Imfinzi® (durvalumab) – New indication

- On June 17, 2024, AstraZeneca announced the FDA approval of Imfinzi (durvalumab), in combination with carboplatin and paclitaxel followed by Imfinzi as a single agent for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR).

- Imfinzi is also approved for the treatment of non-small cell lung cancer, small cell lung cancer, biliary tract cancer, and hepatocellular carcinoma.

- The approval of Imfinzi for the new indication was based on DUO-E, a randomized, double-blind, placebo-controlled study in patients with advanced or recurrent endometrial cancer. Randomization was stratified by tumor mismatch repair (MMR) status (proficient or deficient), disease status (recurrent or newly diagnosed), and geographic region (Asia or rest of the world). Patients were randomized to three arms: (1) Imfinzi plus carboplatin and paclitaxel, followed by Imfinzi as a single agent; (2) placebo plus carboplatin and paclitaxel, followed by placebo, or (3) an additional investigational combination regimen. The major outcome measure was progression-free survival (PFS). Additional outcome measures included overall response rate (ORR) and overall survival (OS).

    - While a statistically significant improvement in PFS was observed in the overall population for Imfinzi with carboplatin and paclitaxel compared to carboplatin and paclitaxel alone, based on an exploratory analysis by MMR status, the PFS improvement in the overall population was primarily attributed to patients with dMMR tumors (n = 95).
    - In dMMR patients, median PFS was not reached in the Imfinzi arm vs. 7.0 months in the chemotherapy arm (hazard ratio 0.42, 95% CI: 0.22, 0.80). The ORR was 71.4% (95% CI: 55.4, 84.3) in the Imfinzi arm vs. 40.5% (95% CI: 25.6, 56.7) in the chemotherapy arm. The OS data in this subpopulation at the time of PFS analysis were immature with 26% of patients who died.

- The most common adverse reactions (≥ 20% of patients with endometrial cancer) with Imfinzi, in combination with carboplatin and paclitaxel, followed by Imfinzi as a single agent were peripheral neuropathy, musculoskeletal pain, nausea, alopecia, fatigue, abdominal pain, constipation, rash, decreased magnesium, increased alanine transaminase, increased aspartate transaminase, diarrhea, vomiting, cough, decreased potassium, dyspnea, headache, increased alkaline phosphatase, and decreased appetite.

- The recommended intravenous dose of Imfinzi for the treatment of endometrial cancer is based on weight:

    - Patients with a body weight of ≥ 30 kg: 1,120 mg in combination with carboplatin and paclitaxel every 3 weeks (21 days) for 6 cycles, followed by Imfinzi 1,500 mg every 4 weeks as a single agent
    - Patients with a body weight of < 30 kg: 15 mg/kg in combination with carboplatin and paclitaxel every 3 weeks (21 days) for 6 cycles, followed by Imfinzi 20 mg/kg every 4 weeks as a single agent
    - Treatment should be continued until disease progression or unacceptable toxicity.

- Refer to the Imfinzi drug label for dosing for all its other indications.