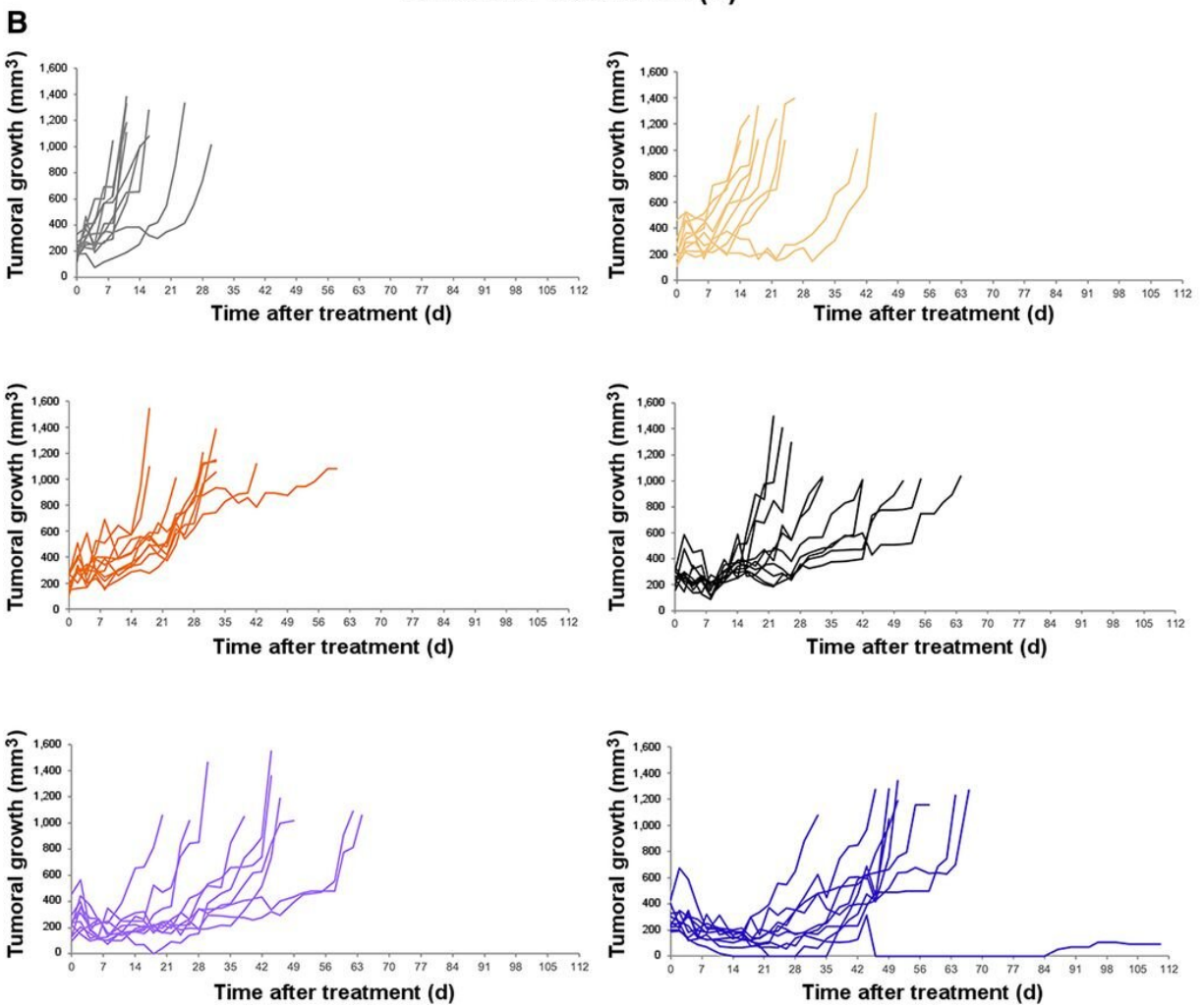
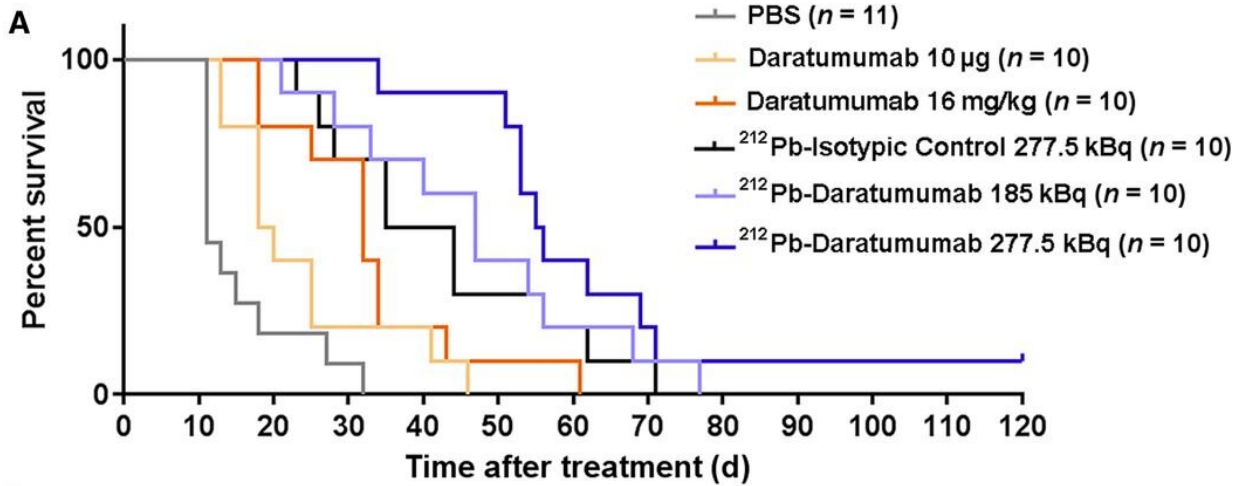


New multiple myeloma therapy shows promise in preclinical study

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Efficacy of ^{212}Pb -daratumumab treatment on Rag2 $^{-/-}$ - $\gamma\text{C}^{-/-}$ bearing subcutaneous xenograft of MM cells. Thirteen days after engraftment, mice received PBS, daratumumab (10 μg or 16 mg/kg), ^{212}Pb -isotypic control (277.5

kBq), or ^{212}Pb -daratumumab (185 or 277.5 kBq). (A) Kaplan–Meier survival analysis. Data were analyzed with log-rank test. (B) Individual tumoral growth evolution. Tumor volume was measured 3 times per week. Mice were euthanized when tumors were 1 cm^3 or when 120 d of survival was reached (end of experiment). Credit: Society of Nuclear Medicine and Molecular Imaging

A new alpha-radioimmunotherapy, ^{212}Pb -anti-CD38, has proven effective in preventing tumor growth and increasing survival in multiple myeloma tumor-bearing mice, according to new research published in the July issue of the *Journal of Nuclear Medicine*. Given the long half-life, central production and worldwide distribution of ^{212}Pb -anti-CD38, researchers have determined that the α -radioimmunotherapy is not only effective but also clinically feasible as a multiple myeloma treatment.

Multiple [myeloma](#) is a plasma cell cancer that occurs in bone marrow. It is the second most common type of blood cancer, with more than 32,000 new cases projected in 2020, according to the American Cancer Society. Despite new treatments and protocols, the prognosis of multiple myeloma patients remains poor, as remission is often followed by relapse. Innovative therapies with a distinct mechanism of action are therefore needed.

"Targeted radioimmunotherapy using antibodies against proteins expressed at the [cell membrane](#) on tumoral [cells](#) has already shown efficacy with beta-emitters, but with severe side effects," said Isabelle Quelven-Bertin, PharmD, radiopharmacist at Limoges University Hospital in Limoges, France. "Using alpha particles is very attractive because their much shorter path-length reduces unwanted radiation exposure on normal tissues, thereby reducing side effects. As such, we investigated the potential of the α -radioimmunotherapy ^{212}Pb -anti-CD38 in the treatment of multiple myeloma."

In the study, researchers developed human myeloma cell lines, which were analyzed for cell proliferation after incubation with various concentrations of ^{212}Pb monoclonal antibodies. Mice received subcutaneous grafts of human myeloma cell lines and were injected with ^{212}Pb -anti-CD38, ^{212}Pb -anti-mCD38 (mice-specific) or ^{212}Pb -isotypic control. Biodistribution, toxicity and dose-range-finding studies were performed, as well as radioimmunotherapy experiments that measured tumor volume and overall survival.

The human myeloma cell line saw a significant inhibition of cell proliferation three days after incubation with ^{212}Pb -anti-CD38. Likewise, the [mouse model](#) showed marked inhibition of [cell proliferation](#) for mice treated with ^{212}Pb -anti-CD38, with a median survival of 55 days; mice that received the isotypic control had a median survival of 11 days. Biodistribution studies showed a specific tumoral accumulation of ^{212}Pb -anti-CD38, and toxicity experiments with ^{212}Pb -anti-mCD38 established a toxic activity of 277.5 kBq.

While ^{212}Pb monoclonal antibodies effectively inhibited [tumor growth](#) and increased survival, whole-body SPECT/CT imaging was not possible due to the low ^{212}Pb activity injected and the detection sensitivity. Instead, researchers performed SPECT/CT imaging with ^{203}Pb , a chemically identical radiometal.

"This radioelement allowed us to consider a theranostic approach for ^{212}Pb α -radioimmunotherapy, preventing the need for a radionuclide with different physical-chemical properties that would likely result in different pharmacokinetics. Combining therapy and imaging could provide an effective approach to optimizing therapeutic doses using specific dosimetry calculation and to monitoring the patient's response. Moving forward, this could be considered as an innovative theranostic approach," noted Michel Cogné, MD, Ph.D., professor of immunology at Limoges Medical School in Limoges, France.

More information: Isabelle Quelven et al, ^{212}Pb α -Radioimmunotherapy Targeting CD38 in Multiple Myeloma: A Preclinical Study, *Journal of Nuclear Medicine* (2019). [DOI: 10.2967/jnumed.119.239491](https://doi.org/10.2967/jnumed.119.239491)

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