Karyopharm® Therapeutics

GLOBAL MEDICAL & SCIENTIFIC AFFAIRS

Selinexor Supportive Care

Guidelines in r/r MM

A brief summary of prophylactic support and supportive care

US-XPOV-06/19-00004

THROMBOCYTOPENIA

Prophylaxis

- Monitor CBC and standard electrolyte / chemistry; monitor more frequently during first three months of treatment

Management

- Platelet transfusions per institutional guidelines
- In the STORM study, romiplostim[1,2,3,*] (5 µg/kg QW) or eltrombopag [2,3,*] (100-150 mg QD) was used.

Dosage Modification Guidelines

First 3 months

close monitoring and consider early intervention

Adverse Reaction	Action	
Platelet count: <LLN to 75,000/mcL	• **Maintain** Dose	
Platelet count: 25,000 to <75,000/mcL	**Without Bleeding** • **Consider** platelet growth factors per institutional guidelines. • **Reduce** selinexor by 1 dose level (see Table 1).	**With Bleeding** • **Interrupt** selinexor. • **Start** selinexor at 1 dose level lower (see Table 1), after bleeding has resolved and the patient is clinically stable.
Platelet count: <25,000/mcL	• **Interrupt** selinexor. • **Consider** platelet growth factors and transfuse per clinical institutional guidelines. • **Monitor** until platelet count returns to ≥ 50,000/mcL. • **Restart** selinexor at 1 dose level lower (see Table 1).	

Dose can be re-escalated when platelets have stabilized above 50K/µL or baseline at physician discretion.

**are not indicated to normalize platelet counts*

NAUSEA/ VOMITING

Prophylaxis

- **5-HT3** antagonist[2,3]
- **Olanzapine**[2,3,4]

Management

- **NK1R antagonist**[2,3]**:** rolapitant, aprepitant or equivalent for emesis
- **Olanzapine**[2,3,4]

Dosage Modification Guidelines

Rule out other causes of nausea.

Adverse Reaction	Action
Grade 1 or 2 nausea OR Grade 1 or 2 vomiting (≤5 episodes per day)	• **Maintain** selinexor dose and initiate additional anti-nausea medications.
Grade 3 Nausea OR Grade 3 or higher vomiting (≥episodes per day)	• **Interrupt** selinexor. • **Monitor** until nausea or vomiting has resolved to ≤Grade 2 or baseline. • **Restart** selinexor at 1 dose level lower (see Table 1).

WEIGHT-LOSS / ANOREXIA

Prophylaxis

- Consult dietitian or nutritionist at start of Rx.
- Nutritional supplements: Boost®, Ensure®, etc.

Management

- Nutritional counseling
- **Megestrol acetate[5]:** 400 mg QD
- **Olanzapine[6]:** Low dose QPM until weight is within 5lbs of starting weight

Dosage Modification Guidelines

- **Monitor** closely and consider early intervention.
- **Rule out** other causes.
- **Consider** nutritional consultation.
- **Institute** supportive care medications per NCCN guidelines[1].

Adverse Reaction	Action
Grade 2 weight loss of 10% to <20% OR anorexia associated with significant weight loss or malnutrition.	• **Interrupt** dose and institute supportive care. • **Monitor** until weight returns to more than 90% of baseline weight. • **Restart** selinexor at 1 dose level lower (see Table 1).

Dose can be re-escalated when weight has returned to ≥90% of baseline after ≥4 weeks.

HYPONATREMIA

Prophylaxis

- Maintain fluid intake.
- Recommend 8 glasses of electrolyte-containing fluids QD.
- Weekly office visit for labs (electrolytes/CBC) and body weight for cycle 1.

Management

- IV saline as needed
- Salt tablets
- Dietary modification

Dosage Modification Guidelines

- **Monitor** closely and consider early intervention.
- **Rule out** other causes including drug (e.g., diuretic) effects. Be certain that reported sodium level is corrected for concurrent hyperglycemia (serum glucose >150 mg/dL).
- **Treat** hyponatremia per institutional guidelines including dietary review.
- **Consider** addition of salt tablets to patient's diet.

Adverse Reaction	Action*
Sodium level: ≤130 mmol/L	• **Interrupt** selinexor provide appropriate supportive care. • **Monitor** until sodium levels return to ≥130 mmol/L. • **Restart** selinexor at 1 dose level lower (see Table 1).

Dose can be re-escalated when sodium levels have stabilized above 130 mmol/L or baseline at physician discretion.

** Correct for hyperglycemia as outlined under Grade 1.*

FATIGUE

Prophylaxis

- Check for underlying causes of preexisting or predisposition to developing fatigue (e.g. hydration status, anemia).

Management

- **Dexamethasone**[7] supportive care dose
- **Methylphenidate***[,2,3] (5-10 mg PO QAM)

Dosage Modification Guidelines

- Rule out other causes of fatigue (dehydration and anemia).
- If anemic, consider transfusing for hemoglobin <8 g/dL.
- Institute supportive care medications per institutional and NCCN guidelines[1].

Adverse Reaction	Action
Grade 1 OR Grade 2 lasting ≤7 days	• **Maintain Dose**
Grade 2 (lasting >7 days) or Grade 3	• **Interrupt** selinexor: - **Monitor** until fatigue resolves to Grade 1 or baseline. - **Restart** selinexor at 1 dose level lower (see Table 1).

**Optimal dosing and schedule have not been established for use of psychostimulants in older adults and patients with cancer*

SUPPORTIVE CARE AND MONITORING

- **monitor closely and consider early intervention**

Adverse Reaction	Action
Nausea and vomiting	• 5-HT3 antagonist combination antiemesis regimen for standard anti-emetic moderate risk protocol or olanzapine[2,3,4]. • Add NK1 receptor antagonist, or olanzapine if not started as prophylaxis[2,3,4]
Anorexia	• Add appetite stimulant (e.g. olanzapine[6] or megestrol[5]) and weight monitoring
Fatigue	• Add psychostimulant[2,3], physical activity
Cytopenias *anemia/neutropenia/thrombocytopenia	• Consider blood transfusions, colony-stimulating or growth factors[1,2,3]
Cytopenias; hyponatremia; hydration	• Weekly CBC, standard chemistry and serum sodium monitoring for first 8 weeks, and at least monthly thereafter[2,3]

Table 1

Recommended Starting Dosage	First Reduction	Second Reduction	Third Reduction	
80 mg Days 1 and 3 of each week (160 mg total per week)	100 mg once weekly	80 mg once weekly	60 mg once weekly	**DISCONTINUE**

Any and all treatment decisions are soley at the discretion of the treating physician or healthcare professional.

1. Soff, GA., et al., Romiplostim Treatment of Chemotherapy Induced Thrombocytopenia, J Clin Oncol. 2019; 37:2892-2898 **2.** Gavariatopoulou, M., et al., Integrated Safety Profile of Selinexor in Multiple Myeloma: Experience from 437 Patients Enrolled in Clinical Trials, Leukemia. 2020; 10.1038: s41375. **3.** Mikhael, J., el al., Consensus Recommendations for the Clinical Management of Patients With Multiple Myeloma Treated With Selinexor. Clinical Lymphoma, Myeloma & Leukemia 2020; 10.1016. Ruiz Garcia V, et al. **4.** Navari, R., et al., Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting. 2016; 375:134-142. **5.** Megestrol acetate for treatment of anorexia-cachexia syndrome. Cochrane Database Sys Rev 2013; 3:CD004310 **6.** Okamoto, H, et al. Low dose of olanzapine has ameliorating effects on cancer-related anorexia. Cancer Manag Res. 2019; 11: 2233-2239. **7.** Yennurajalingam S, et al. Reduction of cancer-related fatigue with dexamethasone: a double-blind, randomized trial. J Clin Oncol 2014; 32:3221-3228.

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Please contact your local Medical Science Liason with any questions.