IMMUNO-ONCOLOGY FROM CHECKPOINT-INHIBITORS TO TIL AND CAR-T THERAPY

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DISCLOSURE INFORMATION

I have the following financial relationships to disclose:

I have provided consultation, attended advisory boards, and/or provided lectures for: Agenus, AZ, BMS, CureVac, GSK, Imcyse, Iovance Bio, Immunocore, Ipsen, Merck Serono, MSD, Molecular Partners, Novartis, Orgenesis, Pfizer, Roche/Genentech, Sanofi, Third Rock Ventures

I participated in the SAB of Achilles Tx, BioNTech, Instil Bio, PokeAcell, T-Knife, Scenic and Neogene Therapeutics (AZ).

Through my work NKI received grant support from Amgen, Asher Bio, BioNTech, BMS, MSD, Novartis, Sastra Cell Therapy

I am Editor-in-Chief of ESMO IOTECH

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Antoni van Leeuwenhoek

CANCER IMMUNOTHERAPY

…fighting cancer by unleashing or harnessing the immune system to combat cancer…

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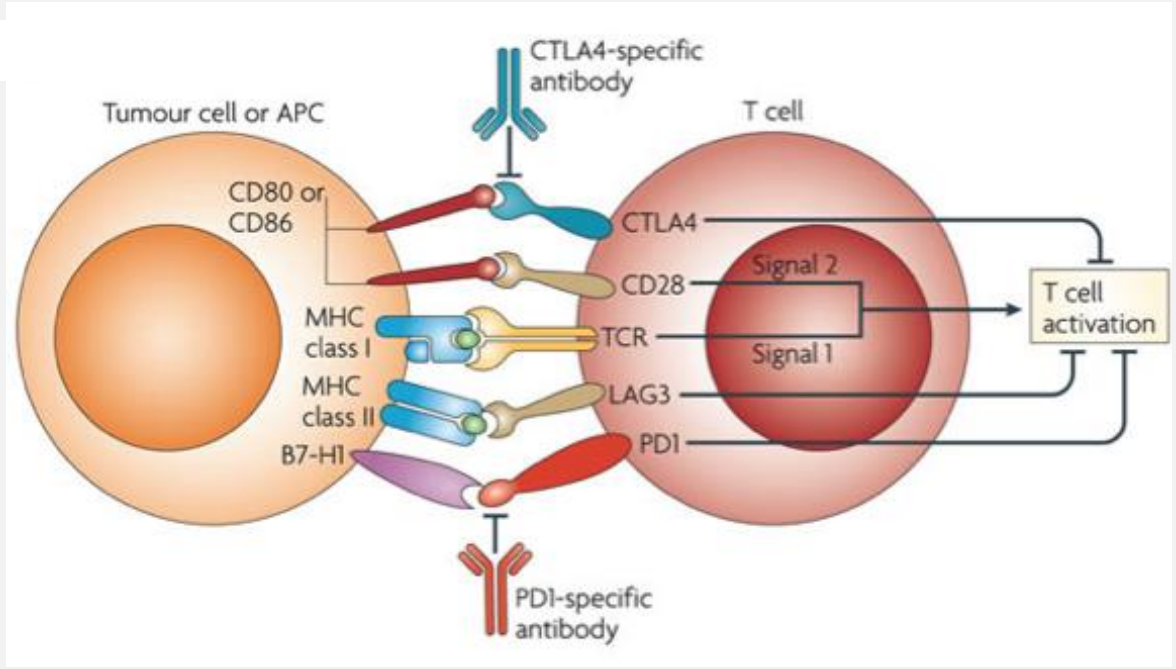
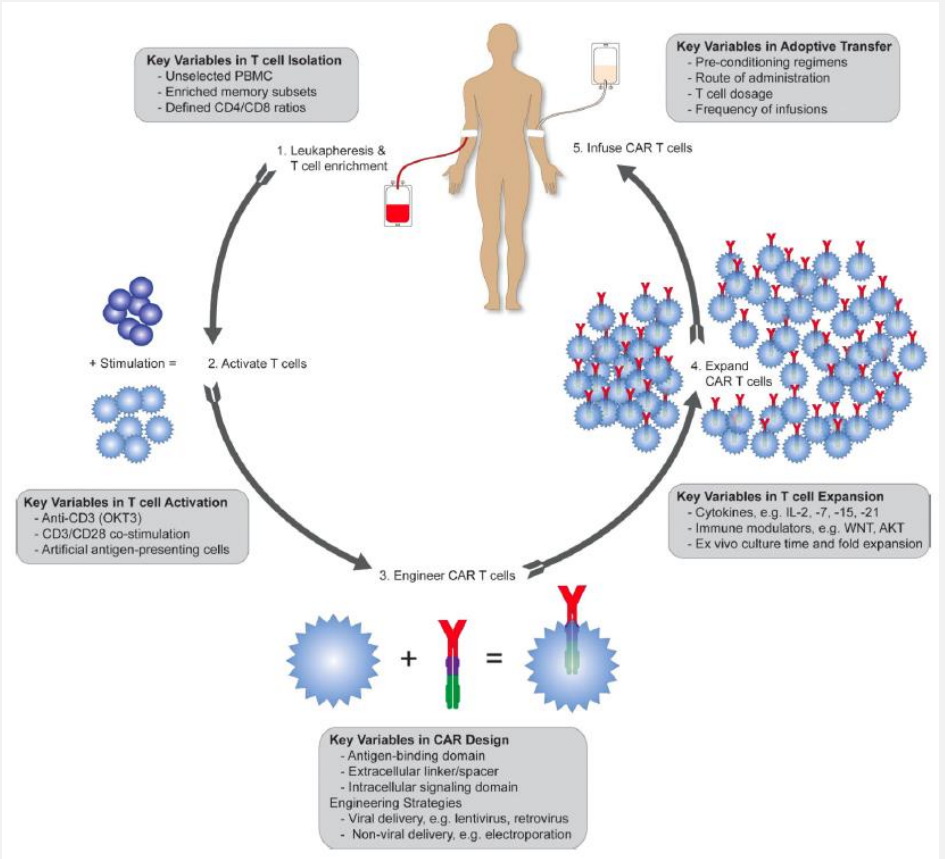


Priceman et al. Curr Opin Immunol 2015



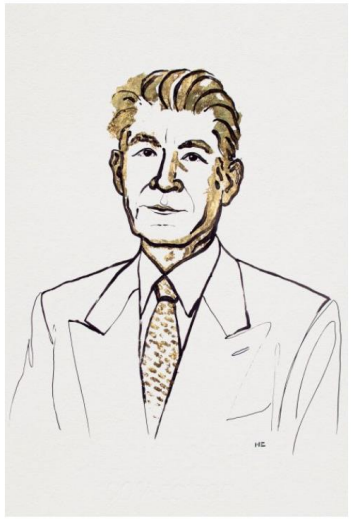
Nobelförsamlingen
The Nobel Assembly at Karolinska Institutet

The Nobel Prize in Physiology or Medicine 2018

Ill. Niklas Elmehed. © Nobel Media

James P. Allison

Prize share: 1/2



Ill. Niklas Elmehed. © Nobel Media

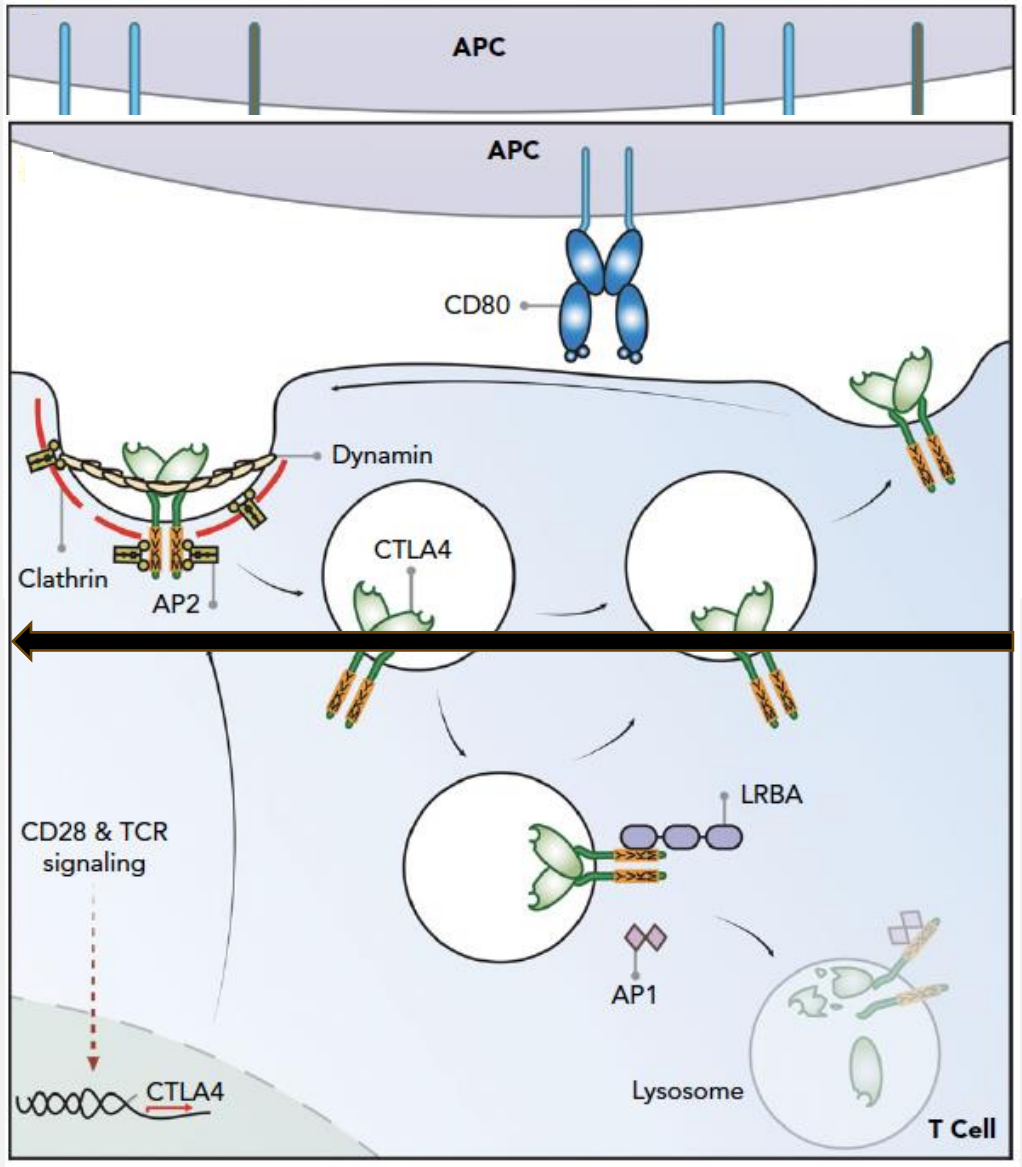
Tasuku Honjo

Prize share: 1/2

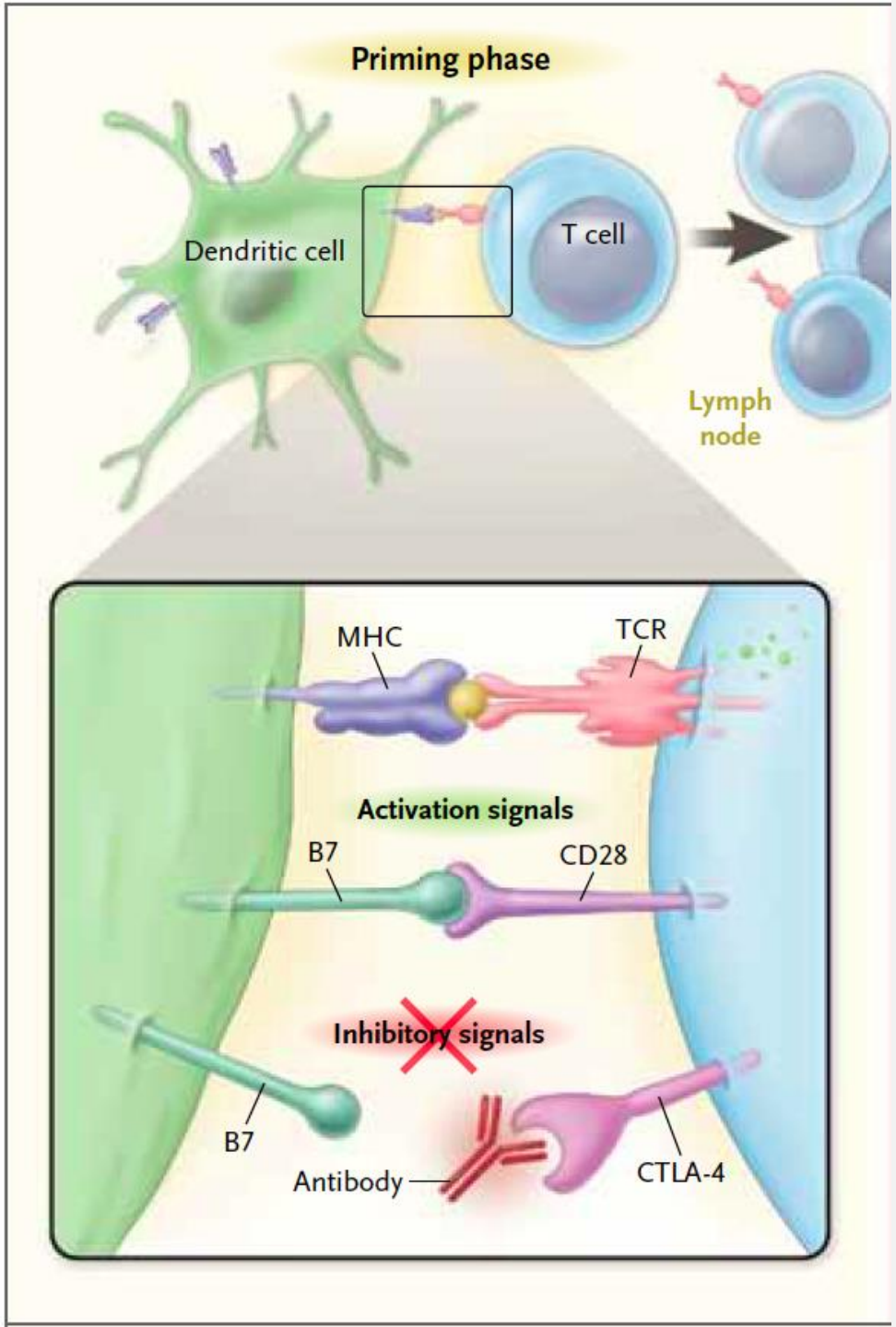
The Nobel Prize in Physiology or Medicine 2018 was awarded jointly to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation."

CD28 AND CTLA4

- CD28 and CTLA4 bind the same targets CD80 and CD86
- CTLA4 binds however these targets with higher affinity
- Timing of expression is different. CTLA4 expression is initiated following TCR/CD28 triggering
- CTLA4 is highly expressed on Tregs



Rowshanravan et al., Blood 2018



ANTI-CTLA4 BLOCKS CTLA4-CD80/86 INTERACTION?

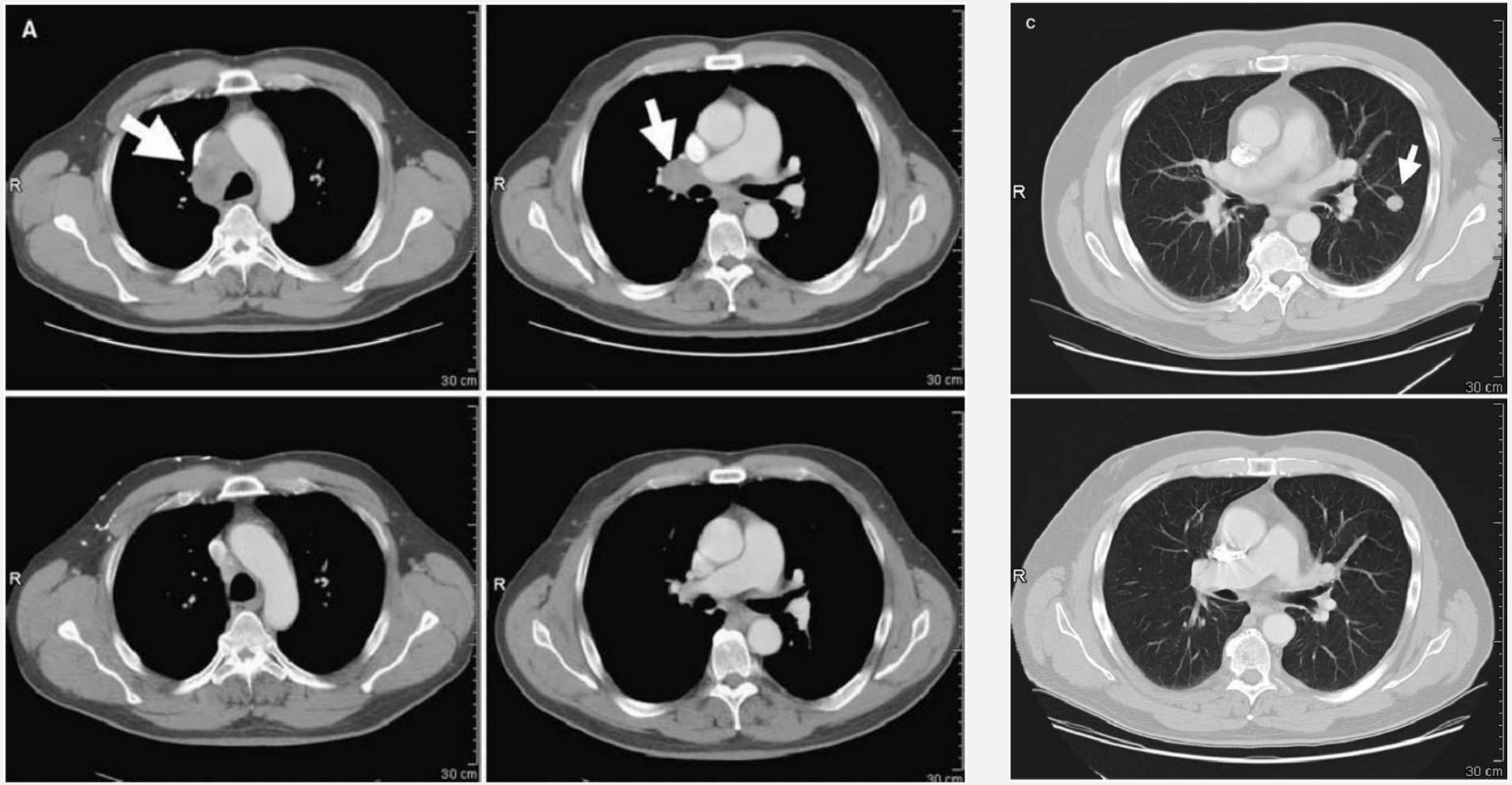
- Newly emerged data show that anti-CTLA4 is still active without blocking CTLA4 - CD80/86 interaction
- Anti-CTLA4 is highly effective in depleting Tregs
- Lineage-specific KO of *ctla4* in Tregs is enough to recapitulate the auto-immune phenomenon observed in *ctla4* -/- mice

Ribas. N Engl J Med 2012; Du et al., Cell Research 2018

TREATMENT WITH ANTI-CTLA-4 MAB

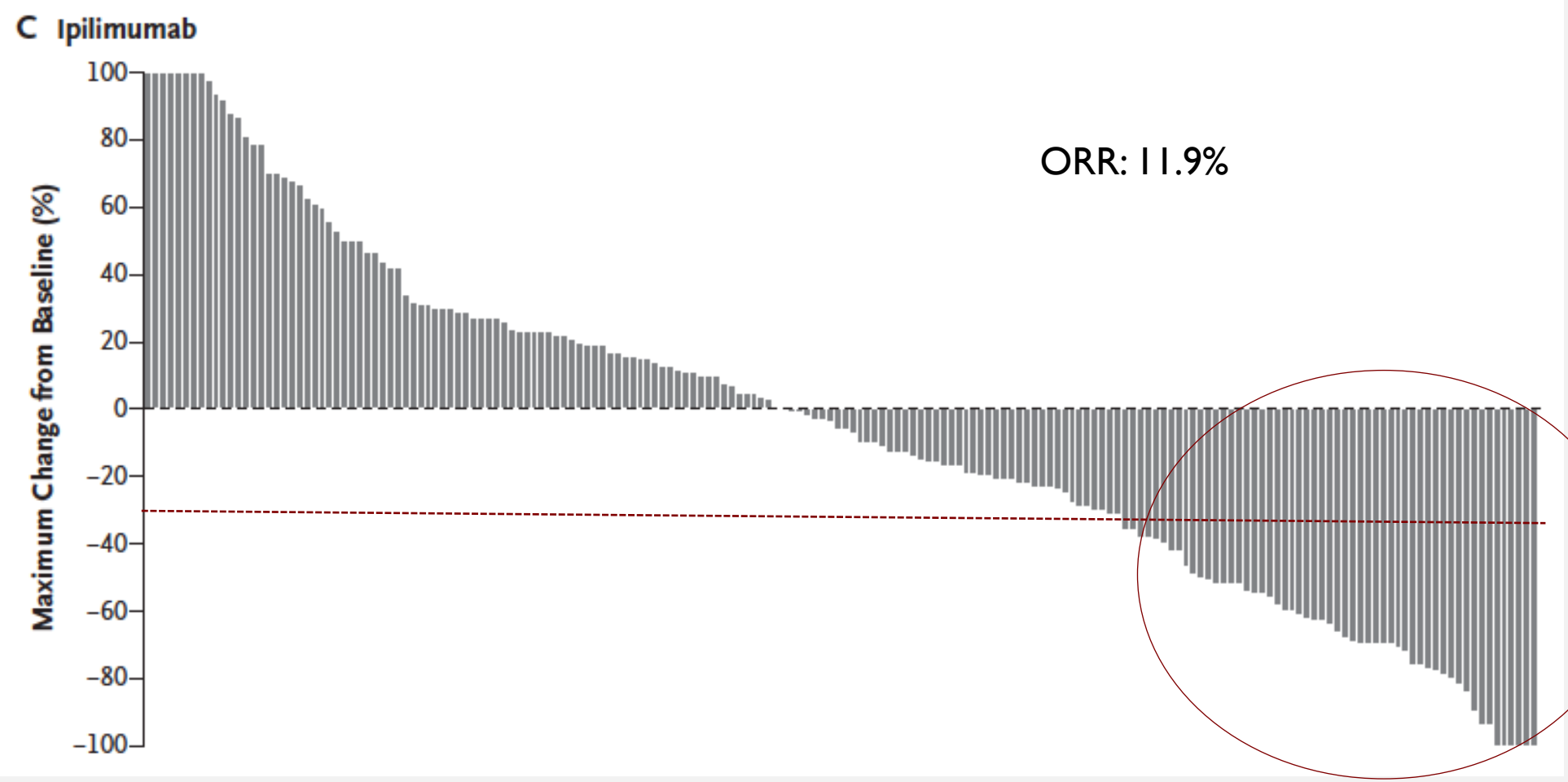
before

after



Maker et al., Ann Surg Oncol 2005

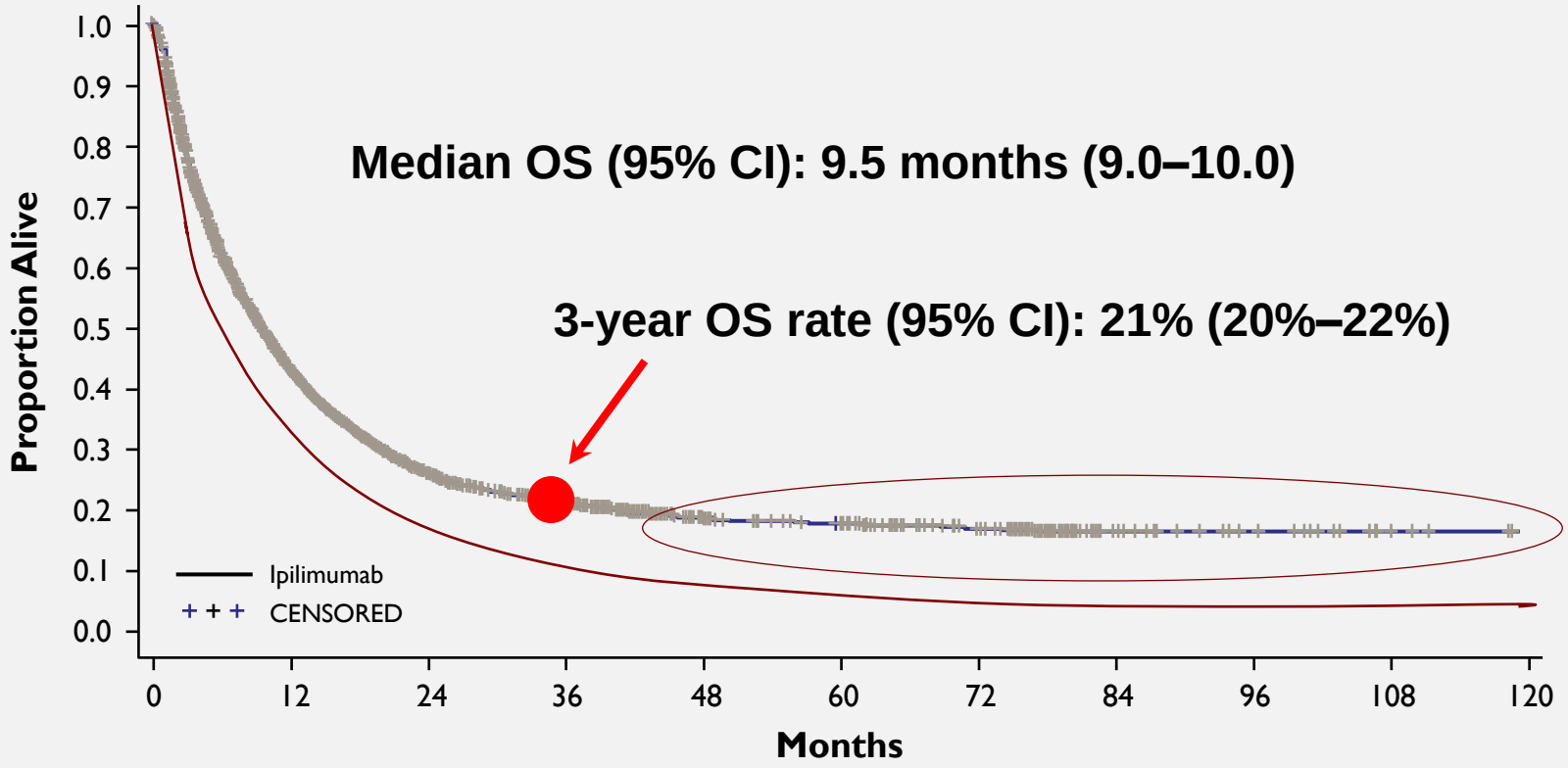
EFFICACY OF IPILIMUMAB AS FIRST LINE TREATMENT FOR MELANOMA



Robert et al., NEJM 2015

CTLA-4 blockade (ipilimumab) can induce long-term survival

(pooled overall survival analysis including Expanded Access Program data from 4846 patients)

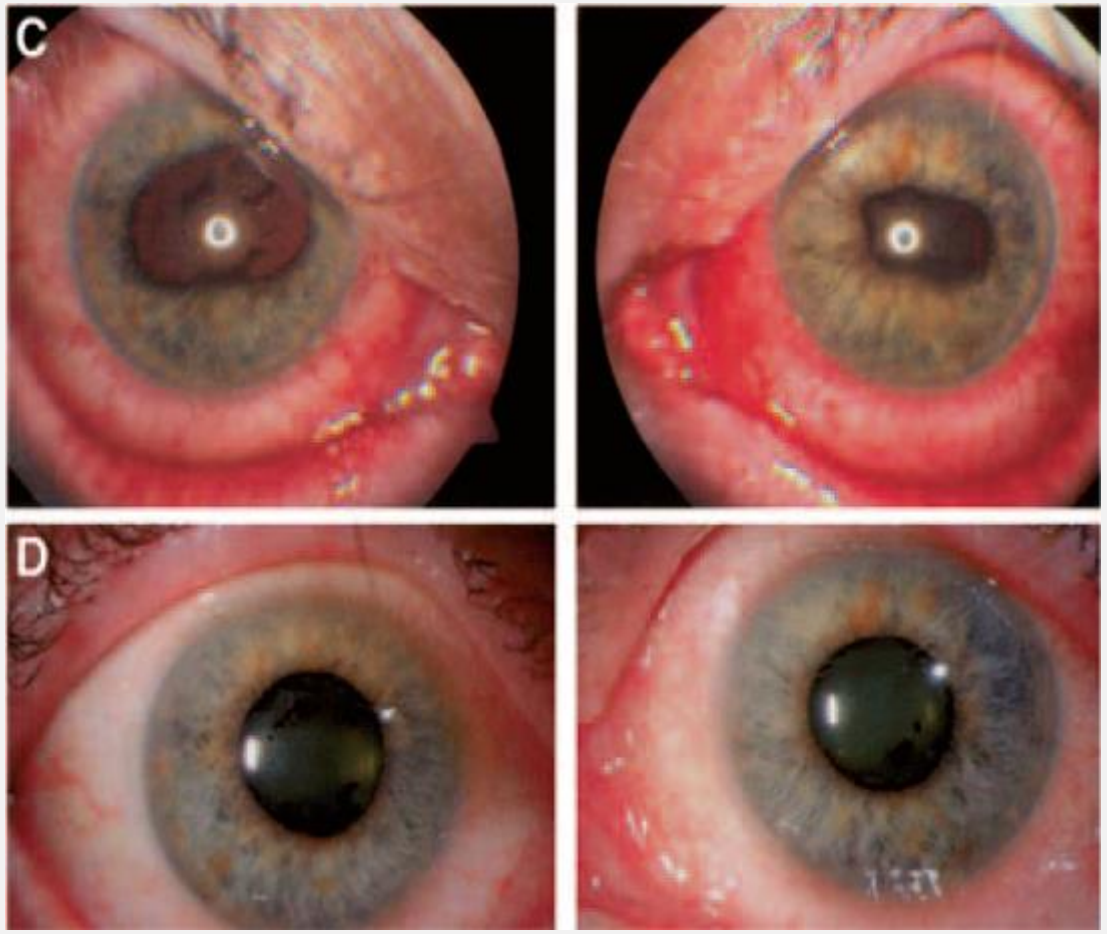


Patients at Risk

Ipilimumab	4846	1786	612	392	200	170	120	26	15	5	0

Schadendorf D, et al. J Clin Oncol 2015

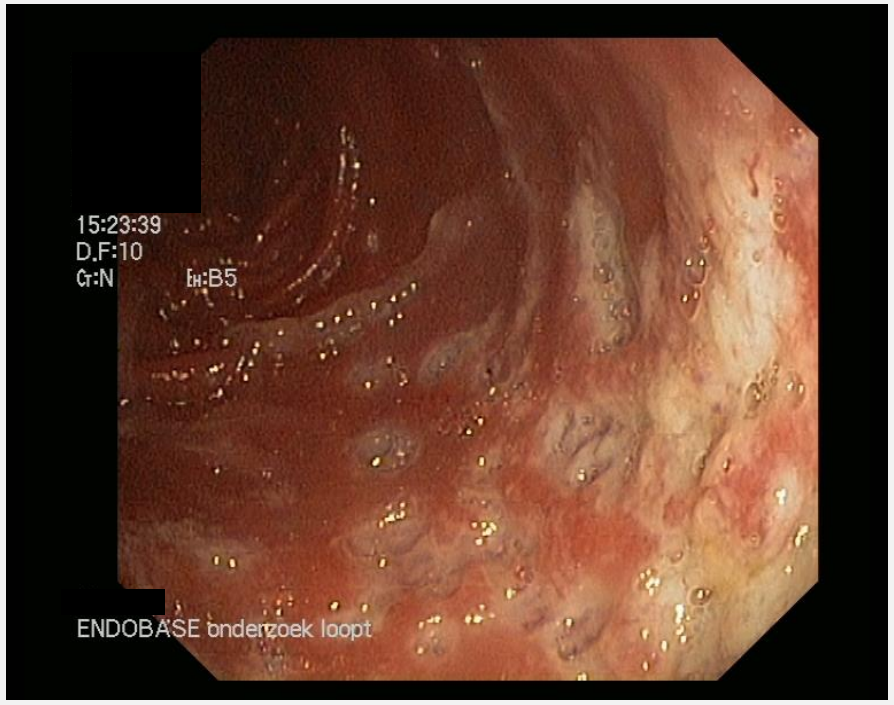
AUTO-IMMUNE UVEITIS AFTER ANTI-CTLA-4 TREATMENT



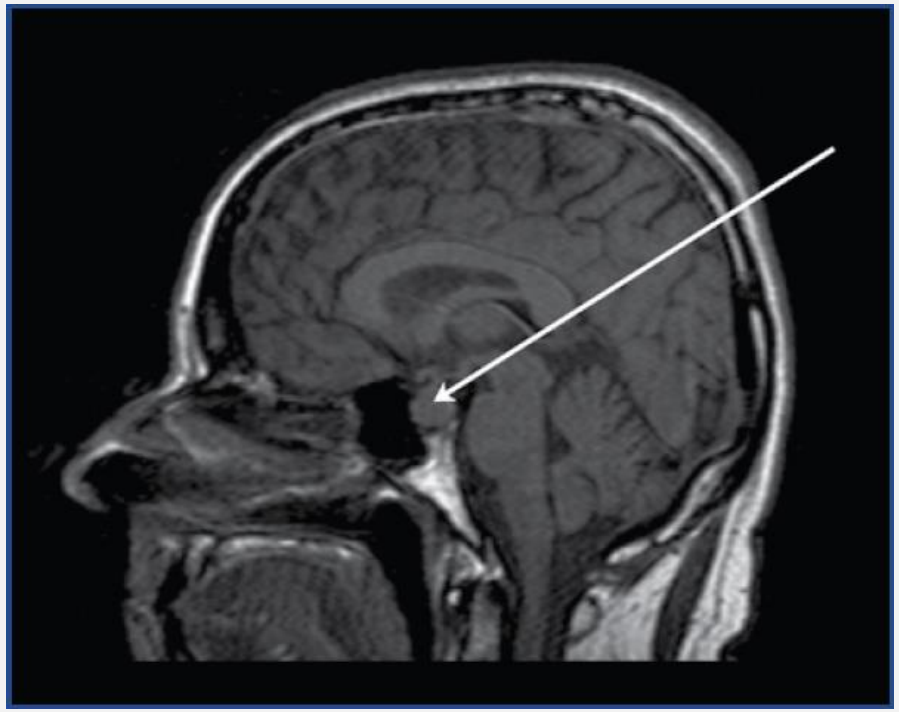
After treatment

IMMUNE RELATED ADVERSE EVENTS UPON ANTI-CTLA-4 MAB TREATMENT

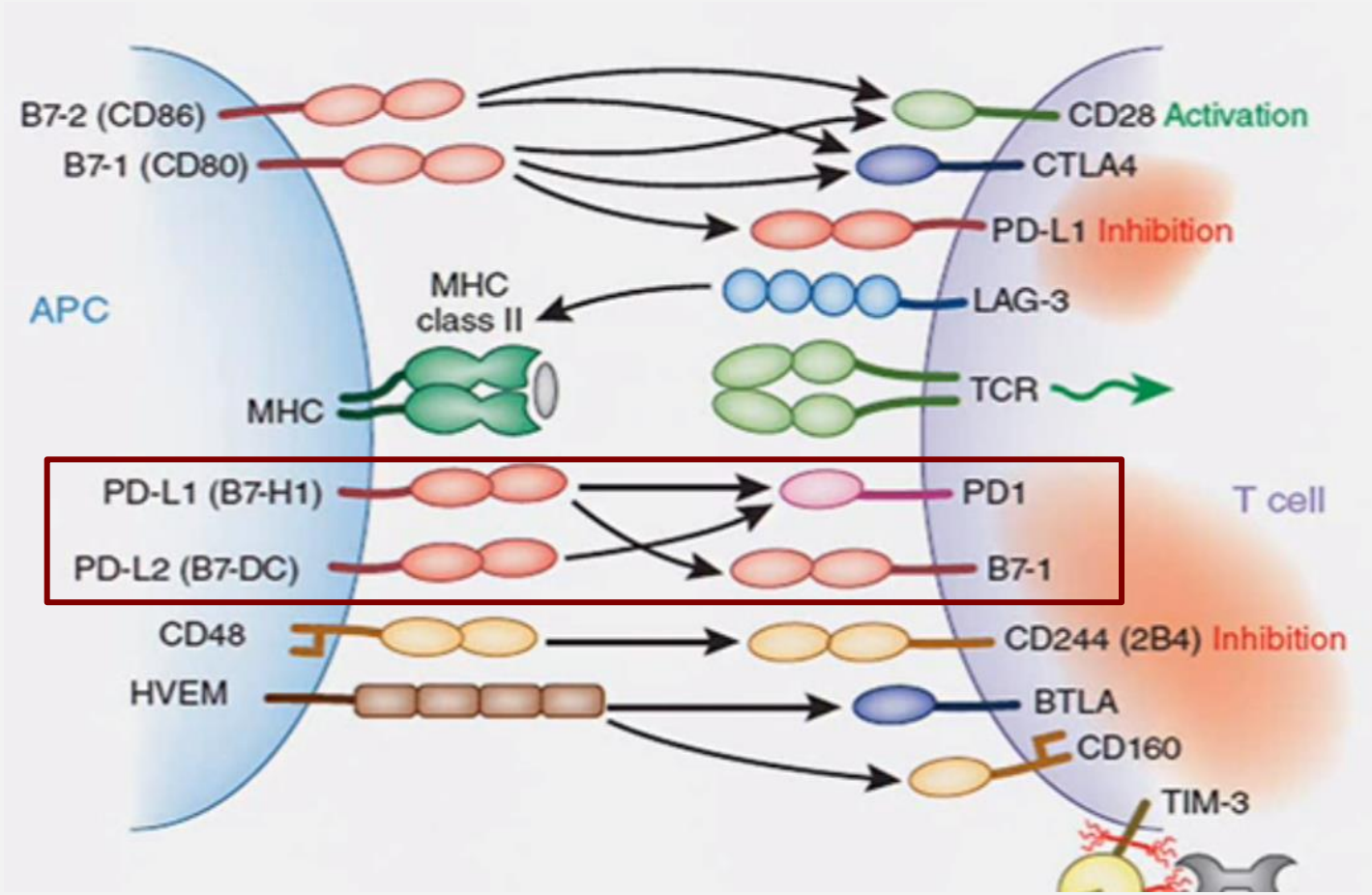
colitis



hypophysitis



PD1 AND PD-L1 IMMUNE CHECKPOINTS

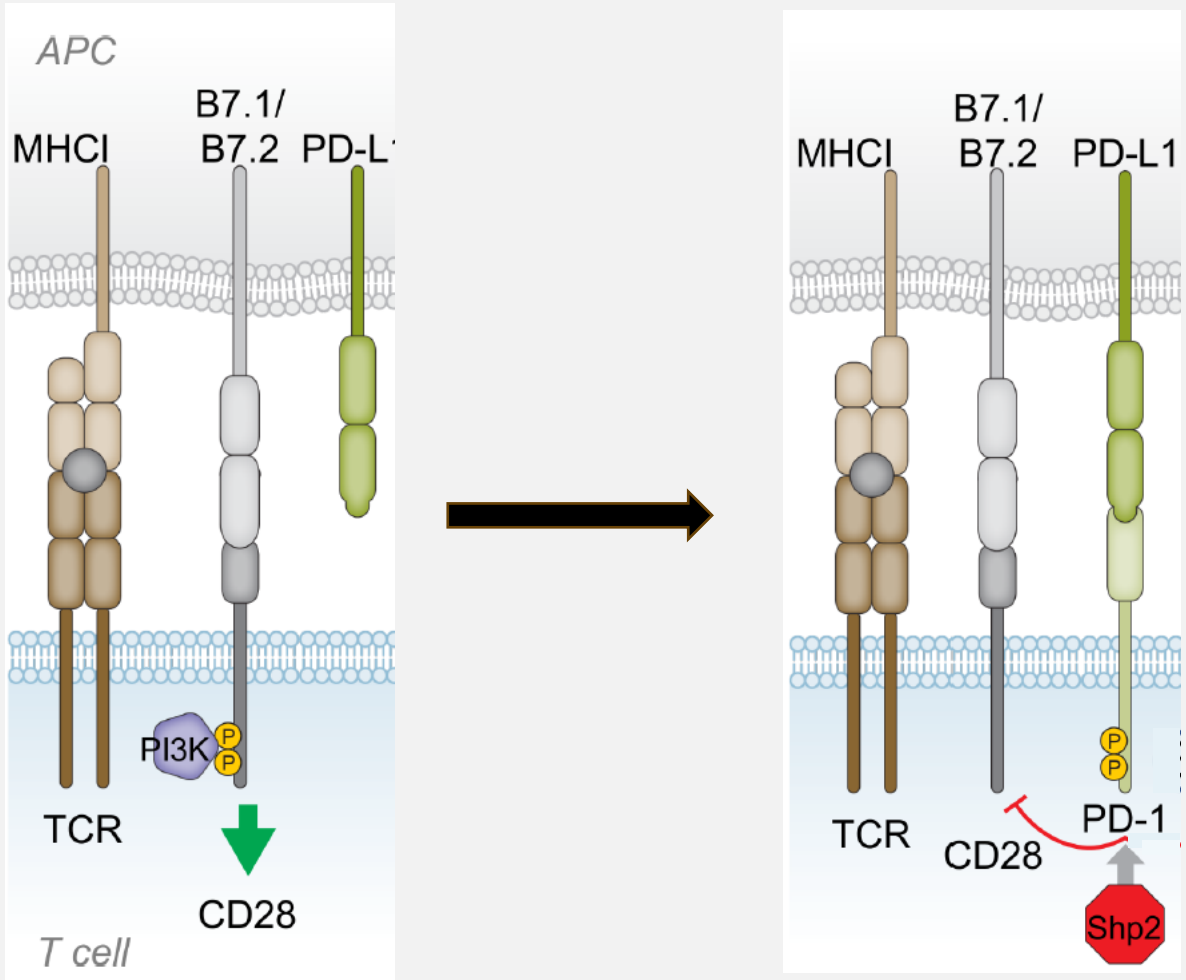


Freeman & Sharpe. Nat Immunol 2013

PROGRAMMED DEATH-1 RECEPTOR (PD1)

- Discovered in 1992 by Honjo and coworkers
  - Upregulated gene in relation to apoptosis
- Member of the Ig superfamily
- Cytoplasmic domains with ITIM and ITSM
  - Recruites phosphatases
  - Inhibits PI3K and AKT activity
- Inducibly expressed by CD4 and CD8 T cells, NKT cells, B cells, monocytes and subtypes of DC
- Expressed by both effector and regulatory T cells
- PD1/PD-L1 interaction involved in tolerance and chronic inflammation
- PD1/PD-L1 contributes to functional T cell exhaustion during chronic infection and cancer

PD-1 pathway inhibits T cell response directly downstream of the TCR and CD28



Adopted from Chiang & Mellman, JiTC 2022

Immunity, Vol. 11, 141–151, August, 1999, Copyright ©1999 by Cell Press

Development of Lupus-like Autoimmune Diseases by Disruption of the *PD-1* Gene Encoding an ITIM Motif-Carrying Immunoreceptor

Hiroyuki Nishimura,* Masato Nose,§
Hiroshi Hiai,† Nagahiro Minato,‡
and Tasuku Honjo*‖

(reviewed by Miller and Flavell, 1994). Similar,
tight, self-tolerance mechanisms are also consid
operate in B cells (reviewed by Goodnow et al.,

Autoimmune Dilated Cardiomyopathy in PD-1 Receptor–Deficient Mice

Hiroyuki Nishimura,[1] Taku Okazaki,[1] Yoshimasa Tanaka,[2]
Kazuki Nakatani,[6] Masatake Hara,[3] Akira Matsumori,[3]
Shigetake Sasayama,[3] Akira Mizoguchi,[4] Hiroshi Hiai,[5]
Nagahiro Minato,[2] Tasuku Honjo[1]*

Nishimura et al. Immunity 1999; Nishimura et al., Science 2001

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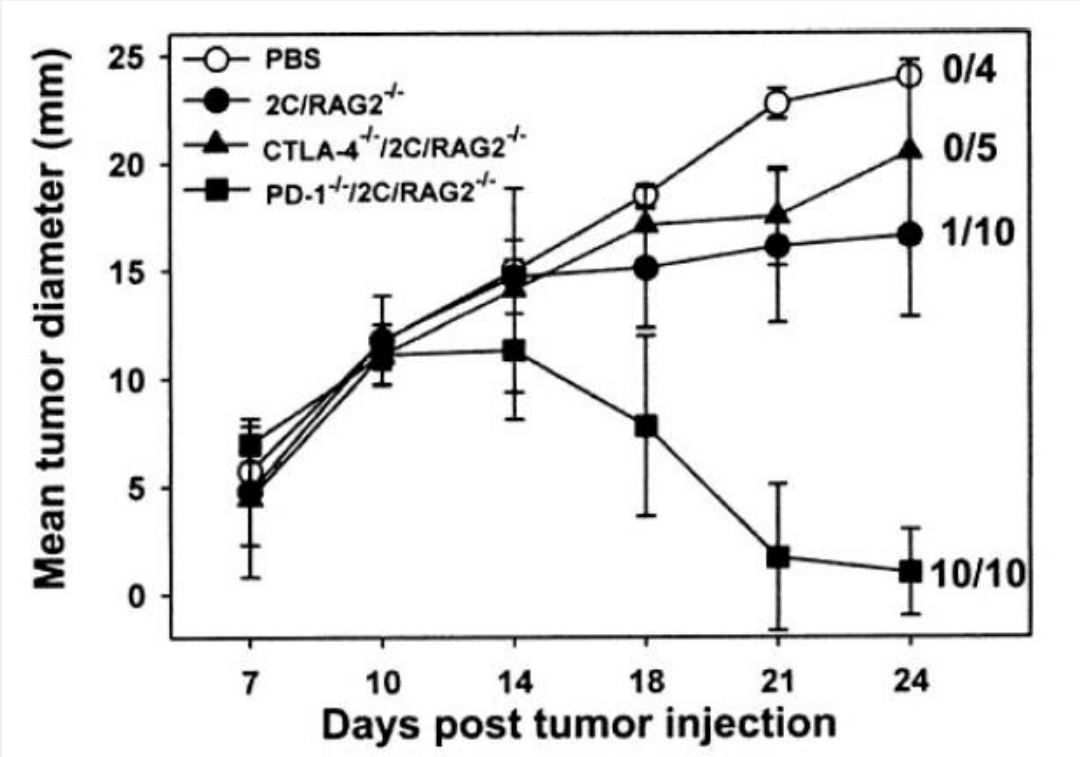
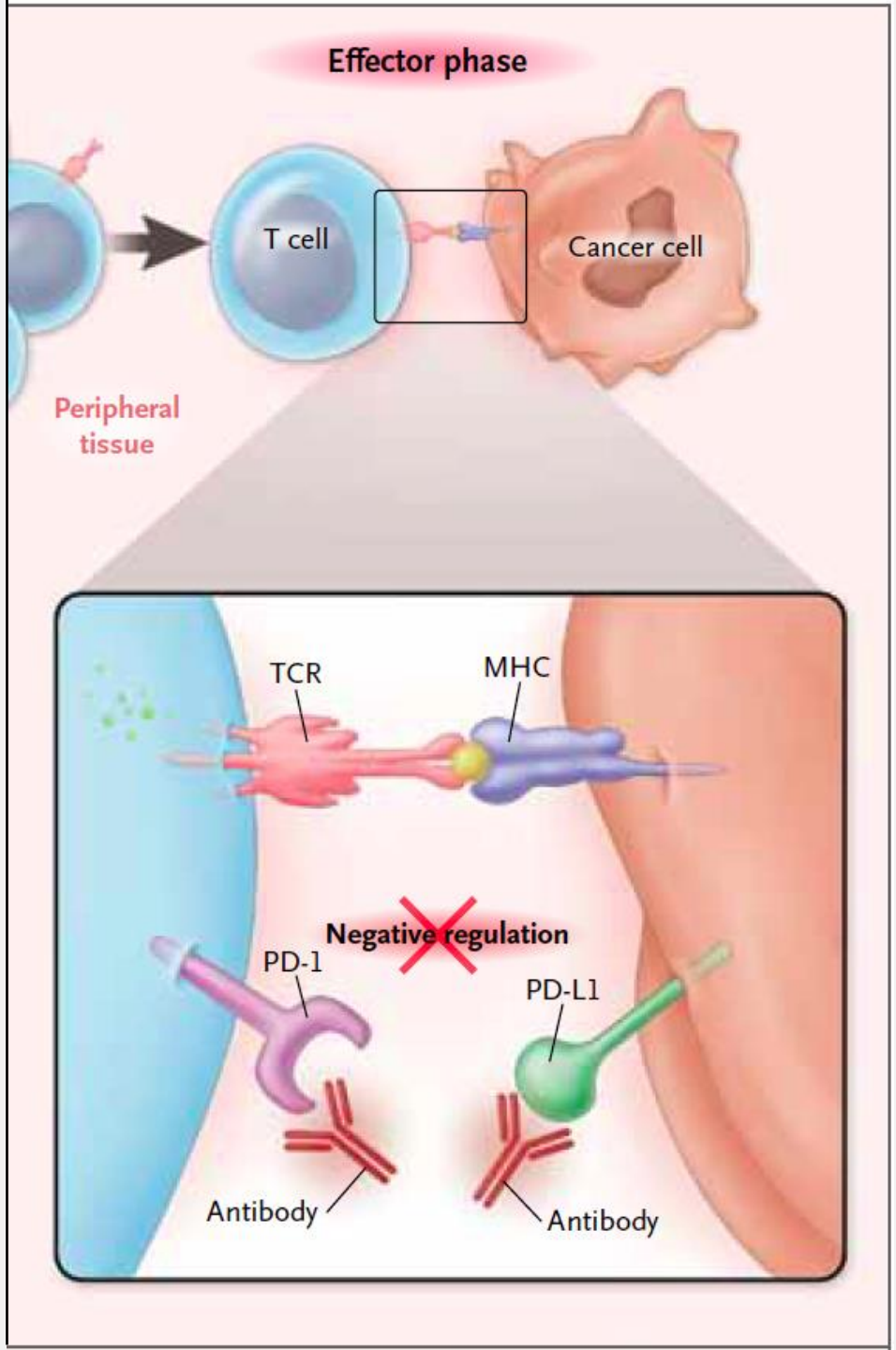
Adoptive cell transfer of tumor-specific TCR transgenic 2C PD-1-/- T cells rejected tumor cells



Blank et al., Cancer Res 2004



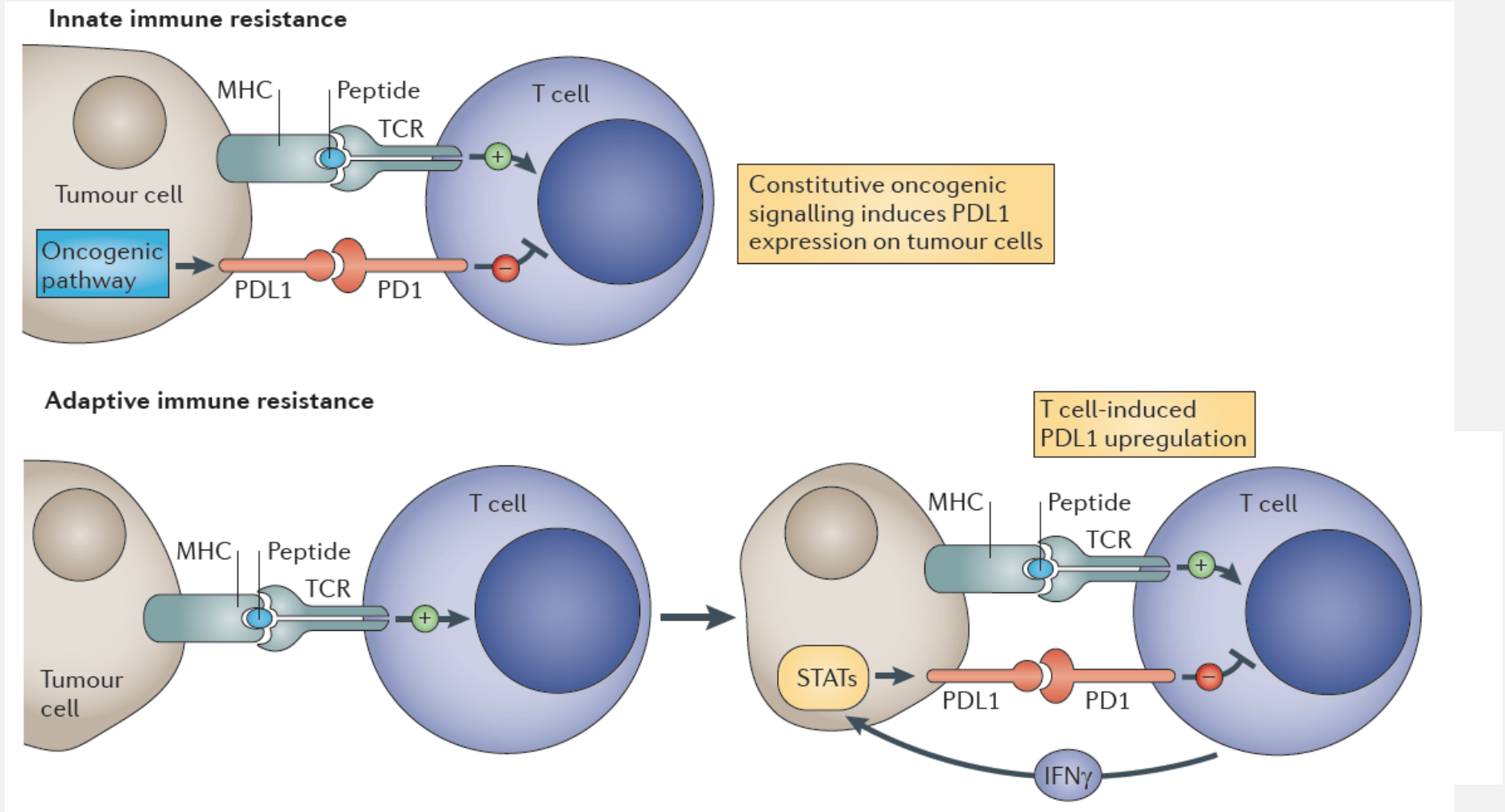
PD1/PD-L1 PLAY A ROLE AT THE TUMOR/EFFECTOR PHASE

- Nivolumab: anti-PD-1
- Pembrolizumab: anti-PD-1
- Cemiplimab: anti-PD-1
- Spartalizumab: anti-PD-1
- Dostarlimab: anti-PD-1

- Atezolizumab: anti-PD-L1
- Durvalumab: anti-PD-L1
- Avelumab: anti-PD-L1

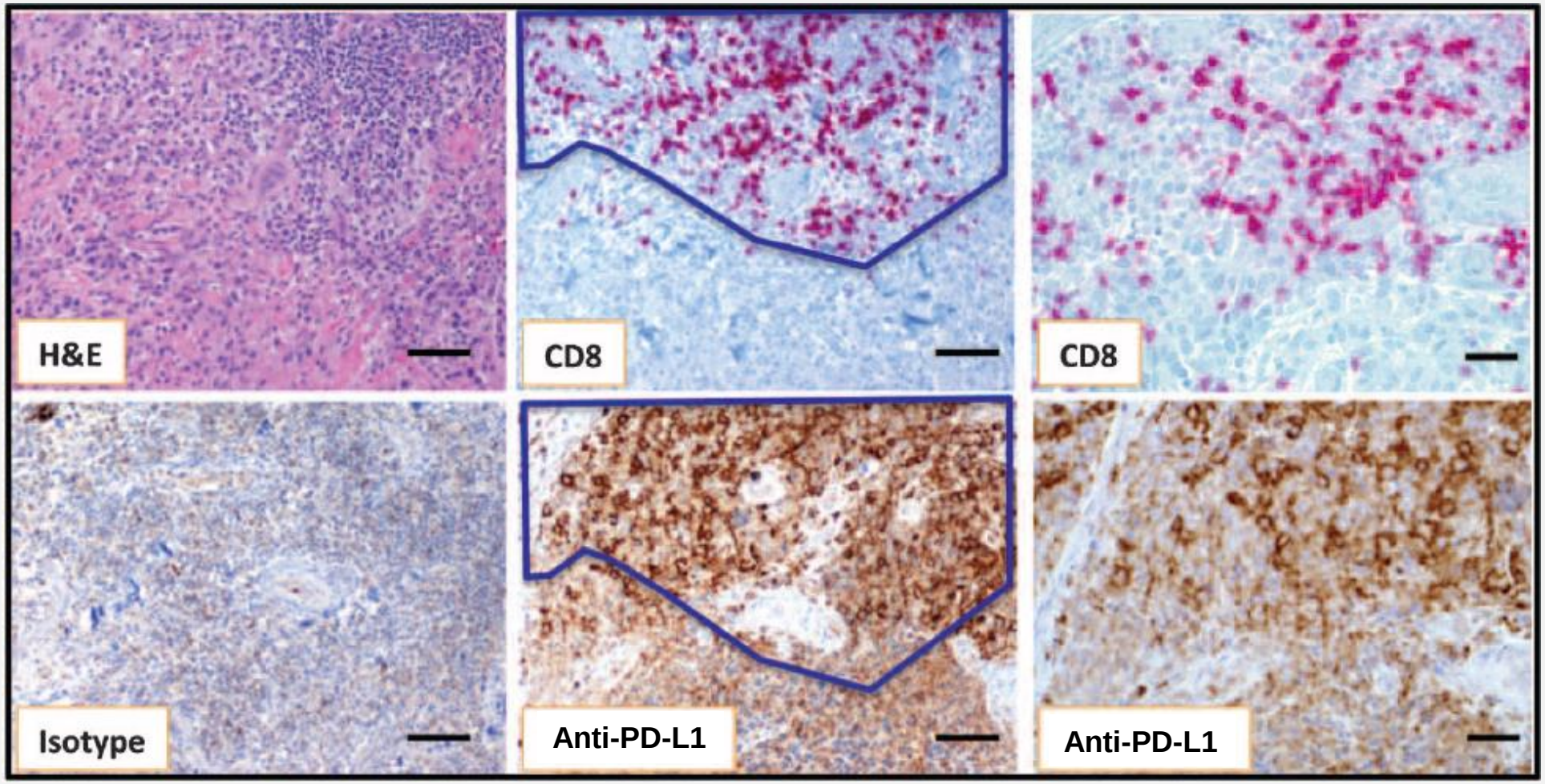
Ribas. N Engl J Med 2012

PD-L1 ON HUMAN TUMOR CELLS MEDIATES T CELL INHIBITION



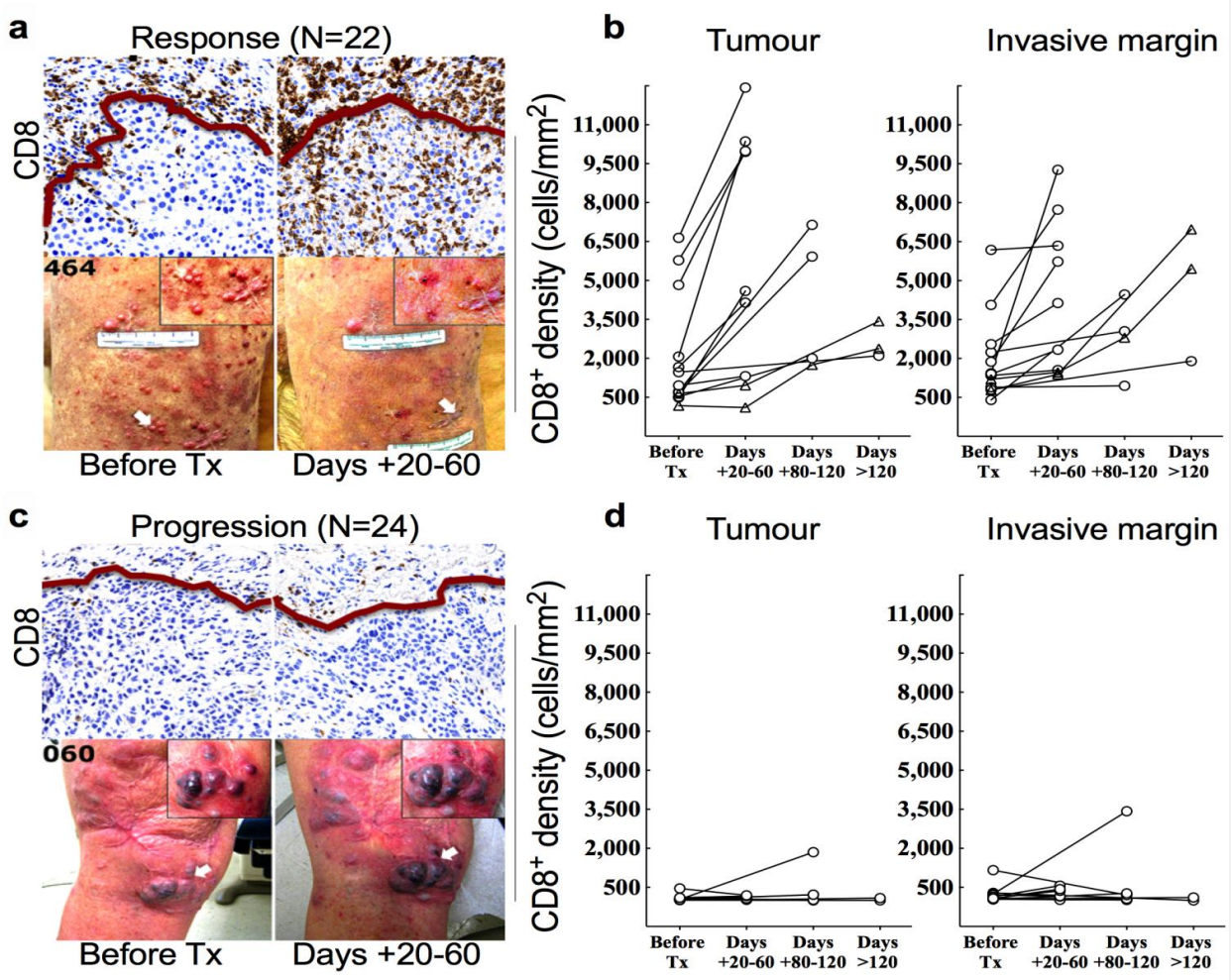
Pardoll DM, Nat Rev Cancer 2012

EXPRESSION OF PD-L1 CO-LOCALIZES WITH TILS



Taube et al. Science Transl Med 2012

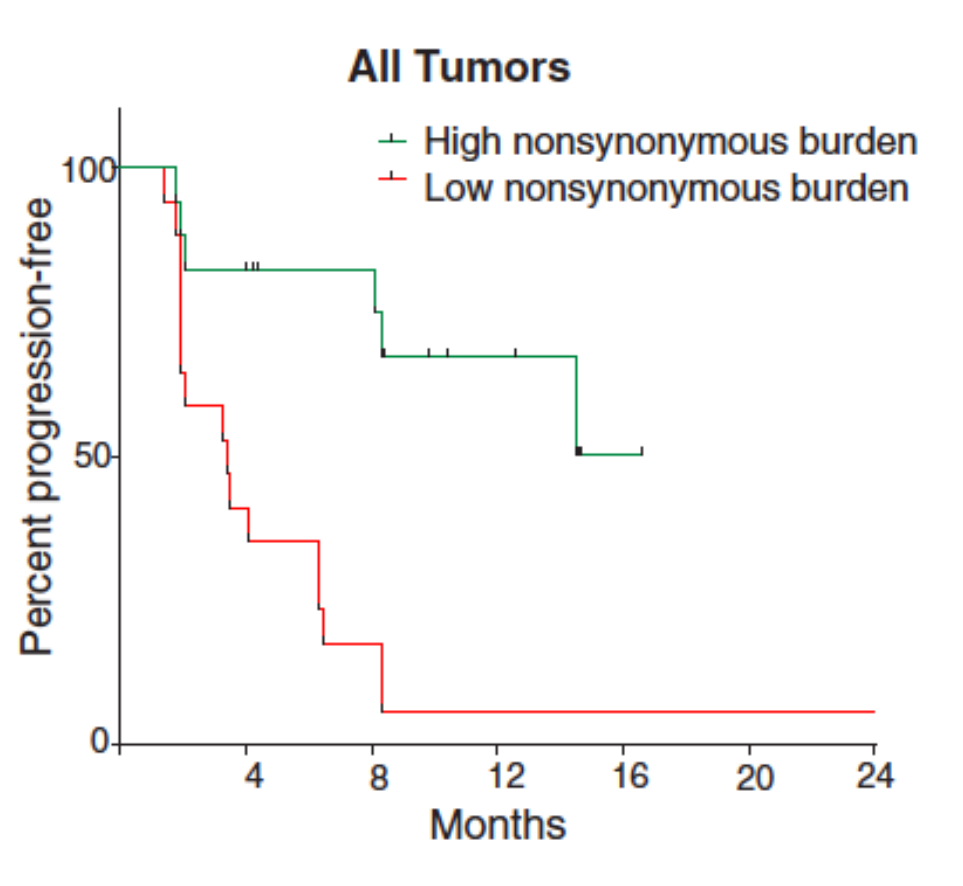
Evolution of CD8+ T-cells, according to treatment outcome



IHC Analysis of CD8+ T-cells in samples obtained before and during anti-PD1 treatment

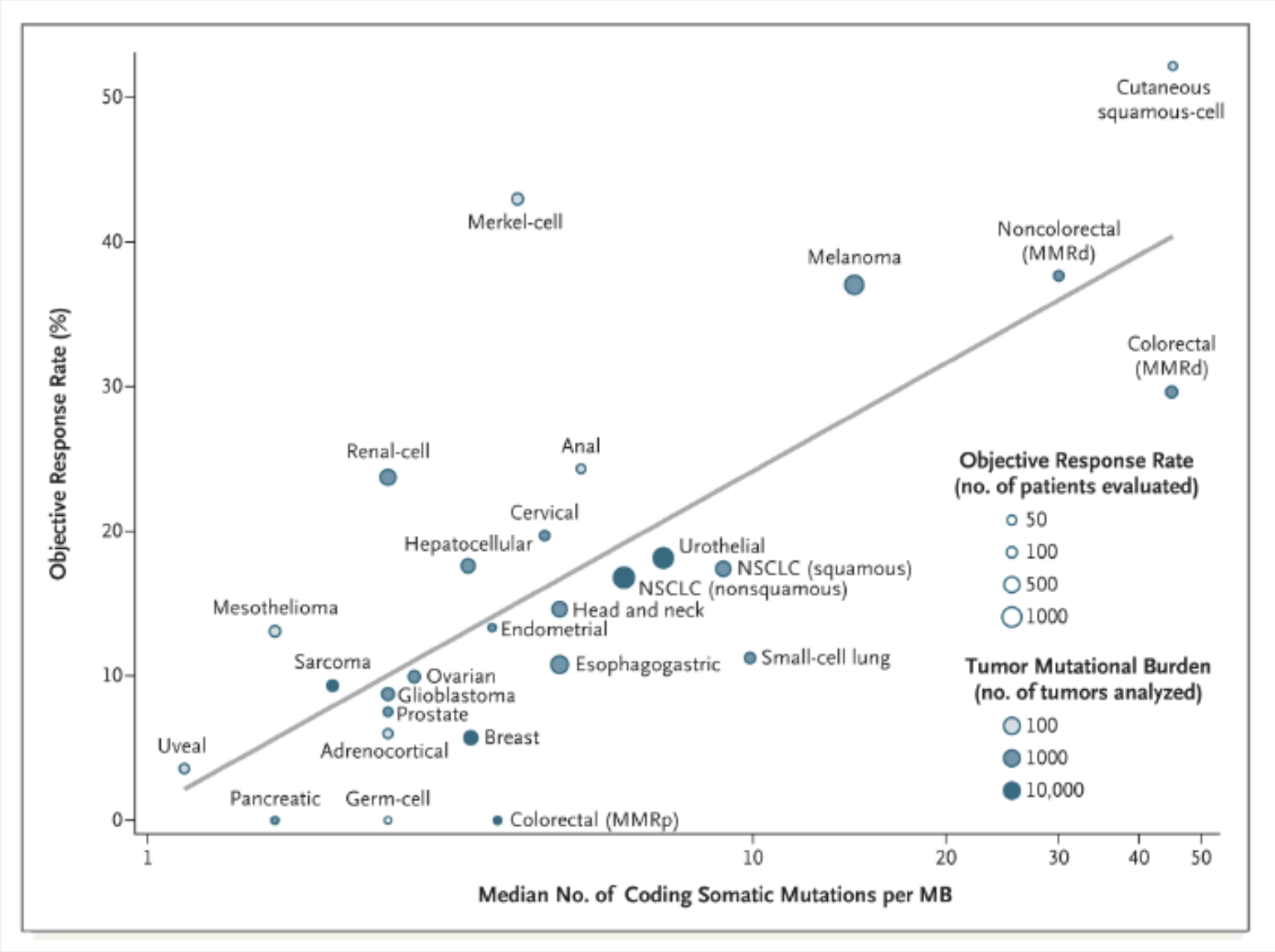
Tumeh *et al.* Nature 2014

MUTATIONAL BURDEN AND CLINICAL BENEFIT FROM ANTI-PD1 IN NSCLC



Rizvi et al., Science 2015

CORRELATION BETWEEN TMB AND RESPONSE TO ICB



Yarchoan et al. NEJM 2017

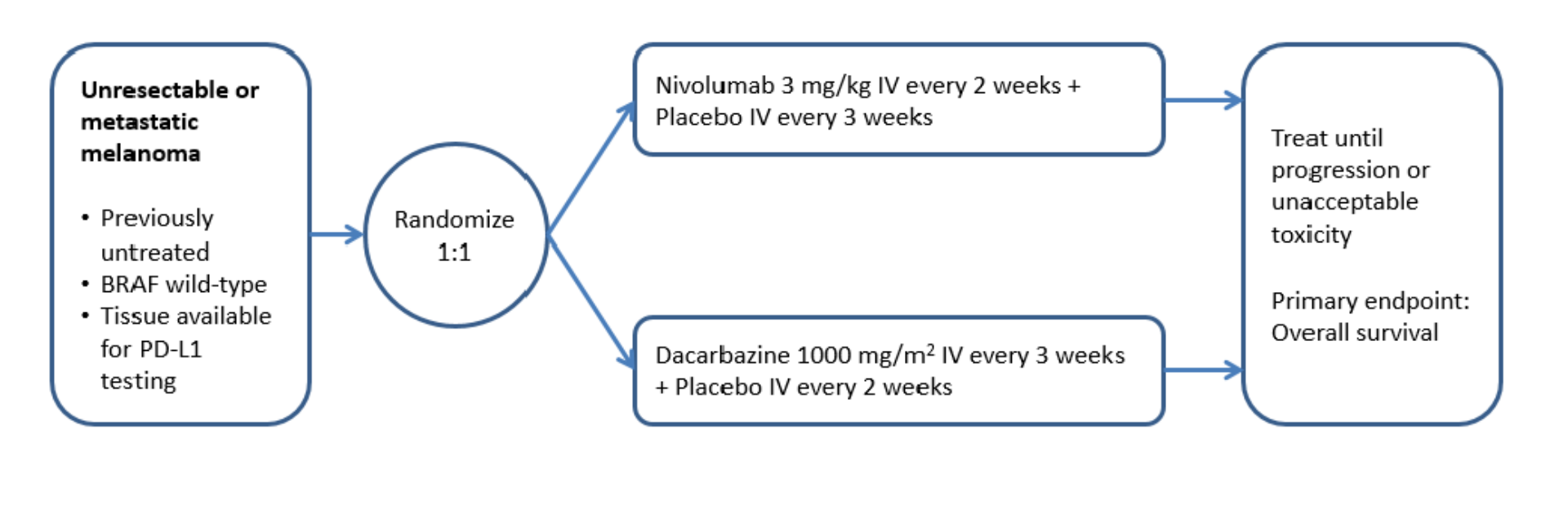
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

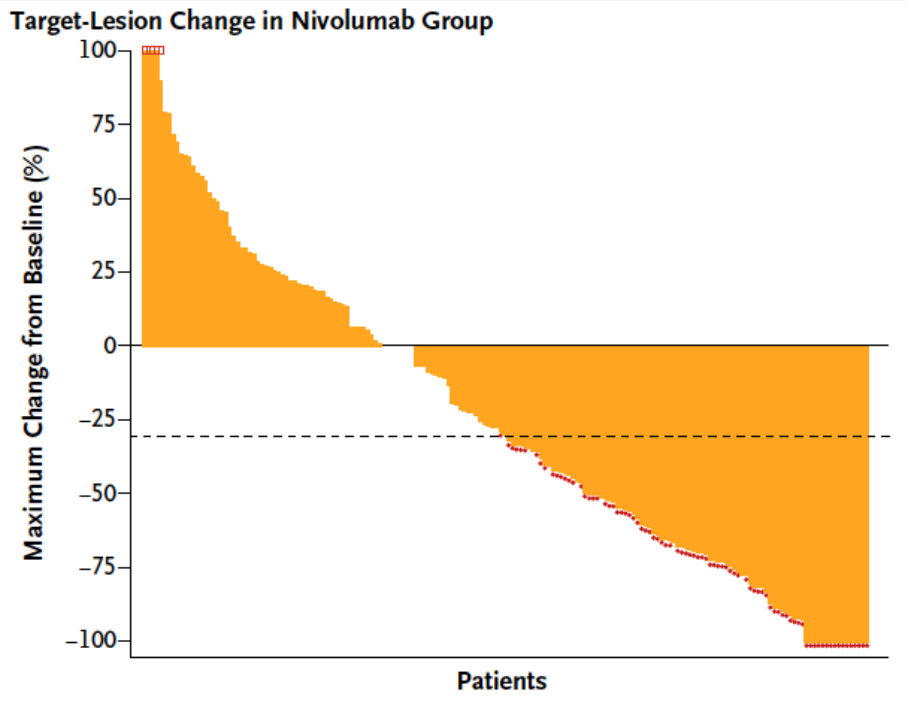
Nivolumab in Previously Untreated Melanoma without *BRAF* Mutation

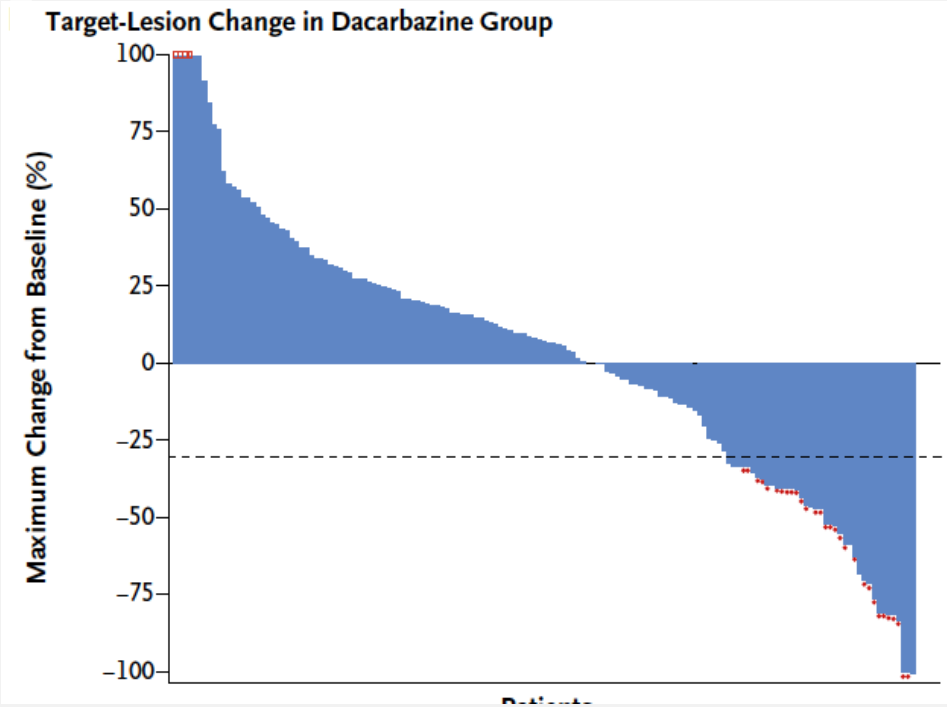
Caroline Robert, M.D., Ph.D., Georgina V. Long, M.D., Ph.D., Benjamin Brady, M.D., Caroline Dutriaux, M.D., Michele Maio, M.D., Laurent Mortier, M.D., Jessica C. Hassel, M.D., Piotr Rutkowski, M.D., Ph.D., Catriona McNeil, M.D., Ph.D., Ewa Kalinka-Warzocha, M.D., Ph.D., Kerry J. Savage, M.D., Micaela M. Hernberg, M.D., Ph.D., Celeste Lebbé, M.D., Ph.D., Julie Charles, M.D., Ph.D., Catalin Mihalcioiu, M.D., Vanna Chiarion-Sileni, M.D., Cornelia Mauch, M.D., Ph.D., Francesco Cognetti, M.D., Ana Arance, M.D., Ph.D., Henrik Schmidt, M.D., D.M.Sc., Dirk Schadendorf, M.D., Helen Gogas, M.D., Lotta Lundgren-Eriksson, M.D., Christine Horak, Ph.D., Brian Sharkey, Ph.D., Ian M. Waxman, M.D., Victoria Atkinson, M.D., and Paolo A. Ascierto, M.D.

DESIGN OF CHECKMATE 066

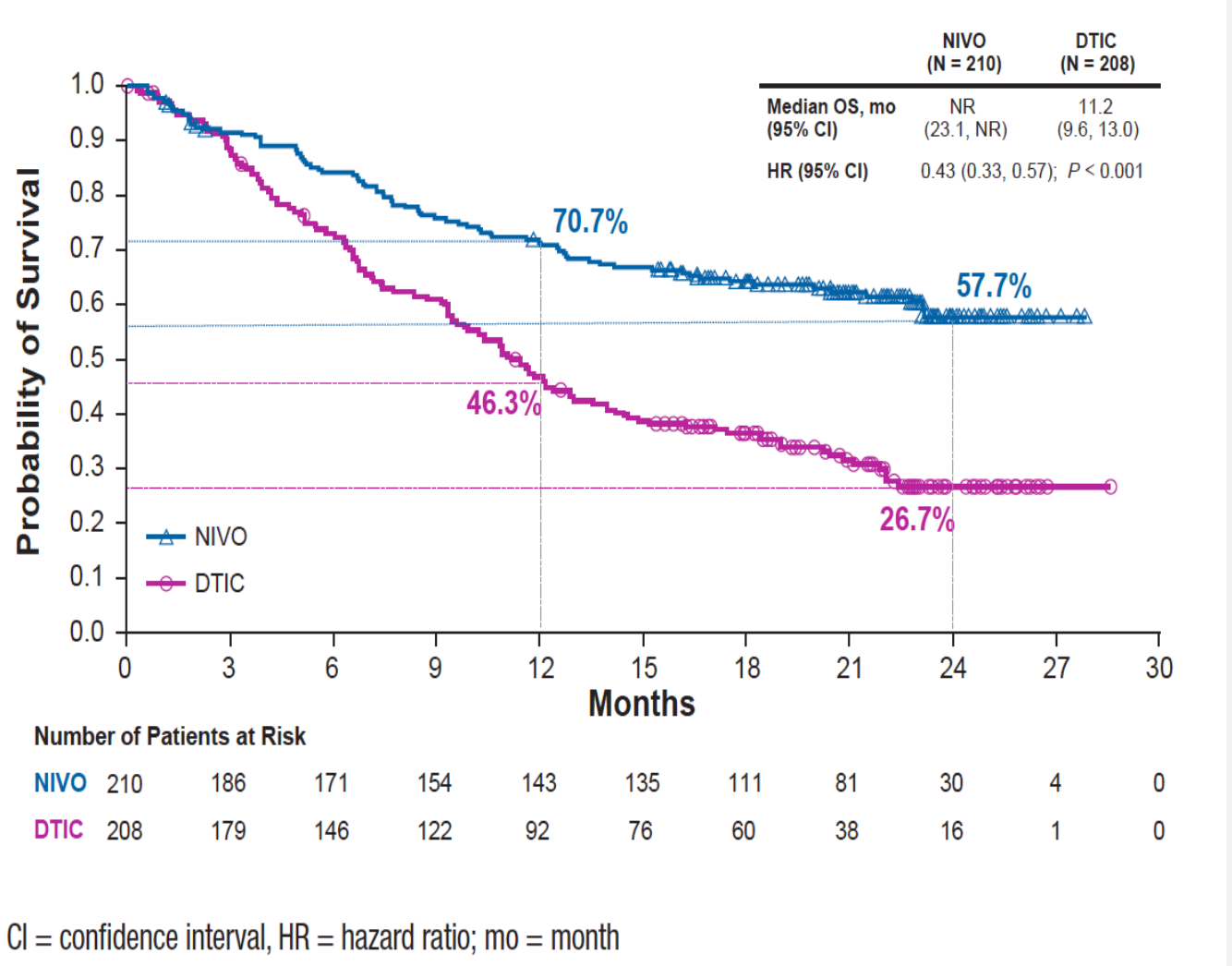


RESULTS OF THE CHECKMATE 066





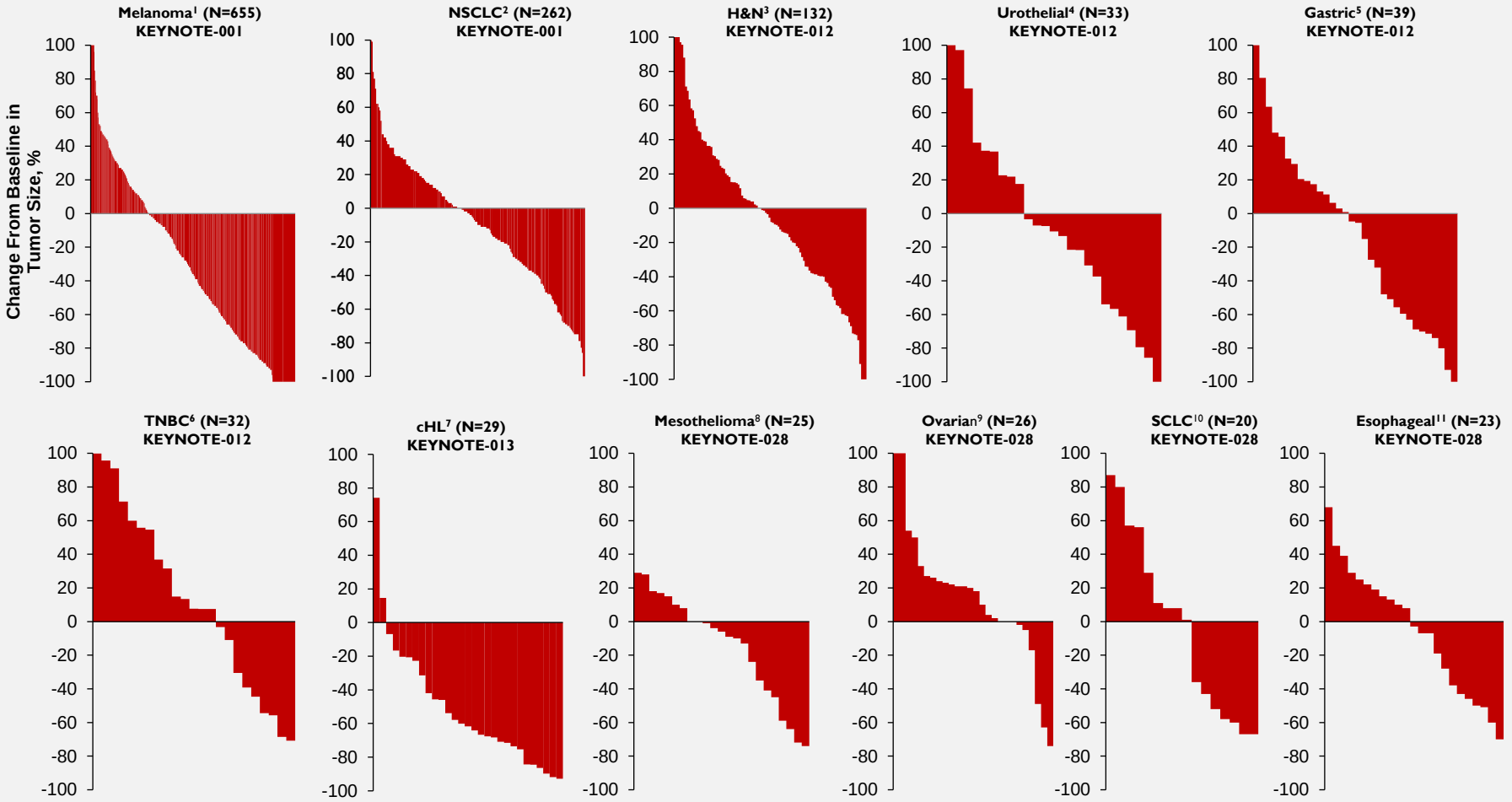
NIVOLUMAB IMPROVES PFS AND OS COMPARED TO DACARBAZINE



CI = confidence interval, HR = hazard ratio; mo = month

Atkinson et al. abstract 3774 SMR 2015

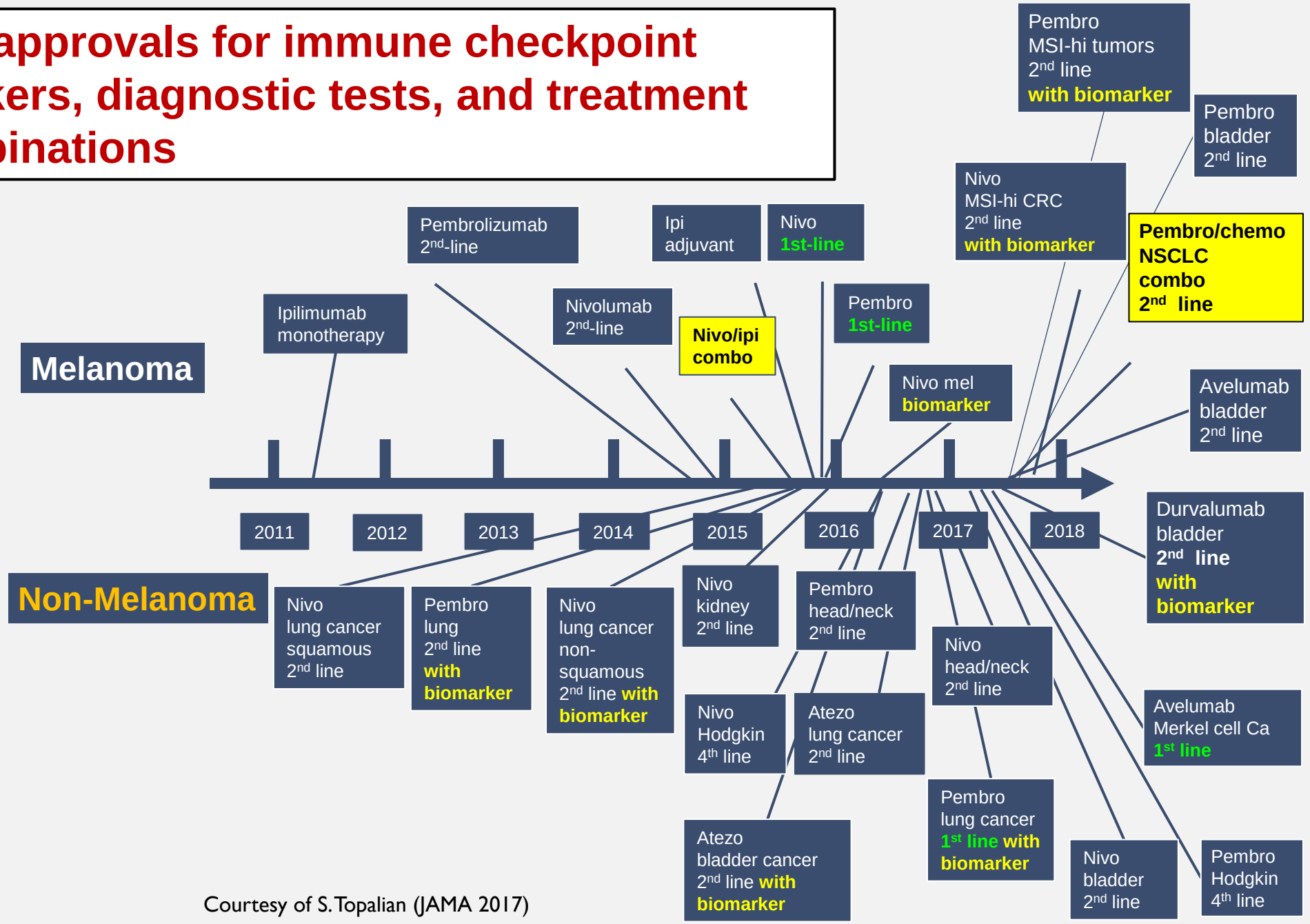
ANTI-PD1 DEMONSTRATES BROAD ANTITUMOR ACTIVITY



Courtesy of G Long

1. Daud A et al. 2015 ASCO; 2. Garon EB et al. ESMO 2014; 3. Seiwert T et al. 2015 ASCO; 4. Plimack E et al. 2015 ASCO; 5. Bang YJ et al. 2015 ASCO; 6. Nanda R et al. SABCS 2014; 7. Moskowitz C et al. 2014 ASH Annual Meeting; 8. Alley EA et al. 2015 AACR; 9. Varga A et al. 2015 ASCO; 10. Ott PA et al. 2015 ASCO; 11. Doi T et al. 2015 ASCO.

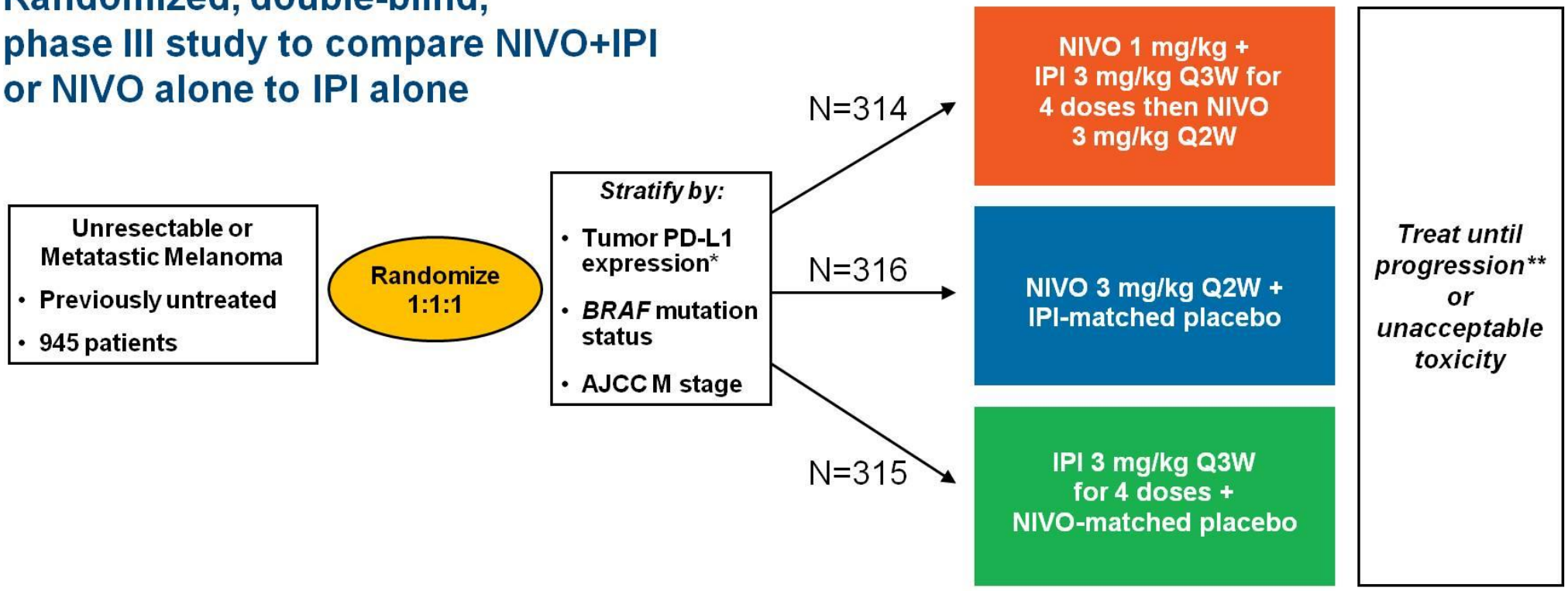
FDA approvals for immune checkpoint blockers, diagnostic tests, and treatment combinations



Courtesy of S. Topalian (JAMA 2017)

COMBINING CTLA-4 AND PD-1 BLOCKADE
CHECKMATE 067 TRIAL

Randomized, double-blind, phase III study to compare NIVO+IPI or NIVO alone to IPI alone

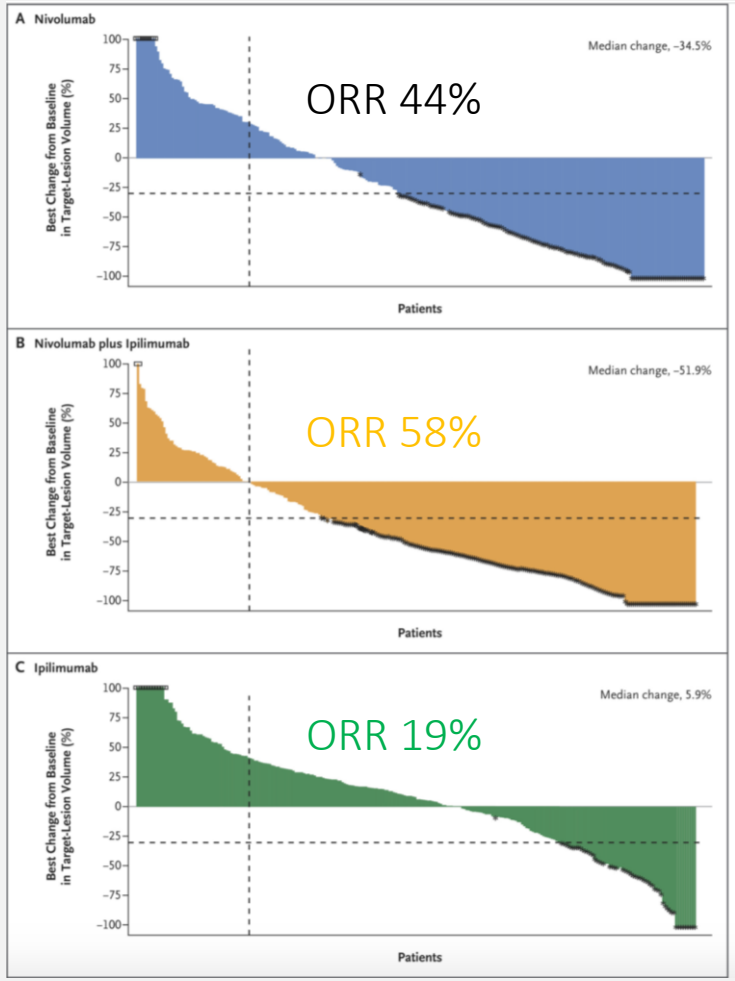


*Verified PD-L1 assay with 5% expression level was used for the stratification of patients; validated PD-L1 assay was used for efficacy analyses.

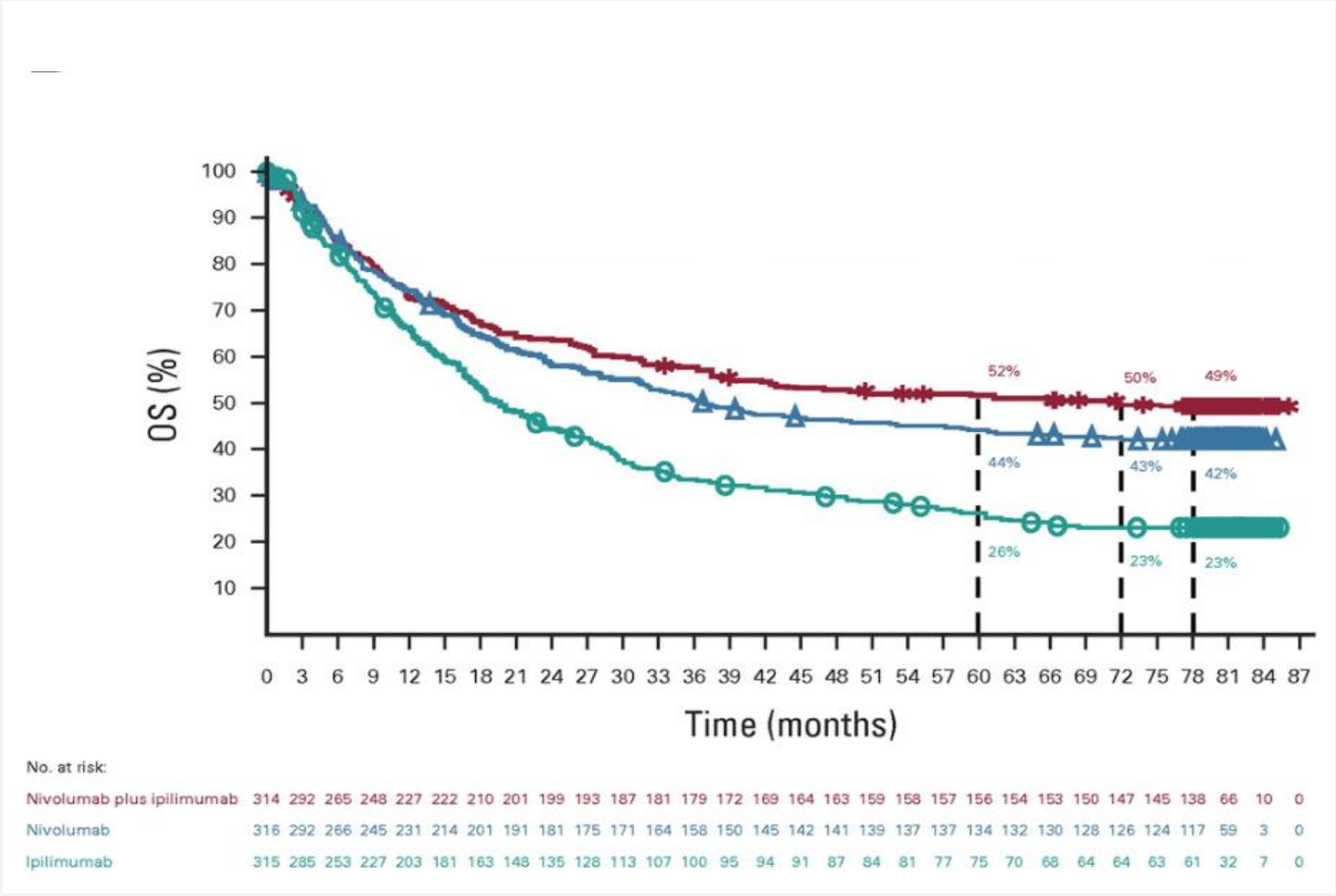
**Patients could have been treated beyond progression under protocol-defined circumstances.

Larkin et al. NEJM. 2015; Larkin et al. NEM 2019

RESPONSE RATE AND (6.5Y) OVERALL SURVIVAL



Larkin et al. NEJM. 2015; Larkin et al. NEM 2019



Wolchok JD. et al. J Clin Oncol. 2022

SAFETY SUMMARY

- With an additional 19 months of follow-up, safety was consistent with the initial report[1]

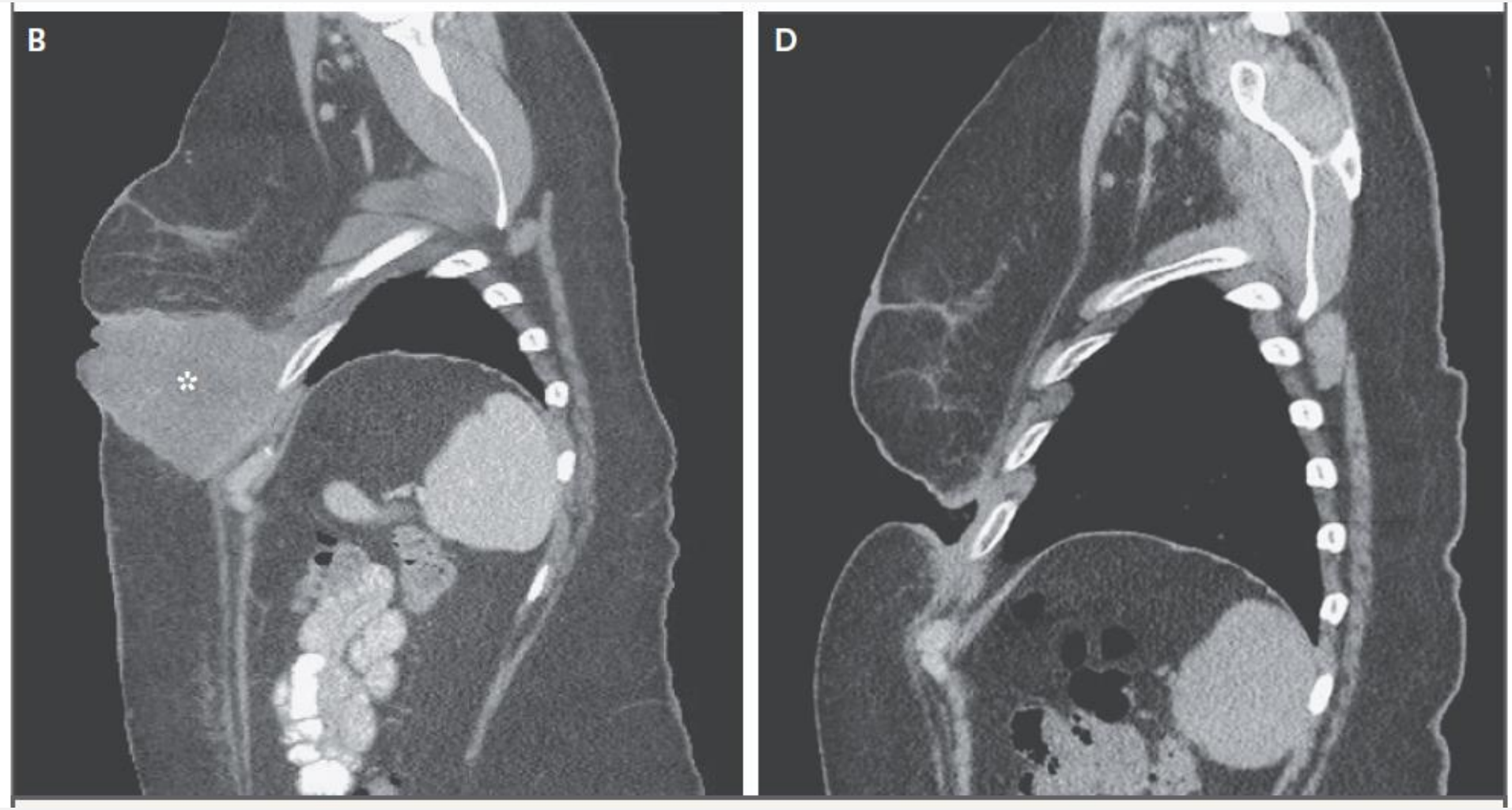
	NIVO+IPI (N=313)		NIVO (N=313)		IPI (N=311)	
Patients reporting event, %	Any Grade	Grade 3-4	Any Grade	Grade 3-4	Any Grade	Grade 3-4
Treatment-related adverse event (AE)	95.8	**58.5**	86.3	**20.8**	86.2	**27.7**
Treatment-related AE leading to discontinuation	39.6	31.0	11.5	7.7	16.1	14.1
Treatment-related death, n (%)	2 (0.6)[a]		1 (0.3)[b]		1 (0.3)[b]	

- Most select AEs were managed and resolved within 3-4 weeks (85–100% across organ categories)
- ORR was 70.7% for pts who discontinued NIVO+IPI due to AEs, with median OS not reached

[a]Cardiomyopathy (NIVO+IPI, n=1); Liver necrosis (NIVO+IPI, n=1). Both deaths occurred >100 days after the last treatment.
[b]Neutropenia (NIVO, n=1); colon perforation (IPI, n=1).[1]

Larkin J, et al. NEJM 2015;373:23–34.

RAPID COMPLETE REMISSION AFTER COMBINATION IMMUNOTHERAPY WITH ANTI-CTLA4 AND ANTI-PD1

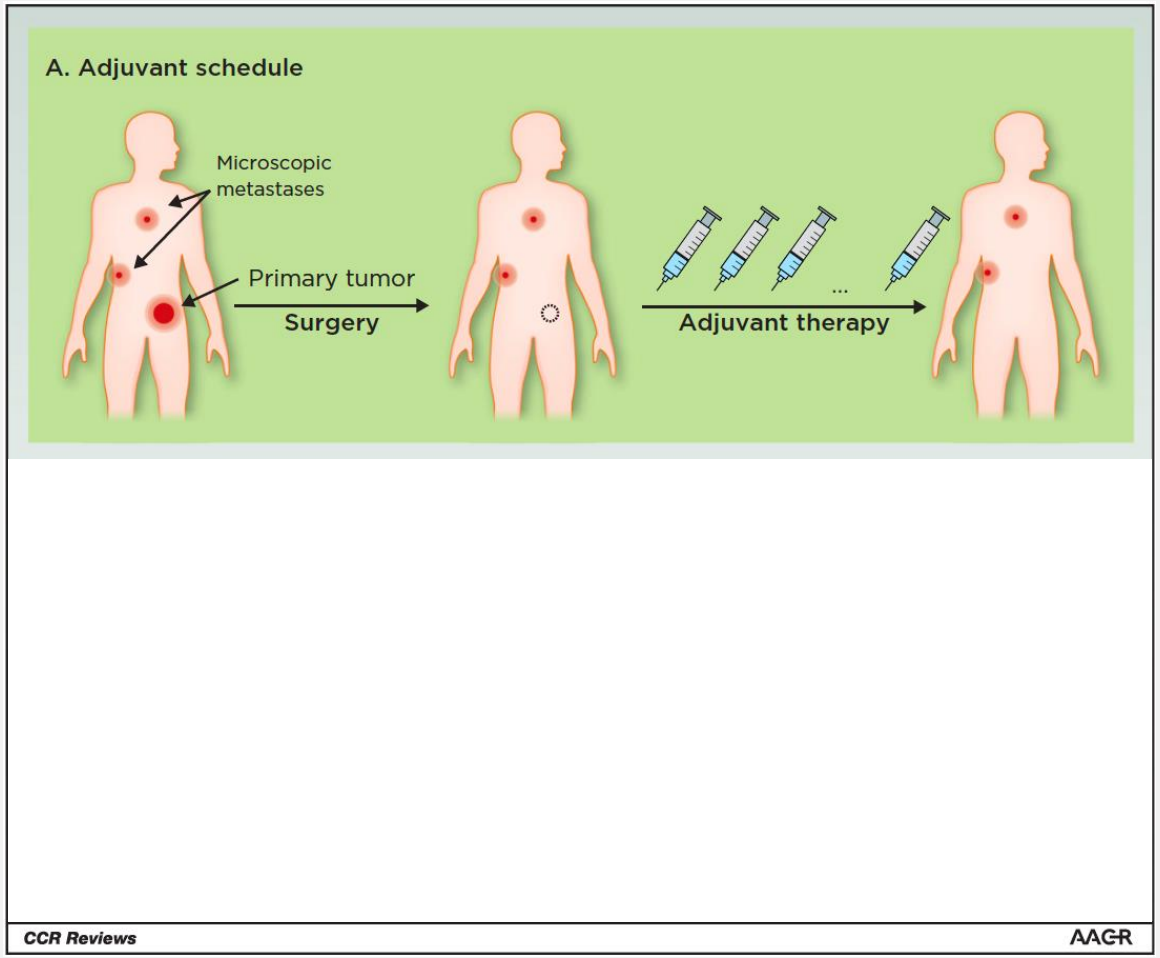


Chapman et al., NEJM 2015

CONCLUSIONS

- After decennia of having lots of promise, immunotherapy became a breakthrough in cancer treatment (2013)
- Immune checkpoint inhibitors target the T-cell compartment of the immune system
- Immunotherapy with immune checkpoint inhibition has been approved in over 40 cancer indications
- Immunotherapy with immune checkpoint inhibitors has been approved alone or in combination with chemotherapy (NSCLC, TNBC, HNSCC) or VEGF-R targeting agents (RCC, HCC, endometrial cancer)
- Immunotherapy (in contrast to chemotherapy and targeted therapy) can result in cures even in metastatic setting, even in brain metastases patients
- Immune checkpoint inhibitors can induce sometimes severe and long-lasting autoimmune adverse events, and should be used by experiences doctors

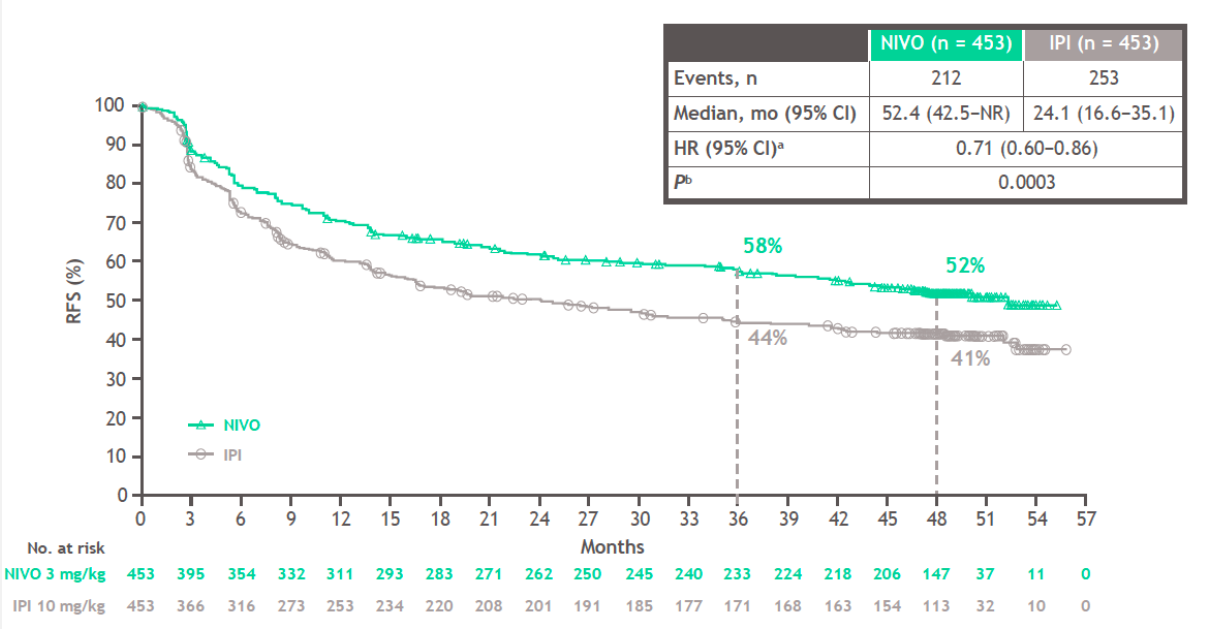
MOVING IMMUNOTHERAPY TO EARLIER STAGES



O'Donnell et al., CCR 2019

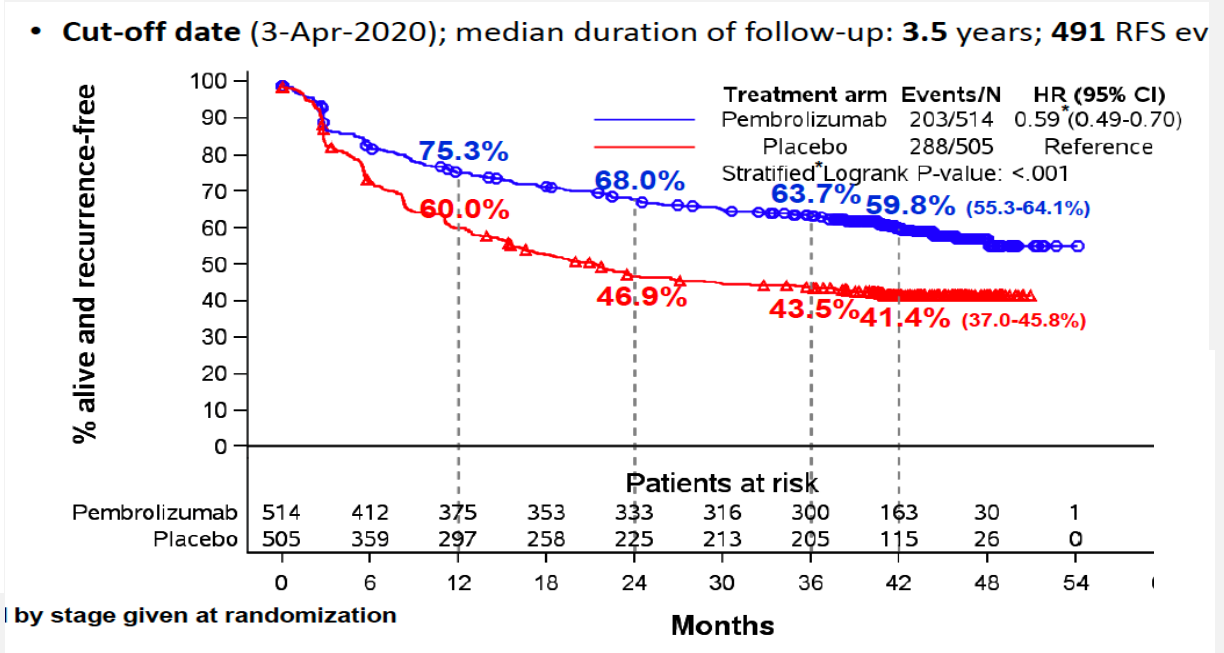
IMPROVEMENT IN RFS WITH ADJUVANT ANTI-PD-1 IN STAGE III MELANOMA

4-year RFS Checkmate-238



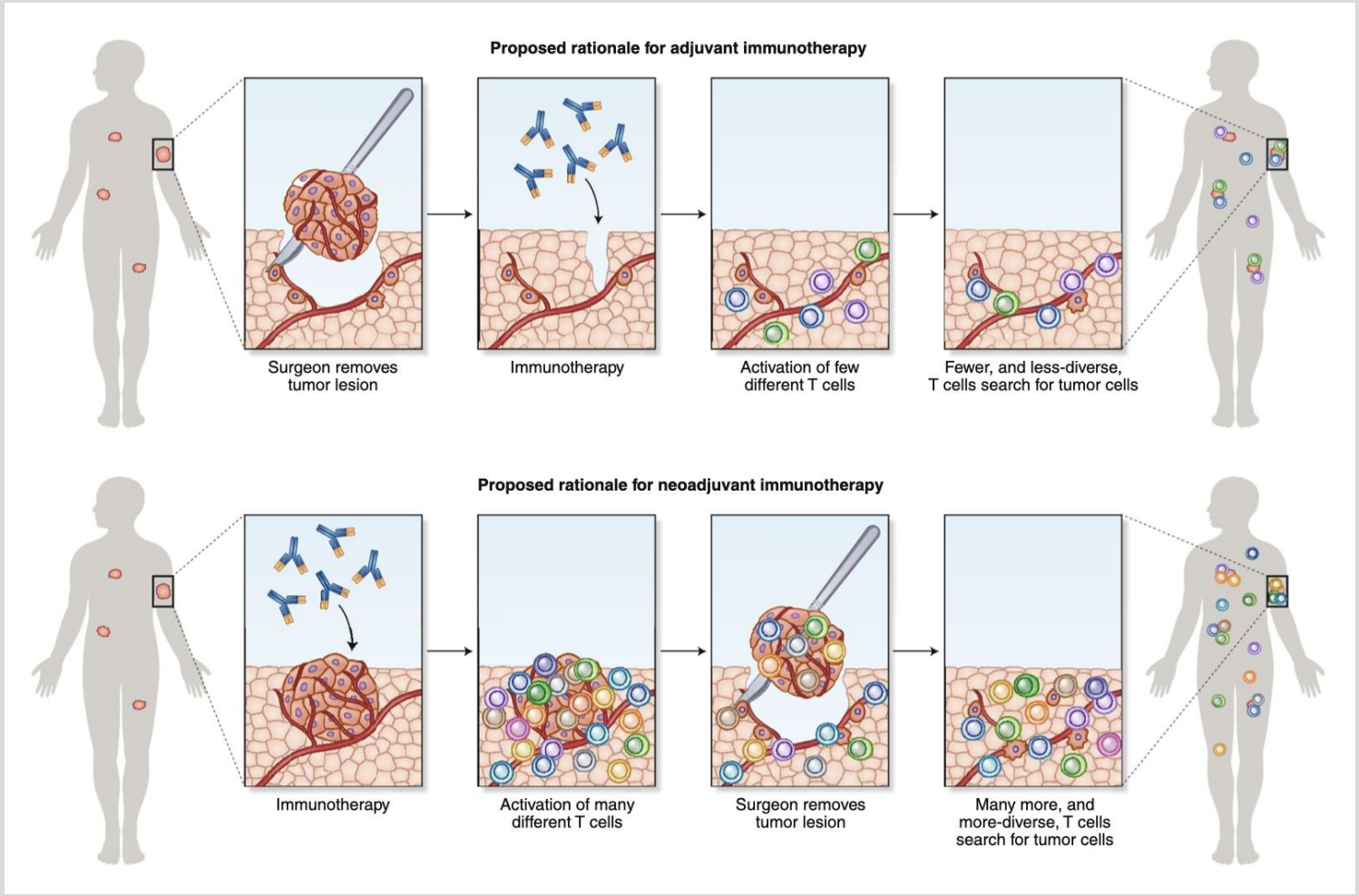
Presented by J Weber ESMO 2020

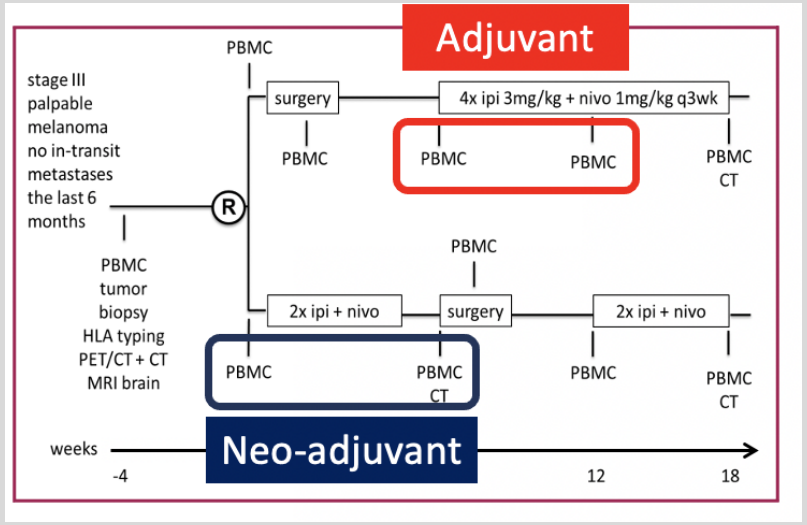
3.5 year RFS Keynote-54

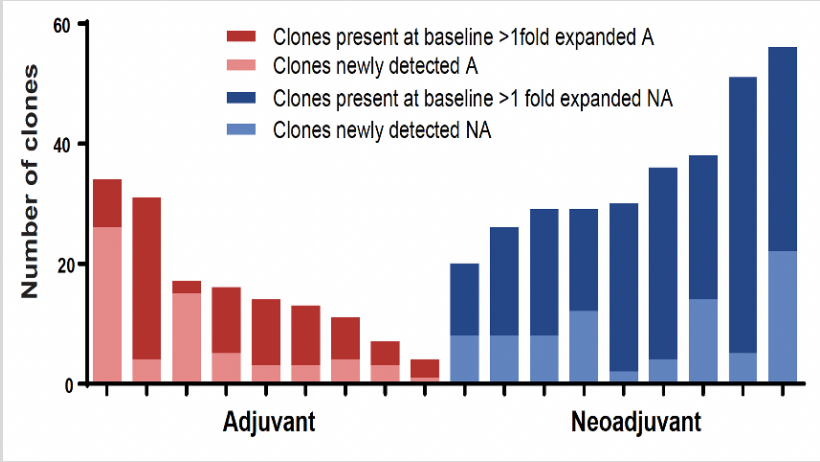


Presented by A Eggermont ESMO 2020

IMMUNOLOGICAL PRIMING APPEARS BETTER WITH NEOADJUVANT THAN ADJUVANT IT







Versluis, Long, and Blank, Nat Med 2020; Blank et al., Nat Med 2018

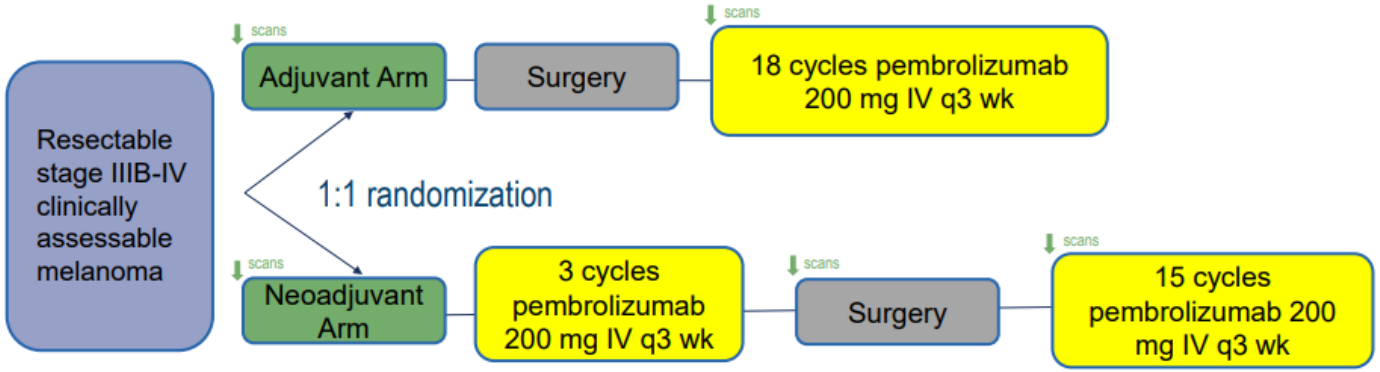
NEOADJUVANT–ADJUVANT OR ADJUVANT-ONLY PEMBROLIZUMAB IN ADVANCED MELANOMA

Trial

- Phase 2
- Open-label
- Randomized
- 313 Adults
- Histologically confirmed, clinically detectable, resectable stage IIIB to IVC melanoma

S1801 Study Schema

Primary endpoint: Event-free survival



⬇ radiographic assessment (scans)

Additional criteria: strata included AJCC 8th ed. stage and LDH, adjuvant radiation allowed, concomitant radiation & pembrolizumab was not allowed, brain metastasis excluded, uveal melanoma excluded

Surgery type and extent was required to be pre-specified and carried out regardless of radiologic response to therapy

PARIS 2022 ESMO congress Sapna P. Patel, MD SWOG NCI NCI

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Patel SP. NEJM. 2023

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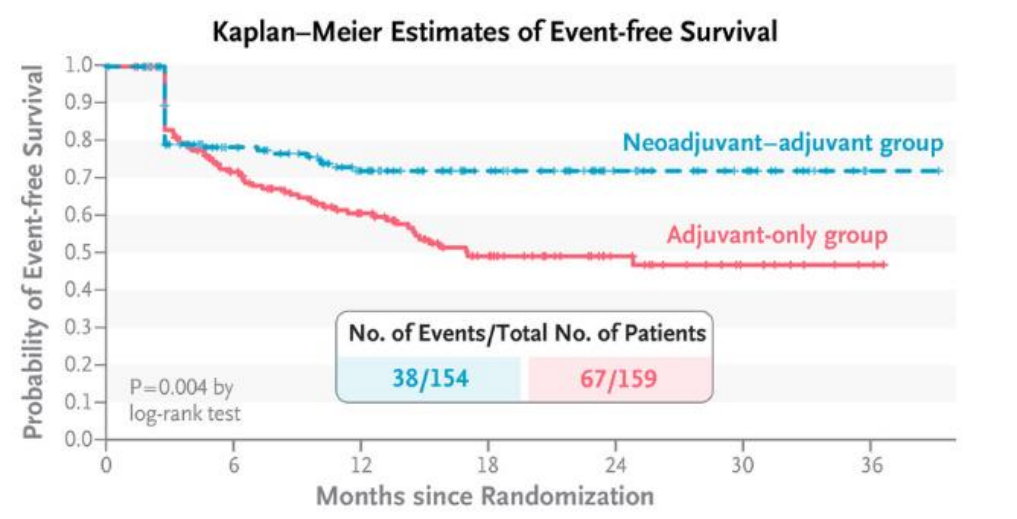
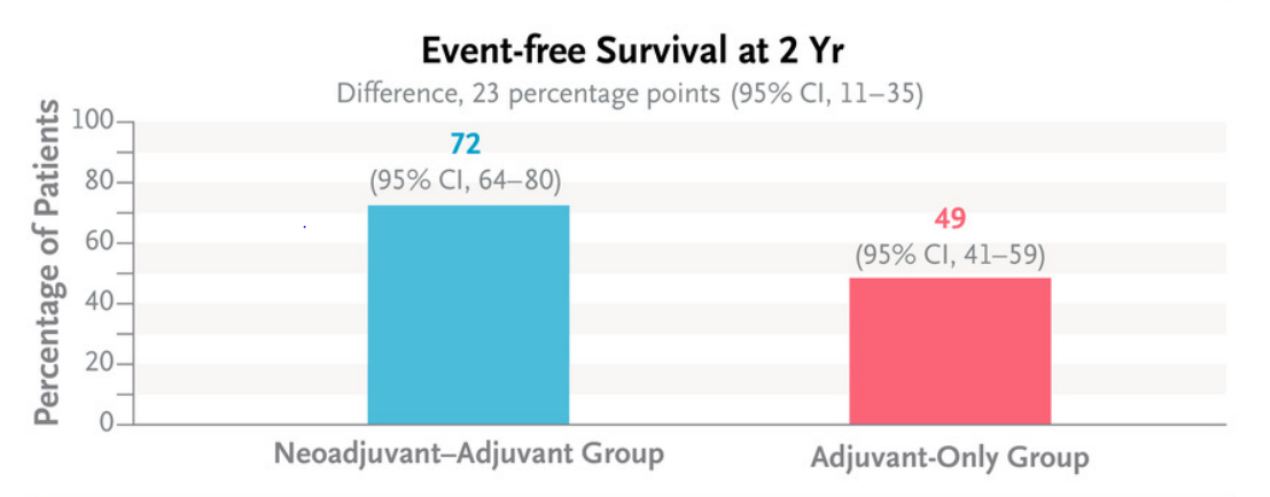
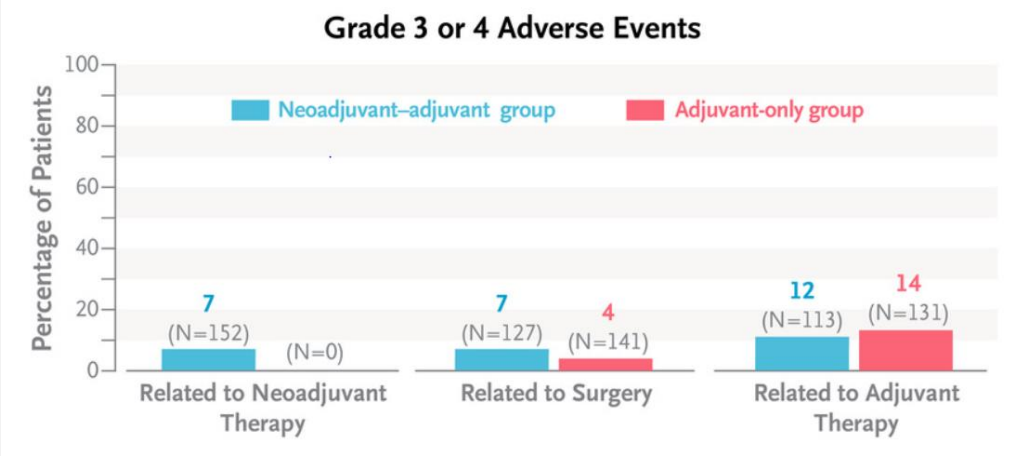






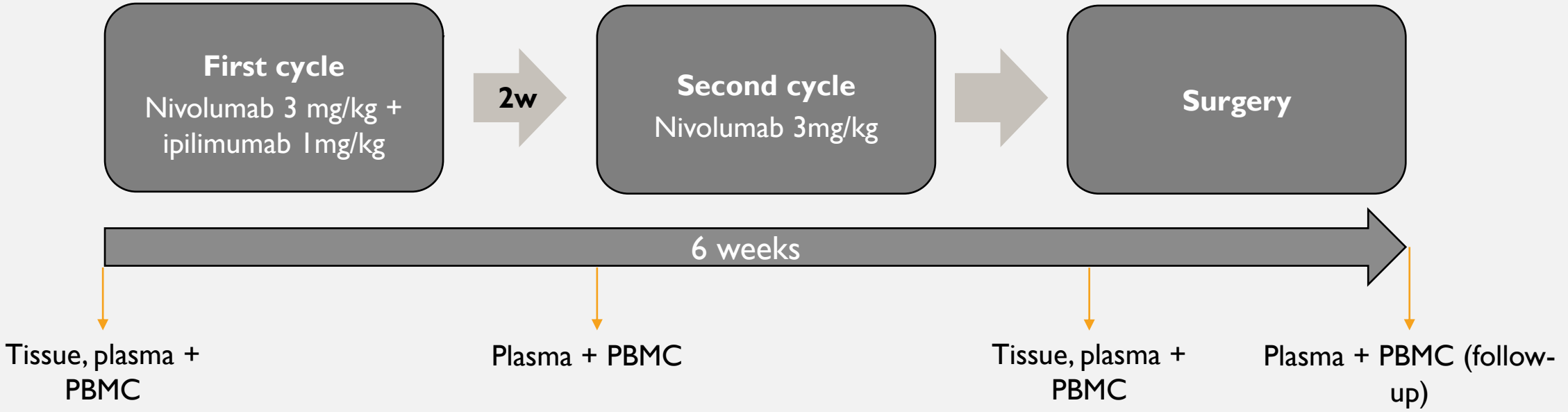
CONCLUSIONS

Among patients undergoing surgical resection for stage III or IV melanoma, event-free survival was longer with neoadjuvant plus adjuvant pembrolizumab therapy than with adjuvant pembrolizumab alone.

Patel SP. NEJM. 2023

NICHE- STUDY DESIGN IN DMMR STAGE 2-3 COLON CANCER

- Investigator-initiated, non-randomized multicenter*



*6 participating hospitals in the Netherlands
PBMC = peripheral blood mononuclear cells

Chalabi, Haanen et al. ESMO 2022

MAJOR PATHOLOGIC RESPONSE IN 95% OF PATIENTS; 67% PCR

Pathologic response (RVT)		Patients *n*= 107
Yes	**(≤ 50%)**	**106 (99%)**
Major	(≤10%)	**102 (95%)**
Complete	(0%)	**72 (67%)**
Partial	(10% - 50%)	4 (4%)
No	**(≥50%)**	**1 (1%)**

RVT = residual viable tumor

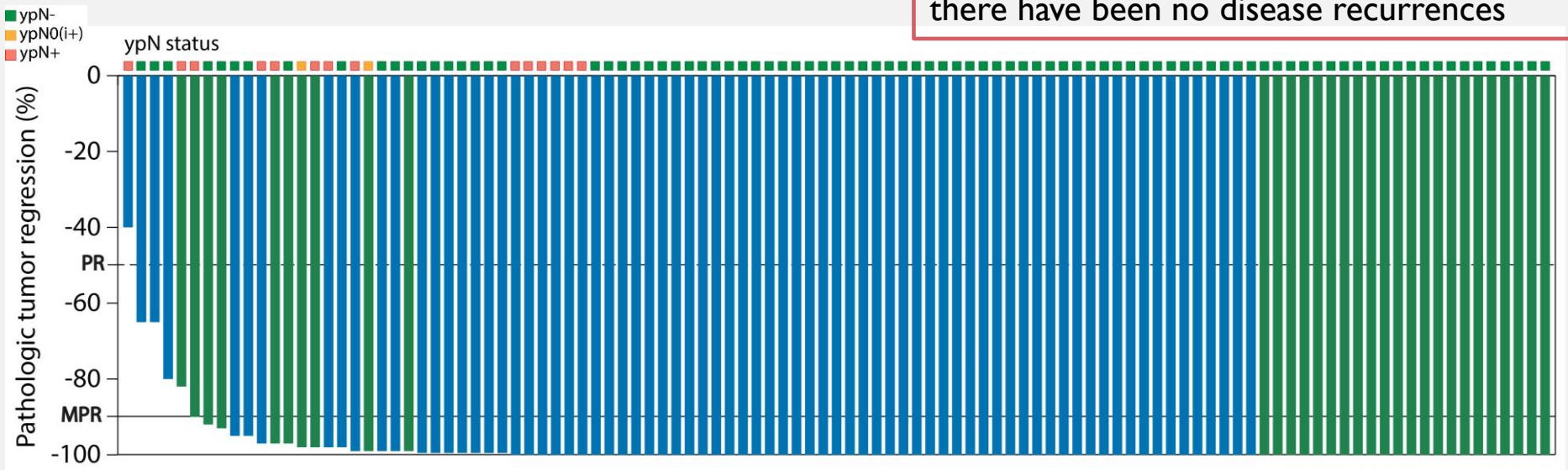
Adjuvant chemotherapy (CTx)

14 patients with ypN+ disease
- 3 patients received adjuvant CTx*
- 5 patients >70 years
- 6 patients refused

* 1 non-responder, 1 partial responder and 1 MPR

Disease recurrence

With a median follow-up of 13.1 months (1.4 -57.4), there have been no disease recurrences

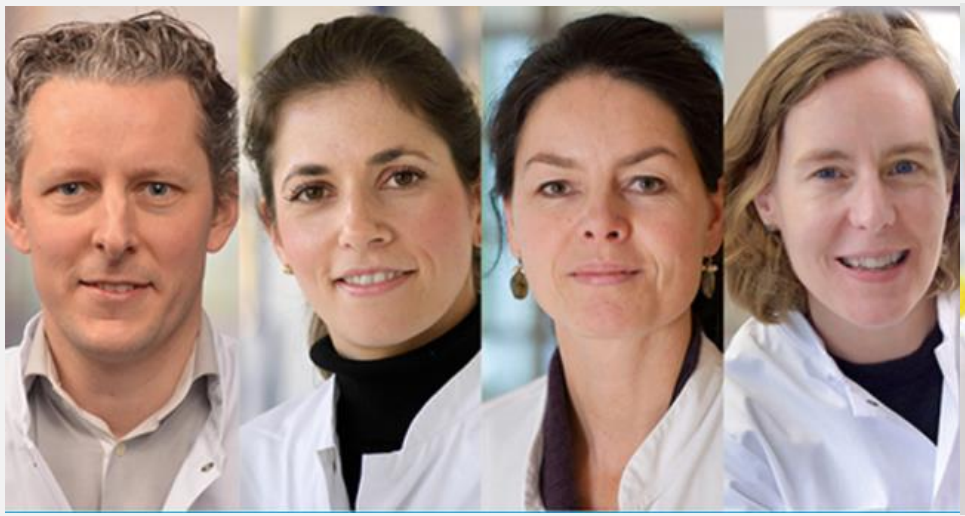


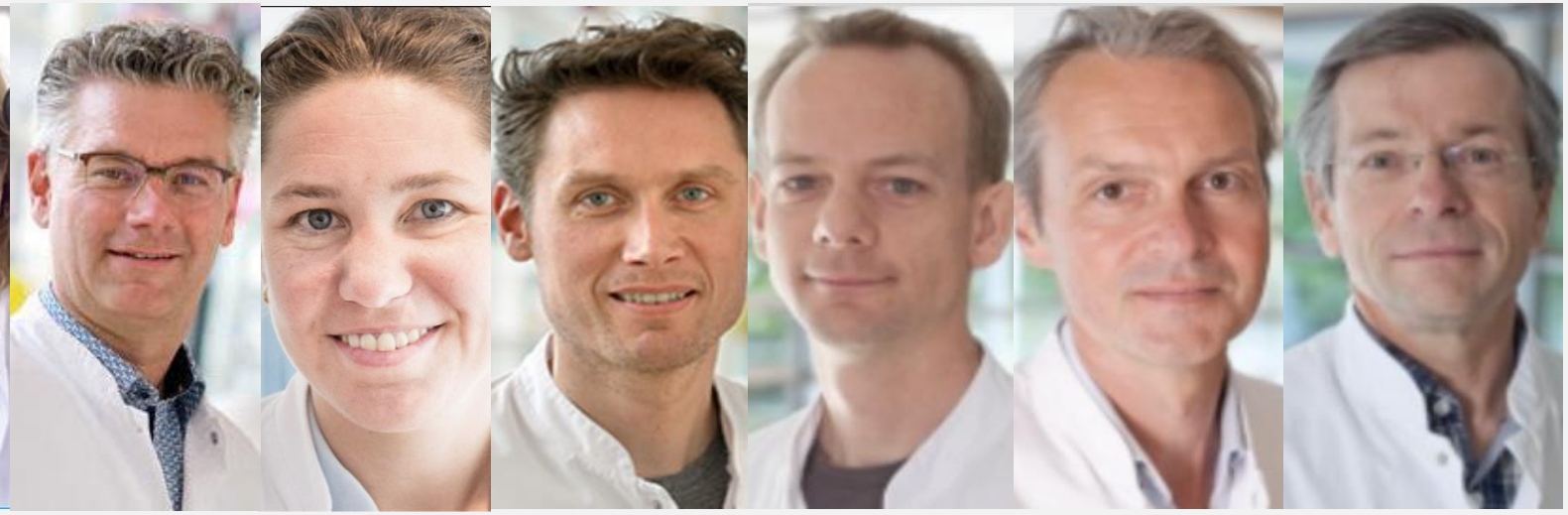
Green bars = NICHE-1 cohort
Blue bars = NICHE-2 cohort

ypN- = tumor-free lymph nodes; ypN+ = lymph nodes with tumor, including micrometastases; ypN(i+) = lymph nodes with isolated tumor cells

Chalabi, Haanen et al. ESMO 2022

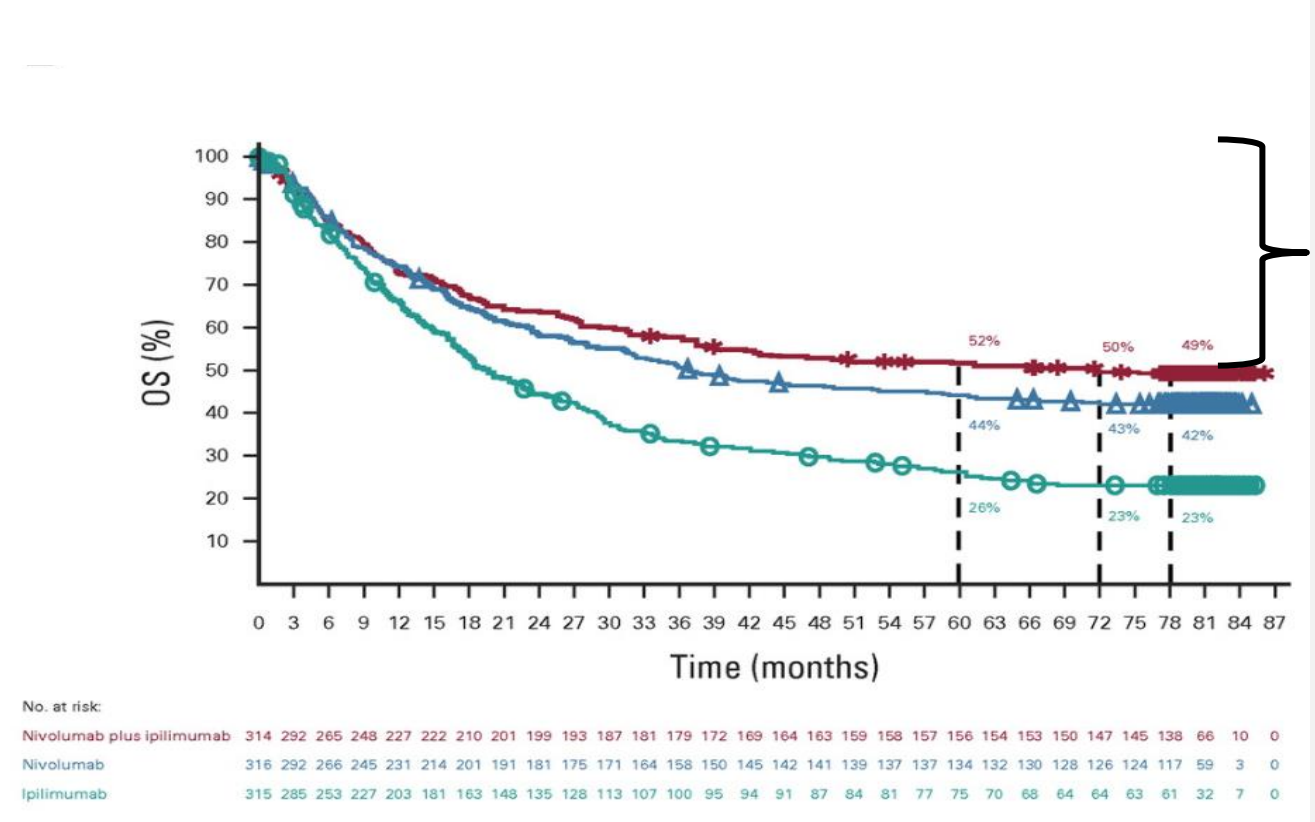
NEOADJUVANT TRIALS AT THE NKI





Bladder	CRC, Gastric	SCCHN, cSCC	TNBC	Melanoma	NSCLC	NSCLC	RCC	RCC	Melanoma, RCC
M. vd Heijden	M. Chalabi	L. Zuur	M. Kok	C. Blank	W. Theelen	J. de Langen	H. v. Thienen	A. Bex.	J. Haanen

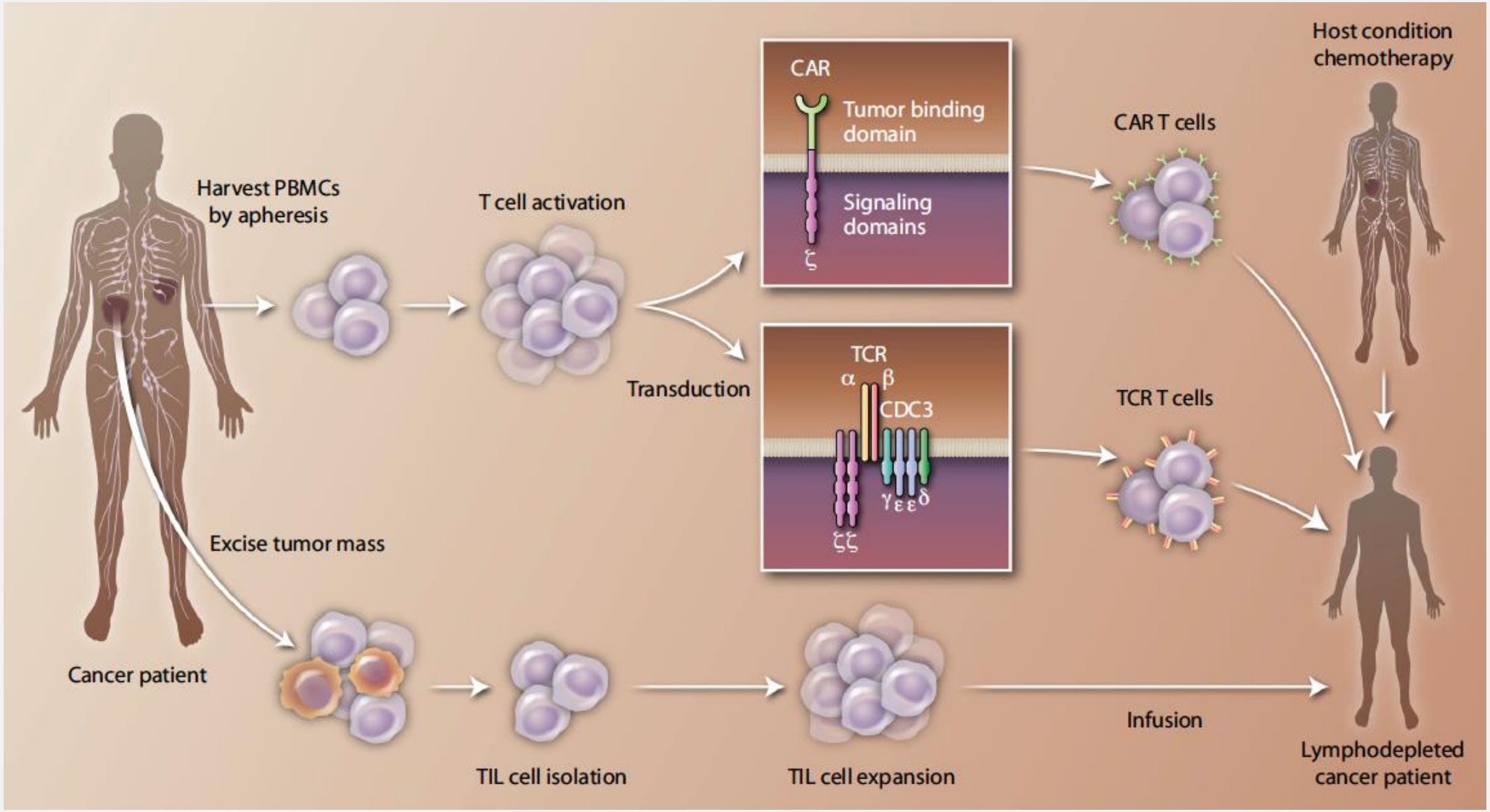
ONLY A MINORITY OF PATIENTS RESPOND LONG-TERM TO ICB-BASED THERAPIES



>50% dies from melanoma

Wolchok JD. et al. J Clin Oncol. 2022

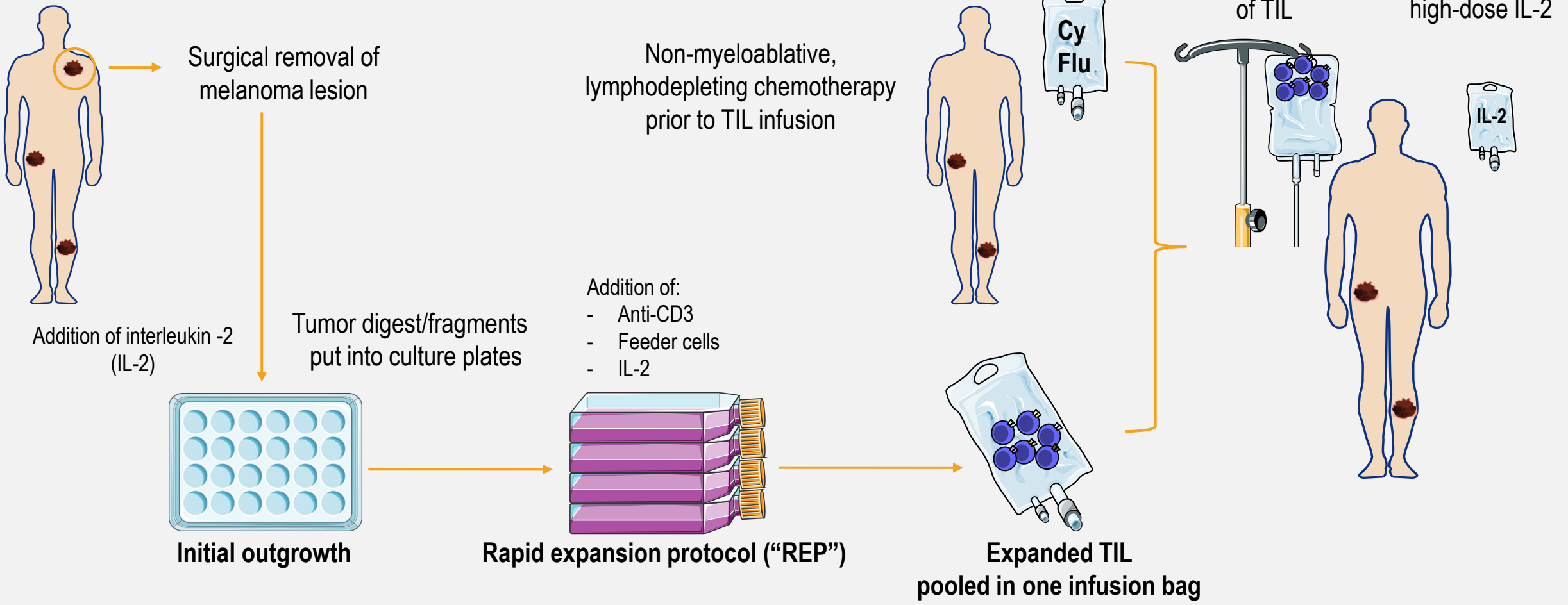
ADOPTIVE CELLULAR THERAPY PLATFORMS FOR SOLID CANCERS



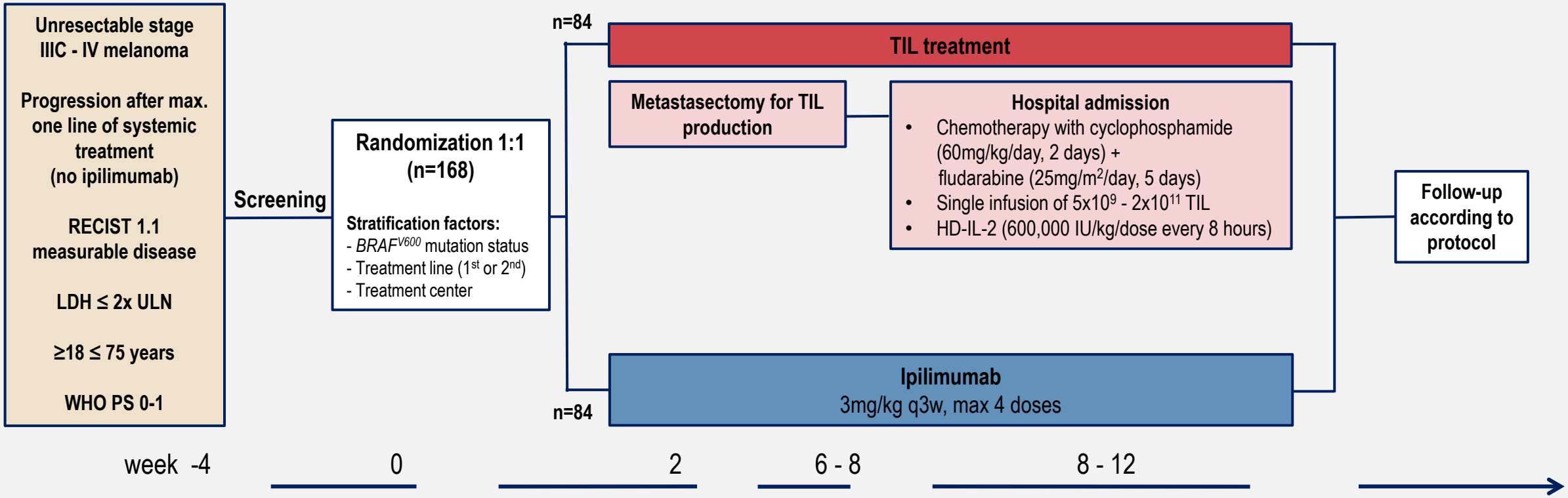
June, Riddell & Schumacher Sci Transl Med 2015

TUMOR-INFILTRATING LYMPHOCYTES (TIL)

Preparation and treatment



TRIAL DESIGN OF PHASE 3 RCT IN MELANOMA

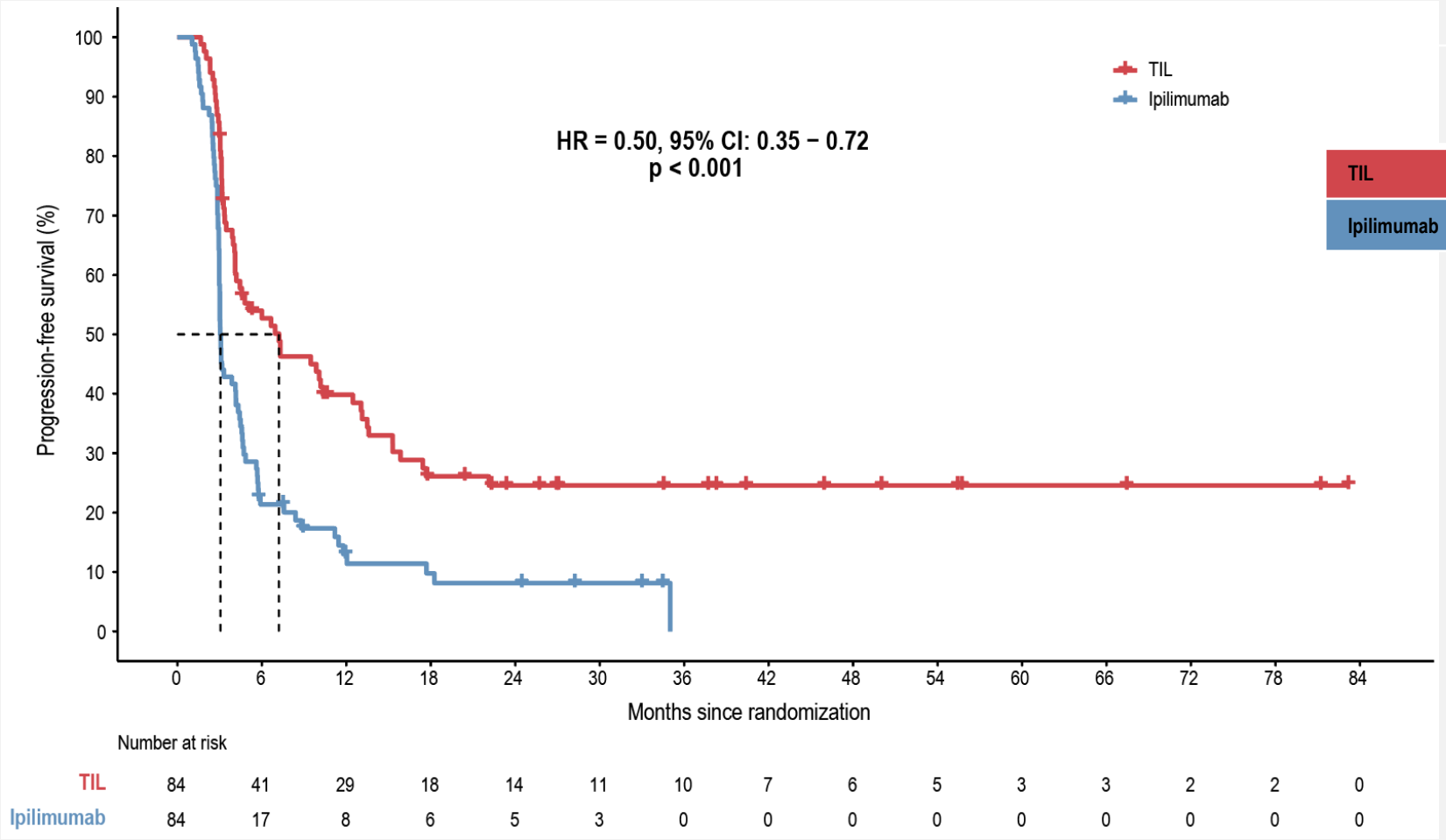


Primary endpoint: Progression-free survival (PFS) according to RECIST 1.1 per investigator review in the intention-to-treat population (ITT)*

*Using the stratified (unweighted) log-rank test and the stratified cox regression model. The study was considered to be positive when PFS after TIL is significantly longer than ipilimumab, based on the log-rank test with a two-sided p-value below 0.05.

Rohaan et al., NEJM 2022

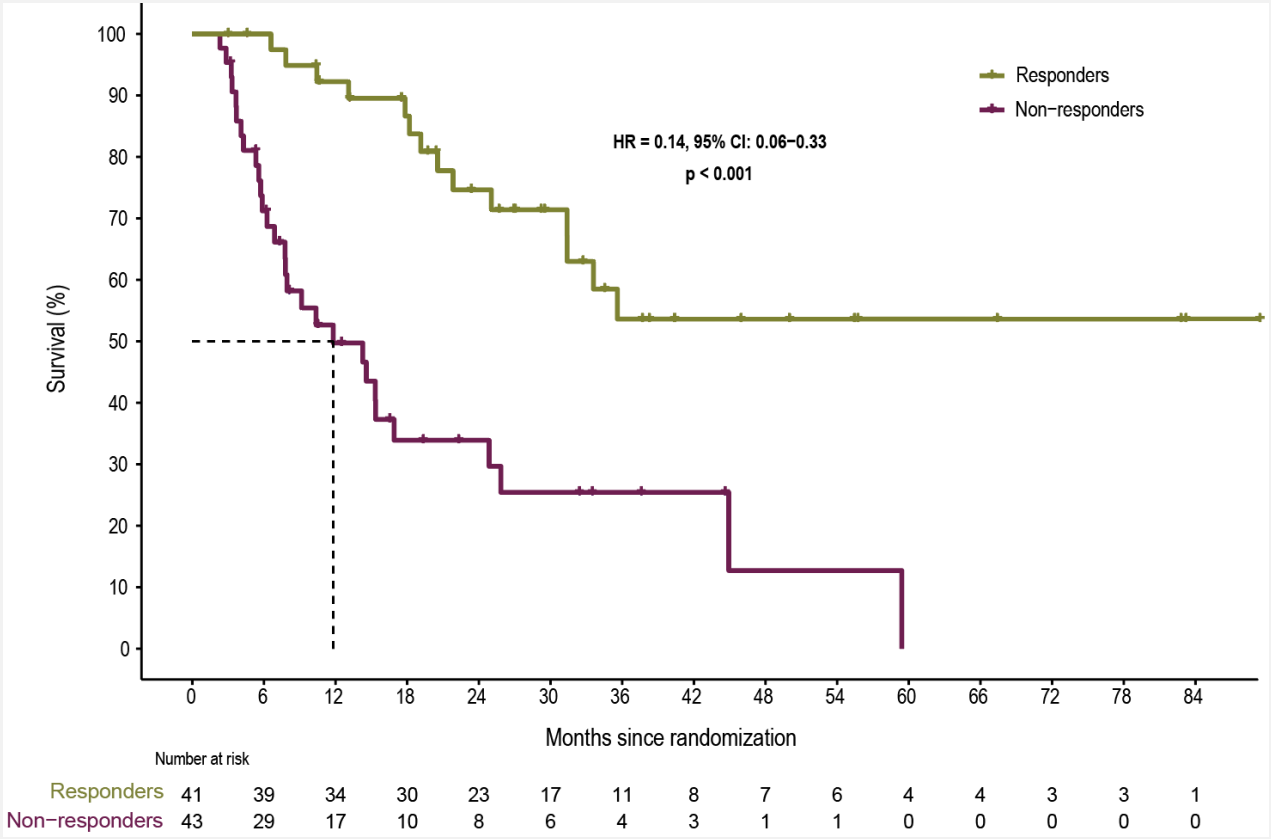
PFS ACCORDING TO RECIST 1.1 IN THE ITT POPULATION

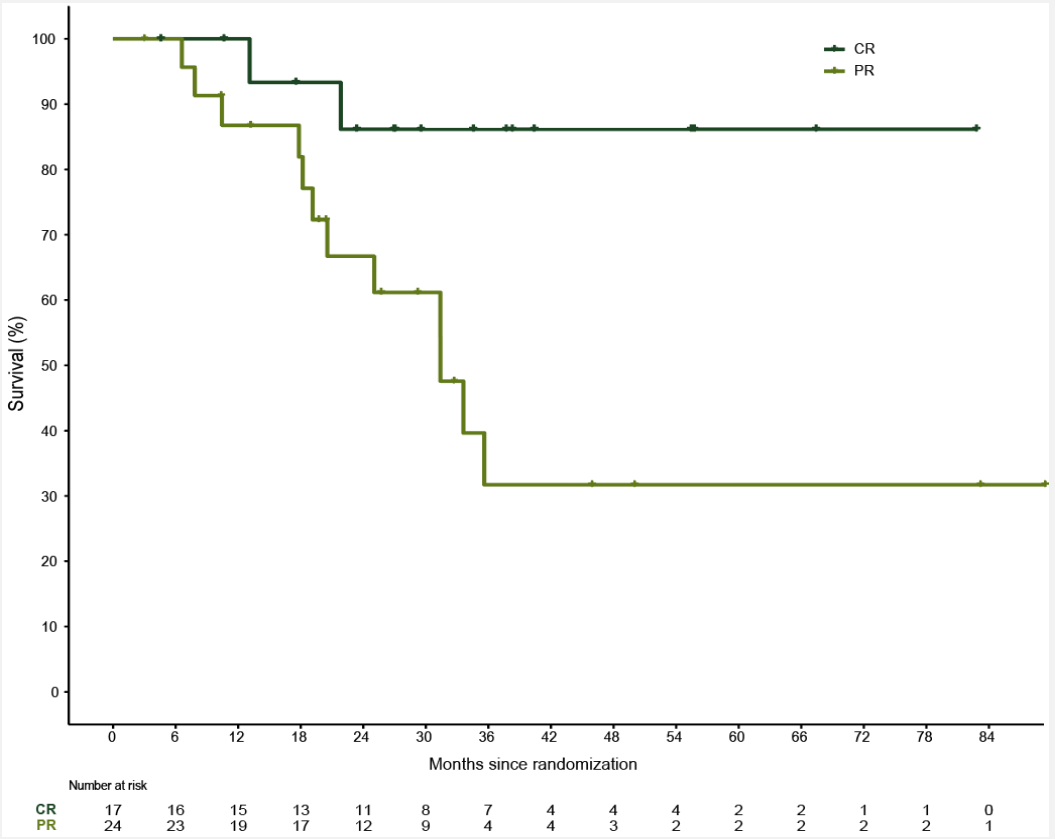


	Median follow-up (months)	Median PFS (months)	95% CI	6 month PFS (%)	95% CI
TIL	33.5	7.2	4.2 - 13.1	52.7	42.9 - 64.7
Ipilimumab	33.0	3.1	3.0 - 4.3	21.4	14.2 - 32.2

Rohaan et al., NEJM 2022

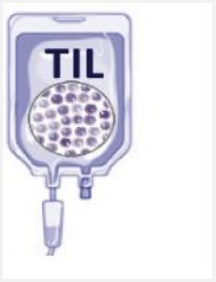
OVERALL SURVIVAL IN TIL ARM (ITT)





Rohaan et al. NEJM 2022

TIL THERAPY: AREAS OF POSSIBLE IMPROVEMENT



TIL THERAPY: AREAS OF POSSIBLE IMPROVEMENT CY/ FLU & IL-2

Issues: Toxicity of Cy/ Flu
Toxicity of IL-2
Activity of IL-2 on other cell types, such as Tregs

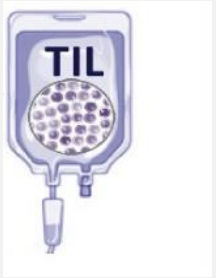
TIL THERAPY: AREAS OF POSSIBLE IMPROVEMENT CY/ FLU & IL-2

Issues: Toxicity of Cy/ Flu
Toxicity of IL-2
Activity of IL-2 on other cell types, such as Tregs

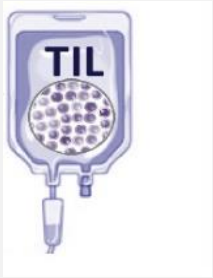
Approach: Engineer immunocytokines that selectively induce the expansion of cells of interest

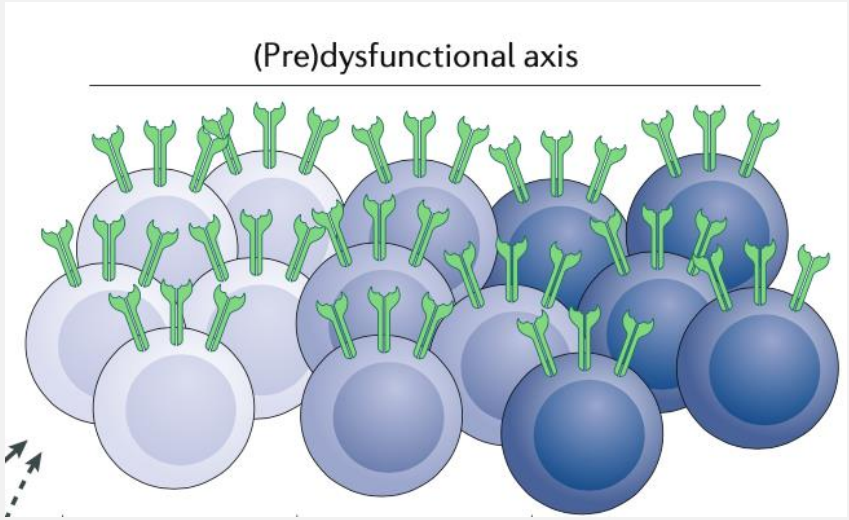
Benefits Potential to use reduced intensity host conditioning
Avoidance of IL-2 toxicity & avoidance of IL-2 activity on other cell types

TIL THERAPY: AREAS OF POSSIBLE IMPROVEMENT
THE T CELLS THEMSELVES



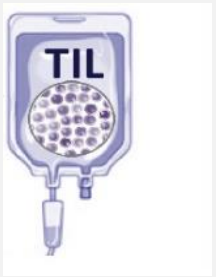
TIL THERAPY: AREAS OF POSSIBLE IMPROVEMENT THE T CELLS THEMSELVES

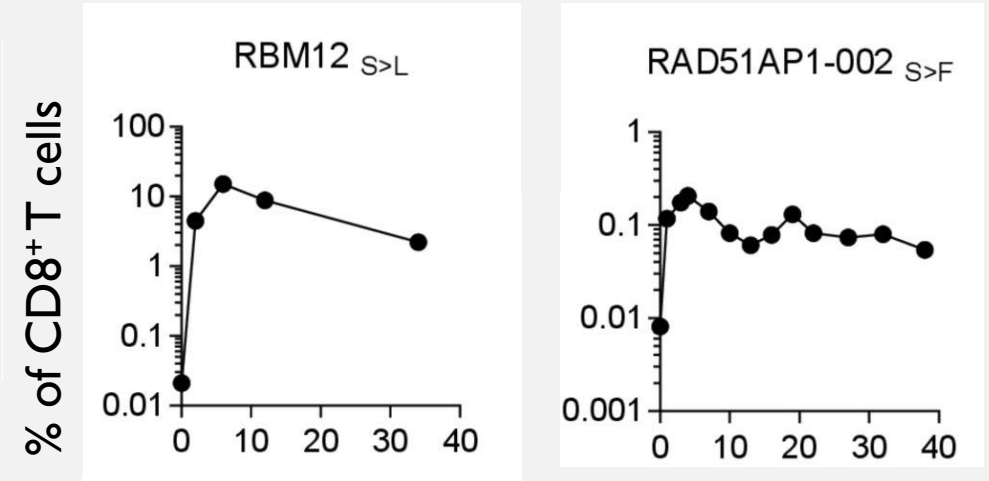




Many of the T cells are exhausted/dysfunctional

TIL THERAPY: AREAS OF POSSIBLE IMPROVEMENT
THE T CELLS THEMSELVES

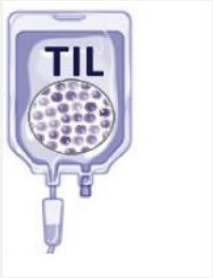


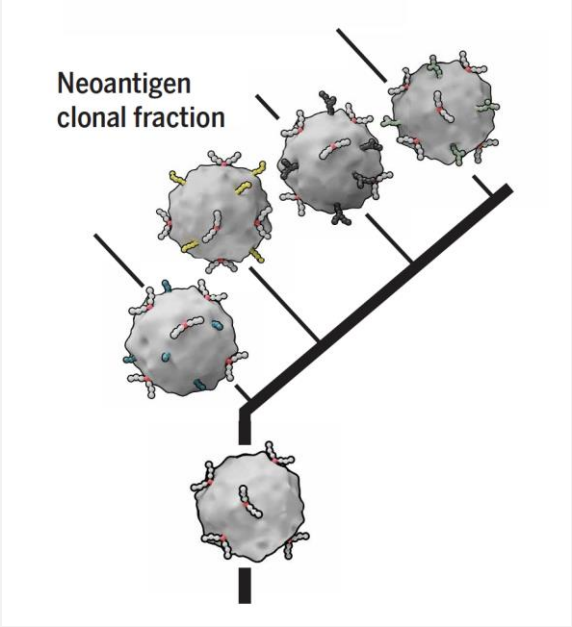


The frequency of neoantigen-specific T cells in TIL products is highly variable (Post TIL PB: <0.1% - >10%)

Van den Berg et al. JITC 2020

TIL THERAPY: AREAS OF POSSIBLE IMPROVEMENT THE T CELLS THEMSELVES

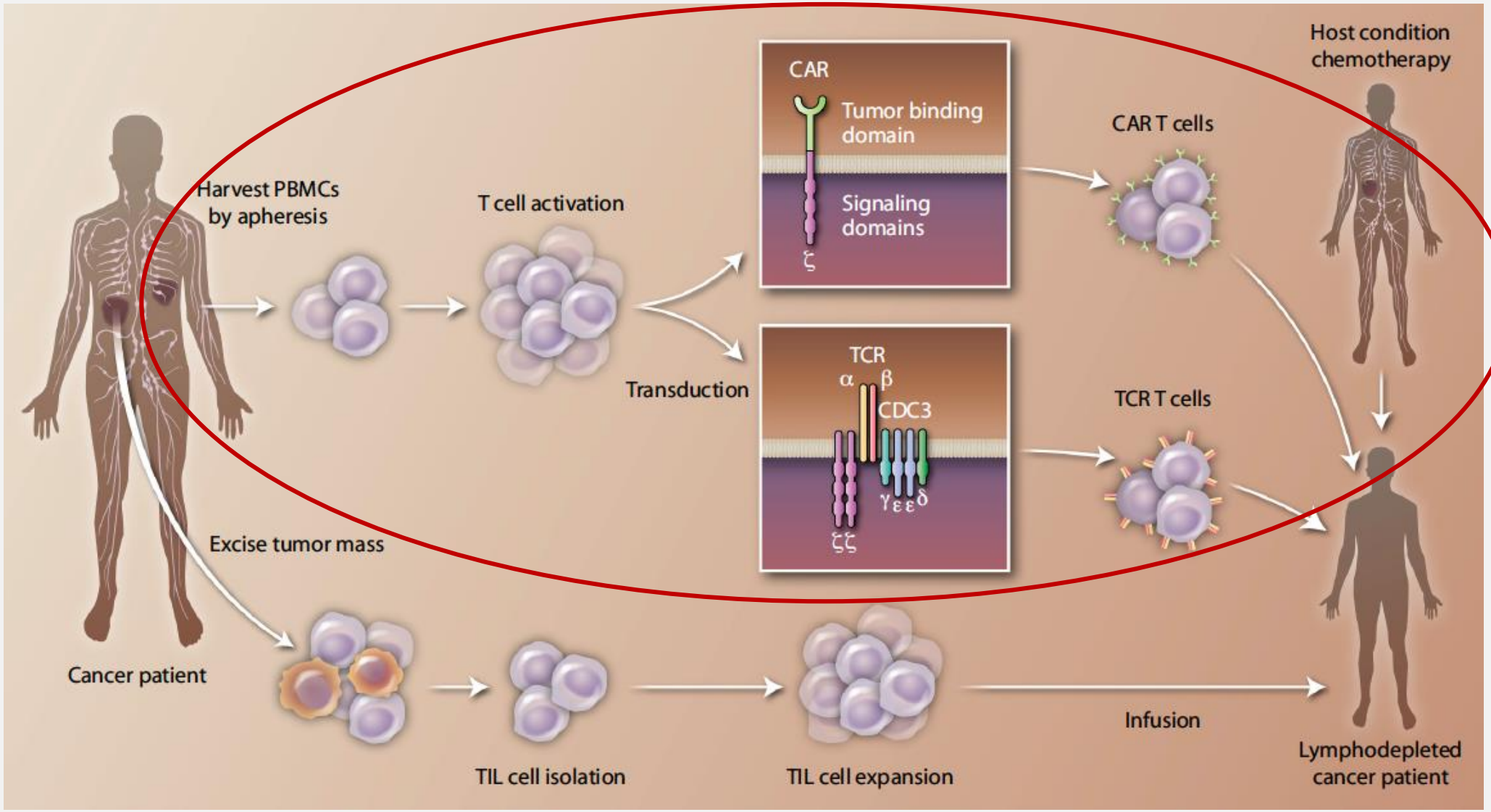




& part of the T cell-recognized neoantigens is subclonal

McGranahan and Swanton. STM 2019

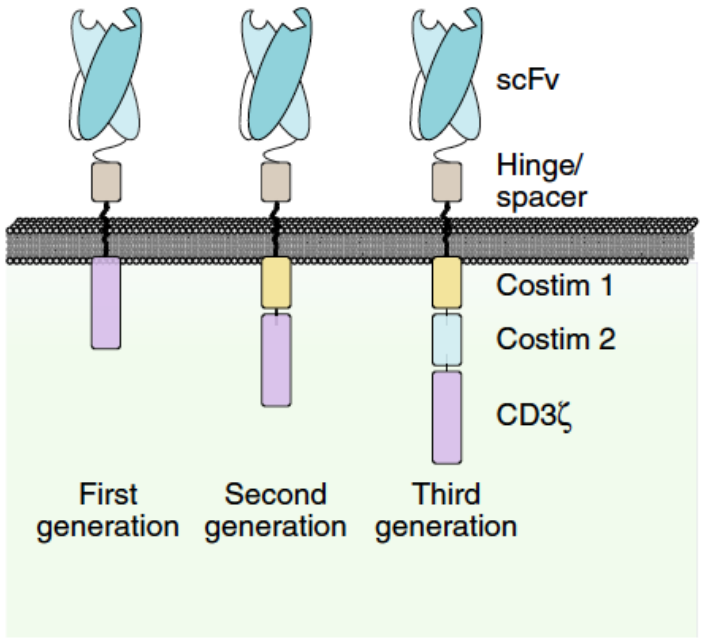
ADOPTIVE CELLULAR THERAPY PLATFORMS FOR SOLID CANCERS



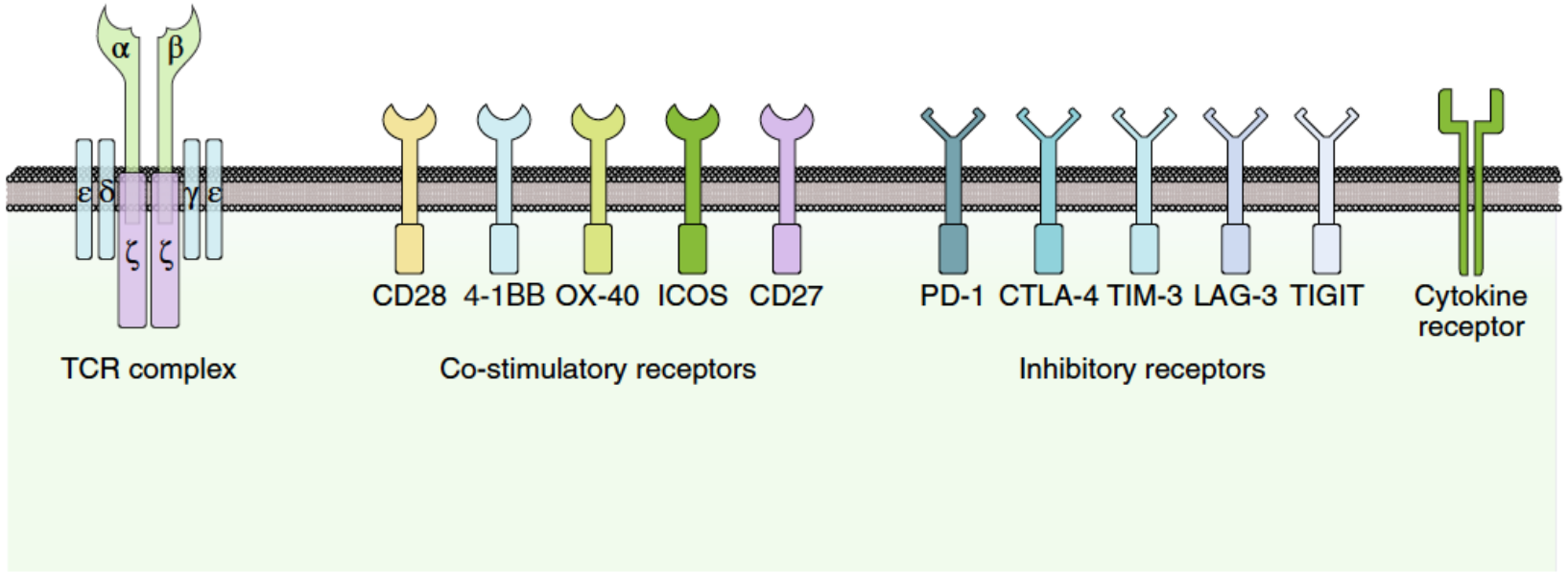
June, Riddell & Schumacher Sci Transl Med 2015

CAR VERSUS TCR

CAR

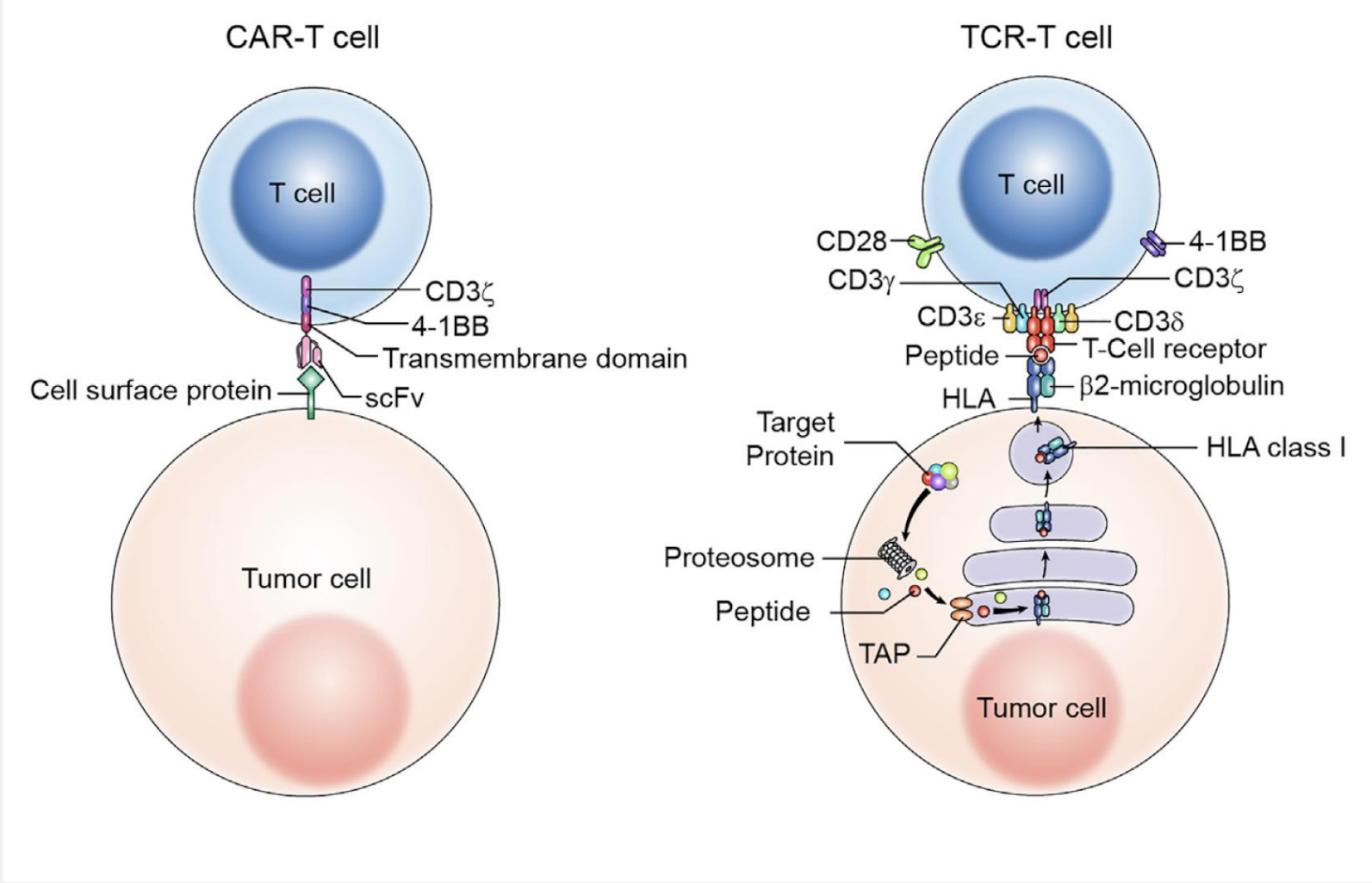


TCR



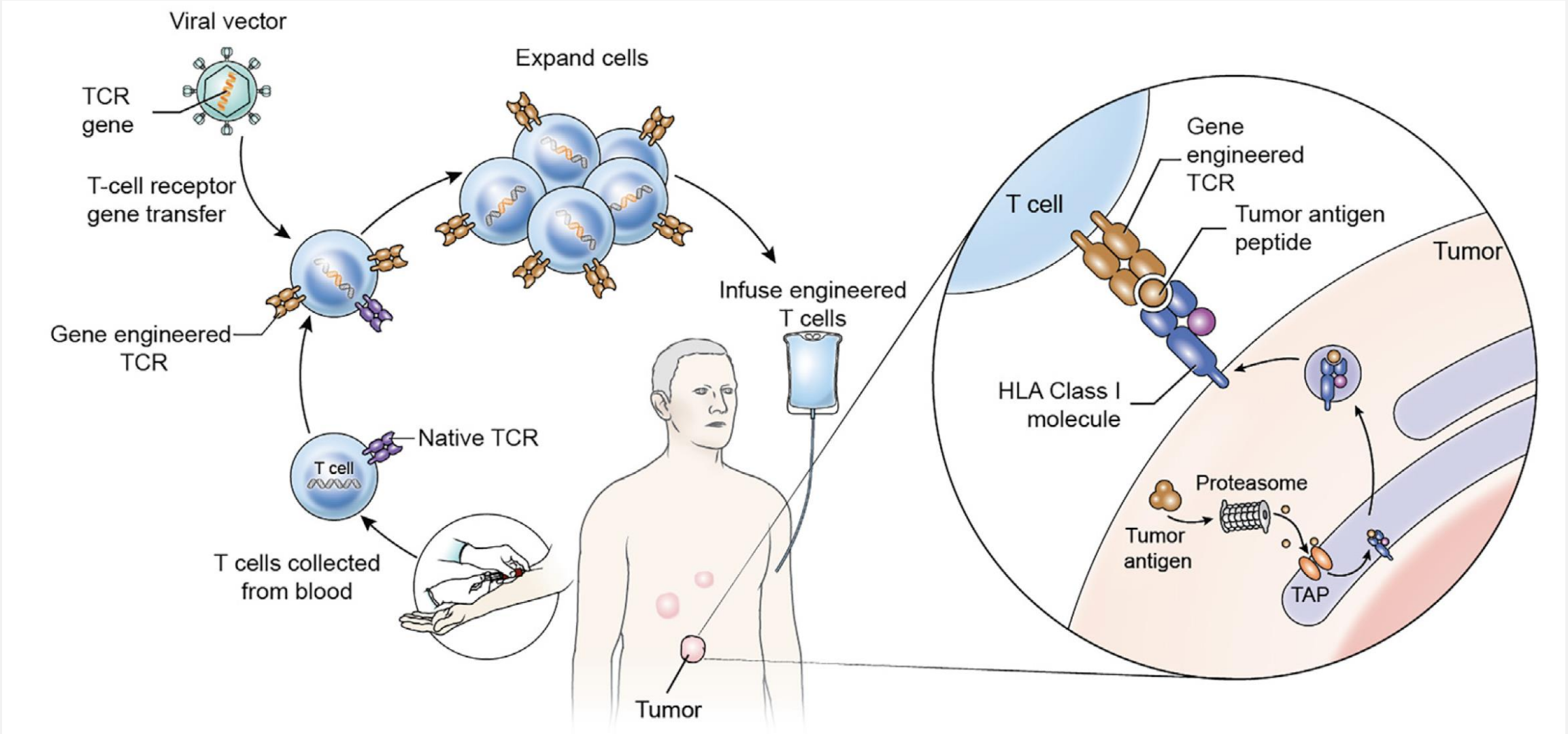
Labanieh et al., Nat Biomed Engin 2018

ANTIGEN RECOGNITION BY CAR-T AND TCR-T



Norberg & Hinrichs, Cancer Cell 2023

T CELL RECEPTOR GENE-ENGINEERED T CELLS



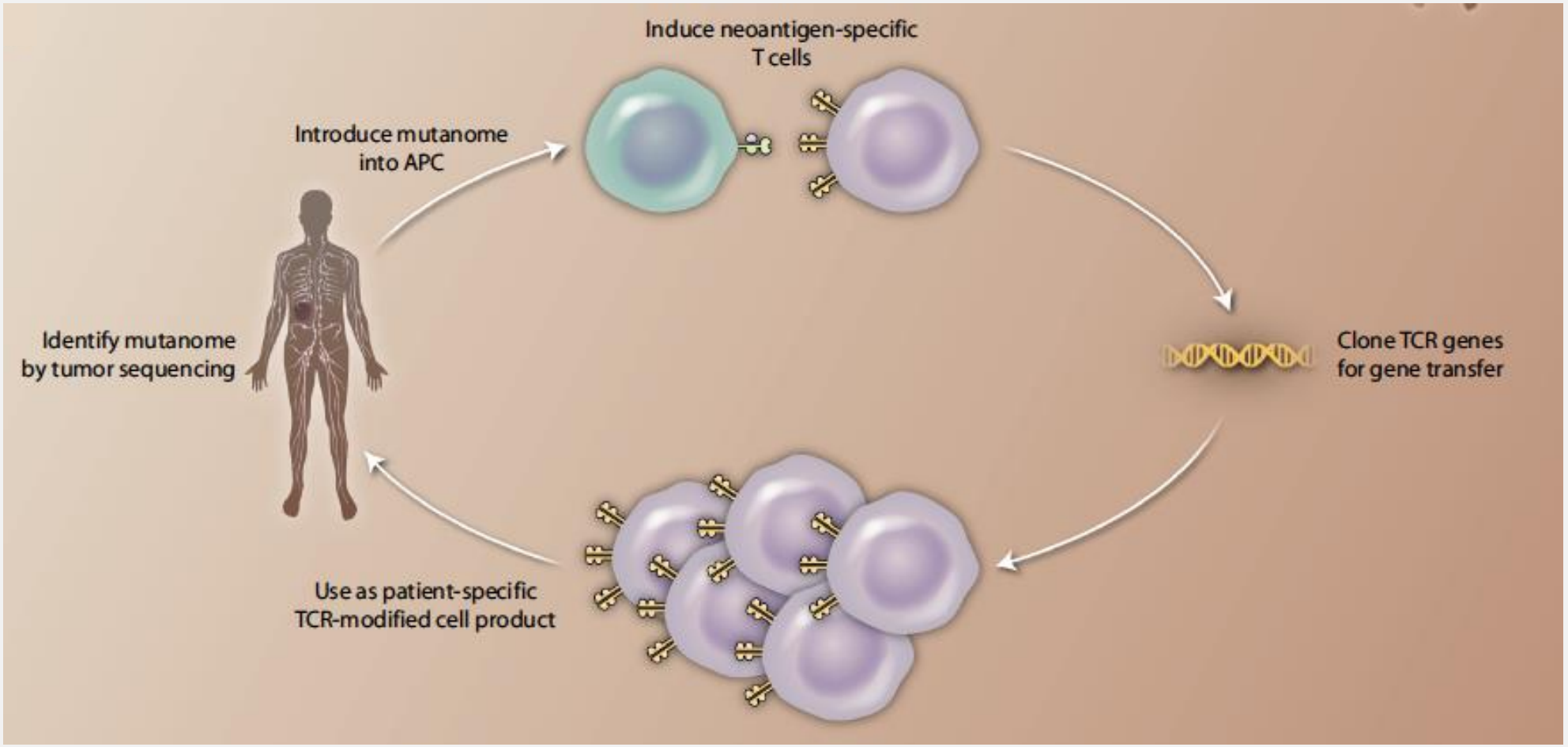
TRIALS WITH ENGINEERED T CELLS DEMONSTRATING CLINICAL ACTIVITY IN SOLID CANCERS

Antigen-targeting receptor	Conditioning regimen	Maximum cell dose	Transduction efficiency (median/range)	Systemic cytokine therapy	Tumor responses (responses/N)
MART1 TCR	cyclophosphamide 60 mg/kg × 2 days fludarabine 25 mg/m^2 × 5 days	107 × 10^9	71	aldesleukin 720,000 IU/kg q8hrs	6/20
gp100 TCR	cyclophosphamide 60 mg/kg × 2 days fludarabine 25 mg/m^2 × 5 days	110 × 10^9	82	aldesleukin 720,000 IU/kg q8hrs	3/16
NY-ESO-1 TCR	cyclophosphamide 60 mg/kg × 2 days fludarabine 25 mg/m^2 × 5 days	130 × 10^9	78, 62[b]	aldesleukin 720,000 IU/kg q8hrs	22/38
NY-ESO-1 TCR	cyclophosphamide 1,800 mg/m^2 × 2 days fludarabine 30 mg/m^2 × 4 days	14 × 10^9	N/A[c]	none	6/12
NY-ESO-1 TCR	cyclophosphamide 600–1,800 mg/m^2 × 2–3 days fludarabine 30 mg/m^2 × 3–4 days	N/A[c]	N/A[c]	none	9/30
MAGE-A3 TCR	cyclophosphamide 60 mg/kg × 2 days fludarabine 25 mg/m^2 × 5 days	120 × 10^9	90	aldesleukin 720,000 IU/kg q8hrs	4/17
MAGE-A3/A9/A12 TCR	cyclophosphamide 60 mg/kg × 2 days fludarabine 25 mg/m^2 × 5 days	79 × 10^9	85	aldesleukin 720,000 IU/kg q8hrs	5/9
E6 TCR	cyclophosphamide 60 mg/kg × 2 days fludarabine 25 mg/m^2 × 5 days	134 × 10^9	60	aldesleukin 720,000 IU/kg q8hrs	2/12
E7 TCR	cyclophosphamide 30 or 60 mg/kg × 2 days fludarabine 25 mg/m^2 × 5 days	120 × 10^9	96	aldesleukin 720,000 IU/kg q8hrs	6/12
CLDN18.2 CAR[10]	cyclophosphamide 250 mg/m^2 × 3 days fludarabine 25 mg/m^2 × 2 days Nab-paclitaxel 100 mg or gemcitabine 1,000 mg × 1 day	5 × 10^8	N/A[c]	none	18/37

[a]Clinical trials with ≥2 objective responses by RECIST criteria.
[b]CD8$^+$ and CD4$^+$ T cells, respectively.
[c]Not available.

Norberg & Hinrichs, Cancer Cell 2023

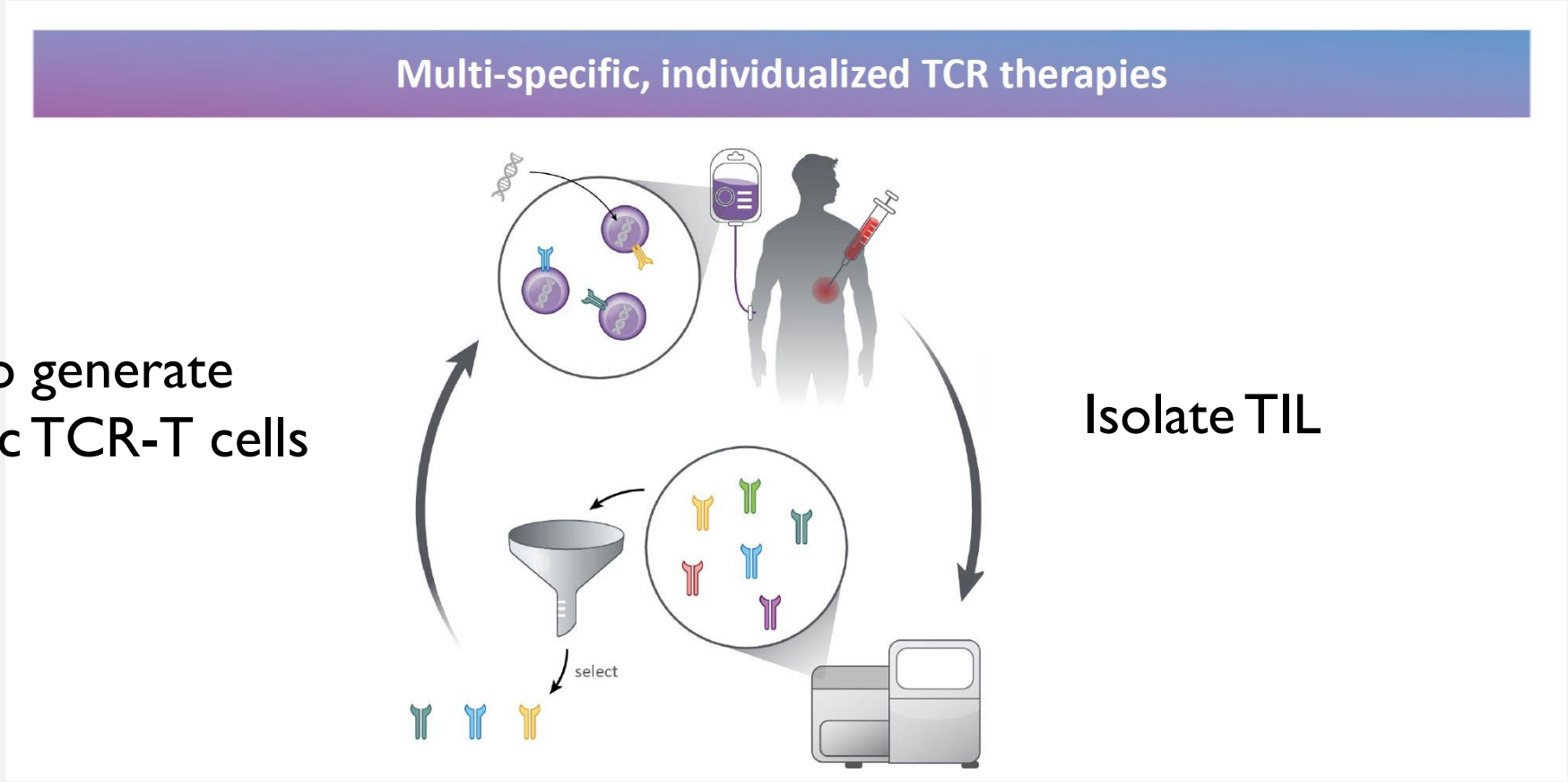
GENERATION OF NEOANTIGEN-SPECIFIC TCR GENE THERAPY



June, Riddel & Schumacher, STM 2015

FROM TIL THERAPY TO AUTOLOGOUS TCR THERAPY?

Use TCRs to generate multi-specific TCR-T cells

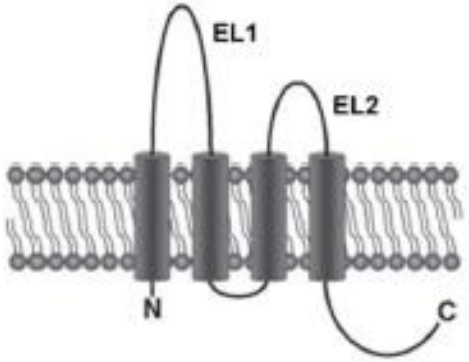


Isolate TIL

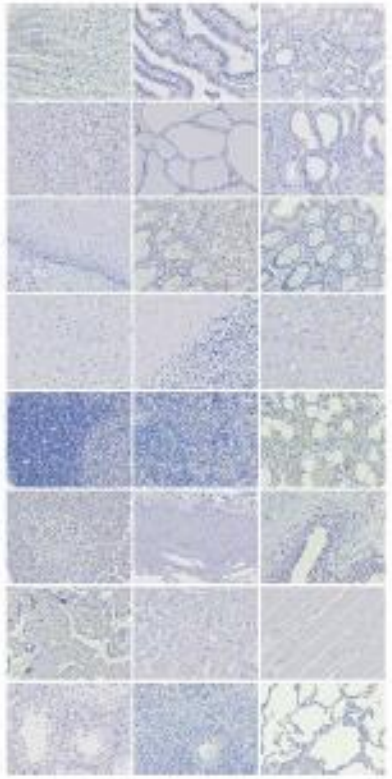
Identify neo-antigen reactive TCRs

CLAUDIN-6 (CLDN6) IS AN IDEAL TARGET FOR CAR-T CELL THERAPY

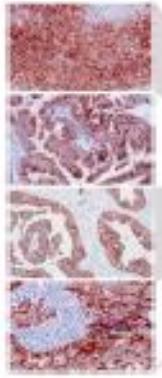
Targetable extracellular loops (EL)



Absent in healthy tissue

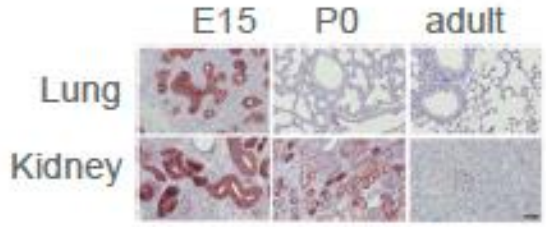


Expressed in various cancers



Indication	% CLDN6+
Testicular cancer	93
Ovarian cancer	56
Endometrial cancer	23
Lung cancer	11
Rare tumors	Up to 30

Silenced during organogenesis



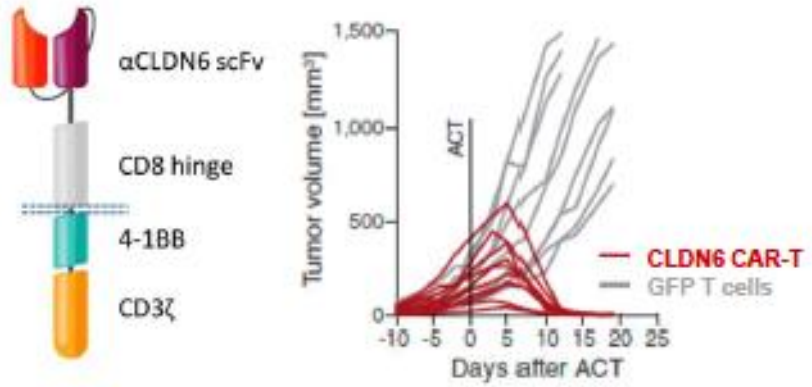
E15 = Embryonic week 15; P0 = at birth.
Reinhard, Rengstl, Oehm et al. Science 2020

Correlation with disease progression

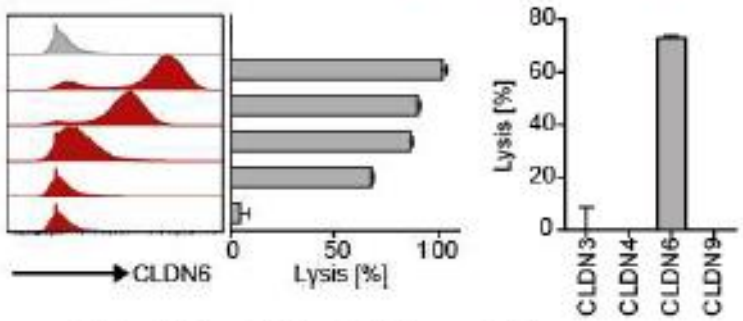
BIONTECH

CO-DEVELOPMENT OF A CLDN6 CAR AND CARVAC

Potent 2nd generation CAR

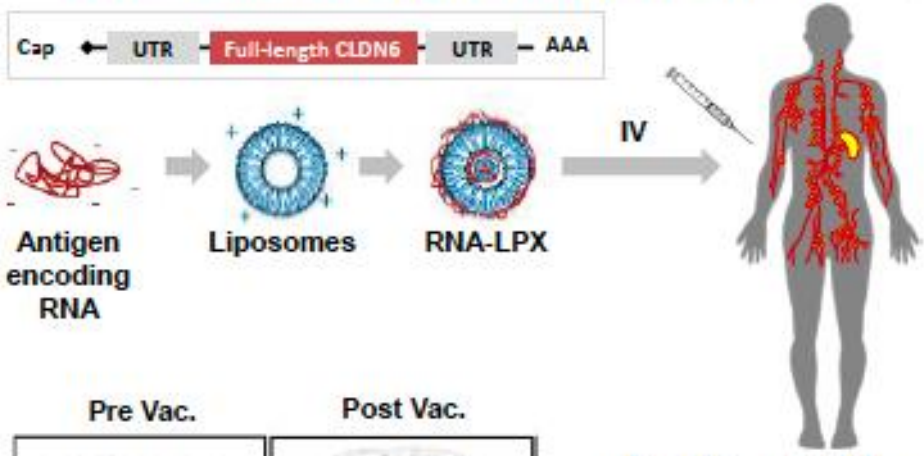


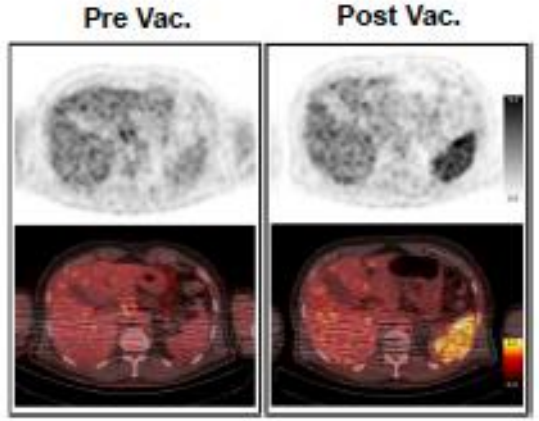
High sensitivity & specificity

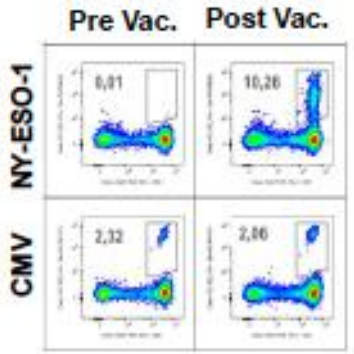


4 Reinhard, Rengstl, Oehm et al. Science 2020

RNA Lipoplexes (LPX) targeting APCs



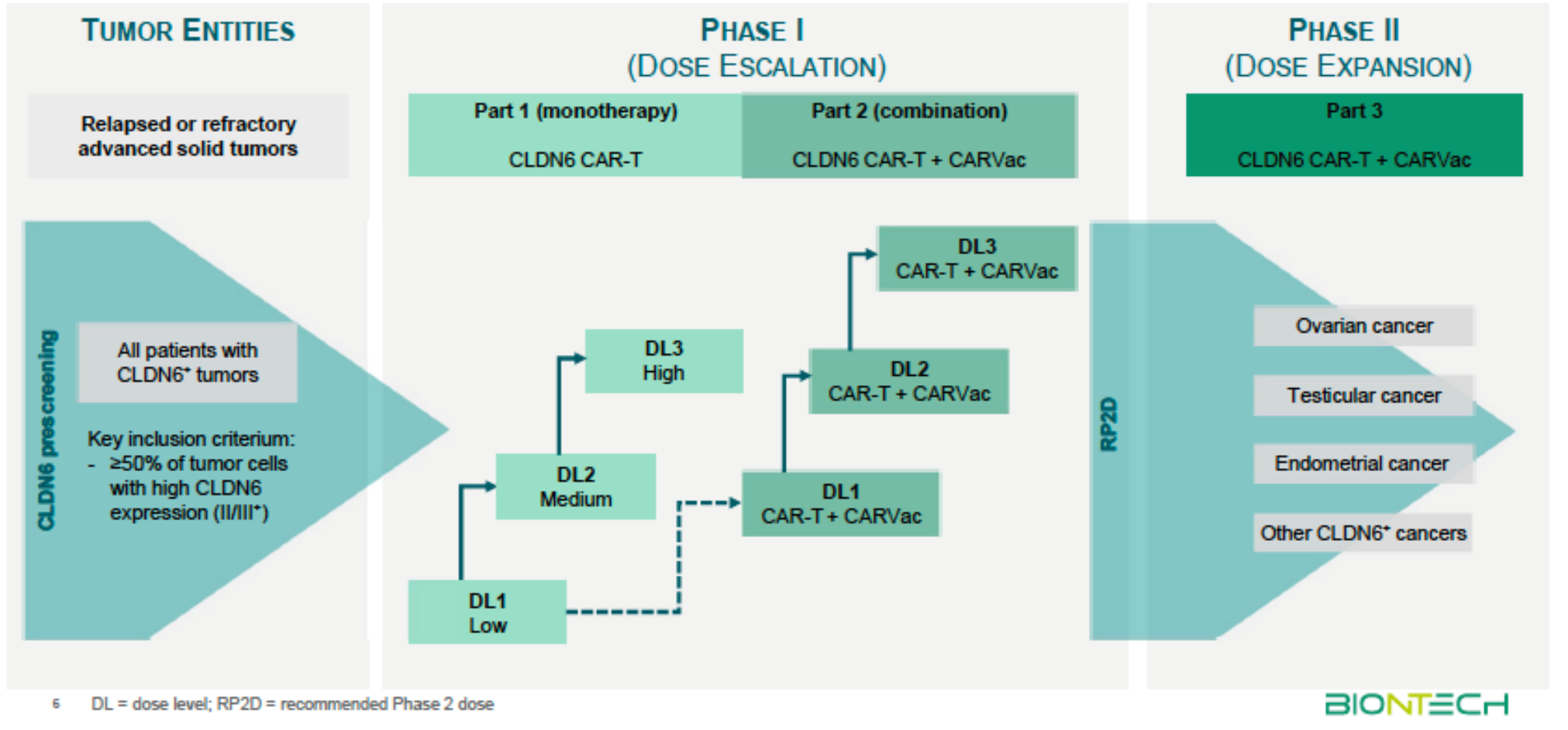




Kranz et al. Nature 2016, Sahin et al. Nature 2020

BIONTECH

DESIGN OF PHASE I TRIAL: 3 + 3 DOSE ESCALATION WITH BIFURCATION



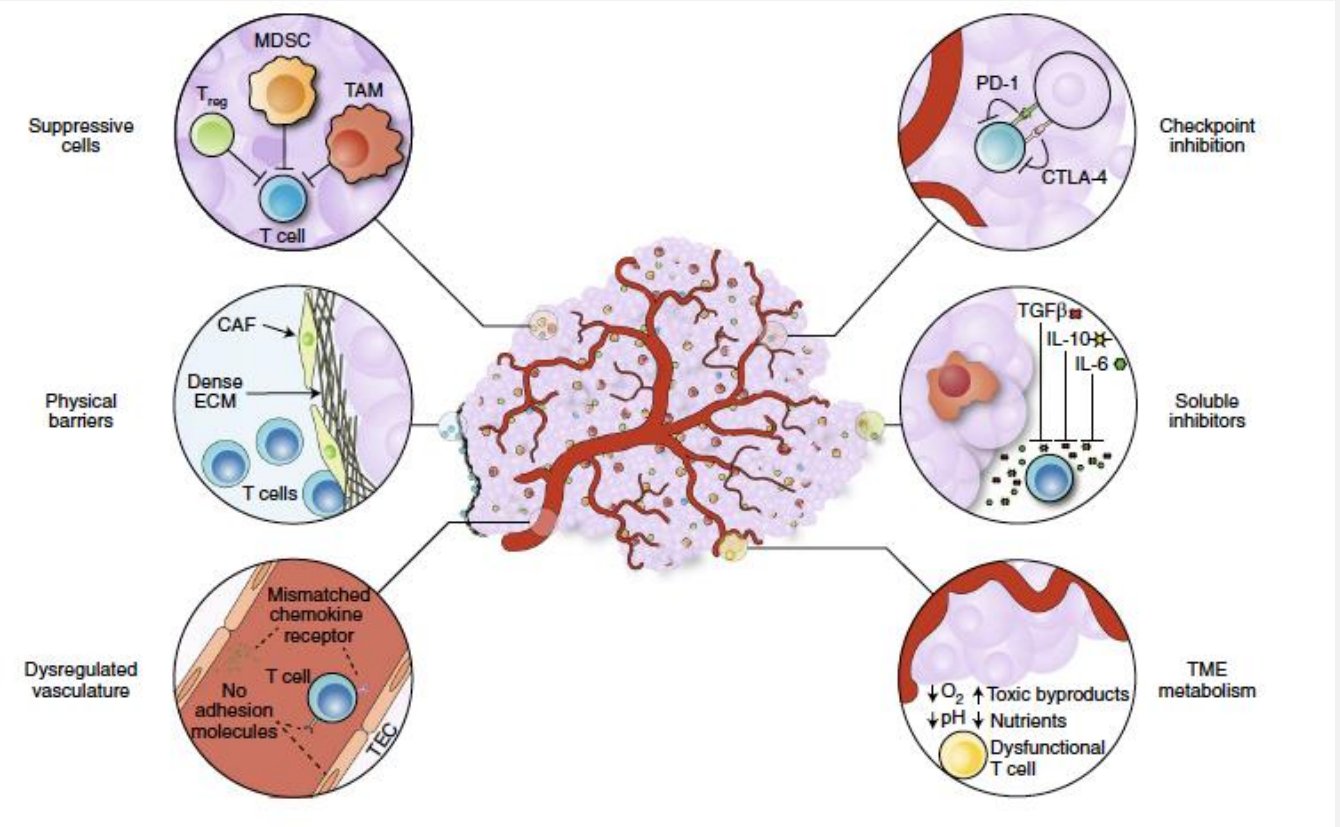
6 DL = dose level; RP2D = recommended Phase 2 dose

TAKE HOME MESSAGES

- There is growing interest (both pharma and academia) for adoptive cell therapy of solid cancers
- Currently, data from TIL treatment (melanoma, cervical cancer, NSCLC) are most mature and convincing. Targeting more than one antigen may be important.
- For solid cancers, no cell therapy has been approved yet
- TCR and CAR gene therapy is upcoming and early efficacy data hold promise
- It is likely that for solid cancers, cell therapy requires combination with other agents (ICB, vaccines) to maximize efficacy

OVERCOMING HURDLES OF ACT IN SOLID TUMORS

- Hostile TME
- Persistence of cells
- Lack of infiltration
- Development of exhaustion



Labanieh et al., Nat Biomed Engin 2018

THANK YOU!