

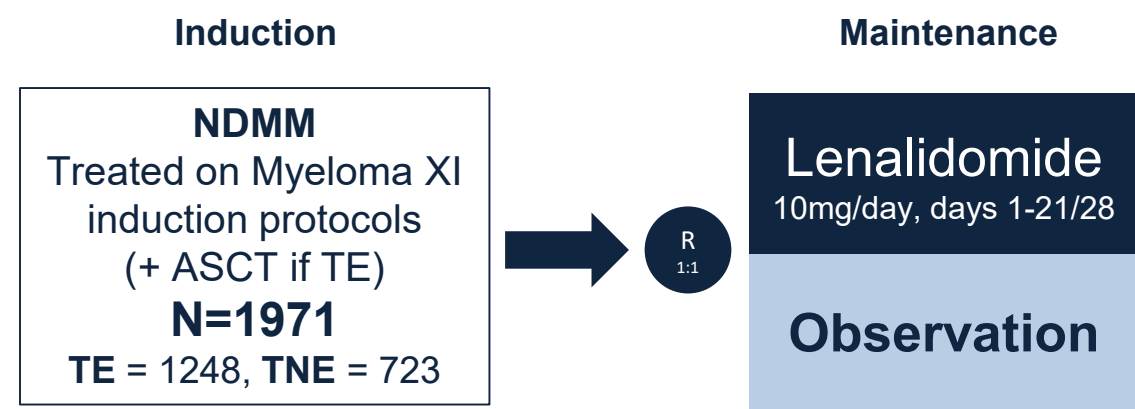
Charlotte Pawlyn<sup>1,2</sup>, Faith Davies<sup>3</sup>, Kara-Louise Royle<sup>4</sup>, David Cairns<sup>4</sup>, Gordon Cook<sup>4</sup>, Mark Drayson<sup>5</sup>, Walter Gregory<sup>4</sup>, Matthew Jenner<sup>6</sup>, John Jones<sup>1</sup>, Martin Kaiser<sup>1,2</sup>, Roger Owen<sup>7</sup>, Nigel Russell<sup>8</sup>, Gareth Morgan<sup>3</sup> and Graham Jackson<sup>9</sup>

## Background

- The impact of the selective pressure of maintenance treatment has been suggested to have the potential to enhance disease aggressiveness at relapse which would shorten the time to next therapy.
- Previously we have shown that Lenalidomide (Len) maintenance therapy in myeloma is associated with improved progression-free survival (PFS).
- This initial analysis defined PFS as the time to biochemical progression based on IMWG criteria. However, at that time point not all patients go on to second line treatment, with the time to treatment being variable dependent on the aggressiveness of disease behaviour at relapse.
- We have used time between biochemical relapse and commencing next treatment as a marker of the impact of maintenance on disease behaviour by analysing long-term follow-up data from 1971 patients in the Myeloma XI trial.

## Myeloma XI

- Myeloma XI is a phase III trial with pathways for transplant eligible (TE) and transplant ineligible (TNE) newly diagnosed myeloma patients.



Median follow up: 47 months (IQR 35-66)

### Exclusion criteria

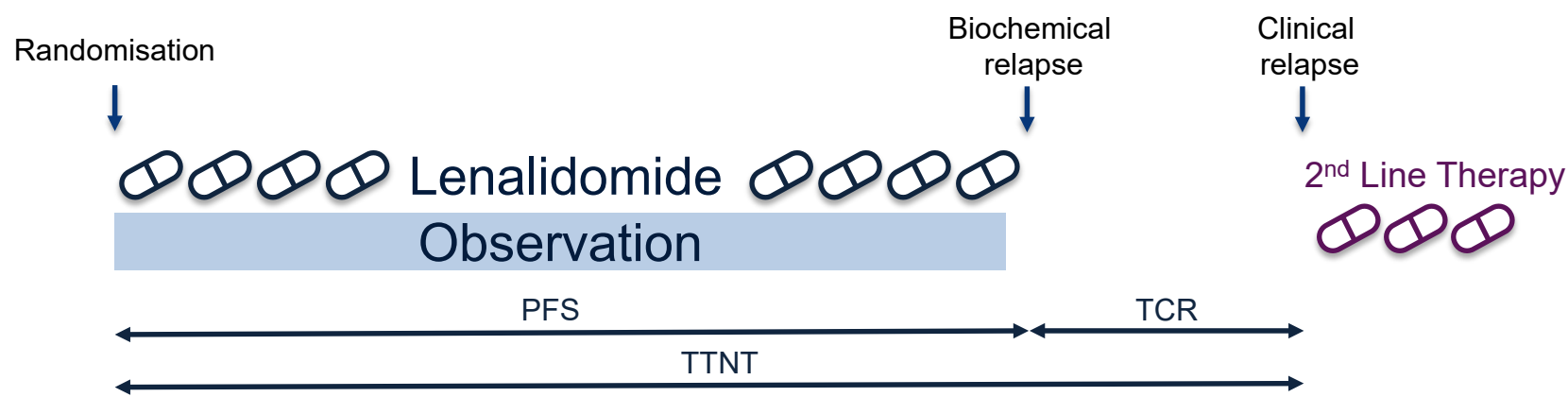
- Failure to respond to lenalidomide as induction IMiD or progressive disease
- Previous or concurrent active malignancies

- Maintenance Len ceased at the time of biochemical progression.

- Neither the timing of commencement, nor agents used for second line therapy were mandated in the protocol.

## Methods

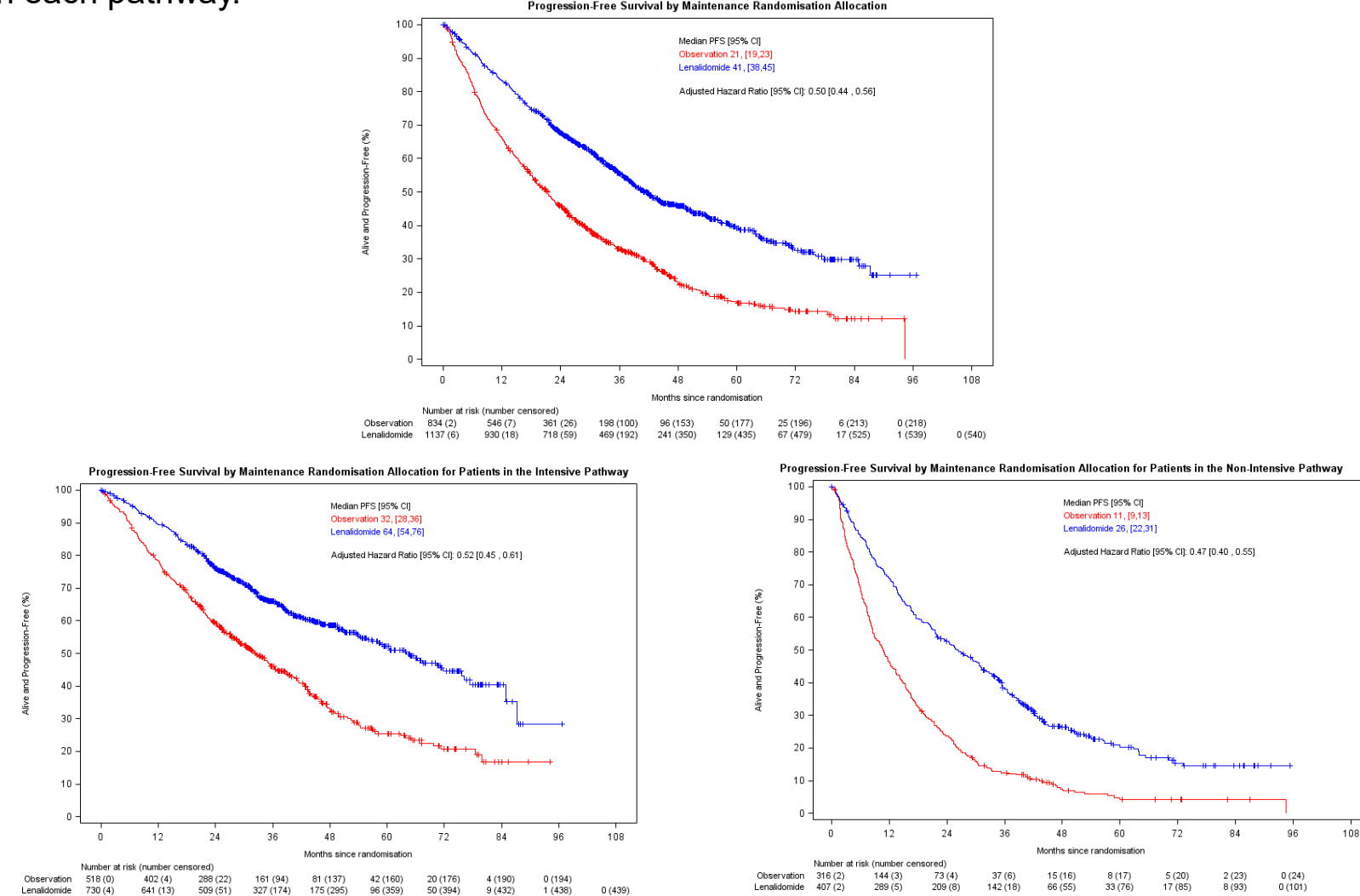
- Updated progression-free survival (PFS) and time to next treatment (TTNT) are presented with a longer follow up than previously (median 47 months).
- An exploratory analysis to compare an estimate of the aggressiveness of relapse was conducted.
  - Time to Clinical Relapse (TCR) was defined as the time from biochemical progression to the start of next line of therapy. We included all patients who progressed on trial excluding those for whom progression was defined by death:



- Hazard ratios (HR) were adjusted for induction/consolidation treatment and pathway.

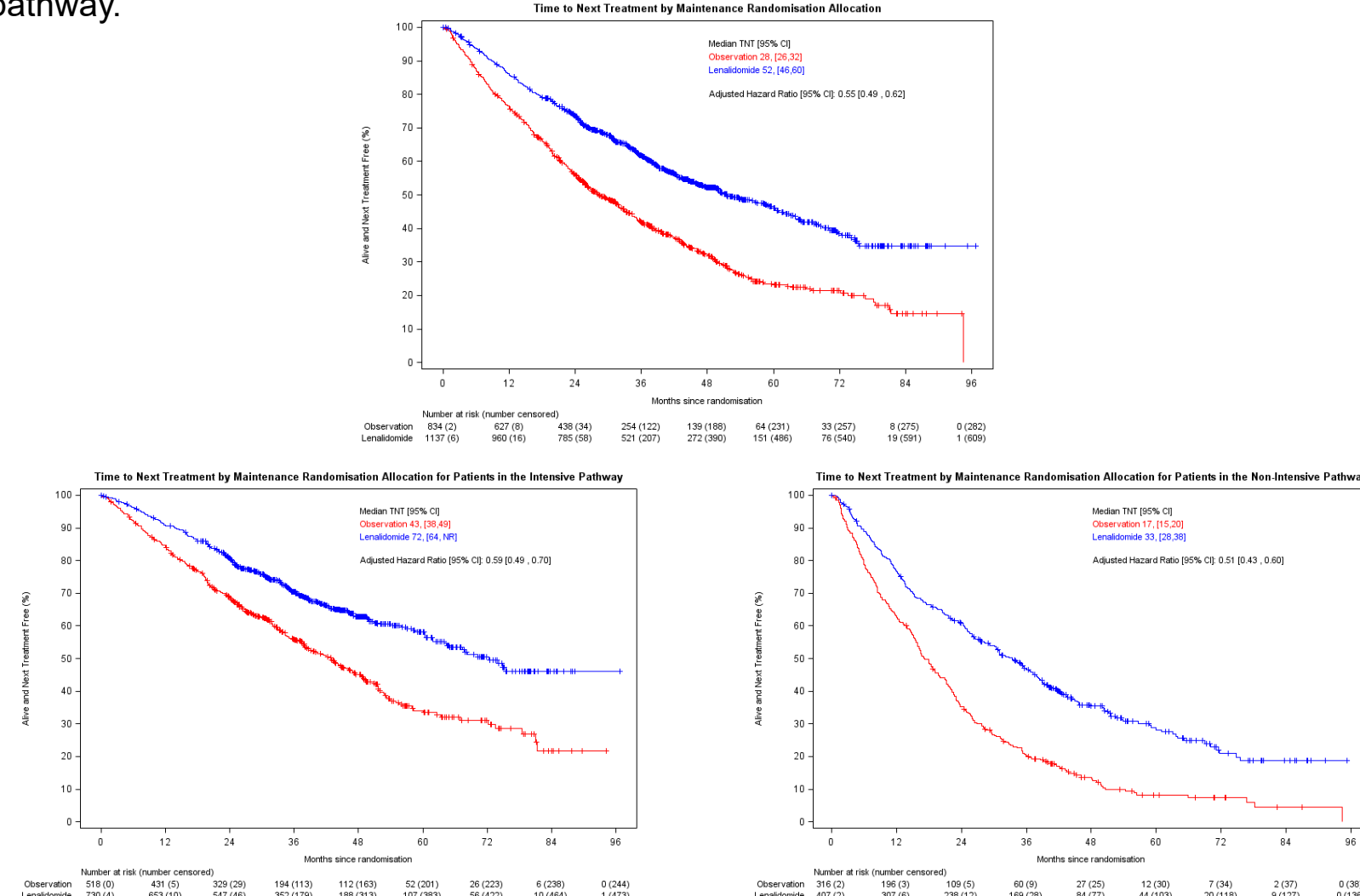
## Progression-free survival

- Len was associated with a significant improvement in PFS compared to observation overall and in each pathway.

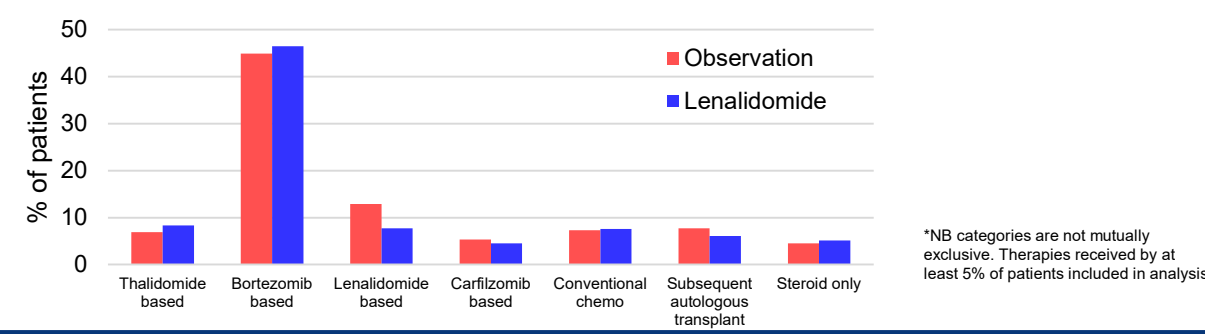


## Time to next therapy

- TTNT was also significantly longer with Len compared to observation overall and in each pathway.

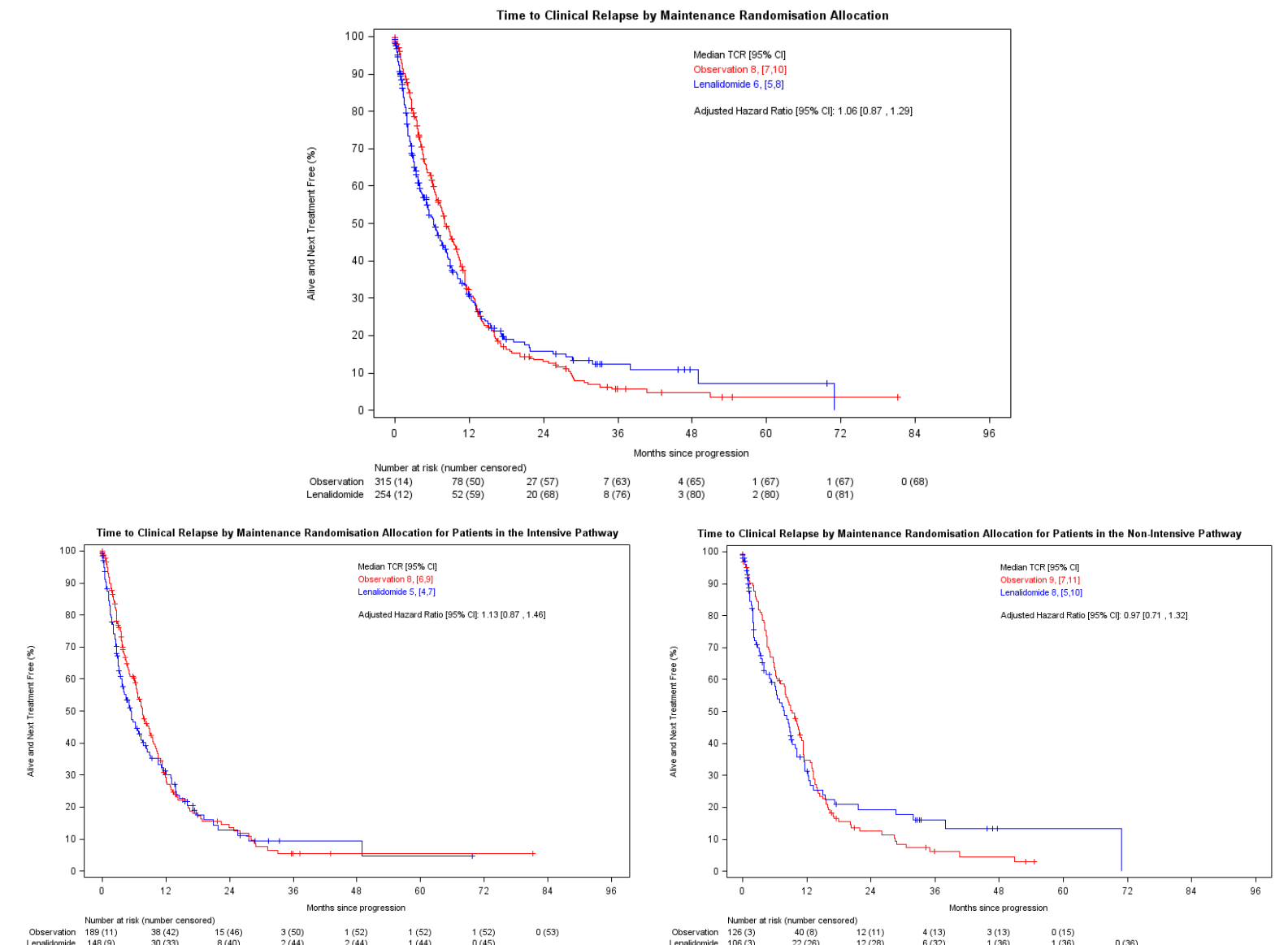


- The most frequently administered second line therapy was bortezomib based.

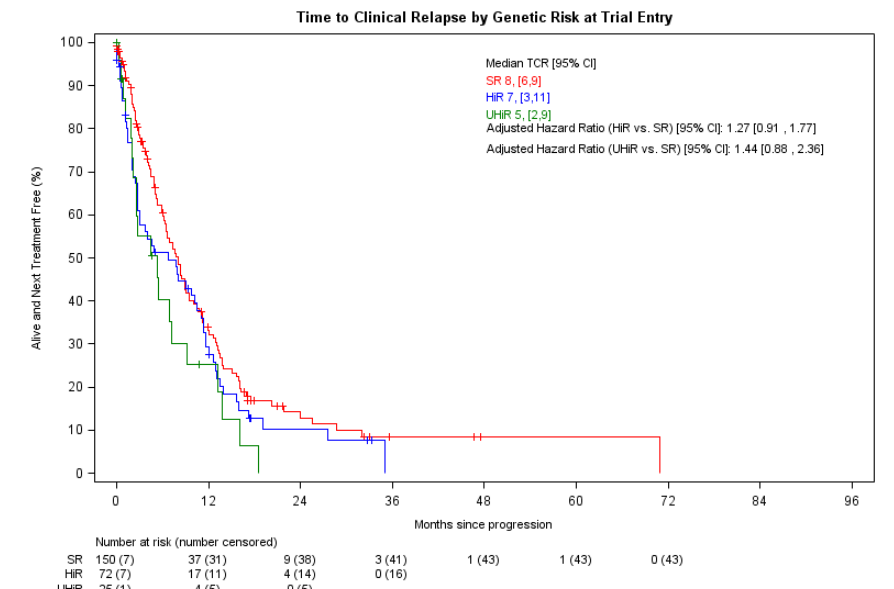


## Time to clinical relapse

- At the time of analysis 569 patients had progressed on trial without progression defined by death. Of these 254 (148 TE, 106 TNE) were receiving Len and 315 (189 TE, 126 TNE) were under observation.
- The median TCR was 7.6 months [95%CI 6.4, 8.5]. There was no difference in TCR between patients receiving Len and those under observation.



- Patient with standard risk disease had a longer (non-significant) median TCR than those with high or ultra-high risk disease.



Adverse molecular risk lesions were defined as gain(1q), t(4;14), t(14;16), t(14;20), or del(17p): standard risk (SR, no adverse lesions), high risk (HiR, one adverse lesion), or ultra-high risk (UHR, two or more adverse lesions).

- There was no difference between the TCR with Len vs observation within each of the risk groups.

## Conclusions

- We found no difference in the aggressiveness of relapse between patients receiving Lenalidomide maintenance or undergoing observation, using long term follow-up data and an exploratory analysis of time to clinical relapse.
- This is consistent with our data showing no significant change in mutational landscape between the groups (Jones J et al. *Haematologica*, 2019) and the meta-analysis showing improved PFS and OS with Lenalidomide used after ASCT (McCarthy P et al. *JCO*, 2017), further supporting the use of maintenance strategies with IMiD drugs for myeloma patients.

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## Conflicts

CP has received honoraria and/or travel support from Amgen, Celgene, Janssen, Oncopeptides and Takeda. For full details of other authors please see abstract book. CP is an NIHR Academic Clinical Lecturer.

