Cosela™ (trilaciclib) – New drug approval

- On February 12, 2021, the FDA announced the approval of G1 Therapeutics' Cosela (trilaciclib), to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC).

- Chemotherapy drugs can cause damage to the bone marrow. When damaged, the bone marrow produces fewer red blood cells, white blood cells, and platelets which can lead to symptoms such as fatigue, increased risk of infection, and bleeding.

- Cosela may help protect bone marrow cells from damage caused by chemotherapy by inhibiting cyclin-dependent kinase (CDK) 4/6.

    — Hematopoietic stem and progenitor cells (HSPCs) in the bone marrow give rise to circulating neutrophils, red blood cells, and platelets. HSPC proliferation is dependent on CDK4/6 activity.

- The efficacy of Cosela was established in three randomized, double-blind, placebo-controlled studies in patients with ES-SCLC. Combined, these studies enrolled 245 patients to receive either an infusion of Cosela or placebo before chemotherapy. Study 1 enrolled adult patients receiving carboplatin, etoposide, and atezolizumab for newly diagnosed ES-SCLC. Study 2 enrolled adult patients receiving etoposide/carboplatin for newly diagnosed ES-SCLC. Study 3 enrolled adult patients receiving topotecan for previously treated ES-SCLC. The primary endpoints in the studies was the proportion of patients with severe neutropenia and the duration of severe neutropenia (DSN) in the first cycle of chemotherapy.

    — In study 1, the mean number of days with DSN was 0 in the Cosela group vs. 4 days with placebo (mean difference -3.6, 95%: -4.9, -2.3; $p < 0.0001$). The percentage of patients experiencing severe neutropenia was 1.9% vs. 49.1%, respectfully (adjusted relative risk 0.038, 95% CI: 0.008, 0.195; $p < 0.0001$).
    — In study 2, the mean number of days with DSN was 0 in the Cosela group vs. 3 days with placebo. The percentage of patients experiencing severe neutropenia was 5.1% vs. 42.1%, respectfully.
    — In study 3, the mean number of days with DSN was 2 in the Cosela group vs. 7 days with placebo. The percentage of patients experiencing severe neutropenia was 40.6% vs. 75.9%, respectfully.

- Warnings and precautions for Cosela include injection-site reactions, including phlebitis and thrombophlebitis; acute drug hypersensitivity reactions; interstitial lung disease/pneumonitis; and embryo-fetal toxicity.

- The most common adverse reactions (≥ 10% of patients with ≥ 2% difference in incidence vs. placebo) with Cosela use were fatigue, hypocalcemia, hypokalemia, hypophosphatemia, increased aspartate aminotransferase, headache, and pneumonia.

- The recommended dose of Cosela is 240 mg/m^2 per dose. Cosela should be administered as a 30-minute intravenous infusion completed within 4 hours prior to the start of chemotherapy on each day chemotherapy is administered.

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    - The interval between doses of Cosela on sequential days should not be greater than 28 hours.

- G1 Therapeutics plans to launch Cosela in early March. Cosela will be available as a 300 mg lyophilized cake in a single-dose vial.