

BC Cancer Protocol Summary for Maintenance Therapy of FLT3-ITD Acute Myeloid Leukemia Using Quizartinib

Protocol Code

LKAMLQMTN

Tumour Group

Leukemia/BMT

Contact Physician

Dr. David Sanford

ELIGIBILITY:

Patient must have:

- 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,
- Complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following consolidation chemotherapy,
- Last consolidation chemotherapy treatment within the preceding 60 days or undergone allogeneic hematopoietic stem cell transplant (HSCT) within the preceding 180 days,
- No active or Grade 3 or higher Graft Versus Host Disease (GVHD) if patient underwent HSCT,
- Less than 5% of bone marrow blasts before start of maintenance therapy (confirmed on post-induction or most recent bone marrow biopsy)
- Treatment initiated by Leukemia/BMT Program physicians

Patient should have:

- Good performance status
- Adequate hematologic, renal, and hepatic function
- QT interval corrected by Fridericia's formula (QTcF) less than or equal to 450 ms

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

TESTS:

- Baseline: CBC & Diff, creatinine, total bilirubin, ALT, LDH, albumin, creatine kinase, sodium, potassium, magnesium, calcium, ECG
- 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, sodium, potassium, magnesium, calcium, urea
- ECG monitoring: weekly during Cycle 1, prior to Cycle 2 and 3, then every 3 cycles thereafter (physician responsible to review ECG results and advise patient)
- If clinically indicated: creatine kinase, total bilirubin, ALT, albumin, HBV viral load (see [SCHBV](#))

PREMEDICATIONS:

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

TREATMENT:**Cycle 1:**

Drug	Dose	BC Cancer Administration Guideline
quizartinib	<u>Days 1 to 14:</u> 26.5 mg once daily continuously <u>Days 15 to 28:</u> If QTcF is less than or equal to 450 ms during Days 1 to 14*: 53 mg once daily continuously If QTcF is greater than 450 ms during Days 1 to 14: 26.5 mg once daily continuously	PO

*If QTcF greater than 500 ms was observed during induction and/or consolidation with ULKAMLQUI, maintain 26.5 mg dose for the duration of maintenance treatment.

Cycle 2 and onward:

Drug	Dose	BC Cancer Administration Guideline
quizartinib	If QTcF is less than or equal to 450 ms during Cycle 1*: 53 mg once daily continuously If QTcF is greater than 450 ms during Cycle 1: 26.5 mg once daily continuously	PO

*If QTcF greater than 500 ms was observed during induction and/or consolidation with ULKAMLQUI, continue 26.5 mg dose for the duration of maintenance treatment.

- 1 cycle = 28 days
- Treatment duration: repeat cycles every 28 days until relapsed or refractory disease, unacceptable toxicity, up to a maximum of 36 cycles or 3 years, whichever comes first.

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	
53 mg	26.5 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
53 mg	35.4 mg
35.4 mg	26.5 mg
26.5 mg	Withhold treatment
17.7 mg	

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

QTcF Interval	Suggested 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 ▪ Monitor for QT prolongation with weekly ECGs during the first month 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 month after resuming treatment
Torsades de pointes, polymorphic ventricular tachycardia, signs/symptoms of life-threatening arrhythmia	Permanently discontinue quizartinib

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 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 obtain a baseline ECG and any electrolyte abnormalities should be corrected. ECG and electrolyte monitoring should be done regularly throughout treatment. Potassium and magnesium levels should be maintained within normal ranges during quizartinib 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.