Opdivo® (nivolumab) and Yervoy® (ipilimumab) – New indication

- On April 16, 2017, Bristol-Myers Squibb announced the FDA approval of Opdivo (nivolumab) plus Yervoy (ipilimumab) for the combination treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma (RCC).
    - Opdivo was previously approved as a single agent for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy.
- Opdivo is also indicated for the treatment of unresectable or metastatic melanoma, adjuvant treatment of melanoma, metastatic non-small cell lung cancer, classical Hodgkin lymphoma, squamous cell carcinoma of the head and neck, urothelial carcinoma, microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer, and hepatocellular carcinoma.
- Yervoy is also indicated for the treatment of unresectable or metastatic melanoma and for adjuvant treatment of melanoma.
- According to the American Cancer Society, approximately 63,340 new cases of RCC will occur in 2018. Of those with advanced RCC, 75% – 80% have one or more risk factors and are considered intermediate or poor risk patients.
- The efficacy of Opdivo in combination with Yervoy for the new indication is based on a clinical study of 847 patients with intermediate or poor risk, previously untreated advanced RCC. Patients were randomized to Opdivo plus Yervoy followed by Opdivo monotherapy vs. Sutent® (sunitinib).The co-primary endpoints were overall survival (OS), objective response rate (ORR), and progression-free survival (PFS).
    - Opdivo plus Yervoy reduced the risk of death by 37% versus sunitinib (HR = 0.63, [99.8% CI: 0.44 to 0.89]; $p < 0.0001$).
    - Opdivo plus Yervoy was associated with a 41.6% ORR vs. 26.5% for sunitinib ($p < 0.0001$).
    - However, PFS did not reach statistical significance for Opdivo plus Yervoy vs. sunitinib (11.6 months vs. 8.4 months) at alpha level of 0.009.
- Yervoy carries a boxed warning regarding the risk of immune-mediated adverse reactions.
- In RCC patients, the most common adverse reactions with Opdivo plus Yervoy use were fatigue, rash, diarrhea, musculoskeletal pain, pruritus, nausea, cough, pyrexia, arthralgia, and decreased appetite.
- In patients with intermediate or poor risk, previously untreated advanced RCC, the recommended dose is Opdivo 3 mg/kg administered as an intravenous (IV) infusion, followed by Yervoy 1 mg/kg administered as an IV infusion on the same day, every 3 weeks for 4 doses.
    - After completing 4 doses of the combination, administer Opdivo as a single agent, either 240 mg every 2 weeks or 480 mg every 4 weeks as an IV infusion until disease progression or unacceptable toxicity.

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- Refer to the Opdivo and Yervoy drug labels for dosing information for all other indications.