Overview of Pixintronide Dimaleate Activity in Non-Hodgkin's Lymphoma

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BACKGROUND

Anti-CD20 therapy: 
- Among the most active classes of agents in non-hodgkin's lymphomas (NHL)
- Standard of care CHOP for low grade aggressive NHL
- Frequently used in relapse, even in insensitive patients, due to cumulative cardiac toxicity

In fact, doxorubicin and paclitaxel are not infrequently used in relapse, even in sensitive patients, due to cumulative cardiac toxicity. 

Reduced oxygen free radical formation and subsequent cardiotoxicity

Higher affinity and avidity for topoisomerase II than doxorubicin

Enhanced hydrogen bonding with greater DNA adduct formation

ACTIVE AS A SINGLE AGENT AND IN COMBINATION WITH OTHER CHEMOTHERAPEUTIC AGENTS

Greater activity than mitoxantrone and doxorubicin in hematologic tumor models

INDOLENT NHL IN CLINICAL STUDIES

Table: Studies with Pixintronide

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Indication</th>
<th>No. of Patients</th>
<th>Age, Median Years (Range)</th>
<th>Response Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single agent</td>
<td>Relapsed Aggressive NHL and CPOP</td>
<td>17</td>
<td>66 (26-76)</td>
<td>CR 8 (11.4), PR 19 (28.6)</td>
</tr>
<tr>
<td>Controlled controlled</td>
<td>Relapsed Aggressive NHL and CPOP</td>
<td>50</td>
<td>66 (26-76)</td>
<td>CR 20 (40.0), PR 30 (60.0)</td>
</tr>
</tbody>
</table>

INTEGRATION WITH VARIOUS THERAPIES

Relapsed/Refractory Indolent NHL and Pixintronide-Hitazone, Phase 2A

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Age, Median Years (Range)</th>
<th>Line of therapy</th>
<th>Treatment Response, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/68 (8.8)</td>
<td>61 (52-77)</td>
<td>3rd line, 2+ prior lines of therapy</td>
<td>CR 2 (7), PR 5 (7)</td>
</tr>
<tr>
<td>3/67 (4.5)</td>
<td>58.5 (45-74)</td>
<td>3rd line, 2+ prior lines of therapy</td>
<td>CR 3 (7), PR 11 (23)</td>
</tr>
</tbody>
</table>

Summary and Conclusions for Phase 2 Study

The study demonstrated that relapsed/refractory aggressive NHL patients treated with pixintronide in combination with other chemotherapy agents, achieved:

- Significant increase in CR rate of 21%
- Significant improvement in ORR of 20% of patients with responses lasting at least 6 months
- 66% of patients in CR/CRu at 6 months
- No increase in treatment related mortality
- No increase in cardiac toxicity
- Significant improvement in PFS and percentage of all patients with responses lasting at least 6 months
- Overall survival at 12 months, 81%

OVERALL SUMMARY

In conclusion, pixintronide dimaleate combined with rituximab and doxorubicin, pixintronide activity is greater in hematologic tumor models and in clinic in tumor models with significantly reduced cardiotoxicity compared to other models.

REFERENCES

4. Pan Pacific Lymphoma 2009