is probably a major cause of renal damage in TLS. As such alkalisation should be withheld using rasburicase.

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References

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Combination therapy of Thalidomide and Peginterferon in patients with progressive multiple myeloma

The rationale of this study was to investigate the safety and therapeutic effect of a combination therapy of Thalidomide (Thal) and IFN-α. Both agents are known to exert immunomodulatory and anti-angiogenic effects and are used for therapy in multiple myeloma (MM) [1]. In a phase I/II study, Thal was started at a dose of 100 mg and increased daily, up to 400 mg. Peginterferon (PegIntron®) has to be injected subcutaneously once a week at a starting dose of 20 µg, which was increased to 50 µg. For both medications, the dose was escalated over a period of 4 weeks.

From March to October 2001, 15 heavily pretreated MM patients were included in the study (eight females, median age 60 years (range: 56–79), 12 patients stage III MM, median of 10 chemotherapy cycles (range: 5–27), at least one cycle of HDCT in 11 patients). One patient died because of progressive disease (PD) and one patient continued PD during an initial treatment period of only 1 month. After a treatment period of 3 months, 13 patients were evaluable: 1 patient developed partial remission (PR), 5 patients minimal response (MR), 6 patients stable disease (SD), and 1 patient developed PD. Five patients had to stop therapy of PegIntron® because of adverse effects, 1 patient had PD, so that 6 patients were evaluated after 6 months: 1 patient PR, 2 patients MR, and 3 patients SD. We found an overall response rate of 40%; another 6 patients showed SD (Table 1). Progression-free survival (PFS) during the evaluation period of 14 months was 8.23 months (range: 3–14). However, compared to Thal monotherapy data [2, 3] combination with PegIntron® was not able to increase overall response rate.

WHO grade I/II adverse effects were observed: somnolence (54%), constipation (46%), dryness of mouth (69%), tingling or numbness (46%), fatigue or weakness (54%), tremor (39%), infection (0%), dizziness (23%), rash (8%) and mood changes (31%). We first reduced dosage of PegIntron® because Thal is more effective in relapsed MM than IFN-α. While therapy of PegIntron® had to be stopped in 7 patients between 3 and 9 months after start of treatment, dose reduction of Thal was sufficient to reduce adverse effects, so that therapy of Thal could be continued. However, in 8 of 13 evaluable patients the daily Thal dosage

Table 1. Decline in monoclonal protein levels (n = 15), evaluated on the basis of the percent changes from base line to the time of maximal response

<table>
<thead>
<tr>
<th>Maximum decline in monoclonal protein levels</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete remission (CR)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>&gt;50% of monoclonal protein (PR)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>&gt;25% of monoclonal protein (MR)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>No change (SD)</td>
<td>6 (44.0)</td>
</tr>
<tr>
<td>Progressive disease (PD)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (6.7)</td>
</tr>
</tbody>
</table>
had to be reduced. No WHO III/IV adverse effects were observed. In comparison to Thal as single agent [2] in the therapy of patients with relapsing MM, it seems that combination of Thal and PegIntron® led to higher percentages of adverse effects concerning dryness of mouth (69% versus 36%), fatigue or weakness (54% versus 28%), tremor (39% versus 26%) and mood changes (31% versus 16%), while other adverse effects were similar using Thal as a single agent.

In summary, we present a new treatment option for MM patients relapsing after HDCT or after conventional chemotherapy using the combination of Thalidomide and Peginterferon.

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