Understanding Cardiac Issues in Multiple Myeloma patients: An ongoing Prospective Observation of Cardiac Safety with Proteasome Inhibition (PROTECT) study

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Background and Rationale: The prospective observation of cardiac safety with proteasome inhibition (PROTECT); studies patients with relapsed and/or refractory multiple myeloma (RRMM) treated with proteasome inhibitors (PIs). Bortezomib (BOR) is considered a first-line agent, while carfilzomib (CAR) is often used in the relapsed/refractory setting. PIs are generally well-tolerated, but have exhibited some specific adverse cardiac events (CE); however, the epidemiology of cardiac toxicity remains largely undefined.

Methods: One hundred thirty patients with RRMM starting a PI-based therapy will be enrolled being treated with either (1) BOR-based or (2) CAR-based therapy. Adverse CE include: heart failure, arrhythmia, hypertension and vascular events. Baseline and interval assessments include myeloma evaluation, ECG, 6-minute walk test, transthoracic echocardiogram, cardiac MRI, the MD Anderson Symptom Inventory Heart Failure (MDASI-HF), BNP and troponin I.

Results: To date, 54 patients have been enrolled in the study and 45 have completed at least 2 cycles of chemotherapy, either BOR (n=14) or CAR (n=31). The overall median age was 69 years (range, 40 - 86 years). There have been 30 CE to date in 16 patients. There appears to be a higher incidence of CE in patients treated with CAR (n=13, 41%) when compared to BOR (n=3, 21%). One patient discontinued PI-based therapy after the CE.

Conclusion: Cardiac events are common in patients with RRMM undergoing treatment with PI, in particular CAR. The majority of these events can be managed and the patient can continue chemotherapy.

Table 1. Baseline Characteristics and Cardiac Events

Baseline Characteristics	**Bortezomib n=14 (%)**	**Carfilzomib n=31 (%)**
Age (median, (range))	68 (40-86)	69 (42-85)
Male	7 (50)	24 (77)
Hx of Hypertension	7 (50)	13 (42)
Hx of Dyslipidemia	5 (35)	14 (45)
Hx of Diabetes Mellitus	2 (14)	6 (19)
Hx of Coronary Artery Disease	2 (14)	5 (16)
Hx of Heart Failure	2 (14)	0
Hx of Arrhythmia	3 (21)	6 (19)
Cardiac events	Total CE (n=3) HF: (n=1) Cardiac chest pain: (n=1) Thromboembolic Event: (n=0) Other: (n=1)	Total CE (n=27) HF: (n=4) Cardiac chest pain: (n=5) Thromboembolic Event: (n=2) Other: (n=16)