The Myeloma XI Trial for Newly Diagnosed Multiple Myeloma (NDMM); second primary malignancy (SPM) incidence when lenalidomide is used as an induction and maintenance treatment option.

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Background

As a consequence of improved treatment patients with multiple myeloma are living longer. Long term comorbidity may include the risk of developing a second primary malignancy (SPM). A recent meta-analysis inclusive of seven trials suggested an increased risk of SPM development in patients treated with long term low dose oral melphalan in combination with lenalidomide. No increased risk was associated with lenalidomide in combination with other agents (1). These findings were in contrast to earlier studies that suggested an increased risk of MDS and AML development in patients treated with lenalidomide (2-4).

Methods

All adverse events flagged as possible SPMs are reviewed by the Myeloma XI clinical review. All cases are presented to the SPM committee.

Results 2 – Breakdown of cases

<table>
<thead>
<tr>
<th>Breakdown of TNE confirmed SPM cases</th>
<th>Breakdown of TE confirmed SPM cases</th>
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</thead>
<tbody>
<tr>
<td>TNE SPM cases (incidence %)</td>
<td>TE SPM cases (incidence %)</td>
</tr>
<tr>
<td>Haemat</td>
<td>Non-Haemat</td>
</tr>
<tr>
<td>CTD(a) (%)</td>
<td>CTD(b) (%)</td>
</tr>
<tr>
<td>31.0(0.2)</td>
<td>29.2(0.8)</td>
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<tr>
<td>16(3.9)</td>
<td>10(2.3)</td>
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<td>1.8</td>
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</table>

Overall haematological SPM incidence is <1% for both pathways. The overall SPM incidence is higher in the TNE pathway, 5.0% vs 2.3% in the TE pathway.

Results 3 - According to induction, maintenance received and age

Overall SPM incidence is lower in patients treated with lenalidomide (4) vs non lenalidomide maintenance (5) (3yr) is 6.5% vs 9.7% respectively. The incidence is further reduced to 3.9% when lenalidomide is used for maintenance (6)

Conclusions

1. Committee review of all SPM’s has led to the appropriate rejection of 18.8%.
2. Overall trial SPM incidence is low, 3 year CI of 3.8% and IR 1.6 per 100 person years.
3. Low risk SPM form a significant proportion of SPMs (3 yr CI 2.9% if CTD excluded).
4. Haematological SPM incidence is very low with an overall incidence of <1%
5. Age appears to be an important factor with incidence highest in those >74 yrs, enrolled to the TNE pathway.
6. Small numbers of patients have been on maintenance for >3 yrs but the SPM incidence is greater in those receiving len. Ongoing monitoring is required.

Acknowledgments

We would like to thank all the patients and staff at over 100 centres throughout the UK whose participation made this study possible.

We are grateful to all principle investigators for their dedication and commitment to recruiting patients to the study.