Alecensa® (alectinib) – Expanded indication, new warning

- On November 6, 2017, Genentech announced the FDA approval of Alecensa (alectinib) for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.
    - Previously, Alecensa was only approved for this indication in patients who had progressed on or were intolerant to Xalkori® (crizotinib).
    - The FDA also converted Alecensa's initial accelerated approval to a full approval.
- The expanded indication for Alecensa was based on an open-label, active-controlled study (ALEX) of 303 patients with ALK-positive NSCLC who had not received prior systemic therapy for metastatic disease. Patients were treated with Alecensa or Xalkori. The major efficacy outcome was progression free survival (PFS).
    - Patients treated with Alecensa demonstrated a significant improvement in PFS vs. the Xalkori group (hazard ratio = 0.53 [95% CI 0.38, 0.73]; $p < 0.0001$).
    - The median PFS was 25.7 months (95% CI: 19.9, not estimable) vs. 10.4 months (95% CI: 7.7, 14.6) for patients treated with Alecensa vs. Xalkori.
    - The ORR was 79% (95% CI: 72, 85) with Alecensa vs. 72% (95% CI: 64, 79) with Xalkori. In addition, 13% vs. 6% of patients achieved a complete response with Alecensa vs. Xalkori, and 66% of patients in both groups achieved a partial response.
- The *Warnings and Precautions* section of the Alecensa drug label was also updated with information regarding renal impairment. Renal impairment occurred in 8% of patients in studies NP28761, NP28673, and ALEX.
    - The incidence of grade ≥ 3 renal impairment was 1.7%, of which 0.5% were fatal events.
    - Dose modifications for renal impairment were required in 3.2% of patients. Median time to grade ≥ 3 renal impairment was 3.7 months (range 0.5 to 14.7 months).
    - Alecensa should be permanently discontinued for grade 4 renal toxicity. Alecensa should be withheld for grade 3 renal toxicity until recovery to ≤ 1.5 times the upper limit of normal, then resumed at a reduced dose.
- The recommended dosage of Alecensa is 600 mg orally twice daily with food until disease progression or unacceptable toxicity.
    - Patients should be selected for the treatment of metastatic NSCLC with Alecensa based on the presence of ALK positivity in tumor specimens.