FIRST AND ONLY mIDH1 INHIBITOR FOR R/R MDS[1,2]

LASER-FOCUSED ON REMISSION

39 % Complete Remission (95% CI, 17.3-64.3)[1,a]

69 % Remission at 12 Months per Kaplan-Meier estimation[3]

67 % Transfusion Independence of patients who were transfusion-dependent at BL[1,b]

TIBSOVO®
ivosidenib tablets 250mg

Ivosidenib (TIBSOVO) is recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a targeted treatment option for certain patients with R/R MDS with *IDH1* mutations[4,c]

[a]CR was defined as bone marrow ≤5% myeloblasts with normal maturation of all cell lines, hemoglobin ≥11 g/dL, platelets ≥100 x 10^9/L, neutrophils ≥1.0 x 10^9/L, and response lasting at least 4 weeks.[3] 43% of CR responders had baseline bone marrow blasts <5%.[1]
[b]Six out of 9 patients who were transfusion-dependent at BL achieved transfusion independence.[1] Postbaseline transfusion independence was defined as a period of ≥56 days with no RBC and/or platelet transfusions after the start of study treatment and on or before the end of study treatment.[3]
[c]Category 2A recommendation for lower-risk disease, including for patients with symptomatic anemia, and higher-risk disease.[4]

BL, baseline; CI, confidence interval; mIDH1, mutated IDH1; NCCN, National Comprehensive Care Network; RBC, red blood cell; R/R, relapsed or refractory.

INDICATION

TIBSOVO is indicated for the treatment of adult patients with relapsed or refractory myelodysplastic syndromes (MDS) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME IN MDS
Patients treated with TIBSOVO have experienced symptoms of differentiation syndrome, which can be fatal. Symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

Please see additional Important Safety Information on page 11 and Full Prescribing Information, including BOXED WARNING for MDS patients.

TIBSOVO HELPS FILL AN IMPORTANT TREATMENT GAP IN R/R MDS

Treatment options are limited in MDS[5]

First-line therapies for MDS often result in relapse or a lack of response.[6,7] Historically, patients with R/R MDS have had limited therapeutic options.[6]

Supportive care agents

- **ESAs and EMAs** are used to treat anemia in MDS, but **primary resistance to ESA is common, and 70% of patients relapse**[7]
- **~90% of MDS patients develop chronic anemia and may require long-term transfusion dependence,** which can lead to long-term complications such as iron toxicity[8-10]

HMA therapy

- Although HMAs are widely used in MDS, **patients rarely achieve CR and most experience HMA failure**[5,11]
- **Outcomes for patients after HMA failure are poor,** with a median survival of less than 6 months[12]

HCT

- HCT is the only curative option for MDS, but **only around one-third of higher-risk patients are eligible**[5,13]
- **Relapse occurs in 20% to 50%** of patients[14]

m*IDH1* is an early driver mutation in the progression of MDS[15,16]

- ***IDH1* mutations can arise anytime during the course of MDS** and can occur in up to 4% of patients, and the mutation rate may double in patients who progress to AML[5,17]
- **m*IDH1* MDS is associated with a higher incidence of neutropenia, higher rate of transformation to AML, and poorer overall and leukemia-free survival**[17-19]
  - 2-year survival rate for patients with m*IDH1* MDS was 14% compared to 52% of patients with wt*IDH1* MDS[17]
  - 67% of patients with m*IDH1* MDS transformed to AML compared to 28% of patients with wt*IDH1* MDS[17]
- **NCCN Guidelines® recommend genetic testing for somatic mutations** (ie, acquired mutations) in genes associated with MDS[4]

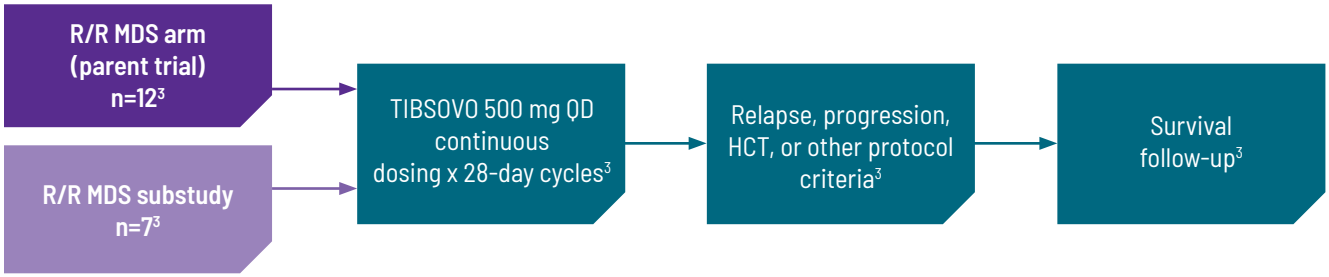
Retest your patients for *IDH1* mutations at the first suspicion of clinical change.[5]
Consider TIBSOVO for patients with m*IDH1* MDS experiencing their first relapse.[1]

CR, complete remission; EMA, erythroid maturation agent; ESA, erythropoiesis-stimulating agent; HCT, hematopoietic cell transplantation; HMA, hypomethylating agent; wtIDH1, wild type IDH1.

TIBSOVO WAS STUDIED IN THE FIRST CLINICAL TRIAL SPECIFICALLY FOR PATIENTS WITH m*IDH1* MDS

TIBSOVO was evaluated in an open-label, single-arm, multicenter study[1]

IDH1 mutations were detected in peripheral blood or bone marrow[1,a]



Efficacy was established on the basis of rate of CR + partial remission (PR)[b], duration of CR + PR (DOCR+PR), and rate of conversion from transfusion dependence to transfusion independence.[1] All observed responses were CRs.

Selected baseline demographics and disease characteristics[1]

	TIBSOVO (500 mg daily) (N=18)
Demographics	
Median age, years (min, max)	74 (61, 82)
Disease characteristics	
ECOG PS, %	
0	28
1	56
2	17
Cytogenic risk status, %	
Good	22
Intermediate	44
Poor	28
Missing	6
Baseline bone marrow blasts, %	
<5%	39
≥5%	61
Prior therapies, %	
Intensive chemotherapy	17
Nonintensive chemotherapy	83
1 line of HMA-based therapy	78
2 lines of HMA-based therapy	6

[a]Identified by a local or central diagnostic test and confirmed retrospectively using the Abbott RealTi*m*e IDH1 Assay.
[b]Rate of CR or PR per 2006 Working Group response criteria for MDS.
ECOG PS, Eastern Cooperative Oncology Group Performance Status; QD, once a day.

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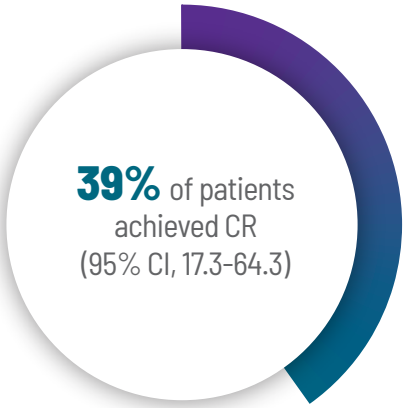
TIBSOVO DEMONSTRATED DEEP AND DURABLE REMISSIONS

TIBSOVO helped patients achieve CR[1,a]



Rapid remissions: median time to CR was 1.9 months (range, 1.0-5.6)

Durability of remissions with TIBSOVO

- **Median DOCR was not reached** by data cutoff (range, 1.9-80.8+ months; 95% CI, 1.9-NE)[1,3,b]

of patients who achieved CR remained in remission at 12 months[3,c]

- **43% of patients who achieved CR remained in remission for more than 5 years**[3,c]

Patients treated with TIBSOVO achieved hematologic improvements, including rapid neutrophil recovery[3]

- **Rapid neutrophil recovery** was seen in all patients with CR and more than half of patients (4/7) who did not achieve CR (57%)
  - **Median time to neutrophil recovery** was 0.97 months

Of the 8 patients who experienced marrow CR, **50% experienced hematologic improvements in ≥1 lineage,** including RBC, platelet, and/or neutrophil.[3,d]

[a]CR was defined as bone marrow ≤5% myeloblasts with normal maturation of all cell lines, hemoglobin ≥11 g/dL, platelets ≥100 x 10^9/L, neutrophils ≥1.0 x 10^9/L, and response lasting at least 4 weeks.[3] 43% of CR responders had baseline bone marrow blasts <5%.[1]
[b]DOCR was derived based on Kaplan-Meier method and is the date of the first documented CR (lasting ≥4 weeks) to the date of the first documented relapse or death, whichever was earlier.[1] Plus sign (+) indicates a censored observation.
[c]Per Kaplan-Meier estimation.[3]
[d]Of those experiencing hematologic improvements in >1 lineage, 25% (2/8) had improved RBC counts, 25% (2/8) had improved platelet counts, and 50% (4/8) had improved neutrophil counts.[3]
NE, not estimable.

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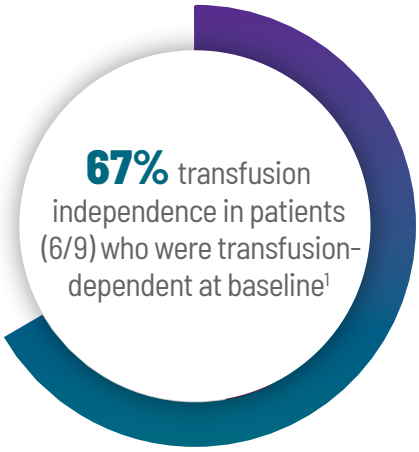
TIBSOVO DELIVERED SUSTAINED TRANSFUSION INDEPENDENCE

Majority of patients achieved or maintained transfusion independence[1,e]



Median time to transfusion independence was 2.43 months in patients who were transfusion-dependent at baseline[3]

of patients (7/9) who were transfusion-independent at baseline maintained transfusion independence[1]

- **100% of patients** who were platelet transfusion-independent at baseline maintained transfusion independence[3]

Duration of transfusion independence with TIBSOVO[3]

- 67% of patients (4/6) who were transfusion-dependent at baseline and achieved transfusion independence **had a duration of transfusion independence >4 months**, with the longest lasting 272+ days and maintained it through the end of treatment
- Of the 72% of patients who achieved or maintained transfusion independence, median duration of transfusion independence was not reached, but ranged between 1.9 and 78.8 months[e,f]

One (6%) patient went on to receive stem cell transplantation following treatment with TIBSOVO.[3]

[e]Postbaseline transfusion independence was defined as a period of ≥56 days with no RBC and/or platelet transfusions after the start of study treatment and on or before the end of study treatment.[3]

[f]Nine observations were censored.[3]

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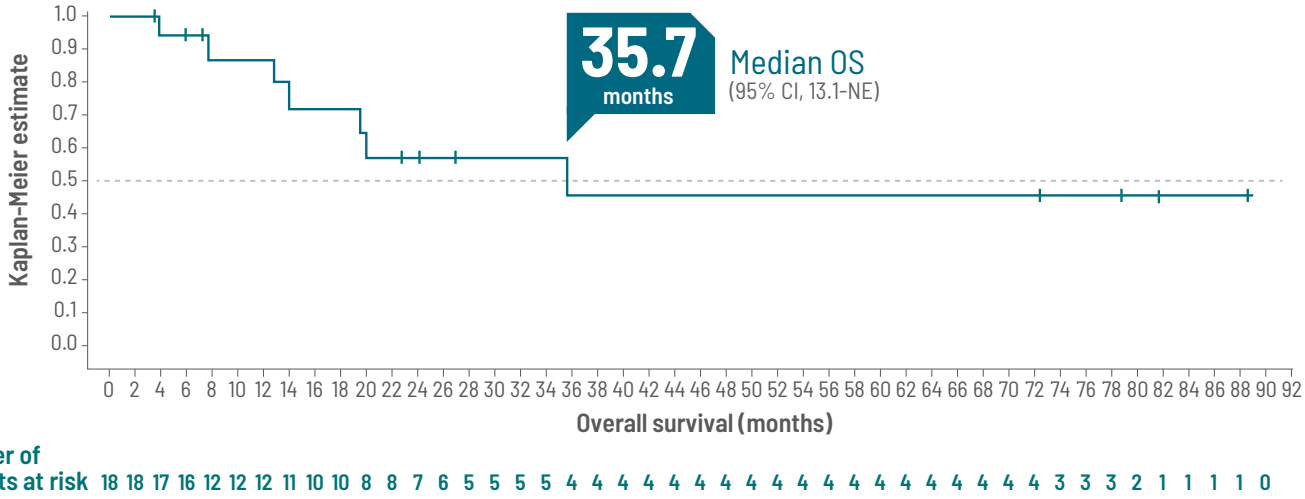
OVERALL SURVIVAL WITH TIBSOVO

Median OS was estimated to be 35.7 months[3]



Number of patients at risk	18	18	17	16	12	12	12	11	10	10	8	8	7	6	5	5	5	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	3	3	3	2	1	1	1	1	0

- Median OS follow-up was 27.1 months[3]
- **87% survival rate at 12 months** per Kaplan-Meier estimation[3]
- Because there was no control arm in this study, OS results should be interpreted cautiously[1]

Only 11% of patients treated with TIBSOVO progressed from MDS to AML.[3]

TIBSOVO is a recommended treatment option for MDS[4]

- **NCCN Guidelines recommend ivosidenib (TIBSOVO) as a targeted treatment option** for certain patients with R/R MDS with *IDH1* mutations[a]

[a]Category 2A recommendation for lower-risk disease, including for patients with symptomatic anemia, and higher-risk disease.[4]
OS, overall survival.

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TIBSOVO IS NONMYELOSUPPRESSIVE, WITH A WELL-CHARACTERIZED SAFETY PROFILE

- The majority of adverse reactions with TIBSOVO were Grades 1 or 2[1]
- Serious adverse reactions in ≥5% of patients included differentiation syndrome (11%), fatigue (5%), and rash (5%)[1]
- The median duration of exposure to TIBSOVO was 9.3 months (range, 3.3-78.8)[1]

Adverse reactions ≥10% in patients with R/R MDS[1]

	TIBSOVO (500 mg daily) (N=19)	
Body system Adverse reaction	All grades %	Grade 3 or 4 %
Musculoskeletal and connective tissue disorders		
Arthralgia	42	16
Myalgia	26	0
General disorders and administration site conditions		
Fatigue	37	11
Respiratory, thoracic, and mediastinal disorders		
Cough	32	0
Dyspnea	21	0
Gastrointestinal disorders		
Diarrhea	32	0
Mucositis	26	5
Constipation	16	0
Nausea	16	0
Skin and subcutaneous tissue disorders		
Pruritus	26	0
Rash	26	0
Metabolism and nutrition disorders		
Decreased appetite	26	0
Blood system and lymphatic system disorders		
Leukocytosis	16	5
Differentiation syndrome	11	0
Nervous system disorders		
Headache	16	0
Vascular disorders		
Hypertension	16	16
Investigations		
ECG QT prolonged	11	0

ECG, electrocardiogram.

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MOST COMMON LABORATORY ABNORMALITIES WITH TIBSOVO

Select laboratory abnormalities (≥15%) that worsened from baseline in patients with R/R MDS[1,a]

	TIBSOVO (500 mg daily) (N=19)	
Laboratory abnormality	All grades %	Grade 3 or 4 %
Creatinine increased	95	5
Hemoglobin decreased	42	32
Albumin decreased	37	0
Aspartate aminotransferase increased	37	5
Sodium decreased	32	5
Phosphate decreased	26	5
Alanine aminotransferase increased	21	5
Bilirubin increased	21	0
Magnesium decreased	21	0
Alkaline phosphatase increased	16	0
Potassium increased	16	0

[a]Laboratory abnormality is defined as new or worsened by at least one grade from baseline, or if baseline is unknown.[1]

Dose discontinuations, interruptions, and reductions[1]

- Permanent discontinuation of TIBSOVO due to an adverse reaction occurred in 1 (5%) patient. The adverse reaction that resulted in permanent discontinuation was fatigue
- Adverse reactions leading to dose interruption of TIBSOVO occurred in 16% of patients. Adverse reactions that required dose interruption in ≥5% were differentiation syndrome, leukocytosis, and rash
- Dose reductions of TIBSOVO due to an adverse reaction occurred in 16% of patients. Adverse reactions that required a dose reduction in ≥5% included differentiation syndrome, fatigue, and rash

Identifying and managing differentiation syndrome[1]

- Symptoms of differentiation syndrome in patients treated with TIBSOVO included noninfectious leukocytosis, peripheral edema, pyrexia, dyspnea, pleural effusion, hypotension, hypoxia, pulmonary edema, pneumonitis, pericardial effusion, rash, fluid overload, tumor lysis syndrome, and creatinine increased
- If differentiation syndrome is suspected, initiate dexamethasone 10 mg IV every 12 hours (or an equivalent dose of an alternative oral or IV corticosteroid) and hemodynamic monitoring until improvement
- If concomitant noninfectious leukocytosis is observed, initiate treatment with hydroxyurea or leukapheresis, as clinically indicated
- Taper corticosteroids and hydroxyurea after resolution of symptoms, and administer corticosteroids for a minimum of 3 days. Symptoms of differentiation syndrome may recur with premature discontinuation of corticosteroid and/or hydroxyurea treatment
- If severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids, interrupt TIBSOVO until signs and symptoms are no longer severe

TIBSOVO IS THE FIRST AND ONLY DIFFERENTIATION THERAPY APPROVED TO TARGET mIDH1 IN R/R MDS

TIBSOVO releases the block on myeloblast differentiation and helps to restore normal cellular function[1]

- Mutated IDH1 proteins produce 2-hydroxyglutarate (2-HG), an oncometabolite that causes histone hypermethylation, which in turn leads to impaired cellular differentiation and increased cellular proliferation[3,20]
- TIBSOVO inhibits mutant IDH1 proteins and subsequently reduces 2-HG levels by >95%, helping to restore normal cell function and myeloid differentiation[3]

For patients without disease progression or unacceptable toxicity, **treat for a minimum of 6 months to allow time for clinical response.**[1]

TIBSOVO offers convenient, once-daily oral dosing for patients with m*IDH1* MDS[1]

- The recommended dose for TIBSOVO is 500 mg taken orally once daily, with or without food

500 mg
(2 x 250-mg film-coated tablets)

Tablets not shown at actual size.

Monitoring and dose modifications[1]

- Obtain an ECG prior to treatment initiation. Monitor ECGs at least once weekly for the first 3 weeks of therapy and then at least once monthly for the duration of therapy. Manage any abnormalities promptly
- Assess blood counts and blood chemistries prior to the initiation of TIBSOVO at least once weekly for the first month, once every other week for the second month, and once monthly for the duration of therapy
- Monitor blood creatine phosphokinase weekly for the first month of therapy
- Interrupt dosing or reduce dose for toxicities. See Full Prescribing Information for dose modification guidelines

TIBSOVO is the only therapy approved by the FDA to target mIDH1 R/R MDS.[1,2] **Retest your patients for *IDH1* mutations** at the first suspicion of clinical change to determine if TIBSOVO may be right for them if and when they relapse.[1,5]

References: 1. Tibsovo. Package insert. Servier Pharmaceuticals LLC; 2023. **2.** Servier announces FDA approval of TIBSOVO® (ivosidenib tablets) for the treatment of IDH1-mutated relapsed or refractory (R/R) myelodysplastic syndromes (MDS). Servier Pharmaceuticals LLC. 2023. Accessed February 20, 2024. https://servier.us/blog/servier-announces-fda-approval-of-tibsovo-ivosidenib-tablets-for-the-treatment-of-idh1-mutated-relapsed-or-refractory-r-r-myelodysplastic-syndromes-mds/ **3.** Data on file. Servier Pharmaceuticals LLC. **4.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myelodysplastic Syndromes V.1.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed February 20, 2024. To view the most recent and complete version of the guideline, 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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LOOKING BEYOND THE BLAST PERCENTAGE THRESHOLD IN MDS AND AML

Fixed blast cutoffs are suboptimal in distinguishing MDS from AML[21]

- Clinical classifications systems continue to evolve to **de-emphasize morphologic features and fixed blast cutoffs** in categorizing MDS and AML[22]
- Updated 2022 WHO and ICC guidelines focus **heavily on molecular and genetic features when characterizing MDS and AML**[22]

MDS exists on a biologic continuum with AML[21]

WHO 2022[22]	ICC 2022[23]
MDS with increased blasts 2 (MDS-IB2)	**MDS/AML**
10% to 19% blasts in the bone marrow in the absence of AML-defining genetic abnormalities	Cytopenic myeloid neoplasm with 10% to 19% blasts in the blood or bone marrow in the absence of AML-defining recurrent genetic mutations

- **Approximately 20% of patients can be classified as MDS/AML** and may have poorer OS outcomes and a greater possibility of progressing to AML[24-27]

AML can be diagnosed in the presence of certain genetic abnormalities, regardless of blast count[22]

WHO 2022[22]	ICC 2022[22]
AML with defining genetic abnormalities	**AML with recurrent genetic abnormalities**
AML can be diagnosed in the presence of certain mutations and/or defined genetic abnormalities, **irrespective of blast count**[a]	All entities defined by the presence of certain recurrent genetic abnormalities and other genetically related entities can be diagnosed as **AML if ≥10% blasts are present**[b]

- **NCCN recognizes that patients with certain genetic abnormalities are considered to have AML even if the marrow blast count is less than 20%**[4,c]

Consider how updated classifications may impact how your patients are diagnosed and managed.[23,28]

[a] *RUNX1::RUNX1T1* fusion, *CBFB::MYH11* fusion, *DEK::NUP214* fusion, *RBM15::MRTFA* fusion, *KMT2A* rearrangement, *MECOM* rearrangement, *NUP98* rearrangement, *NPM1* mutation, myelodysplasia-related genetic abnormalities, and other defined genetic alterations.[28]

[b] t(8;21)(q22;q22.1)/*RUNX1::RUNX1T1*, inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB::MYH11*, t(6;9)(p22.3;q34.1)/*DEK::NUP214*, t(9;11)(p21.3;q23.3)/*MLLT3::KMT2A*, other *KMT2A* rearrangements, inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*; *MECOM*(EVI1), other *MECOM* rearrangements, other rare recurring translocations, mutated *NPM1*, and in-frame bZIP *CEBPA* mutations.[23]

[c] t(8;21)(q22;q22.1)/RUNX1::RUNX1T1, inv(16)(p13.1q22) or t(16;16 (p13.1;q22)/CBFB::MYH11, t(9;11)(p21.3;q23.3)/MLLT3::KMT2A, other KMT2A rearrangements, t(6;9)(p22.3;q34.1)/DEK::NUP214, inv(3)(q21.3q26.2), t(3;3)(q21.3;q26.2)/GATA2; MECOM(EVI1), other MECOM rearrangements, mutated NPM1), in-frame bZIP CEBPA mutations (ICC only), RBM15::MRTFA fusion (WHO only), NUP98 rearrangement (WHO only).

AML, acute myeloid leukemia; ICC, International Consensus Classification; WHO, World Health Organization.

References (cont'd): **5.** Platzbecker U et al. *Leukemia*. 2021;35(8):2182-2198. doi:10.1038/s41375-021-01265-7 **6.** Rodriguez-Sevilla JJ et al. *Cell Rep Med*. 2023;4(2):100940. doi:10.1016/j.xcrm.2023.100940 **7.** Kubasch AS et al. *Int J Mol Sci*. 2019;20(16):3853. doi:10.3390/ijms20163853 **8.** Gangat N et al. *Am J Hematol*. 2016;91(1):76-89. doi:10.1002/ajh.24253 **9.** Balducci L. *Cancer*. 2006;106(10):2087-2094. doi:10.1002/cncr.21860 **10.** Germing U et al. *Hemasphere*. 2019;3(6):e314. doi:10.1097/HS9.0000000000000314 **11.** Gangat N et al. *Am J Hematol*. 2023;98(2):225-228. doi:10.1002/ajh.26781 **12.** Steensma DP. *Blood Cancer J*. 2018;8(5):47. doi:10.1038/s41408-018-0085-4 **13.** Bhatt VR et al. *J Oncol Pract*. 2016;12(9):786-792. doi:10.1200/JOP.2016.015214 **14.** Courville EL et al. *BMC Clin Pathol*. 2017;17:28. doi:10.1186/s12907-017-0066-8 **15.** Guess T et al. *Blood Cancer Discov*. 2022;3(4):316-329. doi:10.1158/2643-3230.BCD-21-0128 **16.** DiNardo CD et al. *Leukemia*. 2016;30(4):980-984. doi:10.1038/leu.2015.211 **17.** Thol F et al. *Haematologica*. 2010;95(10):1668-1674. doi:10.3324/haematol.2010.025494 **18.** Jin J et al. *PLoS One*. 2014;9(6):e100206. doi:10.1371/journal.pone.0100206 **19.** Komrokji R et al. *Haematologica*. 2023;108(4):1168-1172. doi:10.3324/haematol.2022.281607 **20.** Molenaar RJ et al. *J Histochem Cytochem*. 2022;70(1):83-97. doi:10.1369/00221554211062499 **21.** Estey E et al. *Blood*. 2022;139(3):323-332. doi:10.1182/blood.2021011304 **22.** Falini B et al. *Am J Hematol*. 2023;98(3):481-492. doi:10.1002/ajh.26812 **23.** Arber DA et al. *Blood*. 2022;140(11):1200-1228. doi:10.1182/blood.2022015850 **24.** Cazzola M. *Hematology Am Soc Hematol Educ Program*. 2022;2022(1):375-381. doi:10.1182/hematology.2022000349 **25.** Huber S et al. *Leukemia*. 2023;37(4):942-945. doi:10.1038/s41375-023-01855-7 **26.** Chaudhuri D et al. *Cureus*. 2023;15(6):e40124. doi:10.7759/cureus.40124 **27.** IPSS-M Risk Calculator. Accessed February 20, 2024. https://www.mds-risk-model.com **28.** Khoury JD et al. *Leukemia*. 2022;36(7):1703-1719. doi:10.1038/s41375-022-01613-1

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IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME IN MDS
Patients treated with TIBSOVO have experienced symptoms of differentiation syndrome, which can be fatal. Symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

WARNINGS AND PRECAUTIONS

Differentiation Syndrome in MDS: Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal. Symptoms of differentiation syndrome in patients treated with TIBSOVO included noninfectious leukocytosis, peripheral edema, pyrexia, dyspnea, pleural effusion, hypotension, hypoxia, pulmonary edema, pneumonitis, pericardial effusion, rash, fluid overload, tumor lysis syndrome, and creatinine increased.

If differentiation syndrome is suspected, initiate dexamethasone 10 mg IV every 12 hours (or an equivalent dose of an alternative oral or IV corticosteroid) and hemodynamic monitoring until improvement. If concomitant noninfectious leukocytosis is observed, initiate treatment with hydroxyurea or leukapheresis, as clinically indicated. Taper corticosteroids and hydroxyurea after resolution of symptoms and administer corticosteroids for a minimum of 3 days. Symptoms of differentiation syndrome may recur with premature discontinuation of corticosteroid and/or hydroxyurea treatment. If severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids, interrupt TIBSOVO until signs and symptoms are no longer severe.

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. Conduct monitoring of electrocardiograms (ECGs) and electrolytes. In patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or 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

The most common adverse reactions including laboratory abnormalities (≥25%) in patients with relapsed or refractory MDS are creatinine increased, hemoglobin decreased, arthralgia, albumin decreased, aspartate aminotransferase increased, fatigue, diarrhea, cough, sodium decreased, mucositis, decreased appetite, myalgia, phosphate decreased, pruritus, and rash.

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

Advise women not to breastfeed.

TIBSOVO IS BUILT ON EXPERIENCE

- **39% of patients achieved CR** (95% CI, 17.3-64.3)[1,a]
- **69% of patients who achieved CR remained in remission at 12 months**[3,b]
- **67% transfusion independence in patients** who were transfusion-dependent at baseline[1,c]
- **First and only FDA-approved therapy** to target mIDH1 in R/R MDS[1,2]
- **Nonmyelosuppressive, with a well-characterized** safety profile[1,3]
- **Over 5 years of real-world experience** with more than 2300 patients treated across multiple indications[1,3]

NCCN Guidelines recommend ivosidenib (TIBSOVO) as a targeted treatment option for certain patients with R/R MDS with *IDH1* mutations[4,d]

[a]CR was defined as bone marrow ≤5% myeloblasts with normal maturation of all cell lines, hemoglobin ≥11 g/dL, platelets ≥100 x 10^9/L, neutrophils ≥1.0 x 10^9/L, and response lasting at least 4 weeks.[3] 43% of CR responders had baseline bone marrow blasts <5%.[1]
[b]Per Kaplan-Meier estimation.
[c]Postbaseline transfusion independence was defined as a period of ≥56 days with no RBC and/or platelet transfusions after the start of study treatment and on or before the end of study treatment.[3]
[d]Category 2A recommendation for lower-risk disease, including for patients with symptomatic anemia, and higher-risk disease.[4]

INDICATION

TIBSOVO is indicated for the treatment of adult patients with relapsed or refractory myelodysplastic syndromes (MDS) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME IN MDS
Patients treated with TIBSOVO have experienced symptoms of differentiation syndrome, which can be fatal. Symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

Please see additional Important Safety Information on page 11 and Full Prescribing Information, including BOXED WARNING for MDS patients.

SERVIER

TIBSOVO®
ivosidenib tablets 250mg