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Analysis of time to next treatment (TTNT) in melflufen and dexamethasone (dex)-treated patients (pts) with relapsed/refractory multiple myeloma (RRMM).

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Background: Melflufen is a novel peptide-conjugated alkylator potentiated by intracellular aminopeptidases, which are markedly overexpressed in MM. Melflufen + dex had encouraging activity in pts with RRMM and ≥2 prior lines of therapy in the phase 1/2 O-12-M1 study (overall response rate 31%; median overall survival of 20.7 mo; Richardson et al. ASH 2017. Abs. 3150). TTNT is used in Real World Evidence (RWE) to assist treatment decisions and support economic reimbursement modeling. We report TTNT after melflufen + dex in O-12-M1. **Methods**: Pts with RRMM and ≥2 prior lines of therapy, including bortezomib and lenalidomide (len) received 40 mg IV melflufen on d 1 of each 28-d cycle + 40 mg weekly dex until progressive disease (PD)/unacceptable toxicity. Pts were followed up for 2 y after PD, and TTNT was retrospectively reviewed for subsequent therapy. **Results:** As of 9 Nov 2017, 45 pts were treated: median age, 66 y (47-78); ISS stage II/III, 60%; high-risk cytogenetics, 44%. Pts had 4 median prior lines of therapy; 87% were refractory to last line of therapy including alkylators (24%), proteasome inhibitors (PIs; 27%), IMiDs (56%), and monoclonal antibodies (mAbs, 9%); 11% were last-line double refractory. At data cutoff, 44 pts (98%) discontinued melflufen + dex, mainly due to adverse events (40%) and PD (29%). 26 pts received subsequent therapy. Median time from start of melflufen + dex to first subsequent therapy or death, whichever occurred first, (TTNT) was 7.9 mo (95% CI: 5.7-11.0); next therapy included alkylators (27%), PIs (38%), IMiDs (58%), and mAbs (8%). **Conclusions:** Types of subsequent salvage therapy used after melflufen + dex were similar to studies of approved agents in RRMM; TTNT was also similar (Table). Further trials are ongoing, including melflufen + dex vs pomalidomide (pom) + dex in pts with RRMM refractory to len (Phase 3 OCEAN study; NCT03151811).

Drug/study	Median TTNT (mo)	Reference
Pom + dex	6.2	Rabin et al. IMW 2015
Carfilzomib-len-dex 2-4th line	8.9	Chari et al. *Blood*. 2017; 130: 1818
Austrian RWE 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 + dex	7.9	

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