Recent Advances of Immunotherapy in Urologic Malignancies

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For metastatic renal cell carcinoma (mRCC), immunotherapy has been proved effective since the 1990s, before the era of targeted therapy. Cytokines like Interleukin-2 (IL-2) and interferon (IFN-α) have response rates about 15% and durable response about 7%, but now they are occasionally used in select patients due to their toxicities. Recently there is a resurgence of research in immune check point inhibitors in mRCC. In CheckMate 025 phase III clinical trial, 821 patients with advanced clear-cell RCC whose disease progressed after one or two antiangiogenic therapies were randomly assigned to receive nivolumab (an anti-PD-1 agent) or everolimus. The median overall survival was 25.0 months with nivolumab versus 19.6 months with everolimus. (Hazard ratio for death: 0.73) The objective response rate was 25% with nivolumab compared with 5% with everolimus.

For metastatic castration-resistant prostate cancer (mCRPC), Sipuleucel-T is an autologous active cellular immunotherapy and a type of therapeutic cancer vaccine. In IMPACT phase III clinical trial, 512 patients with mCRPC were randomly assigned to receive Sipuleucel-T or placebo. The median overall survival was 25.8 months with Sipuleucel-T versus 21.7 months with placebo. (Hazard ratio for death: 0.78) On the other hand, one phase III trial evaluated the efficacy of ipilimumab (an anti-CTLA4 agent) in comparison with placebo after radiotherapy in 799 patients with mCRPC that progressed after docetaxel chemotherapy. In terms of primary endpoint this study was negative, with median overall survival 11.2 months with ipilimumab versus 10.0 months with placebo. (Hazard ratio for death: 0.85; $p = 0.053$). However, subgroup analyses suggested that ipilimumab might provide an OS benefit for patients with favorable prognostic features (ALP<1.5 x ULN, Hb≥11g/dL and no visceral metastases).

For bladder cancer (BC), Bacillus Calmette–Guérin (BCG) was used as an intravesical immunotherapy to treat superficial BC for almost 40 years. As for new check point inhibitors, atezolizumab (an anti-PD-L1 agent) demonstrated clinical benefit in patients with metastatic urothelial carcinoma who progressed during or following platinum-based chemotherapy. In IMvigor 210 phase II clinical trial, 311 patients received atezolizumab administration on the first day of each 21-day cycle until no

further clinical benefit. According to the results of PD-L1 immunohistochemistry (IHC), the objective response rate was 27% for IC2/3 group, 10% for IC1 group and 9% for IC0 group.