341 A PHASE IB EXPANSION COHORT OF PIXATIMOD PLUS NIVOLUMAB IN PREVIOUSLY TREATED, MICROSATELLITE STABLE METASTATIC COLORECTAL CANCER (MSS MCRC)

[1]Charlotte Lemech*, [2]Keith Dredge, [2]Darryn Bampton, [2]Edward Hammond, [3]Andrew Clouson, [4]Nigel Waterhouse, [4]Amanda Stanley, [4]Lucie Leveque-ElMouttie, [4]Grace Chojnowski, [5]Andrew Haydon, [6]Nick Pavlakis, [3]Matthew Burge, [7]Michael Brown, [8]David Goldstein. *[1]Scientia Clinical Research Pty Ltd, Randwick, Australia; [2]Zucero Therapeutics Ltd, Brisbane, Australia; [3]Royal Brisbane and Women's Hospital, Brisbane, Australia; [4]QIMR Berghofer, Brisbane, Australia; [5]The Alfred Hospital, Melbourne, Australia; [6]Royal North Shore Hospital, Sydney, Australia; [7]Royal Adelaide Hospital, North Ice, Adelaide, SA, Australia; [8]Prince of Wales Hospital, Sydney, Australia*

Background Pixatimod is a novel immunomodulatory agent which stimulates dendritic cells (DC) via Toll-Like Receptor 9 (TLR9) pathway to activate natural killer (NK) cells.[1] It also enhances T cell infiltration into tumors when combined with PD1 inhibitors in vivo.[2] We report on safety, pharmacodynamics (PD), and antitumor activity of pixatimod plus nivolumab in a cohort of previously treated MSS mCRC subjects.

Methods Eligible MSS mCRC patients (ECOG≤1) with a median of 3 lines of previous treatment received 25 mg pixatimod once weekly as a 1-hour i.v. infusion plus nivolumab (240 mg, every other week) until disease progression or discontinuation due to intolerability. Primary and secondary objectives included the assessment of safety and antitumor activity per RECIST v1.1 at the recommended dose, and evidence of immune activation in peripheral blood mononuclear cells (PBMC), plasma cytokines/chemokines, and paired tumor tissue biopsies, where available.

Results Thirty-three subjects with MSS mCRC (42% male) started treatment. Median age was 58 (range 35–80), median number of previous lines of chemotherapy was 3 (range 1–6), ECOG PS 0/1 was 67%/33%, 64% had target liver metastases, and primary tumor site was right-sided/transverse colon in 21% and left-sided colon/rectum 79%. Median number of cycles completed was 2 (range 0–13). Treatment-related AEs led to treatment discontinuation in 2 patients (autoimmune hepatitis and pneumonitis). Ten Grade 3 treatment-related AEs were reported in 4 subjects (12%). Thirty subjects received at least one cycle of treatment (1-month), with 25 subjects having initial post-baseline assessment scans > 6 weeks (as per RECIST v1.1). Of these, 3 subjects had confirmed partial responses and 8 had stable disease. Lower Pan-immune-Inflammatory Value (PIV = Neutrophils x Platelets x Monocytes/Lymphocytes) at screening were associated with clinical benefit (PR/SD). Post-treatment increases in plasma IP-10 and IP-10/IL-8 ratio, effector memory (CD45RA-CCR7-) CD4+ and CD8+ T cells, and Ki-67 expression in CD4+ and CD8+ T cells from PBMC were also detected in the clinical benefit cohort compared to subjects with progressive disease. Conversely, plasma levels of IL-6 were significantly lower in patients with clinical benefit. Analyses of pre- & on-treatment biopsies from the only PR patient with available paired biopsies demonstrated an increase in T cell infiltration.

Conclusions Pixatimod is well tolerated at 25 mg in combination with a standard dose of nivolumab. The efficacy signal and pharmacodynamic changes in MSS mCRC warrants further investigation of pixatimod plus nivolumab for this patient population.

Acknowledgements Research Funding provided by Zucero Therapeutics Ltd and Bristol Myers Squibb (BMS), Australia.

Trial Registration

Clinical trial information ACTRN12617001573347

REFERENCES

1.. Brennan TV, Lin L, Brandstadter JD, Rendell VR, Dredge K, Huang X, *et al*. Heparan sulfate mimetic PG545-mediated antilymphoma effects require TLR9-dependent NK cell activation. *J Clin Invest* 2016;**126**(1):207–19.

2.. Hammond E, Haynes NM, Cullinane C, Brennan TV, Bampton D, Handley P, *et al*. Immunomodulatory activities of pixatimod: emerging nonclinical and clinical data, and its potential utility in combination with PD-1 inhibitors. *J Immunother Cancer* 2018;**6**(1):54.

Ethics Approval The clinical trial entitled "An open-label, multi-centre Phase Ib study of the safety and tolerability of IV infused PG545 in combination with nivolumab in patients with advanced solid tumours with an expansion cohort in patients with metastatic pancreatic cancer. Protocol ZU545102" obtained ethics approval from the Royal Adelaide Hospital (HREC Reference number, HREC/17/RAH/195 and the CALHN Reference number, R20170515) and Bellberry Limited (Application No: 2018-08-695). All participants in the study gave informed consent before taking part in ZU545102.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.341

J Immunother Cancer: first published as 10.1136/jitc-2021-SITC2021.341 on 10 November 2021. Downloaded from http://jitc.bmj.com/ on September 9, 2024 by guest. Protected by copyright.