SNMMI SOCIETY OF NUCLEAR MEDICINE & MOLECULAR IMAGING ANNUAL MEETING

Pre-Clinical Evaluation of Anti-uPAR Antibody as a Radiolabeled PET Imaging Candidate in Solid Tumors

Raji Nair, PhD, Andrew Cittadine, MS, Eric Kawamoto, PhD, Aidan Kelly and Chandler Robinson, MD.

Monopar Therapeutics, Wilmette, Illinois, USA

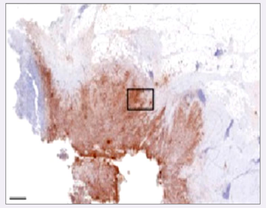
Monopar Therapeutics

uPAR: Promising Cancer Target

The urokinase plasminogen activator receptor (uPAR) is:

- Highly expressed in several aggressive cancers and the tumor microenvironment, but rarely in healthy tissues
- A well credentialed target; present on the surface of cancer cells
- Involved in cancer progression, invasion, and metastasis

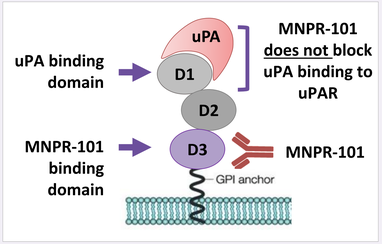
Cancer Type	% Patients with uPAR Expression
Breast	97%
Bladder	89%
Pancreatic	87%
Colorectal	85%
Ovarian	88%
Gastric	88%



Urothelial cell carcinoma showing uPAR expression in brown in both tumor cells and tumor-associated stroma (adapted from Baart 2021)

MNPR-101: First-in-class uPAR-targeting antibody

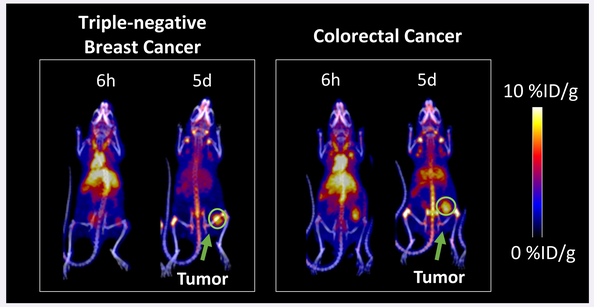
- A well-characterized humanized monoclonal antibody against uPAR
- Highly-selective, with a strong binding affinity at << nM range
- Binds to uPAR even when its ligand uPA is bound
- No adverse findings in animal toxicology and human tissue cross reactivity studies



uPAR structure adapted from Blasi 2002 showing MNPR-101 binding domain

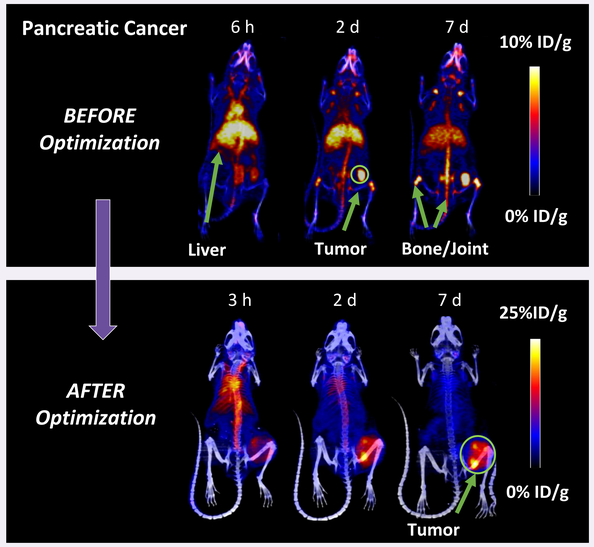
MNPR-101-Zr: PET imaging for uPAR-positive cancers

Robust tumor uptake in multiple xenograft models



PET Imaging after ~250 μCi injection of MNPR-101-Zr in nude mice implanted with MDA-MB-231 (Triple-negative Breast) and HT-29 (Colorectal) tumor cells

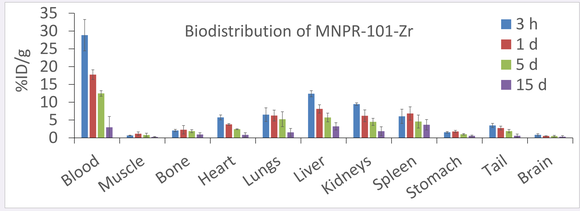
Rigorous optimization achieved markedly higher tumor uptake while minimizing accumulation in bone and healthy tissue



PET Imaging after ~250 μCi injection of MNPR-101-Zr in nude mice implanted with MIA-PaCa2 (pancreatic) tumor cells. Note difference in %ID/g scale

MNPR-101-Zr: Biodistribution and Dosimetry

Encouragingly low uptake in normal tissues



Ex-vivo distribution in naïve mice after 100 μCi injection of optimized MNPR-101-Zr

Predicted dosimetry is well within accepted safety limits

- Projected human absorbed dose from 74 MBq (2 mCi) injection is comparable to other Zr-89 imaging agents. Human effective dose (tissue weighted average) is estimated to be ~ 0.035 Sv.

Target Organ	MNPR-101-Zr Absorbed Dose Estimate (Gy)	Organ Safety Limit (Gy)
Liver	0.053	30
Kidneys	0.044	18
Lungs	0.028	15
Spleen	0.043	-
Red Marrow	0.033	2

OLINDA/EXM was used for mouse to human dosimetry prediction. For Zr-89 1 Gy = 1 Sv

Recently initiated Phase 1 Study

- Clinical Trial for MNPR-101-Zr was launched in April 2024
- PET imaging and dosimetry of 12 patients with Solid Tumors

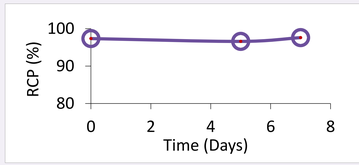
NIH National Library of Medicine
National Center for Biotechnology Information
ClinicalTrials.gov
RECRUITING
ClinicalTrials.gov ID NCT06337084
Sponsor Monopar Therapeutics

MNPR-101-Zr: Synthesis and Stability

Production validated for patient dosing

Run	Chemical Purity (%)	Radiochemical Purity (%)
1	96.5	97.6
2	96	97
3	96.3	97.1

Highly stable at 7 days



HPLC analysis Radiochemical Purity (%) at 2- 8°C

Conclusions

- MNPR-101-Zr shows durable tumor uptake across multiple cancers
- Optimization improved biodistribution and stability
- Lengthy shelf-life enables worldwide distribution

Advancing MNPR-101 Therapy Candidate

- MNPR-101 labeled with therapeutic isotopes shows near complete tumor elimination after single injection in pre-clinical studies
- Targeting therapeutic Phase 1 Clinical Study initiation in solid tumors as early as Q4 2024 or Q1 2025

Citations: