Targeted Therapies Are Preferred First-Line Options in Patients With Oncogenic Drivers[1]

GAVRETO™ pralsetinib 100mg capsules

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) NSCLC panel recommends molecular testing for actionable biomarkers in eligible patients with metastatic NSCLC and strongly advises broad molecular profiling[1]

Knowing your metastatic NSCLC patients' biomarker status, including RET, is critical to determining the optimal treatment plan. Patients with mNSCLC who are candidates for targeted therapy could be missed if comprehensive biomarker testing is not performed.[2,3] Testing with next generation sequencing (NGS) can be effective with liquid biopsies when tissue is limited or unavailable.[4,5]

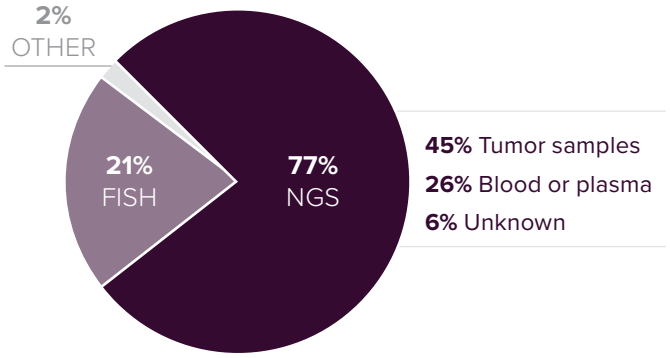
RET fusions

mNSCLC

ARROW clinical trial assays

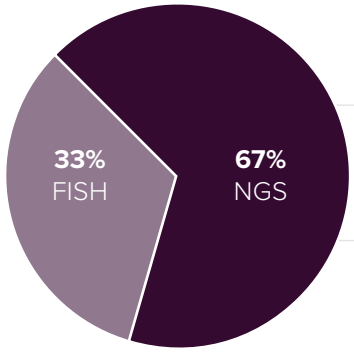
In the ARROW clinical trial, identification of a RET gene alteration in mNSCLC patients was determined by local laboratories using NGS, FISH, and other tests. The most commonly used diagnostic for patient identification was NGS.[6]

Patient identification of previously platinum treated NSCLC patients



45% Tumor samples
26% Blood or plasma
6% Unknown

Patient identification of treatment-naive NSCLC patients



41% Tumor samples
22% Blood or plasma
4% Unknown

Test to find out if a RET fusion is driving your patient's mNSCLC.

The most common adverse reactions (≥25%) in GAVRETO-treated patients were fatigue, constipation, musculoskeletal pain, and hypertension.[6]

Please see the Important Safety Information for GAVRETO on page 3.

Please click here to see the full Prescribing Information for GAVRETO.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for NSCLC provide recommendations for individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

FISH=fluorescence in situ hybridization; mNSCLC=metastatic non–small cell lung cancer; NCCN=National Comprehensive Cancer Network®; RET=rearranged during transfection.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.8.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed September 24, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Barlesi F, Mazières J, Merlio JP, et al. Routine molecular profiling of cancer: results of a one-year nationwide program of the French Cooperative Thoracic Intergroup (IFCT) for advanced non-small cell lung cancer (NSCLC) patients. *Lancet.* 2016;287(10026):1415-1426. **3.** Kris MG, Johnson BE, Berry LD, et al. Using multiplexed assays of oncogenic drivers in lung cancers to select targeted drugs. *JAMA*. 2014;311(19):1998-2006. **4.** Leighl NB, Page RD, Raymond VM, et al. Clinical utility of comprehensive cell-free DNA analysis to identify genomic biomarkers in patients with newly diagnosed metastatic non–small cell lung cancer. *Clin Cancer Res*. 2019;25(15):4691-4700. **5.** Lindeman NI, Cagle PT, Aisner DL, et al. Updated molecular testing guideline for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors: guideline from the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. *Arch Pathol Lab Med.* 2018;142(3):321-346. **6.** GAVRETO™ (pralsetinib). Prescribing Information. Blueprint Medicines Corporation; Cambridge, MA. September 2020.

Consult With Your Pathologist to Determine the Appropriate Laboratory and Test for Your Patients

GAVRETO™ pralsetinib 100mg capsules

Laboratory	Test	Mutations	Fusions	Website
ARUP	Solid Tumor Mutation Panel	✓	✗	aruplab.com
	Gene Rearrangements by FISH*	✗	✓	
Biodesix	GeneStrat®	✗	✓	biodesix.com
Caris Life Sciences	MI Comprehensive Tumor Profile	✓	✓	carislifesciences.com
	MI Tumor Seek	✓	✓	
Foundation Medicine	FoundationOne® CDx	✓	✓	foundationmedicine.com
	FoundationOne® Liquid	✓	✓	
GenPath/BioReference	Solid Tumor NTRK Gene Fusion Assay	✗	✓	genpathdiagnostics.com
	Onkosight Solid Tumor	✓	✗	
Guardant Health	Guardant360	✓	✓	guardant360.com
Inivata	InVision First Lung	✓	✓	inivata.com
Integrated Oncology/ LabCorp	OmniSeq℠ Advance Assay	✓	✓	integratedoncology.com
	OmniSeq℠ Comprehensive Profiling Assay	✓	✓	
	FISH*	✗	✓	
	Resolution Bioscience ctDx Lung Assay	✓	✓	
Mayo Clinic Laboratories	Lung Cancer-Targeted Gene Panel with Rearrangement	✓	✓	mayocliniclabs.com
	Lung Cancer Rearrangement Testing*	✓	✓	
	(10q11) Rearrangement	✗	✓	
NeoGenomics	NeoTYPE® Discovery	✓	✓	neogenomics.com
	Lung NGS Fusion Profile	✗	✓	
	NeoTYPE® Lung Tumor Profile*	✗	✓	
	NGS Fusion Profile	✗	✓	
	InVision First Lung	✓	✓	
PathGroup	Endeavor	✓	✓	pathgroup.com
ParadigmDx	PCDx™	✓	✓	paradigmdx.com
Quest	IBM Watson Genomics	✓	✓	inivata.com
	PTC Rearrangement Thyroid	✓	✓	testdirectory.questdiagnostics.com jdos.nicholsinstitute.com
	Thyroid Cancer Mutation Panel	✗	✓	
	50SEQ® with FISH (MedFusion)*	✓	✓	
	LungSeq with FISH (MedFusion)*	✓	✓	
Tempus	TEMPUS xT	✓	✓	tempus.com
	TEMPUS xF	✓	✓	

*Test uses fluorescence in situ hybridization (FISH). Current as of 10/2020.

INDICATION

GAVRETO™ (pralsetinib) is indicated for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

Pneumonitis occurred in 10% of patients who received GAVRETO, including 2.7% with Grade 3/4, and 0.5% with fatal reactions. Monitor for pulmonary symptoms indicative of interstitial lung disease (ILD)/pneumonitis. Withhold GAVRETO and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.

Hypertension occurred in 29% of patients, including Grade 3 hypertension in 14% of patients. Overall, 7% had their dose interrupted and 3.2% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate GAVRETO in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating GAVRETO. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue GAVRETO based on the severity.

Hepatotoxicity: Serious hepatic adverse reactions occurred in 2.1% of patients treated with GAVRETO. Increased AST occurred in 69% of patients, including Grade 3/4 in 5.4% and increased ALT occurred in 46% of patients, including Grade 3/4 in 6%. The median time to first onset for increased AST was 15 days (range: 5 days to 1.5 years) and increased ALT was 22 days (range: 7 days to 1.7 years). Monitor AST and ALT prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue GAVRETO based on severity.

Grade ≥ 3 **hemorrhagic events** occurred in 2.5% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.

Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, GAVRETO has the potential to adversely affect wound healing. Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.

Based on findings from animal studies and its mechanism of action, GAVRETO can cause **fetal harm** when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with GAVRETO and for 2 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the final dose. Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the final dose.

Common adverse reactions (≥25%) were fatigue, constipation, musculoskeletal pain, and hypertension. **Common Grade 3-4 laboratory abnormalities (≥2%)** were decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected) and increased alanine aminotransferase (ALT).

Avoid coadministration with **strong CYP3A inhibitors**. Avoid coadministration of GAVRETO with **combined P-gp and strong CYP3A inhibitors**. If coadministration cannot be avoided, reduce the GAVRETO dose. Avoid coadministration of GAVRETO with **strong CYP3A inducers**. If coadministration cannot be avoided, increase the GAVRETO dose.

Please click here to see the full Prescribing Information for GAVRETO.

GAVRETO™
pralsetinib 100mg capsules