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Aim: Multiple myeloma is a B-cell malignancy of terminally differentiated plasma cells within the bone marrow. In spite of a very active search for new treatments, cure is almost never achieved. Alpha-radioimmunotherapy (RIT) is a new cancer treatment modality with tumour specific antibodies coupled to alpha particle-emitting radionuclides. CD138 (Syndecan-1) is found mainly in epithelial cells, but was shown to be expressed by most myeloma cells, both in human and in the mouse. The aim of the study was to evaluate the biodistribution, toxicity and efficacy of a rat Astatin-211-labelled anti-mouse CD138 antibody (^{211}At-9E7.4) in a syngeneic mouse myeloma model. **Materials and methods:** C57BL/KaLwRij mice were grafted with 10^6 5T33 cells (murine myeloma cell line). Biodistribution was studied 15 min, 1h, 4h, 7h, 14h and 21h post-administration of ^{211}At-9E7.4 mAb. Toxicity (animal weight, blood cell counts and transaminase) and RIT efficacy were studied after a dose escalation using 370, 555, 740 and 1110 kBq of ^{211}At-9E7.4 and two control groups ^{211}At-IgG2a isotype control at 555 kBq or no treatment, 10 days after tumour engraftment. **Results:** Studies demonstrated a highly statistical survival benefit for the mice treated with ^{211}At-9E7.4 at 555 kBq ($p=0,0006$) and 740 kBq ($p<0,0001$). At 555 kBq, the survival median was increase by 34 days and at 740 kBq 65% of the mice survived 160 days after engraftment. For treatments with 370 kBq with ^{211}At-9E7.4 or ^{211}At-isotype control at 555 kBq no significant benefit was observed. The higher activity with 1110 kBq of ^{211}At-9E7.4 was clearly radio-

toxic since mice were euthanized after a lost more than 30% of baseline weight 14 days after radiopharmaceutical injection. For the other groups, except transient decreases of leukocytes and red cells, no other toxicity could be demonstrated, especially on liver function, which does not seem to be affected. Concerning red blood cells, the effect is much weaker than that observed with the use of Bismuth-213 at an injected activity of 3.7 MBq. **Conclusions:** RIT of MM using Astatine-211 coupled to monoclonal antibody directed against murine CD138 is effective. The activity in astate-211 which allows 60% survival corresponds to an activity injected in Bismuth-213 located between 3.7 and 7.4 MBq, which seems to reflect the influence of the half life of the two radionuclides. In addition, the upper half-life of astatine appears to be a benefit, particularly because of the lower toxicity observed in this syngeneic model of MM.