DANSKE KRÆFTFORSKNINGSDAGE 2022

den nærmeste

Hvad er fremtiden indenfor immunterapi

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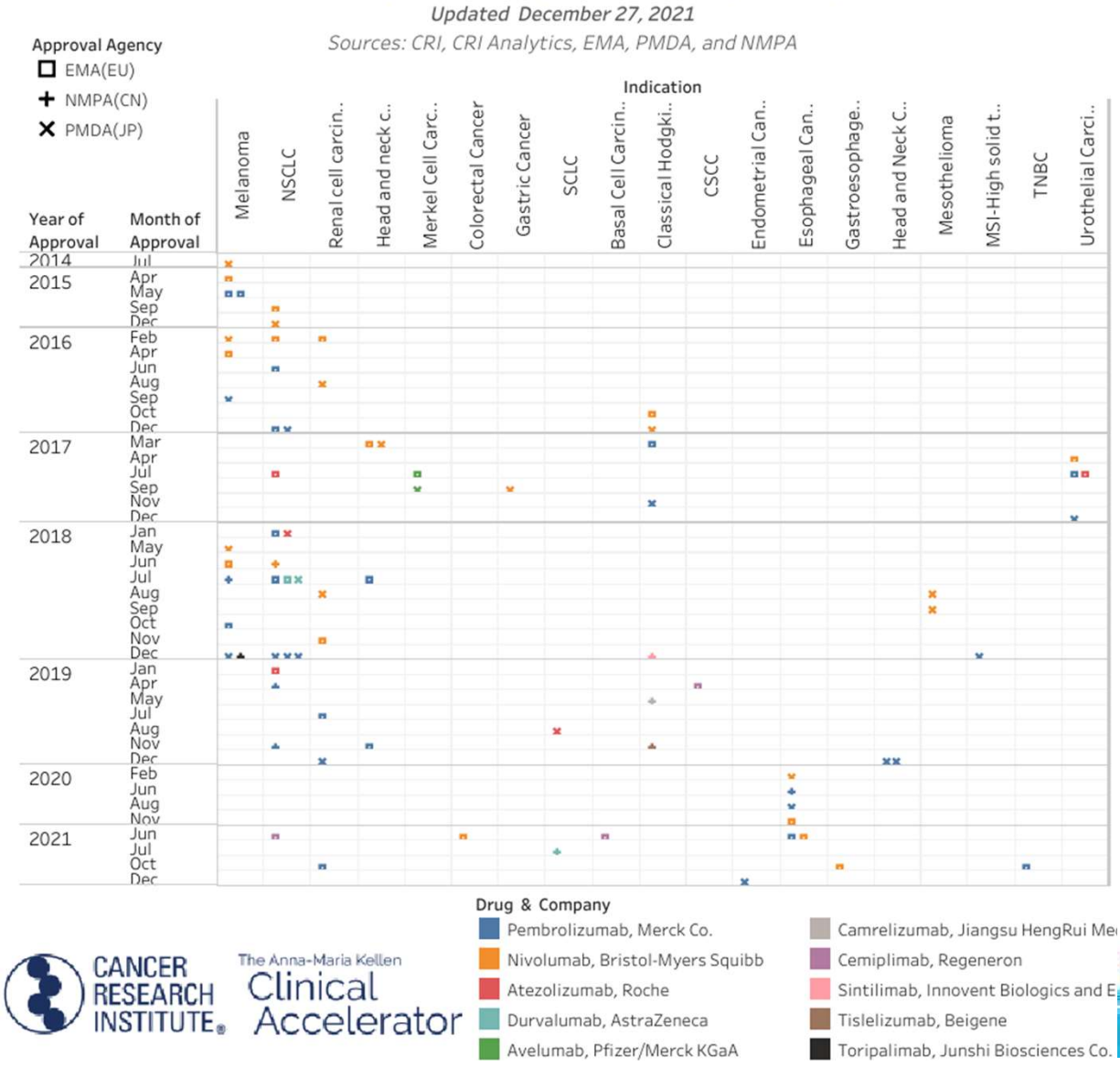
#DKD2022
#SamarbejdeOmKræft

Sli.do
#131525

What have we achieved until now ?

The ongoing wave: Timeline for EMA approval of anti-PD1/PDL1 indications



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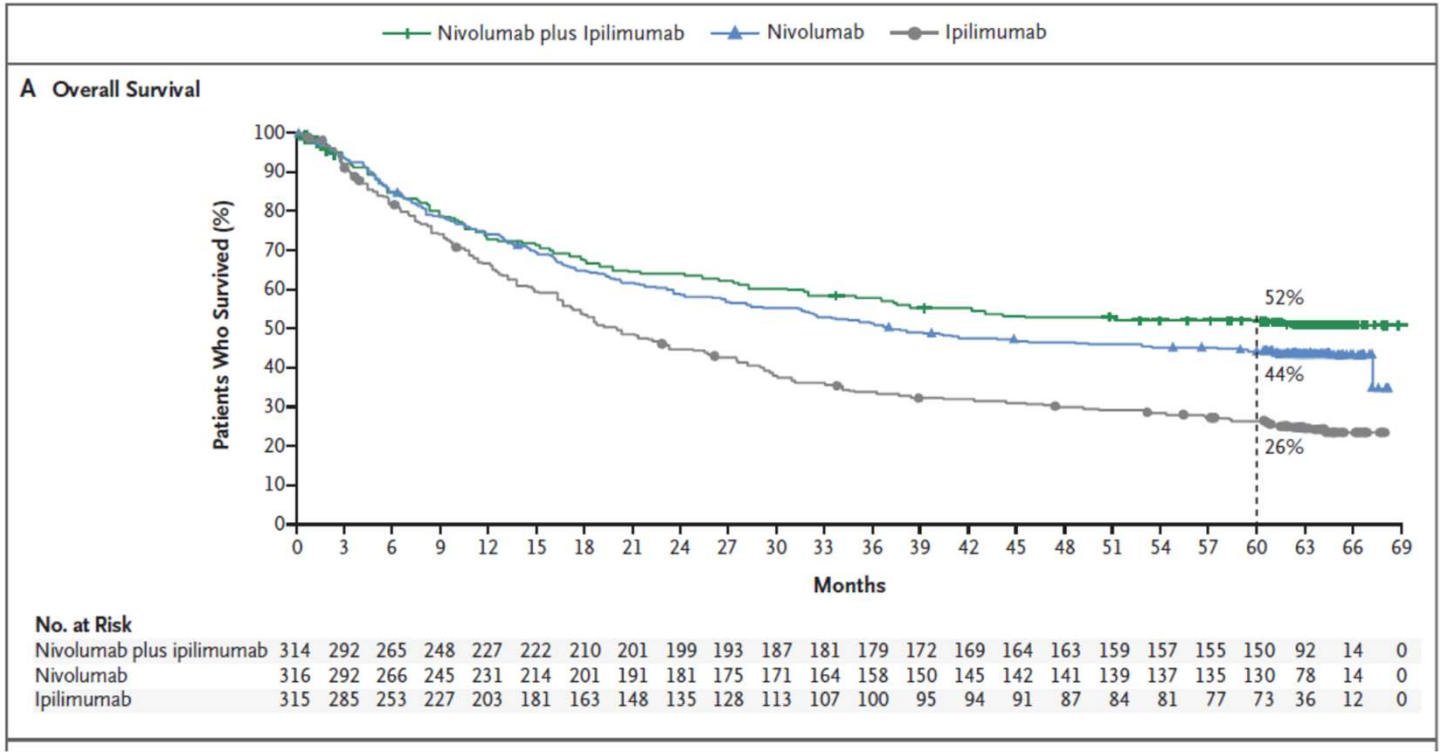
CANCER RESEARCH INSTITUTE

The Anna-Maria Kellen Clinical Accelerator

Durable efficacy of immunotherapy metastatic setting

Checkpoint inhibitors for metastatic melanoma patients



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NEJM 2019

Durable efficacy of immunotherapy adjuvant setting

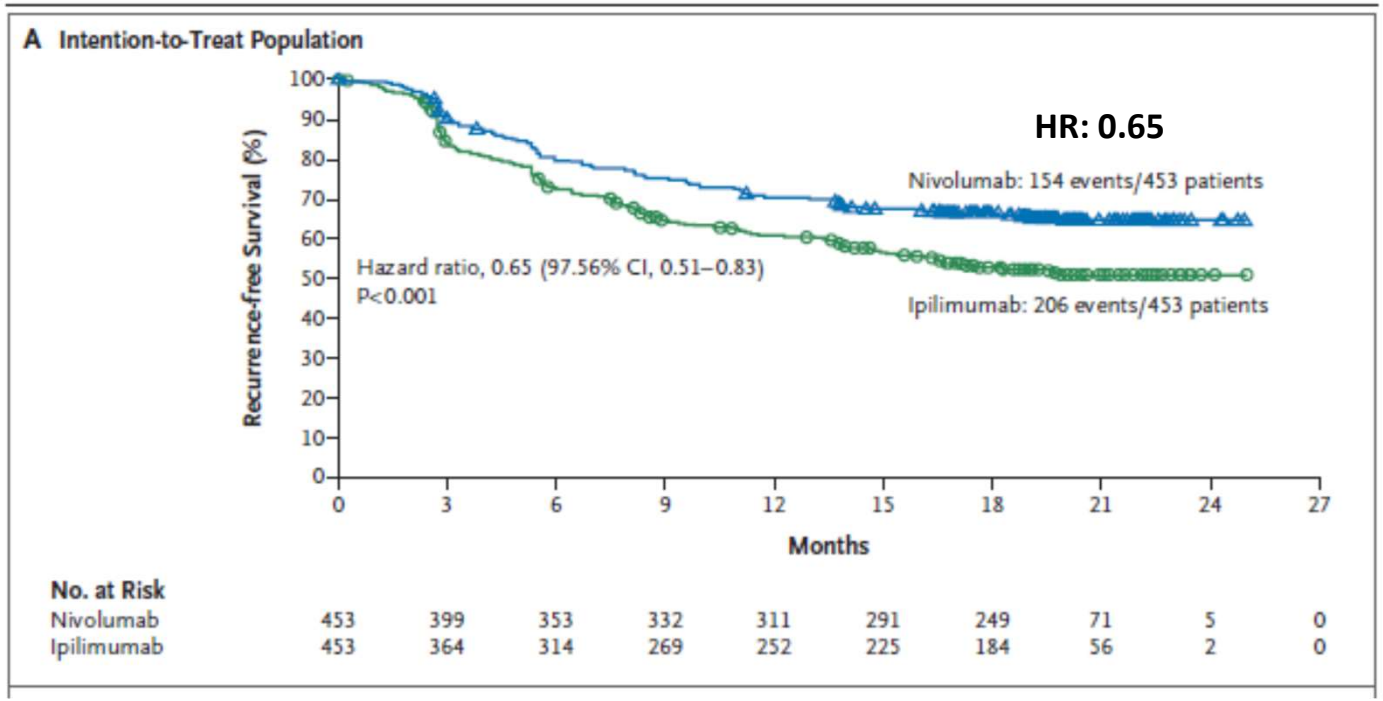
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma

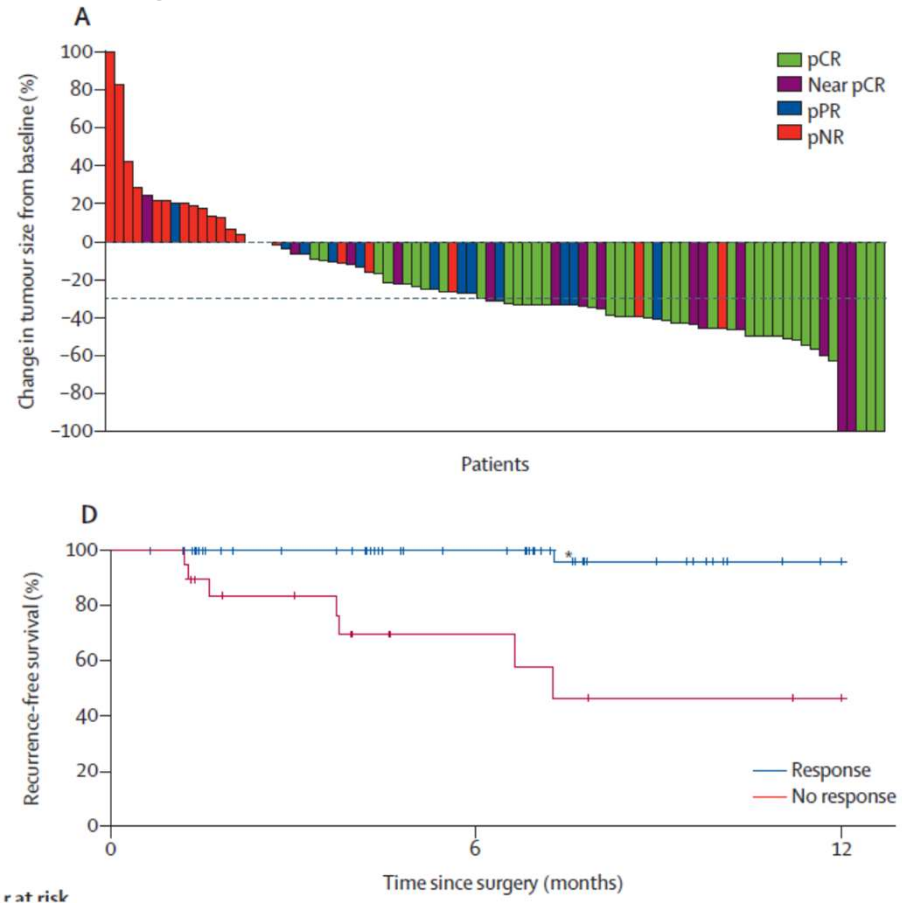
J. Weber, M. Mandala, M. Del Vecchio, H.J. Gogas, A.M. Arance, C.L. Cowey, S. Dalle, M. Schenker, V. Chiarion-Sileni, I. Marquez-Rodas, J.-J. Grob, M.O. Butler, M.R. Middleton, M. Maio, V. Atkinson, P. Queirolo, R. Gonzalez, R.R. Kudchadkar, M. Smylie, N. Meyer, L. Mortier, M.B. Atkins, G.V. Long, S. Bhatia, C. Lebbé, P. Rutkowski, K. Yokota, N. Yamazaki, T.M. Kim, V. de Pril, J. Sabater, A. Qureshi, J. Larkin, and P.A. Ascierto, for the CheckMate 238 Collaborators*

Adjuvant anti PD1 in stage III melanoma



Durable efficacy of immunotherapy neoadjuvant setting

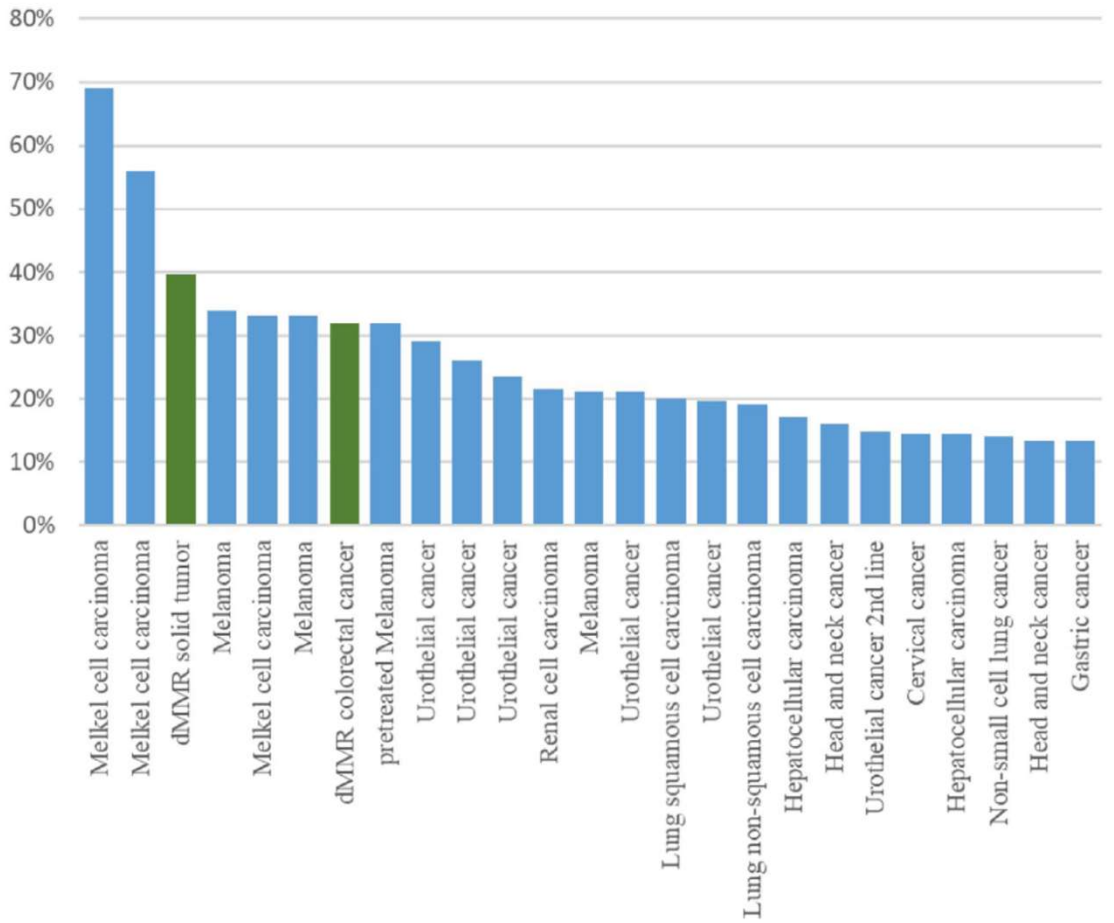
Neodadjuvant ipilimumab plus nivolumab in stage III melanoma



Blank, Lancet Oncol 2019

The challenge: Not all patients benefit from immunotherapy

Objective response rate with PD-1/PD-L1 inhibitors by cancer type



Therapeutic gap = progressive disease

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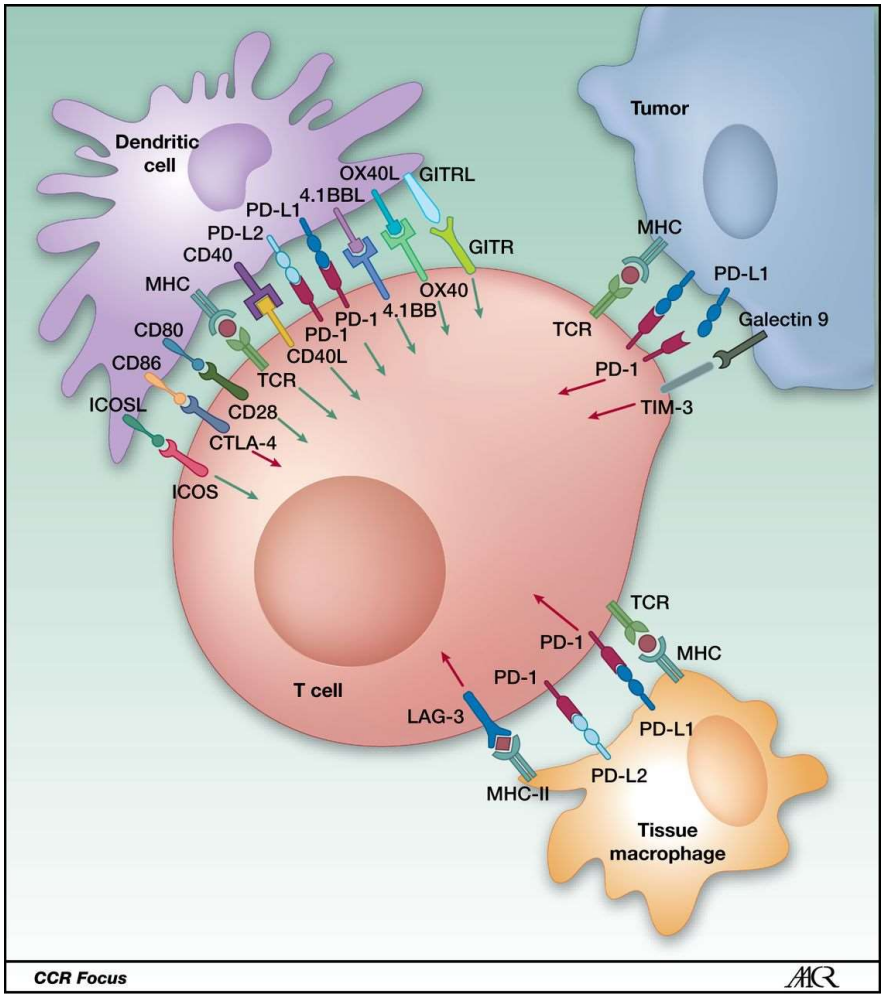
Mishima et al, Int J Clin Oncol 2019

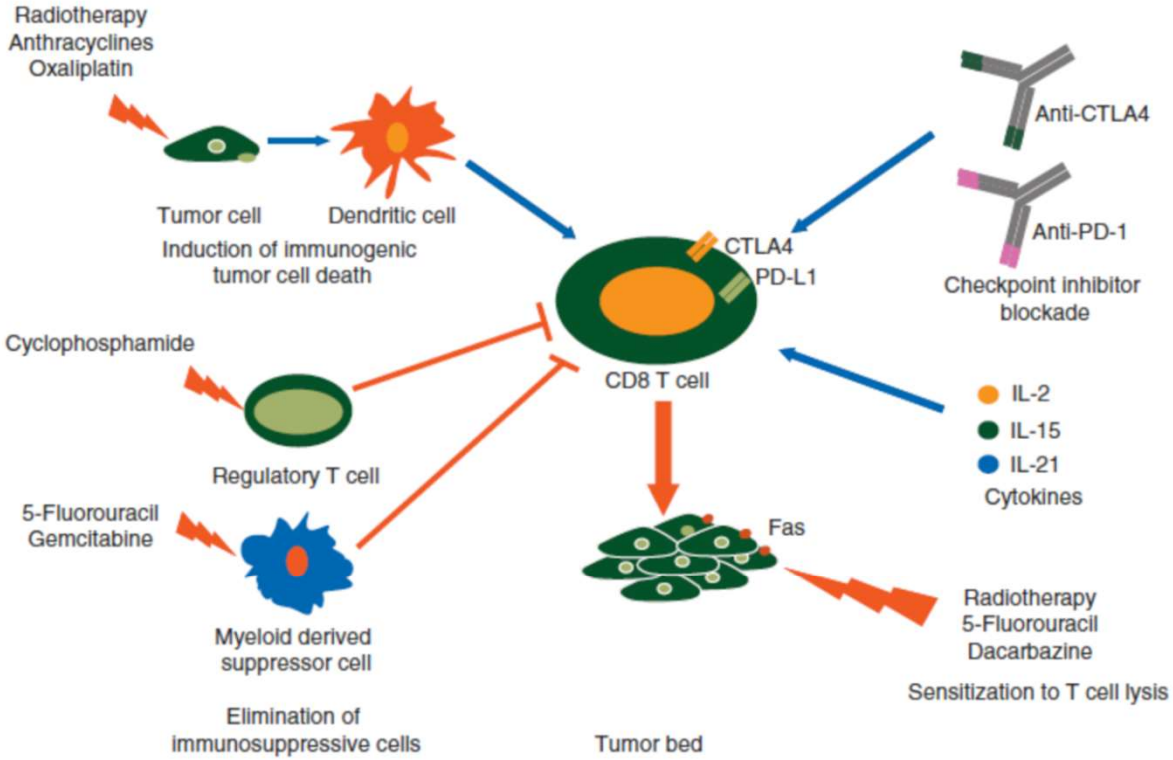
How can we increase the fraction of patients responding to immunotherapy?

More of the same: Many more immune check points are being explored for therapeutic targeting



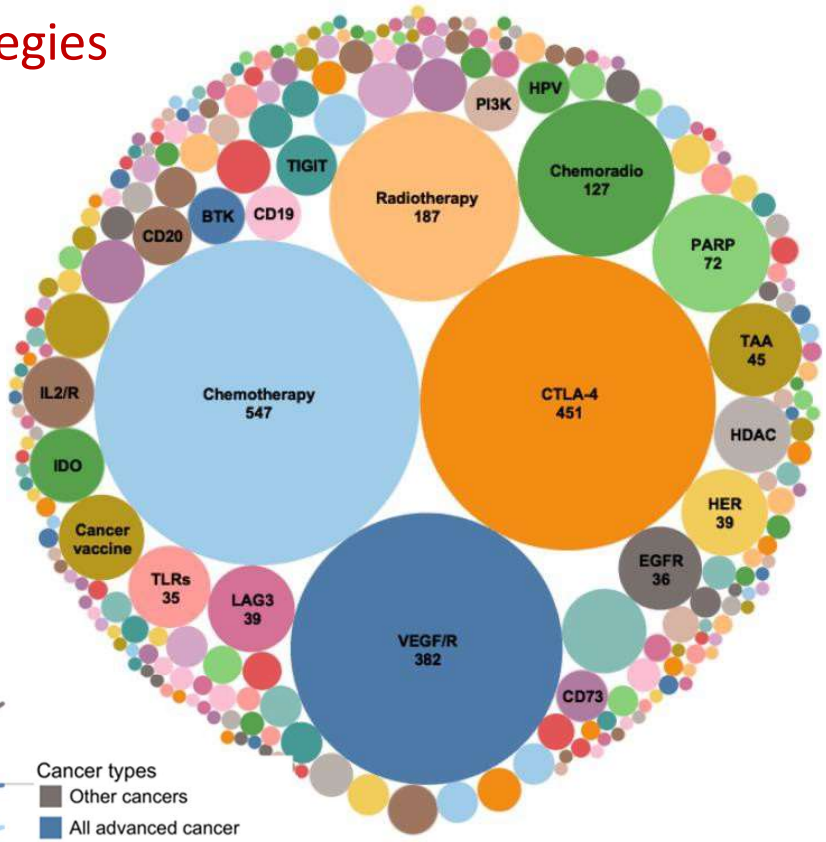
Ott P A et al. Clin Cancer Res 2013

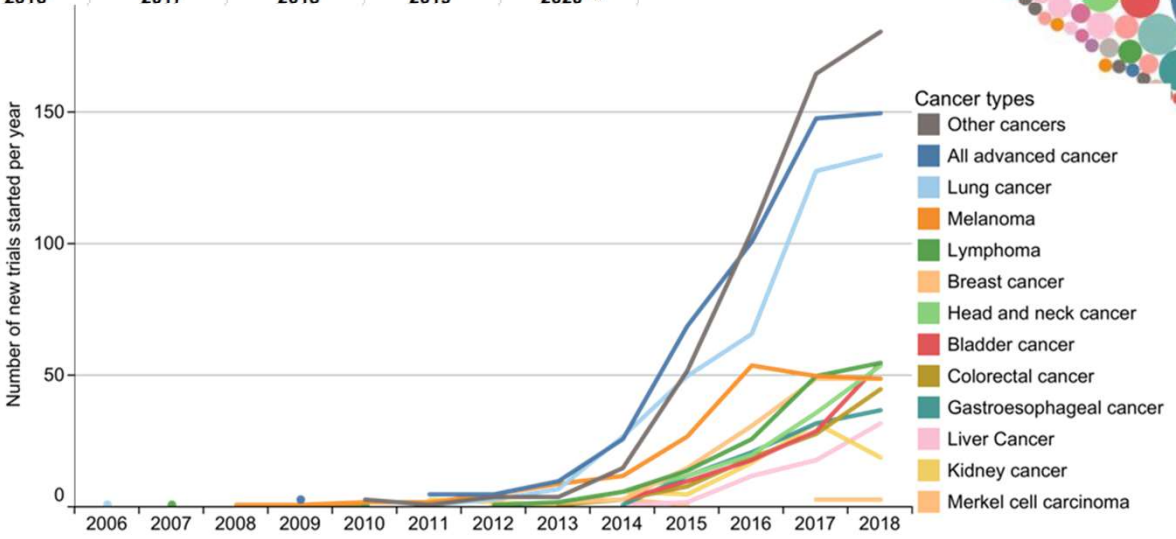
A look into the closet: Synergi with standard therapy



Apetoh et al, Annal Oncol 2015

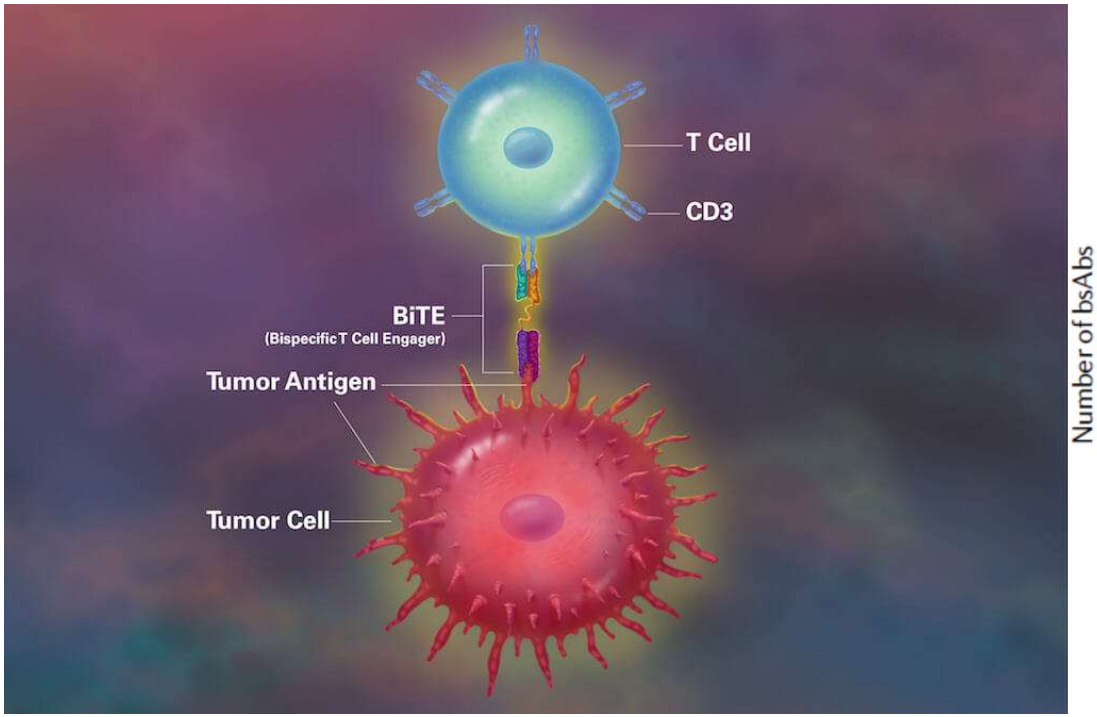
Development in check point inhibitor combination strategies



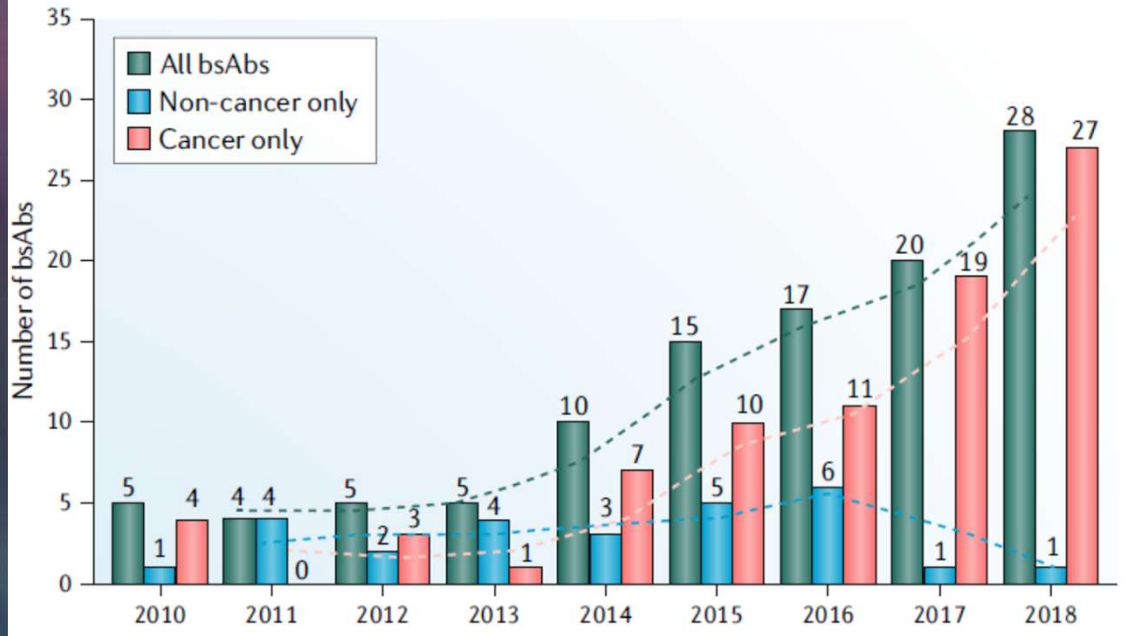


Upadhaya et al Nat Rev Drug Dev 2021

New strategies: Bispecific Antibodies



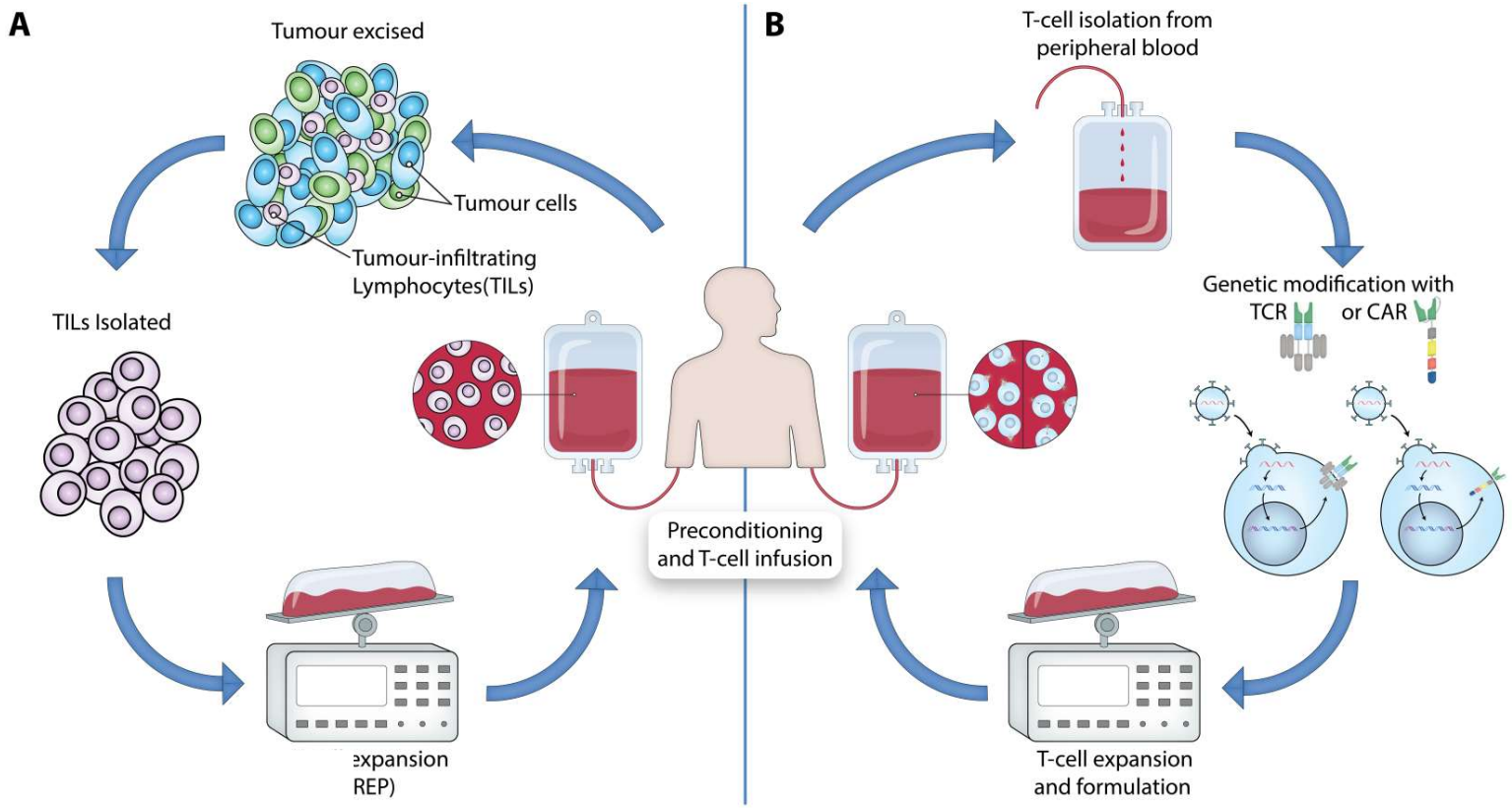
https://blog.dana-farber.org/insight/2019/05/how-are-bispecific-antibodies-being-used-to-treat-blood-cancers/



Labrijn et al Nat Rev Drug Dev 2019

New strategies: Adoptive Cell Therapies

Tumor infiltrating lymphocytes (TIL) and genetic modified T cells



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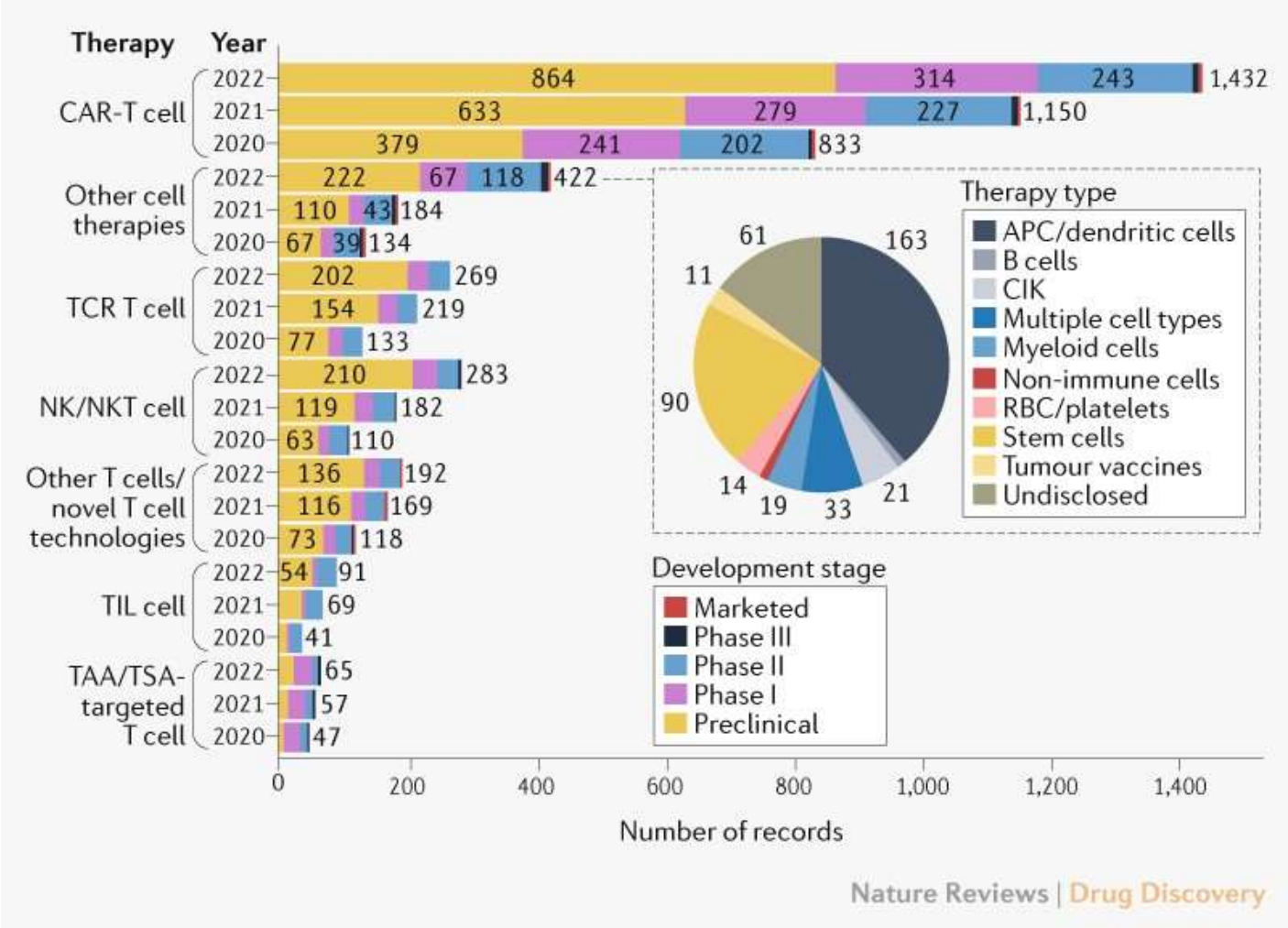
Met, Donia & Svane. ESMO Handbook of Immuno Oncology 2018

Developments in cellular therapy strategies



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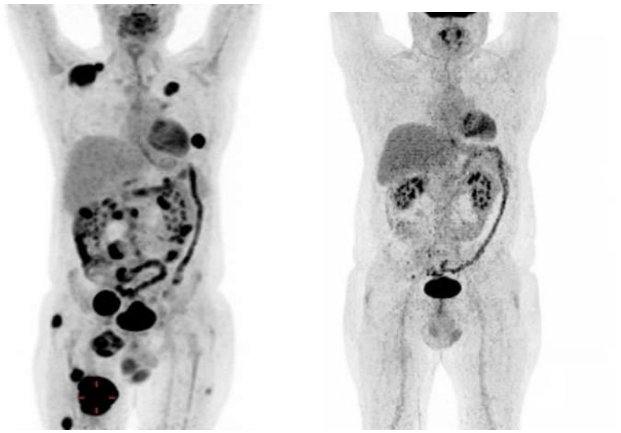
Saez-Ibanez et al Nat Rev Drug Discovery 2022

Academic Randomized phase III study comparing T cell therapy to standard therapy in melanoma patients

Durable response of T-cell therapy



2012 **2022**

Late Breaking Abstract on Presidential Session at ESMO 2022

Treatment with tumor-infiltrating lymphocytes (TIL) versus ipilimumab (IPI) for advanced melanoma: results from a multicenter, randomized phase 3 trial

John B.A.G. Haanen[a,b,c], Maartje W. Rohaan[a], Troels Holz Borch[d], Joost H. van den Berg[e], Özcan Met[d], Marnix H. Geukes Foppen[a], Joachim Stoltenborg Granhøj[d], Bastiaan Nuijen[f], Cynthia Nijenhuis[e], Jos H. Beijnen[f], Inge Jedema[b], Maaike van Zon[e], Inge Mansfield Noringriis[d], Rob Kessels[g], Sofie Wilgenhof[a], Johannes V. van Thienen[a], Ferry Lalezari[h], Alexander C.J. van Akkooi[i], Marco Donia[d], Inge Marie Svane[d]

July 2022 NKI and CCIT announce that the trial has met its primary endpoint

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T cell therapy version 2.0: Non-antigen specific modification of T cells

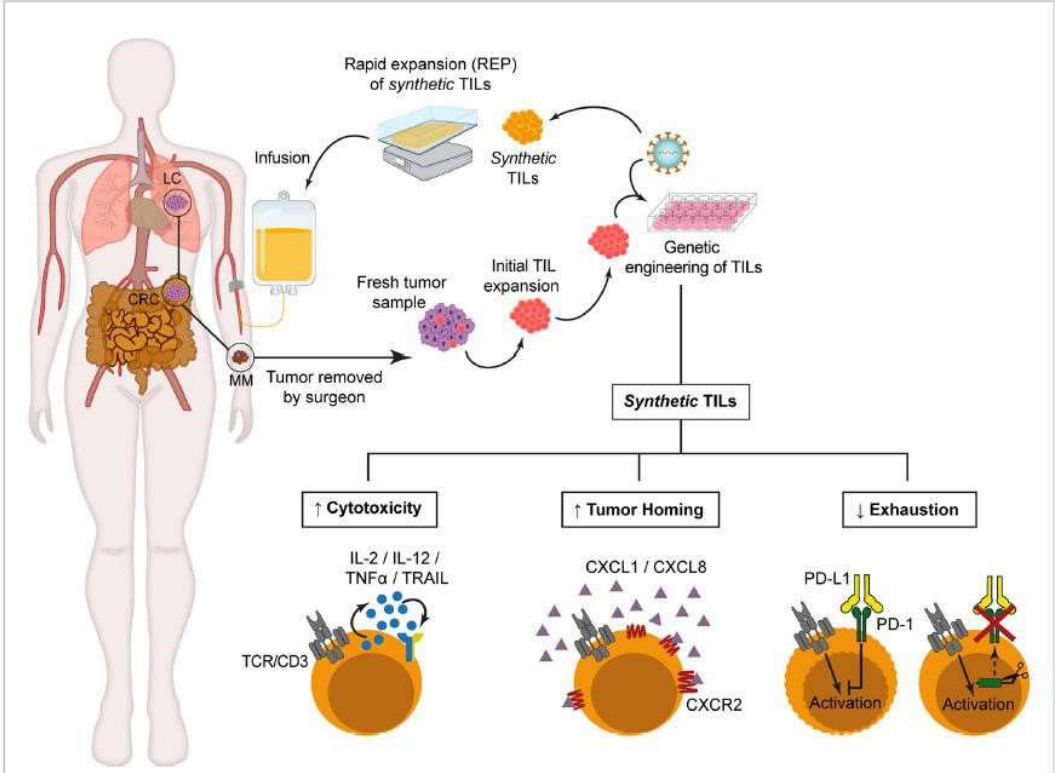
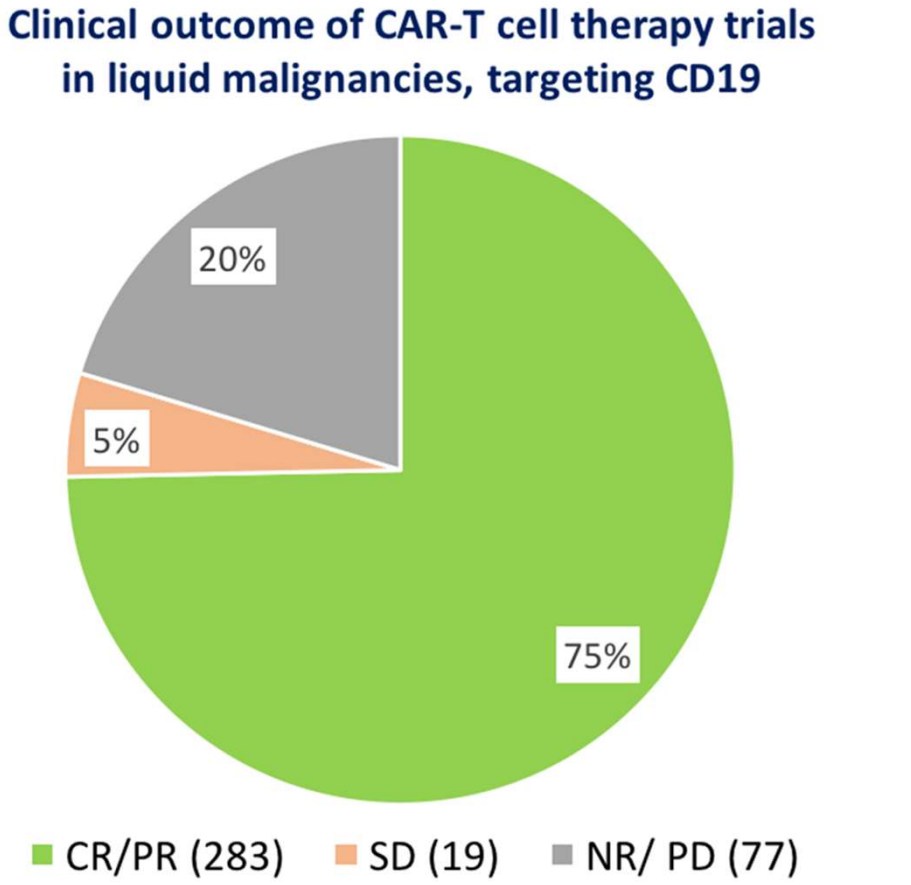


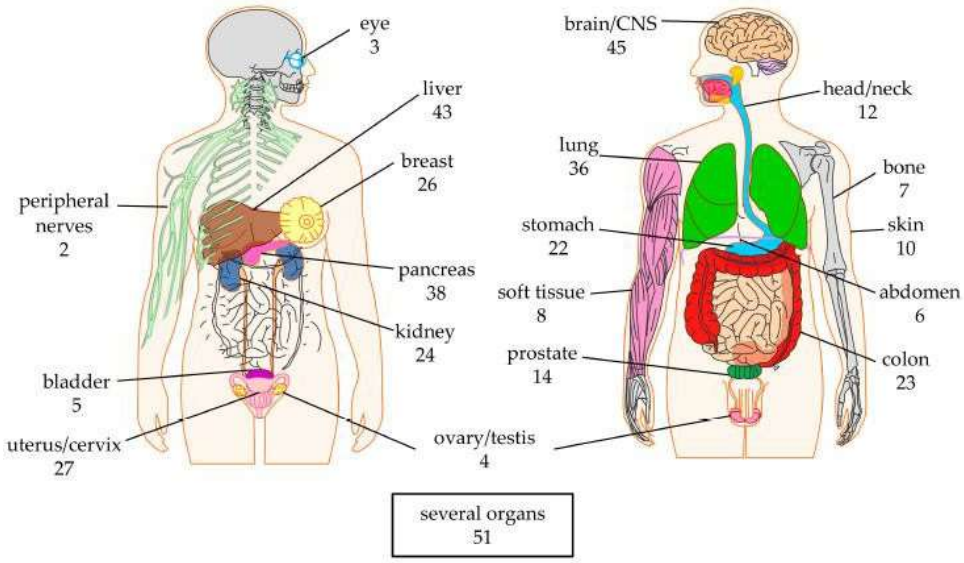
FIGURE 1 | *Synthetic* TILs manufacturing. After initial TILs isolation from fresh tumor fragments, retroviral or lentiviral vectors are used to genetically modified TILs in order to improve cytotoxicity, enhance tumor homing or reduce T cell exhaustion. Then, *synthetic* TILs are ex vivo expanded for 14 days in the presence of allogeneic irradiated peripheral blood mononuclear cells, soluble anti-CD3 antibodies and IL-2. Prior to synthetic TIL infusion, the patients receive lymphodepleting chemotherapy to ensure TIL persistence and expansion. CRC, Colorectal Cancer. LC, Lung Cancer. MM, Metastatic Melanoma..

Jiménez-Reinoso et al Front Oncol 2021

Gene modified T cells for adoptive therapy: CAR-T



CAR-T trials targeting solid tumors

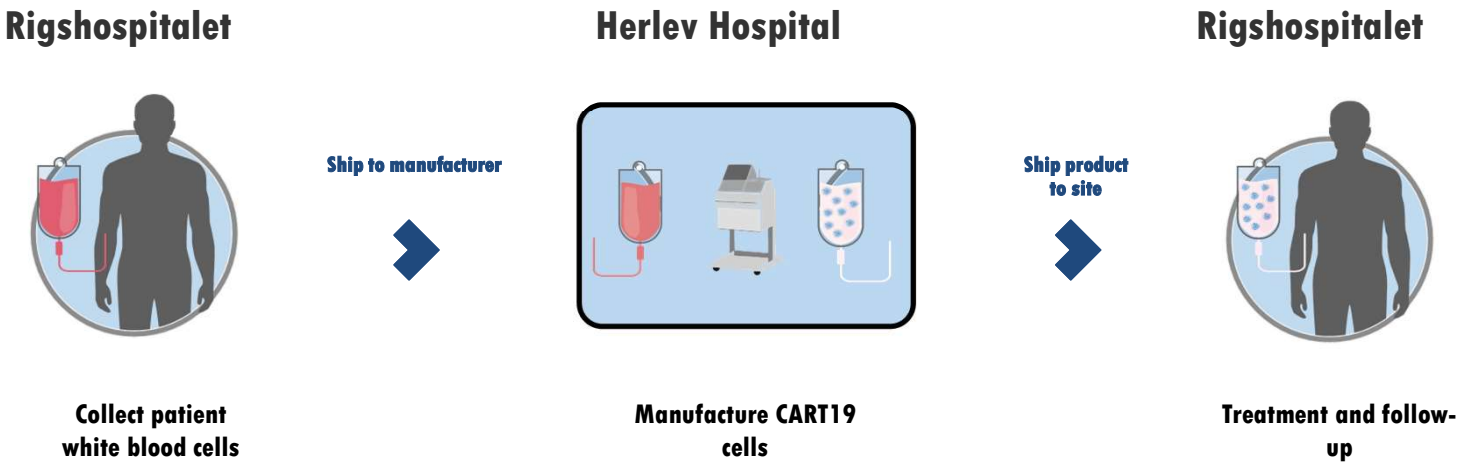


Response rate in general low in solid cancers

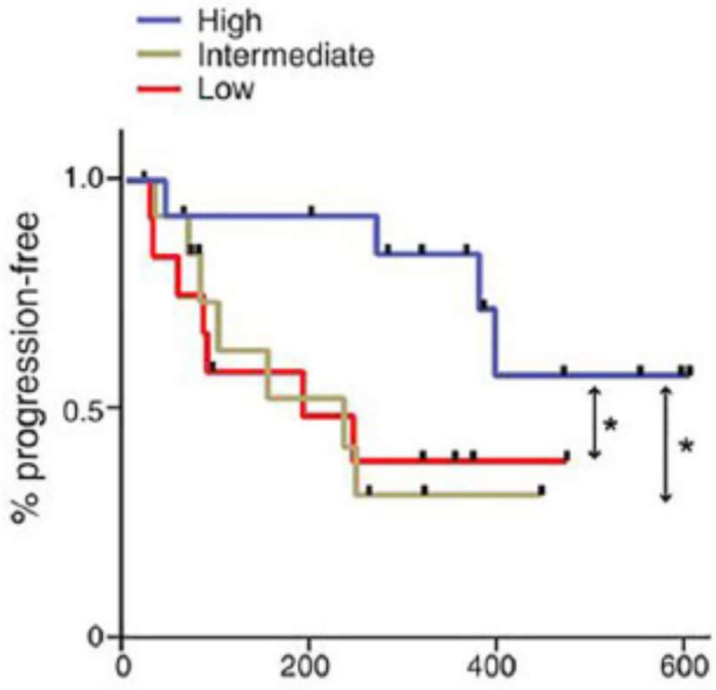
Cancers 2020, 12, 2567

Academic clinical trial on CAR-T

DK-CLIC-1901 CAR T-cells for treatment of patients with relapsed/refractory CD19-positive ALL and NHL (DAN-CART 1901)



Influencers: Gut microbiome influence response to immunotherapy

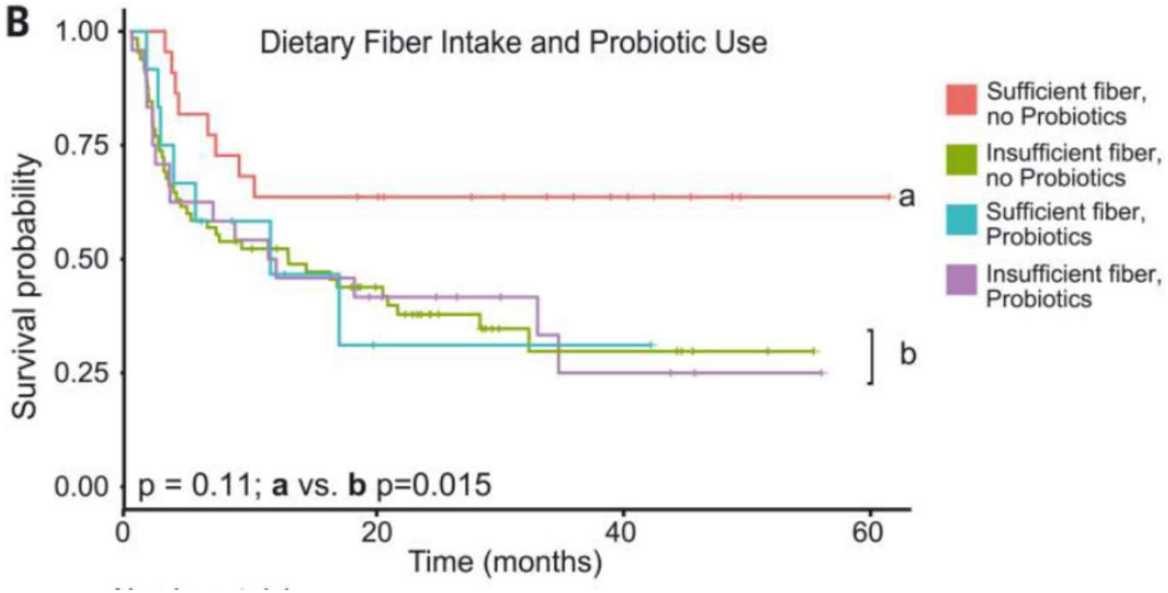


Enhanced gut microbiome diversity is associated with improved response to anti-PD-1 immunotherapy in patients with metastatic melanoma

Gopalakrishnan et al, Science 2018

Dietary influence: fiber and probiotics influence the gut microbiome and melanoma immunotherapy response

Progression free survival of melanoma patients during anti-PD1 therapy



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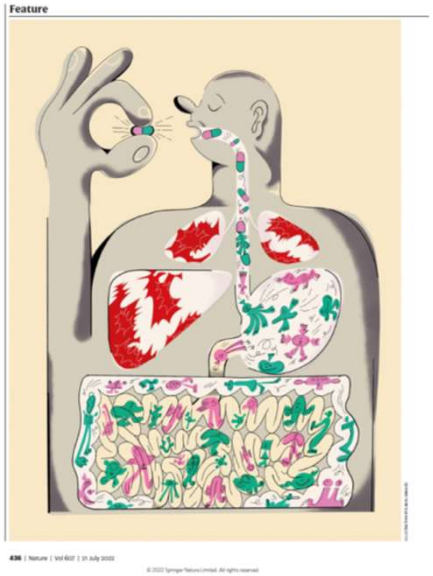
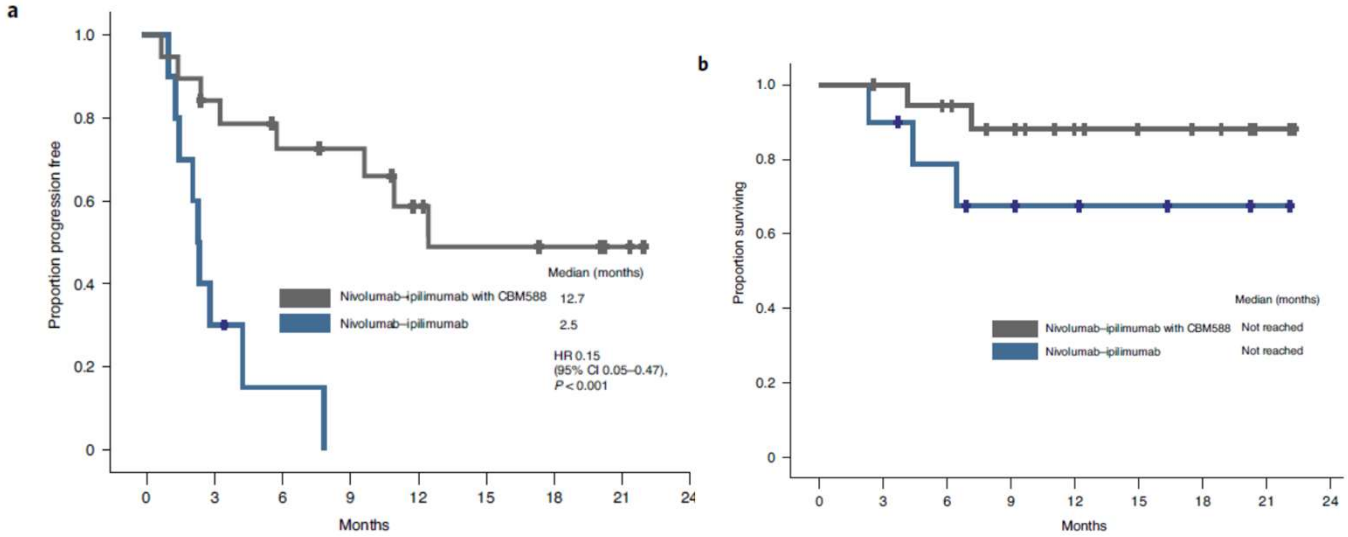
Spencer et al, Science 2021

Therapeutic manipulation: Bacterial supplementation increase immunotherapy efficacy



Nivolumab plus ipilimumab with or without live bacterial supplementation in metastatic renal cell carcinoma: a randomized phase 1 trial



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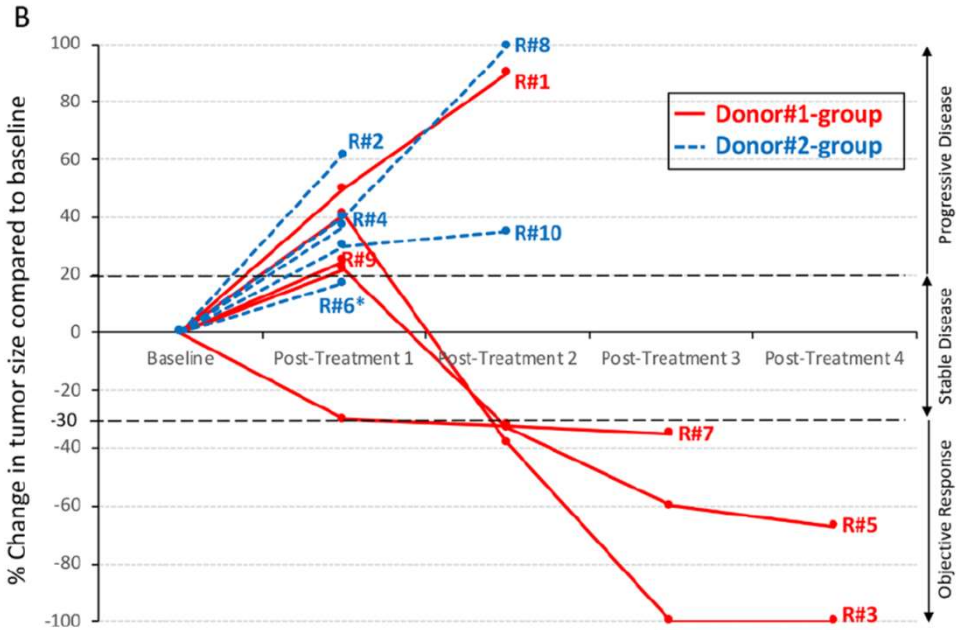
Dizman et al, Nature Medicine 2022

Therapeutic stool: Fecal microbiota transplantation from responder patient induce response to immunotherapy in refractory patients

Two FMT donors who had previously been treated with anti-PD-1 monotherapy for metastatic melanoma and achieved a CR for at least one year



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Baruch et al, Science 2020

A look in the crystal ball

Standard combinations

More checkpoint inhibitors

Influencers

Cellular Therapies

Bispecifics

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