

Länger leben mit Immuntherapie?

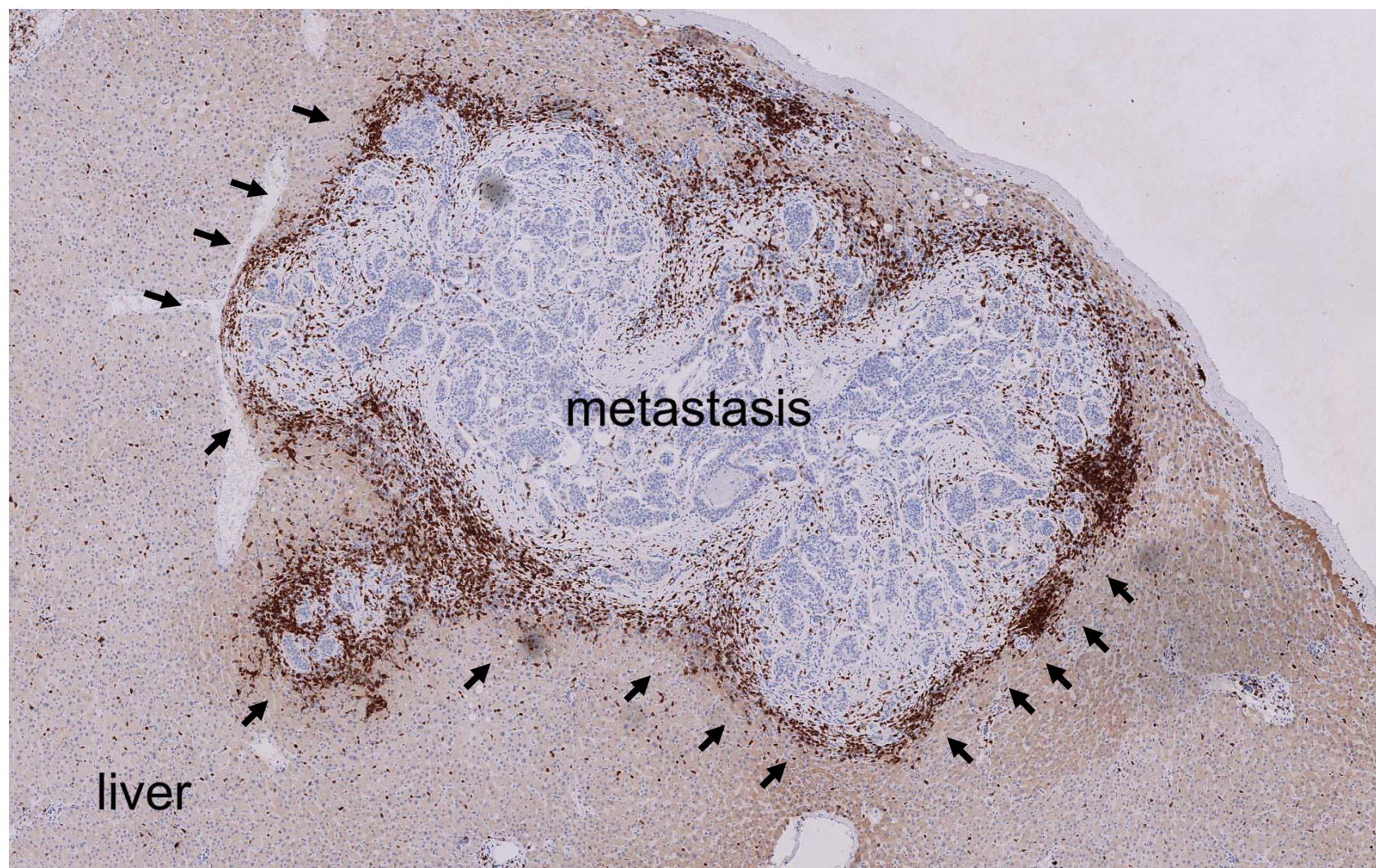
Dirk Jäger
Medizinische Onkologie
Nationales Centrum für Tumorerkrankungen
Universitätsklinik Heidelberg



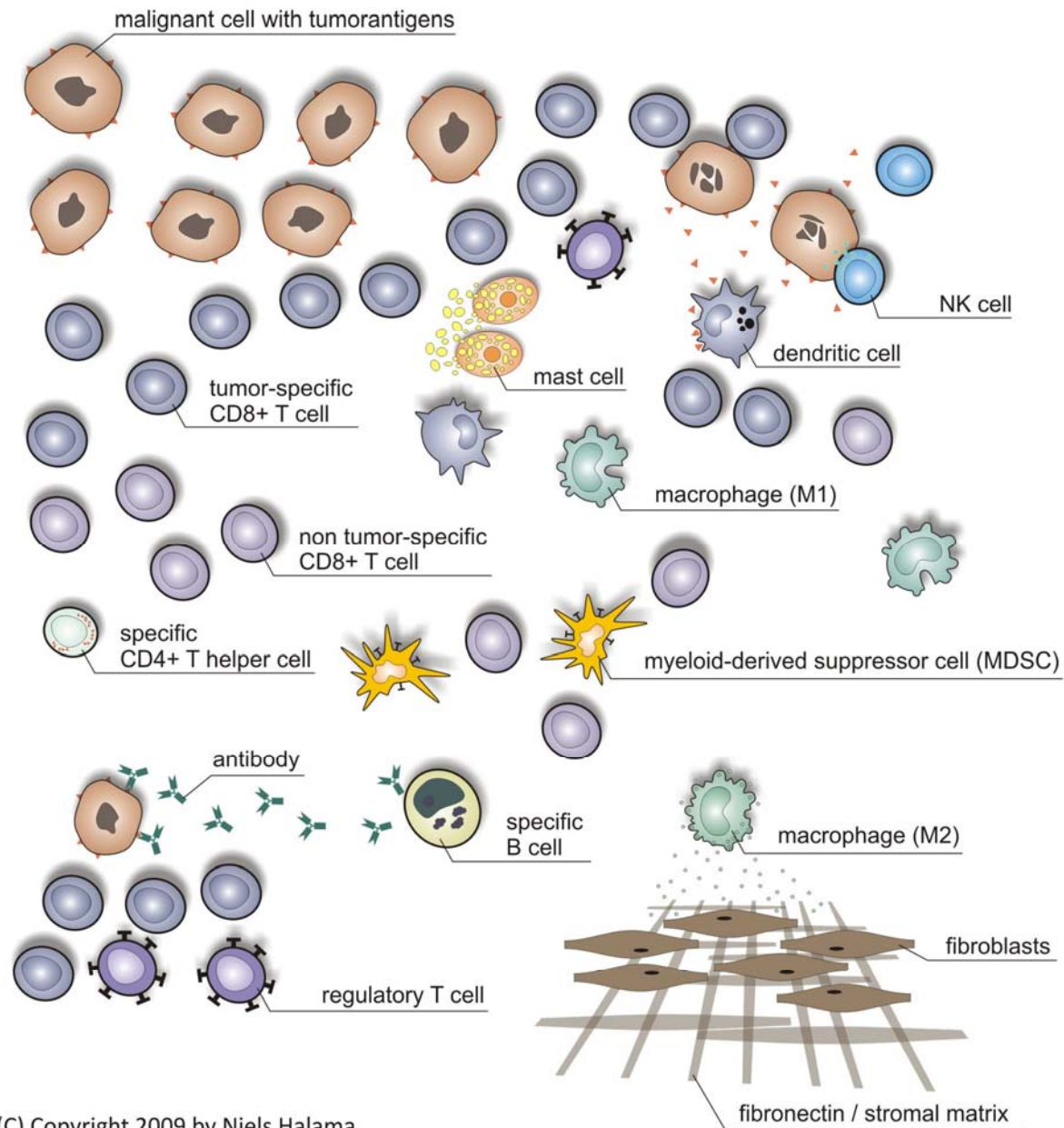
Therapiestrategien in der Onkologie

- Medikamentöse Therapien:
 - Chemotherapie
 - Hormontherapie
 - Signalhemmer (TKI)
 - Immuntherapien:
 - Impfung
 - Monoklonale Antikörper (Target Tumorzelle)
 - Immunmodulation
 - Zellbasierte Therapien (evtl. mit genveränderten Zellen)



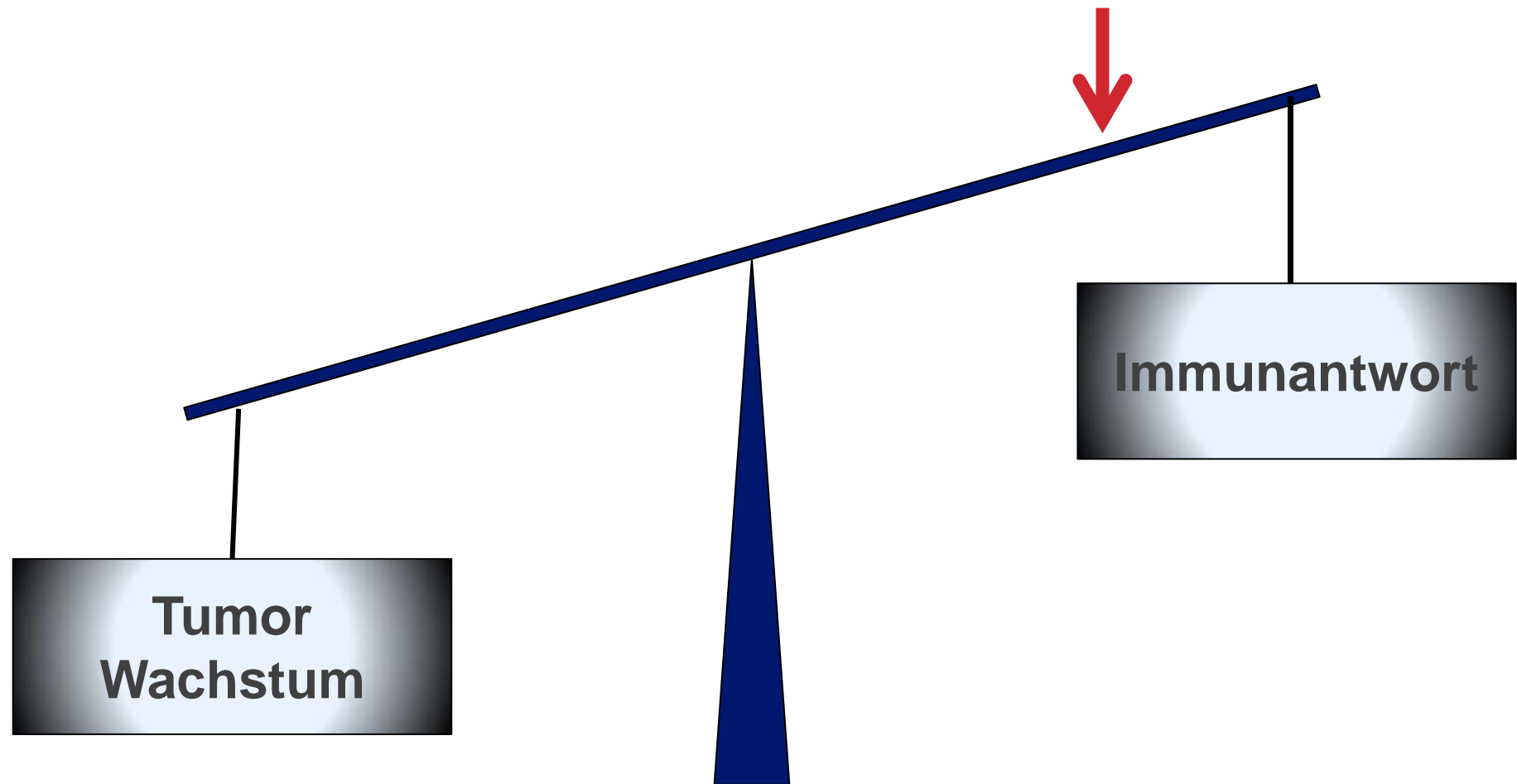


The immunological tumorenvironment

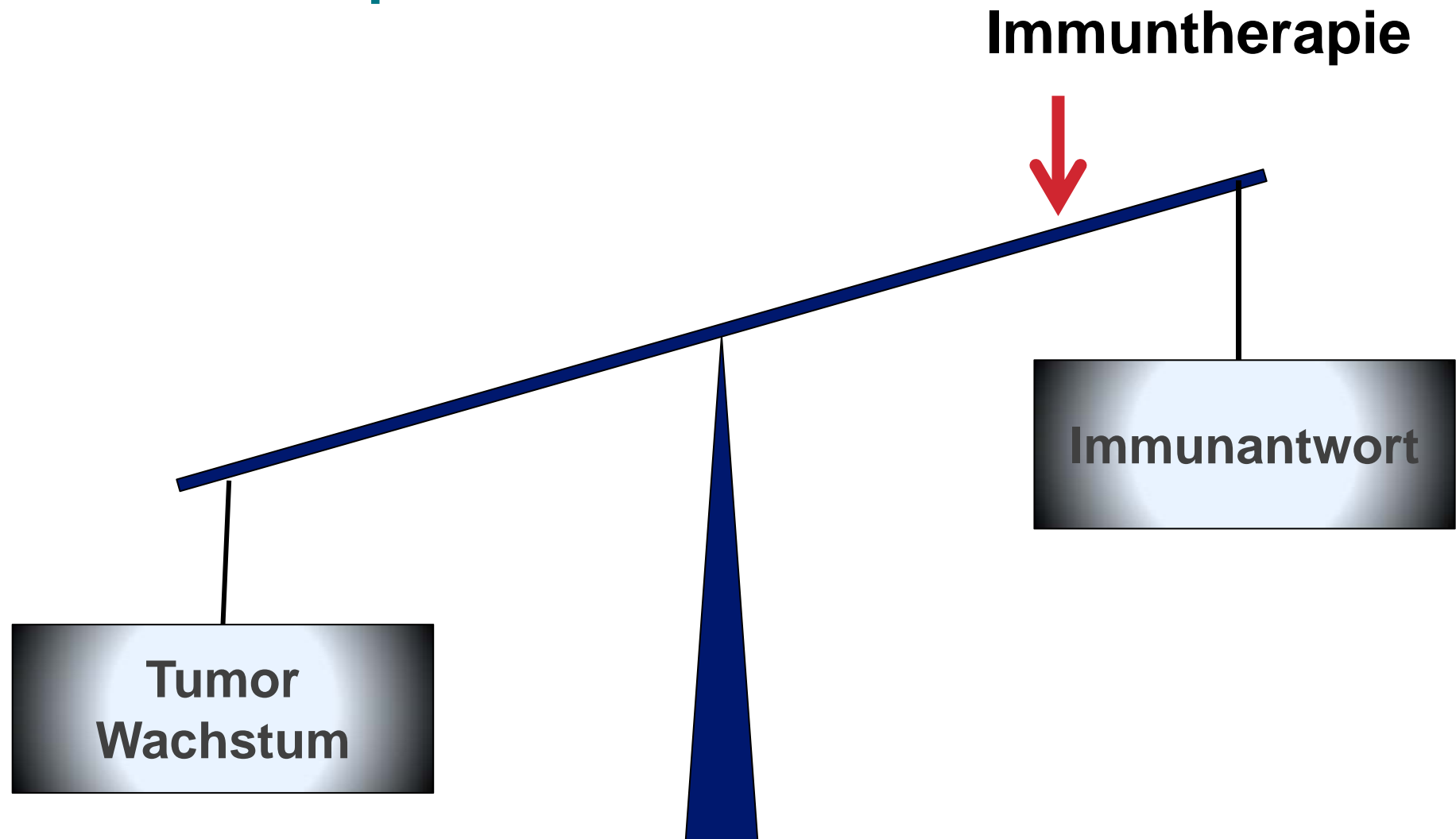


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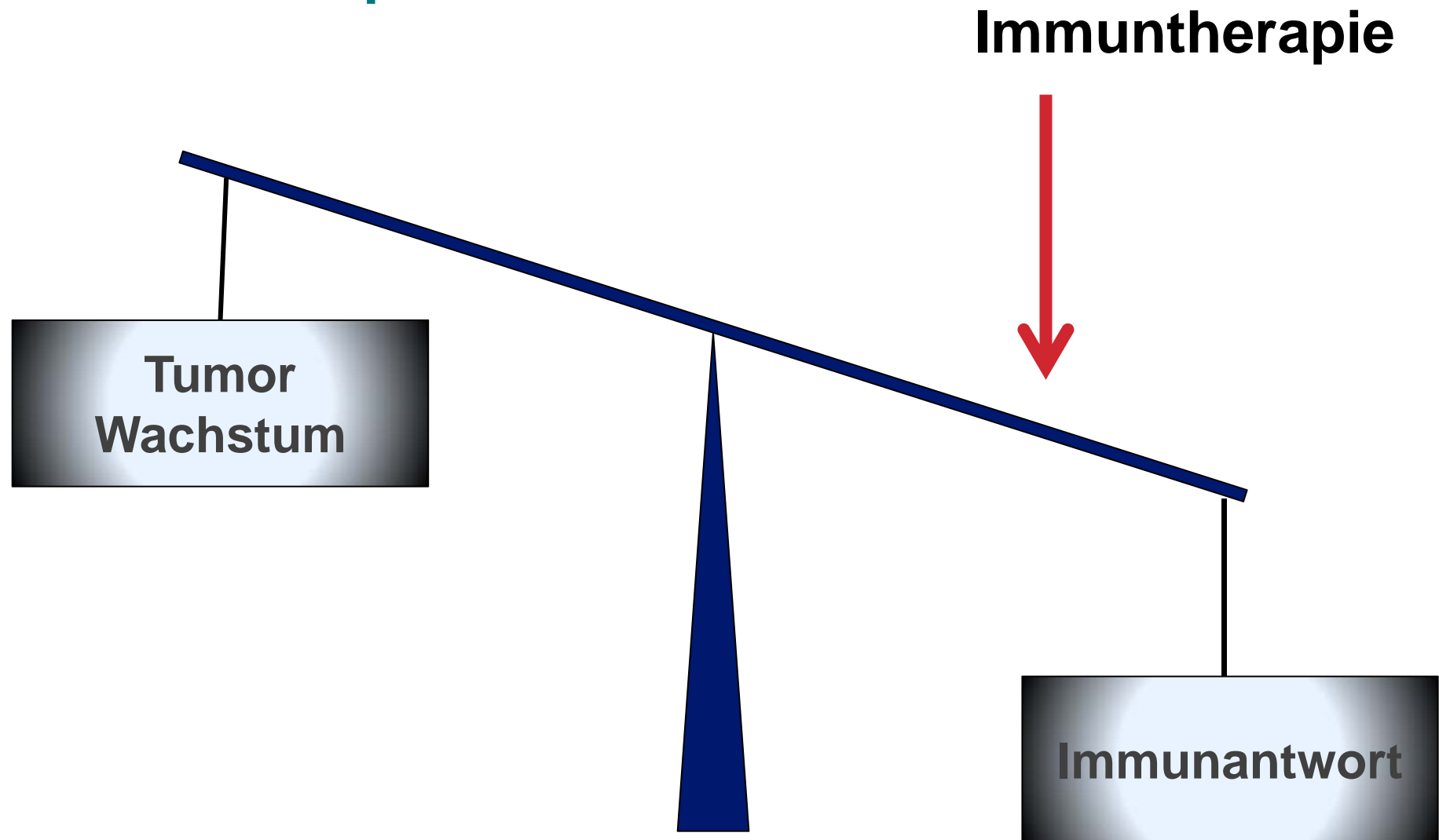
Immuntherapie



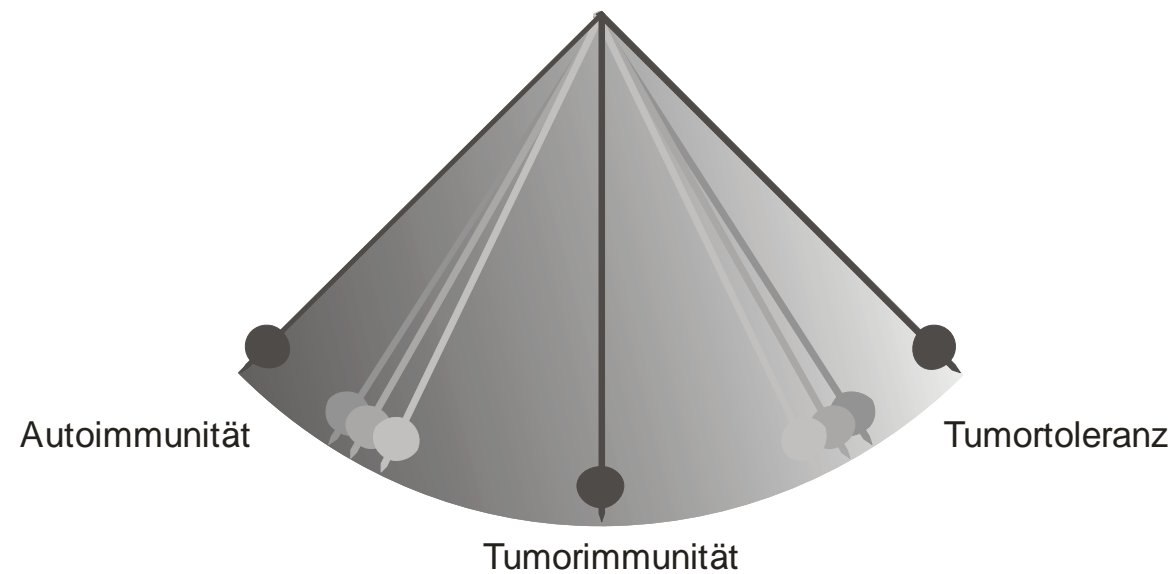
Immuntherapie



Immuntherapie



Was soll bewegt werden?



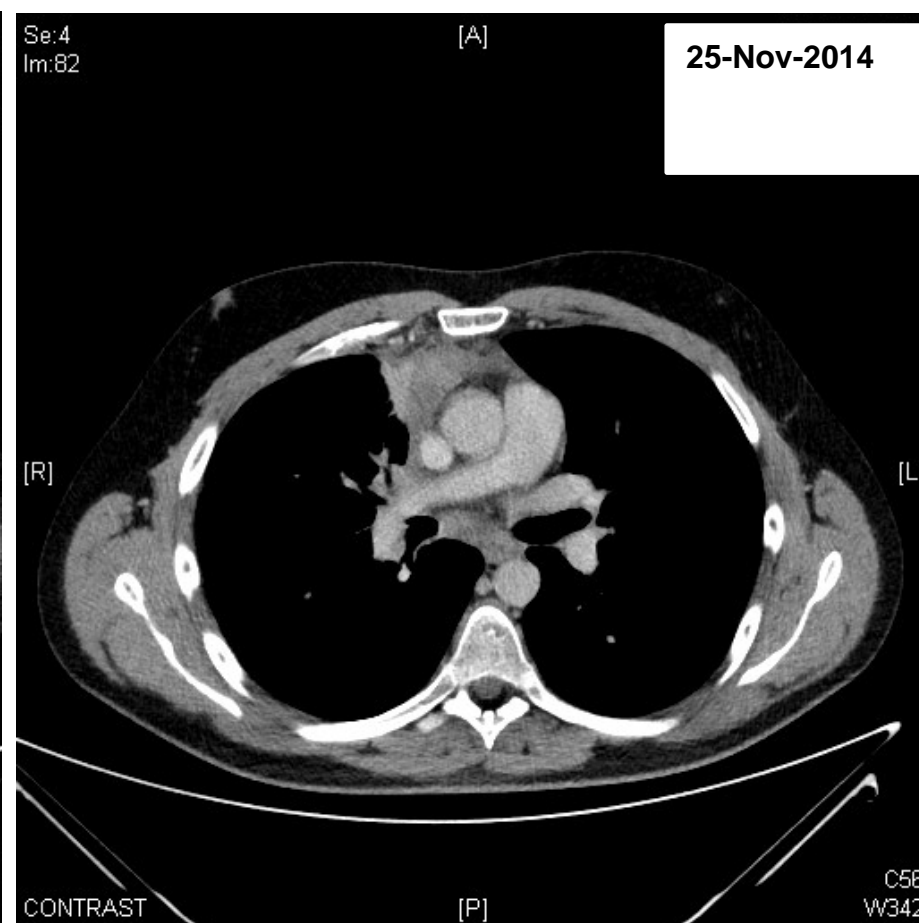
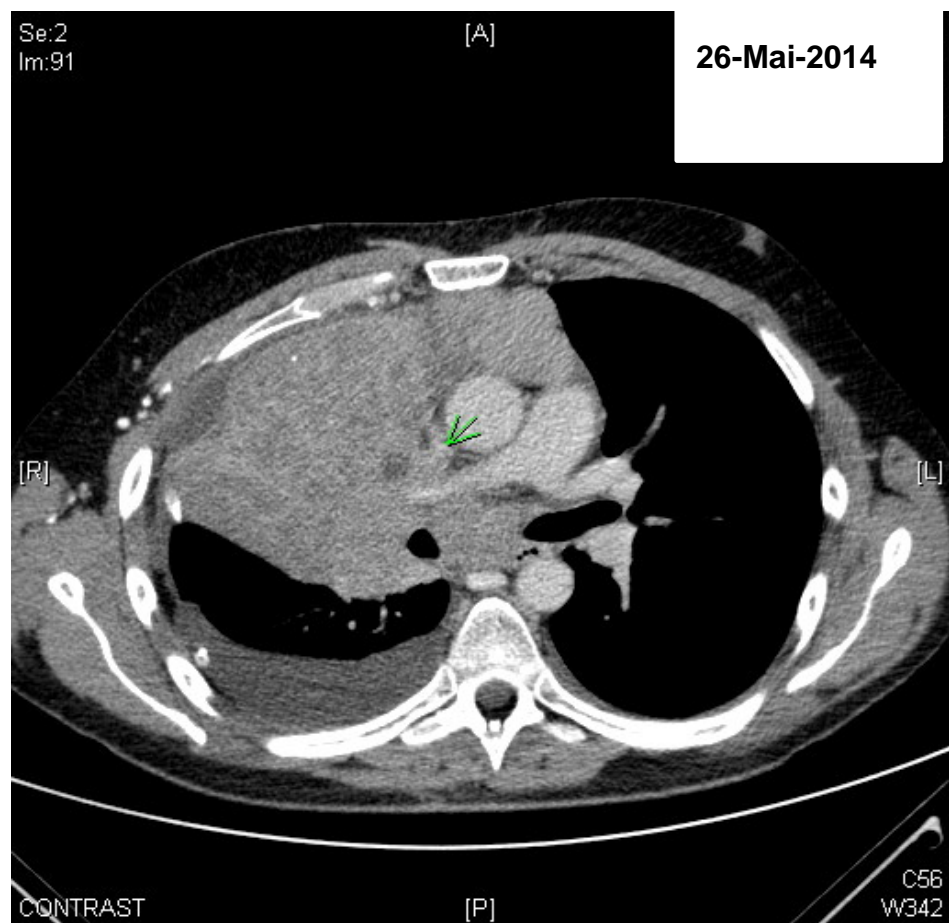
Herr K. G. *04.07.1987

Onkologische Hauptdiagnose

Datum	Diagnose
01/2014	NSCLC re. Lungenoberlappen initiales Stadium: cT4 cN3 cM1a (ossär, pleural, lymphonodulär) G3 Histologie: Plattenepithelkarzinom, nicht verhornend Immunhistologie: CK20-, CD45 -, CK7-, TTF1-, Napsin A-, SynA-, CD56 -, ki-67 90% Mutationsstatus: BRAF WT
Therapie und Verlauf	
02-05/2014	4 Zyklen Cisplatin 80 mg/m² d1 + Paclitaxel 175 mg/m² d1, q22d
05/2014	CT-morphologisch progredienter Pleuraerguss re., Komplet- atelektase re. ML/ OL, weiterhin hochgradige Kompression der V. cava superior
06/2014-01/2015	17 Zyklen eines monoklonalen immunchekpoint inhibitors im Rahmen einer Phase I Studie Komplikationen: Diarrhoe I° , Psoriasis palmaris

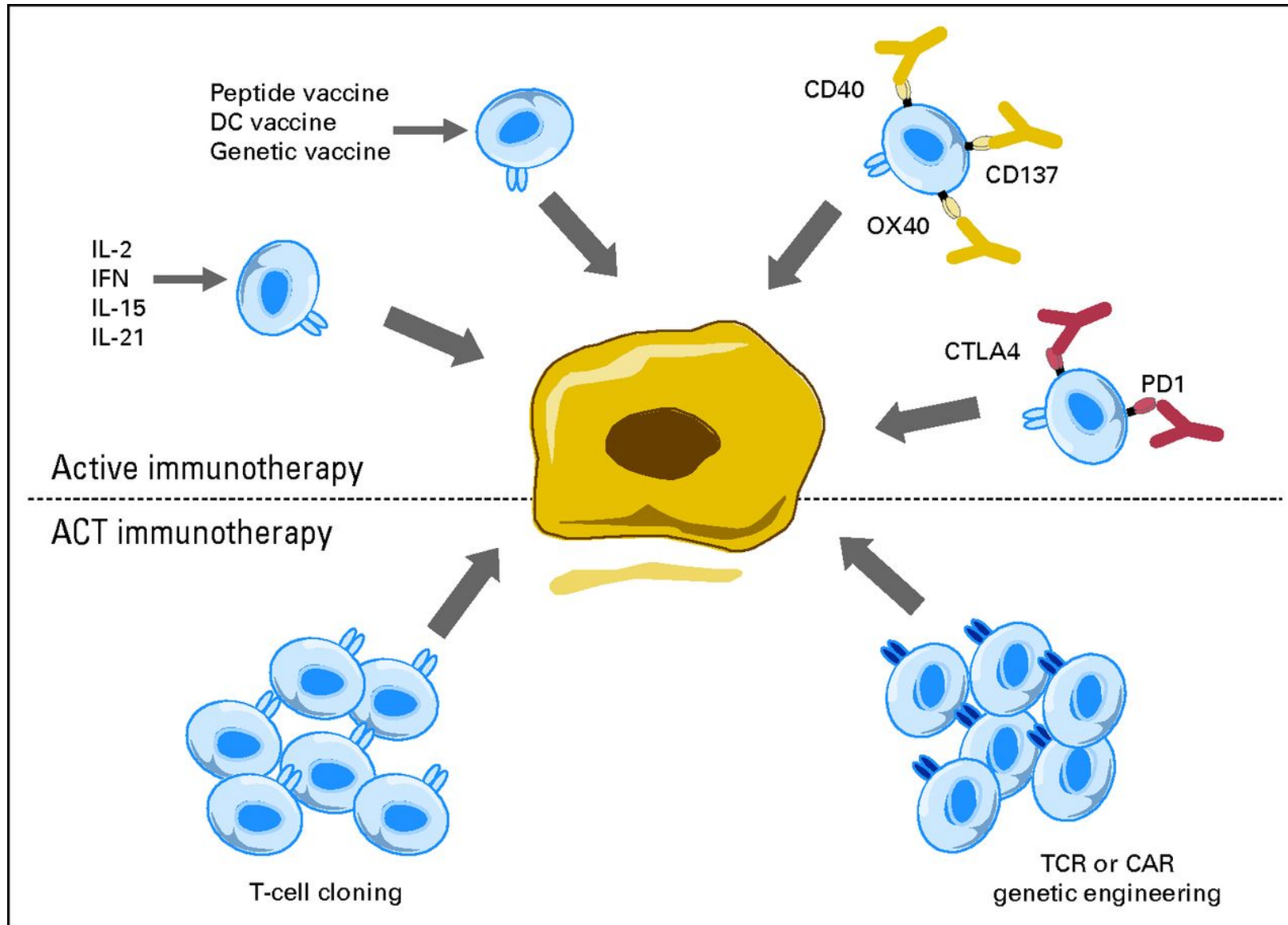


Herr K. G. *04.07.1987



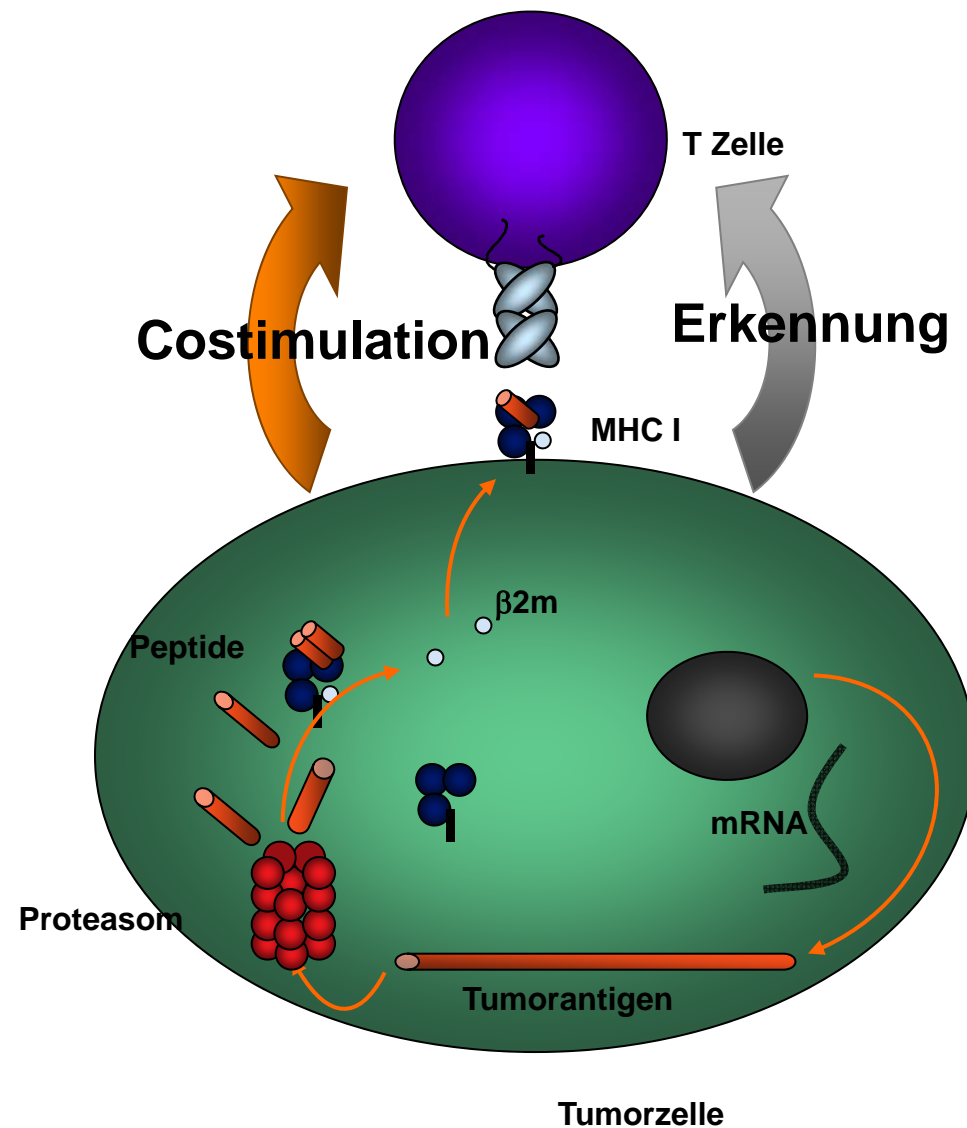
Insgesamt very good partial remission, Therapiefortsetzung bis Juni 2015 über 1 Jahr gefolgt von follow up, bei Progress dann erneute Antikörperbehandlung über ein weiteres Jahr

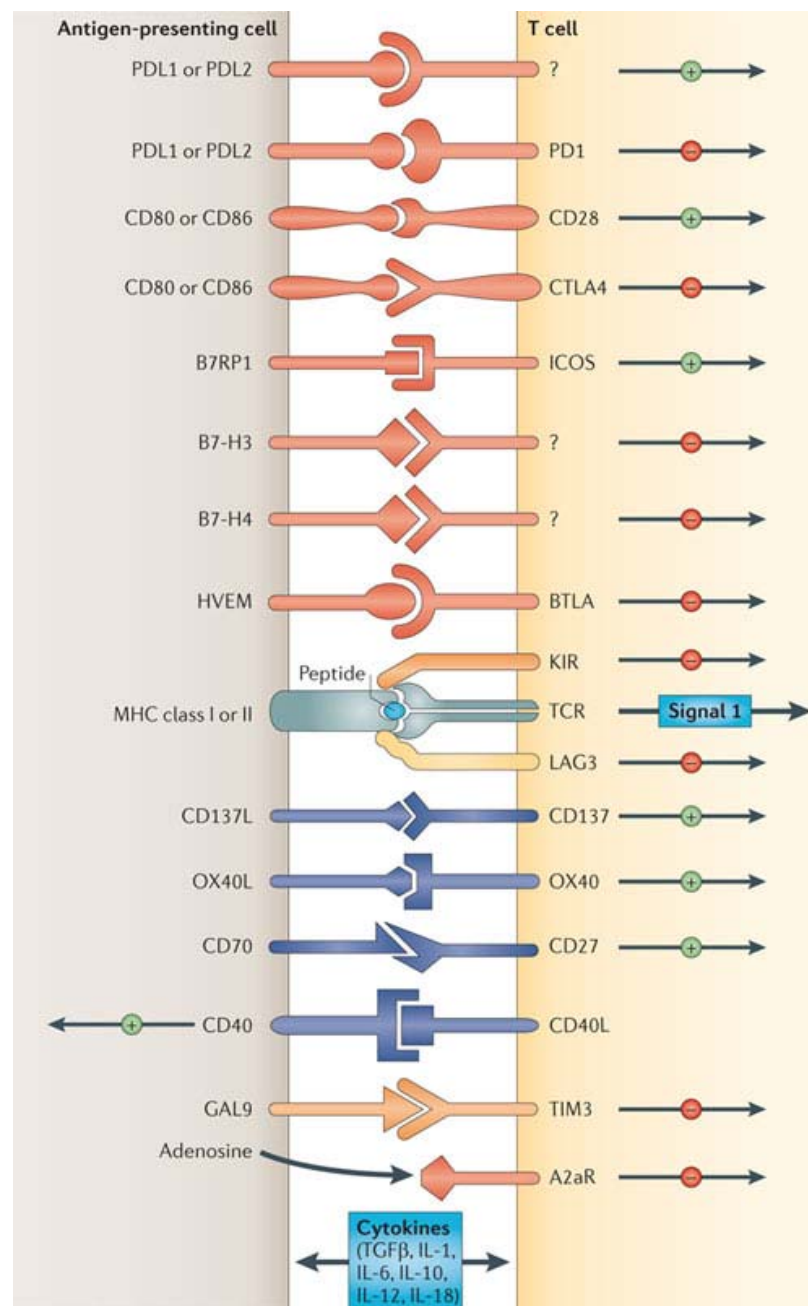
Strategien Immuntherapie



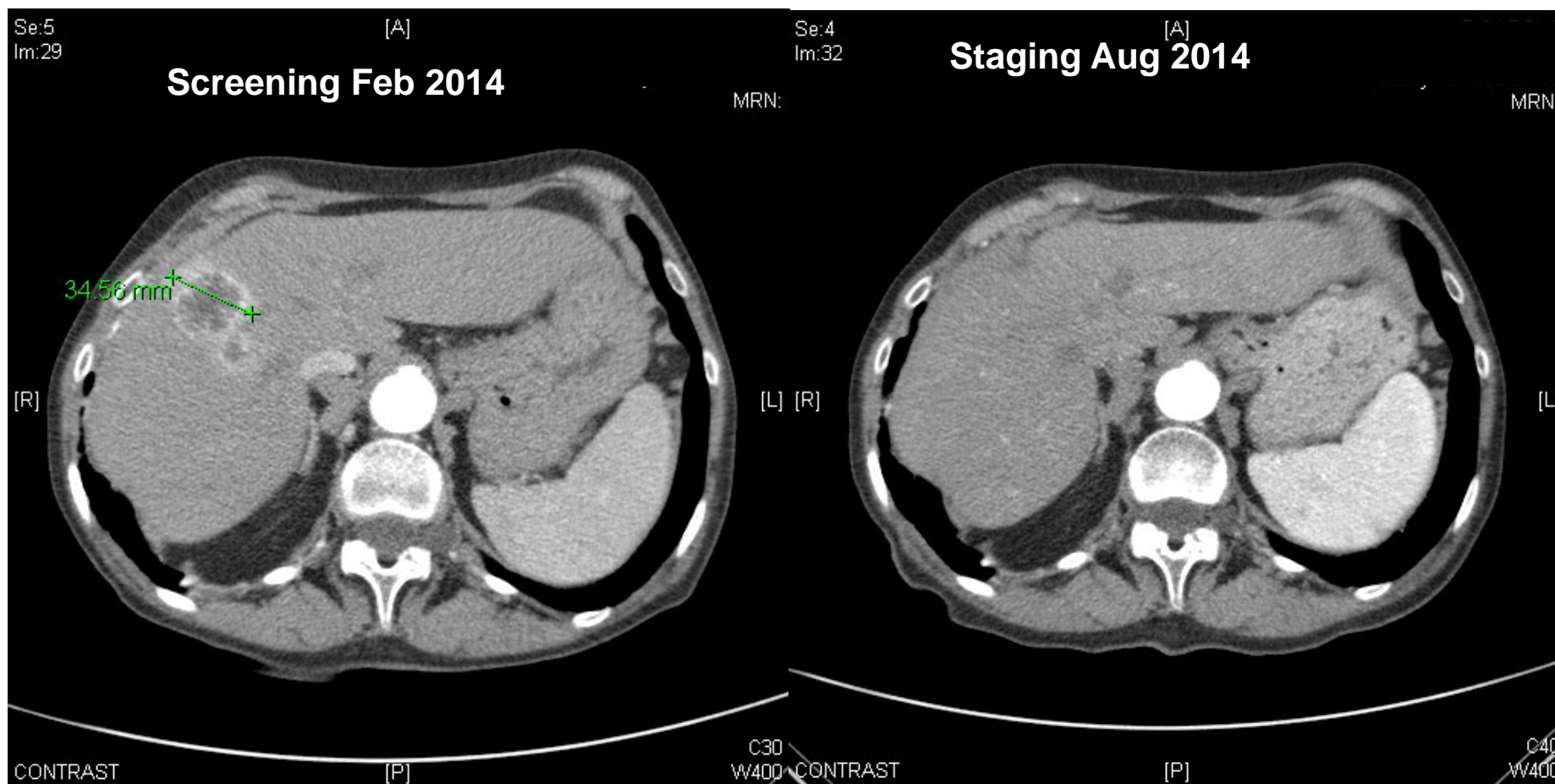
Cytotoxic T-Lymphocyte Killing Target

© James A. Schrier
Immunofundus
Charlottesville, VA USA

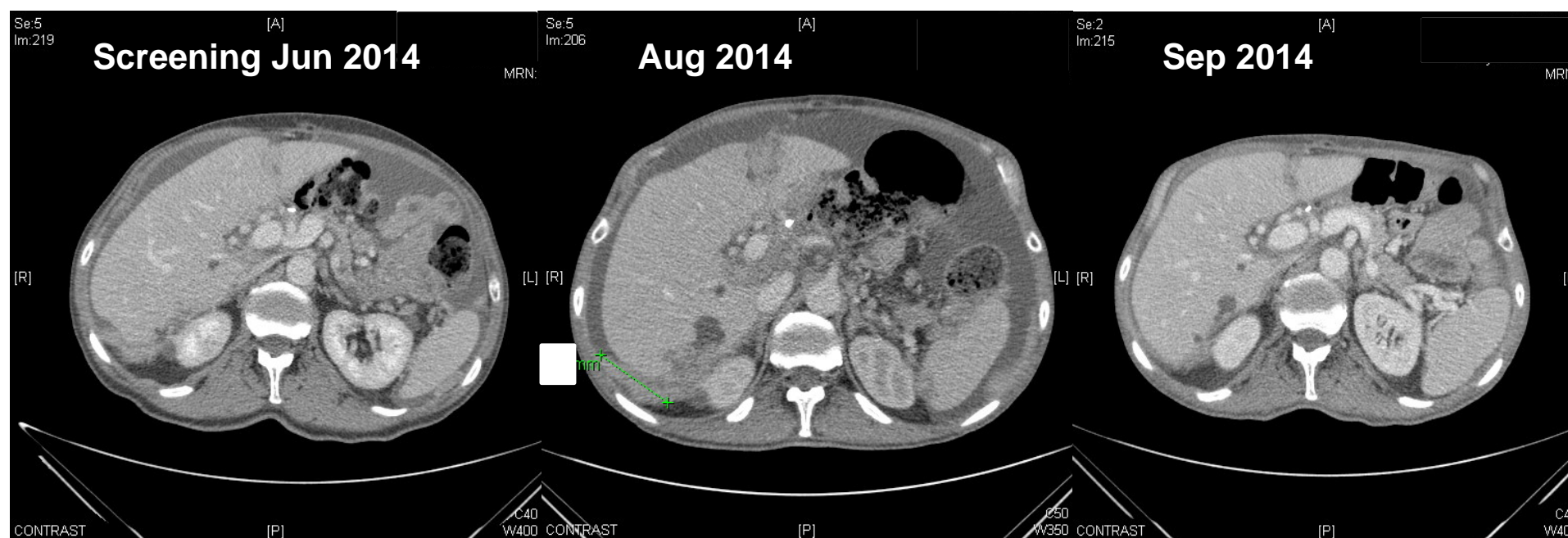




SCLC, extensive disease, 3rd line treatment with PD1 after failing 2 prior chemotherapy regimens



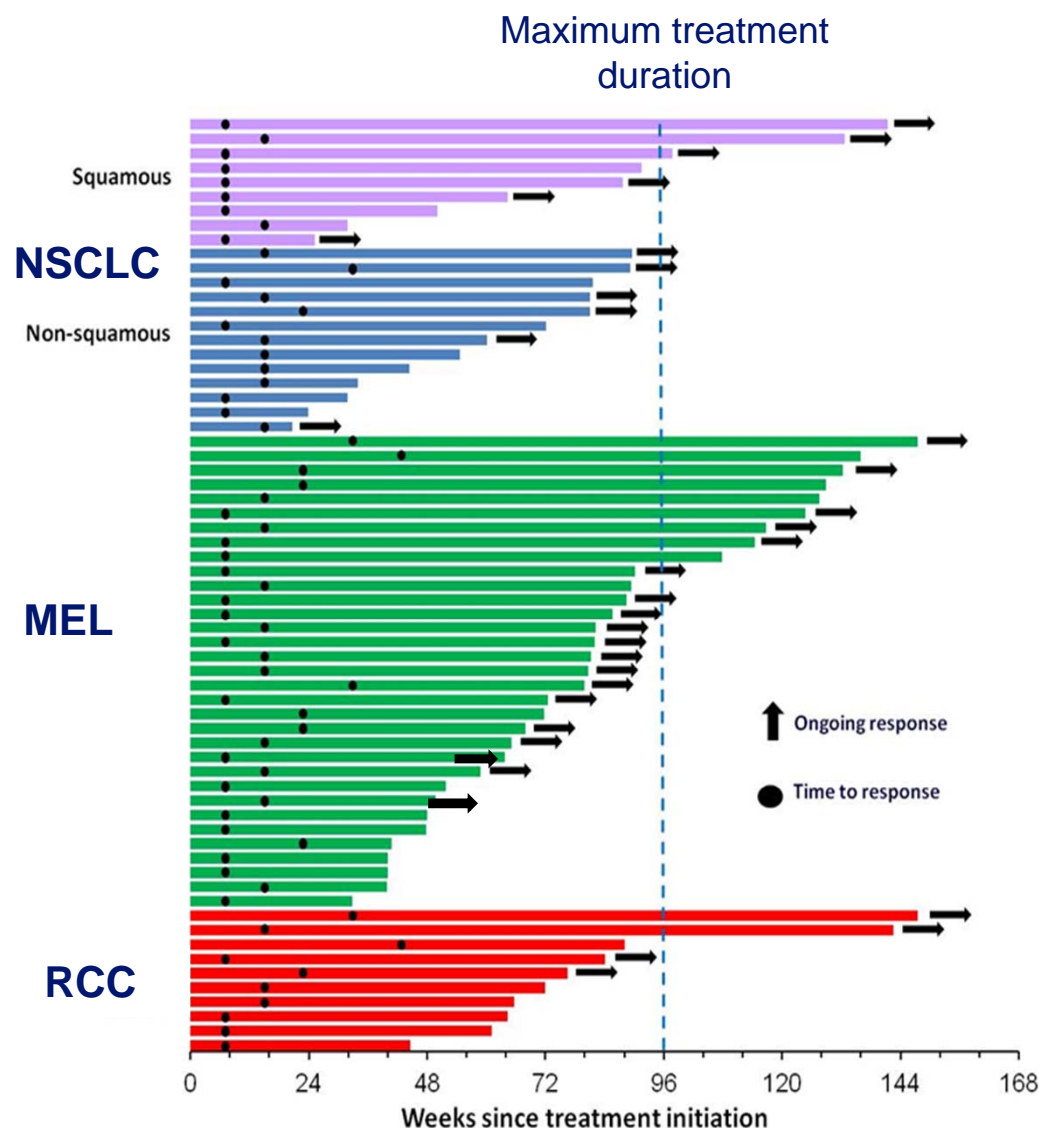
Magenkarzinom, Progress unter Chemotherapie, Einschluss in Studie mit anti-PD1



**Peritoneal progression upon
3 cycles Nivolumab with
weekly ascites tapering**

**Ascites disappeared
completely after 6 cycles
Nivolumab, PR (-34% SLD)**

Durability of Objective Responses Induced by Nivolumab in Patients with Advanced NSCLC, MEL and RCC



Sixty-five of 306 patients had ORs (CR/PR):

- 30 of 65 (**46%**) responses were evident at first tumor evaluation (8 weeks)
- 42 of 65 (**65%**) patients had responses lasting >1 year
- 35 of 65 (**54%**) responses were ongoing at time of data analysis
- Responses persisted off-drug

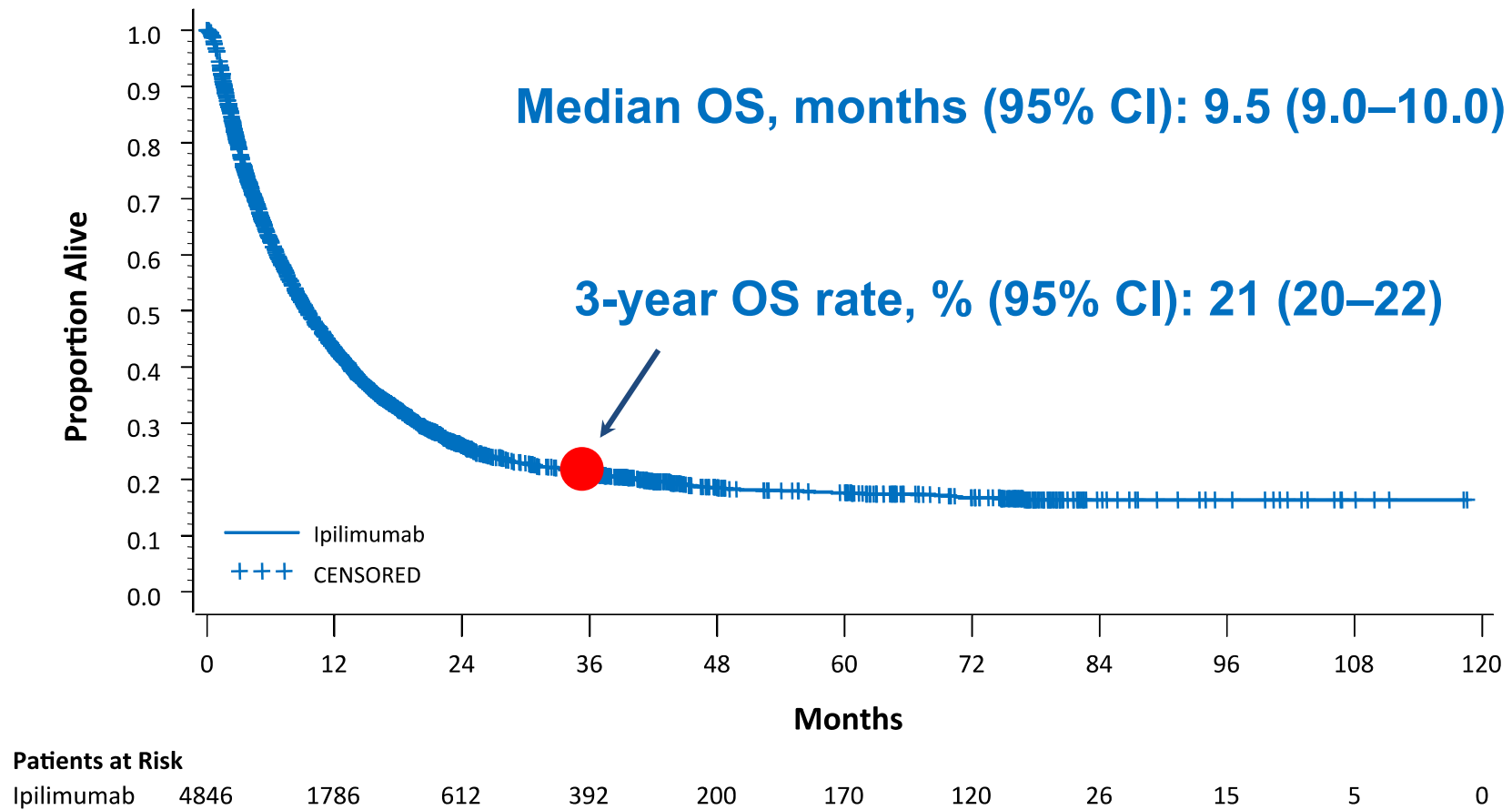
Topalian S et al ASCO 2013

Checkpoint Inhibition

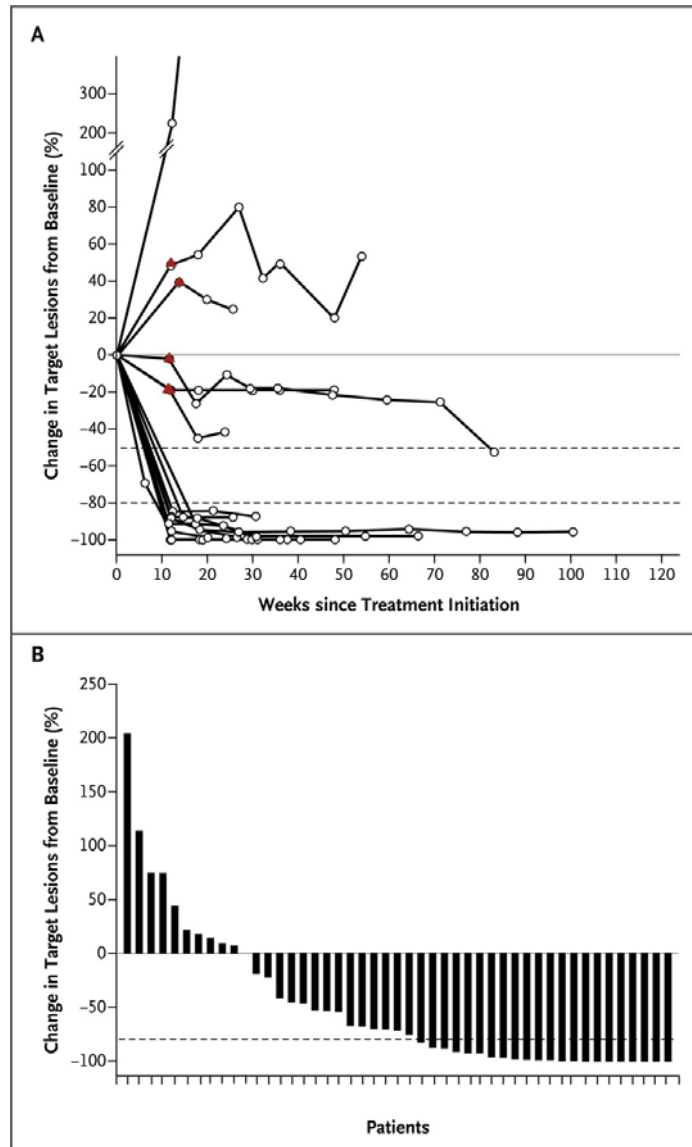
- Hohe Ansprechraten bei verschiedenen Tumoren wie Melanom, Bronchialkarzinom, Blasenkarzinom, Nierenkarzinom und anderen....
- Niedrigere Ansprechraten bei GI Tumoren
- Anhaltende Remissionen bei einigen Patienten
- Moderate Nebenwirkungen



Melanom Stadium IV:

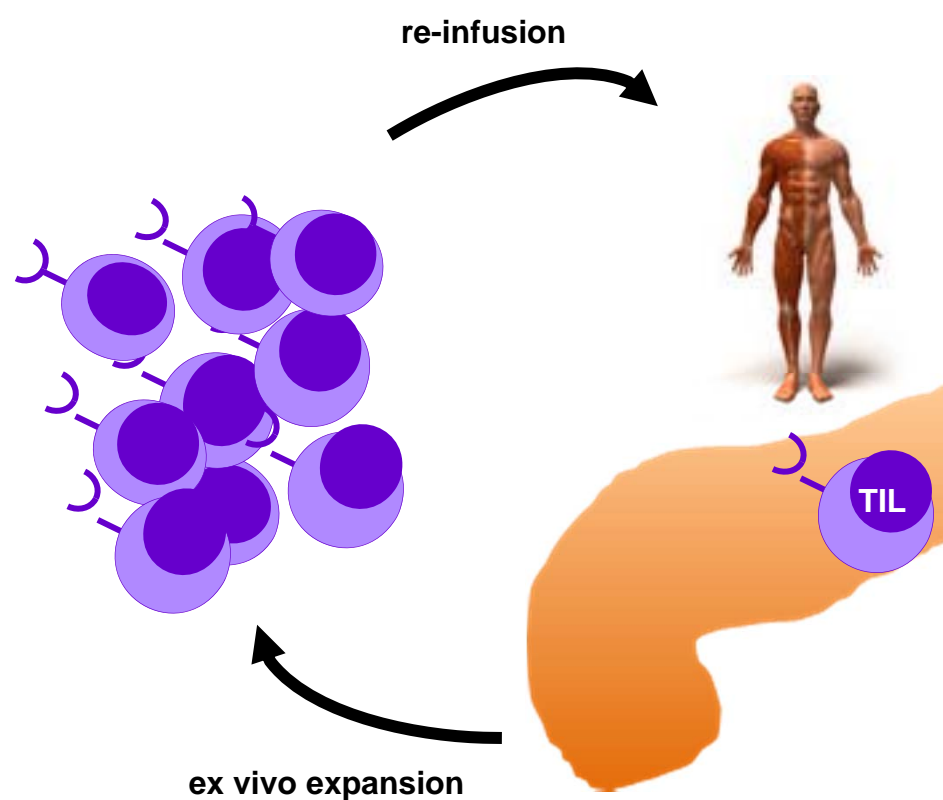


Kombination von PD1 + CTLA4 Ak



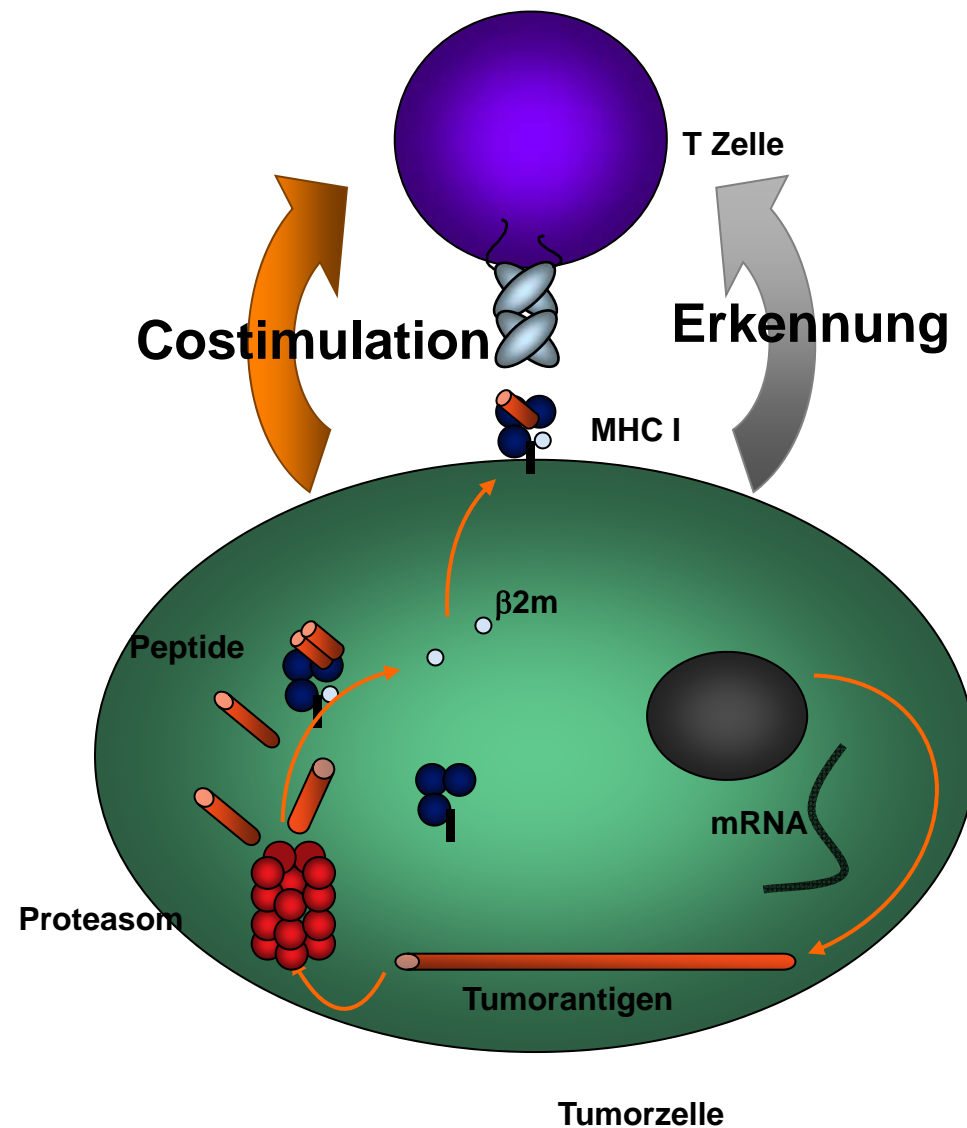
Wolchok JD et al. N Engl J Med 2013;369:122-133.

TIL Therapie

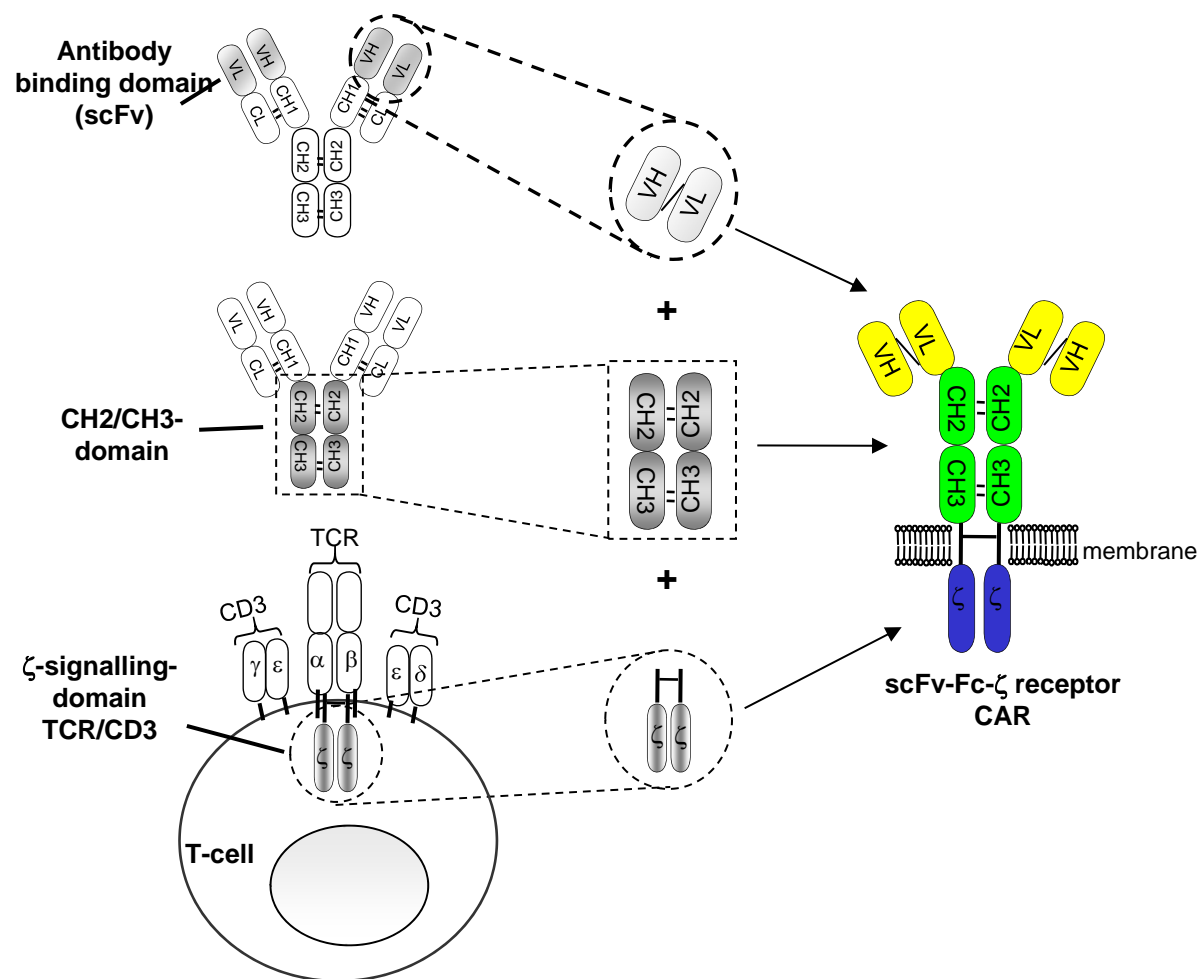


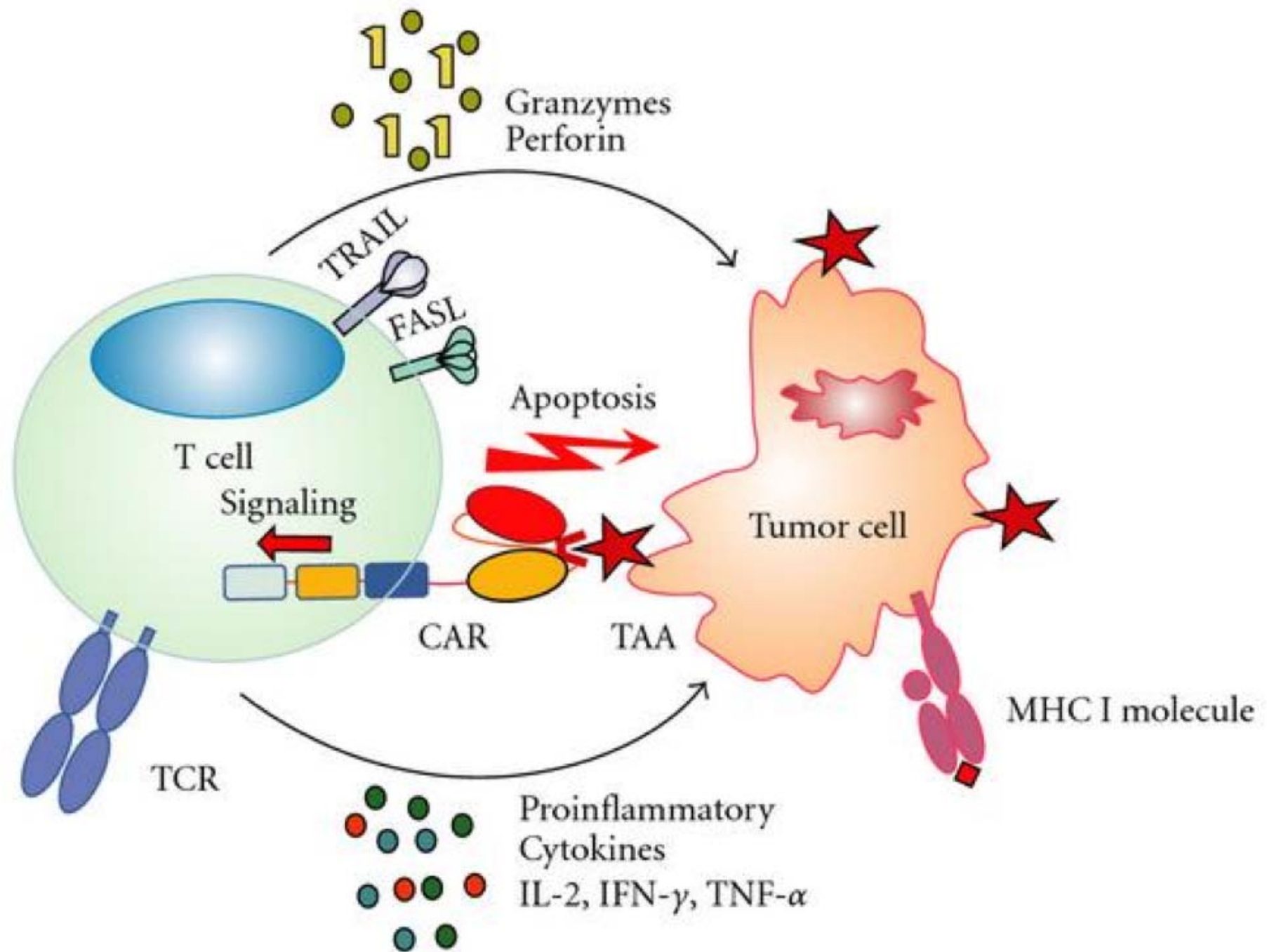
Cytotoxic T-Lymphocyte Killing Target

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Immunofundamentals
Charlottesville, VA USA



CARs





The NEW ENGLAND JOURNAL of MEDICINE

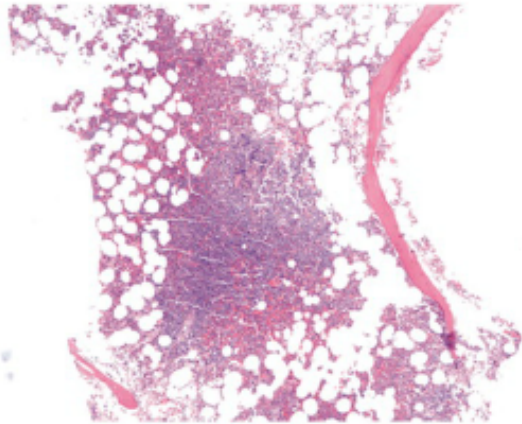
BRIEF REPORT

Chimeric Antigen Receptor–Modified T Cells in Chronic Lymphoid Leukemia

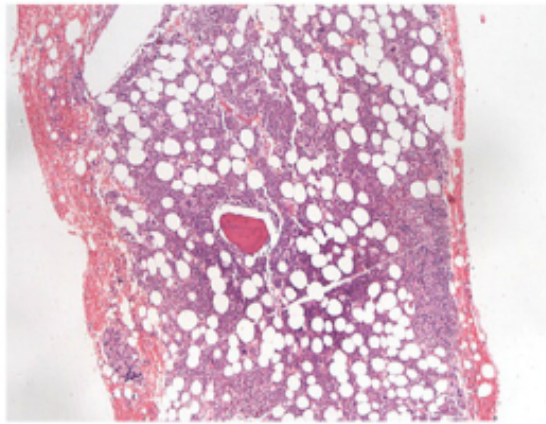
David L. Porter, M.D., Bruce L. Levine, Ph.D., Michael Kalos, Ph.D.,
Adam Bagg, M.D., and Carl H. June, M.D.

C Bone Marrow–Biopsy Specimens

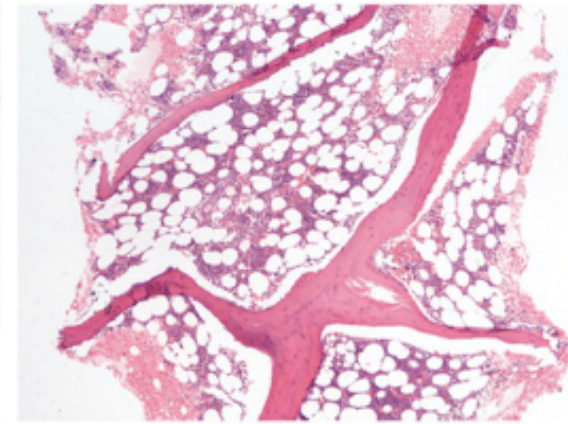
Day -1 (baseline)



Day 23



6 Mo



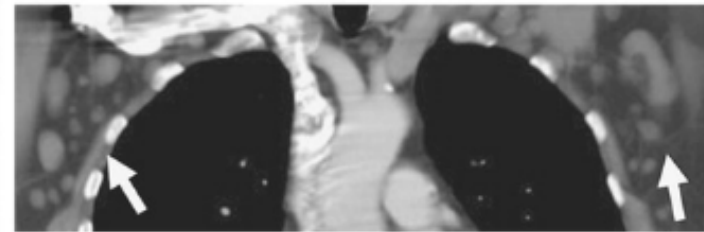
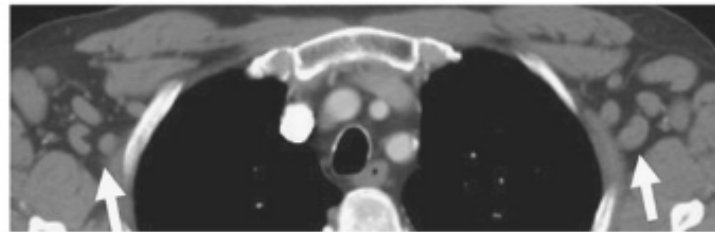
T

D Contrast-Enhanced CT

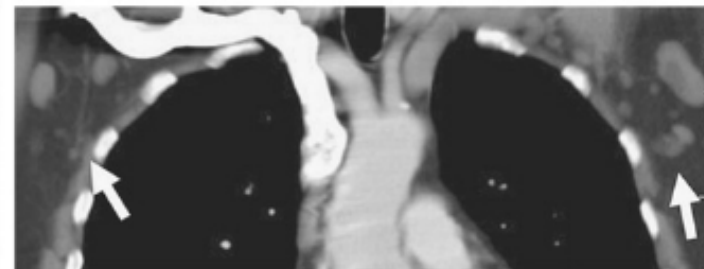
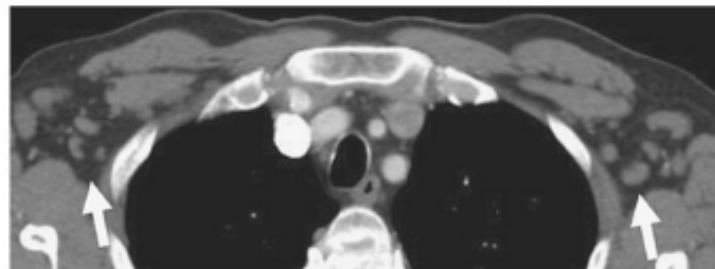
Axial

Coronal

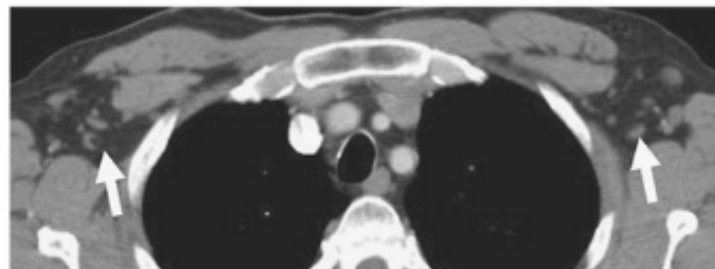
Before Therapy



1 Mo of Treatment



3 Mo of Treatment



Chemotherapy-Refractory Diffuse Large B-Cell Lymphoma and Indolent B-Cell Malignancies Can Be Effectively Treated With Autologous T Cells Expressing an Anti-CD19 Chimeric Antigen Receptor

James N. Kochenderfer, Mark E. Dudley, Sadik H. Kassim, Robert P.T. Somerville, Robert O. Carpenter, Maryalice Stetler-Stevenson, James C. Yang, Giao Q. Phan, Marybeth S. Hughes, Richard M. Sherry, Mark Raffeld, Steven Feldman, Lily Lu, Yong F. Li, Lien T. Ngo, Andre Goy, Tatyana Feldman, David E. Spaner, Michael L. Wang, Clara C. Chen, Sarah M. Kranick, Avindra Nath, Debbie-Ann N. Nathan, Kathleen E. Morton, Mary Ann Toomey, and Steven A. Rosenberg

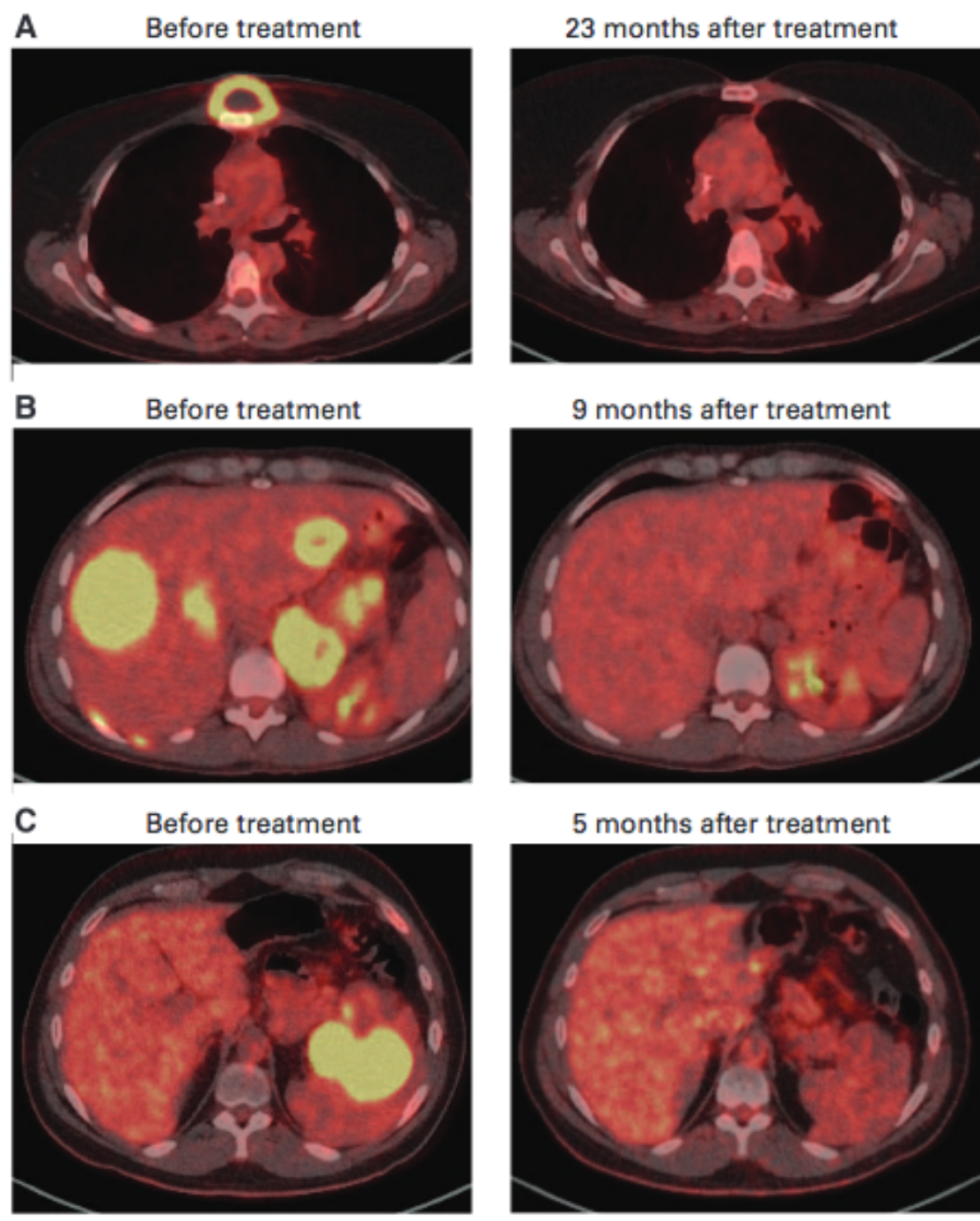
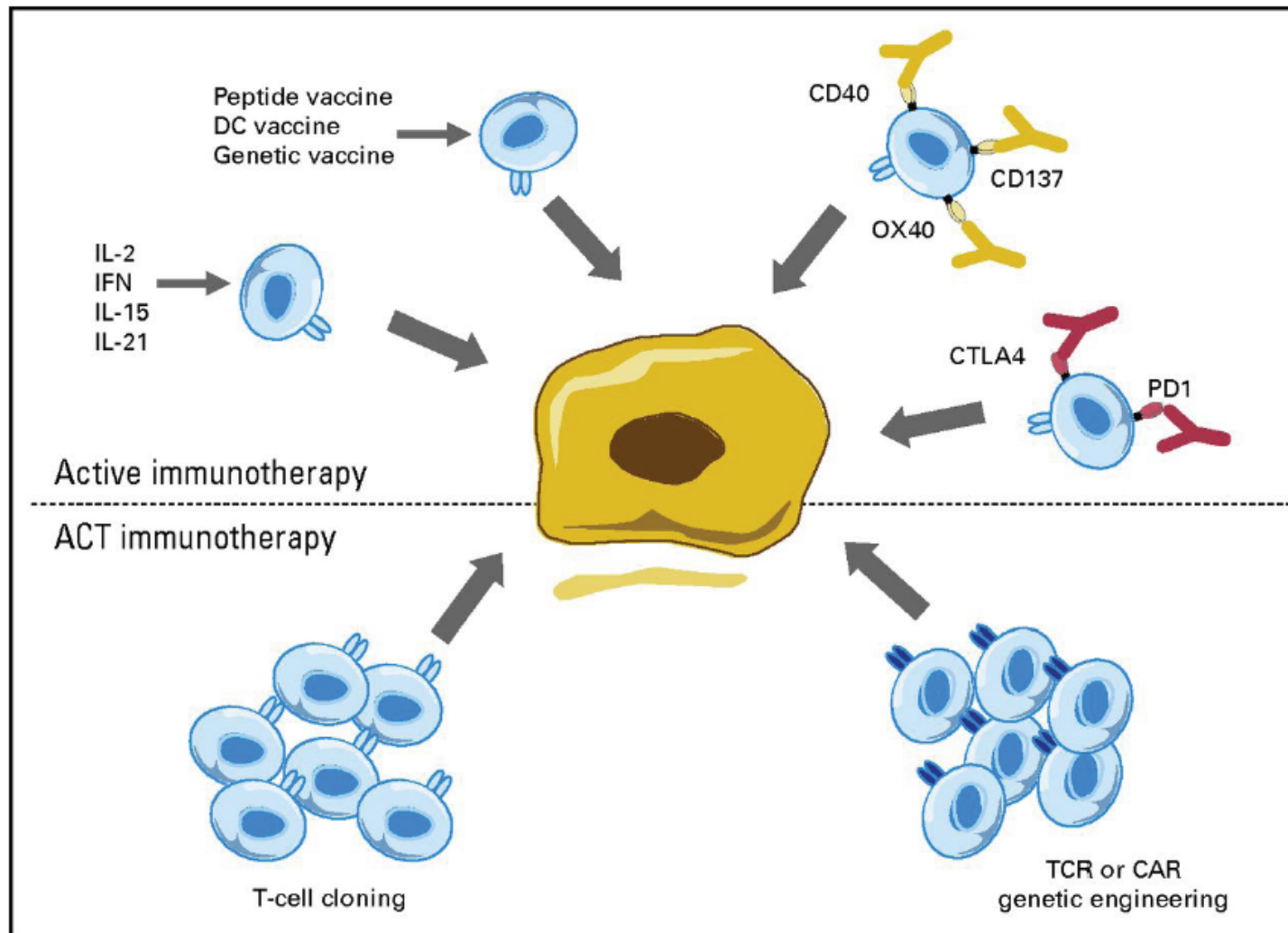
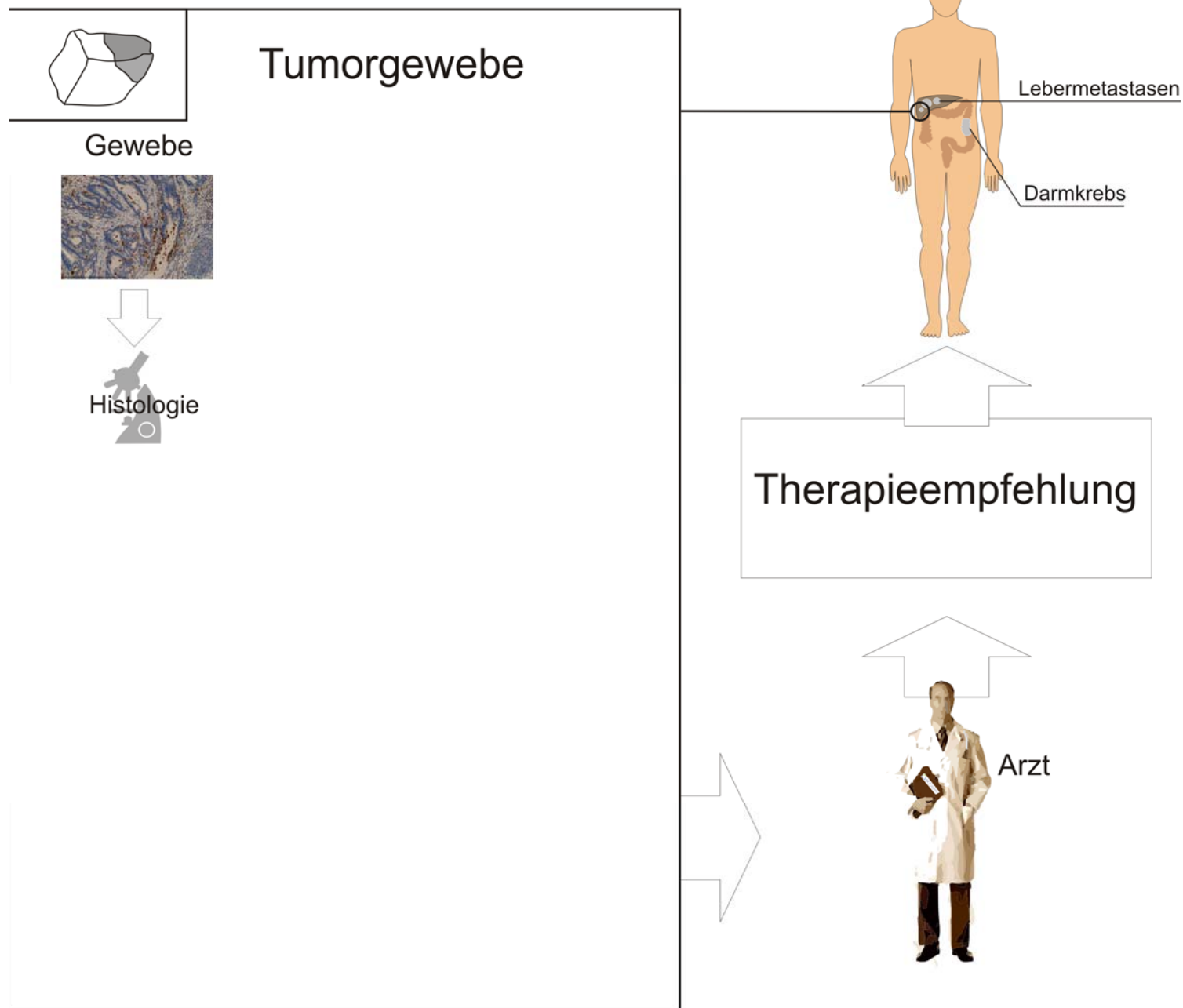


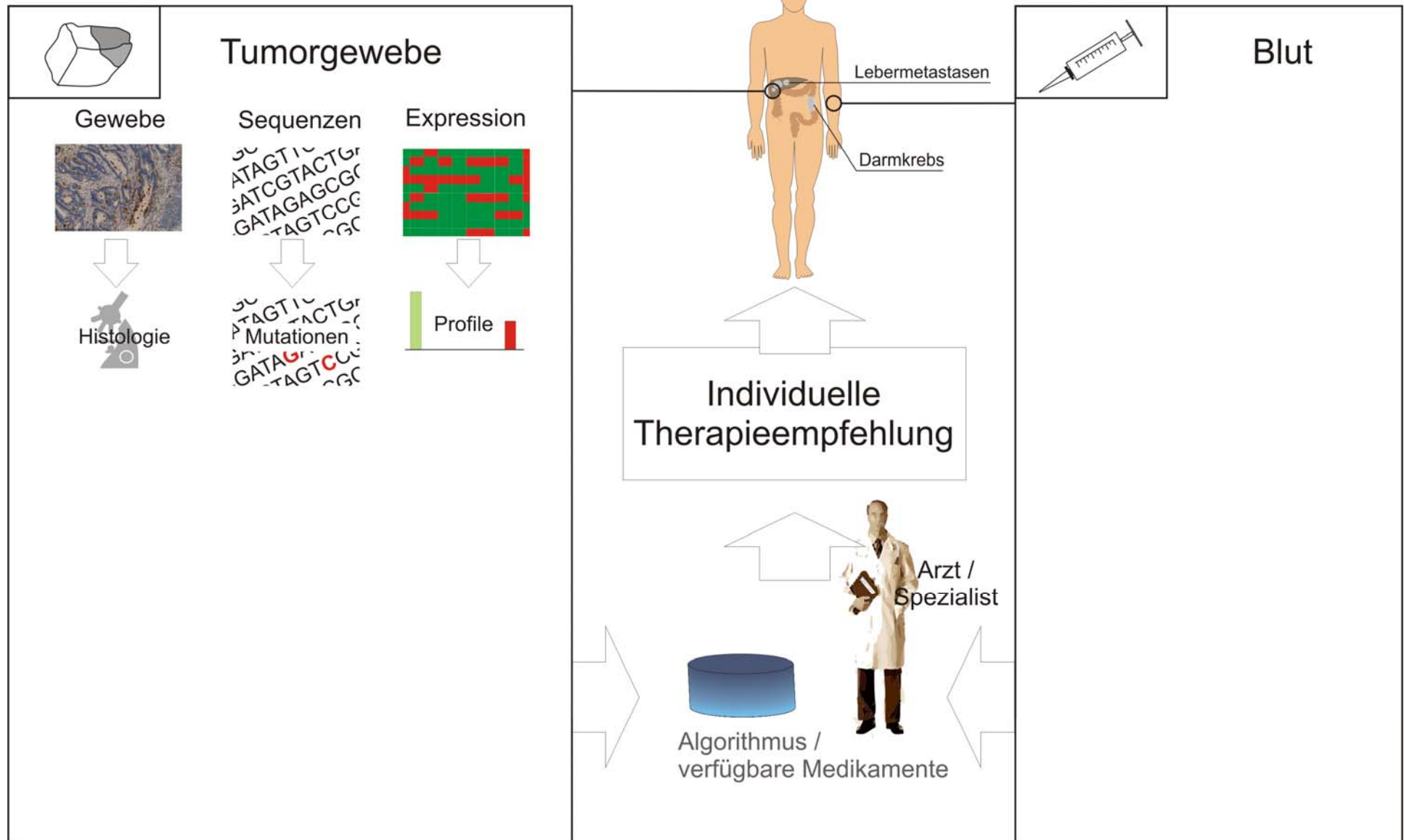
Fig 2. Complete remissions (CRs) of chemotherapy-refractory large-cell lymphomas in patients receiving anti-CD19 chimeric antigen receptor T cells. (A) Positron emission tomography (PET)/computed tomography (CT) scans show CR of chemotherapy-refractory primary mediastinal B-cell lymphoma (PMBCL) in patient No. 2. (B) PET/CT scans demonstrate CR of lymphoma in patient No. 8 who had chemotherapy-refractory PMBCL with extensive liver involvement. (C) PET/CT images show CR of diffuse large B-cell lymphoma, not otherwise specified, in patient No. 14, who had extensive splenic lymphoma.

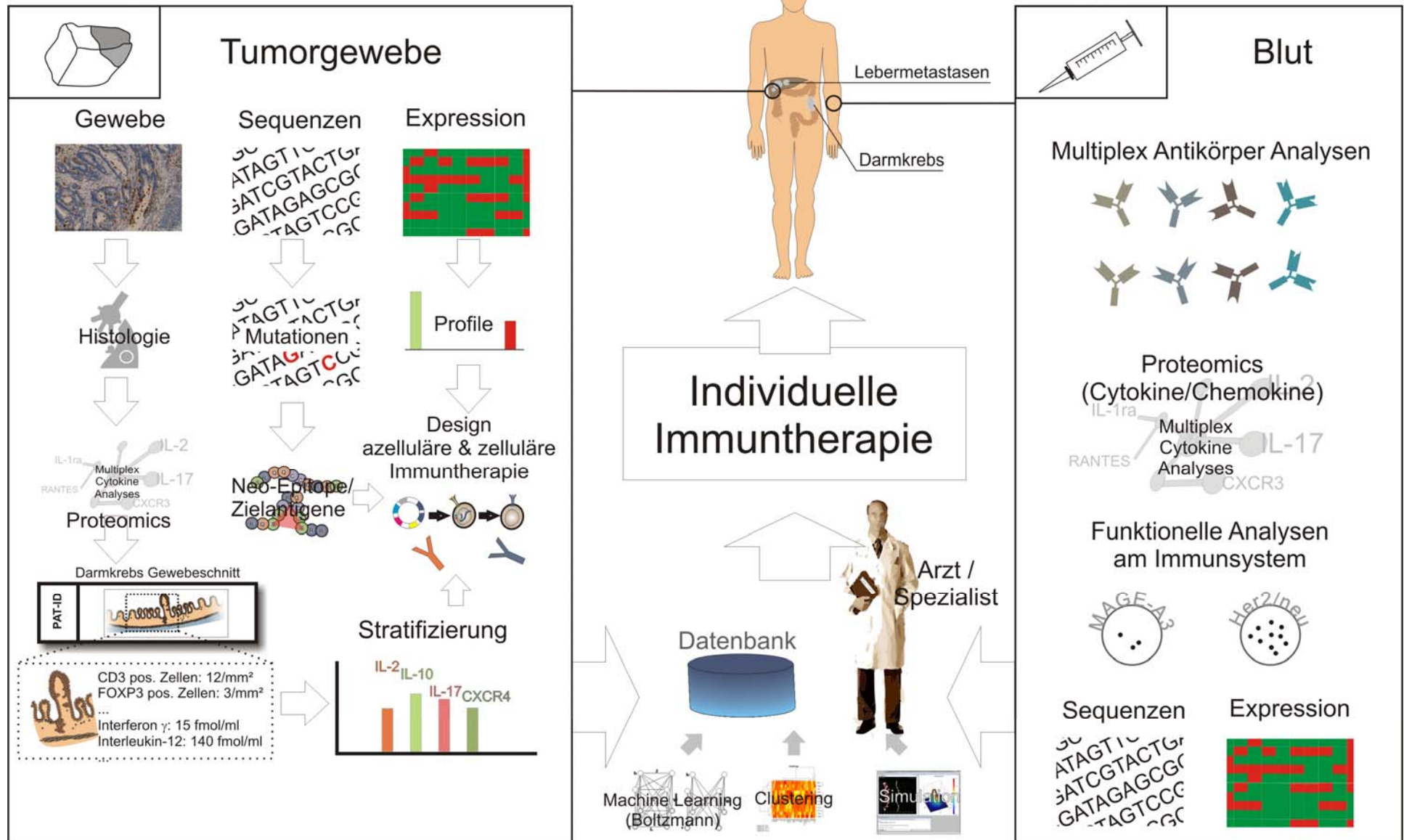
Strategien Immuntherapie



McArthur G A , and Ribas A JCO 2013;31:499-506







Personalisierte Therapie

- Molekulare Diagnostik individueller Tumorerkrankungen einschließlich Genetik und Immunologie
- Integration aller molekularen und immunologischen Daten in ein Modell der individuellen Erkrankung
- Ableitung der individuellen optimalen Therapie:
 - Targeted Drugs (TKI etc)
 - Immunmodulation
 - Individuelle Vakzine
 - Zellbasierte Therapie (T Zellen, genetisch veränderte T Zellen)
 - Intelligente Kombinationen
- Therapie mit Monitoring des Therapieeffektes im Tumor (sequentielle Biopsien)
- Rückkopplung der erhobenen Daten und Verbesserung der Modellierungsalgorithmen



