal entity responsible for the study

Akesobio Australia Pty Ltd.

Funding

Akesobio Australia Pty Ltd.

Disclosure

M. Millward: Advisory/Consultancy, Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy, Travel/Accommodation/Expenses: Bristol-Myers Squibb; Advisory/Consultancy: Merck Sharp & Dohme; Advisory/Consultancy: Pfizer; Advisory/Consultancy, Travel/Accommodation/Expenses: Roche; Advisory/Consultancy: Novartis; Advisory/Consultancy: Takeda. A. Prawira: Research grant/Funding (institution): Akeso Biopharma; Research grant/Funding (institution): Five Prime; Research grant/Funding (institution): Arcusbio;
Research grant/Funding (institution): Pfizer; Research grant/Funding (institution): Bayer; Research grant/Funding (institution): Beigene; Research grant/Funding (institution): Roche/Genentech; Research grant/Funding (institution): BMS; Research grant/Funding (institution): Apollomics; Research grant/Funding (institution): Corvus; Research grant/Funding (institution): Macrogenics; Research grant/Funding (institution): Henlius; Research grant/Funding (institution): Eli Lilly; Research grant/Funding (institution): MSD; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Virogin; Research grant/Funding (institution): Janssen; Research grant/Funding (institution): GSK; Research grant/Funding (institution): QBiotics. B. Tran: Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Research grant/Funding (institution), Travel/Accommodation/Expenses: Amgen; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self), Travel/Accommodation/Expenses: Astellas; Advisory/Consultancy, Research grant/Funding (self), Travel/Accommodation/Expenses: Bayer; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self); BMS; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self); Research grant/Funding (institution), National Coordinator for THOR study: Janssen-Cilag; Advisory/Consultancy, Research grant/Funding (self), Research grant/Funding (institution): MSD; Advisory/Consultancy, Research grant/Funding (institution): Novartis; Advisory/Consultancy, Travel/Accommodation/Expenses: Sanofi; Advisory/Consultancy: Tolmar; Advisory/Consultancy, Research grant/Funding (self): Ipsen; Advisory/Consultancy: IQVIA; Research grant/Funding (self), Research grant/Funding (institution): AstraZeneca; Research grant/Funding (self): Pfizer; Research grant/Funding (self), Research grant/Funding (institution): Akeso Biopharma; Research grant/Funding (institution): MedImmune; Research grant/Funding (institution): Aptevo. X. Jin, B. Li, M. Wang, K.Y. Kwek: Shareholder/Stockholder/Stock options, Full/Part-time employment, Officer/Board of Directors: Akeso Biopharma. Y. Xia: Shareholder/Stockholder/Stock options, Full/Part-time employment, Officer/Board of Directors: Akeso Biopharma. J. Desai: Advisory/Consultancy: Amgen; Advisory/Consultancy, Research grant/Funding (institution): Novartis; Advisory/Consultancy, Research grant/Funding (institution): Eli Lilly; Advisory/Consultancy, Research grant/Funding (institution): GSK; Advisory/Consultancy: Pierre-Fabre; Advisory/Consultancy: Eisai; Research grant/Funding (institution): Roche/Genentech; Research grant/Funding (institution): BMS; Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Beigene. All other authors have declared no conflicts of interest.