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

- On April 30, 2018, Novartis announced the FDA approval of Tafinlar (dabrafenib) in combination with Mekinist (trametinib) for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.

- 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.
    - In combination with Mekinist, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations.
    - In combination with Mekinist, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation.
    - Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma or wild-type BRAF NSCLC.

- Mekinist is also approved for the following:

    - 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.
    - In combination with Tafinlar, for the treatment of patients with metastatic NSCLC with BRAF V600E mutation.
    - Mekinist is not indicated for treatment of patients with melanoma who have progressed on prior BRAF inhibitor therapy.

- The new indication is based on efficacy and safety data of Tafinlar in combination with Mekinist in a placebo-controlled study of 870 patients with completely resected, stage III melanoma with BRAF V600E or V600K mutations. The primary end point was relapse-free survival.

    - At a median follow-up of 2.8 years, the estimated 3-year rate of relapse-free survival was 58% in the Tafinlar/Mekinist group vs. 39% in the placebo group (HR for relapse or death = 0.47; 95% CI: 0.39, 0.58; $p < 0.001$).
    - The 3-year overall survival rate was 86% in the Tafinlar/Mekinist group vs. 77% in the placebo group (HR for death = 0.57; 95% CI: 0.42, 0.79; $p = 0.0006$); however, this difference was not significant because it did not cross the prespecified interim analysis boundary of $p = 0.000019$.

- The most common adverse reactions (≥ 20%) for Tafinlar in combination with Mekinist use for the adjuvant treatment of melanoma were pyrexia, fatigue, nausea, headache, rash, chills, diarrhea, vomiting, arthralgia, and myalgia.

- 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.

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- Treatment for the adjuvant indication should be continued until disease progression or unacceptable toxicity occurs for up to one year.
- Treatment for all other indications should be continued until disease progression or unacceptable toxicity occurs.

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