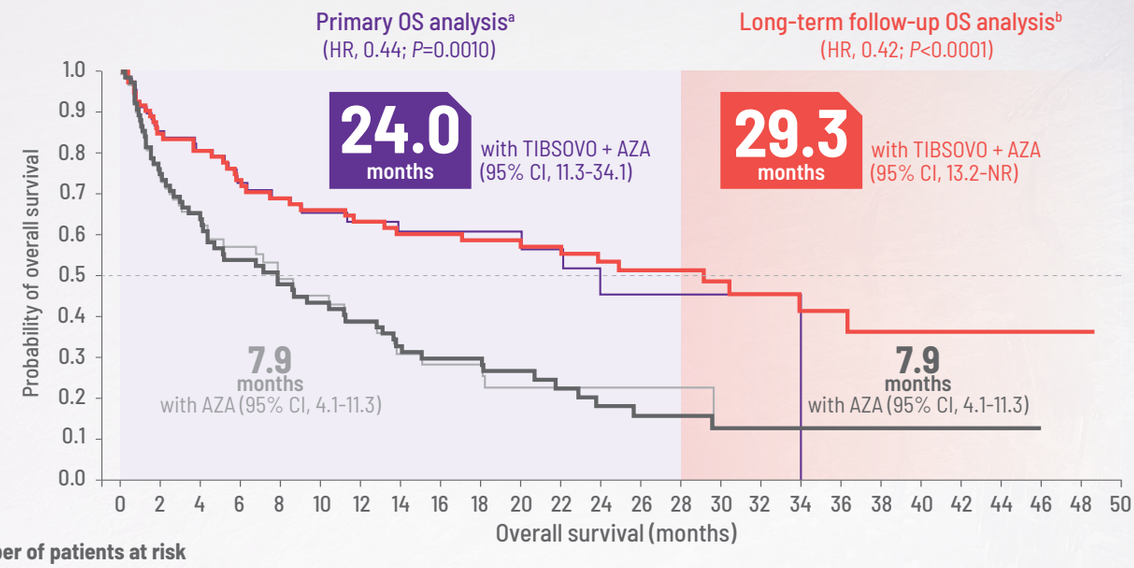
In patients with newly diagnosed, IC-ineligible m*IDH1* AML

TIBSOVO® IS THE FIRST-IN-CLASS mIDH1 INHIBITOR PROVEN TO SIGNIFICANTLY INCREASE OVERALL SURVIVAL (OS)

More than threefold improvement in mOS with TIBSOVO + AZA vs AZA alone[1,2]



Number of patients at risk

Primary OS analysis																									
TIBSOVO+AZA	72	58	53	42	38	33	29	24	21	19	15	13	7	4	4	2	2	1	0						
PLACEBO+AZA	74	53	38	29	23	21	15	11	9	9	6	5	4	3	3	0									
Long-term follow-up OS analysis																									
TIBSOVO+AZA	73	60	56	50	47	45	43	40	39	37	36	32	27	23	20	17	13	11	8	5	4	3	3	1	1	0
PLACEBO+AZA	75	55	45	37	32	28	25	21	19	19	13	10	8	6	5	4	4	3	2	2	1	1	1	1	0	

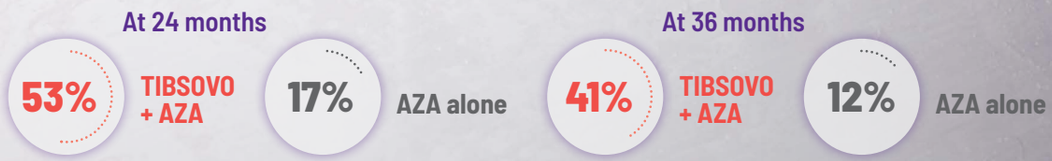
OVER 5 YEARS #1 PRESCRIBED mIDH1 INHIBITOR OF REAL-WORLD EXPERIENCE

- **56% reduction in risk of death** per the primary OS analysis (95% CI, 0.27-0.73)[1]
- **58% reduction in risk of death** per the long-term follow-up OS analysis (95% CI, 0.27-0.65)[2]

[a]In the primary analysis from the AGILE study, 146 patients were 1:1 randomized: 72 to TIBSOVO + AZA and 74 to AZA. The data cutoff date was March 2021 with a median follow-up of 15.1 months for the OS analysis.[1,3]

[b]In the long-term follow-up analysis from the AGILE study, 148 patients were 1:1 randomized: 73 to TIBSOVO + AZA and 75 to AZA. The data cutoff date was June 2022 with a median follow-up of 28.6 months for the OS analysis.[2]

Greater than 3X increase in OS rates with TIBSOVO + AZA[2]



Ivosidenib (TIBSOVO) + azacitidine is recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a category 1 preferred treatment option[4,c]

[c]For patients with m*IDH1* AML who are not candidates for intensive induction therapy.[4]

AZA, azacitidine; CI, confidence interval; HR, hazard ratio; IC, induction chemotherapy; mIDH1, mutated IDH1; mOS, median OS; NCCN, National Comprehensive Cancer Network; NR, not reached.

INDICATIONS

TIBSOVO is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for patients with a susceptible IDH1 mutation as detected by an FDA-approved test with:

Newly Diagnosed Acute Myeloid Leukemia (AML)

- In combination with azacitidine or as monotherapy for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude the use of intensive induction chemotherapy

Relapsed or Refractory AML

- For the treatment of adult patients with relapsed or refractory AML

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME IN AML

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 and Full Prescribing Information, including BOXED WARNING for AML patients.

TIBSOVO®
ivosidenib tablets 250mg

TIBSOVO + AZA DELIVERS STRONG AND DURABLE RESPONSES

Significantly higher rates of CR and CR+CRh compared with AZA ($P<0.0001$)[1,a]

TIBSOVO + AZA **47%**
CR (95% CI, 35-59)
51% CR+CRh (95% CI, 39-63)

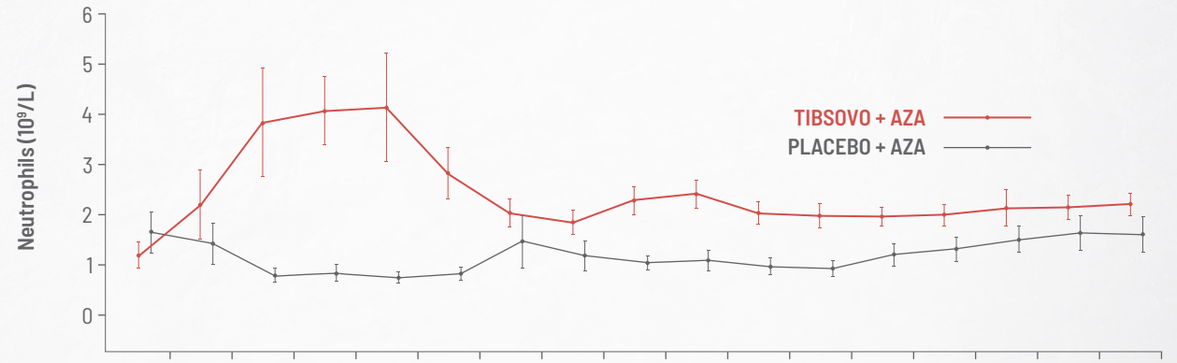
AZA alone **15%**
CR (95% CI, 8-25)
18% CR+CRh (95% CI, 10-28)

- **Median duration of CR was not estimable** (NE) as of the data cutoff date in the TIBSOVO + azacitidine arm (95% CI, 13.0-NE) and was 11.2 months in the azacitidine arm (95% CI, 3.2-NE)[1]
- Of the patients who achieved CR with TIBSOVO + azacitidine, **88% remained in remission at 12 months** (95% CI, 67.5-96.2) per Kaplan-Meier estimation[3,5]

[a]CR was defined as <5% blasts in the bone marrow and no Auer rods, absence of extramedullary disease, full recovery of peripheral blood counts (absolute neutrophil count ≥1000/µL and platelets ≥100,000/µL), and independence of red blood cell transfusions.[5] CRh was defined as <5% blasts in the bone marrow and no Auer rods, absence of extramedullary disease, and partial recovery of peripheral blood counts (absolute neutrophil count >500/µL and platelets >50,000/µL).

Rapid increases in absolute neutrophil count recovery by the end of Cycle 1 with TIBSOVO + AZA[5,6]

Change in absolute neutrophil count from baseline



Visit		BL	C1D8	C1D15	C1D22	C2D1	C2D15	C3D1	C3D15	C4D1	C4D15	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1
TIBSOVO + AZA	n =	70	65	62	60	57	53	50	48	45	44	44	39	36	31	29	28	27
PLACEBO + AZA	n =	72	67	67	58	55	50	38	35	34	30	27	23	19	16	15	14	11

BL denotes baseline, defined as the last assessment before start of study treatment; CxDy indicates Cycle x Day y; error bars indicate mean +/- standard error.

TIBSOVO is proven to deliver a long-term overall survival advantage in combination with azacitidine for newly diagnosed, IC-ineligible m*IDH1* AML patients.[1-3] Visit TibsovoPro.com/aml to learn more.

CR, complete remission; CRh, complete remission with partial hematologic recovery.

INDICATIONS

TIBSOVO is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for patients with a susceptible IDH1 mutation as detected by an FDA-approved test with:

Newly Diagnosed Acute Myeloid Leukemia (AML)

- In combination with azacitidine or as monotherapy for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude the use of intensive induction chemotherapy

Relapsed or Refractory AML

- For the treatment of adult patients with relapsed or refractory AML

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME IN AML
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 and Full Prescribing Information, including BOXED WARNING for AML patients.

TIBSOVO® ivosidenib tablets 250mg

IMPORTANT SAFETY INFORMATION (cont'd)

WARNING: DIFFERENTIATION SYNDROME IN AML
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 AML: In the combination study AG120-C-009, 15% (11/71) of patients with newly diagnosed AML treated with TIBSOVO plus azacitidine experienced differentiation syndrome. 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. Of the 11 patients with newly diagnosed AML who experienced differentiation syndrome with TIBSOVO plus azacitidine, 8 (73%) recovered. Differentiation syndrome occurred as early as 3 days after start of therapy and during the first month on treatment.

In the monotherapy clinical trial AG120-C-001, 25% (7/28) of patients with newly diagnosed AML and 19% (34/179) of patients with relapsed or refractory AML treated with TIBSOVO experienced differentiation syndrome. Of the 7 patients with newly diagnosed AML who experienced differentiation syndrome, 6 (86%) patients recovered. Of the 34 patients with relapsed or refractory AML who experienced differentiation syndrome, 27 (79%) patients recovered after treatment or after dose interruption of TIBSOVO. Differentiation syndrome occurred as early as 1 day and up to 3 months after TIBSOVO initiation and has been observed with or without concomitant leukocytosis.

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, 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.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

- **In patients with AML,** the most common adverse reactions including laboratory abnormalities (≥25%) are leukocytes decreased, diarrhea, hemoglobin decreased, platelets decreased, glucose increased, fatigue, alkaline phosphatase increased, edema, potassium decreased, nausea, vomiting, phosphate decreased, decreased appetite, sodium decreased, leukocytosis, magnesium decreased, aspartate aminotransferase increased, arthralgia, dyspnea, uric acid increased, abdominal pain, creatinine increased, mucositis, rash, electrocardiogram QT prolonged, differentiation syndrome, calcium decreased, neutrophils decreased, and myalgia

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.

References: 1. Tibsovo. Package insert. Servier Pharmaceuticals LLC; 2022. **2.** de Botton S, Montesinos P, Vives Polo S, et al. Updated efficacy and safety data from the AGILE study in patients with newly-diagnosed acute myeloid leukemia treated with ivosidenib + azacitidine compared to placebo + azacitidine. Poster presented at: 2023 American Society of Clinical Oncology Annual Meeting; June 2-6, 2023; Chicago, IL. **3.** Montesinos P, Recher C, Vives S, et al. Ivosidenib and azacitidine in IDH1-mutated acute myeloid leukemia. *N Engl J Med*. 2022;386(16):1519-1531. doi: 10.1056/NEJMoa2117344 **4.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.4.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed July 21, 2023. 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. **5.** Data on file. Servier Pharmaceuticals LLC. **6.** Montesinos P, Recher C, Vives S, et al. Ivosidenib and azacitidine in IDH1-mutated acute myeloid leukemia: supplementary appendix. *N Engl J Med*. 2022;386(16):1519-1531.

Please see additional Important Safety Information and Full Prescribing Information, including BOXED WARNING for AML patients.

SERVIER

TIBSOVO® ivosidenib tablets 250mg