Radioimmunotherapy of Non Hodgkins Lymphomas

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Introduction
Several antigens have been targeted in both B-cell and T-cell lymphomas for radioimmuno-
therapy. The B-cell antigens targeted most frequently is CD20; whereas the T-cell antigens
targeted are CD5 and CD25.

B-Cell Lymphoma
Two major antibodies directed against CD20 have been predominantly used to target NHL: B1
(tositumomab) and 2B8 (ibritumomab). Two basic approaches have been evaluated using either
non-myeloablative doses of I-131 B14,5 or myeloablative therapy with marrow rescue.6 Both
strategies in have resulted in good tumor responses.

A similar strategy has been pursued using the murine antibody 2B8 (Y-90 ibritumomab
tiuxetan). This murine IgG1 has been radiolabeled with In-111 for imaging and Y-90 for therapy.
This is a non-myeloablative approach7 that has resulted in good tumor responses8 and has recently
been approved by the FDA.

T-Cell Lymphoma and Leukemia
T101 is a murine IgG2a that recognizes CD5 antigen.2 It has shown high sensitivity of tumor
detection using In-111 T101 in patients with cutaneous T-cell lymphoma.9 Although radioim-
munotherapy trials have been performed with I-131 T101 by Rosen et al.10,11 the results were
suboptimal. This was likely related to antigen modulation with rapid breakdown of the anti-
body.12,13 Radioimmunotherapy results with Y-90 T101 showed improved results.14

Waldmann et al. discovered anti-Tac, an IgG2a murine antibody that is directed against the IL-
2Rα. A phase I/II trial with murine anti-Tac showed promising results with partial responses and
2 CR.15 Because HAMA was a impediment to repeat treatment a trial utilizing a humanized anti-
Tac is currently in progress.
Future Directions

The NeoRx group has developed a pretargeting approach. Clinical trials have shown the feasibility of using this approach to deliver large radiation doses to target tissue. At NIH, preliminary studies with this approach using anti-Tac streptavidin have shown encouraging results that warrant further clinical development.

Summary

Radioimmunotherapy of lymphoma has shown encouraging responses and is already approved for therapy of B-cell NHL. On going trials to further optimize delivery of higher doses of labeled antibodies are promising and suggest that other reagents may soon be available to target NHL.

References