**Myeloma XI trial for newly diagnosed multiple myeloma (NDMM); Long term second primary malignancy (SPM) incidence in the context of lenalidomide maintenance.**

**Background**

As a consequence of improved treatment patients with multiple myeloma are living longer. Long term co-morbidity may include the risk of developing a second primary malignancy (SPM). Early trials of long-term lenalidomide reported an increased incidence of second primary malignancy (SPM), particularly AML and MDS (1-3). Later, meta-analysis suggested the link to be secondary to lenalidomide in combination with melphalan (4). We have previously reported on SPM incidence in the context of this trial and shown that haematological SPM (hSPM) incidence was not increased in association with lenalidomide (5). Here we present a long-term analysis of SPM incidence in patients who have received maintenance therapy versus observation in the context of the Myeloma XI trial.

**Myeloma XI**

Myeloma XI is a phase III, randomised, multi-centre, parallel-group design, open-label trial comparing thalidomide, lenalidomide, carfilzomib and bortezomib induction combinations and lenalidomide 1 vs 0 onostatin as maintenance in newly diagnosed myeloma patients (n=4358). The trial includes both transplant eligible (TE) and non-eligible (TNE) pathways.

**SPM incidence according to pathway and induction therapy received**

- **TE pathway – induction therapy**
  - Incident in the TNE pathway was greatest with 180 patients developing an SPM with an overall incidence of 9.8%. 138 patients in the TE pathway developed an SPM with an overall incidence of 5.5%.
  - SPM incidence was well matched in each pathway suggesting that the induction treatment received did not impact on the likelihood of SPM development.

- **TNE pathway – induction therapy**

**Overall SPM incidence**

4358 patients were randomised to treatment with a further 1971 patients being randomised to either lenalidomide maintenance or active observation.

**Proportion of patients who developed an SPM and breakdown of cases**

- 94.20% of patients in the TE pathway have not developed an SPM.
- Solid tumours occurred in 3.1%.
- Haematological second malignancies were rare, seen in 1.4% of patients (n=57/2532).

- 89.6% of patients in the TNE pathway have not developed an SPM.
- Solid tumours occurred in 5.6%.
- Haematological second malignancies were very rare, seen in 0.7% of patients (n=1/1328).

**Cause of death according to maintenance strategy (TE and TNE combined)**

- In patients undergoing active observation or receiving lenalidomide maintenance the incidence of death due to SPMs was low. Most deaths in both groups were due to myeloma.

**Conclusions**

- Haematological SPM incidence is low in all patient groups including those receiving lenalidomide maintenance.
- The highest incidence of SPM (all types) is seen in transplant non-eligible patients receiving lenalidomide maintenance. This suggests that advanced age is an important risk factor.
- Low risk non-melanoma skin cancers form a large proportion of SPM cases.
- Death due to second malignancy is rare with most patients dying of advanced myeloma or other causes.

**Contact**

[Links to contact information]

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**Conflicts**

[Links to conflict of interest statement]

**myelomaXI.org**