Braftovi® (encorafenib) – New indication

- On April 8, 2020, Pfizer announced the FDA approval of Braftovi (encorafenib), in combination with Erbitux® (cetuximab), for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy.
    - Braftovi is not indicated for treatment of patients with wild-type BRAF melanoma or wild-type BRAF CRC.
- Braftovi is also approved in combination with Mektovi® (binimetinib), for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.
- In the U.S., an estimated 147,950 people will be diagnosed with cancer of the colon or rectum in 2020, and approximately 53,000 are estimated to die of their disease each year. BRAF mutations are estimated to occur in up to 15% of people with metastatic CRC and represent a poor prognosis for these patients.
    - The BRAF V600E mutation is the most common BRAF mutation and the risk of mortality in CRC patients with the BRAF V600E mutation is more than two times higher than for those with wild-type BRAF.
- The approval of Braftovi for the new indication was based on a randomized, active-controlled, open-label study in patients with BRAF V600E mutation-positive metastatic CRC. A total of 220 patients were randomized to the Braftovi plus Erbitux arm and 221 to the control arm (irinotecan with Erbitux or FOLFIRI with Erbitux). The major efficacy outcome measure was overall survival (OS). Additional efficacy outcome measures included progression-free survival (PFS), overall response rate (ORR), and duration of response (DOR).
    - Median OS was 8.4 months in the Braftovi plus Erbitux arm vs. 5.4 months in the control arm (hazard ratio [HR] 0.60; 95% CI: 0.45, 0.79; $p = 0.0003$).
    - Median PFS was 4.2 months in the Braftovi plus Erbitux arm vs. 1.5 months in the control arm (HR 0.40; 95% CI: 0.31, 0.52; $p < 0.0001$).
    - The ORR was 20% (95% CI: 13, 29) and 2% (95% CI: 0, 7) for the Braftovi plus Erbitux and control arm, respectively ($p < 0.0001$).
    - Median DOR was 6.1 months (95% CI: 4.1, 8.3) and not reached (2.6, not reached) for the Braftovi plus Erbitux and control arm, respectively.
- The most common adverse reactions (≥ 25%) with Braftovi use, in combination with Erbitux, were fatigue, nausea, diarrhea, dermatitis acneiform, abdominal pain, decreased appetite, arthralgia, and rash.
- The recommended dose of Braftovi for the treatment of CRC is 300 mg (four 75 mg capsules) orally once daily in combination with Erbitux until disease progression or unacceptable toxicity.
    - If Erbitux is discontinued, Braftovi should also be discontinued.

Continued . . .

— Refer to the Erbitux drug label for recommended Erbitux dosing information.
— Refer to the Braftovi drug label for dosing in metastatic melanoma.

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