

Positive Quality Intervention: Pralsetinib (Gavreto®) 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 seen in 75% 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 Pralsetinib is also indicated in RET fusion-positive thyroid and RET-mutated medullary thyroid cancer.

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)
- 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
- Review patient's current prescriptions for potential drug interactions
 - Avoid P-gp substrates and strong CYP3A4 inhibitors and inducers
- 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

Important notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



PQI Process continued:

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/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
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 \leq 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.

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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]. J Clin Oncol 2020;38:Abstract 9515.

Supplemental Information:

YourBlueprint patient support program

- Co-pay assistance for commercially insured patients
- Free drug program for uninsured and underinsured patients
- Case managers available
- Enroll online or by calling 1-888-BLUPRNT (1-888-258-7768)

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