Braftovi™ (encorafenib) and Mektovi® (binimetinib) – New drug approval

- On June 27, 2018, Array BioPharma announced the FDA approval of Braftovi (encorafenib) and Mektovi (binimetinib), in combination for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.
    - Braftovi is not indicated for the treatment of patients with wild-type BRAF melanoma.
- Melanoma develops when unrepaired DNA damage to skin cells triggers mutations that may lead them to multiply and form malignant tumors. Metastatic melanoma is the most serious and life-threatening type of skin cancer and is associated with low survival rates. BRAF mutations occur in about half of the new cases of melanoma diagnosed each year.
    - There are about 200,000 new cases of melanoma diagnosed worldwide each year.
- Braftovi is a BRAF kinase inhibitor and Mektovi is a MEK inhibitor which target key enzymes in the MAPK signaling pathway. Inappropriate activation of proteins in this pathway has been shown to occur in many cancers including melanoma.
- The efficacy of Braftovi and Mektovi was demonstrated in the COLUMBUS study enrolling 383 patients with BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma. Patients received Braftovi + Mektovi or Zelboraf® (vemurafenib) until disease progression or unacceptable toxicity. The major efficacy outcome measure was progression-free survival (PFS).
    - The median PFS was 14.9 months for the Braftovi + Mektovi treated patients vs. 7.3 months for the Zelboraf treated patients (HR = 0.54 [95% CI: 0.41, 0.71]; $p < 0.0001$).
    - In addition, the overall response rate and duration of response was 63% and 16.6 months for the Braftovi + Mektovi patients vs. 40% and 12.3 months for the Zelboraf patients.
- Warnings and precautions of Braftovi include new primary malignancies, tumor promotion in BRAF wild-type tumors, hemorrhage, uveitis, QT prolongation, embryo-fetal toxicity, risks associated with Braftovi as a single agent, and risks associated with combination treatment.
- Warnings and precautions of Mektovi include cardiomyopathy, venous thromboembolism, ocular toxicities, interstitial lung disease, hepatotoxicity, rhabdomyolysis, hemorrhage, embryo-fetal toxicity, and risks associated with combination treatment.
- The most common adverse reactions (≥ 25%) with combination therapy with Braftovi and Mektovi use were fatigue, nausea, vomiting, abdominal pain, and arthralgia.
- The recommended dosage of Braftovi is 450 mg orally taken once daily in combination with Mektovi 45 mg orally taken twice daily, approximately 12 hours apart, until disease progression or unacceptable toxicity.
- Array BioPharma has launched Braftovi and Mektovi through specialty pharmacies. Braftovi is available as 50 mg and 75 mg capsules, and Mektovi is available as a 15 mg tablet.