Publication Number: S1-04
Title: Avelumab (MSB0010718C), an anti-PD-L1 antibody, in patients with locally advanced or metastatic breast cancer: A phase Ib JAVELIN solid tumor trial
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Body: Background: The programmed death-1 receptor (PD-1) and its ligand (PD-L1) are key therapeutic targets in the reactivation of the immune response against cancer. Avelumab* (MSB0010718C) is a fully human anti-PD-L1 IgG1 antibody being investigated in clinical trials. We report clinical activity of avelumab in a cohort of patients (pts) with locally advanced (LA) or metastatic breast cancer (MBC) refractory to or progressing after standard-of-care therapy (NCT01772004).

Methods: Pts received avelumab at 10 mg/kg Q2W until confirmed progression, unacceptable toxicity, or any criterion for withdrawal occurred. Tumors were assessed every 6 wks (RECIST 1.1). Unconfirmed best overall response was evaluated. Adverse events (AEs) were graded by NCI-CTCAE v4.0. Biopsy or surgical specimens were collected within 90 days prior to 1st dose of avelumab for biomarker analyses. Tumor PD-L1 expression was assessed by immunohistochemistry using various cutoff criteria.

Results: As of 27 Feb 2015, 168 pts (167 female, 1 male) with MBC, including ductal (56.5%), carcinoma NOS (9.5%), lobular (3.6%), or other (30.4%), were treated with avelumab and followed for a median of 10 mo (range 6-15). Median age was 55y (range 31-81), ECOG performance status was 0 (49.4%) or 1 (50.6%), and pts had received a median of 3 prior therapies for LA/M disease (range 0-10; pts must have received prior treatment with taxane and anthracycline, unless contraindicated). Pts were HER2-/ER+ or PR+ (69 [41.1%]), triple negative (TNBC = HER2-/ER-/PR-; 57 [33.9%]), HER2+ (26 [15.5%]), or had unknown biomarker status (16 [9.5%]). Median duration of treatment was 8 wks (range 2-50), and 9 pts (5.4%) remained on avelumab. Any grade treatment-related treatment-emergent AEs (TEAEs) occurred in 120 pts (71.4%); the most common (>10%) were fatigue (33 [19.6%]), nausea (24 [14.3%]), and infusion-related reactions (20 [11.9%]). Treatment-related grade ≥3 TEAEs occurred in 24 pts (14.3%) and included ≥1% fatigue, anemia, increased GGT, and autoimmune hepatitis (each 1 [0.6%]), and arthralgia (2 [1.2%]). There were 2 treatment-related deaths (acute liver failure, respiratory distress). Unconfirmed objective response rate (ORR) in the entire cohort was 5.4% (9 pts; 95% CI: 2.5, 9.9), with 1 CR and 8 PRs. Five of 9 responses were ongoing at time of cutoff. Stable disease was observed in additional 40 pts (23.8%), for an overall disease control rate of 29.2%. Evidence of tumor reduction by ≥30% was seen in 15 pts (8.9%). There were responders in all biomarker subgroups, including 5 PRs in TNBC (n=57 [8.8%; 95% CI: 2.9, 19.3%]). PD-L1 expression was evaluable in 136 pts. Among all pts with PD-L1 expressing immune cells within the tumor, 33.3% (4 of 12) had PRs. In pts with TNBC who had PD-L1+ immune cells within the tumor, 44.4% (4 of 9) had PRs, compared with 2.6% (1 of 39) for TNBC and PD-L1- immune cells. Conclusions: Avelumab showed an acceptable safety profile and had clinical activity in a subset of pts with MBC. In pts with TNBC, presence of PD-L1 expressing immune cells within the tumor may be associated with clinical responses to avelumab. Further analyses of PD-L1 expression and clinical activity of avelumab in MBC are ongoing. *Proposed INN.