ONUREG® is indicated for continued treatment of adult patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

ONUREG™ (azacitidine) tablets 300 mg • 200 mg

WHAT'S IMPORTANT TO YOUR PATIENTS WITH AML?

EXTENDING LIFE AFTER FIRST REMISSION WITH ONUREG[1,2*]

AN FDA-APPROVED *AML CONTINUED TREATMENT* YOUR PATIENTS CAN TAKE AT HOME[1,2]

NCCN Recommends | ONLY Category 1 preferred National Comprehensive Cancer Network® (NCCN®) treatment option in the maintenance setting for certain patients with AML: oral azacitidine (ONUREG®)[3†‡]

*QUAZAR® AML-001[1]

The efficacy of ONUREG® (azacitidine) was evaluated in QUAZAR® AML-001, a multicenter, randomized, double-blind, placebo-controlled, phase III study. Eligible patients were aged 55 years or older, had AML, and were within 4 months of achieving first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) with intensive induction chemotherapy. Patients were excluded if they were candidates for hematopoietic stem cell transplantation at the time of screening. A total of 472 patients who completed induction with or without consolidation therapy were randomized 1:1 to receive ONUREG® 300 mg (n=238) or placebo (n=234) orally on Days 1 through 14 of each 28-day treatment cycle. Efficacy was established on the basis of OS. The trial demonstrated a statistically significant improvement in OS for patients randomized to ONUREG® compared with placebo. In the trial, ONUREG® showed a median OS of 24.7 months (95% CI: 18.7, 30.5) vs 14.8 months (95% CI: 11.7, 17.6) for patients receiving placebo (HR 0.69 [95% CI: 0.55, 0.86; *P*=0.0009]).

CI, confidence interval; HR, hazard ratio; OS, overall survival.

†NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[3]

Category 1 Preferred recommendation applies to patients in the maintenance setting with intermediate or adverse risk AML that are aged ≥55 (Category 2A for other age groups) and who have received prior intensive chemotherapy and whose disease is now in remission; completed no consolidation, some consolidation or a recommended course of consolidation; and for whom no allogeneic HCT is planned. This is not intended to replace consolidation chemotherapy. In addition, fit patients with intermediate and/or adverse risk cytogenetics may benefit from HCT in first CR, and there are no data to suggest that maintenance therapy with oral azacitidine can replace HCT. The panel also notes that the trial did not include patients <55 years of age or those with CBF-AML; it was restricted to patients ≥55 years of age with intermediate or adverse cytogenetics who were not felt to be candidates for HCT. Most patients received at least 1 cycle of consolidation prior to starting oral azacitidine.

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‡The definition of continued and maintenance treatment by the FDA and NCCN differ based on the AML treatment period in patients with or without CR.[3,4]

AML, acute myeloid leukemia; CR, complete response; FDA, Food and Drug Administration; NCCN, National Comprehensive Cancer Network® (NCCN).

CBF, core binding factor; HCT, hematopoietic cell transplantation.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ONUREG® is contraindicated in patients with known severe hypersensitivity to azacitidine or its components.

WARNINGS AND PRECAUTIONS

Risks of Substitution with Other Azacitidine Products

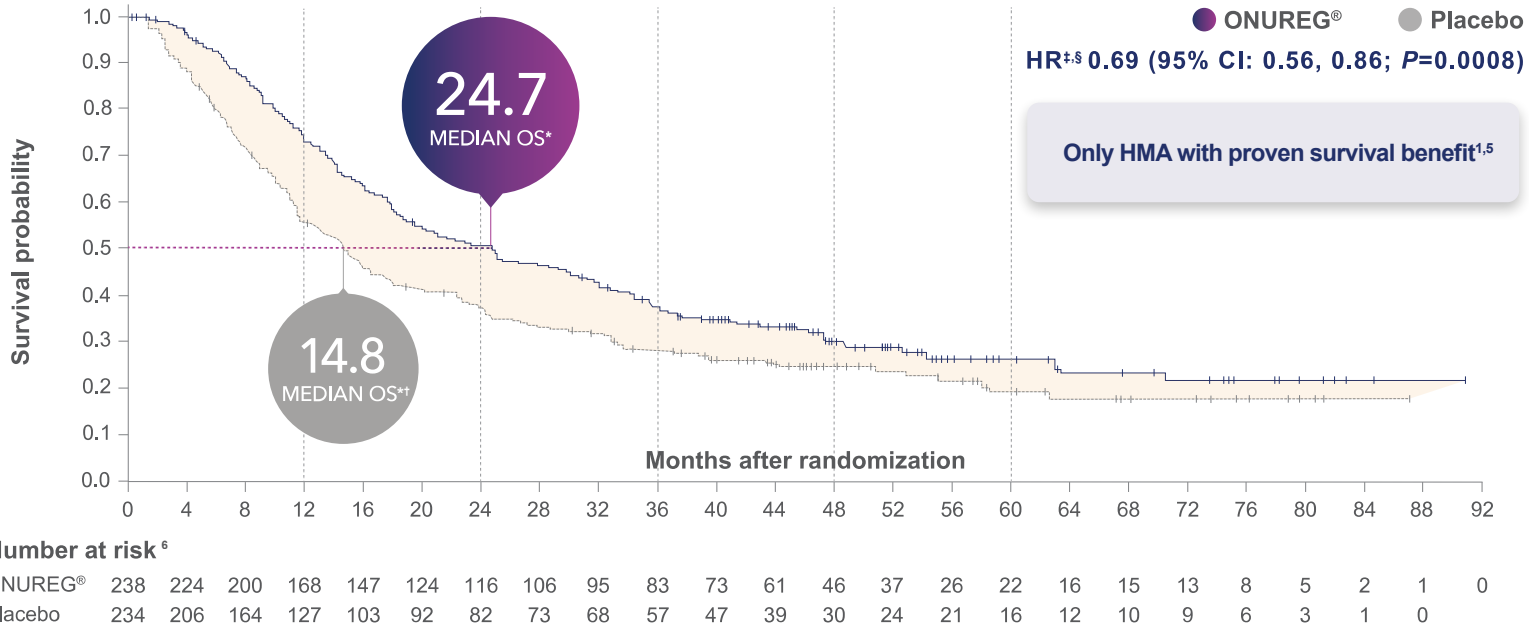
Due to substantial differences in the pharmacokinetic parameters, the recommended dose and schedule for ONUREG® are different from those for the intravenous or subcutaneous azacitidine products. Treatment of patients using intravenous or subcutaneous azacitidine at the recommended dosage of ONUREG® may result in a fatal adverse reaction. Treatment with ONUREG® at the doses recommended for intravenous or subcutaneous azacitidine may not be effective. Do not substitute ONUREG® for intravenous or subcutaneous azacitidine.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for ONUREG®.

After First AML Remission,

Help Your Patients Extend Life With ONUREG®[1,5]

Over 2 years overall survival[1†]



Number at risk [6]

ONUREG®	238	224	200	168	147	124	116	106	95	83	73	61	46	37	26	22	16	15	13	8	5	2	1	0
Placebo	234	206	164	127	103	92	82	73	68	57	47	39	30	24	21	16	12	10	9	6	3	1	0	

*ONUREG® (95% CI: 18.7, 30.5); placebo (95% CI: 11.7, 17.6). †Data cutoff for extended follow-up data was September 2020, with a median follow-up of 51.7 months. Median follow-up in initial dataset was 41.2 months with data cutoff July 2019. ‡The HR is from a Cox proportional hazards model stratified by age (55 to 64 vs ≥65 years), cytogenetic risk category at time of induction therapy (intermediate risk vs poor risk), and received consolidation therapy (yes vs no). §HR for initial follow-up was 0.69 (95% CI: 0.55, 0.86; *P*=0.0009).

AML, acute myeloid leukemia; CI, confidence interval; HR, hazard ratio; OS, overall survival.

Safety[1]

- The majority of adverse reactions (ARs) were mild to moderate (Grade 1 or 2) with ONUREG®
- 1 fatal AR (sepsis) occurred in a patient who received ONUREG®
- Serious ARs occurred in 15% of patients receiving ONUREG®
- Serious ARs in ≥2% of patients who received ONUREG® were pneumonia (8%) and febrile neutropenia (7%)
  - The most common (≥10%) adverse reactions were nausea, vomiting, diarrhea, fatigue/asthenia, constipation, pneumonia, abdominal pain, arthralgia, decreased appetite, febrile neutropenia, dizziness, and pain in extremity

ONUREG™ (azacitidine) tablets 300 mg • 200 mg

Discover OS in patients with *NPM1* mutations at ONUREGPRO.com

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Myelosuppression

New or worsening Grade 3 or 4 neutropenia and thrombocytopenia occurred in 49% and 22% of patients who received ONUREG®. Febrile neutropenia occurred in 12%. A dose reduction was required for 7% and 2% of patients due to neutropenia and thrombocytopenia. Less than 1% of patients discontinued ONUREG® due to either neutropenia or thrombocytopenia. Monitor complete blood counts and modify the dosage as recommended. Provide standard supportive care, including hematopoietic growth factors, if myelosuppression occurs.

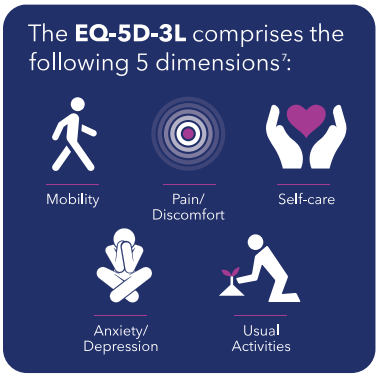
Increased Early Mortality in Patients with Myelodysplastic Syndromes (MDS)

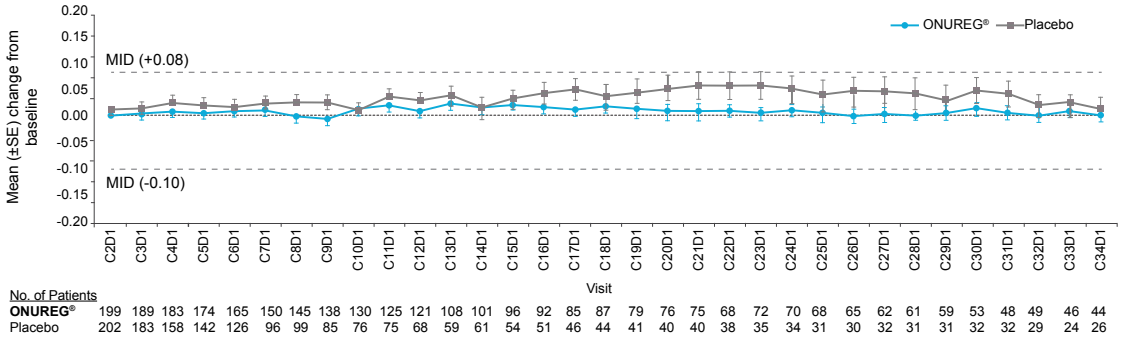
In AZA-MDS-003, 216 patients with red blood cell transfusion-dependent anemia and thrombocytopenia due to MDS were randomized to ONUREG® or placebo. 107 received a median of 5 cycles of ONUREG® 300 mg daily for 21 days of a 28-day cycle. Enrollment was discontinued early due to a higher incidence of early fatal and/or serious adverse reactions in the ONUREG® arm compared with placebo. The most frequent fatal adverse reaction was sepsis. Safety and effectiveness of ONUREG® for MDS have not been established. Treatment of MDS with ONUREG® is not recommended outside of controlled trials.

QoL Was Assessed in QUAZAR-AML-001 by Patient Reported EQ-5D-3L and FACIT-Fatigue Scores

Mean QoL scores remained at or above baseline levels at almost all assessments in the ONUREG® or placebo treatment arms across visits[5*†]

EQ-5D-3L Health Utility Index‡



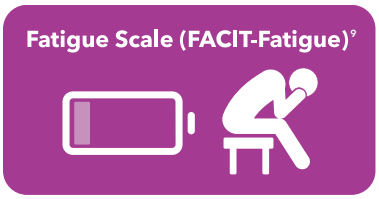


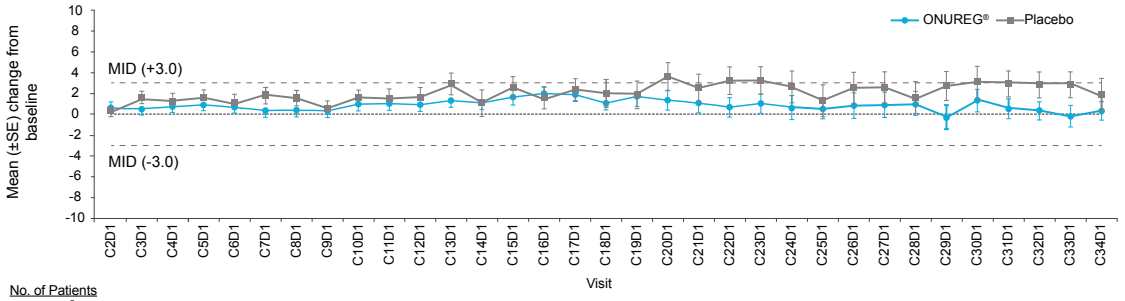
No. of Patients

ONUREG®	199	189	183	174	165	150	145	138	130	125	121	108	101	96	92	85	87	79	76	75	68	72	70	68	65	62	61	59	53	48	49	46	44
Placebo	202	183	158	142	126	96	99	85	76	75	68	59	61	54	51	46	44	41	40	40	38	35	34	31	30	32	31	31	32	32	29	24	26

Analysis Limitation: The EQ-5D-3L assessment is not associated with AML or the individual patient's treatment. This assessment is related to the individual patient's general health status.[8]

FACIT-Fatigue§





No. of Patients

ONUREG®	200	190	185	176	167	152	146	139	130	125	121	109	102	96	92	86	87	79	76	75	68	72	70	68	65	62	61	59	53	48	49	46	44
Placebo	205	183	160	144	128	98	100	87	78	78	71	60	62	65	51	47	44	41	40	40	38	35	34	31	30	32	31	31	32	32	29	24	26

Analysis Limitation: The FACIT-Fatigue Scale is considered relevant to the disease state (AML) rather than the treatment.[10]

No clinically meaningful mean decreases in QoL were observed in ONUREG® or placebo across visits.[7]

STUDY LIMITATIONS:

This analysis is exploratory in nature and definitive conclusions should not be drawn. HRQoL data are not in the Prescribing Information and should be interpreted with caution. The completion rates, based on the number of subjects in the ITT population, declined over time for both groups, with the ONUREG® group having a significantly higher proportion of completion than the placebo group at the Cycle 4 Day 1 visit and thereafter.[9]

A potential limitation is that assessments were conducted on Day 1 of each 28-day treatment cycle, allowing for 14 days of recovery after each 14-day dosing period.

*For the EQ-5D-3L health utility index, a 0.08 and 0.10-point or greater change from baseline was used to define clinically meaningful improvement and worsening, respectively. A change from baseline of ≥3 points was used to define clinically meaningful improvement and worsening at the individual level for the FACIT-Fatigue Scale.[9] Data are presented up to Cycle 34, the last cycle with ≥25 patients in both treatment groups. ‡The EQ-5D-3L (EQ-5D 3-level version) is a generic instrument that includes a descriptive questionnaire that assesses impairment across 5 dimensions at 3 levels (no problems, some problems, and extreme problems).[8] §The FACIT (Functional Assessment of Chronic Illness Therapy)-Fatigue Scale is a 13-item questionnaire that measures an individual's level of fatigue during daily activities over the previous week.[10]

AML, acute myeloid leukemia; EQ-5D-3L, European quality of life-five dimensions-three levels; FACIT, functional assessment of chronic illness therapy; HRQoL, health-related quality of life; ITT, intent-to-treat; MID, minimally important difference; QoL, quality of life; SE, standard error.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

ONUREG® can cause fetal harm when administered to a pregnant woman. Azacitidine caused fetal death and anomalies in pregnant rats via a single intraperitoneal dose less than the recommended human daily dose of oral azacitidine on a mg/m^2 basis. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ONUREG® and for at least 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with ONUREG® and for at least 3 months after the last dose.

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ONUREG® is indicated for continued treatment of adult patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

Over 2 years median OS[1]*

- 24.7-month median OS with ONUREG® vs 14.8-month median OS with placebo in ITT population[1]

HR†: 0.69 (95% CI: 0.55, 0.86; *P*=0.0009)[1]

0 infusions required while taking ONUREG® for AML[1‡]

- ONUREG® offers convenient, once-daily, oral dosing that patients can take at home[1]
- The recommended dosage of ONUREG® is one 300-mg tablet orally, once daily, with or without food on Days 1 to 14 of each 28-day treatment cycle[1]

12 median cycles of ONUREG® in the QUAZAR AML-001 trial[1]

- Range of treatment was 1 to 82 cycles (1 cycle=28days)
- Continue ONUREG® until disease progression or unacceptable toxicity

92% of patients taking ONUREG® did not permanently discontinue due to an AR in the QUAZAR® AML-001 trial[1]

- ARs which resulted in permanent discontinuation in >1% of patients included nausea (2.1%), diarrhea (1.7%), and vomiting (1.3%)[1]

Patients should take an antiemetic 30 minutes prior to each dose of ONUREG® for the first 2 cycles. Antiemetic prophylaxis may be omitted after 2 cycles if there has been no nausea and vomiting.

*ONUREG® (95% CI: 18.7, 30.5); placebo (95% CI: 11.7, 17.6). †The HR is from a Cox proportional hazards model stratified by age (55 to 64 vs ≥65 years), cytogenetic risk category at time of induction therapy (intermediate risk vs poor risk), and received consolidation therapy (yes vs no). ‡Infusions may still be required for supportive care or comorbidities.

AML, acute myeloid leukemia; AR, adverse reaction; CI, confidence interval; HR, hazard ratio; ITT, intention to treat; OS, overall survival.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

Serious adverse reactions occurred in 15% of patients who received ONUREG®. Serious adverse reactions in ≥2% included pneumonia (8%) and febrile neutropenia (7%). One fatal adverse reaction (sepsis) occurred in a patient who received ONUREG®.

Most common (≥10%) adverse reactions with ONUREG® vs placebo were nausea (65%, 24%), vomiting (60%, 10%), diarrhea (50%, 21%), fatigue/asthenia (44%, 25%), constipation (39%, 24%), pneumonia (27%, 17%), abdominal pain (22%, 13%), arthralgia (14%, 10%), decreased appetite (13%, 6%), febrile neutropenia (12%, 8%), dizziness (11%, 9%), pain in extremity (11%, 5%).

LACTATION

There are no data regarding the presence of azacitidine in human milk or the effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with ONUREG® and for 1 week after the last dose.

Please see full Prescribing Information for ONUREG®

Bristol Myers Squibb™

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ONUREG is a trademark of Celgene Corporation, a Bristol Myers Squibb company.
08/23 2011-US-2300110

References: 1. ONUREG® [Prescribing Information]. Summit, NJ: Celgene Corporation; 2022. **2.** U.S. Food and Drug Administration approves ONUREG® (azacitidine tablets), a new oral therapy, as continued treatment for adults in first remission with acute myeloid leukemia [press release]. Bristol Myers Squibb website. https://news.bms.com/news/corporate-financial/2020/U.S.-Food-and-Drug-Administration-Approves-Onureg-azacitidine-tablets-a-New-Oral-Therapy-as-Continued-Treatment-for-Adults-in-First-Remission-with-Acute-Myeloid-Leukemia/default.aspx. Published September 1, 2020. Accessed June 14, 2022. **3.** 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 24, 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. **4.** Acute myeloid leukemia: developing drugs and biological products for treatment. Guidance for industry; availability. FDA website. August 2020. Updated October 17, 2022. Accessed July 20, 2023. https://www.fda.gov/media/162362/download. **5.** Wei AH, Döhner H, Sayer H, et al. Long-term overall survival (OS) with oral azacitidine (oral-AZA) in patients with acute myeloid leukemia (AML) in first remission after intensive chemotherapy (IC): updated results from the phase 3 QUAZAR AML-001 trial. Abstract presented at: ASH Annual Meeting and Exposition; December 13, 2021; Atlanta, GA. **6.** Data on file. BMS-REF-CC-486-0007. Princeton, NJ; Bristol-Myers Squibb Company; 2023. **7.** Wei AH, Döhner H, Pocock C, et al. *N Engl J Med.* 2020;383(Suppl):1-25. **8.** EQ-5D-3L (About). EQ-5D website. January 11, 2022. Accessed June 14, 2023. https://euroqol.org/eq-5d-instruments/eq-5d-3l-about/. **9.** Data on file. BMS-REF-CC-486-0009. Princeton, NJ: Bristol-Myers Squibb Company; 2023. **10.** FACIT-Fatigue. FACIT website. Accessed June 14, 2023. https://www.facit. org/measures/FACIT-Fatigue.

Discover how ONUREG® may help your patients with AML at ONUREGPRO.com