late-breaking and deferred publication abstracts

**LBA32_PR**

**Pembrolizumab (pembro) as first-line therapy for advanced/unresectable or metastatic urothelial cancer: Preliminary results from the phase 2 KEYNOTE-052 study**


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**Background:** KEYNOTE-052 (NCT02335424), an open-label, multicenter, phase 2 study, evaluated the efficacy and safety of pembro in first-line cisplatin-ineligible pts with u/m UC.

**Methods:** 374 pts have been enrolled. Eligibility included pathologically confirmed and measurable u/m UC, age ≥18 y, no chemotherapy for u/m disease, ECOG PS 0-2, and cisplatin ineligibility (ECOG PS 2, creatinine clearance <60 mL/min, ≥ grade 2 neuropathy or hearing loss, NYHA class III CHF). Pts received pembro 200 mg Q3W until progressive disease, unacceptable toxicity, or 24 mo of treatment. Primary end point was RECIST v1.1 confirmed objective response rate (ORR) by independent review in all pts and in PD-L1-positive pts by combined positive score (CPS) (tumor and immune cell PD-L1 expression). Secondary objective was to determine the CPS-high biomarker cutpoint. Interim analysis was planned to evaluate ORR for the first 100 pts and to determine the CPS-high cutpoint.

**Results:** Median age was 75 years (13% ≥85). 13% received perioperative chemotherapy. 87% had visceral disease. 46% were ECOG 2/3. 45% were cisplatin ineligible because of renal insufficiency only. 11% were cisplatin ineligible because of ECOG 2 performance status and renal insufficiency. The CPS-high cutpoint was determined to be ≥10% PD-L1 expression. As of 6/11/16, data cutoff (median 8 mo follow-up), ORR was as follows:

<table>
<thead>
<tr>
<th>% (95% CI)</th>
<th>All subjects N = 100</th>
<th>CPS ≥1% N = 63</th>
<th>CPS ≥10% N = 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>24.0 (16.0-33.6)</td>
<td>25.4 (15.3-37.9)</td>
<td>36.7 (19.9-56.1)</td>
</tr>
<tr>
<td>CR</td>
<td>6.0 (2.2-12.6)</td>
<td>6.3 (1.8-15.5)</td>
<td>13.3 (3.8-30.7)</td>
</tr>
</tbody>
</table>

Median duration of response (DOR) has not been reached (range, 1.4+ - 9.8+ mo). DOR rate ≥ months was 83% (Kaplan-Meier estimate). 67% of pts experienced a drug-related adverse event (DRAE), most commonly fatigue (14%). 16% experienced a grade 3/4 DRAE. 5% discontinued therapy because of a DRAE.

**Conclusions:** Pembro 200 mg Q3W demonstrates substantial antitumor activity and has a manageable toxicity profile in cisplatin-ineligible pts with u/m UC. CPS high cutpoint was determined to be ≥10% PD-L1 expression. CR rate of 6% for all pts and 13.3% for pts CPS ≥10% is encouraging.

**Clinical trial identification:** NCT02335424

Legal entity responsible for the study: Merck & Co. Inc.

Funding: Merck & Co., Inc.

Disclosure: J. Bellmunt: Advisory board member for Merck, Genentech, Pfizer, Novartis, Sanofi, and Pierre Fabre, and research grants from Takeda, Novartis, and Sanofi. P.H. O’Donnell: Advisory board member for Genentech, AstraZeneca/MedImmune, and Merck, and research grants from Genentech, Merck, and AstraZeneca/MedImmune. P. Grivas: Advisory board member for Merck, Genentech, Bristol-Myers Squibb, Bayer, and Dendreon, and research grants from Merck, Genentech, OncogeneX, Bayer, Mirati, and Pfizer. T. Powles: Honoraria from GlaxoSmithKline, Roche, Merck, and Bristol-Myers Squibb, and research grants from Roche/Genentech. E.R. Plimack: Advisory board member for Acceleron, AstraZeneca, Bristol-Myers Squibb, Genentech/Roche, Eli Lilly Inc., Novartis, Pfizer, and Synergene, and research grants from Acceleron, AstraZeneca, Bristol-Myers Squibb, Eli Lilly Inc., Merck, and Pfizer. N.M. Hahn: Advisory board member for AZ/MedImmune, Inovio, Pieris, Genentech/Roche, Merck, BMS, and OncoGeneX, and research grants to my institution from Novartis, BMS, Heat Biologics, Merck, Genentech/Roche, AZ/MedImmune, Principia Biopharma, Mirati, and OncoGeneX. R. de Wit: Advisory board member for Sanofi, Merck, Lilly, and Roche, and research grants from Sanofi. L. Pang, R. Perini: Employee of and own stock in Merck & Co., Inc. M.J. Savage: Employee of and may own stock in Merck & Co., Inc. S. Keefe: Employee of Merck & Co., Inc. D. Bajorin: Advisory board member for Bristol-Myers Squibb, Roche, Merck, Genentech, Pfizer, and Novartis, and research grants from Roche, Merck, and Novartis. All other authors have declared no conflicts of interest.