

BC Cancer Protocol Summary for Therapy of FLT3-ITD Acute Myeloid Leukemia Using Quizartinib in Combination with Induction and Consolidation Chemotherapy

Protocol Code

ULKAMLQUI

Tumour Group

Leukemia/BMT

Contact Physician

Dr. David Sanford

ELIGIBILITY:

Patient must have:

- Newly primary diagnosed acute myeloid leukemia (AML) or AML secondary to myelodysplastic syndrome or a myeloproliferative neoplasm
- Presence of FLT3-ITD-activating mutation in bone marrow using a validated test
- Planned use in combination with standard cytarabine and anthracycline induction chemotherapy, followed by standard high- or intermediate-dose cytarabine consolidation chemotherapy
- Treatment prescribed by Leukemia/BMT Program physicians and delivered at Vancouver General Hospital
- BC Cancer “Compassionate Access Program” approval prior to treatment

Patient should have:

- Good performance status
- QT interval corrected by Fridericia’s formula (QTcF) less than or equal to 450 ms

Note:

- Patients experiencing intolerance or toxicity from midostaurin (LKAMLMIDO) during induction and/or consolidation chemotherapy may switch to ULKAMLQUI provided all other eligibility criteria are met. Switching after progression is not funded.
- For patients who proceed to hematopoietic stem cell transplant (HSCT), quizartinib should be stopped 7 days before the start of a conditioning regimen.

EXCLUSIONS:

Patient must not:

- Have acute promyelocytic leukemia, French-American-British classification M3 or WHO classification of acute promyelocytic leukemia with translocation, t(15;17) (q22;q12)
- Have *BCR-ABL*–positive leukemia
- Uncontrolled or significant cardiovascular disease, congenital long QT syndrome or history of ventricular arrhythmias or torsades de pointes
- Be less than 18 years of age

TESTS:

- Baseline: sodium, potassium, magnesium, calcium, ECG
- Weekly throughout treatment: ECG
- Prior to each cycle: sodium, potassium, magnesium, calcium
- Refer to induction and consolidation chemotherapy orders for general laboratory monitoring related to induction and consolidation chemotherapy.

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic potential chemotherapy protocols (see [SCNAUSEA](#)).

SUPPORTIVE MEDICATIONS:

- Refer to current Leukemia/BMT program recommendations for antiviral, antifungal and antibiotic prophylaxis related to induction and consolidation chemotherapy.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
quizartinib	Induction: 35.4 mg once daily on Days 8 to 21 of each induction cycle Consolidation*: 35.4 mg once daily for 14 days, to start on day after the last chemotherapy dose of each consolidation cycle	PO

*For patients who achieved complete remission (CR) or complete remission with incomplete hematologic recovery (CRi) with induction treatment

- 1 cycle = 28 days
- **Treatment duration:**
 - Induction: Up to 2 cycles
 - Consolidation: Up to 4 cycles, then proceed to maintenance (see LKAMLQMTN)

DOSE MODIFICATIONS:**If Coadministration with Strong CYP3A Inhibitors is Unavoidable:**

Dose	Dose Reduction for Concomitant Use with Strong CYP3A Inhibitors
26.5 mg	17.7 mg
35.4 mg	

After discontinuation of strong CYP3A inhibitor, resume quizartinib at original dose after 5 half lives of the strong CYP3A inhibitor

Dose Levels for Adverse Reactions:

Dose at Toxicity Occurrence	Dose Reduction
35.4 mg	26.5 mg
26.5 mg	Withhold treatment
17.7 mg	

1. Cardiac – QTcF Prolongation: Physician responsible to review ECG and advise patient

QTcF Interval*	Management
450 to 480 ms	Continue quizartinib at same dose
Greater than 480 ms to less than or equal to 500 ms	- Reduce quizartinib dose to next lower dose level without treatment interruption - Check electrolyte levels and correct any abnormalities - If QTcF decreases to less than 450 ms, resume quizartinib at the previous dose in the next cycle. Monitor for QT prolongation with weekly ECGs during the first cycle at the increased dose
Greater than 500 ms	- Withhold quizartinib - Discontinue other QTc-prolonging medications where possible - Check electrolyte levels and correct any abnormalities - Resume quizartinib at next lower dose level once QTcF returns to less than 450 ms - Monitor for QT prolongation with weekly ECGs during the first cycle after resuming treatment
Recurrence of greater than 500 ms	Permanently discontinue quizartinib if QTcF greater than 500 ms recurs despite dose reduction and elimination of other risk factors
Torsades de pointes, polymorphic ventricular tachycardia, signs/symptoms of life-threatening arrhythmia	Permanently discontinue quizartinib

* QT interval corrected by Fridericia's formula (QTcF)

2. Renal Impairment: Quizartinib is not recommended for patients with severe renal impairment (creatinine clearance less than 30 mL/min) as safety and efficacy have not been evaluated in this patient population.

- 3. Hepatic Impairment:** Quizartinib is not recommended for patients with severe hepatic impairment (Child-Pugh Class C or total bilirubin greater than 3 x upper limit of normal) as safety and efficacy have not been evaluated in this patient population.

4. Other Adverse Reactions:

Toxicity	Management
Grade 3 or 4 non-hematologic toxicity	▪ Interrupt quizartinib until improvement to less than or equal to Grade 2 ▪ If adverse reaction improves to less than or equal to Grade 1, resume at previous dose ▪ If adverse reaction only improves to Grade 2, resume treatment at next lower dose level ▪ Discontinue quizartinib if Grade 3 or 4 adverse reaction persists beyond 28 days
Persistent ANC less than $0.5 \times 10^9/L$ or platelets less than $25 \times 10^9/L$ without active bone marrow disease	Reduce dose to next lower dose level

PRECAUTIONS:

- 1. QT Interval Prolongation:** Torsades de pointes, cardiac arrest, ventricular fibrillation, and sudden death have been reported in patients treated with quizartinib, occurring predominantly during the induction phase of treatment. Prior to treatment initiation, all patients should have a baseline ECG and any electrolyte abnormalities should be corrected. ECG and electrolyte monitoring should be done regularly throughout treatment. Additional close monitoring is indicated for patients with known risk factors for QTc prolongation. Avoid concurrent therapy with other QT prolonging drugs or drugs which disrupt electrolytes. Management of QT interval prolongation may include dose interruption, dose reduction and permanent discontinuation.
- 2. Infections:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- 3. Drug Interactions:** Quizartinib is a CYP 3A4/5 substrate. See BC Cancer Drug Manual for more details.
- Avoid concurrent use with strong CYP3A4/5 inhibitors. If coadministration cannot be avoided, reduce quizartinib dose and monitor closely for toxicity, including QTc prolongation.
 - Grapefruit, grapefruit juice and products containing grapefruit extract may increase quizartinib exposure and should be avoided.
 - Avoid concurrent use of strong or moderate CYP3A4 inducers, as this may lead to decreased quizartinib exposure and reduced efficacy.
- 4. Hepatitis B Reactivation:** See [SCHBV](#) protocol for more details.

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. Erba, HP, Montesinos P, Kim HJ et al. Quizartinib plus chemotherapy in newly diagnosed patients with FLT3-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2023; 401: 1571–83.
2. Quizartinib (VANFLYTA) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. *Canadian Journal of Health Technologies* Aug 2025; 5(8): 1-33.