Initial results from a phase 1a/b study of Etigilimab (OMP-313M32), an anti-T cell immunoreceptor with Ig and ITIM domains (TIGIT) antibody, in advanced solid tumors


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Abstract (updated)

Background: TIGIT is an immunoinhibitory receptor expressed on T and NK cells. Etigilimab is a bow-tie IgG4 anti-TIGIT antibody that functions intrinsically as an ITIM and efficiently, anti-TIGIT demonstrates preclinical activity in vitro with tumor effects as a single agent and with anti-PD-1. Initial results from the phase 1a dose-escalation portion of the study which is shown to have clinical activity in selected tumor types with nivolumab (dose escalation). Objectives included anti-tumor effects as a single agent and with anti-PD-1. Results from the phase 1a dose-escalation portion of the study are shown.

Methods, Study Schema, and Objectives

- Preclinical models demonstrate single-agent and combination (PD-1) efficacy
- Effector function is an important component of efficacy

Treatment Exposure

- PBMC flow cytometry
- Blood-based biomarker analysis reveals significant reduction in Tregs
- Immune-related adverse events were observed in several subjects,

Adverse Events (Treatment-Related)

- Immune-related adverse events included rash (27.8%), pruritus (16.7%), and cough (11.1%). Immune-related adverse events included rash (27.8%), pruritus (16.7%), and abdominal pain, embolism, hypertension, and pulmonary embolism (11.1% each).

Immune-Related Adverse Events

- No confirmed ADA+ patients through cycle 4
- Subject discontinued treatment due to AE (autoimmune hepatitis) but subsequently had the Day 56 CT scan with stable disease

Pharmacokinetics and Immunogenicity

- Etigilimab exhibits linear PK over the dose range of 0.3 – 20 mg/kg
- No confirmed ADA+ patients through cycle 4

Conclusions

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Biomarkers

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Best Overall Tumor Response

- No confirmed ADA+ patients through cycle 4

Waterfall Plot

- Subject noted to be MSI post data-cut for this presentation
- 3 subjects were enrolled and not treated

Adverse Events (all Grades ≥10%)

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Disposition and DLTs

- Safety Population[2] 3 (100%) 3 (100%) 3 (75.0%) 3 (100%) 6 (75.0%) 18 (85.7%)
- Discontinuation
  - DLT 0 0 0 0 0 0
  - Clinical Progression 1 (33.3%) 0 0 0 0 1 (4.8%)
  - Not Eligible For Treatment 0 0 0 0 1 (12.5%) 1 (4.8%)

Baseline Characteristics

- T cell immunoreceptor with Ig and ITIM domains (TIGIT)
  - TIGIT is a receptor similar to PD1 in both structure and expression
  - TIGIT is expressed on CD4, CD8 and NK cells and is elevated upon activation
  - TIGIT mediates an inhibitory signal

Tumor types for inclusion in the dose escalation portion in selected tumor types with nivolumab (dose escalation). Objectives included anti-tumor effects as a single agent and with anti-PD-1. Initial results from the phase 1a dose-escalation portion of the study which is shown to have clinical activity in selected tumor types with nivolumab (dose escalation). Objectives included anti-tumor effects as a single agent and with anti-PD-1. Results from the phase 1a dose-escalation portion of the study are shown.

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