643P M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients with post-platinum esophageal adenocarcinoma (EAC): Preliminary results from a phase I cohort

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Background: TGF-β and PD-(L)1 are 2 mechanisms of immune suppression in the tumor microenvironment; blocking both may enhance antitumor activity. M7824 is an innovative first-in-class bifunctional fusion protein composed of an anti–PD-L1 mAb fused with 2 extracellular domains of TGF-βRII (a TGF-β "trap"). Advanced EAC is treated per gastric cancer guidelines, with ORRs ≤14% with 2L SoC taxane monotherapy. We report results in patients (pts) with EAC that progressed on ≥ 1 platinum-based therapy. Emerging data with immunotherapies show clinical activity in advanced EAC, though none are currently approved in these pts.

Methods: In the ongoing trial NCT02517398, pts with advanced, post-platinum EAC received M7824 1200 mg q2w until confirmed PD per RECIST v1.1, unacceptable toxicity or trial withdrawal. The primary endpoint is BOR per RECIST; secondary endpoints include safety/tolerability. Biomarker analysis included tumor cell PD-L1 expression (antibody clone 73-10).

Results: As of August 23, 2017 (median follow-up, 14.4 [range, 1.3–43.3] weeks), 30 pts with advanced EAC (80% had ≥2 prior lines of therapy) received M7824. The median therapy duration was 6.1 (range, 2.0–40.0) weeks; treatment was ongoing in 4 pts (13.3%). 19 pts (63.3%) had TRAEs; 7 pts (23.3%) experienced grade 3 TRAEs (anemia [2 pts], Bowen's disease, cancer pain, generalized rash, hemorrhagic gastritis, hypophysitis, hypopituitarism, and skin SCC [1 pt each]). No grade 4 TRAEs, study discontinuations, or deaths due to a TRAE were observed. 6 pts (confirmed ORR 20.0%) had a PR with 3 responses ongoing per RECIST (DOR, 1.4+, 2.0, 2.8, 2.9+, 3.6, 6.5+ months), and 4 pts (13.3%) had SD per RECIST by independent committee read. 9 pts (31.0% of 29 evaluable) had PD-L1 + (≥1%) tumors. ORR was 22.2% in pts with PD-L1+ and 20.0% in pts with PD-L1– tumors.

Conclusions: These preliminary data show that M7824 resulted in a manageable safety profile in pts with advanced EAC. Early signs of clinical efficacy in this heavily pretreated population are encouraging, with an ORR of 20%, irrespective of PD-L1 expression. Updated efficacy data and biomarker analysis will be presented.

Clinical trial identification: NCT02517398.

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