Single-dose anti-CD138 radioimmunotherapy: bismuth-213 is more efficient than lutetium-177 for treatment of multiple myeloma in a preclinical model

Abstract:
Objectives: Radioimmunotherapy (RIT) has emerged as a potential treatment option for multiple myeloma (MM). In humans, a dosimetry study recently showed the relevance of RIT using an antibody targeting the CD138 antigen. The therapeutic efficacy of RIT using an anti-CD138 antibody coupled to 213Bi, an α-emitter, was also demonstrated in a preclinical MM model. Since then, RIT with β-emitters has shown efficacy in treating hematologic cancer. In this paper, we investigate the therapeutic efficacy of RIT in the 5T33 murine MM model using a new anti-CD138 monoclonal antibody labeled either with 213Bi for α-RIT or 177Lu for β-RIT. Methods: A new monoclonal anti-CD138 antibody, 9E7.4, was generated by immunizing a rat with a murine CD138-derived peptide. Antibody specificity was validated by flow cytometry, biodistribution, and α-RIT studies. Then, a β-RIT dose-escalation assay with the 177Lu-radiolabeled 9E7.4 mAb was performed in KalwRij C57/BL6 mice 10 days after i.v. engraftment with 5T33 MM cells. Animal survival and toxicological parameters were assessed to define the optimal activity. Results: α-RIT performed with 3.7 MBq of 213Bi-labeled 9E7.4 anti-CD138 mAb increased median survival to 80 days compared to 37 days for the untreated control and effected cure in 45% of animals. β-RIT performed with 18.5 MBq of 177Lu-labeled 9E7.4 mAb was well tolerated and significantly increased mouse survival (54 vs. 37 days in the control group); however, no mice were cured with this treatment. Conclusion: This study revealed the advantages of α-RIT in the treatment of MM in a preclinical model where β-RIT shows almost no efficacy.

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