# 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)

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Abstract #: 2602

## 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

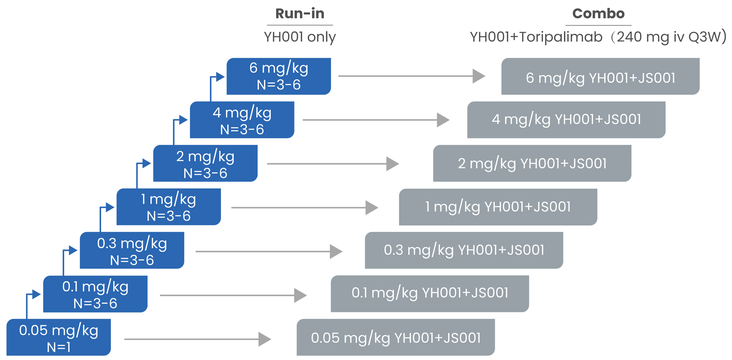
### Dosing regimen:

- 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 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 4 mg/kg dose levels when combined with Toripalimab and has shown encouraging antitumor activity in patients with advanced solid tumors.**

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## RESULTS

As of 31-Dec-2021 data cut-off, 24 pts with advanced solid tumors were enrolled and dosed at 0.05 mg/kg (n = 2), 0.1 mg/kg (n = 3), 0.3 mg/kg (n = 3) ,1mg/kg (n = 5), 2mg/kg (n = 5), 4mg/kg (n = 3) and 6mg/kg (n = 3). Baseline ECOG scores were 0 (n = 14), 1 (n = 10) with all pts progressed after a median of 2 prior lines of available standard therapy (range 1-5) including 5 pts progressed after prior immunotherapy of anti-PD-1 antibody.

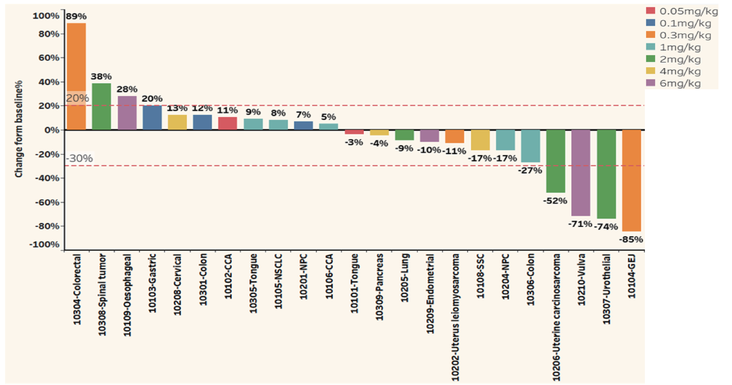
### Safety and Tolerability

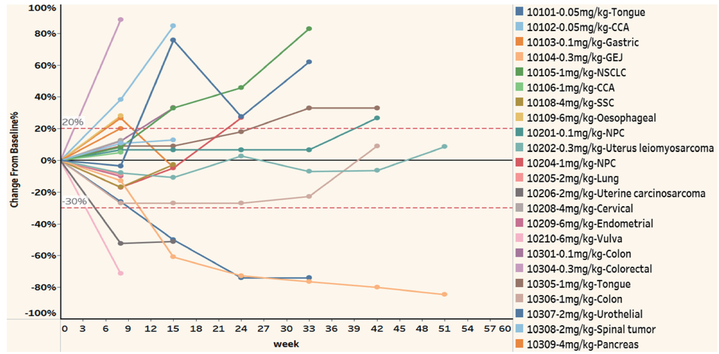
- 18 pts (75%) had 63 TRAEs of any level, including 28 G1 TRAEs, 29 G2 TRAEs.
- 6 cases of G3 or above TRAEs have been reported in 5 pts at 0.3 mg/kg, 4 mg/kg and 6 mg/kg dose level respectively, including 1 G3 colitis, 1 G4 thrombocytopenia, 1 G3 Enterocolitis, 1 G3 Rash, 1 G3 Pruritus and 1 G3 hepatitis.
- 2 of the first 3 pts at MAD (6mg/kg) met protocol defined DLT in Combo phase.
- No death events due to TRAEs.

| | Cohort 1 (0.05mg/kg) N=2 | Cohort 2 (0.1mg/kg) N=3 | Cohort 3 (0.3mg/kg) N=3 | Cohort 4 (1mg/kg) N=5 | Cohort 5 (2mg/kg) N=5 | Cohort 6 (4mg/kg) N=3 | Cohort 7 (6mg/kg) N=3 | Total N=24 |
|---|---|---|---|---|---|---|---|---|
| Any YH001 drug-related TEAEs | 5 | 6 | 11 | 20 | 6 | 1 | 14 | 63 |
| Grade 1 | 5 | 5 | 3 | 1 | 5 | 0 | 6 | 28 |
| Grade 2 | 0 | 1 | 7 | 16 | 1 | 0 | 4 | 29 |
| ≥Grade 3 | 0 | 0 | 1 | 0 | 0 | 1 | 4 | 6 |
| DLT | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 |
| Drug-related SAE | 0 | 0 | 1 | 0 | 0 | 1 | 4 | 6 |
| AE leading to death | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

### *Outcome response for evaluable patients*

- Among the 23 pts having imaging tumor assessment by RECIST v1.1, 4 achieved PR and 9 achieved SD in Best of Response. ORR and DCR were 17.4%, 56.5% respectively.
- 1 subject with gastroesophageal junction carcinoma at 0.3 mg/kg has achieved PR since the 2nd tumor assessment, target lesion decreased by up to 84.5% from baseline.
- 1 subject with urothelial carcinoma at 2mg/kg progressed after prior anti-PD-1 antibody has achieved PR since the 2nd tumor assessment, target lesion decreased by up to 74% from baseline.
- 1 subject with uterine carcinosarcoma at 2mg/kg has achieved PR since the 1st tumor assessment, target lesion decreased by up to 52.3% from baseline.
- 1 subject with vulva adenocarcinoma at 6mg/kg has achieved PR since the 1st tumor assessment, target lesion decreased by up to 71.4% from baseline.




## 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.