Cyramza® (ramucirumab) – Expanded indication

- On May 29, 2020, Eli Lilly announced the FDA approval of Cyramza (ramucirumab), in combination with erlotinib, for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
    - Cyramza is also approved in combination with docetaxel for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy.
- In addition, Cyramza is approved for gastric cancer, colorectal cancer, and hepatocellular carcinoma.
- The approval of Cyramza for the expanded indication was based on RELAY, a randomized, double-blind, placebo-controlled study in 449 patients with previously untreated metastatic NSCLC whose tumors have EGFR exon 19 deletion or exon 21 (L858R) substitution mutations. Patients received either Cyramza or placebo, in combination with erlotinib until disease progression or unacceptable toxicity. The major efficacy outcome measure was progression-free survival (PFS). Additional efficacy outcome measures included overall survival (OS), objective response rate (ORR), and duration of response (DOR).
    - Median PFS was 19.4 months for Cyramza plus erlotinib vs. 12.4 months for placebo plus erlotinib (hazard ratio [HR] 0.59; 95% CI: 0.46, 0.76; $p < 0.0001$).
    - The ORR was 76% (95% CI: 71, 82) in the Cyramza plus erlotinib arm and 75% (95% CI: 69, 80) in the placebo plus erlotinib arm, with median DOR 18.0 months (95% CI: 13.9, 19.8) and 11.1 months (95% CI: 9.7, 12.3), in each arm respectively.
    - At the time of the final analysis of PFS, OS data were not mature as only 26% of planned events for the final analysis had occurred (HR 0.83; 95% CI: 0.53, 1.30).
- The most common adverse reactions (≥ 30% and ≥ 2% higher than placebo) with Cyramza with erlotinib use were infections, hypertension, stomatitis, proteinuria, alopecia, and epistaxis. The most common laboratory abnormalities were increased alanine aminotransferase, increased aspartate aminotransferase, anemia, thrombocytopenia, and neutropenia.
- The recommended dosage of Cyramza for metastatic NSCLC whose tumors EGFR exon 19 deletions or exon 21 (L858R) substitution mutations is 10 mg/kg every 2 weeks administered by intravenous (IV) infusion over 60 minutes. If the first infusion is tolerated, all subsequent Cyramza infusions may be administered over 30 minutes. Cyramza should be continued until disease progression or unacceptable toxicity.
    - Prior to each Cyramza infusion, all patients should be premedicated with an IV histamine-1 receptor antagonist (eg, diphenhydramine).
    - Refer to the drug label for erlotinib for dosage information.
    - Refer to the Cyramza drug label for dosing for all its other indications.