New Drug Overview

Ibtrozi (taletrectinib)

PDL Category: Antineoplastics

Introduction

Disease Background:

- The most common lung cancer, accountable for the greatest number of cancer deaths in the world, includes non-small cell lung cancers (NSCLC). This malignant tumor of the lung accounts for approximately 85-90% of lung cancer occurrences (*Eapen et al 2024*).
- There are two subtypes of non-small cell carcinoma, including non-squamous carcinoma (adenocarcinoma and large cell carcinoma) and squamous cell carcinoma (*Eapen et al 2024*).
- It has been reported that tumors certain for proto-oncogene tyrosine protein kinase-1 (*ROS1*) gene fusions make up 0.9%-2.6% of NSCLCs. In addition, a majority are lung adenocarcinomas (*Li et al 2024*).
- Genetic predisposition and environmental exposures are listed as risk factors for NSCLC, but tobacco use is the main risk factor (*Eapen et al 2024*).
  - The Surgeon General has reported that both active smoking and second-hand smoke can cause lung cancer (*NCCN 2025*).
- This cancer generally affects older adults ≥65 years of age, and men are generally more commonly diagnosed with lung cancer as compared with females (*Eapen et al 2024*).
- While roughly 25% of patients can be asymptomatic, common symptoms of lung cancer comprise of cough, dyspnea, chest pain, hemoptysis, wheezing, and nonspecific chest discomfort or pleuritic chest pain (*Eapen et al 2024*).
- Ibtrozi was FDA approved in 2025.

Pharmacology/Usage

- Ibtrozi (taletrectinib) is a kinase inhibitor. It is an inhibitor of tyrosine kinase ROS1, including ROS1 resistance mutations. Taletrectinib also demonstrated inhibitory effects on tropomyosin receptor kinases (TRKs) TRKA, TRKB, and TRKC. Taletrectinib inhibited growth of cancer cells expressing *ROS1* fusion genes and mutations.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Ibtrozi (taletrectinib)
• For the treatment of adult patients with locally advanced or metastatic *ROS1*-positive non-small cell lung cancer (NSCLC).	✔

(Prescribing information: Ibtrozi 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Ibtrozi (taletrectinib)	Capsules	Oral	Once daily, on an empty stomach (no food intake at least 2 hours before and 2 hours after taking	• Select patients for treatment of locally advanced or metastatic

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
	-Swallow whole; do not open, chew, crush, or dissolve prior to swallowing.		Ibtrozi), until disease progression or unacceptable toxicity. -Take at about the same time each day.	NSCLC with Ibtrozi based on the presence of *ROS1* rearrangement(s) in tumor specimens. An FDA approved test to detect *ROS1* rearrangement(s) for selecting patients for Ibtrozi treatment is not currently available. • Before starting treatment, assess liver function tests (including ALT, AST, and bilirubin), electrolytes, ECG, and uric acid. • Avoid food or drink containing grapefruit during Ibtrozi treatment. • Minimize sun exposure and use sun protection during treatment and for ≥5 days after discontinuation. • If vomiting occurs at any time after taking a dose, take the next dose at its scheduled time on the following day. • There are dosage modifications for adverse reactions.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Ibtrozi was assessed in two multicenter, single-arm, open-label clinical trials (TRUST-I and TRUST-II) that included patients (N=270) with *ROS1*-positive locally advanced or metastatic NSCLC.
- In both trials, patients were required to have histologically confirmed, locally advanced or metastatic, *ROS1*-positive NSCLC, an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

- The main efficacy outcome measures were confirmed overall response rate (ORR) and duration of response (DOR) per RECIST v1.1 as assessed by a blinded independent central review (BICR). Intracranial response per modified RECIST v1.1 was assessed by BICR.
  - The efficacy populations included 157 patients naïve to treatment with a ROS1 TKI and 113 patients who received one prior ROS1 TKI.
  - Patients could be chemotherapy-naïve or have received prior chemotherapy for locally advanced disease.
- *ROS1 TKI-naïve:*
  - TRUST-I included patients (N=103) with ROS1 TKI-naïve NSCLC with a median age of 56 years (range 26 to 78), while 55% were female, 100% were Asian, 73% never smoked, and 81% had ECOG performance status of 1. At baseline, 91% had metastatic disease, 17% had CNS metastases, 96% had adenocarcinoma, and 19% had prior platinum-based chemotherapy for advanced disease.
  - TRUST-II included patients (N=54) with ROS1 TKI-naïve NSCLC with a median age of 57 years (range 27 to 82), while 56% were female, 65% were Asian, 50% never smoked, and 61% had ECOG performance status of 1. At baseline, 91% had metastatic disease, 35% had CNS metastases, 98% had adenocarcinoma, and 19% had prior platinum-based chemotherapy for advanced disease.
  - Efficacy results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

Efficacy Parameters	ROS1 TKI-naïve (N=157)	
	TRUST-I (N=103)	TRUST-II (N=54)
Response Rate, %	90%	85%
Complete Response, %	5%	7%
Partial Response, %	85%	78%
Duration of Response (DOR)	N=93	N=46
Median DOR	Not reached	*
Range (months)	1.1, 46.9+	1.4+, 30.4+
% with DOR ≥12 months	72%	63%

*Median DOR not included for TRUST-II given shorter duration of follow-up

  - Among the 157 ROS1 TKI-naïve patients across TRUST-I and TRUST-II, 15 had measurable CNS metastases at baseline as assessed by BICR and had not received radiation therapy to the brain within 2 months prior to study entry; responses in intracranial lesions were observed in 11 patients.
- *ROS1 TKI-pretreated:*
  - TRUST-I included patients (N=66) with ROS1 TKI-pretreated NSCLC with a median age of 51 years (range 31 to 77), while 61% were female, 100% were Asian, 74% had never smoked, and 71% had ECOG performance status of 1. At baseline, 97% had metastatic disease, 42% had CNS metastases, 92% had adenocarcinoma, 35% had prior platinum-based chemotherapy for advanced disease, and 100% had prior treatment with crizotinib.

- TRUST-II included patients (N=47) with ROS1 TKI-pretreated NSCLC with a median age of 55 years (range 27 to 79), while 57% were female, 47% were Asian, 62% had never smoked, and 55% had ECOG performance status of 1. At baseline, 98% had metastatic disease, 57% had CNS metastases, 98% had adenocarcinoma, 40% had prior platinum-based chemotherapy for advanced disease, 79% had prior treatment with crizotinib, and 21% had prior treatment with entrectinib.
- Efficacy results are presented in the table below, which was adapted from the prescribing information.

Table 4. Efficacy results

Efficacy Parameters	ROS1 TKI-pretreated (N=113)	
	TRUST-I (N=66)	TRUST-II (N=47)
Response Rate, %	52%	62%
Complete Response, %	0%	11%
Partial Response, %	52%	51%
Duration of Response (DOR)	N=34	N=29
Median DOR	13.2	*
Range (months)	1.4, 38.7+	1.7+, 30.4+
% with DOR ≥6 months	74%	83%
% with DOR ≥12 months	44%	45%

*Median DOR not included for TRUST-II given shorter duration of follow-up

- Among the 113 ROS1 TKI-pretreated patients, across TRUST-I and TRUST-II, 24 had measurable CNS metastases at baseline as assessed by BICR and had not received radiation therapy to the brain within 2 months prior to study entry; responses in intracranial lesions were observed in 15 patients.
- Among 32 patients who had re-biopsied samples tested by next-generation sequencing after failure of a prior ROS1 TKI, 15 had resistance mutations. Responses were observed in 8 of these 15 patients; all responding patients had tumors with solvent front mutation G2032R.

Clinical guidelines

- **National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer (NSCLC)** (*NCCN 2025*).
  - This guideline was last updated in December if 2025, but taletrectinib was added in prior update. Taletrectinib is added as a preferred option for ROS1 gene fusion discovered prior to first-line systemic therapy. The updated footnote adds that entrectinib, repotrectinib, or taletrectinib may be best if a patient has brain metastases. Taletrectinib is also listed in subsequent therapy for ROS1 gene fusion. The updated footnote adds that repotrectinib or taletrectinib is an option for resistant mutations (eg ROS1 G2032R). Refer to the guidelines for specific additional information.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Ibtrozi can cause hepatotoxicity, including drug-induced liver injury and fatal adverse reactions. Monitor liver function tests (ALT, AST, bilirubin) prior to administration of Ibtrozi, every 2 weeks during the first 2 months of treatment, and then monthly thereafter as clinically indicated with more frequent testing in patients who develop transaminase elevations. Withhold, then resume at reduced dose upon improvement, or permanently discontinue Ibtrozi based on severity.
  - Ibtrozi can cause severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis. ILD/pneumonitis led to dose interruption of Ibtrozi in 1.1% of patients. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Immediately withhold Ibtrozi in patients with suspected ILD/pneumonitis. Withhold, then reduce the dose or permanently discontinue Ibtrozi if Grade ≥2 ILD/pneumonitis is confirmed.
  - Ibtrozi can cause QTc interval prolongation, which can increase the risk for ventricular tachyarrhythmias or sudden death. Ibtrozi prolongs the QTc interval in a concentration-dependent manner. Monitor ECGs and electrolytes prior to administration of Ibtrozi and then periodically thereafter as clinically indicated during treatment. Adjust the frequency of monitoring based on risk factors such as known long QT syndromes, clinically significant bradyarrhythmia, severe or uncontrolled heart failure, and concomitant medications associated with QTc interval prolongation.
    - Significant prolongation of the QTc interval may occur when Ibtrozi is taken with food, strong and moderate CYP3A inhibitors, and/or drugs with a known potential to prolong QTc. Administer Ibtrozi on an empty stomach. Avoid coadministration of Ibtrozi with strong and moderate CYP3A inhibitors and/or drugs with a known potential to prolong QTc. Withhold, then resume at the same or reduced dose, or permanently discontinue Ibtrozi based on severity.
  - Ibtrozi can cause hyperuricemia. Monitor serum uric acid levels prior to administration of Ibtrozi and periodically during treatment. Start treatment with urate-lowering medications as clinically indicated. Withhold, then resume at the same or reduced dose, or permanently discontinue Ibtrozi based on severity.
  - Ibtrozi can cause myalgia with or without creatine phosphokinase (CPK) elevation. The median time to first onset of myalgia was 11 days. Advise patients to report any unexplained muscle pain, tenderness, or weakness. Monitor serum CPK levels during Ibtrozi treatment every 2 weeks during the first month of treatment and then as clinically indicated in patients reporting unexplained muscle pain, tenderness, or weakness. Withhold, then resume at the same or reduced dose upon improvement.
  - Ibtrozi can increase the risk of fractures. ROS1 inhibitors as a class have been associated with skeletal fractures. Promptly assess patients with signs or symptoms of fractures. There are no data on the effects of Ibtrozi on healing of known fractures and risk of future fractures.

- **Common adverse drug reactions**: Listed % incidence for adverse drug reactions= reported % incidence for Ibtrozi for all grades. Please note that there was no placebo data to compare with in the prescribing information.
  - The most frequently reported adverse reactions included diarrhea (64%), nausea (47%), vomiting (43%), constipation (21%), dizziness (22%), peripheral neuropathy (17%), dysgeusia (15%), rash (22%), fatigue (20%), electrocardiogram QT prolonged (19%), decreased appetite (16%), and cough (16%).
  - Select laboratory abnormalities included hemoglobin decreased (48%), lymphocytes decreased (38%), neutrophils decreased (25%), AST increased (87%), ALT increased (85%), creatine phosphokinase increased (53%), cholesterol

increased (41%), triglycerides increased (41%), creatinine increased (39%), uric acid increased (38%), gamma glutamyl transferase increased (36%), alkaline phosphatase increased (30%), calcium decreased (28%), albumin decreased (25%), bilirubin increased (24%), potassium increased (21%), and sodium increased (20%).

- **Drug interactions:**
  - Taletrectinib is a CYP3A substrate. Avoid concomitant use with strong or moderate CYP3A inhibitors.
  - Avoid concomitant use with strong or moderate CYP3A inducers.
  - Concomitant use of a proton pump inhibitor (PPI) decreases taletrectinib exposure, which may reduce the effectiveness of Ibtrozi. Avoid concomitant use with PPIs and H2 receptor antagonists. Administer locally acting antacids at least 2 hours before or 2 hours after taking Ibtrozi.
  - Ibtrozi causes QTc interval prolongation. Concomitant use of Ibtrozi with other drugs known to prolong the QTc interval may increase the risk of QTc interval prolongation. Avoid concomitant use of Ibtrozi with other drug(s) with a known potential to prolong the QTc interval, such as antiarrhythmic drugs. If concomitant use cannot be avoided, adjust the frequency of monitoring as recommended. Withhold Ibtrozi if the QTc interval is >500 msec or the change from baseline is >60 msec.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that based on literature reports in humans with congenital mutations leading to changes in TRK signaling, findings from animal studies, and its mechanism of action, Ibtrozi can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus.
    - Verify the pregnancy status of females of reproductive potential prior to starting Ibtrozi. In addition, advise females of reproductive potential and male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 weeks after the last dose.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- The most common lung cancer, accountable for the greatest number of cancer deaths in the world, includes non-small cell lung cancers (NSCLC). This malignant tumor of the lung accounts for approximately 85-90% of lung cancer occurrences (*Eapen et al 2024*).
- Ibtrozi is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive NSCLC.
  - It can cause hepatotoxicity and thus liver function tests should be monitored.
  - It can cause severe, life-threatening or fatal ILD/pneumonitis. Monitor for new or worsening pulmonary symptoms.
  - It can cause QTc interval prolongation. Monitor ECGs and electrolytes. Significant prolongation of the QTc interval may occur when Ibtrozi is taken with food, strong and moderate CYP3A inhibitors, and/or drugs with a known potential to prolong QTc. Administer on an empty stomach. Avoid the coadministration of Ibtrozi with strong and moderate CYP3A inhibitors and/or drugs with a known potential to prolong QTc.
- Its efficacy was assessed in two multicenter, single-arm, open-label clinical trials. The main efficacy outcome measures were confirmed ORR and DOR per RECIST v1.1 as assessed by a BICR.
  - The response rates ranged from 85% to 90% in both studies for ROS1 TKI-naïve patients.
  - The response rates ranged from 52% to 62% in both studies for ROS1 TKI-pretreated patients.
- NCCN guidelines have been updated to include Ibtrozi (taletrectinib).

- It is recommended that Ibtrozi should be non-recommended in order to confirm the appropriate diagnosis and clinical parameters for use.

- **PDL Placement:**
  - ☐ Recommended
  - ☒ Non-Recommended with Conditions

References

- Eapen GA, Weiss KS, Ko YJ, et al. Non-small cell lung cancer. Dynamed Web site. Updated May 08, 2024. Accessed February 2, 2026. Non-small Cell Lung Cancer - DynaMed.
- Ibtrozi. Package insert. Nuvation Bio Inc; June 2025.
- Li W, Xiong A, Yang N, et al. Efficacy and safety of taletrectinib in Chinese patients with ROS1+ non-small cell lung cancer: The phase II TRUST-I study. *J Clin Oncol*. 2024; 42(22): 2660-2670.
- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer v3.2026-December 24, 2025. Accessed February 2, 2026. nscl.pdf.

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