Phase 1 study of fianlimab, a human lymphocyte activation gene-3 monoclonal antibody, in combination with cemiplimab: Subgroup analysis

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Background

• Fianlimab (MRG-044) and cemiplimab are both high-affinity, human, IgG1 monoclonal antibodies that bind to LAG-3 and PD-1, respectively.

• Fianlimab is a lymphocyte activation gene-3 (LAG-3) antibody that blocks LAG-3/CD274 interaction (CD274 = PD-L1).

• Fianlimab is currently in clinical development as a stand-alone therapy and in combination with other immunotherapeutic agents.

• Cemiplimab is a programmed cell death-1 (PD-1) antibody that blocks PD-1/PD-L1 interaction.

• Cemiplimab is currently approved for the treatment of squamous cell carcinoma of the skin.

• The combination of fianlimab and cemiplimab is under investigation for the treatment of patients with advanced melanoma.

• Concurrent blockade of LAG-3 may enhance the efficacy of PD-1 therapies.

Methods

• Adult patients with advanced melanoma and no prior anti-PD-1/PD-L1 therapy (trial I: 100 mg + 250 mg; trial II: 100 mg IV every 3 weeks) for 24 weeks (for >21 weeks; ORR 20.0% [95% CI 12.5–30.7]).

• Tumour response assessed every 6 weeks for the first 24 weeks, then every 9 weeks for the subsequent 27 weeks.

• The ORR was 63.8% (95% CI 51.8–75.8) and the DCR was 80.0% (95% CI 70.4–89.6).

• The median duration of response (mDOR) was not reached.

• Across patients in expansion cohorts 6 and 15, those with:

- LDH > ULN (n=13, ORR 69.2% [95% CI 49.8–87.6]);
- M1c stage disease and LDH > ULN at baseline had an ORR of 53.8% (95% CI 26.1–79.4). Median duration of response was not reached.

• Discontinued or withdrawn for any reason (n=3, 30.0) and treatment-emergent AEs (n=30, 30.0).

• Treatment-emergent AEs regardless of causality (n=113, 113.0) and treatment-emergent serious adverse events (n=11, 11.0).

Results

Baseline demographics and disease characteristics

• As of the 1 July 2022 data cutoff, 60 patients had been treated with fianlimab + cemiplimab in expansion cohorts 6 and 15 (Table 2). Patients were evaluable for safety (n=60, 100.0) and tumour response (n=56, 93.3).

• The median age across all anti-PD-1/PD-L1 therapies was 60 years (range 23–88) of which 60% were male and 80% were White.

• The target lesion had a mean diameter of 14.5 mm (range 1.1–60.0 mm) among patients in both cohorts (Table 2).

• Of the 60 evaluable patients with metastatic melanoma, 30% had stage III disease, 49% had stage IV disease, 25% had LDH > ULN, and 16% had any grade 3 adverse event.

• Baseline background characteristics: 6% had more than 20% of tumour burden, 25% of patients had stage III disease, 46% had low metastases, 25% had LDH > ULN, and 16% had any grade 3 adverse event (Table 1).

• Responding patients had the option to continue fianlimab + cemiplimab treatment for an additional 51 weeks.

• Cemiplimab is a programmed cell death-1 (PD-1) antibody that blocks PD-1/PD-L1 interaction.

• Cemiplimab is approved for the treatment of squamous cell carcinoma of the skin.

• Cemiplimab is currently in clinical development as a stand-alone therapy and in combination with other immunotherapeutic agents.

• The combination of fianlimab and cemiplimab is under investigation for the treatment of patients with advanced melanoma.

• Concurrent blockade of LAG-3 may enhance the efficacy of PD-1 therapies.