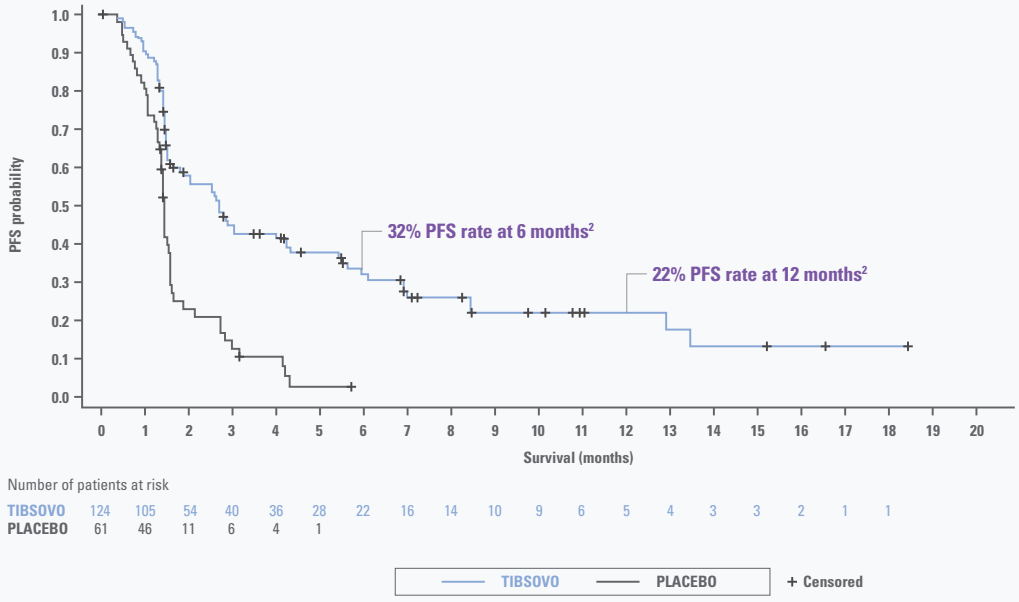
TIBSOVO®
ivosidenib tablets 250mg

IMPROVING PROGRESSION-FREE SURVIVAL IN mIDH1 CHOLANGIOCARCINOMA

TIBSOVO® delivered **significant improvements in PFS** with a 63% reduction in the risk of disease progression or death **(HR, 0.37 [95% CI, 0.25-0.54]; *P*<0.0001)**[1]



TIBSOVO was studied in a phase 3, randomized (2:1), double-blind, placebo-controlled, multicenter trial of 185 adult patients with locally advanced or metastatic m*IDH1* cholangiocarcinoma whose disease had progressed following at least 1 but not more than 2 prior regimens, including at least one gemcitabine- or 5-FU-containing regimen.[1] Patients were randomized to receive either TIBSOVO 500 mg QD orally or matched placebo. The primary endpoint was PFS. Crossover from placebo to TIBSOVO was permitted after confirmed disease progression. Among the 61 patients randomized to placebo, 70% crossed over to receive open-label TIBSOVO.

Patients were censored if they were missing a baseline assessment, missing documented progression or death before data cutoff, started alternate anticancer systemic treatment, or had documented progression or death following 95 days or more from the previous adequate assessment.[2]

- Once-daily oral TIBSOVO is the **first-in-class targeted inhibitor of mIDH1**[1,3]
- Disease control rate[a] was **53% with TIBSOVO** vs 28% with placebo
- The **maximum treatment duration** was **nearly 5X longer with TIBSOVO** vs placebo[4]
- **15% of patients** remained on TIBSOVO for **over a year**[4]
- The most common adverse reactions (≥15%) were fatigue, nausea, abdominal pain, diarrhea, cough, decreased appetite, ascites, vomiting, anemia, and rash[1]

INDICATION

TIBSOVO is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for patients with a susceptible IDH1 mutation as detected by an FDA-approved test for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma who have been previously treated.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

QTc Interval Prolongation: Patients treated with TIBSOVO can develop QT (QTc) prolongation and ventricular arrhythmias. Concomitant use of TIBSOVO with drugs known to prolong the QTc interval (eg, anti-arrhythmic medicines, fluoroquinolones, triazole anti-fungals, 5-HT_3 receptor antagonists) and CYP3A4 inhibitors may increase the risk of QTc interval prolongation.

Please see additional Important Safety Information on back and Full Prescribing Information.

CI, confidence interval; HR, hazard ratio; mIDH1, mutated isocitrate dehydrogenase-1; ORR, objective response rate; PFS, progression-free survival; QD, once a day; SD, stable disease.

[a]The disease control rate (ORR + SD) was due mostly to the SD rate (an ORR of 2% [3 partial responses] and an SD rate of 51% with TIBSOVO vs an ORR of 0% and an SD rate of 28% with placebo).

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend ivosidenib (TIBSOVO®) as a subsequent-line treatment option for unresectable or metastatic cholangiocarcinoma with an *IDH1* mutation following disease progression.[5]

To view the most recent and complete version of the guidelines, visit NCCN.org.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

QTc Interval Prolongation: (cont'd) Conduct monitoring of electrocardiograms (ECGs) and electrolytes. In patients with congenital long QTc syndrome, congestive heart failure, or electrolyte abnormalities, or in those who are taking medications known to prolong the QTc interval, more frequent monitoring may be necessary.

Interrupt TIBSOVO if QTc increases to greater than 480 msec and less than 500 msec. Interrupt and reduce TIBSOVO if QTc increases to greater than 500 msec. Permanently discontinue TIBSOVO in patients who develop QTc interval prolongation with signs or symptoms of life-threatening arrhythmia.

Guillain-Barré Syndrome: Guillain-Barré syndrome can develop in patients treated with TIBSOVO. Monitor patients taking TIBSOVO for onset of new signs or symptoms of motor and/or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, paresthesias, or difficulty breathing. Permanently discontinue TIBSOVO in patients who are diagnosed with Guillain-Barré syndrome.

ADVERSE REACTIONS

- **In patients with cholangiocarcinoma,** the most common adverse reactions (≥15%) were fatigue, nausea, abdominal pain, diarrhea, cough, decreased appetite, ascites, vomiting, anemia, and rash. The most common laboratory abnormalities (≥10%) were hemoglobin decreased, aspartate aminotransferase increased, and bilirubin increased

DRUG INTERACTIONS

Strong or Moderate CYP3A4 Inhibitors: Reduce TIBSOVO dose with strong CYP3A4 inhibitors. Monitor patients for increased risk of QTc interval prolongation.

Strong CYP3A4 Inducers: Avoid concomitant use with TIBSOVO.

Sensitive CYP3A4 Substrates: Avoid concomitant use with TIBSOVO.

QTc Prolonging Drugs: Avoid concomitant use with TIBSOVO. If co-administration is unavoidable, monitor patients for increased risk of QTc interval prolongation.

LACTATION

Because many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed children, advise women not to breastfeed during treatment with TIBSOVO and for 1 month after the last dose.

Please see additional Important Safety Information on front and Full Prescribing Information.

References: 1. Tibsovo. Package insert. Servier Pharmaceuticals LLC; 2022. **2.** Data on file. Servier Pharmaceuticals LLC. **3.** Popovici-Muller J, Lemieux RM, Artin E, et al. Discovery of AG-120 (ivosidenib): a first-in-class mutant IDH1 inhibitor for the treatment of IDH1 mutant cancers. *ACS Med Chem Lett.* 2018;9(4):300-305. **4.** Zhu AX, Macarulla T, Javle MM, et al. Final overall survival efficacy results of ivosidenib for patients with advanced cholangiocarcinoma with IDH1 mutation: the phase 3 randomized clinical ClarIDHy trial. *JAMA Oncol.* 2021;7(11):1669-1677. **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers V2.2022. © National Comprehensive Cancer Network, Inc., 2022. All rights reserved. Accessed July 25, 2022. To view the most recent and complete version of the guidelines, go online to NCCN.org. 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.

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