Tafinlar® (dabrafenib) plus Mekinist® (trametinib) – New indication, new formulation approvals

- On March 16, 2023, Novartis announced the FDA approval of Tafinlar (dabrafenib) plus Mekinist (trametinib), for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

- In addition to the new indication, Tafinlar and Mekinist were both approved in new liquid formulations to support use of the drugs in pediatric patients.

    — Tafinlar is also approved as an oral capsule and Mekinist is also approved as an oral tablet.

- LGG is the most common pediatric brain cancer. BRAF V600 mutations are present in 15% to 20% of pediatric LGGs and are associated with poor survival outcomes.

- Tafinlar and Mekinist are approved as single-agents or in combination with one another for several other indications. Refer to the individual drug labels for a complete list of approved uses.

- The approval of Tafinlar plus Mekinist for the new indication was based on an open-label study in 110 pediatric patients aged 1 to < 18 years of age with BRAF V600E mutation-positive LGG. Patients were randomized to Tafinlar plus Mekinist or carboplatin plus vincristine. The major efficacy outcome measure was overall response rate (ORR). Additional efficacy outcome measures were progression free survival (PFS) and overall survival (OS). The primary analysis was performed when all patients had completed at least 32 weeks of therapy.

    — The ORR was 46.6% vs. 10.8% for Tafinlar plus Mekinist vs. carboplatin plus vincristine, respectively ($p < 0.001$).
    — Median PFS was 20.1 months and 7.4 months for Tafinlar plus Mekinist vs. carboplatin plus vincristine, respectively (hazard ratio 0.31, 95% CI: 0.17, 0.55; $p < 0.001$).
    — The OS results at interim analysis did not reach statistical significance.

- The most common adverse reactions (≥ 20%) with Tafinlar plus Mekinist for LGG were pyrexia, rash, headache, vomiting, musculoskeletal pain, fatigue, diarrhea, dry skin, nausea, hemorrhage, abdominal pain, and dermatitis acneiform.

- The recommended dosage for Tafinlar oral capsules and tablets for oral suspension in pediatric patients is based on body weight.

    — A recommended dosage of Tafinlar capsules has not been established in patients who weigh less than 26 kg.
    — The recommended duration of treatment for pediatric patients with LGG is until disease progression or until unacceptable toxicity.
    — Refer to the Tafinlar drug label for complete dosing recommendations for LGG and all its other indications.

- The recommended dosage for Mekinist tablets and oral solution in pediatric patients is based on body weight.

    — A recommended dosage of Mekinist tablets has not been established in patients who weigh less than 26 kg.

Continued . . .

  - The recommended duration of treatment for pediatric patients with LGG is until disease progression or until unacceptable toxicity.
  - Refer to the Mekinist drug label for complete dosing recommendations for LGG and all its other indications.

- Novartis' launch plans for the liquid formulations of Tafinlar and Mekinist are pending. Tafinlar will be available as a 10 mg tablet for oral suspension. Mekinist will be available as a 4.7 mg oral solution (0.05 mg/mL when reconstituted).