User project report

Antibody-based molecular radiotherapy: assessment of 161Tb-AKIR001 for potential treatment of CD44v6-positive cancer

Marika Nestor
Department of Immunology, Genetics and Pathology
Uppsala University, Sweden

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP). This document reflects only the view of the author(s). The Agency is not responsible for any use that may be made of the information it contains.

1. Authors

Amanda Gustafsson[1], Anja Mortensen[1], Sara Rinne[1], Saloni Chopra[1], Tianqi Xu[1], Jens Hemmingsson[2], Peter Bernhardt[2], Marika Nestor[1]

[1]Department of Immunology, Genetics and Pathology, Uppsala University, Sweden
[2]Department of Medical Radiation Sciences, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden.Department of Medical Physics and Biomedical Engineering, Sahlgrenska University Hospital, Gothenburg, Sweden.

2. Context of the project

This project aims to evaluate 161Tb-labeled AKIR001, a novel CD44v6-targeting antibody, as a candidate for molecular radiotherapy in aggressive cancers. 177Lu-AKIR001 has shown excellent preclinical efficacy, and 161Tb offers promising potential due to combined β, Auger- and conversion electron emissions. Radiolabeling, binding, and therapeutic effects are studied in vitro and in vivo. The goal is to generate comparative data with 177Lu-AKIR001 and identify whether 161Tb may offer improved therapeutic benefit.

3. Results and discussion

161Tb-AKIR001 was successfully radiolabeled with high yield and stability, especially when ascorbate was included to prevent radiolysis. In vitro studies confirmed retained antigen specificity and high affinity. Biodistribution studies in two xenograft models demonstrated high and antigen-specific tumor uptake with low off-target accumulation. In vivo therapy studies revealed dose-dependent tumor regression and survival benefits comparable to or exceeding those of 177Lu-AKIR001. Dosimetry studies are ongoing. Overall, 161Tb-AKIR001 has shown promising efficacy and safety in preclinical models.

4. Conclusions

The study demonstrates that 161Tb-AKIR001 is a viable radiopharmaceutical with high tumor specificity and promising therapeutic effects in preclinical models. Retained binding properties and improved radiobiological effects due to 161Tb emissions may offer advantages over 177Lu. This lays the groundwork for future clinical development using 161Tb and highlights its potential to enhance antibody-based radiotherapy, particularly for CD44v6-positive cancers with poor prognosis.

5. Involvement of the PRISMAP services

PRISMAP provided access to high-purity 161Tb in multiple batches, enabling radiolabeling optimizations, stability testing, and preclinical efficacy studies. The support allowed comparison of 161Tb-AKIR001 to existing 177Lu-AKIR001 data in a translational context, supporting drug development for hard-to-treat CD44v6-positive cancers.

6. Feedback to PRISMAP

We are very grateful for the access to 161Tb and the excellent support from the PRISMAP team. Communication and coordination have worked smoothly throughout. One observation is that chemical purity has varied somewhat between batches, with one batch unfortunately yielding results that could not be used. Despite this, the overall experience has been highly valuable and we truly appreciate the opportunity to be part of the PRISMAP program.

7. Publications and other dissemination activities (conferences etc.)

Conference presentations:

1. EANM 2024 poster: **Biodistribution and in vivo efficacy of ^{161}Tb-labeled AKIR001, a novel anti-CD44v6 antibody.** EP-0991. Anja Mortensen *et. al.* October 2024
2. IWRMR 2025 poster: **Tb, or Not Tb: Exploring Terbium-161 for CD44v6-Targeted Radionuclide Therapy.** Poster. Amanda Gustafsson *et. al.* April 2025
3. EANM 2025 top rated oral presentation: **Tb, or Not Tb – Exploring Terbium-161 for CD44v6 Therapy**. OP-414. Amanda Gustafsson et. al. October 2025
4. EANM 2025 poster: **161Tb-DOTATATE for SSTR2-Targeted Neuroblastoma Therapy**. EP-0068. Saloni Chopra et. el. October 2025

Planned manuscript submissions during 2026:

1)
Tb, or Not Tb – Exploring Terbium-161 for CD44v6-Targeted Radionuclide Therapy
Amanda Gustafsson[1], Anja Charlotte Lundgren Mortensen[1,2], Tianqi Xu[1], Klas Bratteby[4,5], Peter Bernhardt[6,7], Marika Nestor[1]

2)
[^{161}Tb]Tb-DOTATATE as a potential treatment option for neuroblastoma
Saloni Chopra[1], Tianqi Xu[1], Hanna Berglund[1], Amanda Gustafsson[1], & Marika Nestor[1]*

Appendix 1. Dissemination guidelines for user projects as agreed in the signed User Agreement

Dissemination rules

Only user groups that are allowed to disseminate the results which they have generated under the project may benefit from the access, unless they are working for SMEs.

For each user group project, a publishable project summary and a publishable summary of the results will be published on the European Union Horizon 2020 PRISMAP project website www.prismap.eu. The publication of results in journals or at conferences is strongly encouraged.

To ensure the long-term sustainability of the PRISMAP initiative, proper recognition of the contributing facilities, their services and the involved persons is necessary. All participating PRISMAP facilities shall be acknowledged in the publication. Acknowledgement and co-authorship of PRISMAP staff members who participated in the experiment shall be considered according to the research field best practices and verified with the PRISMAP Technical Manager before any publication.

The user group shall contact the PRISMAP Technical Manager 30 days prior to submission of publications or other communications of results that were obtained by making use of services provided by PRISMAP (radionuclides delivered or medical services provided). The Technical Manager will communicate to the user group the list of PRISMAP facilities and persons that have contributed to each specific project and the way this contribution must be acknowledged in the publication/communication or where co-authorship is required to reflect specific scientific contributions.

Users must comply with Horizon 2020 dissemination rules (i.e. acknowledge that their work was financially supported by the European Union's Horizon 2020 Research and Innovation Programme by including the following acknowledgement: "This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP)"), and grant open access to resulting publications and related data.

Dissemination shall take place only once legitimate interests regarding intellectual property have been safeguarded. A maximum publication delay of 90 days may be granted for this purpose.

Acknowledgements

The list of name(s) to be mentioned in the acknowledgment section is sent to the technical manager by the main contact of the involved facilities.

A general sentence will be added by the corresponding author of the article (user side):

"The authors would like to thank the members of the PRISMAP consortium and of the PRISMAP user selection panel, coordination and management team for their advice and support."

Funding acknowledgement

"This work was supported by the European Union's Horizon 2020 research and innovation programme as a user project of PRISMAP – The European medical radionuclides programme (GA 101008571)".