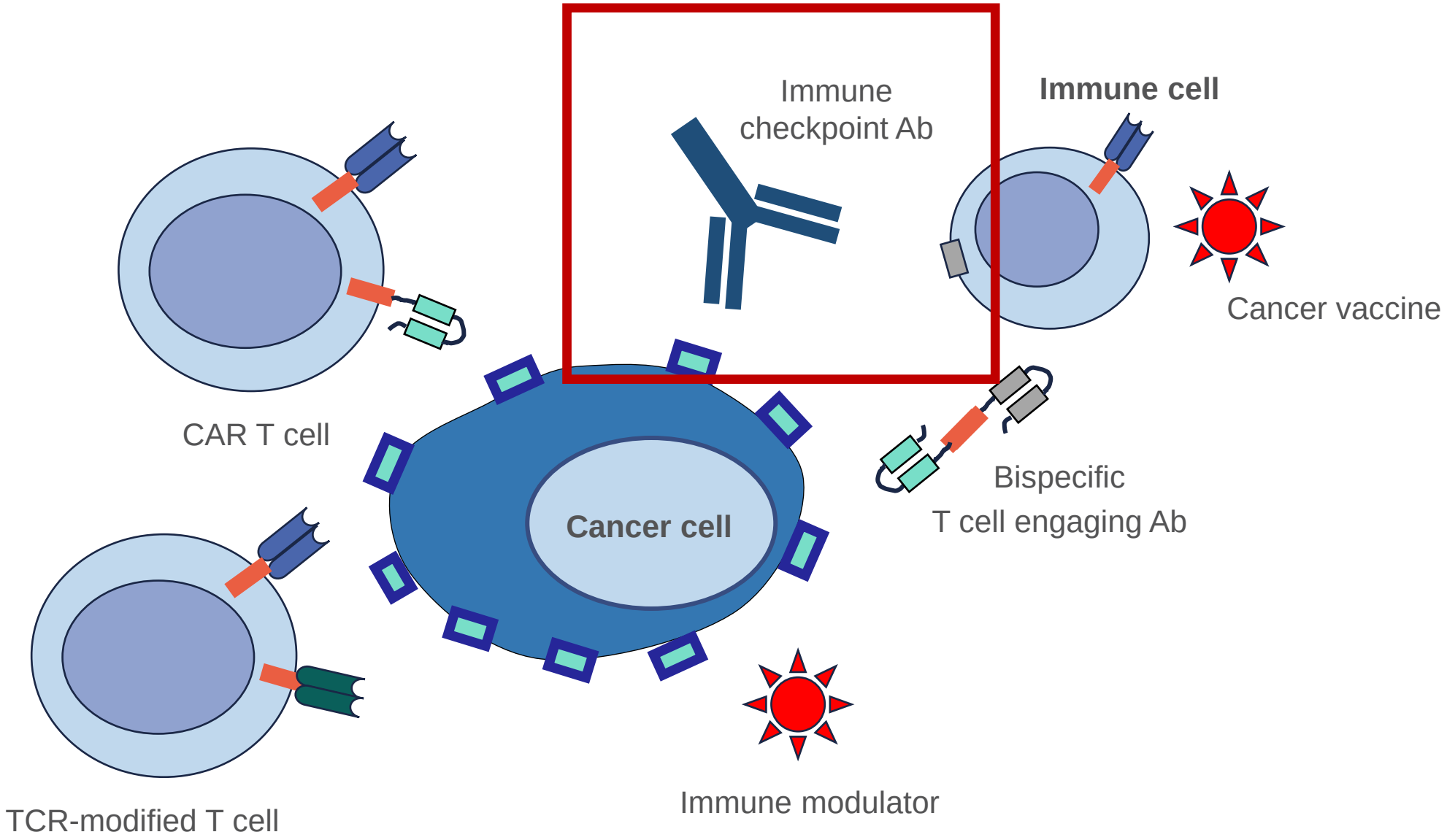
Update Immuno-Oncology 2025

Mascha Binder

Medical Oncology

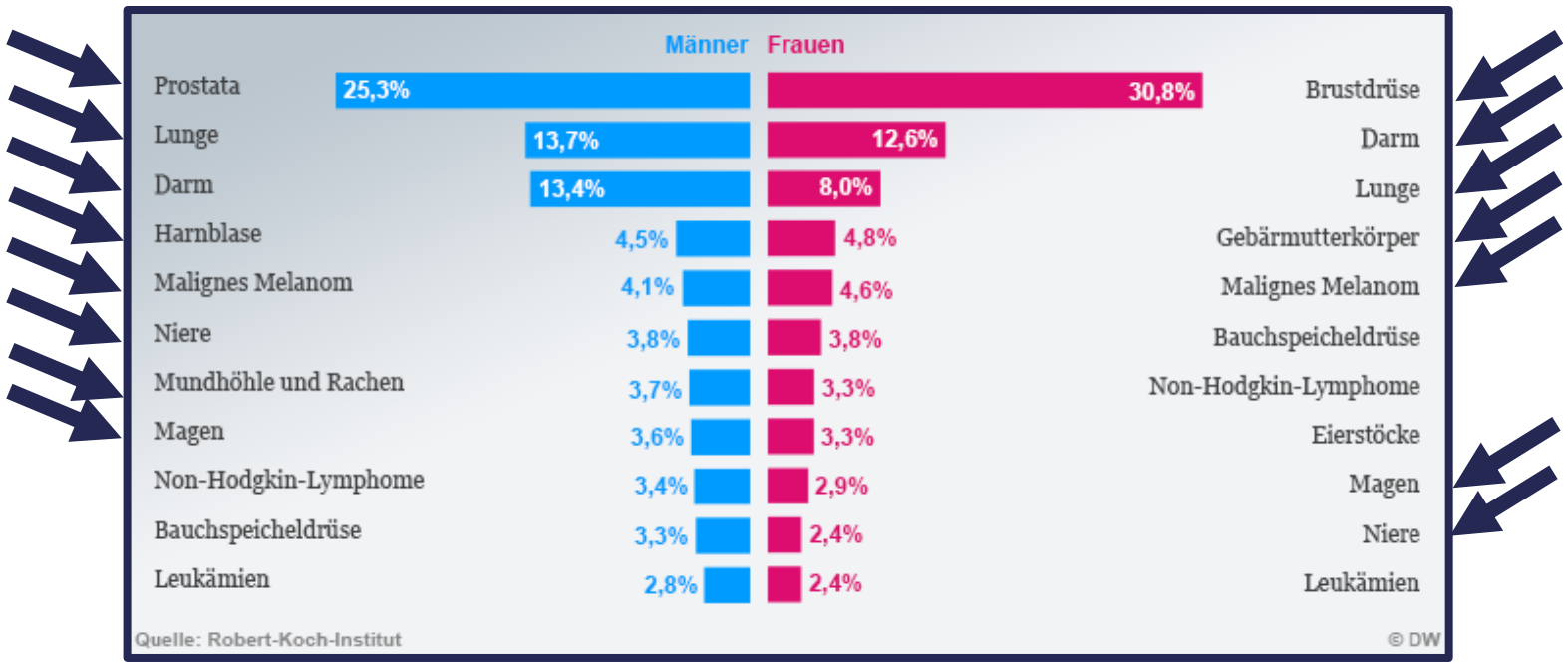
Unispital Basel

Immuno-Oncology – what do we have? For solid tumors?

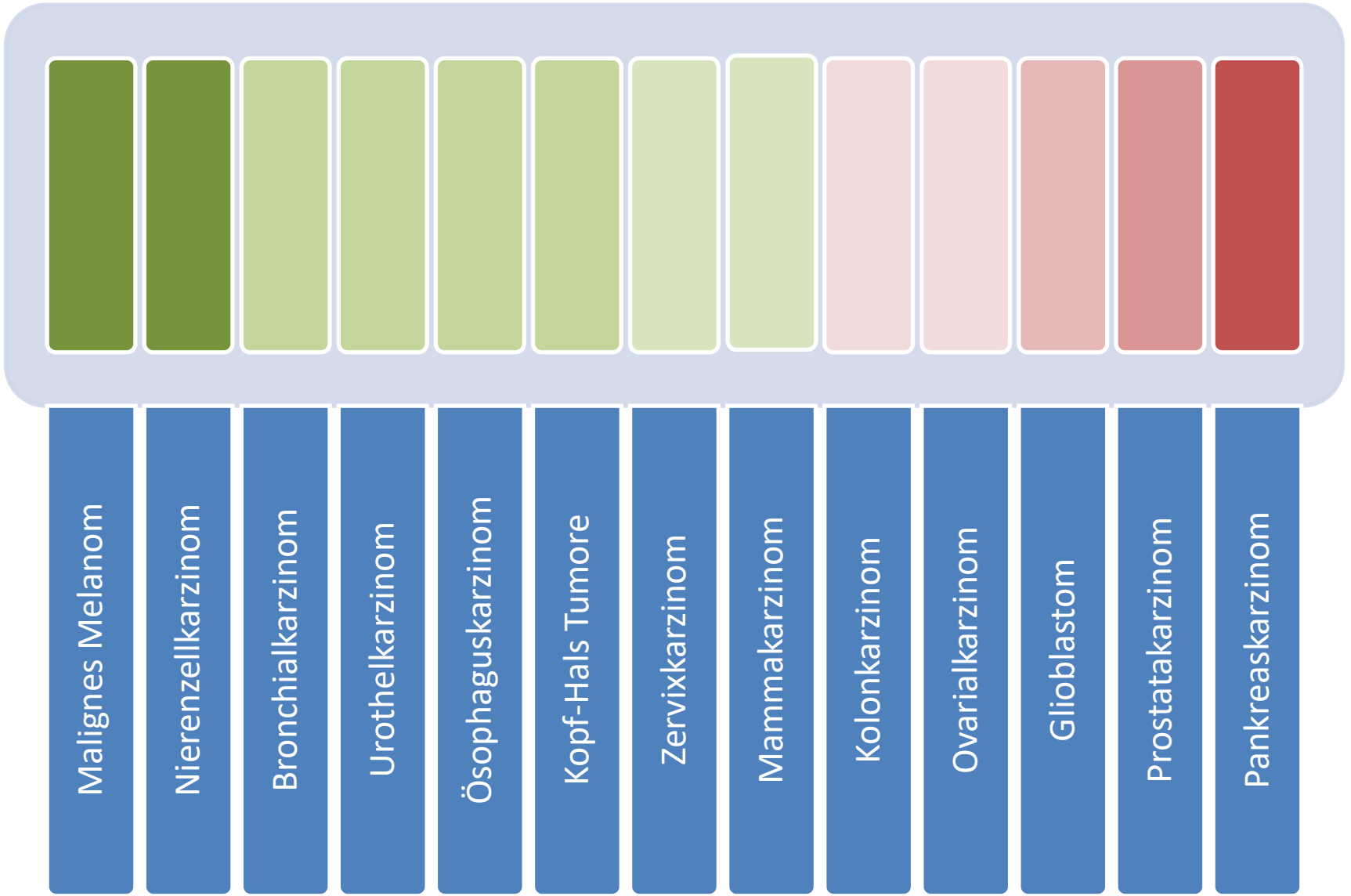


IO Standard

IO Standard



Universitätsspital Basel


Malignes Melanom
Nierenzellkarzinom
Bronchialkarzinom
Urothelkarzinom
Ösophaguskarzinom
Kopf-Hals Tumore
Zervixkarzinom
Mammakarzinom
Kolonkarzinom
Ovarialkarzinom
Glioblastom
Prostatakarzinom
Pankreaskarzinom

The precision paradigm

Immuno-Oncology (IO)

One-size-for-all
PD-L1 insufficient
Scarce molecular data
Resistance multilayered
Unselective T cell activation
Immune-related side effects

Molecular targeted treatment

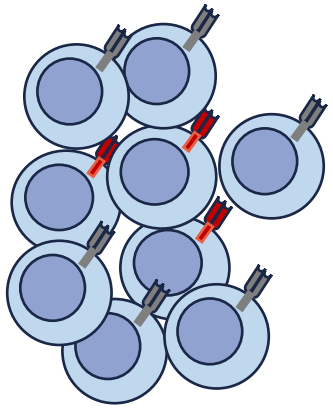
Druggable rearrangements
Some defined resistance
Spare healthy tissues
genomic sequencing
actionable mutations
transcriptomics

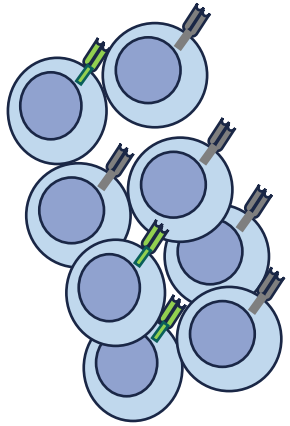
The precision paradigm in IO

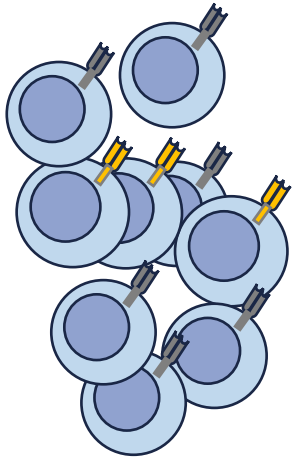
Patient 1 | Patient 2 | Patient 3

One drug for all

BUT: unleashing a tumor-/patient-specific set of T cell clones





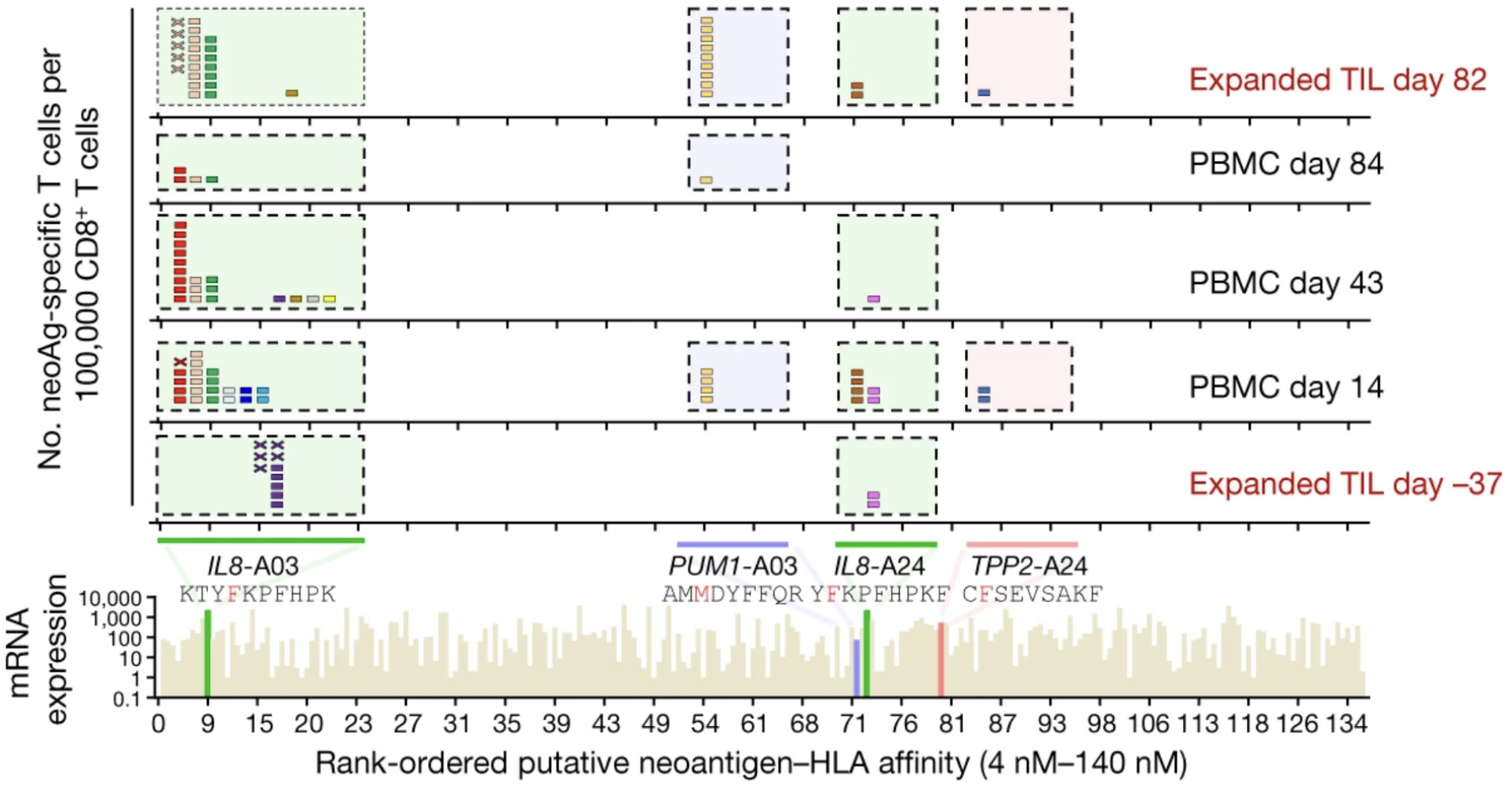


Neoepitope specific

Neoepitope specific

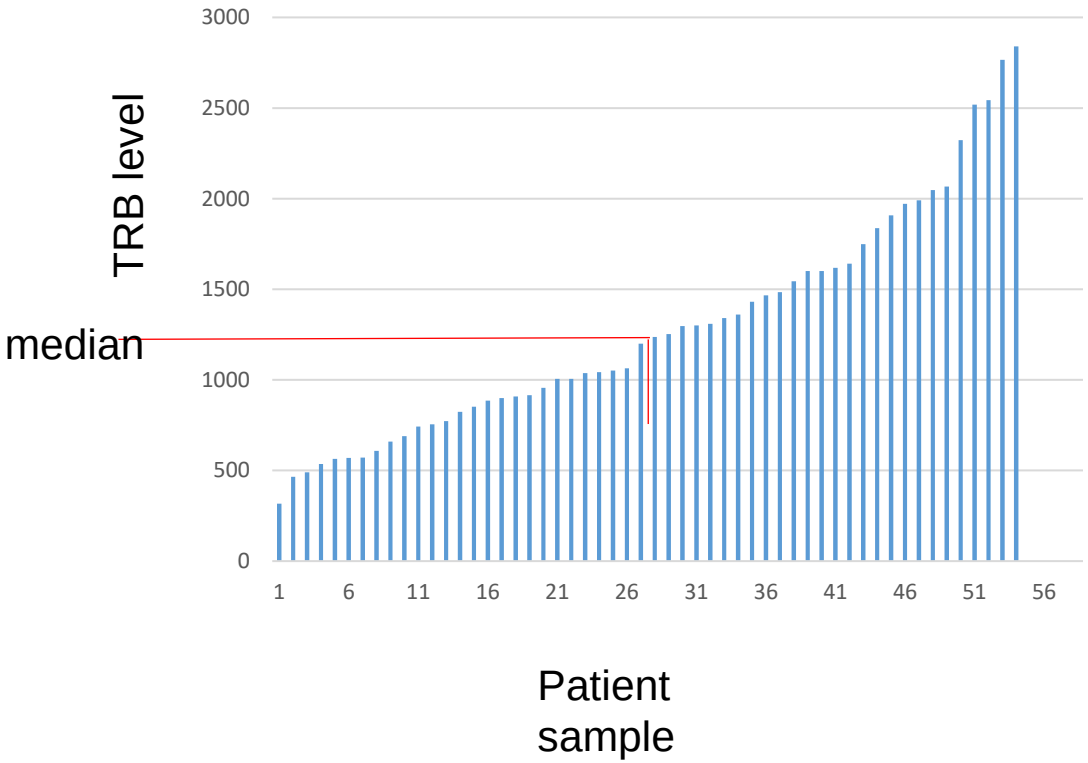
Neoepitope specific

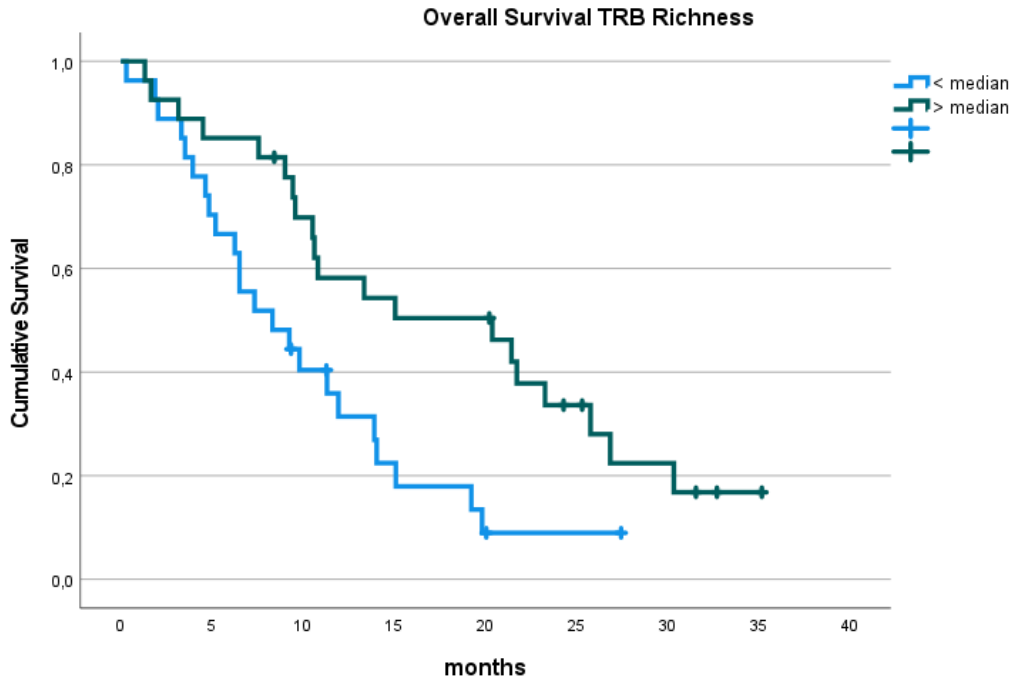
Tapping into the neoantigen-directed T cell response



Puig-Saus et al., Nature 2023

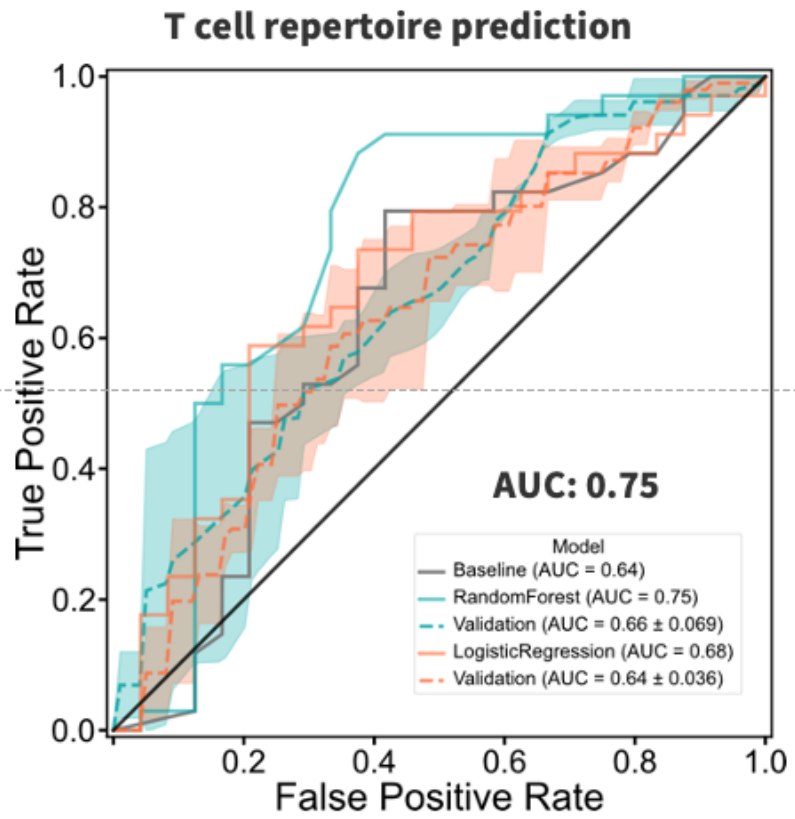
The precision paradigm in IO
Statistics of T cell richness at the TCR repertoire level

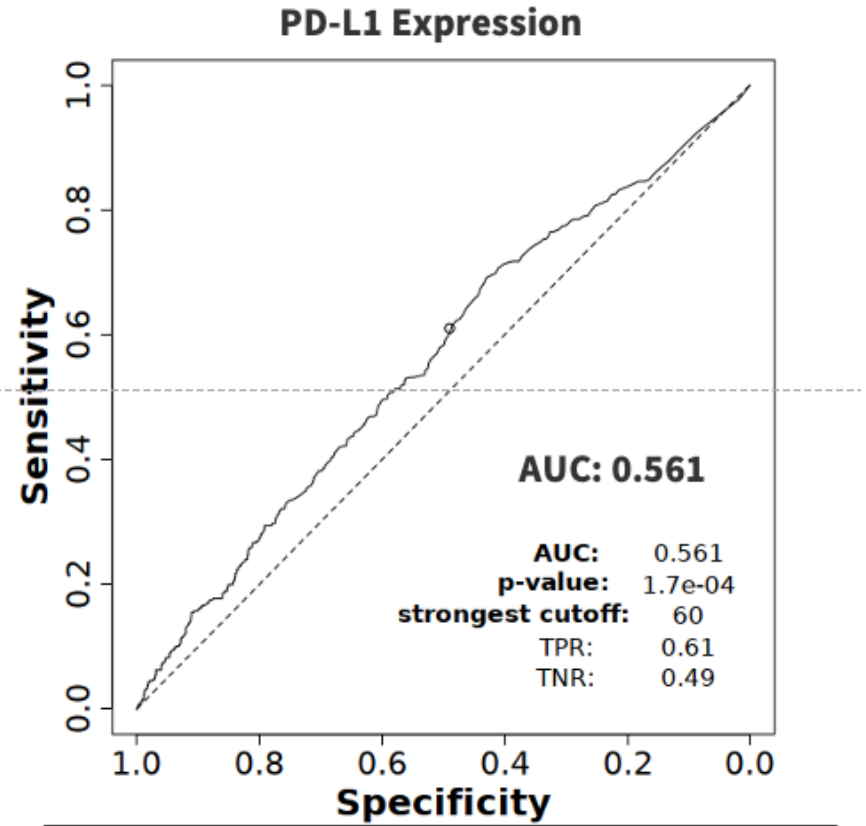




Paschold *et al*, JAMA oncology 2023
Thuss *et al*., JAMA network open 2023
Simnica et al., Journal of Clinical Oncology PO 2022

The precision paradigm in IO
T cell richness and the PD-L1 benchmark

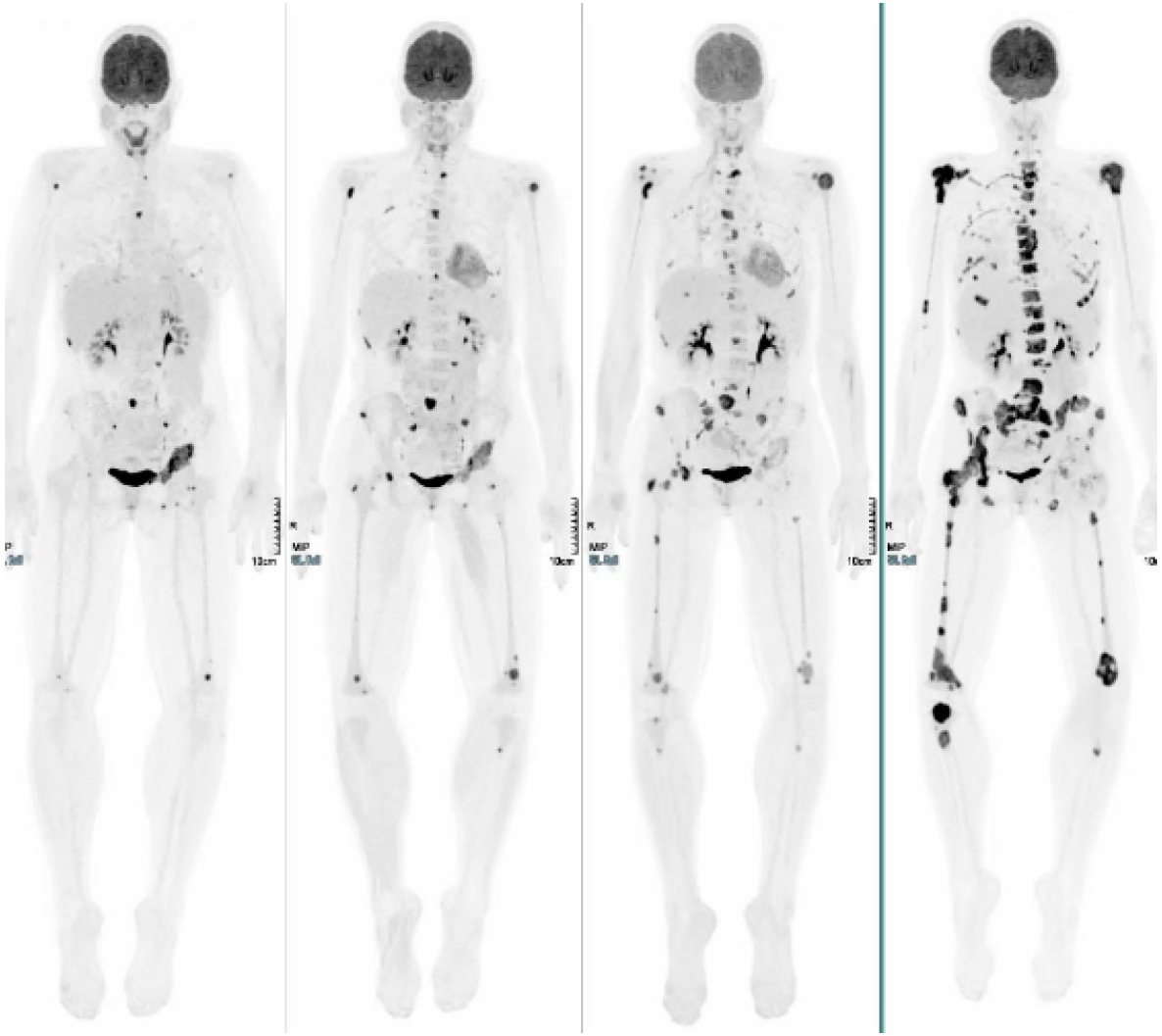




Kovacs SA, Fekete JT, Gyorffy B: Predictive biomarkers of immunotherapy response with pharmacological applications in solid tumors, Acta Pharamcol Sin., 2023

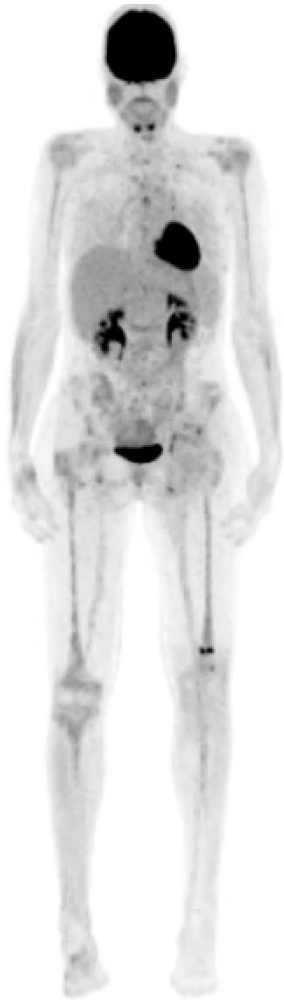
The right T cells can yield powerful outcomes

10. June 2024



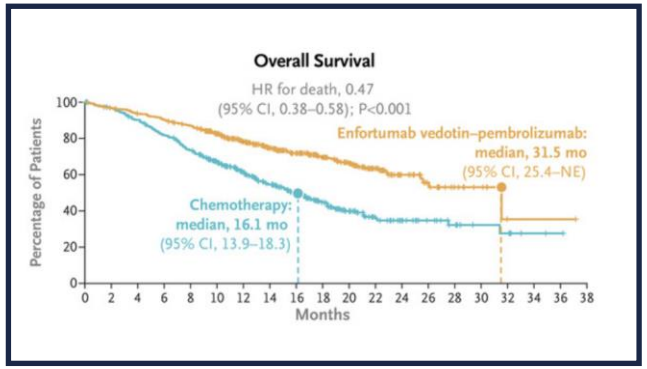
TIL 10.
July 2024

today



Shared by Heinz Läubli and David König USB

How to improve precision in IO?



Antibodies or antibody-drug conjugates

Immune checkpoint Ab

Immune cell

Cancer vaccine

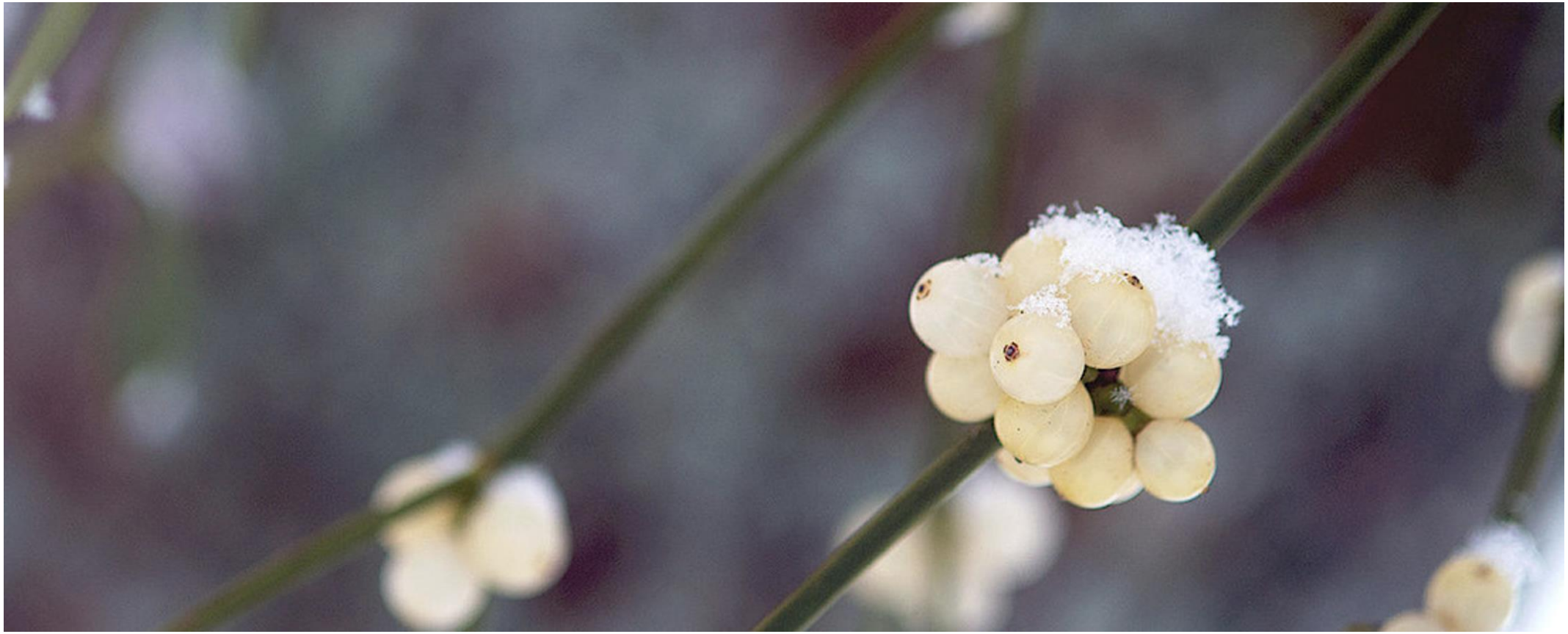
Cancer cell

- mRNA-4157/V940, a personalized mRNA-based cancer vaccine + Pembro
- BNT111 + Cemiplimab

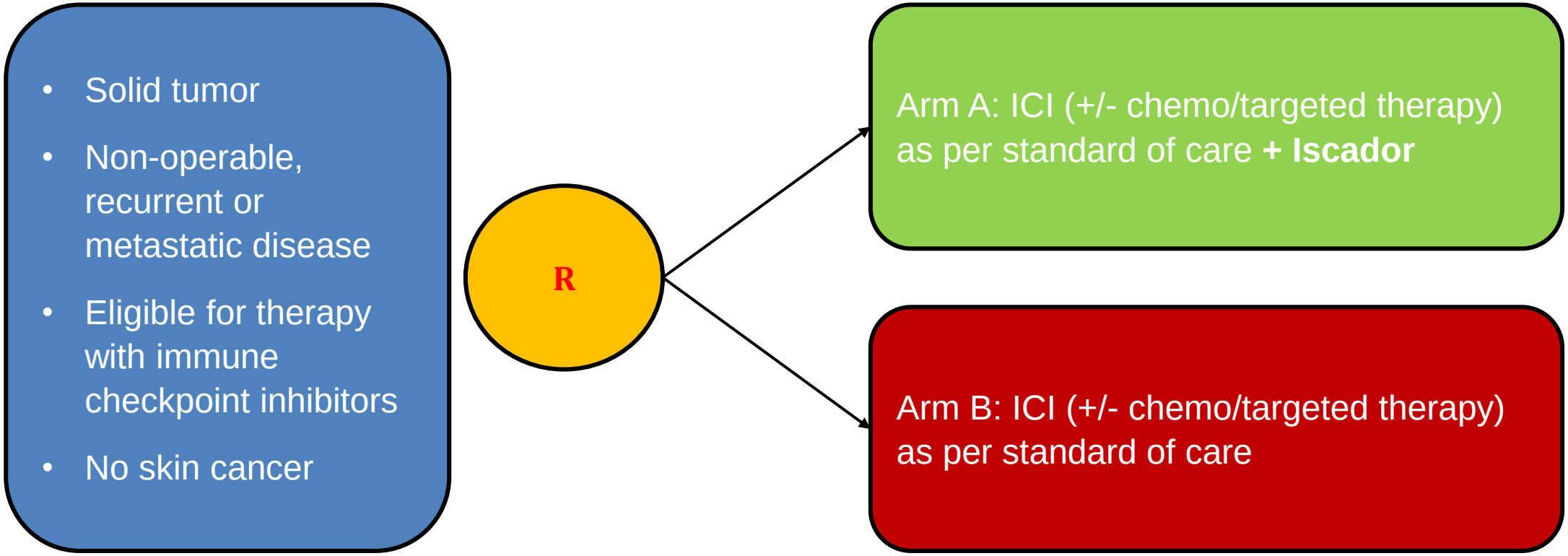
…

Universitätsspital Basel

Combination of IO with other immunomodulatory agents… What about mistletoe?



ISCA-CHECK Trial

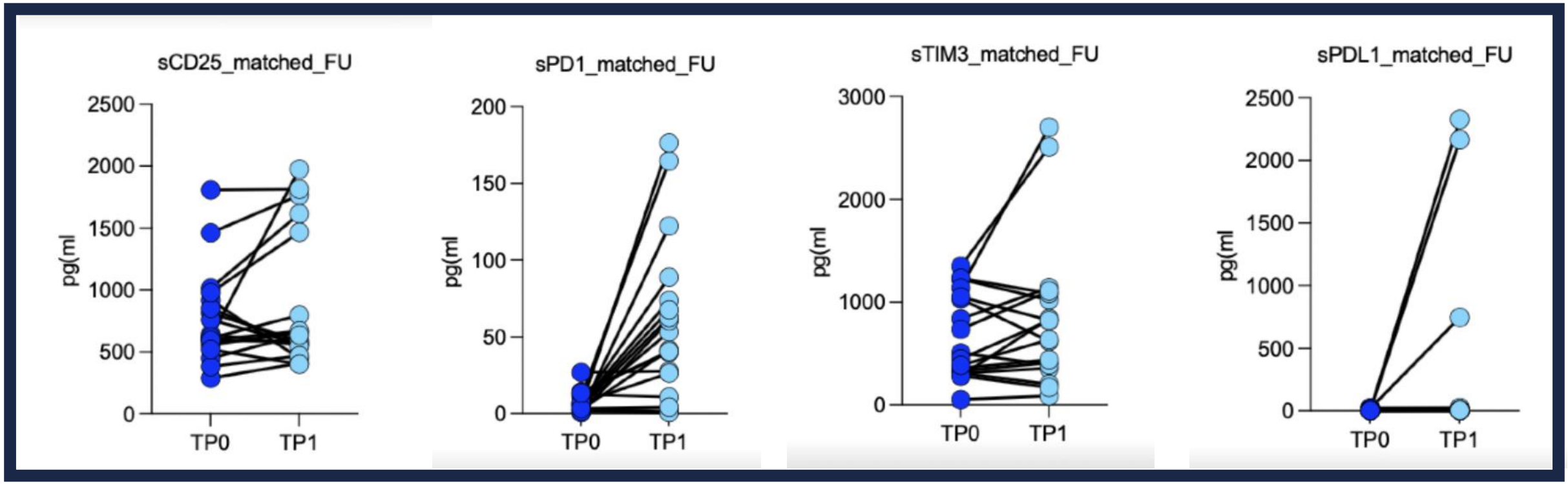


- 100 patients (1:1) from 4 sites over 24 months
- USB
- Liestal
- Baden
- Tumor und Brustzentrum Ostschweiz

Endpoints

- Modulation of adaptive immunity
- Clinical outcomes (PFS, OS)
- Rates of AE/SAE
- QoL

ISCA-CHECK Trial – we are still blinded…



SNIO
Swiss Network for Integrative Oncology

https://integrative-oncology.ch/

Working Groups Research

The primary objective of the SNIO Research Working Group is to promote Swiss **multi-center clinical research projects** that actively involve young researchers, patients, and multiple disciplines, while also addressing key questions in **implementation research** (e.g. Real-World Data Collection).

- **Join us at the monthly SNIO Research WG Meeting to discuss the development of integrative oncology research in Switzerland !** *Dates and Zoom links for 2025*

Wednesday 23. April **16:30 - 17:30**
Monday 26. Mai **11:00-12:00**
Wednesday 2. Juli **16:30 - 17:30**
Monday 25. August **11:00 - 12:00**
Wednesday 1. October **16:30 - 17:30**
Monday 3. November **11:00-12:00**

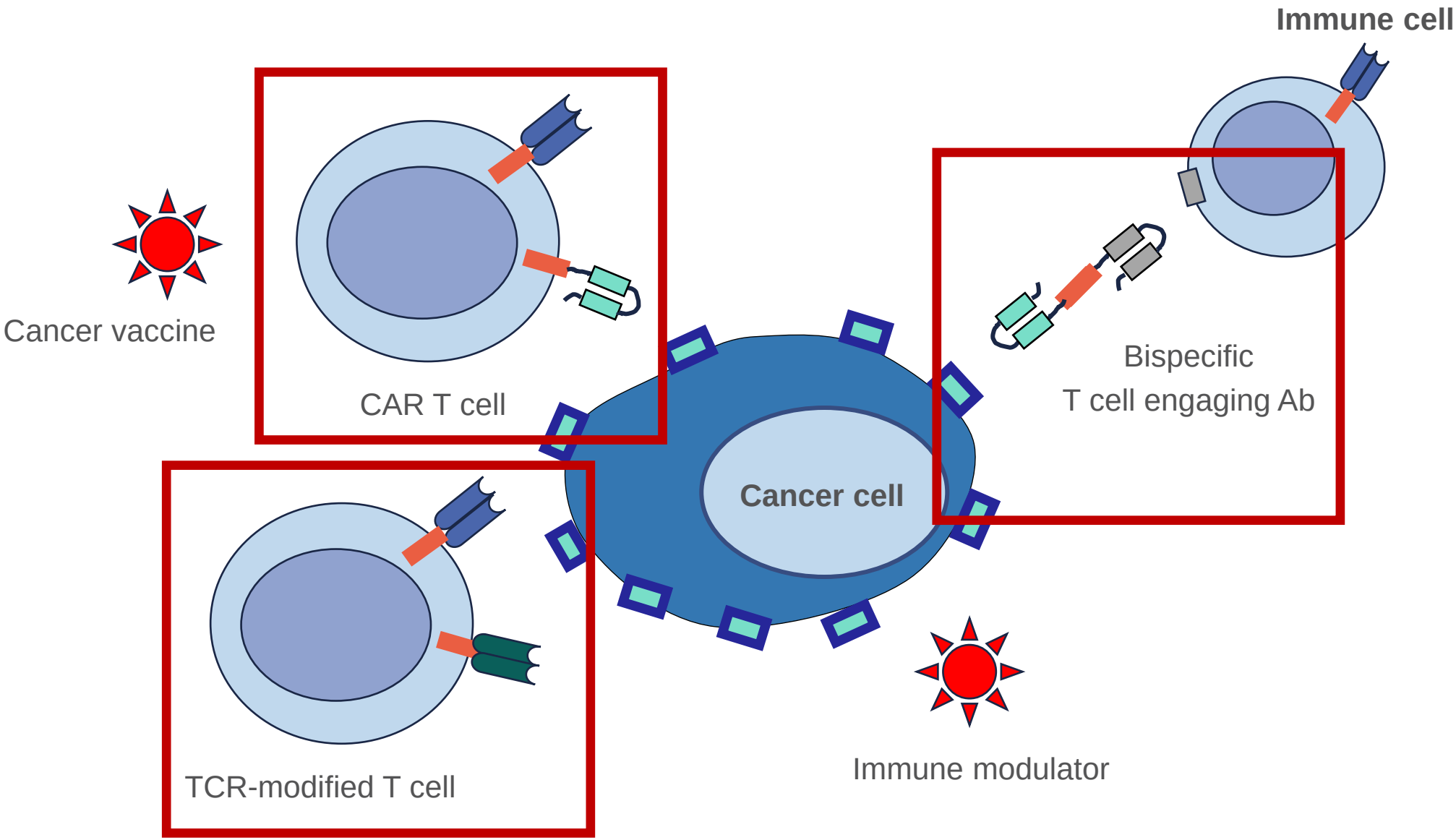
- **Selection of open studies in Switzerland:**

A Selection of Research Projects open for:
a) accrual of patients
b) participation as academic or clinical investigator
c) participation as SNIO study centre

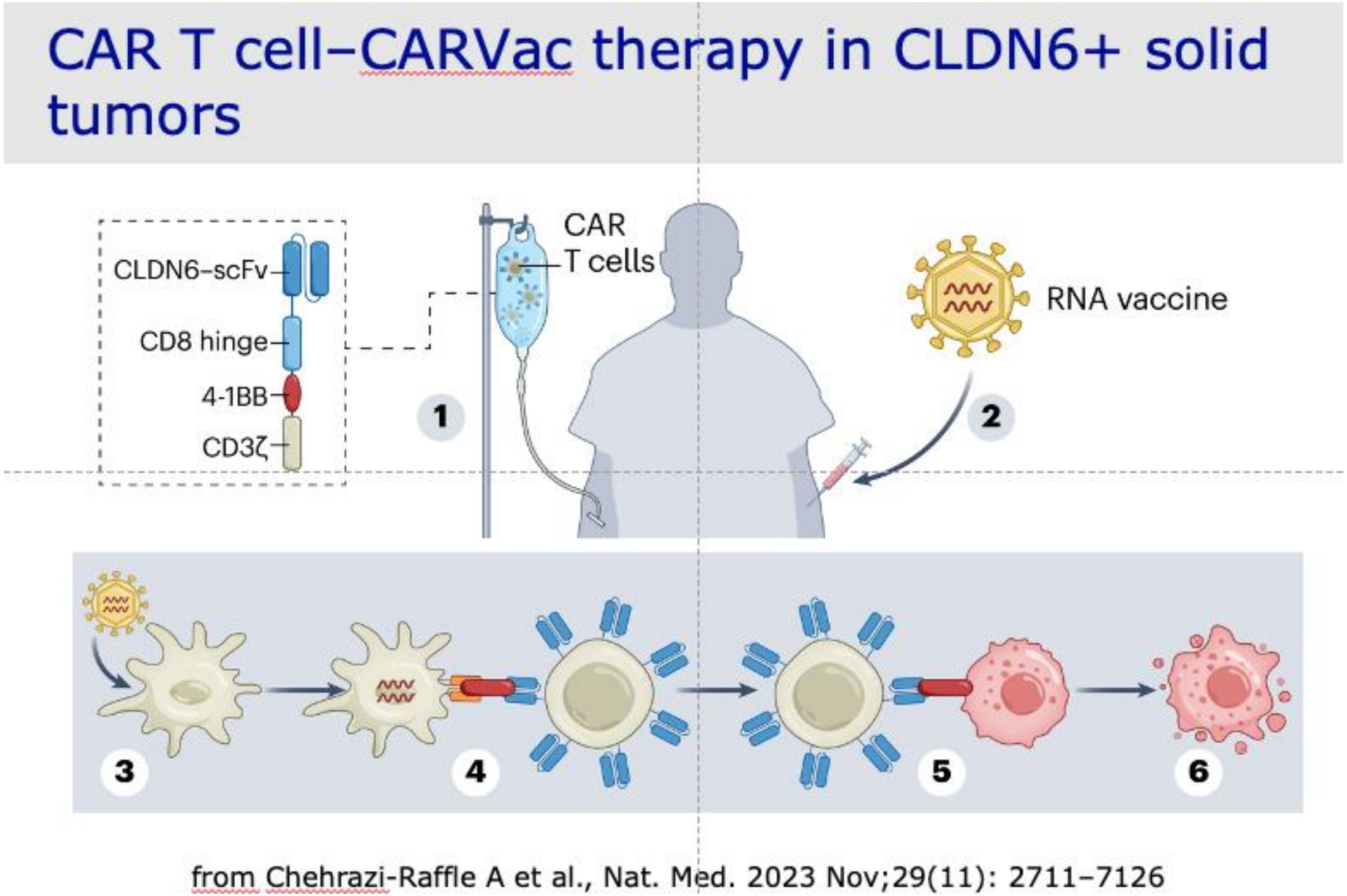
The list is updated at each SNIO WG Research monthly virtual meeting → please mail and attend

For contact (Co-lead SNIO WG Research)
PD Dr. med. Florian Strasser:
flo.strasser@bluewin.ch

Other avenues towards precision IO?

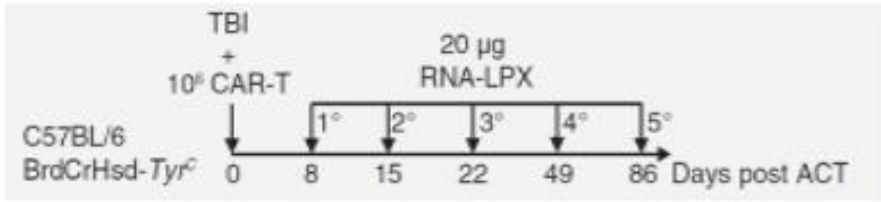


The Future for solid tumors? CAR T cells with a booster vaccine

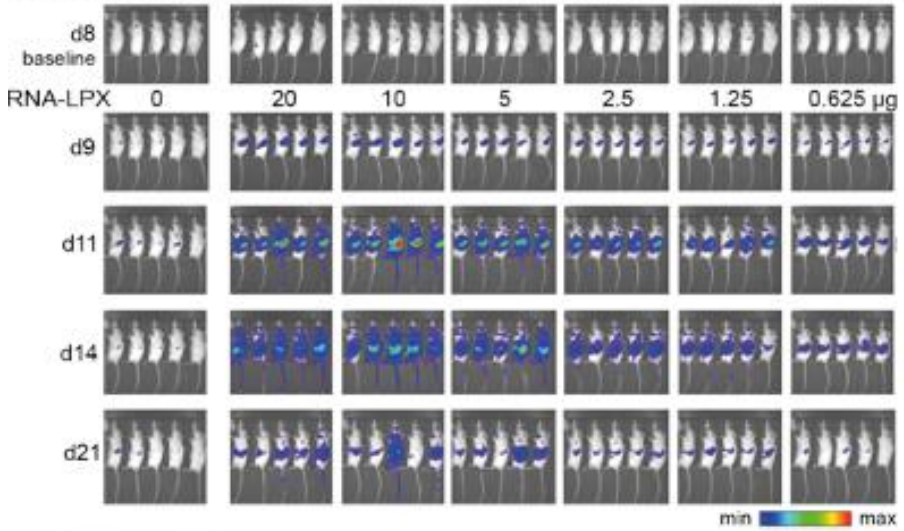


from Chehrazi-Raffle A et al., Nat. Med. 2023 Nov;29(11): 2711–7126

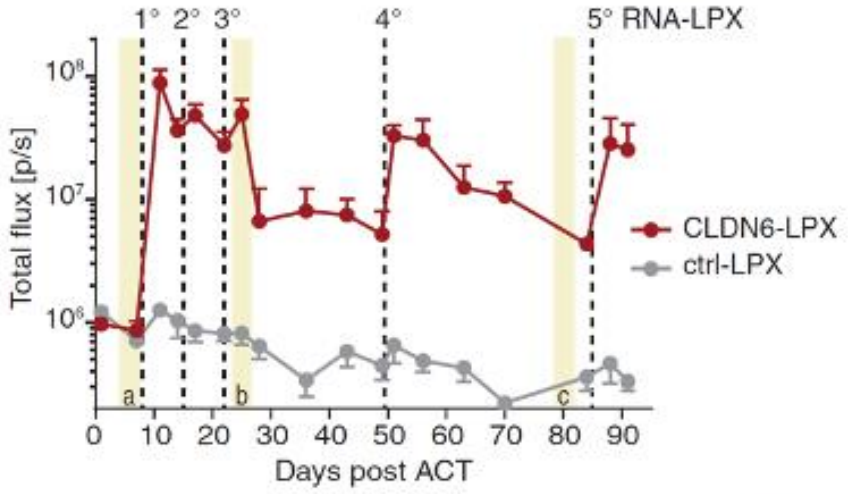
Vaccine drives expansion and efficacy of CAR T cells



CARVac mediates dose dependent *in vivo* expansion of CAR-T



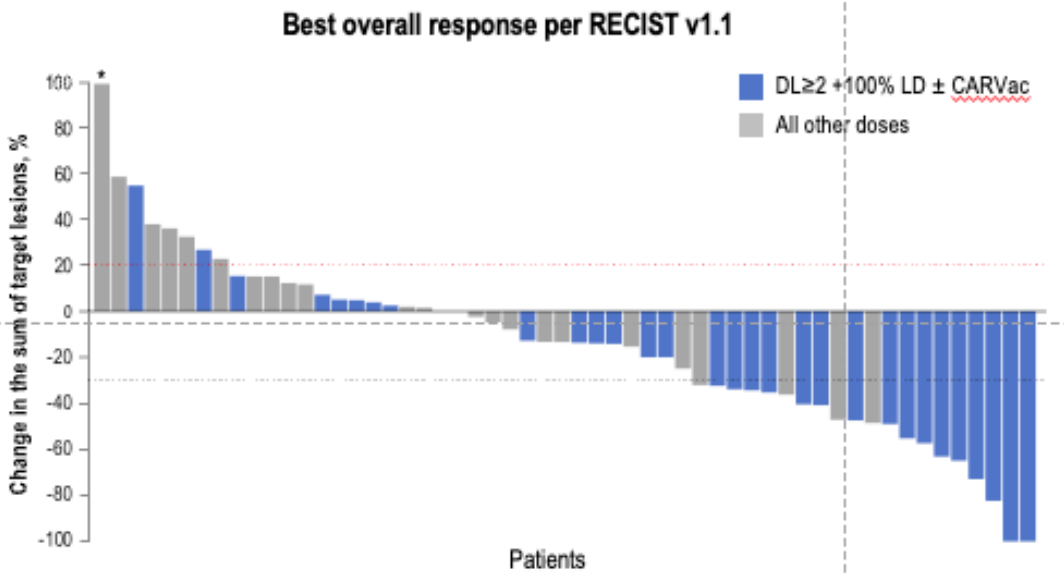
Repetitive administration of CARVac leads to persistence of CAR-T cells



Reinhard, Rengstl et al. Science 2020; 367:446–453
Kranz LM, et al. Nature 2016; 534:396–401
Şahin U, et al. Nature 2020; 585:107–112

Efficacy of vaccine-boostered Claudin6 CAR T cells in patients

BNT211-01: Best overall response



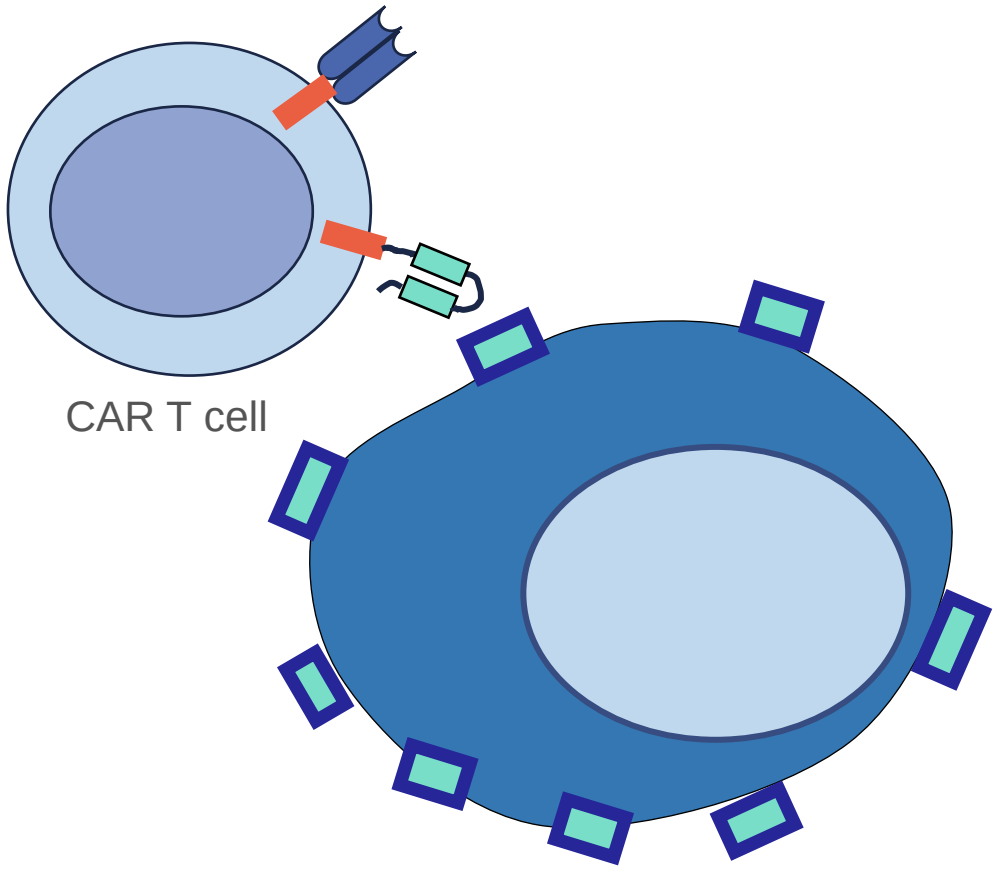
Response[a]	Total (N=74)[b]
Evaluable patients, n	64
ORR, n (%)	**21 (32.8)**
95% CI (%)	18.5–40.1
CR, n (%)	3 (4.1)
PR, n (%)	18 (24.3)
DCR, n (%)	**43 (67.2)**
95% CI (%)	46.1–69.5

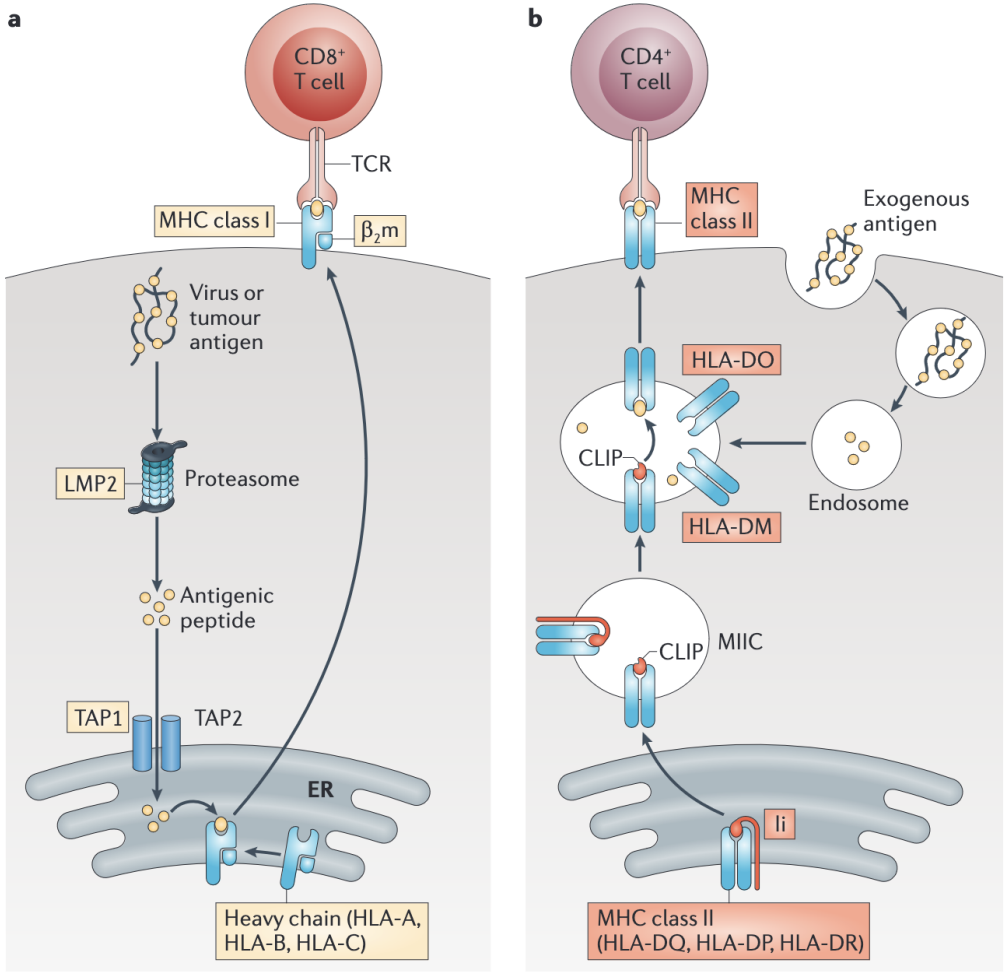
Response[a]	DL≥2 +100% LD ± CARVac (N=41)[b,c]
Evaluable patients, n	33
ORR, n (%)	17 (51.5)
95% CI (%)	26.3–57.9
DCR, n (%)	28 (84.8)
95% CI (%)	51.9–81.9

Data cut off: 16 May 2024. Presented are data from patients who received automated process CAR T and had a tumor assessment at baseline and at least 7 weeks post-ACT (N=77). [a]Includes tumor marker responses. [b]Excludes patients who received an out-of-specification product. [c]DL2=1×10^8; DL3=2–5×10^8 CAR T cells. *Bar truncated at 100% (actual value was 196%). ACT, adoptive cell transfer; CAR, chimeric antigen receptor; CARVac, CAR T-cell amplifying RNA vaccine; CI, confidence interval; CR, complete response; DCR, disease control rate; DL, dose level; LD, lymphodepletion; ORR, objective response rate; PR, partial response.

Exciting frontier making precise CARs more potent!

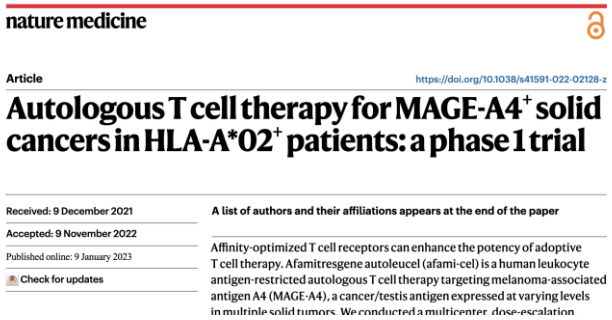
Cell surface proteins are prime targets for immunological treatments!





Kobayashi et al., Nat. Rev. Immunology 2012

How to target intracellular antigens?



nature medicine

Article

https://doi.org/10.1038/s41591-022-02128-z

Autologous T cell therapy for MAGE-A4^{+} solid cancers in HLA-A*02^{+} patients: a phase 1 trial

Received: 9 December 2021

Accepted: 9 November 2022

Published online: 9 January 2023

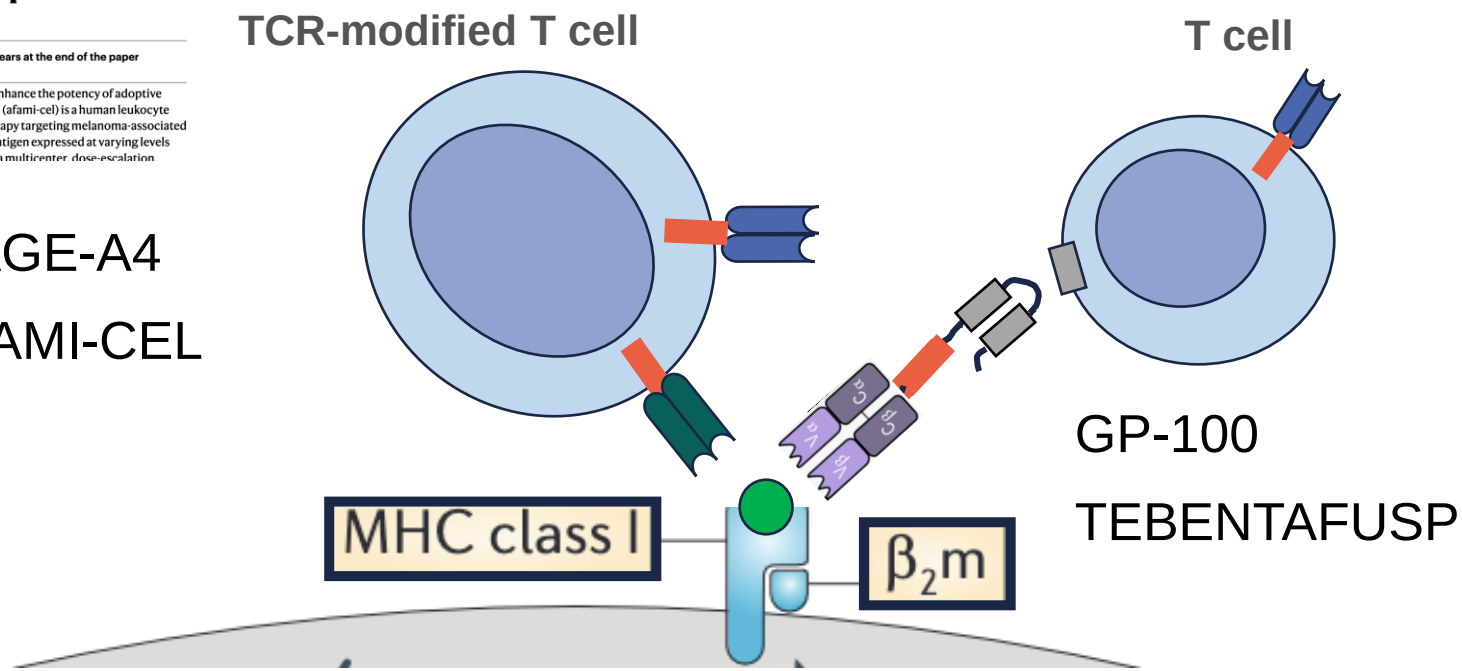
Check for updates

A list of authors and their affiliations appears at the end of the paper

Affinity-optimized T cell receptors can enhance the potency of adoptive T cell therapy. Afamitresgene autoleucel (afami-cel) is a human leukocyte antigen-restricted autologous T cell therapy targeting melanoma-associated antigen A4 (MAGE-A4), a cancer/testis antigen expressed at varying levels in multiple solid tumors. We conducted a multicenter, dose-escalation

MAGE-A4

AFAMI-CEL



GP-100

TEBENTAFUSP

Prêt-à-porter

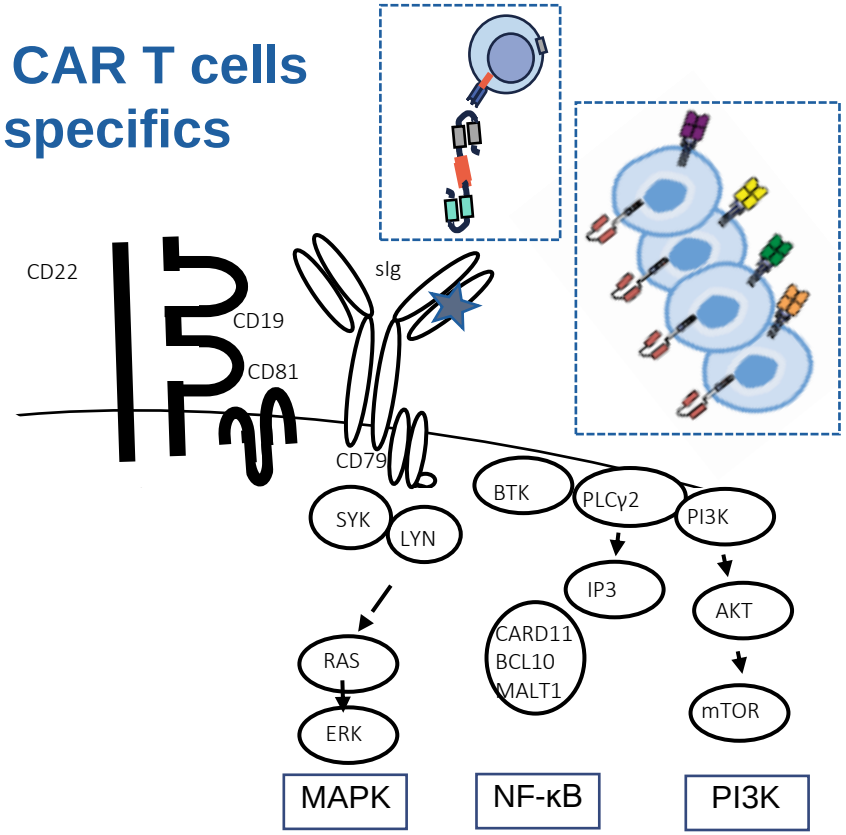
Targeted drug/cell product

Haute couture

Individual cell product

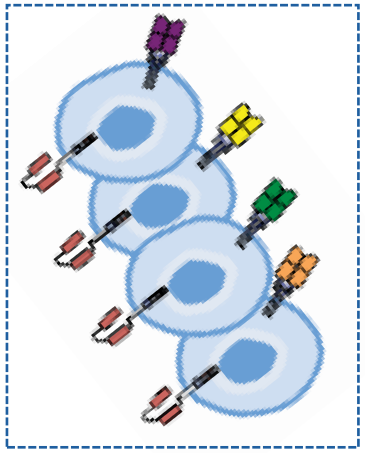
Mutation-specific CAR T cells and bispecifics

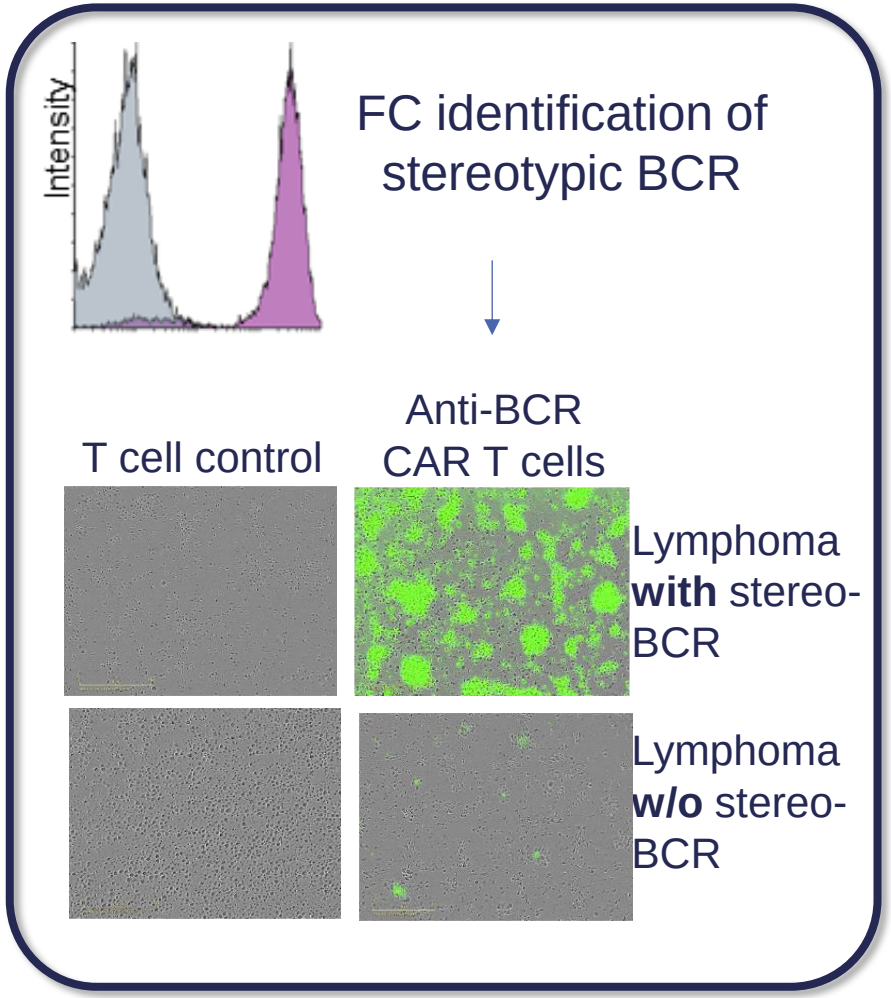
anti-BCR CAR T cells and bispecifics



Schweizerischer Nationalfonds

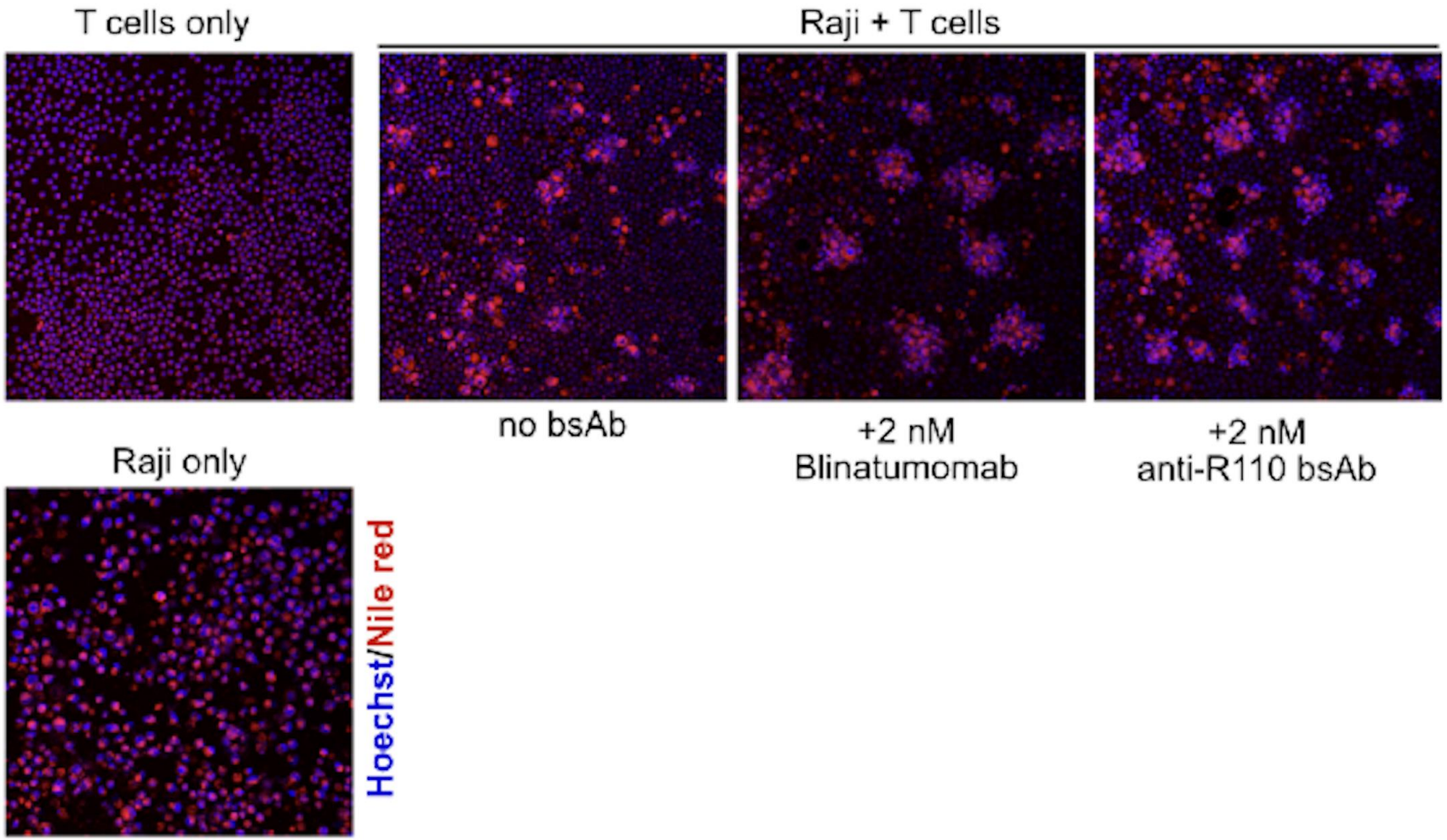
Vision: IGLV3-21-R110 mutation-specific CAR T cells

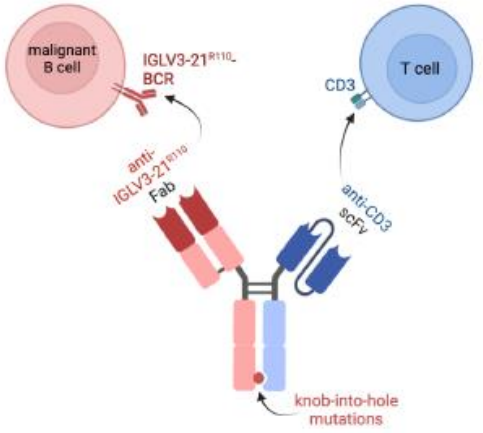




Märkl *et al*., Nat.com. 2024

Vision: IGLV3-21-R110 mutation-specific bispecific T cell engagers





Summary Immunotherapy 2025

Immunotherapy can be highly precise by

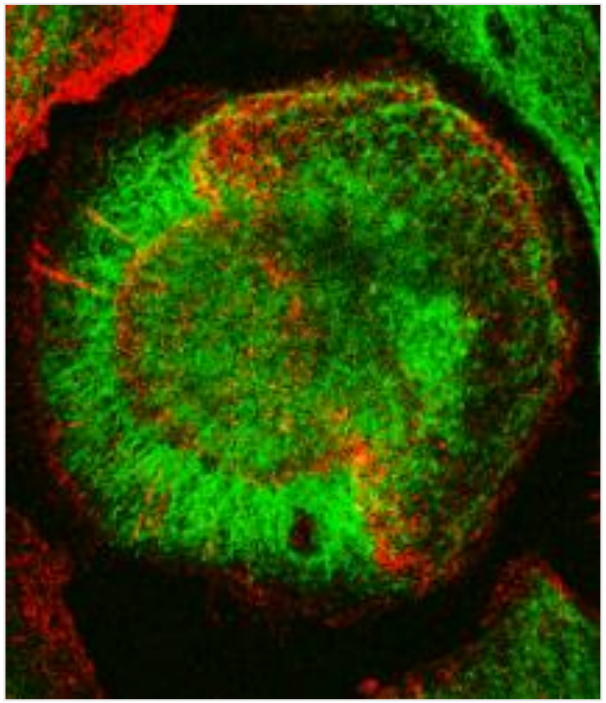
- Unleashing patient-specific neoepitope-directed T cells (checkpoint blockade / TIL)
- Boostering with target-specific vaccines (this may even work for CAR T cells)
- Engineering to target surface-exposed point mutations or sequences

Wat is the interaction of “conventional” Immunotherapy with complementary medicine?

- Often practiced, not well explored
- Trials are needed!

Encapsulating the essence of Precision Oncology:

We need the right treatment for the right patient at the right time!



Unispital Basel

Med Onko Unispital

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