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Prevention Of Selinexor-Induced Nausea/Vomiting and Diarrhea in First Month Of Therapy: A Novel Step-Up Dosing Approach

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Background: Selinexor is an exportin-1 (XPO1) inhibitor, that acts by restoring the nucleus and re-activating tumor suppressor proteins. The FDA approval was based on phase 2 STORM study and in this trial, grade 3 nausea was seen in 10% of participants. Furthermore, drug discontinuation rate due to debilitating nausea was 6%.

Purpose: Previous analyses from the BOSTON trial demonstrated that dose reductions of selinexor (from 100 mg to lower weekly doses) did not compromise efficacy and improved treatment tolerability. Based on these observations, we implemented a step-up dosing strategy in our center to mitigate early gastrointestinal toxicities, particularly nausea, vomiting, and diarrhea, which frequently occur during the first weeks of therapy. We describe a novel dosing strategy aimed at preventing dose reductions, delays, and treatment discontinuations related to selinexor-induced gastrointestinal toxicity. Our secondary outcome is response rate, since improved tolerability may allow treatment continuity and potentially enhance hematologic responses.

Methods: We retrospectively analyzed 8 selinexor-treated patients Patient's age, sex, risk category, myeloma subtype, prior therapies, maximum and minimum selinexor doses, major toxicities beside nausea/vomiting, response rates, prior autologous stem cell transplant (auto-SCT) were recorded. All patients had nausea/vomiting prophylaxis composed of aprepitant/5-HT3 antagonist/dexamethasone and began treatment with 60 mg dose with subsequent weekly 20 mg increments to target 100 mg/week dose per institutional standardized operation procedure. Informed consent was received for each patient.

Results: 6/8 of patients had auto-SCT. Minimum and maximum number of prior lines were 1 and 5. Grade 2 and higher nausea/vomiting and diarrhea was not recorded. 5/8 of patients attained at least partial response.

Conclusions: Step-up dosing from 60 mg to 100 mg with weekly 20 mg increments, lowers the possibility of treatment pauses due to nausea/vomiting and diarrhea. Additionally, there were no efficacy concerns with step-up approach.

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