Phase I/II study of the combination of panobinostat and carfilzomib in patients with relapsed/refractory multiple myeloma

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Supplemental Text

Methods Supplement

Cardiac Exclusion Criteria

Patients with impaired cardiac function, including a history or presence of sustained ventricular tachyarrhythmia, any history of ventricular fibrillation or Torsade de pointes, bradycardia defined as HR <50 bpm, screening ECG with a QTc >450 msec, right bundle branch block + left anterior hemiblock (bifascicular block, myocardial infarction or unstable angina within 6 months of treatment, and other clinically significant heart disease (e.g. CHF NY Heart Association class III or IV, uncontrolled hypertension, history of labile hypertension, or history of poor compliance with an antihypertensive regimen) were excluded from this study. No formal cardiac testing other than EKG was required for study participation.

Dose-limiting toxicities Definitions

Dose limiting toxicities for the Phase I portion of the study were defined as Grade 4 neutropenia for >7 days or febrile neutropenia, Grade 4 thrombocytopenia or Grade 3 thrombocytopenia with ≥ Grade 2 bleeding, Grade 3 or 4 non-hematologic toxicity (excluding alopecia) despite optimal supportive care lasting > 72 hours or requiring a dose reduction in the first cycle, and any toxicity that prevented a patient from receiving at least 75% of the required doses of both carfilzomib and panobinostat.