A First-in-human phase I dose escalation of YH001, an anti-CTLA-4 monoclonal antibody (mAb) in combination with Toripalimab (anti-PD-1 mAb) in patients with advanced solid tumors (NCT04357756)

Vinod Ganju[1],Adam Cooper[2],Kate Wilkinson[2], Gao Bo[3],

1.PSEHOG. Frankston, Australia; 2.St George Private Hospital, Kogarah, Australia, 3.Blacktown Hospital, Blacktown, Australia

Abstract #: 2577

BACKGROUND

- YH001,a humanized anti -hCTLA-4 IgG1 mAb that relieves CTLA-4-mediated immunosuppression, and thereby enhances the T-cell-mediated antitumor immune response.
- Preclinical data have shown potent anti-cancer activity when combined with anti-PD-1 antibodies.

METHODS

Primary endpoint

- safety/tolerability and MTD/RP2D of YH001+Toripalimab

Secondary endpoint

- PK and preliminary anti-tumor activities (ORR, DCR etc.)

Key Inclusion criteria:

- Patients with advanced solid tumor progressed on after treatment with standard therapies or intolerant of standard care.
- Serum creatinine <1.5 x ULN, and calculated creatinine clearance (CrCL) > 40 ml/min

Key Exclusion criteria:

- Grade ≥3 irAEs or irAEs that lead to discontinuation of prior immunotherapy
- Prior anti-CTLA-4 checkpoint inhibitors

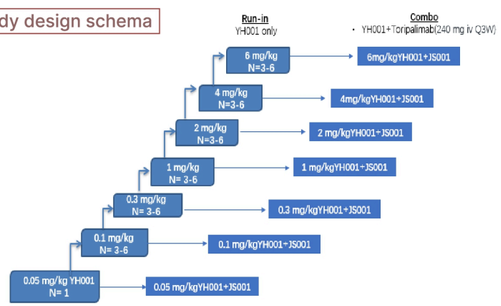
Dosing regimen:

- YH001: 0.05-6 mg/kg
- Toripalimab: 240 mg (fixed)
- iv Q3W

Study design

This is an ongoing phase 1 dose-escalation study conducted in Australia. An accelerated titration method followed by the standard "3 + 3" dose escalation algorithm was utilized. Patients with advanced solid tumors received YH001 by IV administration Q3W as monotherapy at 0.05 to 6.0 mg/kg for the first cycle (21 days) followed by YH001 combination with Toripalimab at 240 mg Q3W in an accelerated "3+3" design.

Figure 1 Study design schema



Main Takeaway

YH001 was well tolerated up to 1 mg/kg dose levels when combined with Toripalimab and has shown disease control activity in patients with advanced solid tumors.

vg@paso.com.au

RESULTS

Table 1: Patient demographics and disease characteristics (n=10)
Cutoff date: 31-Dec-2020

Age; years	Median(range)	62(46-74)
ECOG	0	8
	1	2
Prior lines of therapy	Median(range)	2 (1-4)
Prior immunotherapy	Yes	1
	No	9
Primary tumor type	Tongue Carcinoma	2
	Pancreatic Head Tumor	1
	Nasopharyngeal Carcinoma	1
	Colorectal Carcinoma	2
	Gastric Cancer	1
	Gastroesophageal Junction Cancer	1
	Uterus Leiomyosarcoma	1
	Non-small-cell Lung Cancer	1

Treatment- related Adverse Events

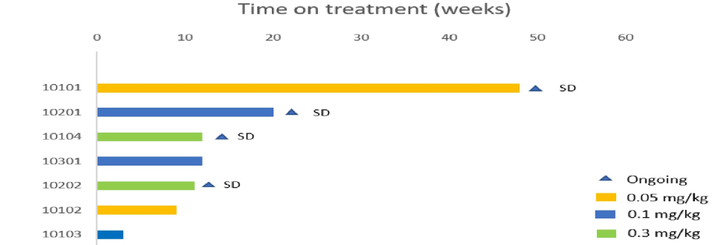
Table 2: All the treatment-related Adverse Events
Cutoff date: 31-Dec-2020

Dose level	AE term	Relationship to YH001	Relationship to Toripalimab	Grade
Cohort 1 (0.05mg/kg)	Hypotension	Possibly Related	Unlikely to be related	1
	Dry skin	Possibly Related	Possibly Related	1
	Pruritus	Probably related	Unlikely to be related	1
	Maculopapular rash	Probably related	Probably related	2
Cohort 2 (0.1mg/kg)	Rash pruritus	Related	Unlikely to be related	1
	Hyperthyroidism	Related	Related	1
	Hypothyroidism	Related	Related	2
	Rash Macular	Related	Related	1
	Rash	Related	Related	1
	Rash pruritus	Possibly Related	Possibly Related	1
Cohort 3 (0.3mg/kg)	Fatigue	Related	Unlikely to be related	1
	Fatigue	Possibly Related	Unlikely to be related	1

As of 31-Dec-2020 data cut-off, no dose limiting toxicities (DLT) were observed. No Serious Adverse Events (SAEs) or AEs leading to treatment discontinuation were reported. Twelve YH001 drug related AEs were reported.

Outcome response for evaluable patients

As of 31-Dec-2020, Among 7 patients having imaging tumor assessment by RECIST v1.1, there were 4 SD, including 1 at 0.05 mg/kg with tongue carcinoma at week 8 assessment, 1 at 0.1 mg/kg with nasopharyngeal carcinoma at week 8 and 15 assessment, 2 at 0.3 mg/kg with gastroesophageal junction cancer and uterus leiomyosarcoma at week 8.



FUTURE DIRECTIONS FOR RESEARCH

We will continue to complete the dose escalation study and initiate a phase II study to further verify the safety of the combination treatment and efficacy in select tumor types.

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For any questions regarding this poster, please contact bd@eucure.com.