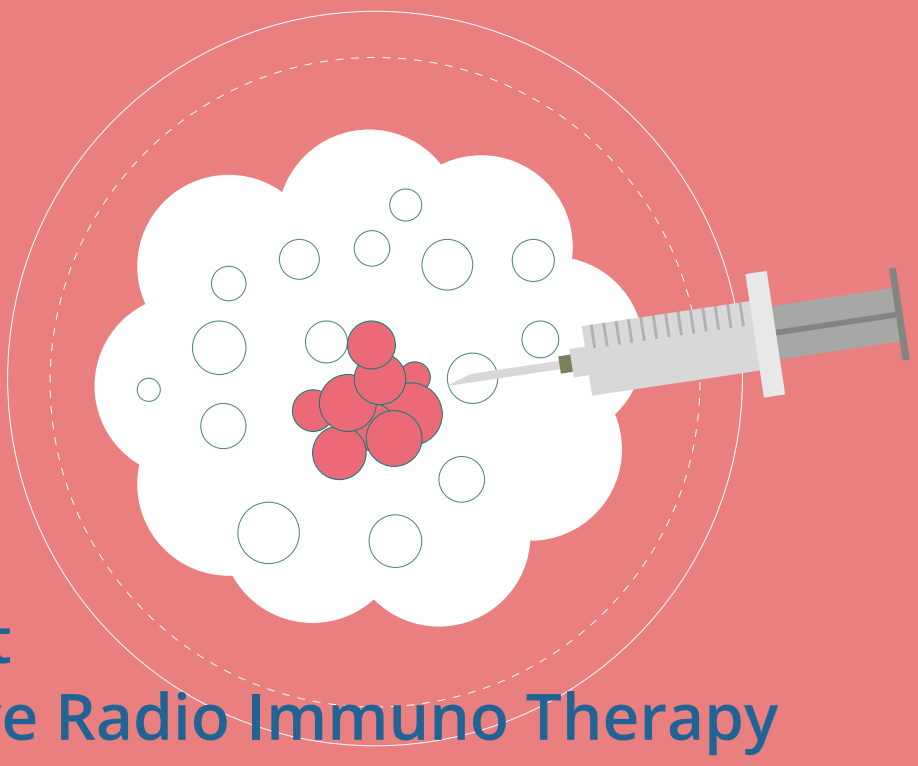
PHASE 2 THERAPY

Phase2Therapy (P2T) wants to make better drugs and new treatment methods available to patients faster and at lower cost. P2T helps shorten Phase 2 studies by enabling clinical investigators in the efficient design and execution of Phase 2 studies

P2T is a not-for-profit organization and relies on donations, grants and crowd-sourcing for operating expenses.



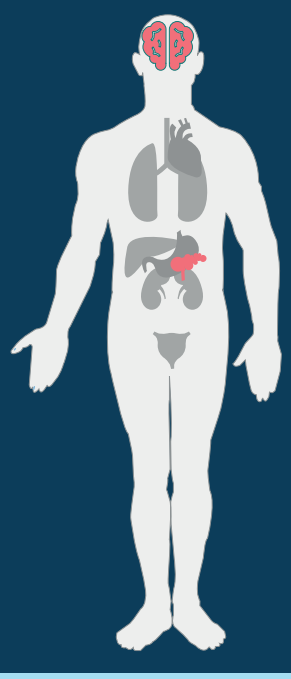
Factsheet
Innovative Radio Immuno Therapy

Phase2Therapy developed a new Radio Immuno Therapy (RIT) against solid tumors.
The precision treatment firmly irradiates the whole tumor matrix, while sparing surrounding healthy tissue, which minimizes side effects from therapy.
P2T avoids misdirected treatment by qualifying patients before start of therapy. The state-of-the-art platform enables complete patient specific dosing to optimize the radioimmuno therapy for each individual patient. The therapy delivers the exact high dose for cancer treatment in order to achieve local-regional control of the tumor, while protecting the patient for overdosing and sparing healthy tissues.

The targeted solid cancers
Phase2Therapy wants to treat the most challenging solid cancers, being:

1. Glioblastoma Multiforme (GBM) a type of very aggressive brain tumor
2. Pancreatic cancer (paCa) without hematogenous metastases.
3. Recurrent cancers and Tenascin-C-positive primary solid tumors with a low chance for cure after radical surgery and post-operation radiation

Common feature of solid cancers: tumor bed
Ninety-five (95) percent of all forms of Cancer are 'solid' tumors. The remaining 5 percent are not-solid ('liquid') tumors, such as lymphomas and leukemia's. The liquid tumors circulate as single cells, but solid tumors have a have a 'tumor bed'.
Phase2Therapy wants to improve the standard rate of cure for patients diagnosed with early stages of a solid tumor by targeting this tumor bed of solid tumors.



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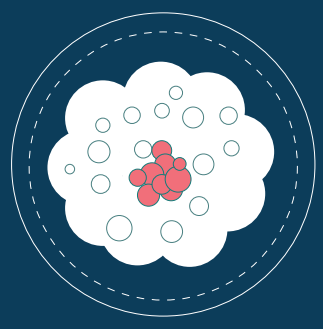
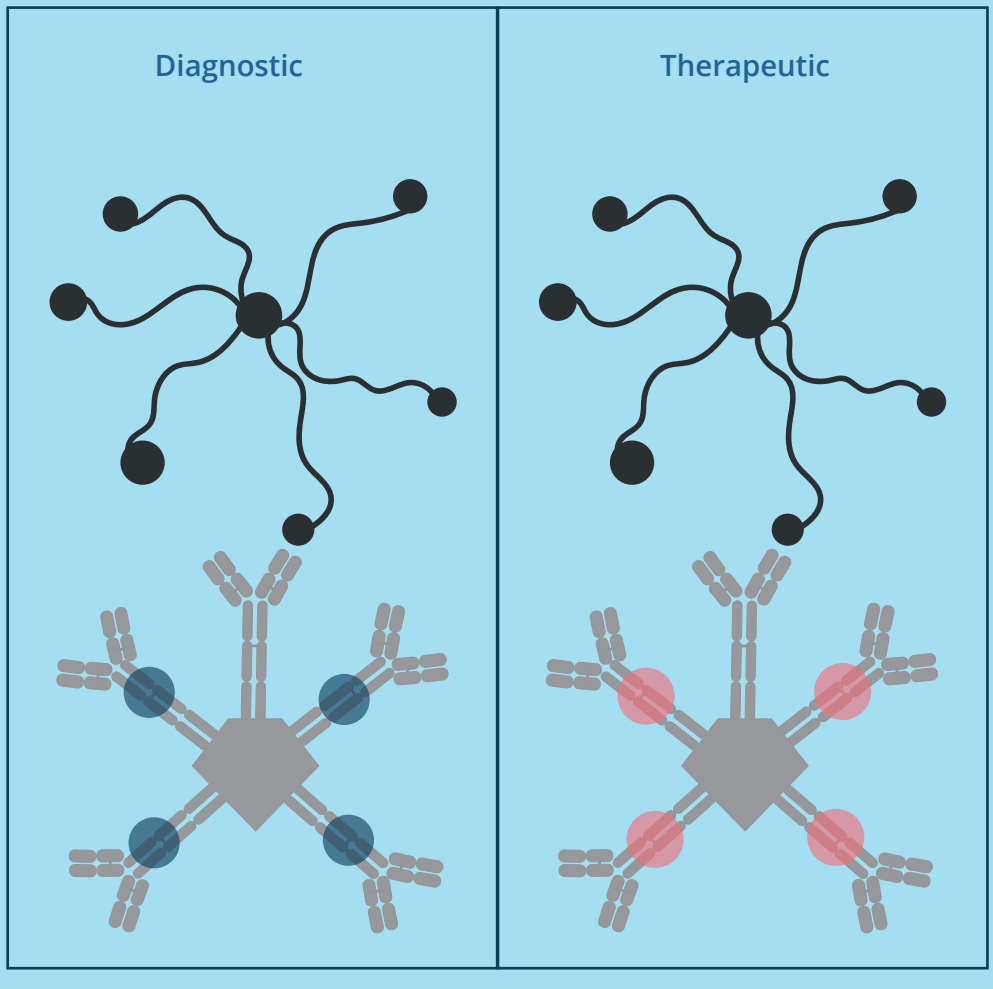


solid cancers



Tenascin-C: present in vast majority of tumor beds
The vast majority of solid cancers display a tumor bed glycoprotein called Tenascin-C (TNC).
Tenascin-C is detected in several cancer types including: brain-, pancreas-, stomach-, mouth-,larynx-, lung-,liver, bone-, colon-, renal- (Grawitz tumor), prostate-, breast- carcinoma, Ewing sarcoma, ovarian cancer and melanoma. In most tumors TNC is detected in the connective tissue surrounding the tumor cells.

Tenascin-C: restricted in healthy tissue
The glycoprotein Tenascin-C expression is restricted in healthy tissue, but is detected in the tumor bed of many solid cancers and the large Tenascin-C variants are abundantly expressed at the invasive tumor front.

Tenascin-C as target for cancer therapy
Tenascin-C seems a good target for cancer therapy as it is abundant in a majority of the solid tumors with limited expression in healthy tissues.

The design of P2T's Tenascin-C targeted Radio Immuno Therapy
Phase2Therapy has developed an antibody that specifically binds to Tenascin-C. The designed antibody is able to diffuse through the entire viable tumor to find Tenascin-C. The Tenascin-C antibody can carry either a safe diagnostic imaging molecule or a therapeutic radioactive molecule. Phase2Therapy does both a diagnostic imaging step and a therapeutic step.

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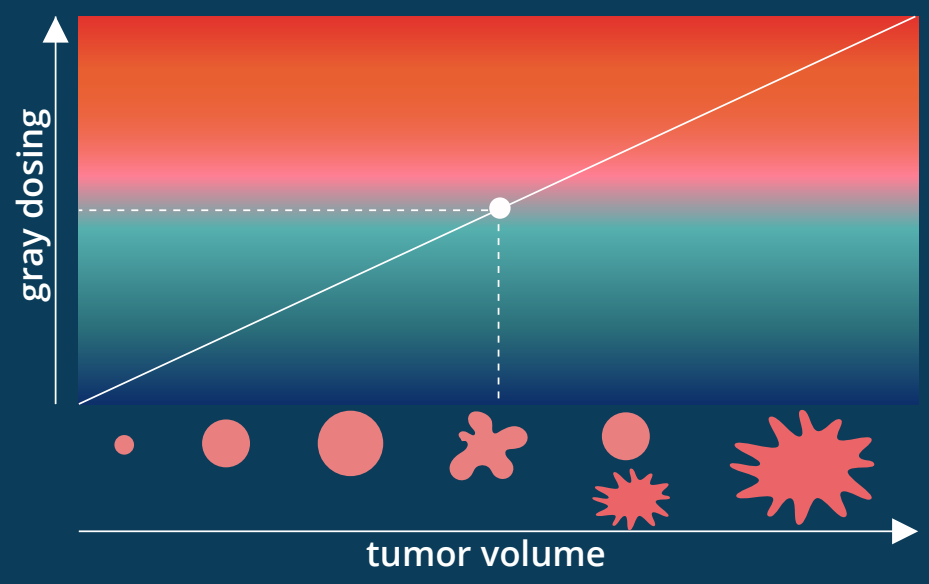
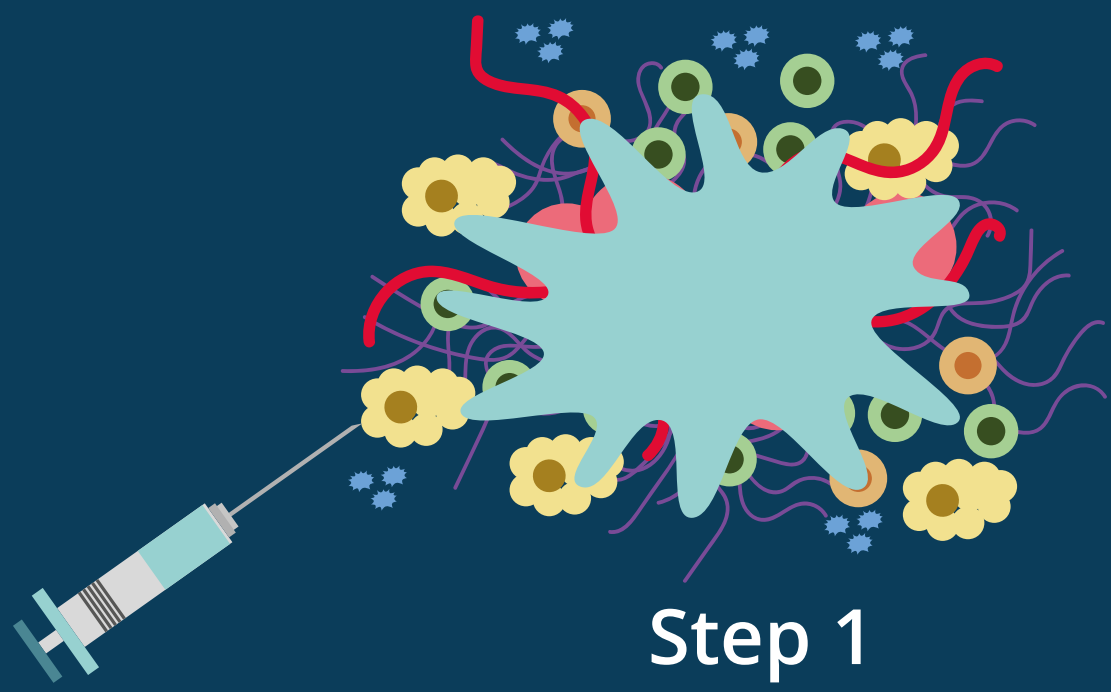
Step 1: The specific targeted diagnostic test
The specific targeted diagnostic test uses the Tenascin-C antibody labelled with Indium-111, a safe isotope used in specialized diagnostic applications for imaging.

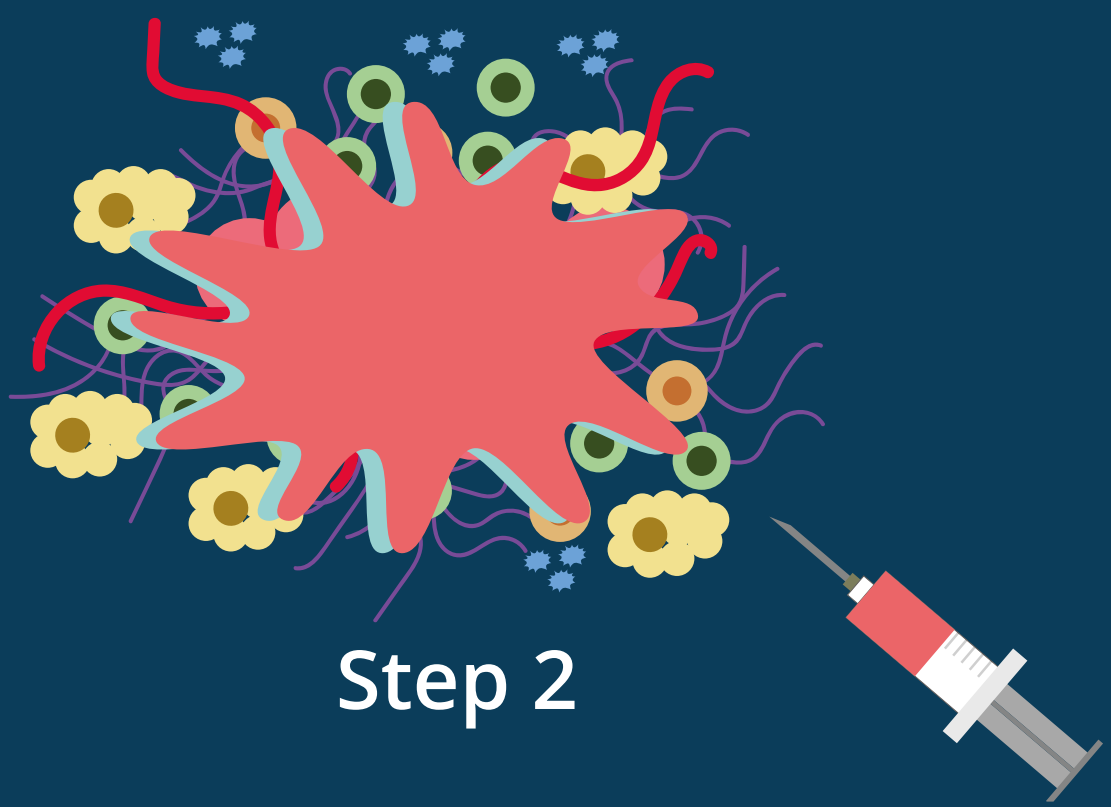
The safe diagnostic step 1:
A. confirms the location of the tumor in vivo
B. determines the stability of the radio-immuno-conjugate
C. determines the residence time of the radio-immuno-conjugate

The resulting data from diagnostic step 1 are used to identify and select the patients, who will benefit from the subsequent therapy: The patients with sufficient radio immuno conjugate in the tumor and an acceptable exposure of radio immunoconjugate in critical normal tissues will benefit from the therapy.
Only these patients will proceed to the therapeutic step 2.





Patient specific dose calculation:
The diagnostic step 1 brings another great benefit. The In-111 biodistribution acts as a predictor of the Y-90 biodistribution and the determined In-111 biodistribution will be used in the therapeutic dose calculation. The resulting dosimetry will therefore be specific to the tumor and normal tissue volumes of each individual patient. The gamma emissions from In-111 are recorded by a gamma camera and reconstructed into 3D volumes. The exact imaging allows tumor staging and tumor responses to be expressed in volume measurements, cc's.



Step 2: The therapeutic treatment with Tenascin-C antibody labelled with Yttrium-90.
The anti-cancer therapy starts with administration of the antibody with a radioactive compound directly into the visualized tumor bed. The antibody strongly binds to the whole tumor bed and the attached radioactive compound, Yttrium-90 irradiates the entire tumor bed and kills the tumor stem cells.

The combination of the Tenascin-C antibody and the radioactive Y-90 isotope allows over 90% of the activity to specifically decay in the tumor. The Y-90 beta radiation will be delivered through the whole tumor. The Yttrium-90 beta irradiates the whole tumor volume with a biologically determined margin of 5mm and destroy the tumor and tumor supporting cells in the tumor bed.

Yttrium-90 is a beta emitter, Beta radiation is a particle (electron) with a strong short range effect. Five mm from the location of a Y-90 molecule it is very cold, 'zero' energy deposition. The Beta radiation is very different from gamma radiation (photons), which deposit energy over a much longer range. The strong effect makes Beta radiation ideal for therapy and the short range allow safe use for therapy.

Conclusion:
P2T's radioimmunotherapy (RIT) is based on Tenascin-C presence in the tumor matrix of solid cancers. The RIT seems capable of treating the majority of solid cancer as Tenascin-C is present in most solid cancers.
P2T selects the patients, who will benefit from therapy in a safe diagnostic step.
Only patients with sufficient radio immuno conjugates in tumors along with an acceptable exposure of radio immunoconjugates in critical normal tissue be benefited from the therapy and treated from cancer

P2T developed a new model for fully patient specific dosing based on the diagnostic step.
The new tumor model dosimetry for radioImunnotherapy will spare healthy tissue as it only delivers Beta radiation to the tumor & tumor bed. The accurate tumor volume specific dosing will reduce the side effects for patient as it avoids overdosing.

Phase2Therapy will demonstrate that tumor treatment could be optimized for individual patient to get the highest possible rate of local regional tumor control and the lowest amount of normal tissue damage.

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