Karyopharm® Therapeutics

GLOBAL MEDICAL & SCIENTIFIC AFFAIRS

Selinexor Supportive Care

Guidelines for r/r DLBCL

A brief summary of prophylactic support and supportive care

ALL-XPOV-06/20-00002

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 SADAL study, **romiplostim**[1,2,3,*] (5 µg/kg QW) or **eltrombopag**[2,3,*] (100-150 mg QD) was permitted.

Dosage Modification Guidelines

Adverse Reaction	Action	
Platelet count: **50,000 to <75,000/mcL**	• **Interrupt** one dose of selinexor • **Restart** selinexor at same dose level	
Platelet count: **25,000 to <50,000/mcL**	**Without Bleeding** • **Interrupt** selinexor • **Monitor** until platelets return to ≥ 50,000/mcL • **Restart** selinexor at 1 dose level lower	**With Bleeding** • **Interrupt** selinexor • **Monitor** until platelet count returns to ≥ 50,000/mcL • **Restart** selinexor at 1 dose level lower after bleeding resolves • **Administer** platelet transfusion per clinical guidelines
Platelet count: **Less than 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	

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]
- **Steroids**

Management

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

Dosage Modification Guidelines

Adverse Reaction	Action
Grade 1 or 2 nausea (oral intake decreased w/o significant weight loss, dehydration or malnutrition) **OR Grade 1 or 2 Vomiting** (≤5 episodes per day)	• **Maintain** selinexor dose and initiate additional anti-nausea medications
Grade 3 Nausea (inadequate oral caloric or fluid intake) **OR** **Grade 3 or higher vomiting** (≥6 episodes per day)	• **Interrupt** selinexor • **Monitor** until nausea or vomiting has resolved to ≤Grade 2 or baseline • **Initiate** additional anti-nausea medications • **Restart** selinexor at 1 dose level lower

Consider consultation with palliative care physician and NCCN guidelines for patients' materials on nausea and vomiting.

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.

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

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

FATIGUE

Prophylaxis

- Check for underlying causes of preexisting or predisposition to developing fatigue (e.g. hydration status, anemia).
- Consider initiating and/or encourage physical activity

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.

Adverse Reaction	Action
Grade 1 OR Grade 2 lasting ≤7 days	• **Maintain** dose • Rule out other causes such as anemia
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

Patients with significant fatigue after several doses of selinexor may have an antitumor response. Consider an unscheduled assessment of tumor response as part of the patient's evaluation.

**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	
60 mg Days 1 and 3 of each week (120 mg total per week)	40 mg Days 1 and 3 (80 mg total per week)	60 mg once weekly	40 mg once weekly	**Discontinue**

Any and all treatment decisions are solely 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.

CONTACT INFORMATION

AE Reporting Line
+1 (888)209-9326

Karyopharm Website
https://www.karyopharm.com

Please contact your local
Medical Science Liason with any questions.

Selinexor At-A-Glance: Supportive Care Guidelines in r/r DLBCL

Table 1

Recommended Starting Dosage	First Reduction	Second Reduction	Third Reduction	
60 mg Days 1 and 3 of each week (120 mg total per week)	40 mg Days 1 and 3 (80 mg total per week)	60 mg once weekly	40 mg once weekly	**DISCONTINUE**

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

THROMBOCYTOPENIA

Platelet Transfusions ► per institutional guidelines

Thrombopoietin (TPO) Agonists[1,3,4]:

- Romiplostim[2] ► **5 - 10** µg/kg SQ QW
- Eltrombopag ► **100 - 150** mg PO QD

WEIGHT-LOSS / ANOREXIA

Olanzapine[5] ► 2.5 - 5.0 mg (low dose) PO QHS

Megestrol acetate ► 400 mg PO QD

Continue until weight is within 5 pounds of goal weight

NAUSEA & VOMITING[3]

5-HT3 Antagonist ► Ondansetron **8 mg** PO or equivalent Q8 hours before selinexor and for 2 days following

Olanzapine ► **2.5 - 5.0** mg PO QHS starting C1D1 or

NK1R Antagonists*

- Rolapitant ► **180 mg** PO within two hours prior to each dose
- Aprepitant ► **125 mg** PO d1, **80 mg** PO d2, 3

FATIGUE

Methylphenidate[3,4] ► **5 - 10 mg** PO QAM

Dexamethasone ► supportive care dose

1. Data on File. 2. Soff, GA., et al., Romiplostim Treatment of Chemotherapy Induced Thrombocytopenia, JClin Oncol. 2019; 37:2892-2898 3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Antiemesis. Version 3.2018 4. Okamoto, H, et al. Low dose of olanzapine has ameliorating effects on cancer-related anorexia. Cancer Manag Res. 2019; 11: 2233-2239. *As per package insert prescribing information

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