Lartruvo™ (olaratumab) – New Orphan Drug Approval

- On October 19, 2016, Eli Lilly announced the FDA approval of Lartruvo (olaratumab) in combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.
    - This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.
- The National Cancer Institute estimates that 12,310 new cases of STS and nearly 5,000 deaths are likely to occur from the disease in 2016.
    - STS includes a wide variety of tumors arising in the muscle, fat, blood vessels, nerves, tendons or the lining of the joints.
    - The most common treatment for STS that cannot be removed by surgery is treatment with doxorubicin alone or with other drugs.
- Olaratumab is a recombinant human IgG1 antibody that binds to platelet-derived growth factor receptor alpha (PDGFR-α). Olaratumab exhibits in-vitro and in-vivo anti-tumor activity against selected sarcoma cell lines and disrupted the PDGFR-α signaling pathway in in-vivo tumor implant models.
- The efficacy and safety of Lartruvo were demonstrated in a clinical study of 133 patients randomized to receive Lartruvo in combination with doxorubicin or doxorubicin as a single agent. The efficacy outcome measures were overall survival (OS), progression-free survival (PFS), and objective response rate (ORR).
    - The combination group demonstrated a statistically significantly greater OS vs. doxorubicin alone (26.5 vs. 14.7 months, respectively; HR = 0.52 [95% CI: 0.34, 0.79]; $p < 0.05$).
    - The median PFS was 8.2 months with combination therapy vs. 4.4 months with doxorubicin alone (HR = 0.74 [95% CI: 0.46, 1.19]).
    - The ORR was 18.2% with combination therapy vs. 7.5% with doxorubicin alone.
- Warnings and precautions of Lartruvo include infusion-related reactions and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) of Lartruvo plus doxorubicin use were nausea, fatigue, musculoskeletal pain, mucositis, alopecia, vomiting, diarrhea, decreased appetite, abdominal pain, neuropathy, and headache.
- The most common laboratory abnormalities (≥ 20%) were lymphopenia, neutropenia, thrombocytopenia, hyperglycemia, elevated aPTT, hypokalemia, and hypophosphatemia.
- The recommended dose of Lartruvo is 15 mg/kg administered intravenously over 60 minutes on days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity. For the first 8 cycles, Lartruvo is administered with doxorubicin.
    - Patients should be premedicated with diphenhydramine and dexamethasone prior to Lartruvo on day 1 of cycle 1.

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- Eli Lilly plans to launch Lartruvo as a 500 mg/50 mL solution in a single-dose vial by the end of October 2016.