BC Cancer Protocol Summary for Maintenance Oral azaCITIDine for Acute Myeloid Leukemia

Protocol Code	*ULKAMLAMTN*
Tumour Group	*Leukemia/BMT*
Contact Physician	*Dr. David Sanford*

ELIGIBILITY:

Patients must have:

- De novo or secondary acute myeloid leukemia (AML),
- Intermediate or poor risk cytogenetics,
- Complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction or consolidation chemotherapy,
- Last dose of chemotherapy within 4 months of starting azaCITIDine maintenance, and
- BC Cancer Compassionate Access Program (CAP) approval

Patients should have:

- ECOG 0 to 3,
- Recovered from induction chemotherapy with adequate marrow function, and
- Adequate hepatic function

EXCLUSIONS:

- Candidate for hematopoietic stem-cell transplantation
- CR/CRi following non-intensive treatment
- Advanced hepatic tumors
- AML associated with presence of t(8;21), inv(16)/t(16;16) or t(15;17) or t(9;22) karyotypes

TESTS:

- Baseline: CBC & Diff, creatinine, urea, GGT, alkaline phosphatase, ALT, total bilirubin, LDH, albumin, sodium, potassium, chloride
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): HBsAg, HBsAb, HBcoreAb
- Prior to each cycle: CBC & Diff, creatinine, urea, GGT, alkaline phosphatase, ALT, total bilirubin, LDH, albumin, sodium, potassium, chloride
- Cycle 1 – Days 8, 15, 22: CBC & Diff
- Cycle 2 – Day 15: CBC & Diff

- If clinically indicated on Day 15 of subsequent cycles: CBC and differential, platelets (for 2 cycles if dose adjusted for myelosuppression)
- If clinically indicated, every 3 months: HBV viral load

PREMEDICATIONS:

- ondansetron 8 mg PO 30 minutes prior to azaCITIDine
- If there has been no nausea and/or vomiting during the first two cycles, antiemetic prophylaxis may be omitted
- If required: prochlorperazine 10 mg PO 30 minutes prior to azaCITIDine

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
azaCITIDine	300 mg once daily on Days 1 to 14	PO

Repeat every 28 days until disease progression or unacceptable toxicity.

DOSE MODIFICATIONS:

azaCITIDine dose level

Starting Dose	First Dose Reduction	Second Dose Reduction
300 mg PO once daily on Days 1 to 14	200 mg PO once daily on Days 1 to 14	200 mg PO once daily on Days 1 to 7*

* Discontinue if further dose reduction required below 200 mg PO once daily on Days 1 to 7

1. **Hematological**

ANC (x10^9/L)	azaCITIDine Dose
Less than 0.5 or 0.5 - 1.0 with fever	First occurrence: Hold until ANC greater than or equal to 1.0 x 10^9/L, then resume at same dose.
	Occurrence in 2 consecutive cycles: Hold until ANC greater than or equal to 1.0 x 10^9/L, then resume at next lower dose.
Platelets (x 10^9/L)	**azaCITIDine Dose**
Less than 25 or 25 to less than 50 with bleeding	First occurrence: Hold until greater than or equal to 50 x 10^9/L, then resume at the same dose.
	Occurrence in 2 consecutive cycles: Hold until greater than or equal to 50 x 10^9/L, then resume at next lower dose.

2. **Non-Hematological**

Toxicity	Grade	Dose
Gastrointestinal (nausea, vomiting or diarrhea) or Other non-hematological toxicity	3 or greater	First occurrence: Hold until grade 1 or lower, then resume at same dose
		Second occurrence: Hold until grade 1 or lower, then resume at next lower dose

3. **Renal dysfunction:** No dose adjustment in patients with mild to moderate renal impairment. No initial dose adjustment in patients with severe renal impairment. Monitor patients with CrCl 15-29 mL/min more frequently and modify dose for adverse reactions**.**

4. **Hepatic dysfunction**: No dose adjustment in patients with mild hepatic impairment (total bilirubin ≤ ULN and ALT or AST > ULN, or total bilirubin 1 to 1.5 × ULN and any ALT or AST). A recommended dosage has not been established in patients with moderate hepatic impairment (total bilirubin > 1.5 to 3 × ULN). Not studied in patients with severe hepatic impairment (total bilirubin > 3 × ULN). Contraindicated in patients with advanced malignant hepatic tumors.

PRECAUTIONS:

1. **Oral azaCITIDine is not interchangeable with azaCITIDine for injection**. **DO NOT SUBSTITUTE** with or for other azaCITIDine formulations.
2. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
3. **Hepatotoxicity**: oral azaCITIDine is contraindicated in patients with advanced malignant hepatic tumors. During injectable treatment with azaCITIDine, patients with extensive tumour burden due to metastatic disease have been rarely reported to experience progressive hepatic coma and death, especially if baseline serum albumin less than 30 g/L.
4. **Renal dysfunction:** monitor patients with severe renal impairment (CrCl 15 to 29 mL/min) more frequently for adverse reactions and modify oral azaCITIDine dosage for adverse reactions.
5. **GI Toxicity**: oral azaCITIDine is associated with GI toxicity including nausea, vomiting, diarrhea, and constipation. Use of prophylactic 5-HT3 antagonists (e.g., ondansetron) is also associated with constipation. Patients should be made aware of potential GI toxicities prior to starting azaCITIDine.
6. **Hepatitis B reactivation:** Low risk of Hepatitis B reactivation. See SCHBV for monitoring requirements.

Call Dr. David Sanford or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References

1. Wei AH, Döhner H, Pocock C, et al. Oral azacitidine maintenance therapy for acute myeloid leukemia in first remission. N Engl J Med 2020;383(26):2526-2537.
2. Celgene Inc. ONUREG® product monograph. Saint-Laurent, QC; January 4, 2021.
3. Ravandi F, Roboz GJ, Wei AH, et al. Management of adverse events in patients with acute myeloid leukemia in remission receiving oral azacitidine: experience from the phase 3 randomized QUAZAR AML-001 trial. J Hematol Oncol 2021;14(1):133.