Abstract Submission

14. Myeloma and other monoclonal gammopathies - Clinical

EHA-2615

O-12-M1: AN EVALUATION OF TIME TO NEXT TREATMENT IN MELFLUFEN AND DEXAMETHASONE-TREATED PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Does the study abide by applicable national and international regulations and guidelines, including but not limited to ethical committees, data protection and privacy regulations, informed consent and off-label use of drugs?: Yes

Background: Melflufen is a novel peptide-conjugated alkylator potentiated by intracellular aminopeptidases, which are markedly overexpressed in multiple myeloma. Melflufen plus dexamethasone had encouraging activity in patients with relapsed/refractory multiple myeloma and ≥2 prior lines of therapy in the phase 1/2 O-12-M1 study (overall response rate, 31%; median overall survival, 20.7 months; Richardson et al. ASH 2017. Abs. 3150). Time to next treatment is used in real world evidence to assist treatment decisions and support economic reimbursement modeling.

Aims: To present a time to next treatment analysis of melflufen plus low-dose dexamethasone in relapsed/refractory multiple myeloma patients exposed to bortezomib and lenalidomide in O-12-M1 (NCT01897714) and how it compares to recently reported relapsed/refractory multiple myeloma studies.

Methods: Patients with relapsed/refractory multiple myeloma and ≥2 prior lines of therapy, including bortezomib and lenalidomide received 40 mg melflufen intravenously on day 1 of each 28-day cycle plus 40 mg weekly dexamethasone until progressive disease or unacceptable toxicity. Patients were followed up for 2 years after PD, and time to next treatment was retrospectively reviewed for subsequent therapy.

Results: As of 9 Nov 2017, 45 patients were treated: median age, 66 years (range, 47-78 years); International Staging System stage II/III, 60%; high-risk cytogenetics, 44%. Patients had 4 median prior lines of therapy; 87% were refractory to last line of therapy including alkylators (24%), proteasome inhibitors (27%), IMiDs (56%), and monoclonal antibodies (9%); 11% were last-line double refractory. At data cutoff, 44 patients (98%) discontinued melflufen plus dexamethasone, mainly due to adverse events (40%) and progressive disease (29%). Twenty-six patients received subsequent therapy. Median time from start of melflufen plus dexamethasone to first subsequent therapy or death, whichever occurred first, (time to next treatment) was 7.9 months (95% CI, 5.7-11.0); next therapy included alkylators (27%), proteasome inhibitors (38%), IMiDs (58%), and monoclonal antibodies (8%).

Image/Pictures:

Drug/study	Median time to next treatment, months	Reference
Pomalidomide + dexamethasone	6.2	Rabin et al. IMW 2015
Carfilzomib-lenalidomide-dexamethasone 2-4th line	8.9	Chari et al. *Blood*. 2017; 130:1818
Austrian Real World Evidence 3-4th line	7.3	Willenbacher et al. *PLoS*. 2016;11:(e)0147381
Daratumumab median 4 prior lines	5.7	Lakshman et al. *Am J Hematol*. 2017;92:1146
Melflufen + dexamethasone	7.9	

Summary/Conclusion: Types of subsequent salvage therapy used after melflufen plus dexamethasone were similar to studies of approved agents in relapsed/refractory multiple myeloma; time to next treatment was also similar (Table). Further trials are ongoing, including a phase 3 study of melflufen plus dexamethasone vs pomalidomide plus dexamethasone in patients with relapsed/refractory multiple myeloma refractory to lenalidomide (NCT03151811).

Keywords: Imids, Multiple myeloma, Phase I/II, Proteasome inhibitor