Recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a category 1 preferred treatment option

TIBSOVO® + azacitidine in newly diagnosed, IC-ineligible m*IDH1* AML

PROVEN TO EXTEND SURVIVAL AND DELIVER STRONG AND DURABLE RESPONSES

Threefold improvement in overall survival (OS) with TIBSOVO + azacitidine[1]
Median OS: 24.0 months (95% CI, 11.3-34.1) vs 7.9 months (95% CI, 4.1-11.3) with placebo + azacitidine (hazard ratio, 0.44 [95% CI, 0.27-0.73]; *P*<0.0010)

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

TIBSOVO®
ivosidenib tablets 250mg

TIBSOVO® is the only therapy that was studied in a phase 3 trial specifically designed for newly diagnosed patients with m*IDH1* AML

CLINICAL TRIAL

146 adult patients with previously untreated m*IDH1* AML who were not candidates for intensive therapy were randomized[1]

- TIBSOVO + azacitidine was studied in a global, phase 3, multicenter, randomized (1:1), double-blind, placebo-controlled trial[1,2]
- The trial was initially powered for 200 participants. However, the Independent Data Monitoring Committee suggested halting enrollment after 146 patients when a statistical difference between the two treatment groups was achieved[3]
- Efficacy was established on the basis of event-free survival (EFS), overall survival (OS), and rate and duration of complete remission (CR)[1]
  - EFS was defined as time from randomization until treatment failure, relapse from remission, or death from any cause, whichever occurred first
  - Treatment failure was defined as failure to achieve CR by Week 24. A CRh response was considered to be a treatment failure

TIBSOVO + azacitidine was studied in an IC-ineligible patient population reflective of that seen in clinical practice[1]

	TIBSOVO® (500 mg daily) + azacitidine (n=72)	Placebo + azacitidine (n=74)
Baseline demographics		
Median age, years (min,max)	76 (58, 84)	76 (45, 94)
Age categories, n (%)		
<65 years	4 (6)	4 (5)
≥65 years to <75 years	29 (40)	27 (36)
≥75 years	39 (54)	43 (58)
Baseline disease characteristics		
ECOG PS, n (%)		
0	14 (19)	10 (14)
1	32 (44)	40 (54)
2	26 (36)	24 (32)
Cytogenetic risk status,[a] n (%)		
Favorable	3 (4)	7 (9)
Intermediate	48 (67)	44 (59)
Poor	16 (22)	20 (27)
Other	3 (4)	1 (1)
Missing	2 (3)	2 (3)
Transfusion dependent at baseline,[b] n (%)	39 (54)	40 (54)
Type of AML, %		
de novo AML	54 (75)	53 (72)
Secondary AML	18 (25)	21 (28)
Therapy-related AML	2 (3)	1 (1)
MDS related	10 (14)	12 (16)
MPN related	4 (6)	8 (11)

[a] Cytogenic risk status: Investigators used the NCCN Guidelines®.
[b] Patients were defined as transfusion dependent at baseline if they received any red blood cell or platelet transfusion within 56 days prior to the first dose of study treatment.

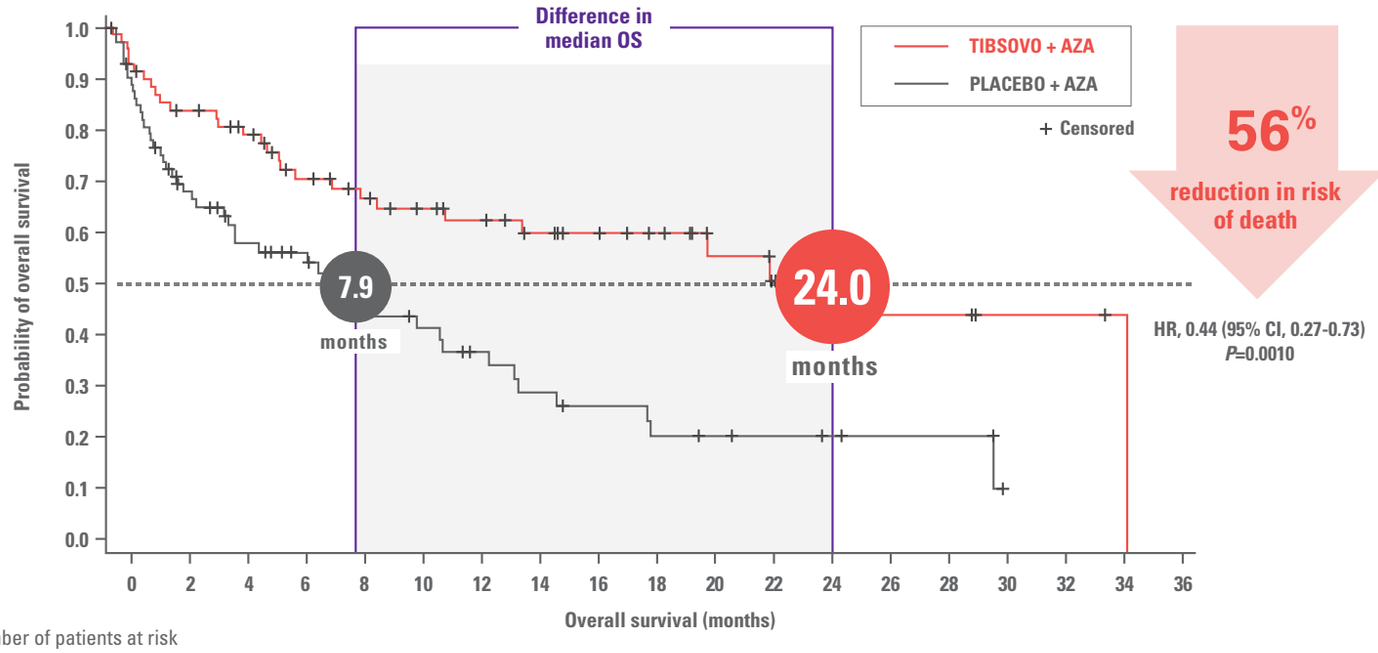
AML, acute myeloid leukemia; CR, complete remission, defined as <5% blasts in the bone marrow and no Auer rods, absence of extramedullary disease, full recovery of peripheral blood counts (absolute neutrophil count ≥1000/µL and platelets ≥100,000/µL), and independence of RBC transfusions[4]; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IDH1, isocitrate dehydrogenase-1; mIDH1, mutated IDH1; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm.

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

TIBSOVO® ivosidenib tablets 250mg

Threefold improvement in overall survival with TIBSOVO® + azacitidine

Overall survival (OS)[1]



Number of patients at risk

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			

Treatment with TIBSOVO + azacitidine resulted in significant improvement in OS compared with azacitidine[1]

	TIBSOVO (500 mg daily) + azacitidine (n=72)	Placebo + azacitidine (n=74)
OS, events (%)	28 (39)	46 (62)
Median OS, months (95% CI)	24.0 (11.3-34.1)	7.9 (4.1-11.3)
Hazard ratio[a] (95% CI)	0.44 (0.27-0.73)	
P value[b]	0.0010	

The two-sided *P* value boundary for OS is 0.0034.
[a]Hazard ratio was estimated using a Cox proportional hazards model stratified by the randomization stratification factors (type of AML and geographic region) with placebo + azacitidine as the denominator.
[b]Two-sided *P* value was calculated from the log-rank test stratified by the randomization stratification factors (type of AML and geographic region).

- Overall survival benefit was consistent across subgroups: de novo status, region, age, baseline ECOG PS score, sex, race, baseline cytogenetic risk status, WHO classification of AML, baseline white blood cell count, and baseline percentage of bone marrow blasts[4]

AML, acute myeloid leukemia; ECOG PS, Eastern Cooperative Oncology Group Performance Status; mIDH1, mutated isocitrate dehydrogenase-1.

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

TIBSOVO® ivosidenib tablets 250mg

TIBSOVO® + azacitidine delivered meaningful improvement in EFS vs azacitidine

Treatment with TIBSOVO + azacitidine resulted in significant improvement in EFS compared with azacitidine[1]

	TIBSOVO (500 mg daily) + azacitidine (n=72)	Placebo + azacitidine (n=74)
EFS, events (%)	47 (65)	62 (84)
Treatment failure	43 (60)	59 (80)
Relapse	3 (4)	2 (3)
Death	1 (1)	1 (1)
Hazard ratio[a] (95% CI)	0.35 (0.17-0.72)	
P value[b]	0.0038	

Two-sided *P* value boundary for EFS is 0.0095.
[a]Hazard ratio was estimated using a Cox proportional hazards model stratified by the randomization stratification factors (type of AML and geographic region) with placebo + azacitidine as the denominator.
[b]Two-sided *P* value was calculated from the log-rank test stratified by the randomization stratification factors (type of AML and geographic region).

- **12-month EFS rate: 37.4% with TIBSOVO + azacitidine** (95% CI, 25.9-48.9) vs 12.2% with azacitidine (95% CI, 4.3-24.4)[3]
- **18-month EFS rate: 33.3% with TIBSOVO + azacitidine** (95% CI, 20.9-46.2) vs 6.1% with azacitidine (95% CI, 0.7-20.9)[3]

AML, acute myeloid leukemia; CI, confidence interval; EFS, event-free survival, defined as time from randomization until treatment failure (ie, failure to achieve complete remission by Week 24), relapse from remission, or death from any cause, whichever occurred first.[1]

IMPORTANT SAFETY INFORMATION

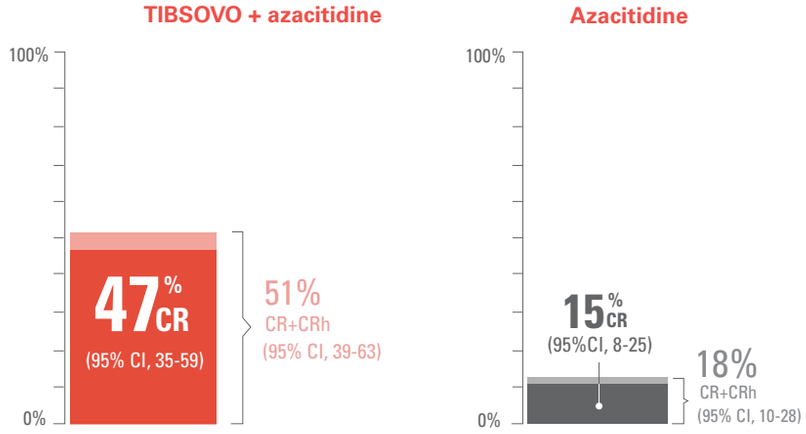
WARNINGS AND PRECAUTIONS

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.

TIBSOVO® + azacitidine: the combination for strong and durable responses in newly diagnosed, IC-ineligible m*IDH1* AML

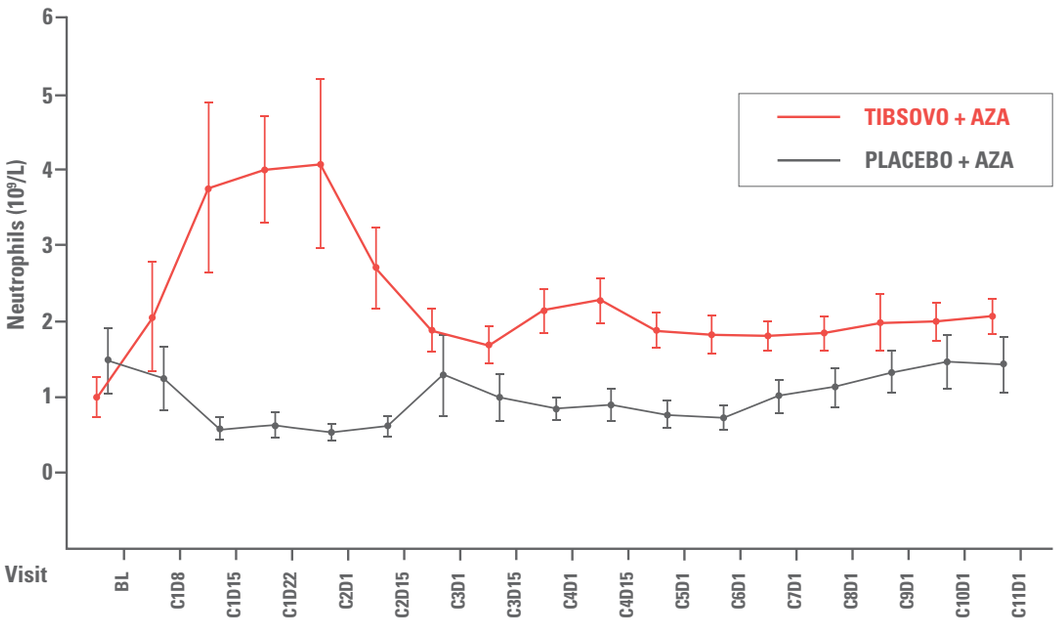
TIBSOVO + azacitidine demonstrated significantly higher rates of CR and CR+CRh compared with azacitidine (*P*<0.0001)[1]



- Median duration of complete response 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 or CRh **with TIBSOVO + azacitidine, 80.5% remained in remission at 12 months (95% CI, 54.4-92.5) and 53.6% remained in remission at 24 months** (95% CI, 17.0-80.3) per Kaplan-Meier estimation[3]

TIBSOVO + azacitidine resulted in rapid neutrophil recovery[4]

Change in absolute neutrophil count from baseline



	BL	C1D8	C1D15	C1D22	C2D1	C2D15	C3D1	C3D15	C4D1	C4D15	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1
TIBSOVO + AZA	70	65	62	60	57	53	50	48	45	44	44	39	36	31	29	28	27
PLACEBO + AZA	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.

AML, acute myeloid leukemia; AZA, azacitidine; CI, confidence interval; CR, complete remission, 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[3]; CRh, complete remission with partial hematological recovery, 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)[3]; IC, induction chemotherapy; mIDH1, mutated isocitrate dehydrogenase-1.

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

TIBSOVO® ivosidenib tablets 250mg

TIBSOVO® + azacitidine helps achieve multiple treatment goals for your patients with IC-ineligible m*IDH1* AML

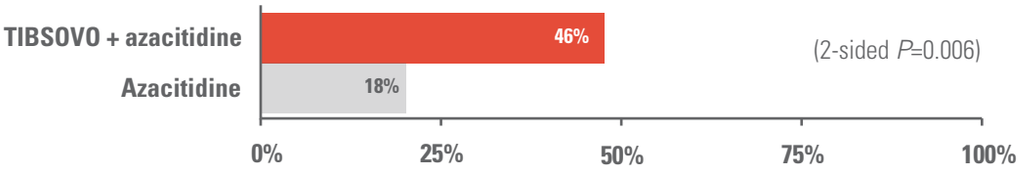
Time to response

Median time to response with TIBSOVO + azacitidine:

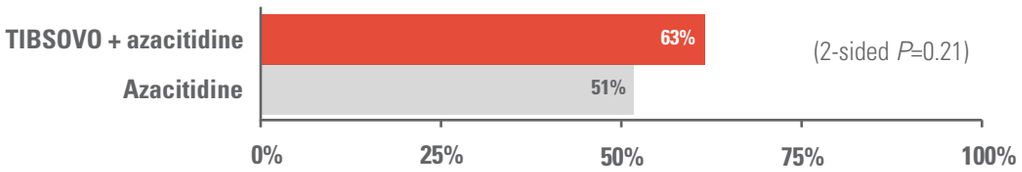
- First response (CR, CRi, CRp, PR, or MLFS): 2 months (range, 2-8)[3]
- CR: 4 months (range, 2-12)[1]
- CR+CRh: 4 months (range, 2-12)[1]

Transfusion independence[a]

Among patients who were transfusion dependent at baseline (~54%), a higher percentage of patients converted to transfusion independence with TIBSOVO + azacitidine than with azacitidine[2,4]



Postbaseline RBC and platelet transfusion independence regardless of baseline transfusion status[4]



[a]Postbaseline transfusion independence is defined as a period of ≥56 days with no transfusion after the start of study treatment and on or before the end of study treatment + 28 days, disease progression, confirmed relapse, death, or data cutoff date, whichever was earlier.[3]

AML, acute myeloid leukemia; CR, complete remission; CRh, complete remission with partial hematological recovery; CRi, complete remission with incomplete hematologic recovery; CRp, complete remission with incomplete platelet recovery; mIDH1, mutated isocitrate dehydrogenase-1; MLFS, morphologic leukemia-free state; PR, partial remission; RBC, red blood cell.

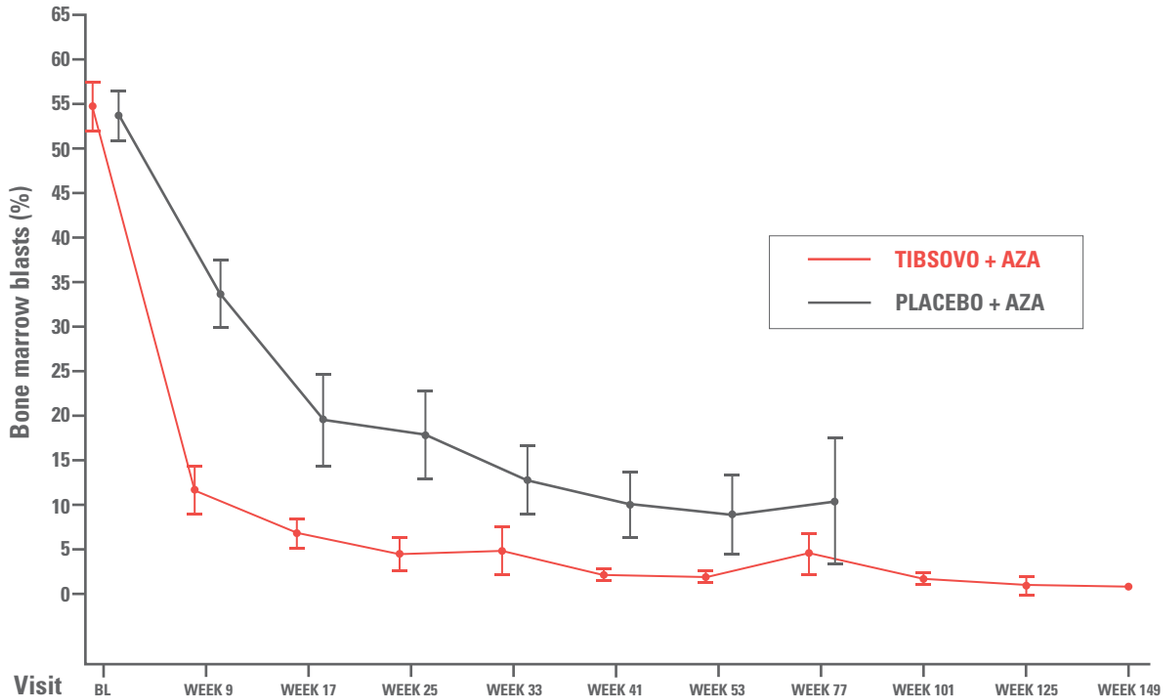
IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Differentiation Syndrome in AML: (cont'd) 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® + azacitidine resulted in decreased bone marrow blasts

Change in bone marrow blasts from baseline[3]



	BL	WEEK 9	WEEK 17	WEEK 25	WEEK 33	WEEK 41	WEEK 53	WEEK 77	WEEK 101	WEEK 125	WEEK 149
TIBSOVO + AZA	70	50	41	34	26	24	21	13	5	2	1
PLACEBO + AZA	72	42	27	22	18	11	6	4			

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

- Participants in the AGILE trial were to follow a study center visit schedule that included a bone marrow aspirate/biopsy and peripheral blood sampling to evaluate *IDH1*-mutated cells and to assess disease status and response[3]
- This was conducted at screening and on Day 1 (+/- 7 days) of Weeks 9, 17, 25, 33, 41, 53, and every 24 weeks thereafter; at end of treatment; and during EFS follow-up[3]

AZA, azacitidine; EFS, event-free survival; IDH1, isocitrate dehydrogenase-1.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

TIBSOVO® has a well-characterized safety profile studied in more than 270 patients with m*IDH1* AML

Adverse reactions (≥10%) in patients with AML who received TIBSOVO + azacitidine with a difference of ≥2% between arms compared with placebo + azacitidine[1]

	TIBSOVO + azacitidine (n=71)		Placebo + azacitidine (n=73)	
Body system Adverse reaction	All grades n (%)	Grade ≥3 n (%)	All grades n (%)	Grade ≥3 n (%)
Gastrointestinal disorders				
Nausea	30 (42)	2 (3)	28 (38)	3 (4)
Vomiting	29 (41)	0	20 (27)	1 (1)
Investigations				
Electrocardiogram QT prolonged	14 (20)	7 (10)	5 (7)	2 (3)
Psychiatric disorders				
Insomnia	13 (18)	1 (1)	9 (12)	0
Blood system and lymphatic system disorders				
Differentiation syndrome[a]	11 (15)	7 (10)	6 (8)	6 (8)
Leukocytosis	9 (13)	0	1 (1)	0
Vascular disorders				
Hematoma	11 (15)	0	3 (4)	0
Musculoskeletal and connective tissue disorders				
Arthralgia	21 (30)	3 (4)	6 (8)	1 (1)
Respiratory, thoracic, and mediastinal disorders				
Dyspnea	14 (20)	2 (3)	11 (15)	4 (5)
Nervous system disorders				
Headache	8 (11)	0	2 (3)	0

[a]Differentiation syndrome can be associated with other commonly reported events such as peripheral edema, leukocytosis, pyrexia, dyspnea, pleural effusion, hypotension, hypoxia, pulmonary edema, pneumonia, pericardial effusion, rash, fluid overload, tumor lysis syndrome, and creatinine increased.

- TIBSOVO + azacitidine was associated with a lower rate of infection of any grade compared with azacitidine (28% vs 49%)[2]

AML, acute myeloid leukemia; mIDH1, mutated isocitrate dehydrogenase-1.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

TIBSOVO® + azacitidine laboratory assessments and dose modifications

Select laboratory abnormalities (≥10%) that worsened from baseline in patients with AML who received TIBSOVO + azacitidine[1,a,b]

Parameter	TIBSOVO + azacitidine (n=71)		Placebo + azacitidine (n=73)	
	All grades n (%)	Grade ≥3 n (%)	All grades n (%)	Grade ≥3 n (%)
Hematology parameters				
Leukocytes decreased	46 (65)	39 (55)	47 (64)	42 (58)
Platelets decreased	41 (58)	30 (42)	52 (71)	42 (58)
Lymphocytes decreased	40 (56)	23 (32)	47 (65)	25 (35)
Neutrophils decreased	18 (25)	16 (23)	25 (35)	23 (32)
Lymphocytes increased	17 (24)	1 (1)	7 (10)	1 (1)
Chemistry parameters				
Glucose increased	40 (56)	9 (13)	34 (47)	8 (11)
Phosphate decreased	29 (41)	7 (10)	25 (34)	9 (12)
Aspartate aminotransferase increased	26 (37)	0	17 (23)	0
Magnesium decreased	25 (35)	0	19 (26)	0
Alkaline phosphatase increased	23 (32)	0	21 (29)	0
Potassium increased	17 (24)	2 (3)	9 (12)	1 (1)

[a]Laboratory abnormality was defined as new or worsened by at least one grade from baseline or if baseline was unknown.
[b]The denominator used to calculate percentages is the number of treated patients who could be evaluated for Common Terminology Criteria for Adverse Events for each parameter in each arm.

- TIBSOVO + azacitidine was associated with fewer severe cytopenias compared with azacitidine

Dose modifications seen with TIBSOVO[1]

- Adverse reactions leading to discontinuation of TIBSOVO in ≥2% of patients were differentiation syndrome (3%) and pulmonary embolism (3%)
- The most common (>5%) adverse reactions leading to dose interruption of TIBSOVO were neutropenia (25%), electrocardiogram QT prolonged (7%), and thrombocytopenia (7%)
- Adverse reactions leading to dose reduction of TIBSOVO included electrocardiogram QT prolonged (8%), neutropenia (8%), and thrombocytopenia (1%)

AML, acute myeloid leukemia.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

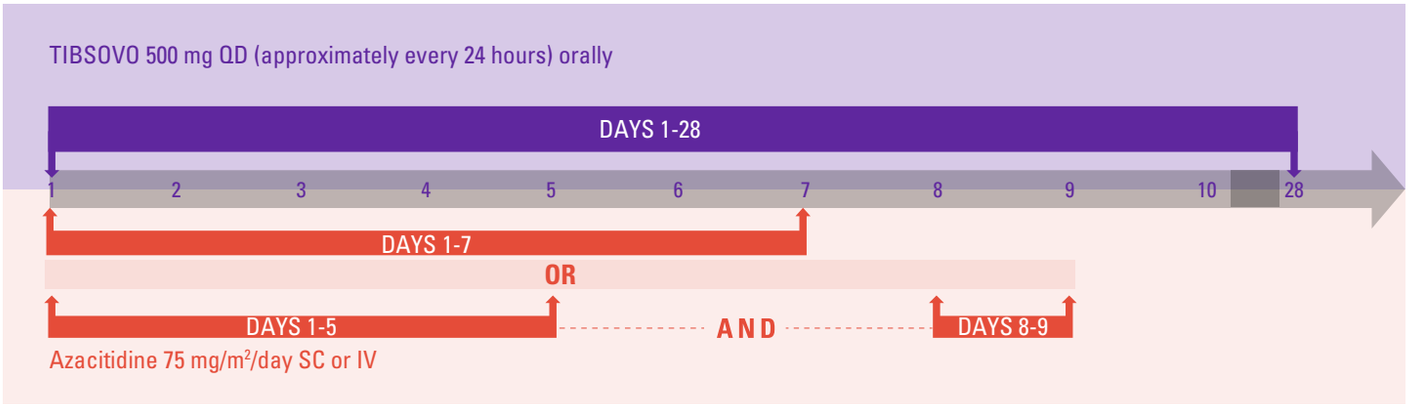
- **In patients with AML,** the most common adverse reactions including laboratory abnormalities (≥25%) are leukocytes decreased, diarrhea, hemoglobin decreased, platelets decreased, glucose increased, fatigue, alkaline phosphatase increased, edema, potassium decreased, nausea, vomiting, phosphate decreased, 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

TIBSOVO® + azacitidine offers a straightforward dosing regimen

Dosing and administration of TIBSOVO + azacitidine[1]

- The recommended dose of TIBSOVO is 500 mg taken orally once daily until disease progression or unacceptable toxicity
  - No dose titration required at treatment initiation
- Start TIBSOVO administration on Cycle 1 Day 1 in combination with azacitidine 75 mg/m^2 subcutaneously or intravenously once daily on Days 1-7 (or Days 1-5 and 8-9) of each 28-day cycle

Dosing schedule for TIBSOVO + azacitidine[1,3]



- Administer TIBSOVO with or without food. Do not administer TIBSOVO with a high-fat meal because of an increase in ivosidenib concentration[a]
- Do not split, crush, or chew TIBSOVO tablets
- Administer TIBSOVO tablets orally about the same time each day
- If a dose of TIBSOVO is vomited, do not administer a replacement dose; wait until the next scheduled dose is due. If a dose of TIBSOVO is missed or not taken at the usual time, administer the dose as soon as possible and at least 12 hours prior to the next scheduled dose. Return to the normal schedule the following day. Do not administer 2 doses within 12 hours
- For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response

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

[a]An example of a high-fat meal includes 2 eggs fried in butter, 2 strips of bacon, 2 slices of white bread with butter, 1 croissant with 1 slice of cheese, and 8 ounces of whole milk (approximately 1000 calories and 58 grams of fat).

AML, acute myeloid leukemia; ECG, electrocardiogram; IV, intravenous; QD, once a day; SC, subcutaneous.

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

TIBSOVO® ivosidenib tablets 250mg

IDH1 mutations are driver mutations that occur in 6% to 10% of patients with AML

IDH1 incidence[2]

- m*IDH1* contributes to oncogenesis by catalyzing the production of D-2-hydroxyglutarate, which leads to disruption of cellular metabolism and epigenetic regulation
- Several studies have suggested that m*IDH1* AML is associated with a poor prognosis

Guidelines

- Both the NCCN Guidelines and ASH-CAP Guidelines recommend testing for *IDH1* mutations in patients with AML[6,7]
  - —"To appropriately stratify available intensive therapy options, expedite test results of molecular and cytogenetic analyses for immediately actionable mutations or chromosomal abnormalities (eg, *CBF*, *FLT3* [ITD and TKD], *NPM1*, *IDH1*, *IDH2*)" —National Comprehensive Cancer Network® (NCCN®)[6]
- NCCN Guidelines recommend ivosidenib (TIBSOVO®) + azacitidine as a category 1 preferred treatment option for newly diagnosed patients ≥60 years of age with m*IDH1* who are not candidates for intensive remission induction therapy[6]

Give your AML patients the chance for **improved overall survival—test and obtain m*IDH1* results** to inform prescribing options.

AML, acute myeloid leukemia; ASH, American Society of Hematology; CAP, College of American Pathologists; IDH1, isocitrate dehydrogenase-1; mIDH1, mutated IDH1; NCCN, National Comprehensive Cancer Network.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

TIBSOVO® + azacitidine in newly diagnosed, IC-ineligible m*IDH1* AML

SIGNIFICANT IMPROVEMENT IN OVERALL SURVIVAL WITH STRONG AND DURABLE RESPONSES

- **Threefold improvement in overall survival** compared with azacitidine[1]
  - TIBSOVO + azacitidine delivered a median overall survival of 24.0 months vs 7.9 months with azacitidine (hazard ratio, 0.44; *P*=0.001)
- **EFS was significantly higher** vs azacitidine (hazard ratio, 0.35; 2-sided *P*=0.0038)[1,2]
  - 12 months: 37.4% vs 12.2%
  - 18 months: 33.3% vs 6.1%
- **CR and CR+CRh was significantly higher** vs azacitidine (*P*=0.0001)[1]
  - CR: 47% vs 15%
  - CR+CRh: 51% vs 18%

Choose **TIBSOVO + azacitidine to extend overall survival** for your m*IDH1* patients.

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.

AML, acute myeloid leukemia; CI, confidence interval; CR, complete remission, 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 RBC transfusions[4]; CRh, complete remission with partial hematological recovery, 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]; EFS, event-free survival, defined as time from randomization until treatment failure (ie, failure to achieve CR by Week 24), relapse from remission, or death from any cause, whichever occurred first; IC, induction chemotherapy; IDH1, isocitrate dehydrogenase-1; mIDH1, mutated IDH1.

References: 1. Tibsovo. Package insert. Servier Pharmaceuticals LLC; 2022. **2.** 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 **3.** Data on file. Servier Pharmaceuticals LLC. **4.** 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. doi:10.1056/NEJMoa2117344. **5.** Montesinos P, Recher C, Zarzycka E, et al. AGILE: A phase 3, double-blind, randomized, placebo-controlled study of ivosidenib in combination with azacitidine in adults with newly diagnosed acute myeloid leukemia and an *IDH1* mutation. Poster presented at: 3rd International Academy for Clinical Hematology (IACH) Annual Meeting; October 1-3, 2020; virtual. https://iachlive.cme-congresses.com/wp-content/uploads/2020/09/Montesinos_AGILE-Phase-3-double-blind-randomized-placebo-controlled-study-of-ivosidenib_29Sept20.pdf **6.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed June 21, 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. **7.** Arber DA, Borowitz MJ, Cessna M, et al. Initial diagnostic workup of acute leukemia: guideline from the College of American Pathologists and the American Society of Hematology. *Arch Pathol Lab Med.* 2017;141(10):1342–1393. doi:10.5858/arpa.2016-0504-CP

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

SERVIER

TIBSOVO®
ivosidenib tablets 250mg