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# POSTER ABSTRACTS

## 654.MULTIPLE MYELOMA: PHARMACOLOGIC THERAPIES

### Optimising the Duration of Therapy for Newly Diagnosed Transplant Ineligible Patients - Analysis of Long Term Follow up Data from the UK MRA Myeloma XI Trial

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**Introduction**

Ongoing therapy to progression has become a standard of care for newly diagnosed myeloma (NDMM) patients but this carries with it an increased burden of treatment administration and potential side effects. This may be of particular importance in the older, frailer, patient group due to increased co-morbidities and polypharmacy. Optimum duration may also differ in subgroups of patients, for example those at different levels of frailty. In a novel analysis, updated data for the transplant ineligible (TNE) pathway of the UKMRA/NCRI Myeloma XI trial after more than 8 years follow up were used to explore this question.

**Methods**

Myeloma XI was a phase III trial with a pathway for TNE NDMM patients who, after immunomodulatory agent-based induction therapy, were randomised between lenalidomide maintenance (Len, 10mg, 21/28 days planned to continue to disease progression) or observation (Obs). Progression-free survival (PFS) and overall survival (OS) data were analysed landmarked from multiple time points (2, 3, and 4 years) after the time of maintenance randomisation, including all patients who had not had an event prior to that time point. Data were analysed for all patients, and within UK-Myeloma Risk Profile groups (UK-MRP: based on WHO performance status, age, ISS and CRP, used as a surrogate for frailty), defined as MRP-low, med and high.

**Results**

In the TNE pathway 723 patients entered the maintenance randomisation and were allocated to observation (n=316) or lenalidomide (n=407). After a median of 101 months (m) of follow up lenalidomide maintenance was associated with a significantly prolonged median PFS in the TNE pathway (11 vs 26m, hazard ratio [HR] 0.49 [95%CI 0.42, 0.58], p<0.001). PFS benefit was seen across all MRP groups (MRP-low 13 vs 32m, HR 0.47 [0.37, 0.60], MRP-med 11 vs 25m, HR 0.51 [0.39, 0.66], MRP-high 10 vs 17m, HR 0.58 [0.43, 0.78]). There was no significant difference in OS with median 59 and 56m respectively, HR 0.98 [95%CI 0.83, 1.15], p=0.813).

The magnitude of the PFS benefit was consistent when landmarked from 2y after randomisation (HR 0.65 [95%CI 0.49, 0.86], p=0.003) but the benefit appeared to diminish at later time points, from the 3y landmark (HR 0.84, [95%CI 0.57, 1.25], p=0.391)

and 4y (HR 0.77 [95%CI 0.47, 1.27], p=0.313). OS remained equivalent from all landmarks with no evidence of an OS detriment from continuing lenalidomide (from 2y HR 1.01 [95%CI 0.84, 1.22], from 3y HR 0.95 [0.77, 1.16] and from 4y HR 0.95 [0.76, 1.20]. This did not appear to differ across MRP groups. When landmarked from 2yr after randomisation all groups had an ongoing benefit from lenalidomide maintenance (MRP-low HR 0.64 [95% CI 0.43, 0.94], MRP-med HR 0.80 [95% CI 0.45, 1.41], MRP-high HR 0.48 [95% CI 0.26, 0.87]). Analogous to the overall population, this benefit appeared lost at later landmarks and there was no evidence of OS detriment from any landmark in any MRP group.

Median duration of maintenance was 19 cycles, range 1, 145, (MRP-low 28 [1,138], MRP-med 15 [1, 128] and MRP-high 11 [1, 145]). More than half of all patients stopping maintenance did so due to disease progression (58.5%). In the remainder the most common reason cited was toxicity (17.1%), and it was cited more for those in the MRP-med/high groups (21.7% and 18.2% respectively) vs MRP-low (12.7%). 72.5% of all patients required a lenalidomide dose modification during their maintenance course (MRP-low 75.4%, MRP-med 68.1%, MRP-high 73.3%). No new specific toxicity signals were identified with longer-term follow up. Cumulative incidence of second primary malignancies at 8 years was 10.4% (95%CI 7.06%, 13.83%) in the observation arm and 16.3% (95%CI 12.81%, 19.71%) in the lenalidomide arm.

**Conclusions**

Long-term follow up of the Myeloma XI trial demonstrates a persistent progression free survival benefit associated with lenalidomide maintenance compared to observation for TNE patients. Exploratory analysis suggests that the benefit of ongoing therapy beyond 2-3 years may be limited, irrespective of MRP subgroup, and randomised studies of limited duration therapy are therefore warranted.

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