Margenza™ (margetuximab-cmkb) – New drug approval

- On December 16, 2020, MacroGenics announced the FDA approval of Margenza (margetuximab-cmkb), in combination with chemotherapy, for the treatment of adult patients with metastatic human epidermal growth factor receptor 2 protein (HER2)-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.

- HER2 is a protein found on the surface of some cancer cells that promotes growth and is associated with aggressive disease and poor prognosis. Approximately 15 to 20% of breast cancer cases are HER2-positive.

- Margenza is a monoclonal antibody that targets the HER2 oncoprotein. Similar to Herceptin® (trastuzumab), Margenza inhibits tumor cell proliferation, reduces shedding of the HER2 extracellular domain and mediates antibody-dependent cellular cytotoxicity (ADCC).

- The efficacy of Margenza was established in SOPHIA, a randomized, open-label study in 536 patients with HER2-positive metastatic breast cancer who had received prior treatment with other anti-HER2 therapies. Patients were randomized to Margenza plus chemotherapy or trastuzumab plus chemotherapy. Major efficacy outcome measures were progression-free survival (PFS) and overall survival (OS). Additional efficacy outcome measures were objective response rate (ORR) and duration of response (DOR).

    - Median PFS was 5.8 months and 4.9 months, for the Margenza and trastuzumab arms, respectively (hazard ratio 0.76, 95% CI: 0.59, 0.98; p = 0.033).
    - The ORR was 22% (95% CI: 17, 27) and 16% (95% CI: 12, 20) for the Margenza and trastuzumab arms, respectively.
    - The median DOR was 6.1 months (95% CI: 4.1, 9.1) and 6.0 months (95% CI: 4.0, 6.9), for the Margenza and trastuzumab arms, respectively.
    - At the protocol pre-specified second interim analysis of OS, the OS data were not mature with 50% of deaths in the overall population. The final OS analysis is expected in the second half of 2021.

- Margenza carries a boxed warning for left ventricular dysfunction and embryo-fetal toxicity.

- An additional warning and precaution for Margenza is infusion-related reactions.

- The most common adverse reactions (> 10%) with Margenza use, in combination with chemotherapy, were fatigue/asthenia, nausea, diarrhea, vomiting, constipation, headache, pyrexia, alopecia, abdominal pain, peripheral neuropathy, arthralgia/myalgia, cough, decreased appetite, dyspnea, infusion-related reactions, palmar-plantar erythrodysesthesia, and extremity pain.

- The recommended dose of Margenza is 15 mg/kg, administered as an intravenous (IV) infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity.

    - Margenza should be administered at 15 mg/kg over 120 minutes for the initial dose, then over a minimum of 30 minutes every 3 weeks for all subsequent doses.
    - On days when both Margenza and chemotherapy are to be administered, Margenza may be administered immediately after chemotherapy completion.
    - Refer to the respective drug labels for each therapeutic agent administered in combination with Margenza for the recommended dosage information, as appropriate.

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- MacroGenics plans to launch Margenza in March 2021. Margenza will be available as a 250 mg/10 mL single-dose vial.

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