GAVRETO demonstrated robust and durable response in treatment-naïve RET+ mNSCLC[1]

GAVRETO pralsetinib 100mg capsules

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.

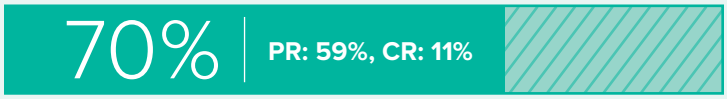
SELECT SAFETY INFORMATION

Serious and sometimes fatal adverse reactions occurred with GAVRETO. Warnings and precautions include interstitial lung disease/pneumonitis, hypertension, hepatotoxicity, hemorrhagic events, tumor lysis syndrome, risk of impaired wound healing, and embryo-fetal toxicity.

EFFICACY RESULTS IN TREATMENT-NAÏVE mNSCLC PATIENTS TREATED WITH GAVRETO[1,2]

PIVOTAL DATA INCLUDED IN THE U.S. PRESCRIBING INFORMATION (USPI)

Overall Response Rate (n=27) (95% CI: 50%-86%)



Median DoR (n=19): 9.0 months (6.3 months-NE)

Median DoR follow up: 7.5 months (3.7 months-8.3 months)[2]

Patients enrolled by July 11, 2019. Data cutoff: Feb 13, 2020

STUDY DESIGN

Efficacy and safety was evaluated in treatment-naïve and previously platinum-treated patients with RET-fusion+ mNSCLC in ARROW, a phase 1/2, nonrandomized, open-label, single-arm, multicohort, multicenter clinical trial. Patients with asymptomatic central nervous system metastases, including patients with stable or decreasing steroid use within 2 weeks prior to study entry, were enrolled.

Per initial protocol, treatment-naïve patients were included if they were deemed not eligible for platinum-based chemotherapy based on investigator assessment.[2]

SELECT BASELINE CHARACTERISTICS

- Median age: 65 years (30-87)
- Gender: Female 52%, Male 48%
- History of or current CNS metastases at baseline: 37%

Adverse reactions (≥15%) and Grade 3-4 laboratory abnormalities (≥2%) in RET fusion-positive mNSCLC patients (n=220)[1]*

- **Adverse Reactions: Fatigue (35%), constipation (35%), musculoskeletal pain (32%), hypertension (28%), diarrhea (24%), cough (23%), pyrexia (20%), edema (20%), pneumonia (17%), and dry mouth (16%)**
- **Laboratory Abnormalities: Decreased lymphocytes (19%), decreased neutrophils (16%), decreased phosphate (11%), decreased hemoglobin (9%), decreased sodium (7%), decreased platelets (3.2%), increased AST (2.3%), and increased ALT (2.3%)**

*The safety of GAVRETO 400 mg orally once daily was evaluated in both treatment-naïve and previously platinum-treated mNSCLC patients.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; CI=confidence interval; CNS=central nervous system; CR=complete response; mNSCLC=metastatic non–small cell lung cancer; NE=not estimable; PR=partial response; RET=rearranged during transfection.

EXPLORATORY FOLLOW-UP ANALYSES[2]

These analyses include treatment-naïve patients enrolled through May 22, 2020, which includes the patients from the pivotal analysis in the USPI. These results are not included in the GAVRETO labeling. **As these were not pre-specified analyses, data must be interpreted with caution.**

ALL TREATMENT-NAÏVE PATIENTS

Overall Response Rate (n=68) (95% CI: 68%-88%)

Duration of Response (n=54)

Median DoR: Not Reached (9 months-NR)

Median DoR follow up: 7.4 months (6.4 months-9.5 months)

POST HOC ANALYSES OF TREATMENT-NAÏVE PATIENTS

Initially, the ARROW protocol included treatment-naïve patients who were not candidates for standard therapy. In July 2019, the protocol was amended to expand the eligibility criteria to include patients who were eligible for standard therapy.

Pre-protocol amendment (n=43):

74% ORR
(95% CI: 59%-87%)
PR=65%, CR=9%

Median DoR (n=32): 11 months (7.4 months-NR)

Baseline Characteristics

- Median age: 65 years (30-87)
- Gender: Female 44%, Male 56%
- History of or current CNS metastases at baseline: 35%

Post-protocol amendment (n=25):

88% ORR
(95% CI: 69%-98%)
All responses were partial.

Median DoR (n=22): Not Reached (NR-NR)

Baseline Characteristics

- Median age: 54 years (35-80)
- Gender: Female 56%, Male 44%
- History of or current CNS metastases at baseline: 28%

All other baseline patient characteristics were generally balanced between the pivotal data included in the USPI and exploratory follow-up populations.

Patients enrolled by May 22, 2020. Data cutoff: Nov 6, 2020

Adverse reactions (≥15%) and Grade 3-4 laboratory abnormalities (≥2%) in RET fusion-positive mNSCLC patients (n=281) were generally consistent with the pivotal data included in the USPI[2]

Please see additional Important Safety Information on the next page and click here to see the full Prescribing Information for GAVRETO.

Test for RET and consider GAVRETO for first-line treatment of RET+ mNSCLC[1]

GAVRETO® pralsetinib 100mg capsules

NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®) recommend pralsetinib (GAVRETO) as a preferred first-line treatment option for RET fusion-positive metastatic NSCLC (Category 2A)[3]*

NCCN=National Comprehensive Cancer Network.
*See the NCCN Guidelines for detailed recommendations, including other preferred treatment options.
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.

GAVRETO is approved across all lines of therapy in RET+ mNSCLC, including first line.[1]
Ensure you have biomarker test results before making therapeutic decisions.[1,4]

IMPORTANT SAFETY INFORMATION

Interstitial Lung Disease (ILD)/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 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 aspartate aminotransferase (AST) occurred in 69% of patients, including Grade 3/4 in 5% and increased alanine aminotransferase (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.

Tumor Lysis Syndrome (TLS): Cases of TLS have been reported in patients with medullary thyroid carcinoma receiving GAVRETO. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

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 constipation, hypertension, fatigue, musculoskeletal pain and diarrhea. **Common Grade 3/4 laboratory abnormalities (≥2%)** were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased calcium (corrected), decreased sodium, increased AST, increased ALT, decreased platelets and increased alkaline phosphatase.

Avoid coadministration of GAVRETO with **strong CYP3A inhibitors or 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.

You may report side effects to the FDA at **1-800-FDA-1088** or www.fda.gov/medwatch. You may also report side effects to Genentech at **1-888-835-2555**.

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

Visit **GAVRETO-hcp.com** for more information.

References: 1. GAVRETO Prescribing Information. Genentech, Inc. April 2021. **2.** Data on file. Blueprint Medicines Corporation. Cambridge, MA 2020. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.4.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed March 31, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **4.** VanderLaan PA, Rangachari D, Costa DB, et al. The rapidly evolving landscape of biomarker testing in non–small cell lung cancer. *Cancer Cytopathol.* 2021;129(3):179-181.

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