Orencia® (abatacept) – New orphan indication

- On December 15, 2021, the FDA announced the approval of Bristol-Myers Squibb's Orencia (abatacept), for the prophylaxis of acute graft versus host disease (aGVHD), in combination with a calcineurin inhibitor and methotrexate, in adults and pediatric patients 2 years of age and older undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated-donor (URD).

- Orencia is also approved for the treatment of adult rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, and adult psoriatic arthritis.

- aGVHD is a potentially fatal complication that can occur after stem cell transplantation when the donor's immune cells view the recipient's body as foreign, and the donated cells attack the body. The chances of developing aGVHD increase when the donor and recipient are not related or are not a perfect match.

    — This is the first FDA drug approval for aGVHD prevention and incorporates real world evidence as one component of the determination of clinical effectiveness.

- The approval of Orencia for the new indication was based on a two-cohort clinical study (Study GVHD-1) in patients age 6 years and older who underwent HSCT from a matched or 1 allele-mismatched URD. Cohort 1 was an open-label, single-arm study of 43 patients who underwent a 7 of 8 Human Leukocyte Antigen (HLA)-matched HSCT (7 of 8 cohort). Cohort 2 was a randomized, double-blind, placebo-controlled study of patients who underwent an 8 of 8 HLA-matched HSCT who received Orencia or placebo in combination with a calcineurin inhibitor (CNI) and methotrexate (MTX) (8 of 8 cohort). Efficacy was established based on overall survival (OS) and grade II-IV aGVHD free survival (GFS) assessed at day 180 post-transplantation.

    — In Cohort 8 of 8, Orencia plus CNI and MTX did not significantly improve grade III-IV GFS vs. placebo plus CNI and MTX at day 180 post-transplantation. Additional results from Cohort 8 of 8 can be found in the table below.

Endpoint	Orencia (+ CNI and MTX)	Placebo (+CNI and MTX)
Gr III-IV GFS	87%	75%
Hazard ratio (95% CI)	0.55 (0.26, 1.18)	
Gr II-IV GFS	50%	32%
Hazard ratio (95% CI)	0.54 (0.35, 0.83)	
OS	97%	84%
Hazard ratio (95% CI)	0.33 (0.12, 0.93)	

    — In an exploratory analysis of the 7 of 8 cohort of Orencia-treated patients, the rates of grade III-IV GFS, grade II-IV GFS, and OS at day 180 post-transplantation were 95% (95% CI 83, 99), 53% (95% CI 38, 67), and 98% (95% CI 85, 100), respectively.

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- In addition, Orencia was approved based on data from the Center for International Blood and Marrow Transplant Research (CIBMTR). The study analyzed outcomes of Orencia in combination with a CNI and MTX vs. CNI and MTX alone. The Orencia plus CNI and MTX-treated group (n = 54) included 42 patients from GVHD-1, in addition to 12 patients treated with Orencia outside of GVHD-1. The comparator group (n = 162) was randomly selected to the Orencia-treated group from the CIBMTR registry from patients who had not received Orencia during the study period. Analyses used propensity score matching and inverse probability of treatment weighting to help address the impact of selection bias. Efficacy was based on OS at day 180 post-HSCT.

    — The OS rate at day 180 in the Orencia combination group was 98% (95% CI: 78, 100) vs. 75% (95% CI: 67, 82) with CNI plus MTX alone.

- The most common adverse reactions (≥ 10%) with Orencia use for prophylaxis of aGVHD were anemia, hypertension, cytomegalovirus (CMV) reactivation/CMV infection, pyrexia, pneumonia, epistaxis, decreased CD4 lymphocytes, hypermagnesemia, and acute kidney injury.

- For patients 6 years and older, Orencia should be administered as a 10 mg/kg (maximum dose of 1,000 mg) intravenous (IV) infusion over 60 minutes on the day before transplantation (day -1), followed by administration on days 5, 14, and 28 after transplantation.

- For patients 2 to less than 6 years old, Orencia should be administered as a 15 mg/kg IV infusion over 60 minutes on the day before transplantation (day -1), followed by 12 mg/kg as an IV infusion over 60 minutes on days 5, 14, and 28 after transplantation.

- Before administering Orencia, recommended antiviral prophylactic treatment for Epstein-Barr virus reactivation should be administered, and continued for six months following HSCT. In addition, prophylactic antivirals should be considered for CMV infection/reactivation during treatment and for six months following HSCT.

- Refer to the Orencia drug label for dosing for all its other indications.