Safety and efficacy of Wnt inhibition with a DKK1 inhibitor, DKN-01, in combination with atezolizumab in patients with advanced oesophageal adenocarcinoma (OGA): Phase Ila results of the WAKING trial

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BACKGROUND

- Dickkopf-1 (DKK1) modulates Wnt/β-catenin signalling and promotes an immunosuppressive tumour microenvironment (TME) by activating MDSCs and downregulating NK cell activity.
- DKK1 is frequently overexpressed in OGA and associated with poor prognosis.

OBJECTIVES

- To evaluate the safety and anti-tumour activity of DKN-01 in combination with atezolizumab.
- To determine recommended phase 2 doses of DKN-01.

METHODS

- Study Design: Double-blind, randomised, placebo-controlled, single cohort phase 1b/2a trial
- Key eligibility criteria
  - Histologically or cytologically confirmed advanced OGA
  - Eastern Cooperative Oncology Group (ECOG) performance status 0-2
  - At least 2 prior lines
- Dosing cohorts
  - 100 mg (n=4), 200 mg (n=4), 400 mg (n=4), 600 mg (n=4), 840 mg (n=2)
  - 50 mg (n=4) for six patients

RESULTS

- 33 patients were enrolled. 22 patients were evaluable for safety and 10 patients were evaluable for response at data cut.
- Safety
  - 3 AE leading to treatment discontinuation
  - No grade 3 or 4 treatment-related adverse events (TRAEs) were observed
  - 3 TRAEs (urticaria) were reported (1 each at 200, 400 mg, 600 mg)
  - Time from initial diagnosis to trial entry: median 61 (IQR 54 – 69) months
  - Performance status: 0 (n=7), 1 (n=12), 2 (n=14)

- Efficacy
  - 4 partial responses (ORR 10%); duration of this response was 2.7 months
  - Disease control rate during treatment was 50%; median duration of disease control was 2.0 months
  - 3 patients experienced clinical disease progression

CONCLUSIONS

- DKN-01 up to 600mg in combination with atezolizumab 840mg was considered safe.
- DKN-01 600mg was determined as the recommended phase 2 dose.
- Phase IIb is now recruiting.
- Time of date cut off (16th August 2021): 18 patients were enrolled in the study across both Phase IIA and III.
- Translational analyses and assessment of PD-1 status are ongoing.