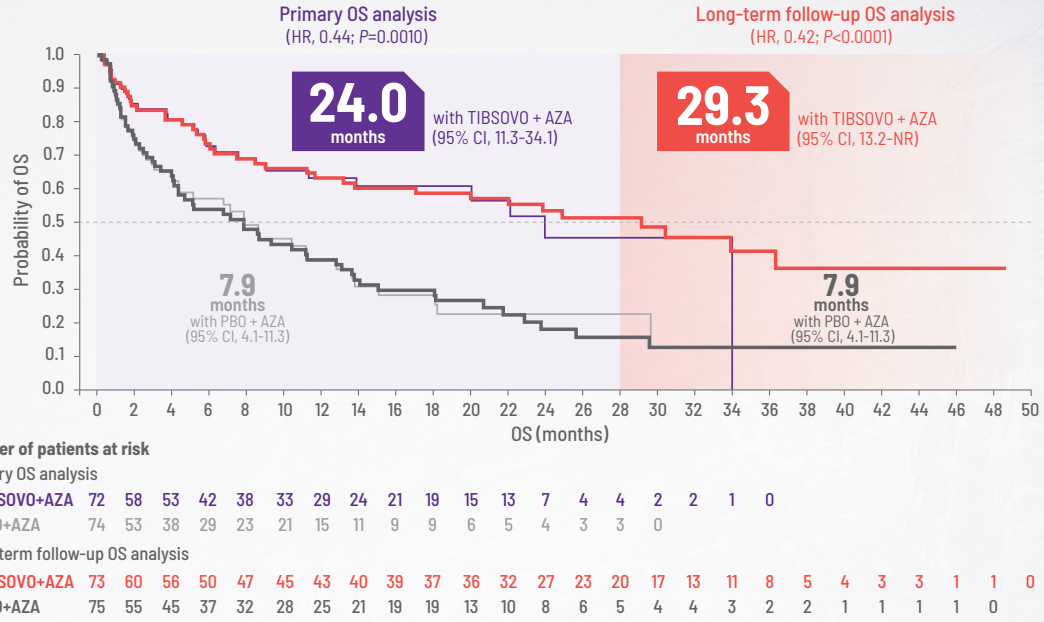
In patients with newly diagnosed, IC-ineligible m*IDH1* AML

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

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



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
PBO+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
PBO+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 7 YEARS #1 PRESCRIBED mIDH1 INHIBITOR[c] 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 PBO + AZA.[1,3] The data cutoff date was March 2021 with a median follow-up of 15.1 months for the OS analysis.[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 PBO + AZA. The data cutoff date was June 2022 with a median follow-up of 28.6 months for the OS analysis.[2] This post hoc analysis was not a prespecified endpoint in the AGILE statistical analysis plan; therefore, any findings should be interpreted with caution.[2,4]

[c]Claims data as of 11/2024.[4]

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

At 24 months

53% TIBSOVO + AZA

17% PBO + AZA

At 36 months

41% TIBSOVO + AZA

12% PBO + AZA

Ivosidenib (TIBSOVO) + AZA is recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as an NCCN Category 1 preferred treatment option[5,d]

[d]For newly diagnosed patients ≥18 years of age with m*IDH1* AML who are not candidates for intensive induction chemotherapy.[5]

AZA, azacitidine; HR, hazard ratio; IC, intensive induction chemotherapy; mIDH1, mutated IDH1; mOS, median overall survival; OS, overall survival; NCCN, National Comprehensive Cancer Network® (NCCN®); NR, not reached; PBO, placebo.

INDICATION

TIBSOVO is indicated in combination with azacitidine or as monotherapy for patients with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

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 on pages 2 and 3 and Full Prescribing Information, including BOXED WARNING for AML patients, accompanying this material or at TibsovoPro.com.

TIBSOVO® ivosidenib tablets 250mg

IMPORTANT SAFETY INFORMATION (cont'd)

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WARNINGS AND PRECAUTIONS

Differentiation Syndrome in AML: 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, 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

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

Advise women not to breastfeed.

References: 1. Tibsovo. Package insert. Servier Pharmaceuticals LLC; 2023. **2.** Montesinos P, Marchione DM, Récher C, et al. Long-term results from the AGILE study of azacitidine plus ivosidenib vs placebo in newly diagnosed IDH1-mutated AML. *Blood Adv*. doi:10.1182/bloodadvances.2025016399 **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.** Data on file. Servier Pharmaceuticals LLC. **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia Version 3.2024. © National Comprehensive Cancer Network, Inc., 2024. All rights reserved. Accessed August 9, 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. **6.** Fathi AT, Smith BD, Angiolillo A, et al. Time to recovery from neutropenia in patients with newly diagnosed IDH-1 mutated acute myeloid leukemia receiving azacitidine and ivosidenib in the AGILE clinical trial. *Leuk Res*. 2025;157:107925. doi:10.1016/j.leukres.2025.107925 **7.** Döhner H, DiNardo CD, Wei AH, et al. Genetic risk classification for adults with AML receiving less-intensive therapies: the 2024 ELN recommendations. *Blood*. 2024;144(21):2169-2173. doi:10.1182/blood.2024025409

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TIBSOVO + AZA DELIVERS DEEP AND DURABLE REMISSIONS

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)

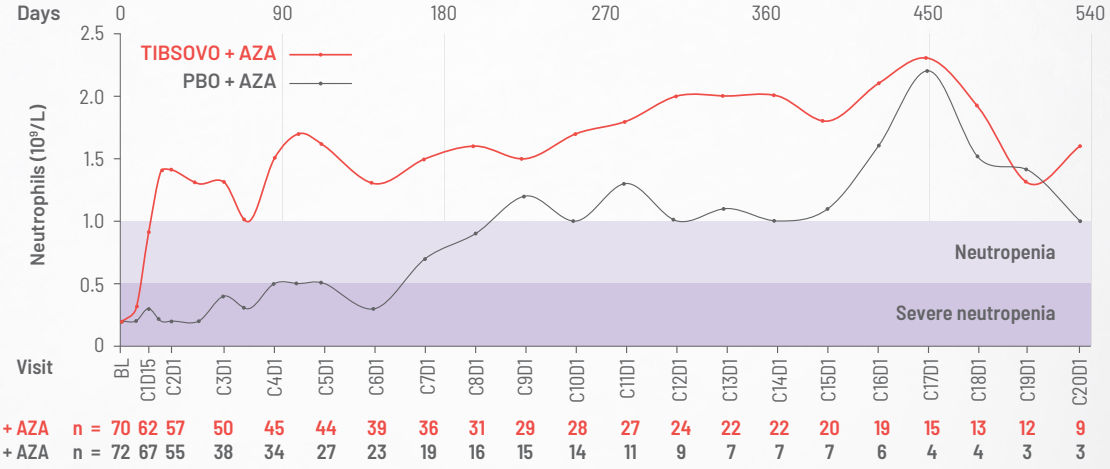
PBO + AZA **15%**
CR (95% CI, 8-25)
18% CR+CRh (95% CI, 10-28)

- **Median duration of CR was not estimable** (NE) as of the data cutoff date in the TIBSOVO + AZA arm (95% CI, 13.0-NE) and was 11.2 months in the AZA arm (95% CI, 3.2-NE)[1]
- Of the patients who achieved CR with TIBSOVO + AZA, **88% were estimated to remain in remission at 12 months** (95% CI, 67.5-96.2) per Kaplan–Meier estimation[3,4]

[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 (ANC ≥1000/µL and platelets ≥100,000/µL), and independence of red blood cell transfusions. 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).[4]

TIBSOVO + AZA resulted in a rapid onset of action and sustained neutrophil recovery[6,b-d]

Within Cycle 1, median ANC reached 1.0 x 10^9/L with TIBSOVO + AZA and was sustained throughout the treatment duration



TIBSOVO + AZA	n =	70	62	57	50	45	44	39	36	31	29	28	27	24	22	22	20	19	15	13	12	9
PBO + AZA	n =	72	67	55	38	34	27	23	19	16	15	14	11	9	7	7	7	6	4	4	3	3

[b]BL denotes baseline, defined as a median ANC value of 0.2 x 10^9/L for the TIBSOVO + AZA arm and placebo + AZA arm; CxDy indicates Cycle x Day y.[6]
[c]Shading denotes neutropenia and severe neutropenia, defined as ANC values of <1.0 x 10^9/L and <0.5 x 10^9/L, respectively.[6]
[d]Median values are presented to avoid the potential masking influence of outliers resulting from differentiation of leukocytosis, which may be possible with reporting the mean values.[6]

ELN states that ivosidenib (TIBSOVO) + AZA has a favorable outcome in adult patients with newly diagnosed, IC-ineligible m*IDH1* AML[7,e]

Scan here or visit TibsovoPro.com/aml to learn more

[e]The ELN 2024 risk classification for patients receiving less intensive therapy categorizes patients into adverse, intermediate, and favorable groups.[7]
ANC, absolute neutrophil count; CR, complete remission; CRh, complete remission with partial hematologic recovery.

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