《招待講演》

Radioimmunotherapy of Non Hodgkins Lymphomas

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Introduction

Several antigens have been targeted in both B-cell and T-cell lymphomas for radioimmunotherapy. The B-cell antigens targeted most frequently is CD20[1]; whereas the T-cell antigens targeted are CD5 and CD25.[2,3]

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 B1[4,5] 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 approach[7] that has resulted in good tumor responses[8] 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 radioimmunotherapy 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 antibody.[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.[16] Clinical trials have shown the feasibility of using this approach to deliver large radiation doses to target tissue.[17] At NIH, preliminary studies with this approach using anti-Tac streptavidin have shown encouraging results that warrant further clinical development.[18]

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.

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