BC Cancer Protocol Summary for Treatment of Symptomatic Myelofibrosis with Momelotinib

Protocol Code	*UMLMFMOM*
Tumour Group	*Myeloid*
Contact Physician	*Dr. Lynda Foltz*

ELIGIBILITY:

Patients must have:

- Primary myelofibrosis (MF), post-essential thrombocythemia MF, or post-polycythemia vera MF,
- Palpable splenomegaly of at least 5 cm,
- Moderate to severe anemia, defined by a hemoglobin level less than 100 g/L,
- DIPSS score:
  - intermediate-2 or high risk, OR
  - intermediate-1 risk associated with symptomatic splenomegaly or hepatomegaly
- A Compassionate Access Program (CAP) approval prior to the initiation of treatment

Patients should have:

- Good performance status
- Adequate hepatic and renal function
- ANC greater than or equal to 0.8 x 10^9/L and platelet count greater than or equal to 25 x 10^9/L

Note:

- Patients with prior first line JAK inhibitor treatment are eligible for momelotinib
- Use of momelotinib in first line precludes ruxolitinib and fedratinib use in subsequent lines of treatment. Switching for intolerance is permitted.
- Patients receiving alternate MF therapies (e.g. fedratinib, ruxolitinib, hydroxyurea) may switch to momelotinib provided all eligibility criteria are met

TESTS:

- Baseline: CBC & Diff, ALT, total bilirubin
- Baseline, if clinically indicated: creatinine, albumin, INR
- 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
- Every 4 weeks during treatment: CBC & Diff, ALT, total bilirubin
- If clinically indicated: creatinine, HBV viral load (see protocol SCHBV)

PREMEDICATIONS:

- Antiemetics usually not required

TREATMENT: Active infections should be resolved prior to initiating treatment

Drug	Dose	BC Cancer Administration Guideline
momelotinib	200 mg once daily	PO

- In patients with severe hepatic impairment (Child-Pugh Class C), the recommended starting dose is 150 mg PO once daily
- Repeat every 28 days until disease progression or unacceptable toxicity
- Discontinue if no response by 6 cycles

DOSE MODIFICATIONS:

Table 1: Dose Levels:

Drug	Starting Dose	Dose Level -1	Dose Level -2
momelotinib	200 mg once daily	150 mg once daily	100 mg once daily

- Discontinue momelotinib in patients who are unable to tolerate a dose of 100 mg daily
- If treatment interruption is required and patient was previously dosed at 100mg daily, treatment may be reinitiated at 100 mg daily
- Treatment may be escalated up to starting dosage as clinically appropriate

1. Hematological:

Thrombocytopenia:

Baseline Platelet Count (x10^9/L)	Platelet Count During Treatment (x10^9/L)	Management
Greater than or equal to 100	Greater than or equal to 50	Continue with current dose
	20 to 49	Reduce daily dose by one dose level
	Less than 20	Interrupt treatment until platelets recover to greater than or equal to 50, then restart at lower dose level
50 to 99	Greater than or equal to 20	Continue with current dose
	Less than 20	Interrupt treatment until platelets recover to greater than or equal to 50, then restart at lower dose level
25 to 49	Greater than or equal to 20	Continue with current dose
	Less than 20	Interrupt treatment until platelets recover to greater than or equal to 50, then restart at lower dose level

Neutropenia: If ANC is less than 0.5 x 10^9/L during treatment, interrupt treatment until ANC recovers to greater than or equal to 0.8 x 10^9/L, then restart at lower dose level.

2. Hepatotoxicity:

Total bilirubin (micromol/L)		ALT and/or AST	Management
Greater than 2 x ULN OR Greater than 2 x baseline, if baseline was abnormal	or	Greater than 5 x ULN OR Greater than 5 x baseline, if baseline was abnormal	Interrupt treatment until ALT recovers to less than or equal to 2 x ULN or baseline* and total bilirubin recovers to less than or equal to 1.5 x ULN or baseline**, then restart at next lower dose level If patient experiences reoccurrence of ALT elevation above 5 x ULN, permanently discontinue

ULN = upper limit of normal
*If baseline was greater than 2 x ULN
**If baseline was greater than 1.5 x ULN

3. Non-Hematologic Toxicity:

Severity†	Management
Grade 3 or higher OR Grade 2 or higher bleeding	Interrupt treatment until recover to Grade 1 or baseline, then restart at next lower dose level

†Graded per CTCAE v5.

PRECAUTIONS:

1. **Serious bacterial and viral infections:** have been reported in patients treated with momelotinib. Active infections should be resolved before initiating treatment and patients should be monitored closely for signs and symptoms of infection throughout treatment. Fever or other evidence of infection must be assessed promptly and treated promptly.
2. **Hepatoxicity:** new or worsening liver enzyme elevation has been reported with momelotinib. Although rare and reversible, drug-induced liver injury has been reported. Reduce starting dose to 150 mg once daily for patients with pre-existing severe hepatic impairment. Monitor liver enzymes regularly throughout treatment for all patients. Management of hepatotoxicity may include treatment interruption and dose reduction. Permanently discontinue momelotinib treatment for reoccurrence of ALT and/or AST elevation to greater than 5 x ULN.
3. **Major cardiovascular events** have been reported with momelotinib use. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if symptoms are experienced.
4. **Peripheral neuropathy,** mostly mild or moderate, has been reported with momelotinib use.
5. **Drug interactions:** momelotinib is a CYP3A4 substrate. Concurrent use of strong CYP3A4 inducers may decrease momelotinib exposure and efficacy. If coadministration cannot be avoided, monitor for decreased momelotinib efficacy. Momelotinib is also a substrate of OATP1B1/1B3 transporter. Coadministration of momelotinib with an OATP1B1/1B3 inhibitor may increase the plasma concentration of momelotinib. Monitor for momelotinib toxicity and consider momelotinib dose reduction based on adverse reactions. Momelotinib is a Breast Cancer Resistance Protein (BCRP) inhibitor and may increase the plasma concentration of BCRP substrates. If coadministration is unavoidable, monitor for toxicity of the substrate. Dose reduction of the substrate may be required.
6. **Hepatitis B Reactivation:** Low risk for hepatitis B reactivation. See SCHBV protocol for monitoring requirements.

Call Dr. Lynda Foltz or tumour group delegate at (236) 317-3083 with any problems or questions regarding this treatment program.

References:

1. Verstovsek, S et al. Momelotinib versus danazol in symptomatic patients with anemia and myelofibrosis (MOMENUM). Lancet 2023: 401: 269-80.
2. Mesa, R et al. SIMPLIFY-1: A phase 3 randomized trial of momelotinib versus ruxolitinib in JAK inhibitor-naïve patients with myelofibrosis. J Clin Oncology 2017, 35(34): 3844-3850.
3. Momelotinib (Ojjaara) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. Canadian Journal of Health Technologies. Feb 2025; 5(2): 1-28.