Carvykti™ (ciltacabtagene autoleucel) – New orphan drug approval

- On February 28, 2022, Janssen announced the FDA approval of Carvykti (ciltacabtagene autoleucel), for the treatment of adult patients with relapsed or refractory multiple myeloma, after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

- Multiple myeloma is an incurable blood cancer that affects plasma cells, which are found in the bone marrow. In 2022, it is estimated that more than 34,000 people will be diagnosed with multiple myeloma, and more than 12,000 people will die from the disease in the U.S.

- Carvykti is a B-cell maturation antigen (BCMA)-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T-cells with a transgene encoding a chimeric antigen receptor (CAR) that identifies and eliminates cells that express the BCMA. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B-cells and plasma cells.

    — The Carvykti CAR protein features two BCMA-targeting single domain antibodies designed to confer high avidity against human BCMA. Upon binding to BCMA-expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells.

- Carvykti is the second CAR T immunotherapy approved for multiple myeloma. Bristol Myers Squibb and bluebird bio's Abecma® (idecabtagene vicleucel) was also approved for this use in March 2021.

- The efficacy of Carvykti was established in CARTITUDE-1, an open-label, single-arm study in adult patients with relapsed or refractory multiple myeloma, who previously received at least three prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The efficacy-evaluable population was 97 patients. Efficacy was established on the basis of overall response rate (ORR), complete response (CR), and duration of response (DRR).

    — ORR was achieved in 97.9% of patients (95% CI: 92.7, 99.7).
    — Stringent CR was achieved in 78.4% of patients (95% CI: 68.8, 86.1).
    — The median DOR was 21.8 months (95% CI: 21.8, not estimable).

- Carvykti carries a boxed warning for cytokine release syndrome (CRS); neurologic toxicities; Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS); and prolonged and recurrent cytopenia.

    — Because of the risk of CRS and neurologic toxicities, Carvykti is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Carvykti REMS. Refer to the Carvykti drug label and www.carvyktirems.com for additional details.

- Additional warnings and precautions for Carvykti include infections; hypogammaglobulinemia; hypersensitivity reactions; secondary malignancies; and effects on ability to drive and use machines.

- The most common nonlaboratory adverse reactions (> 20%) with Carvykti use were pyrexia, CRS, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections-pathogen unspecified, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy,

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constipation, and vomiting. The most common laboratory adverse reactions (≥ 50%) include thrombocytopenia, neutropenia, anemia, aminotransferase elevation and hypoalbuminemia.

- Refer to the Carvykti drug label for dosing and administration recommendations.
- Carvykti will be priced at $465,000 for the one-time dose.
- Janssen's launch plans for Carvykti are pending.