Tafinlar® (dabrafenib) and Mekinist® (trametinib) – New indication

- On June 22, 2017, the FDA announced the approval of Novartis' Tafinlar (dabrafenib) in combination with Mekinist (trametinib) for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test.

- Tafinlar is also approved for the following:

    - As a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.
    - In combination with Mekinist for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test.
    - Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma or wild-type BRAF NSCLC.

- Mekinist is also approved as a single agent or in combination with Tafinlar, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test.

    - Mekinist is not indicated for treatment of patients with melanoma who have progressed on prior BRAF inhibitor therapy.

- The new indication for Tafinlar and Mekinist is the first FDA approval specifically for treatment of patients with BRAF V600E mutation-positive metastatic NSCLC.

- BRAF mutations appear in approximately 1% to 3% of NSCLC cases worldwide. BRAF V600E mutation-positive tumors have been shown to be more aggressive and may lead to a poorer prognosis.

- The FDA also approved the Oncomine™ Dx Target Test, a next generation sequencing test to detect multiple gene mutations for lung cancer in a single test from a single tissue specimen.

    - The test detects the presence of BRAF, ROS1, and EGFR gene mutations or alterations in tumor tissue of patients with NSCLC and can be used to select patients with NSCLC with the BRAF V600E mutation.

- The new indication is based on safety and efficacy data of Tafinlar in combination with Mekinist in an open-label study of 93 patients with stage IV BRAF V600E mutant NSCLC.

    - Among treatment-naïve patients, the overall response rate (ORR) was 61% (95% CI: 44%, 77%).
    - In the previously treated population, patients demonstrated an ORR of 63% (95% CI: 49%, 76%).
    - The median duration of response (DOR) in the treatment-naïve cohort was not estimable (NE) (95% CI: 6.9, NE) and in the previously treated patient cohort the DOR was 12.6 months (95% CI: 5.8, NE).
    - The proportion of responders with a DOR ≥ 6 months was 59% and 64% in the treatment-naïve and previously treated cohorts, respectively.

- The most common adverse reactions (≥ 20%) with Tafinlar in combination with Mekinist use for the treatment of NSCLC were pyrexia, fatigue, nausea, vomiting, diarrhea, dry skin, decreased appetite, edema, rash, chills, hemorrhage, cough, and dyspnea.

Continued . . .

- The recommended doses of Tafinlar and Mekinist for all indications are as follows:
    - Tafinlar: 150 mg orally twice daily, approximately 12 hours apart as a single agent or with Mekinist.
    - Mekinist: 2 mg orally once daily at the same time each day as a single agent or with Tafinlar.
    - Treatment is continued until disease progression or unacceptable toxicity occurs.