National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

Written By: Kayla Randle, PharmD, BCOP
Kaiser Permanente of Georgia

Positive Quality Intervention: Pralsetinib Management for Metastatic RET Fusion-positive Non-Small Cell Lung Cancer

Description:

Pralsetinib is an oral Rearranged during Transfection (RET) tyrosine kinase inhibitor (TKI) that inhibits oncogenic RET fusions and mutations.[1] The purpose of this PQI is to review pralsetinib's role in therapy, management of adverse effects and potential drug interactions, and to recommend patient follow up associated with pralsetinib treatment.

Background:

The phase I/II ARROW trial examined pralsetinib for the treatment of RET fusion-positive metastatic non-small cell lung cancer (NSCLC).[1,2] In the dose expansion phase of the study, all patients received pralsetinib at a dose of 400 mg once daily. The trial included 87 patients who had previously undergone treatment with platinum chemotherapy. Overall response rate in these patients was 57% (95% CI: 46%, 68%) with 5.7% of patients achieving a complete response. Responses of 6 months or greater were observed in 80% of patients who responded to pralsetinib. The study population also included 27 patients who had not yet received any treatment. Overall response rate in these treatment-naïve patients was 70% (95% CI: 50%, 86%) with a complete response observed in 11% of patients. A duration of treatment response of 6 months or greater was seen in 58% of patients.

Adverse effects seen in 25% or more of patients treated with pralsetinib include increase in liver enzymes, alkaline phosphatase and serum creatinine; decrease in hemoglobin, lymphocytes and neutrophils; fatigue, constipation, musculoskeletal pain, and hypertension.[1] Interstitial lung disease (ILD)/pneumonitis occurred in 10% of patients who received pralsetinib, including 2.7% with Grade 3-4, and 0.5% with fatal reactions.[1]

PQI Process:

Upon receipt of an order for pralsetinib:

- Ensure patient is an appropriate candidate based on diagnosis of RET fusion-positive metastatic NSCLC
  - FDA approved companion diagnostic test for RET fusion: Oncomine Dx Target (ODxT) Test (Life Technologies Corporation)
    - Information on FDA-approved tests for RET gene fusion in NSCLC is available at http://www.fda.gov/CompanionDiagnostics.
- Starting dose of pralsetinib is 400 mg by mouth once daily on an empty stomach
  - No food should be eaten for at least two hours prior to and at least one hour after pralsetinib dose
- Review patient's current prescriptions for potential drug interactions
  - Avoid strong CYP3A4 inhibitors and inducers

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PQI Process continued:

- Verify monitoring parameters:
  - Baseline: AST, ALT, blood pressure, pregnancy status in females of reproductive potential
  - AST/ALT every 2 weeks for first 3 months of therapy, then monthly or as clinically indicated
  - Blood pressure after 1 week of therapy then at least monthly or as clinically indicated
  - Signs/symptoms of interstitial lung disease/pneumonitis, hemorrhage, and impaired wound healing

Recommended Pralsetinib Dose Reduction for Adverse Reactions

Dose reduction	Recommended dosage
Usual (initial dose)	400 mg once daily
First dose reduction level	300 mg once daily
Second dose reduction level	200 mg once daily
Third dose reduction level	100 mg once daily
Permanently discontinue pralsetinib if patient unable to tolerate 100 mg once daily	

Pralsetinib Dosage Adjustments for Toxicities

Toxicity	Severity	Pralsetinib dose adjustment
Hemorrhagic events	Grade 3/4	Withhold pralsetinib until recovery to baseline or Grade 0 or 1. Discontinue pralsetinib for severe or life-threatening hemorrhagic events.
Hypertension	Grade 3	Initiate or optimize hypertensive therapy. Withhold pralsetinib for grade 3 hypertension that persists despite management with optimal antihypertensive therapy. Resume pralsetinib at a reduced dose when hypertension is controlled.
	Grade 4	Discontinue pralsetinib.
Hepatotoxicity	Grade 3/4	Withhold pralsetinib and monitor AST/ALT once weekly until resolution to Grade 1 or baseline. Resume at reduced dose. If hepatotoxicity recurs at Grade 3 or higher, discontinue pralsetinib

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Pralsetinib Dosage Adjustments for Toxicities continued

Toxicity	Severity	Pralsetinib dose adjustment
Pulmonary toxicity (interstitial lung disease [ILD])/pneumonitis)	Grade 1/2	Withhold pralsetinib until resolution, then resume pralsetinib at a reduced dose. Permanently discontinue pralsetinib for recurrent ILD/pneumonitis.
	Grade 3/4	Permanently discontinue pralsetinib for confirmed ILD/pneumonitis.
Other adverse reactions	Grade 3/4	Withhold pralsetinib until improvement to ≤ grade 2, then resume pralsetinib at a reduced dose. Permanently discontinue pralsetinib for recurrent grade 4 adverse reactions.

Patient Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet
- Counsel to administer orally
    - Review importance of taking on an empty stomach
- Review baseline labs and chronic medications
- Proper sign/symptom monitoring
- Evaluate if patients have missed any doses between cycles to determine if interventions are needed such as reminders, calendars, pill box, etc.

References:

1. Pralsetinib. Blueprint Medicines Corporation. Available at https://www.blueprintmedicines.com/uspi /GAVRETO.pdf. Accessed December, 2020.
2. Gainor JF, Curigliano G, Kim D-W, et al. Registrational dataset from the phase I/II ARROW trial of pralsetinib (BLU-667) in patients with advanced RET fusion+ non-small cell lung cancer (NSCLC).[abstract]. JClin Oncol 2020;38:Abstract 9515.

Supplemental Information:

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