Immuno-Oncologie 2.0 : vers une Personnalisation des Immunothérapies en Cancérologie

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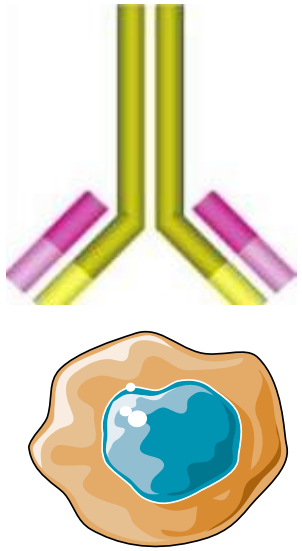
Cancéropole Est, Strasbourg, 13 Mars 2025

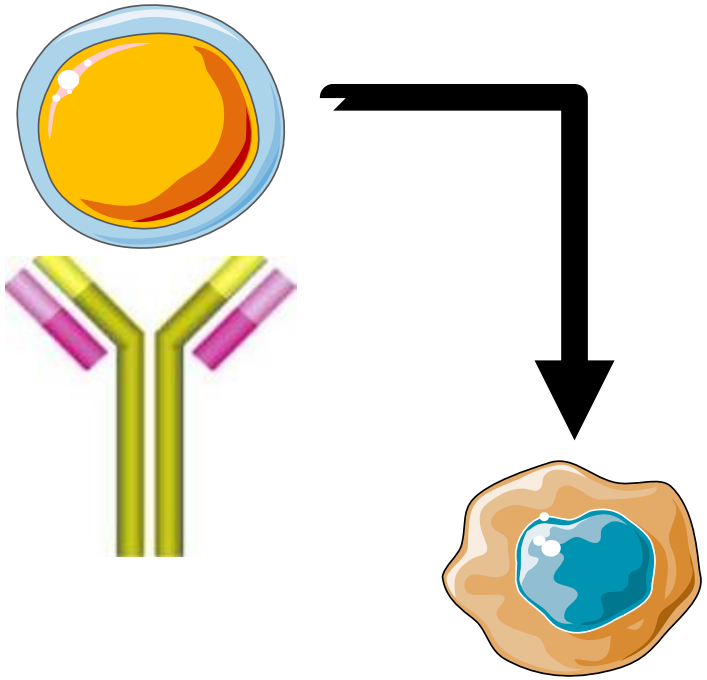
Changement de Paradigme en Cancérologie

Paradigme Historique: Cibler les Cellules Cancéreuses	Nouveau Paradigme: Cibler les Cellules Immunitaires

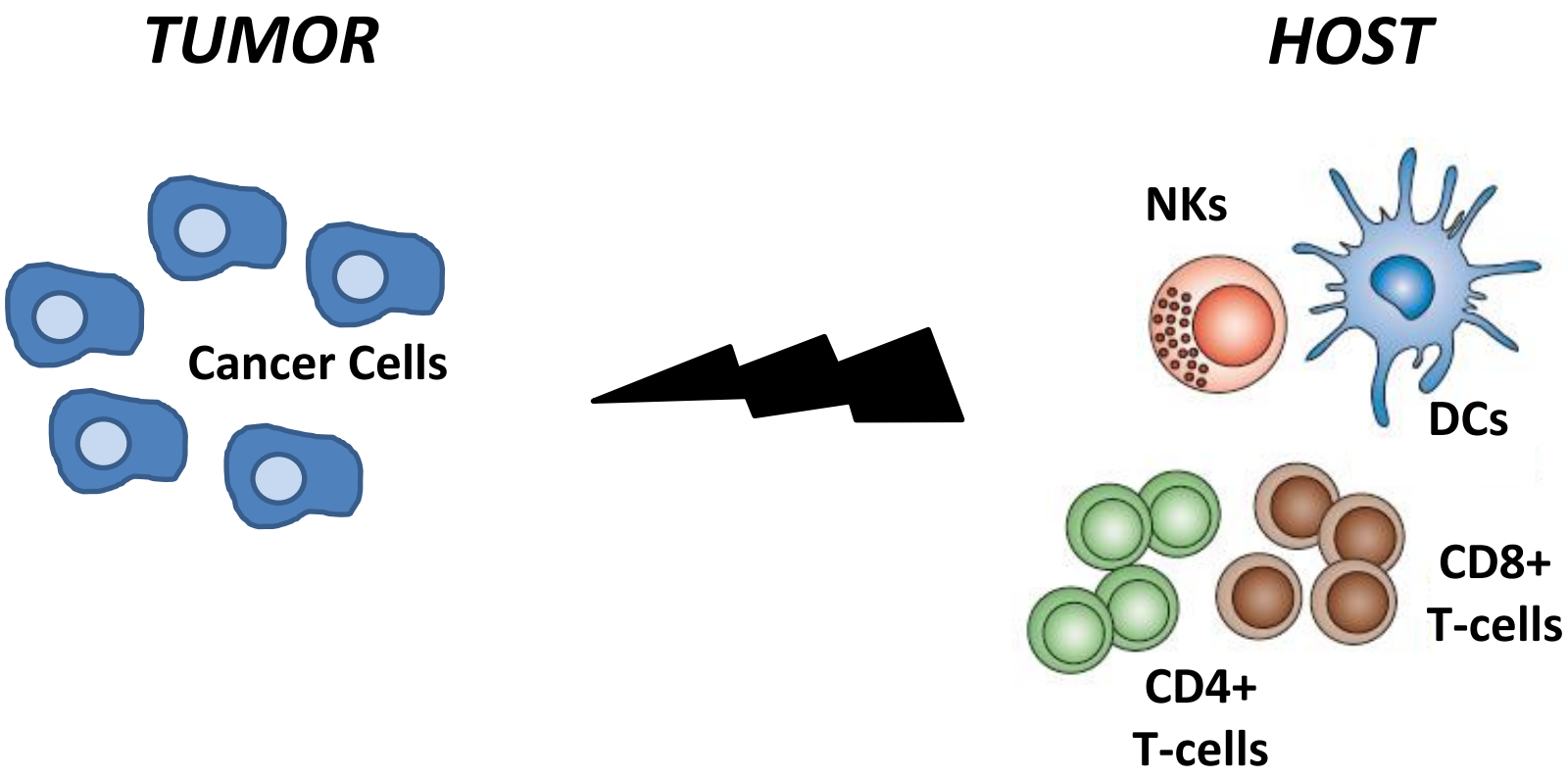


Cellule Cancéreuse

Lymphocyte

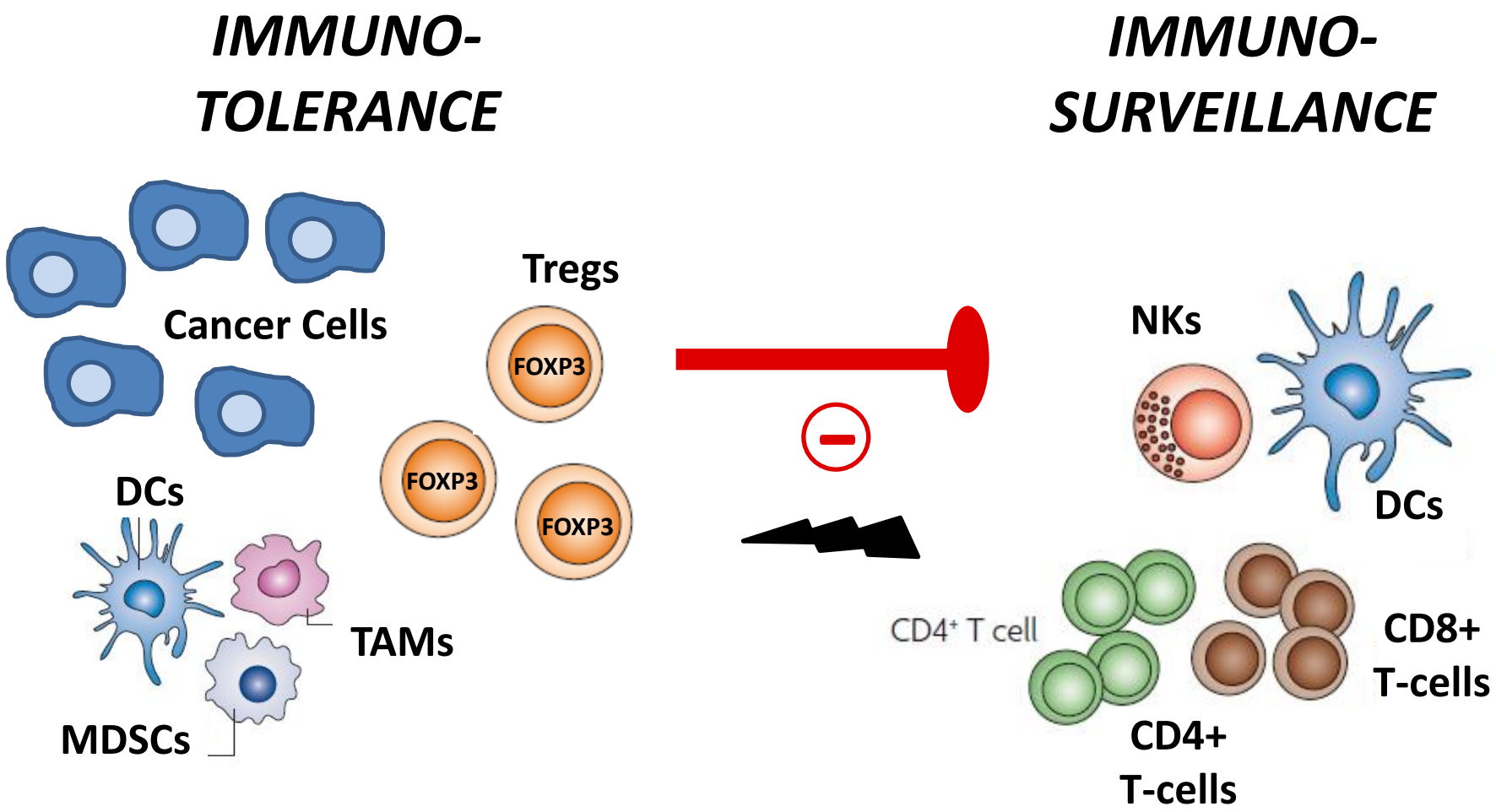


1970 – 2000:
Role or the Immune System = Immuno-Surveillance



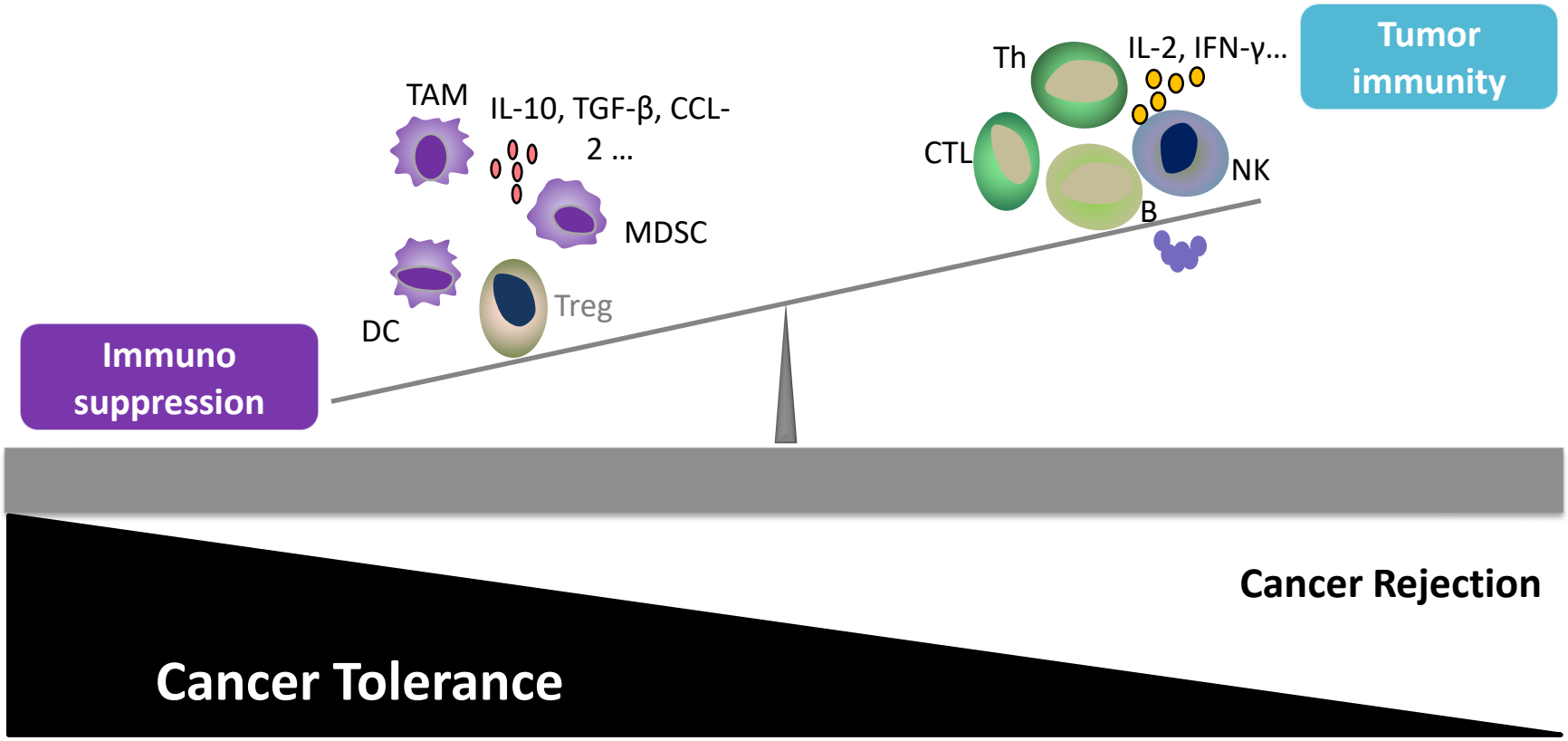
Adapted from Colombo MP, et al Nat Rev Cancer. 2007 Nov;7(11):880-7.

2000-2010:
Subsets of Immune Cells can also Promote Cancers !

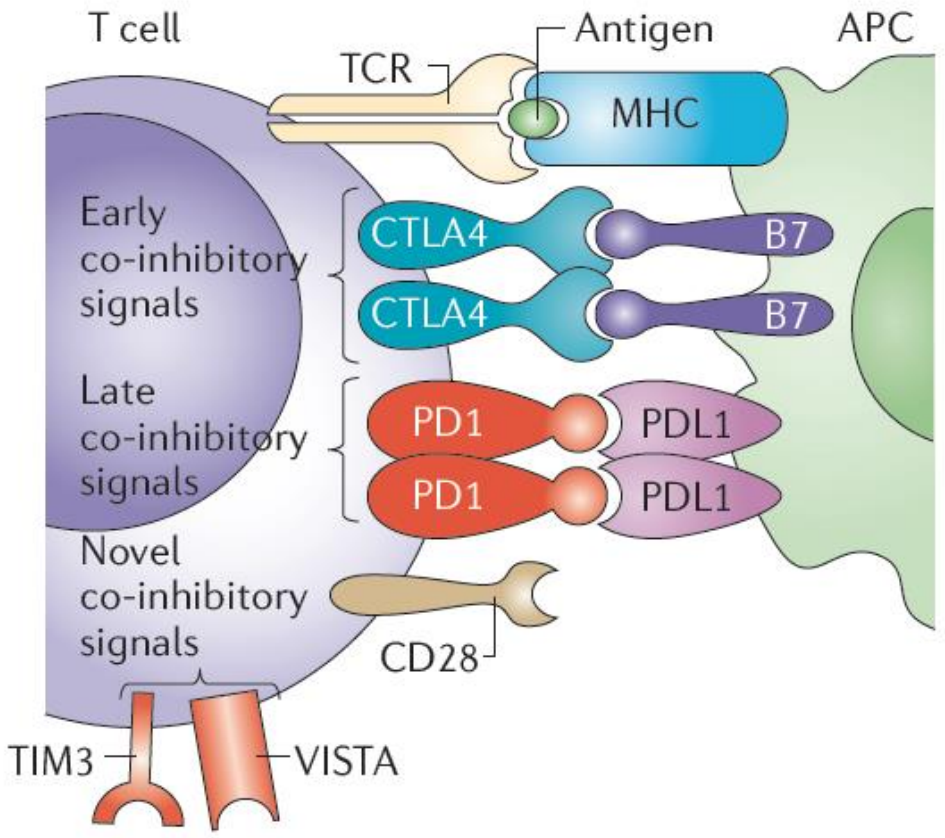


Adapted from Colombo MP, et al Nat Rev Cancer. 2007 Nov;7(11):880-7.

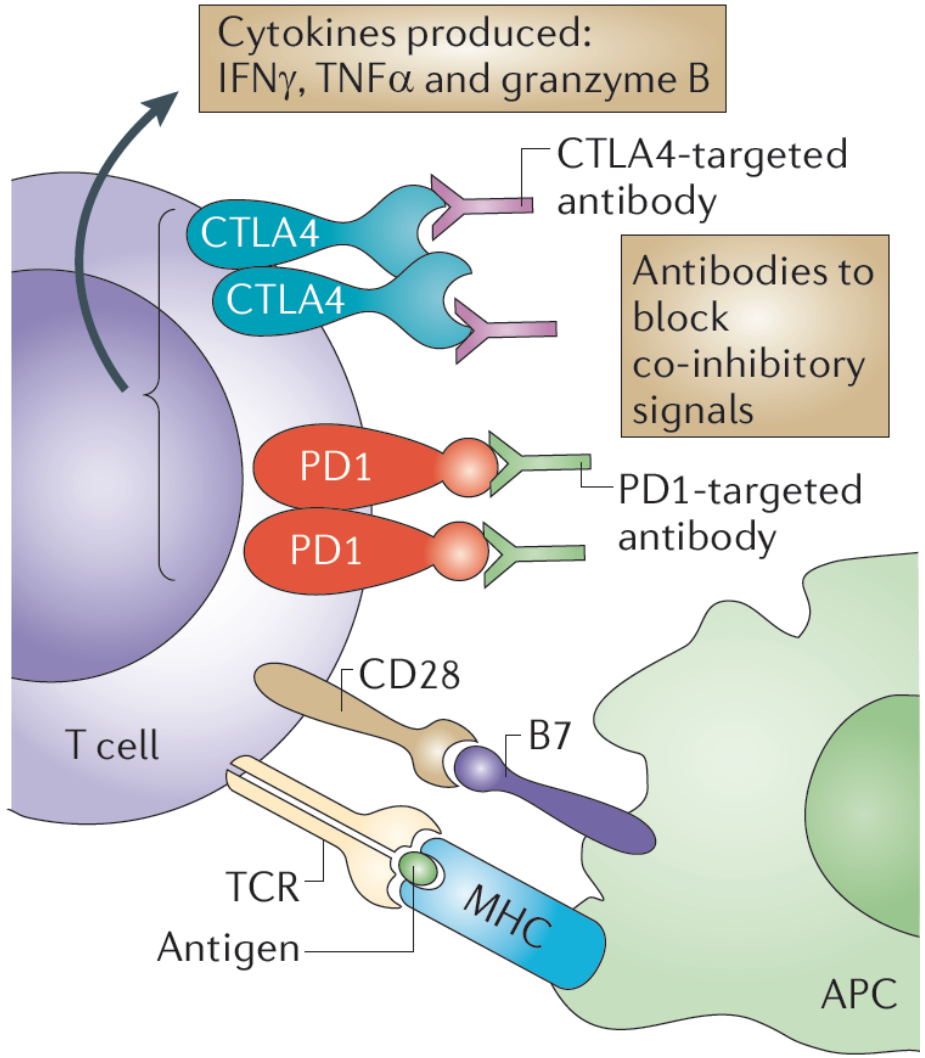
Cancer is a Disequilibrium in favor of Tolerance over Rejection of Cancer Cells



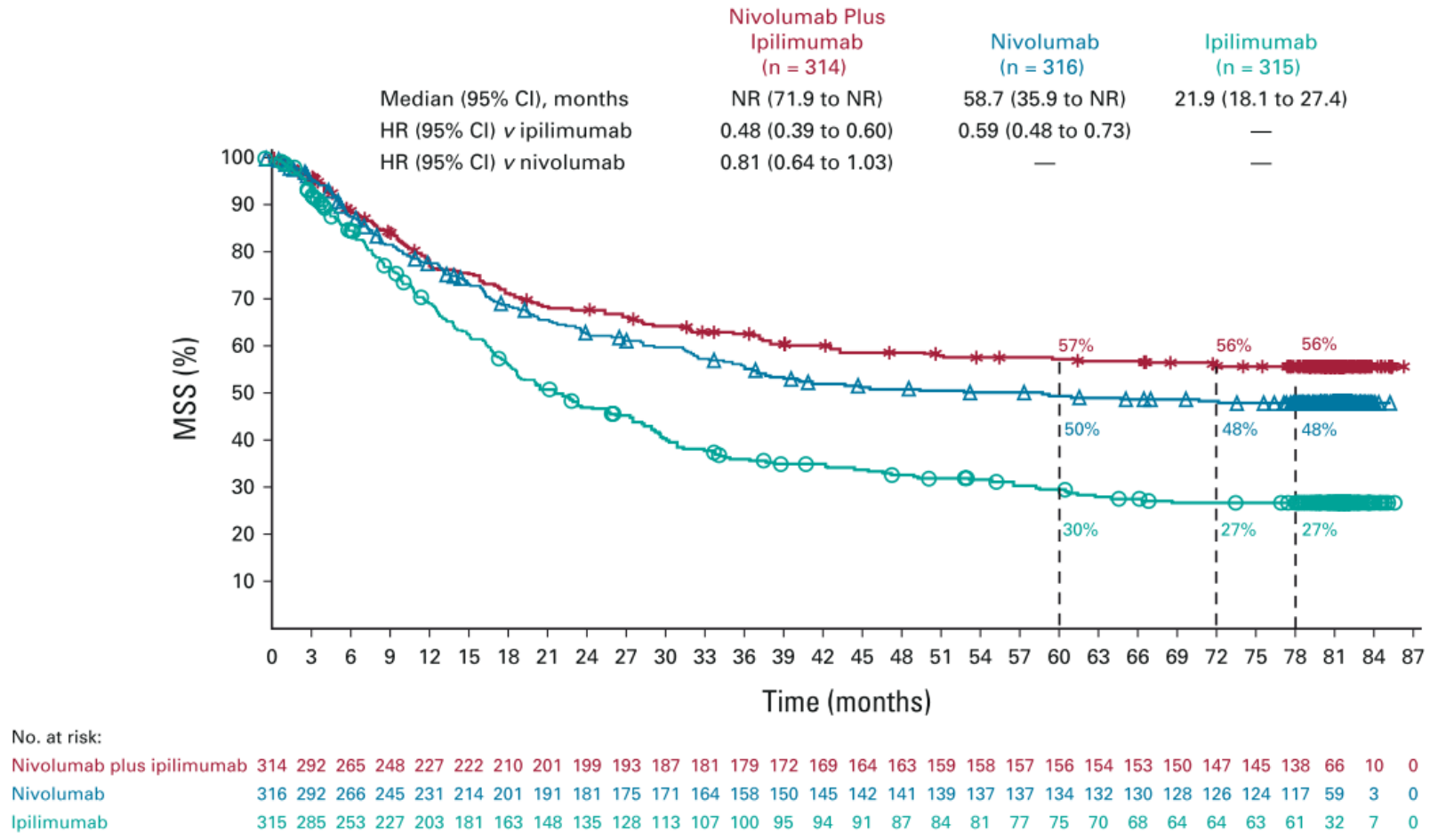
Activation of T-Cells is Suppressed in the TME

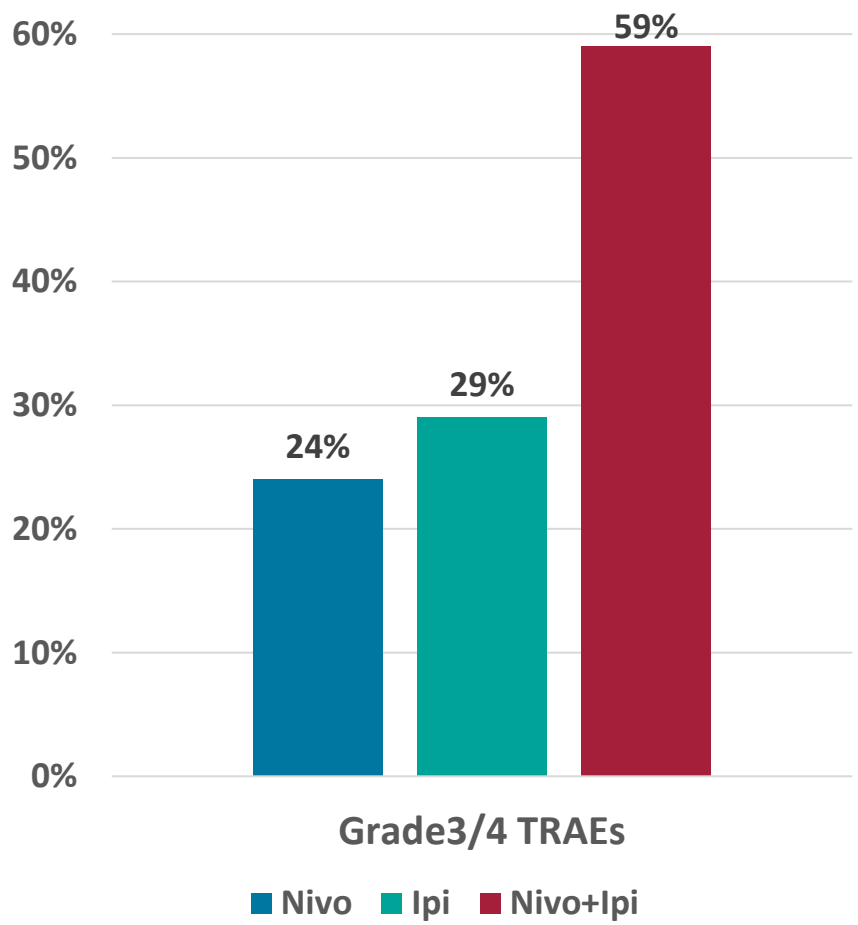


Immune Checkpoint Blockade Therapy to Allow T-Cell Activation in the TME



Anti-PD1 + Anti-CTLA4 IV in 1L Metastatic Melanoma

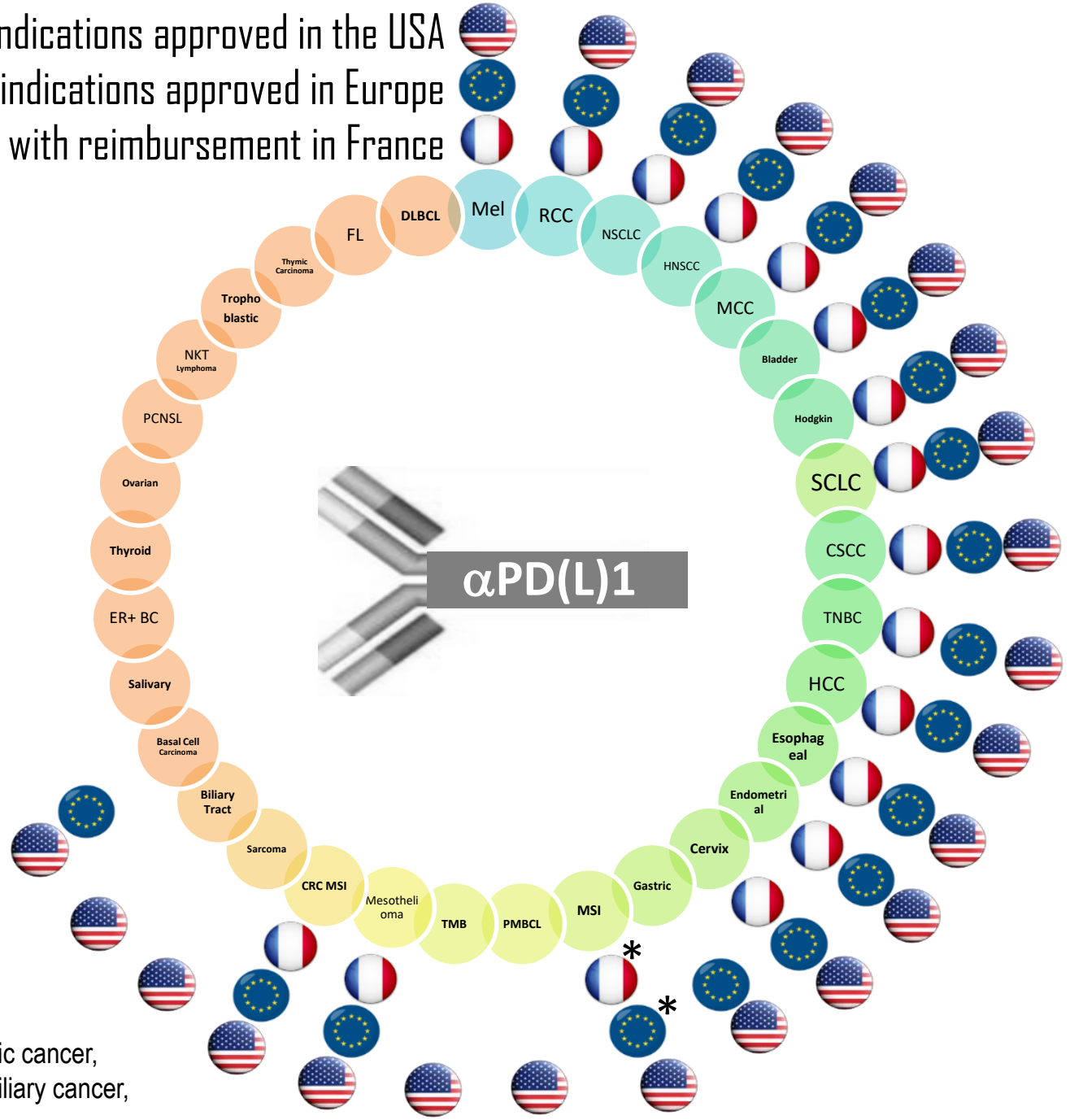




Wolchok, J.D., et al. (2022). Long-Term Outcomes With Nivolumab Plus Ipilimumab or Nivolumab Alone Versus Ipilimumab in Patients With Advanced Melanoma. J. Clin. Oncol. 40, 127–137.

23 Tumor indications approved in the USA
19 Tumor indications approved in Europe
16 Tumor indications with reimbursement in France

La Révolution des Immunothérapies Anti-Checkpoints



* Only for 5 tumor types: colorectal cancer, gastric cancer, endometrial carcinoma, small intestine cancer, biliary cancer,

EMA/FDA Approved Immune Checkpoint Targeted Antibodies

Anti-CTLA-4

Ipilimumab (BMS)

YERVOY™

Tremelimumab (AZ)

IMJUDO®

Anti-PD-1

Nivolumab (BMS)

OPDIVO™

Dostarlimab (GSK)

Jemperli (dostarlimab-gxly) Injection 500 mg

Pembrolizumab (MSD)

KEYTRUDA®

Tislelizumab (Beigene)

TEVIMBRA

Cemiplimab (Regeneron/Sanofi)

LIBTAYO®

Toripalimab (Coherus)

LOQTORZI™

Anti-PD-L1

Atezolizumab (Roche/Genentech)

TECENTRIQ™

Durvalumab (AZ/Medimmune)

IMFINZI™

Avelumab (Pfizer)

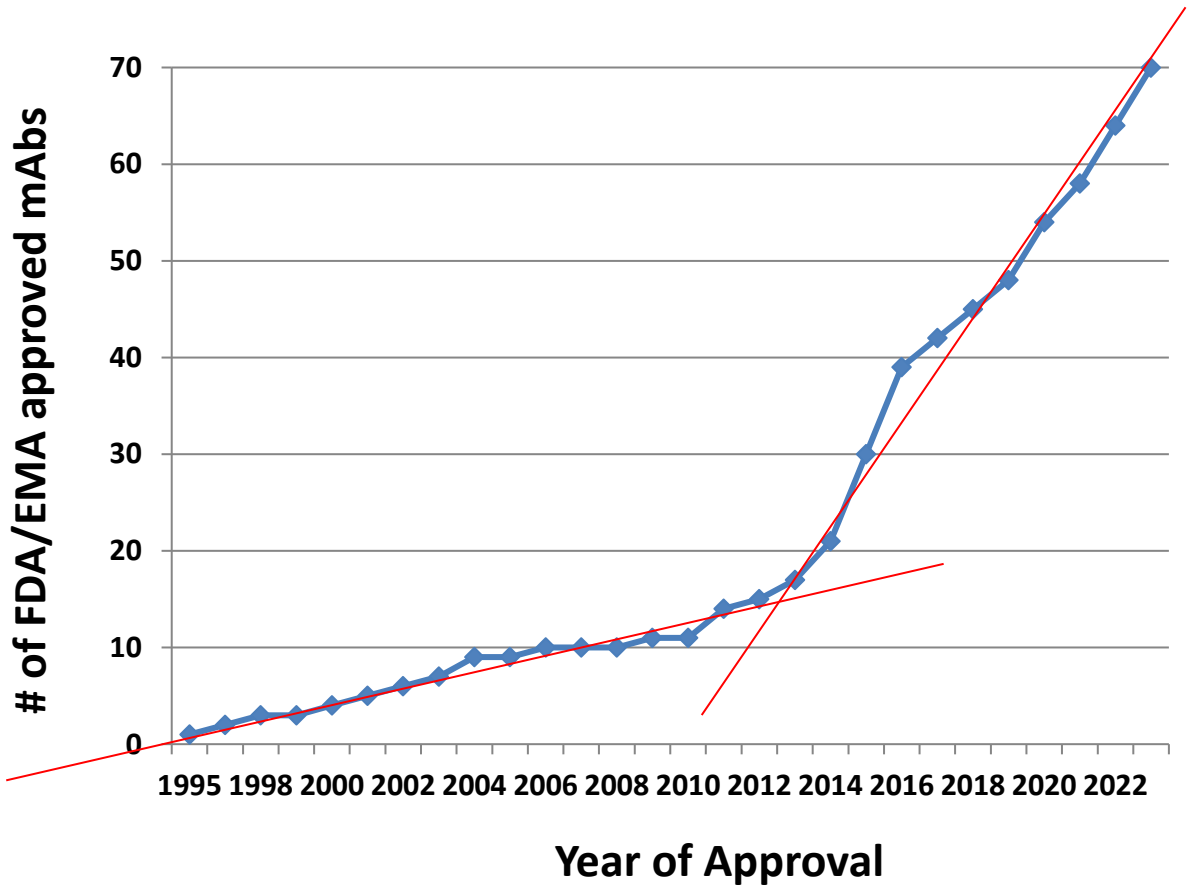
BAVENCIO®

Anti-LAG3

Relatlimab + Nivolumab (BMS)

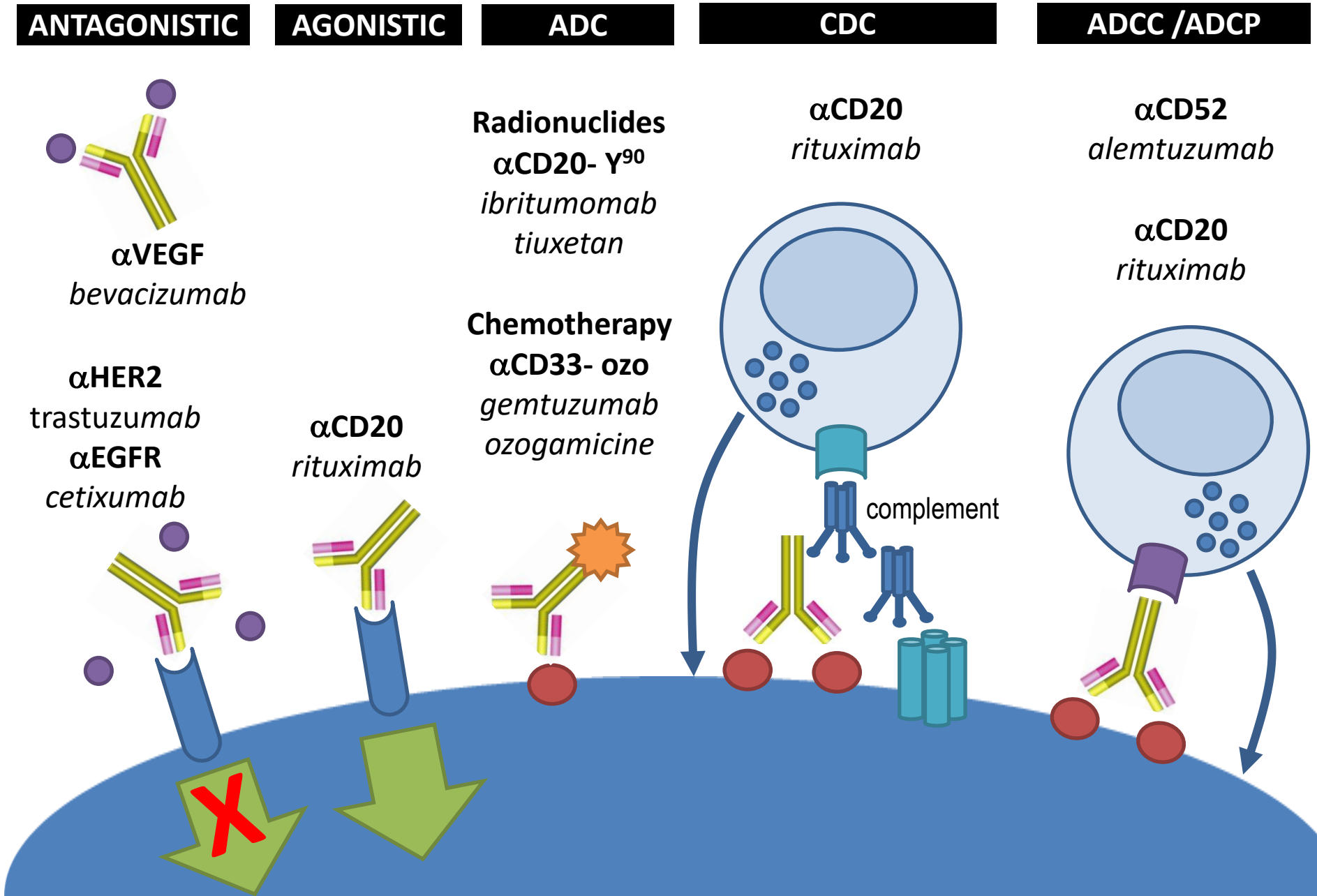
Opdualag™

Accélération des Anticorps Approuvés en Onco-Hématologie



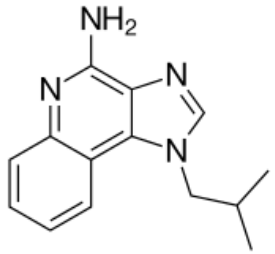
1995	edrecolomab
1997	rituximab
1998	trastuzumab
2000	gemtuzumab ozogamicin
2001	alemtuzumab
2002	ibritumomab tiuxetan
2003	tositumomab
2004	cetuximab, bevacizumab
2006	panitumumab
2009	ofatumumab
2011	ipilimumab, denosumab, brentuximab vedotin
2012	pertuzumab
2013	obinutuzumab, ado-trastuzumab emtansine
2014	ramucirumab, siltuximab, pembrolizumab, nivolumab
2015	secukinumab,dinutuximab, alirocumab, idarucizumab, evolocumab, daratumumab, mepolizumab, necitumumab, elotuzumab
2016	obiltoxaximab, ixekizumab, reslizumab, atezolizumab, daclizumab, adalimumab, ustekinumab, olaratumab, bezlotoxumab
2017	brodalumab, sarilumab, inotuzumab ozogamicin
2018	cemiplimab, moxetumomab pasudotox, mogamulizumab
2019	trastuzumab deruxtecan, enfortumab vedotin, Polatuzumab vedotin
2020	isatuximab, Sacituzumab govitecan, Tafasitamab, Belantamab mafodotin, Naxitamab, Margetuximab
2021	Dostarlimab, Loncastuximab tesirine, Amivantamab, Tisotumab vedotin
2022	Tebentafusp, Relatlimab, Mosunetuzumab, Teclistamab, Tremelimumab, Mirvetuximab soravtansine
2023	Toripalimab, Tislelizumab, Glofitamab, Epcoritamab, Talquetamab, Elranatamab

mAbs: Versatile Platforms for Tumor Targeted Therapies

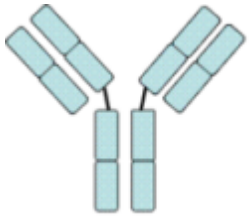


Les Différents Types d'Immunothérapies Approuvées

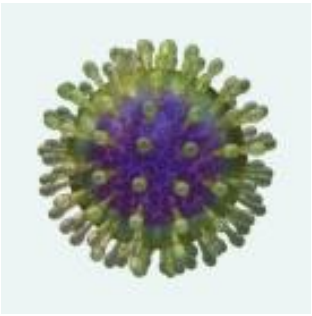
Cytokines
(IL2, IFN)



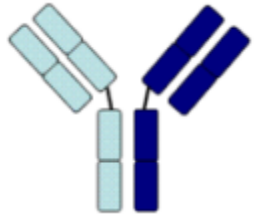
PRR Agonists
(TLR7/8)



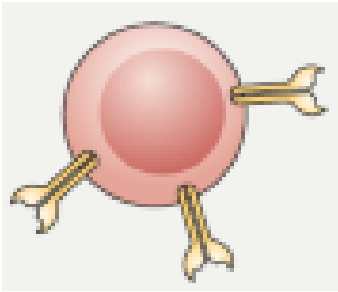
Antibodies
(Immune & Tumor Targeted, ADC)



Oncolytic Virus

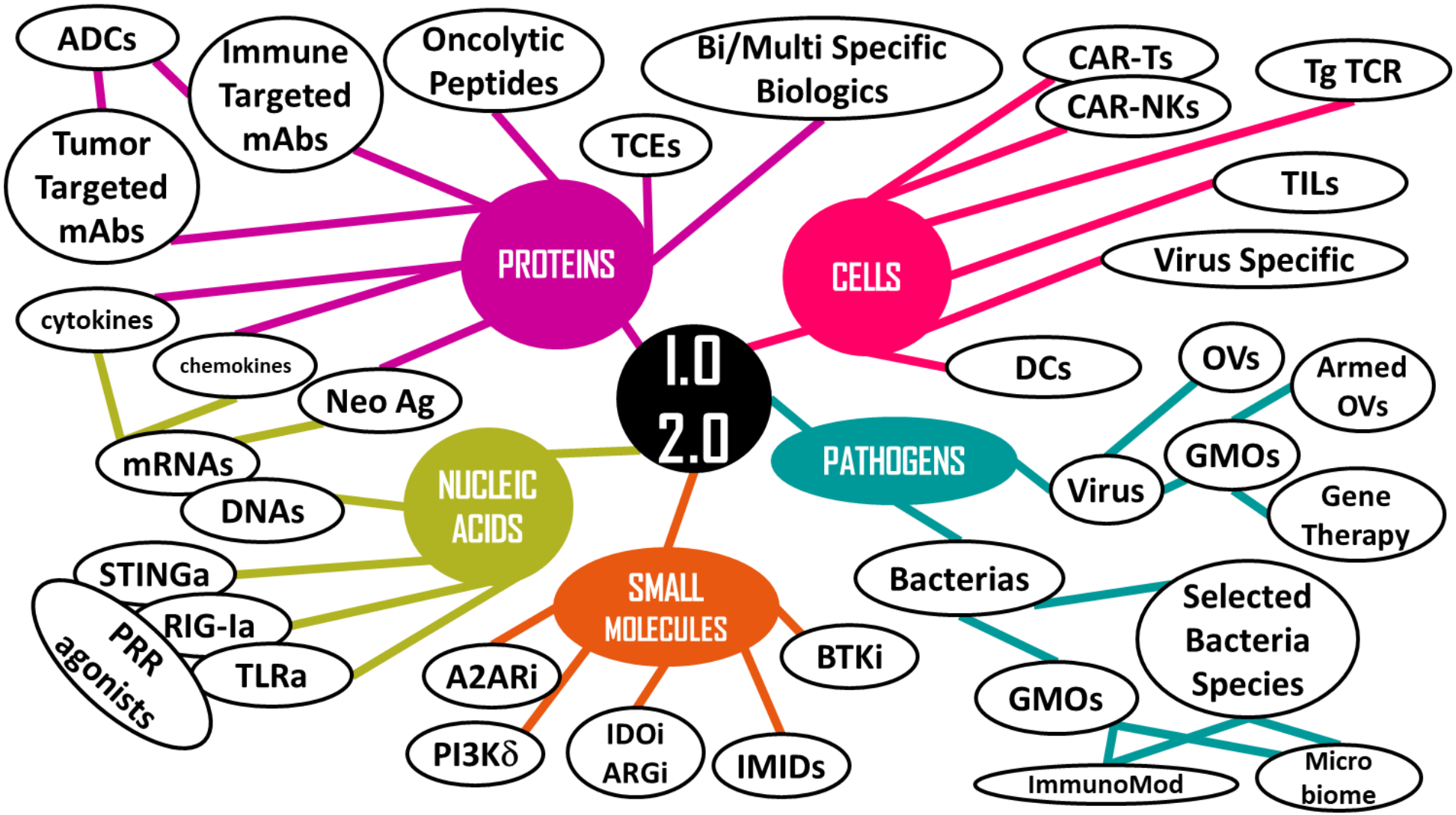


Bispecific T-Cell Engagers

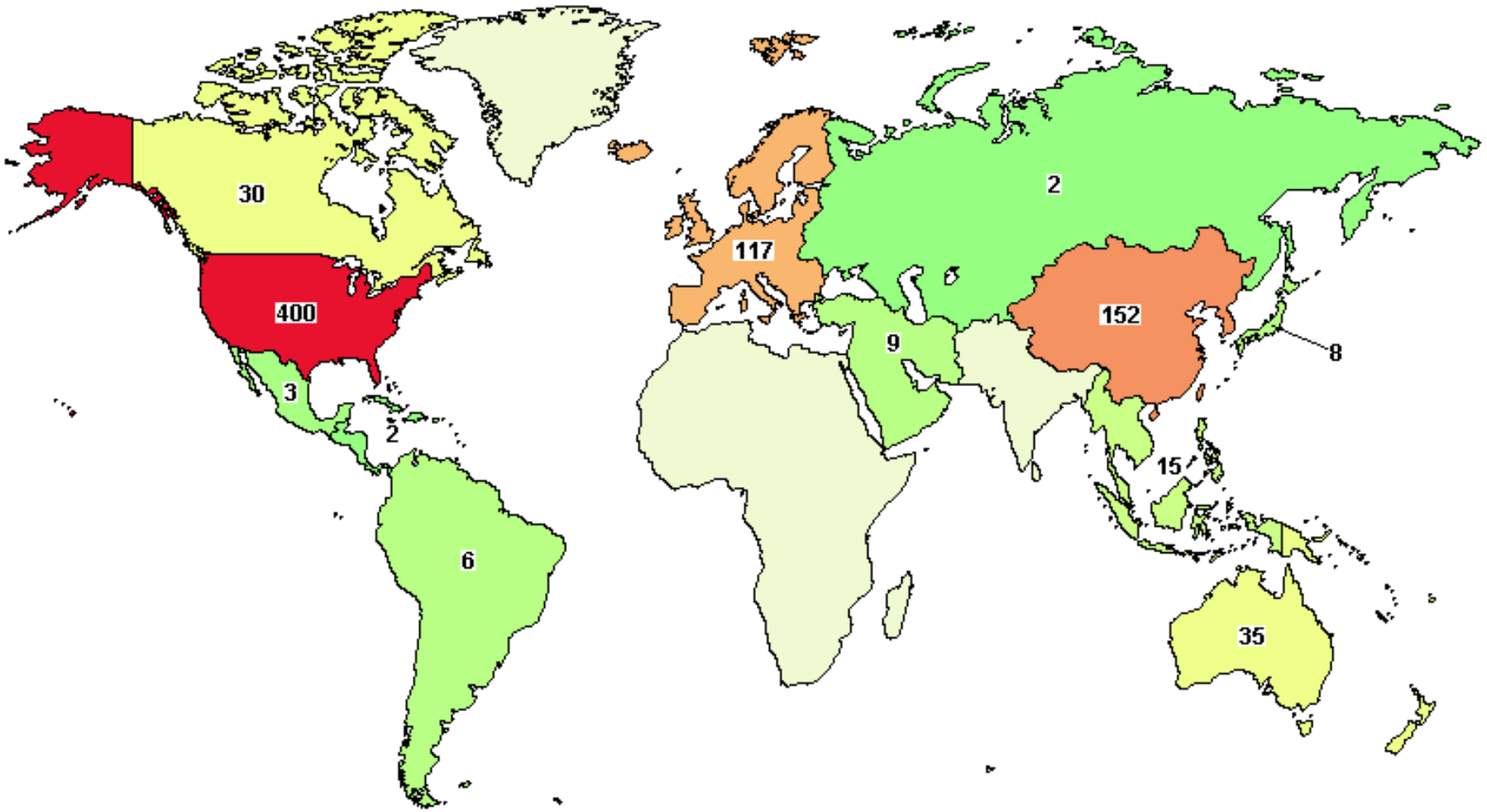


Adoptive Cell Therapies
(CAR-T, TILs)

Immuno-Oncology 2.0

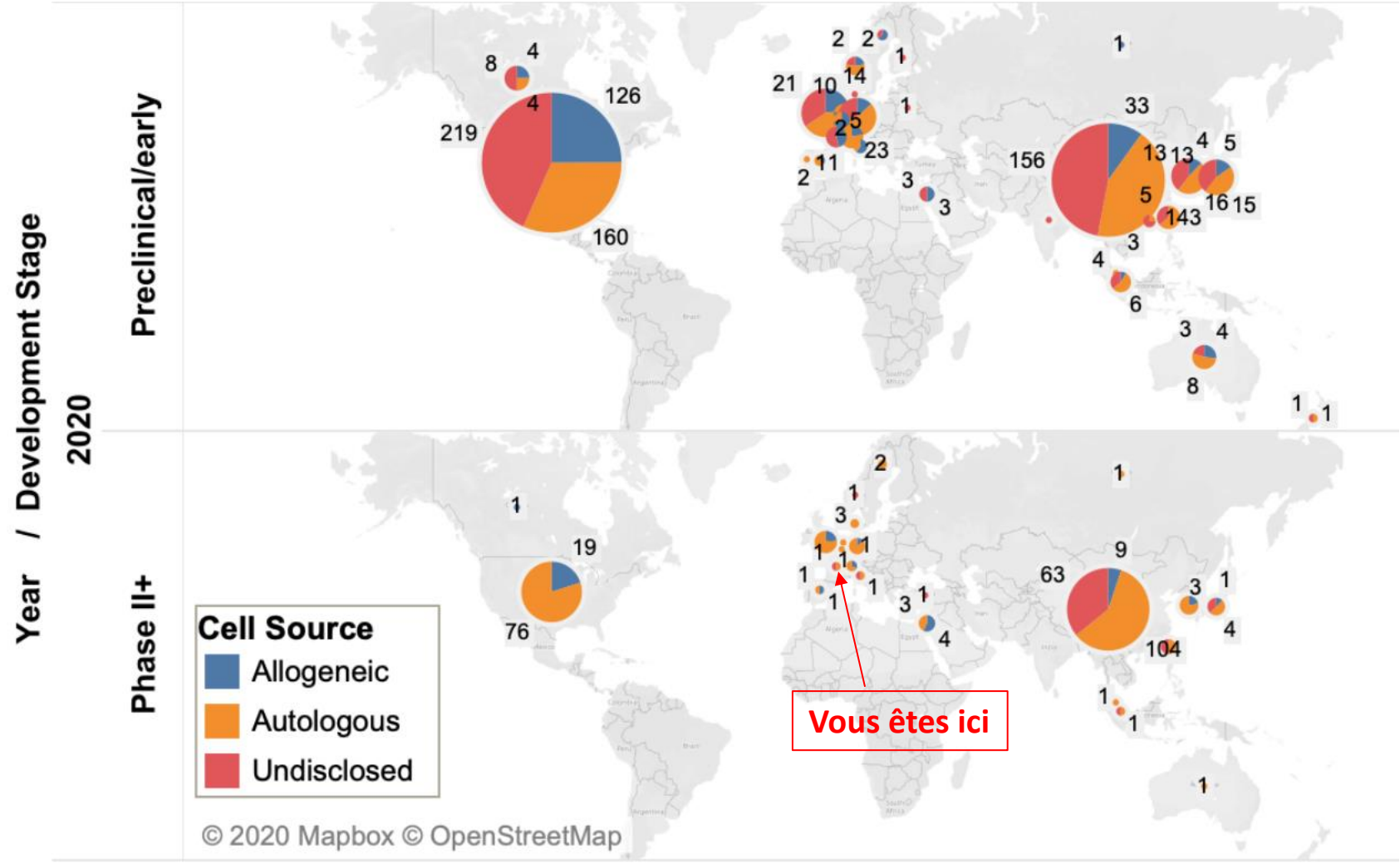


Essais Cliniques de Phase I en Cours d'Inclusion en Immunothérapie des Cancers (Fev 2024)



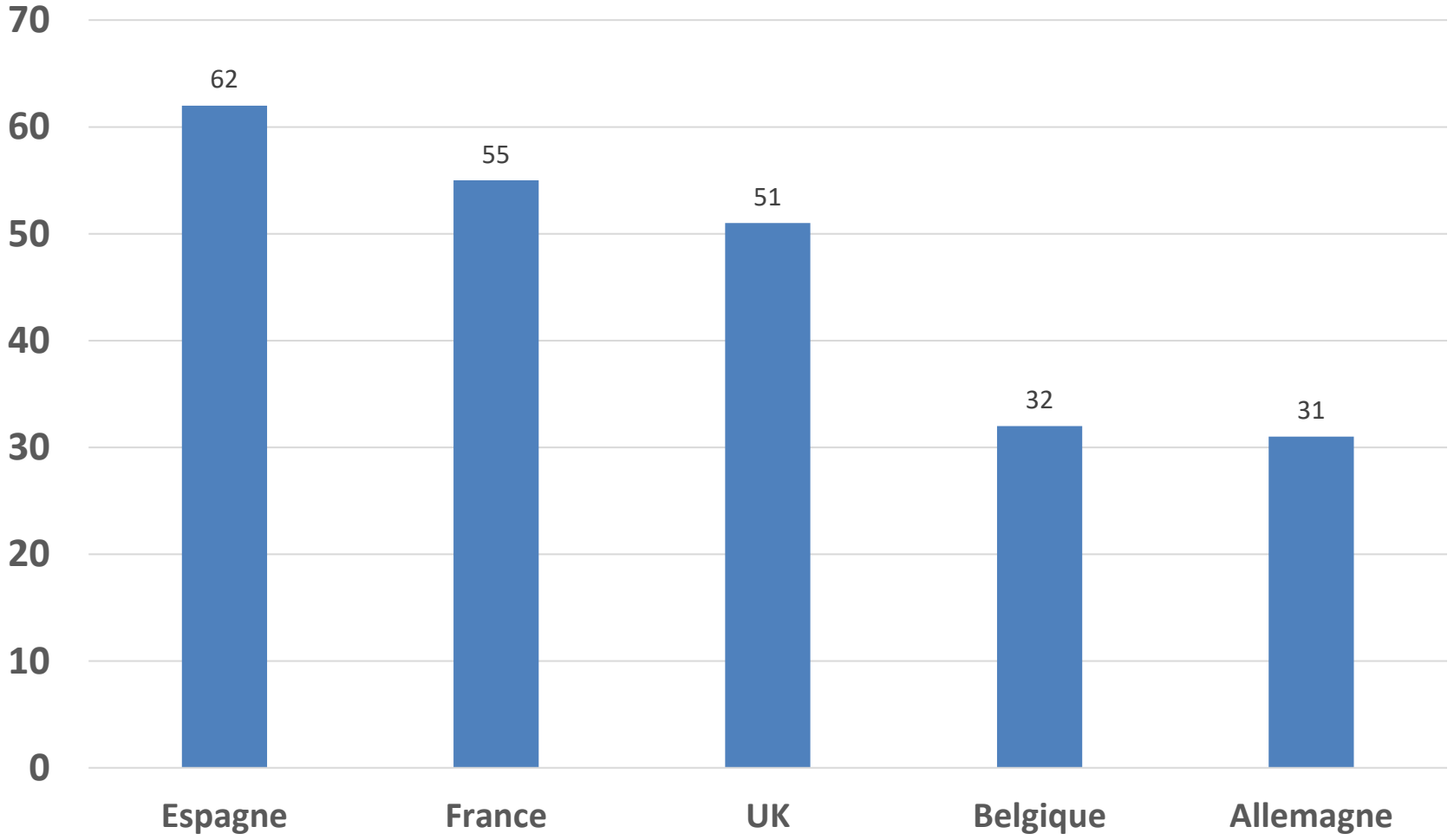
https://classic.clinicaltrials.gov/ct2/results/map?term=immunotherapy&recrs=abf&type=Intr&cond=cancer&phase=04&map=

Illustration du décalage grandissant USA-EU-France: les Immunothérapies par CAR-T cells



Yu JX, et al. Cancer cell therapies: the clinical trial landscape. Nat Rev Drug Discov 2020;

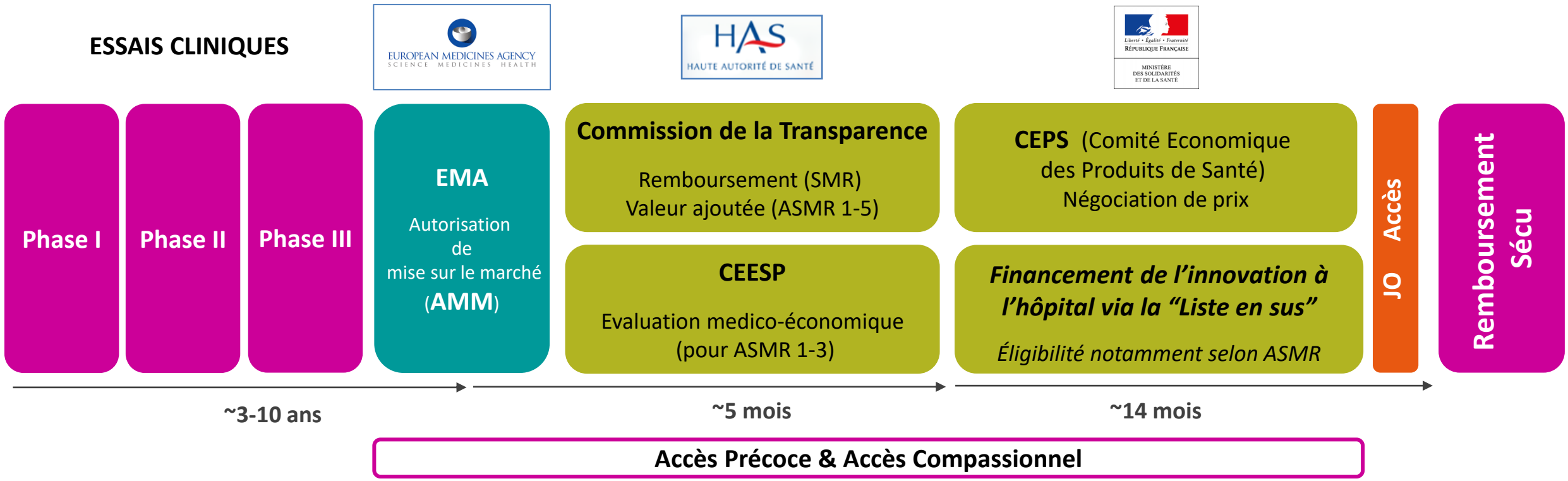
Essais Cliniques de Phase I en Immunothérapie



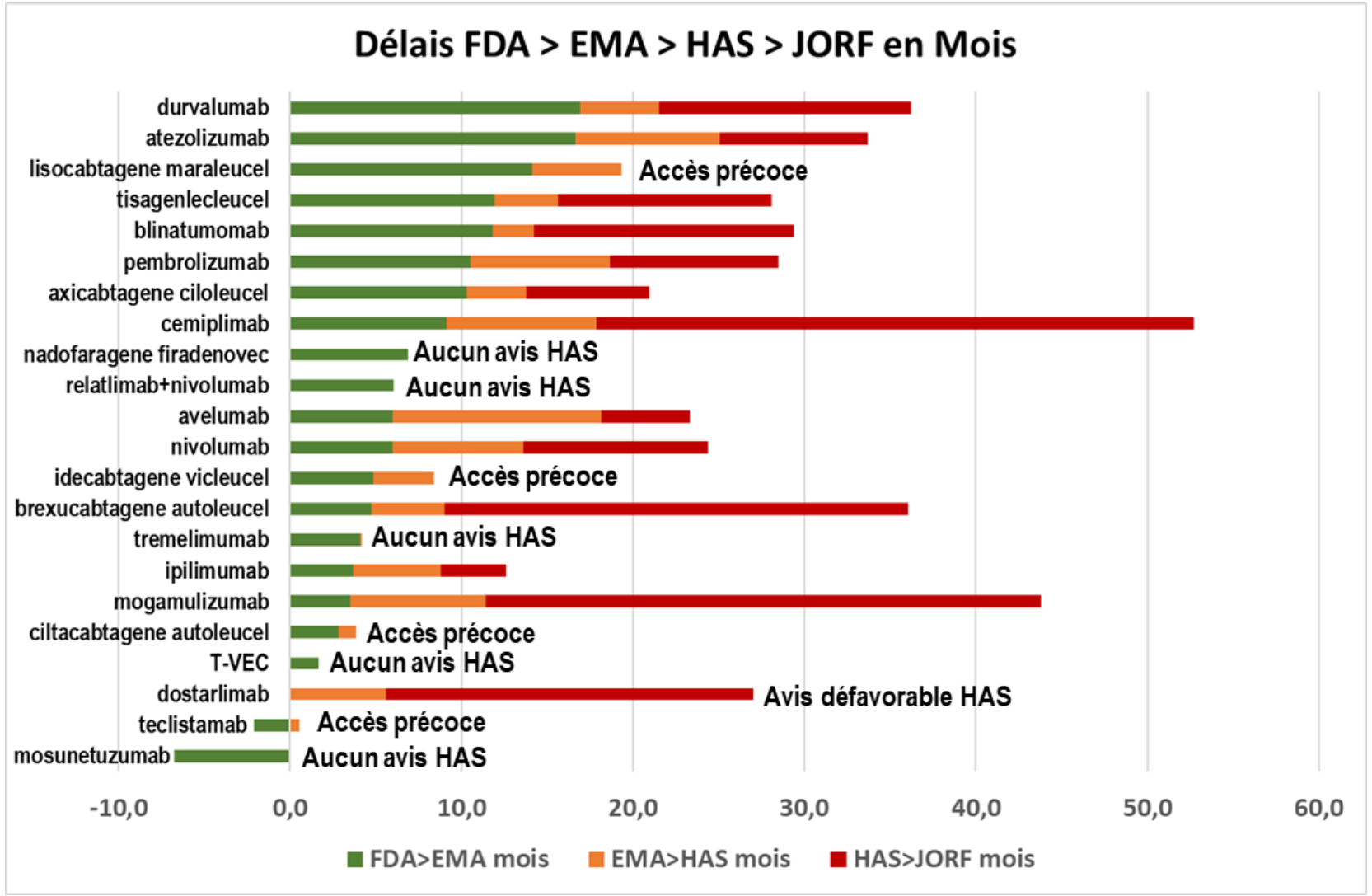
immunotherapy | Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | Interventional Studies | cancer | Phase Early Phase 1, 1

www.clinicaltrials.gov; Fev 2024

Modalités d'Accès aux Nouveaux Traitements en Cancérologie



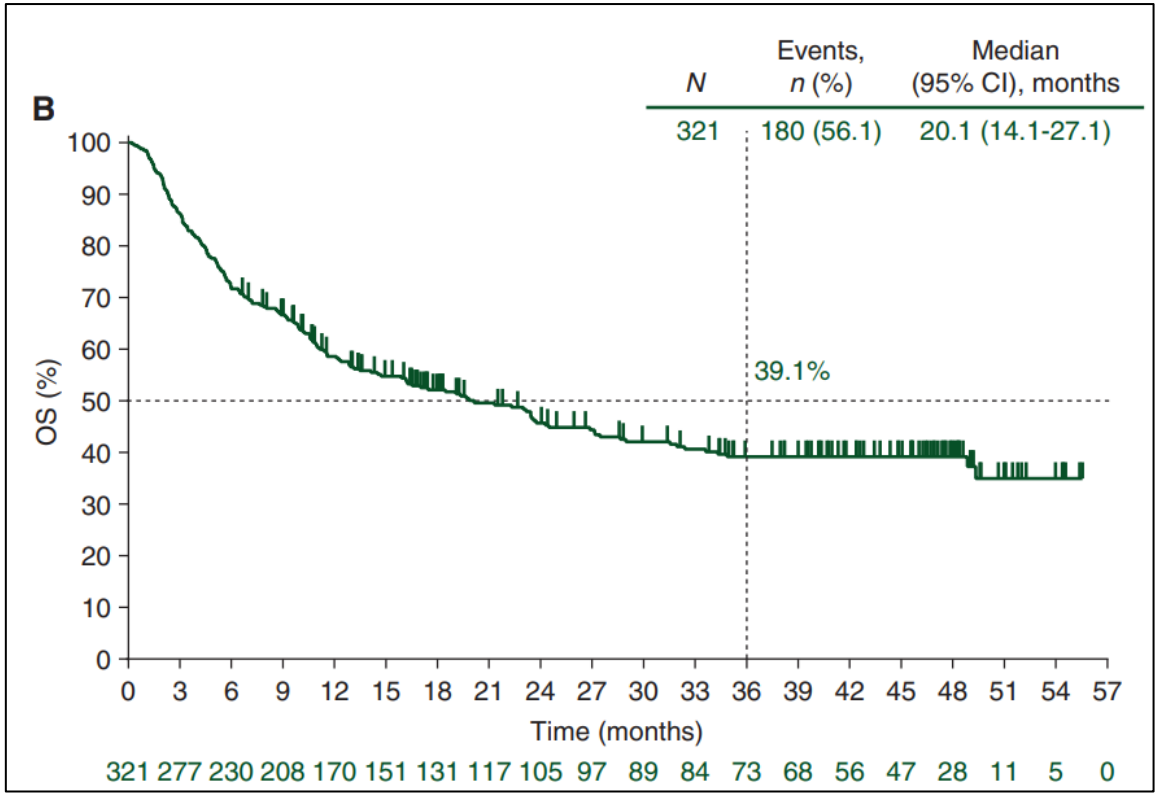
Délais Réglementaires entre FDA, EMA, HAS & JORF



	Médiane	Moyenne
FDA>EMA mois	6,0	6,5
EMA>HAS mois	4,9	5,1
HAS>JORF mois	12,4	15,6
FDA>JORF mois	23,3	27,3

Bilan 2023; d'après www.fda.gov, www.ema.europa.eu, www.has-sante.fr, & www.legifrance.gouv.fr

Exemple: Accès aux Anti-PD1 pour les Patients MSI^{high}



Maio, M., et al. (2022). Pembrolizumab in microsatellite instability high or mismatch repair deficient cancers: updated analysis from the phase II KEYNOTE-158 study. Ann. Oncol. 33, 929–938.

FDA Approval: May 2017

EMA Approval: Apr 2022

(Limited to advanced/recurrent colorectal, endometrial, gastric, small intestine & biliary cancers)

Why Immune Checkpoint Targeted Therapies provide Overall Survival Benefits?

Adaptive anti-tumor immunity is polyclonal:

➔ ***better control of tumor heterogeneity***

Adaptive anti-tumor immunity has memory:

➔ ***durable remissions***

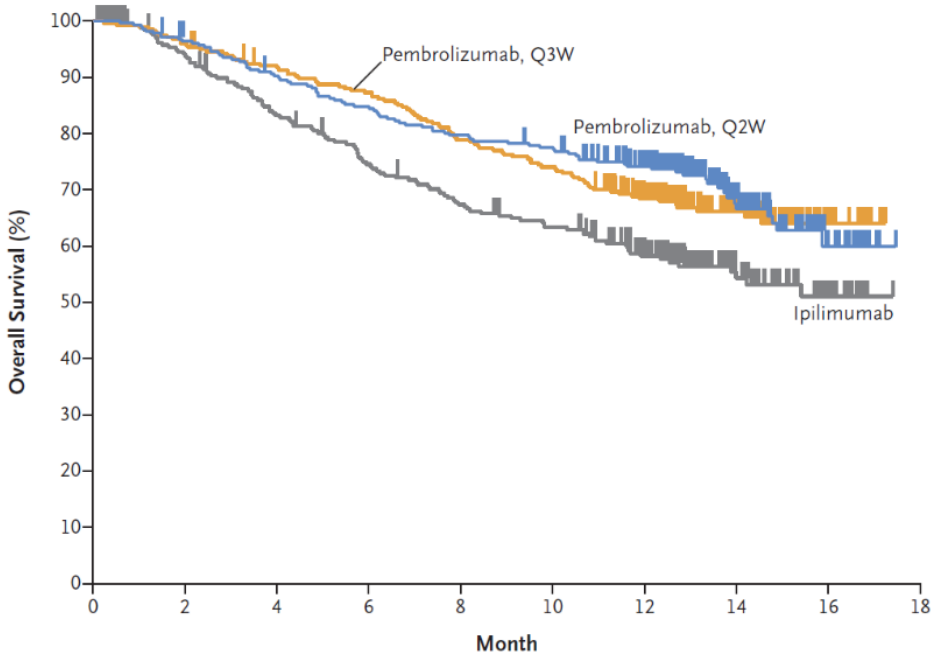
And immune cells can cross the BBB

(whereas most drugs can't)

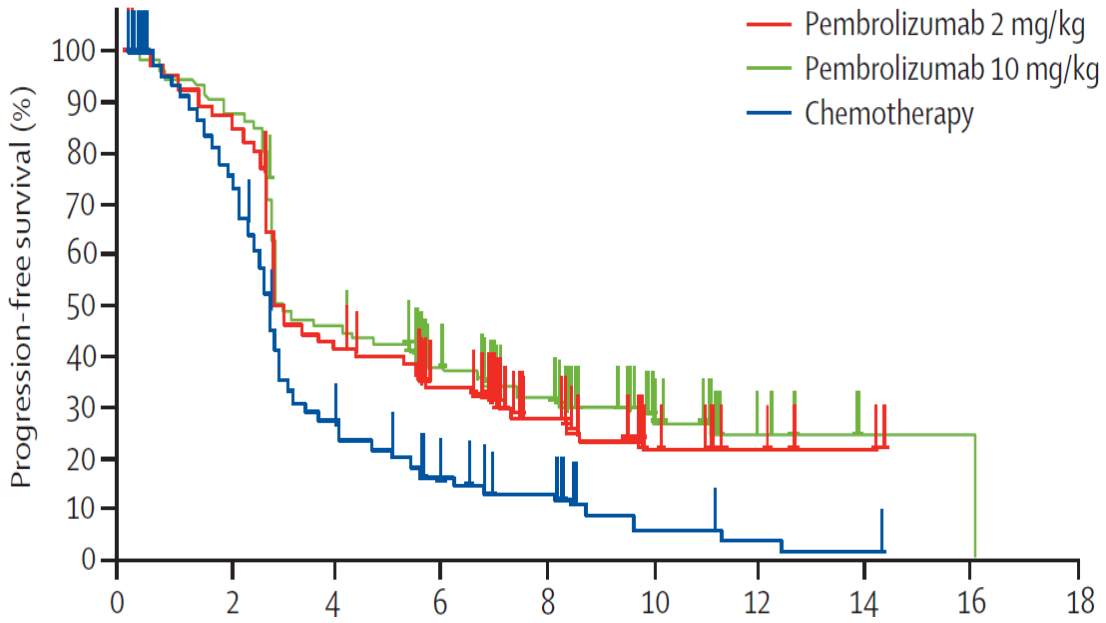
Aurélien Marabelle MD, PhD, Gustave Roussy

Anti-PD-1/PD-L1 = Checkpoint Blockade

No Dose/Efficacy/Toxicity Correlation

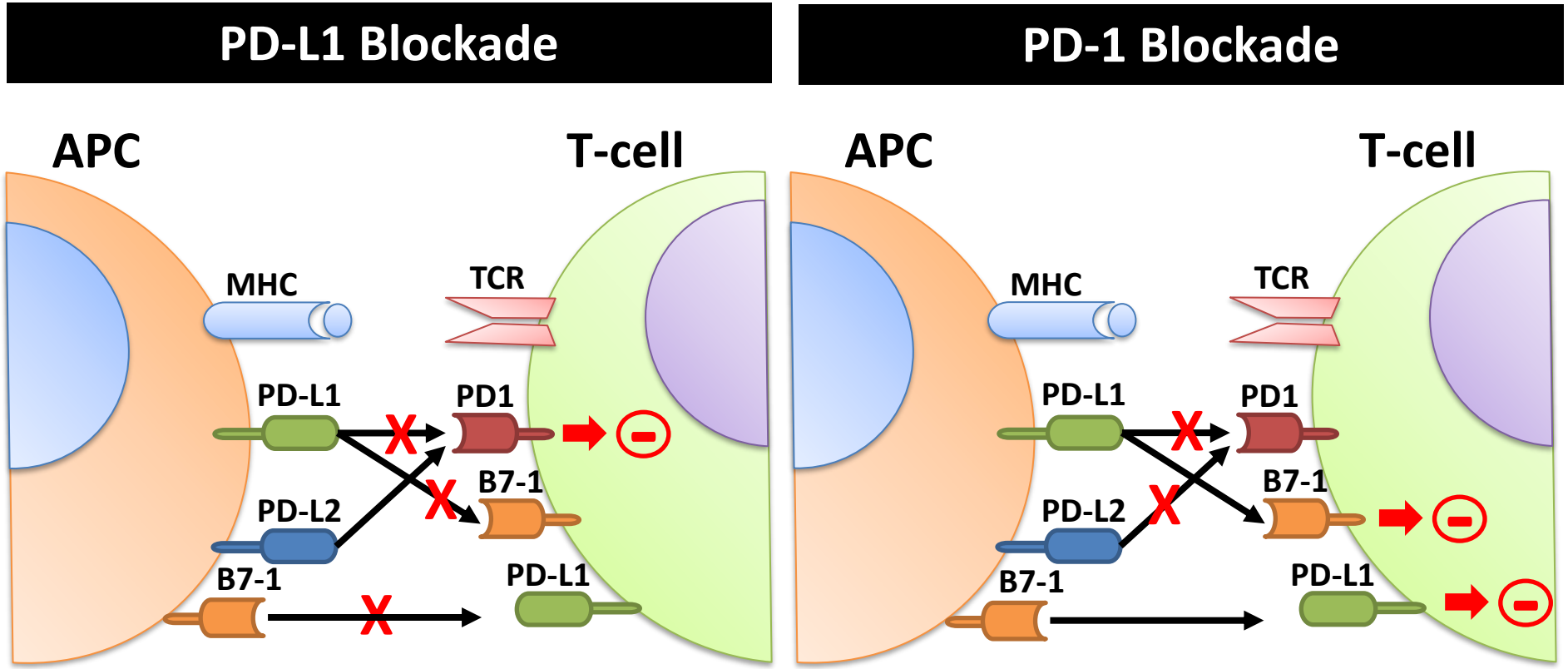


Robert C, et al. Pembrolizumab versus Ipilimumab in Advanced Melanoma.
N Engl J Med. 2015;372:2521–32.



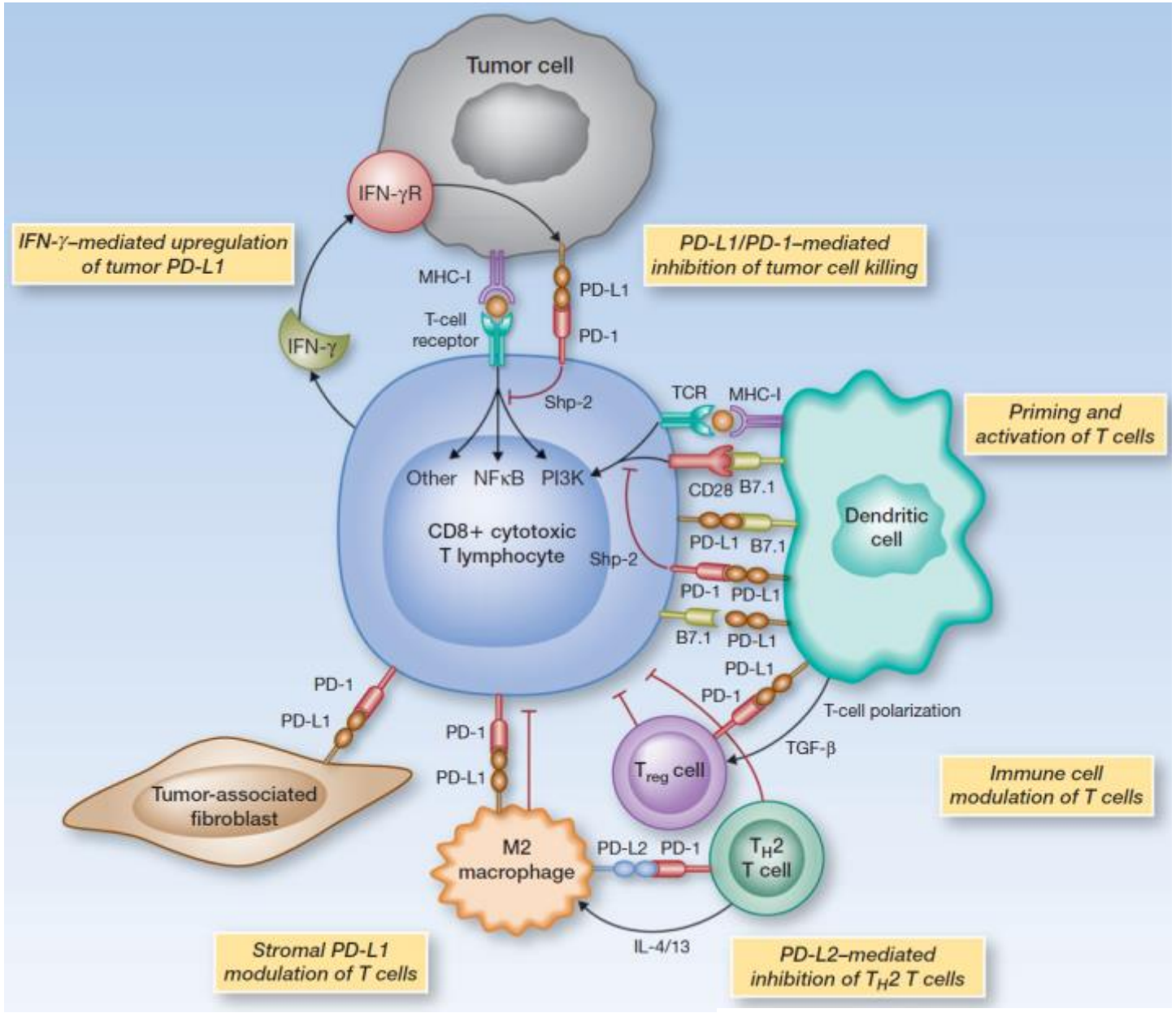
Ribas A, et al. Pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory melanoma (KEYNOTE-002): a randomised, controlled, phase 2 trial. Lancet Oncol. 2015;

PD-1 vs PD-L1 Blocking: Not Strictly Redundant



Adapted from Annu. Rev. Immunol. 2008. 26:677–704

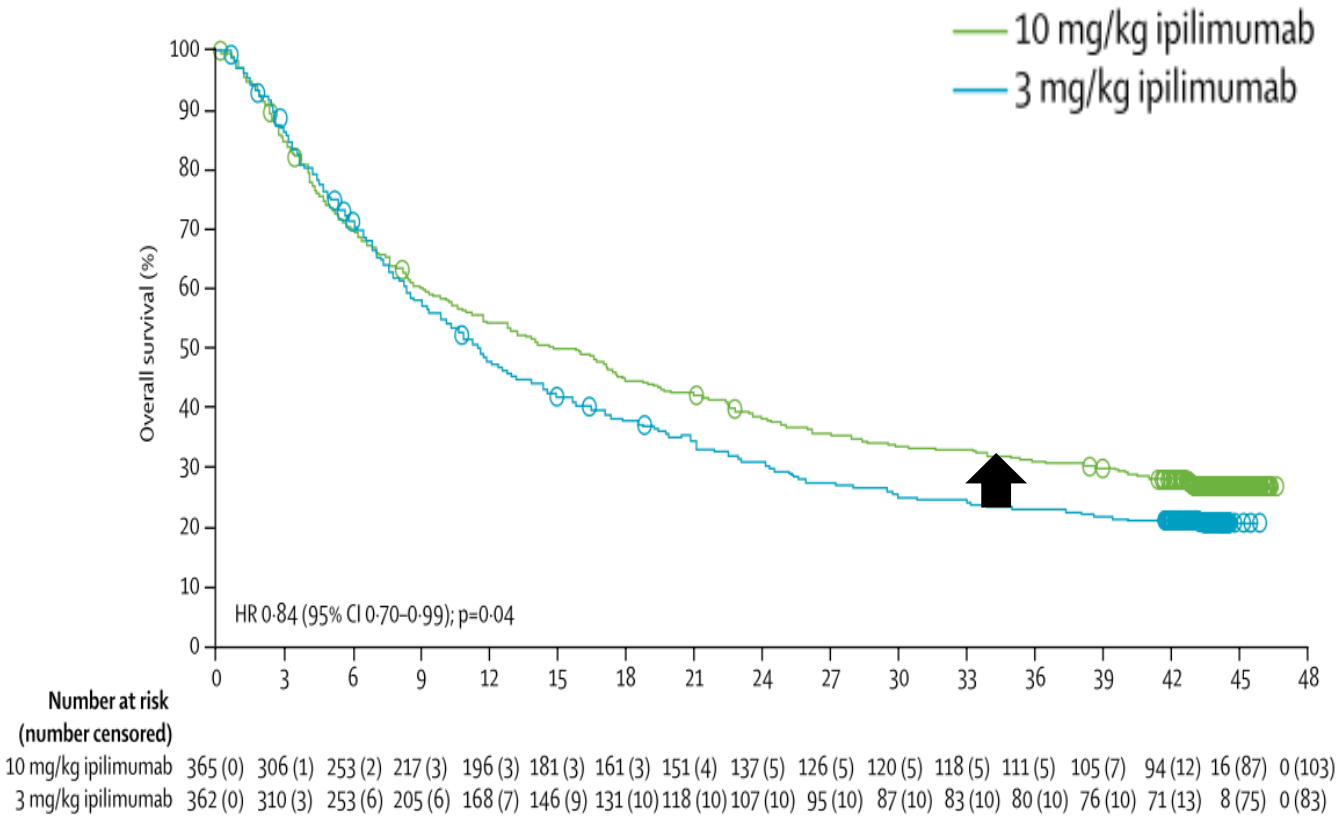
How Do Anti-PD(L)1 Really Work ?



Clin Cancer Res; 18(24) December 15, 2012

How Do Anti-CTLA4 Really Work ?

More Efficacy & Toxicity at Higher Doses



	Ipilimumab 10 mg/kg (n=364)			Ipilimumab 3 mg/kg (n=362)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Any treatment-related adverse event	162 (45%)	99 (27%)	25 (7%)	162 (45%)	57 (16%)	9 (2%)

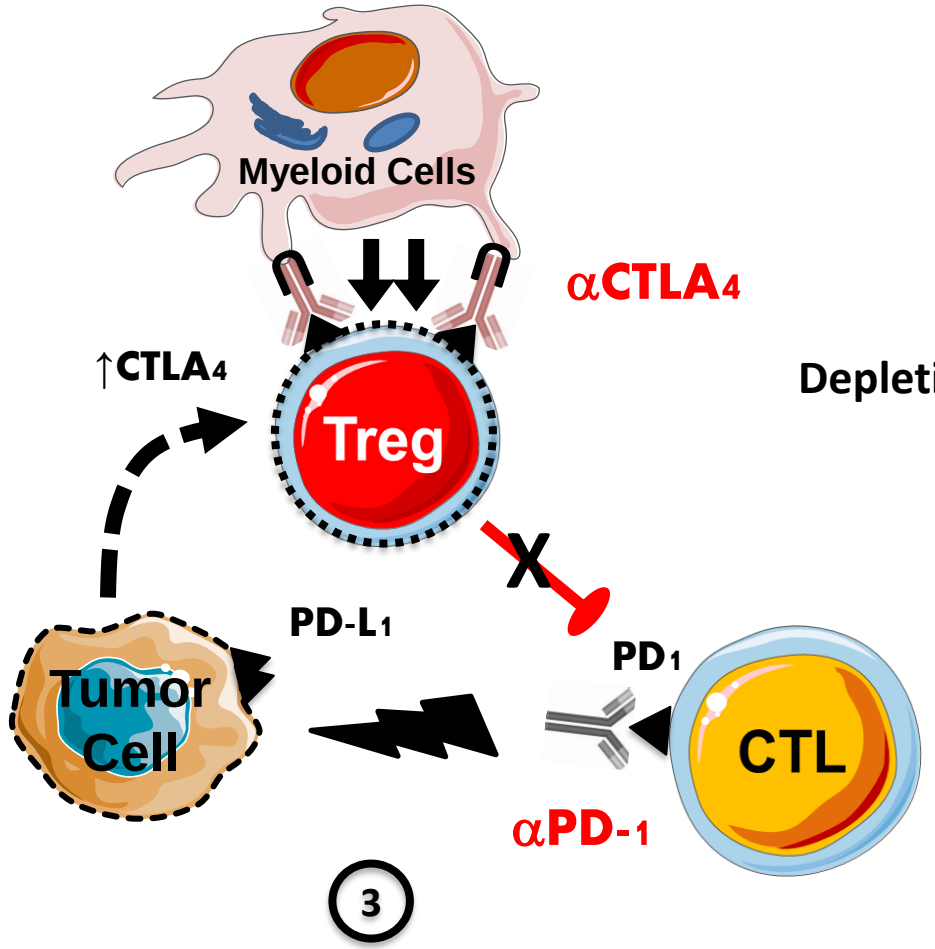
34% ← **18%**

Ascierto PA, et al. Ipilimumab 10 mg/kg versus ipilimumab 3 mg/kg in patients with unresectable or metastatic melanoma: a randomised, double-blind, multicentre, phase 3 trial. Lancet Oncol. 2017;18:611–22.

Anti-CTLA4 = Treg depleter ?

1

Upregulation of Membrane CTLA4 on Tumor Specific Tregs



2

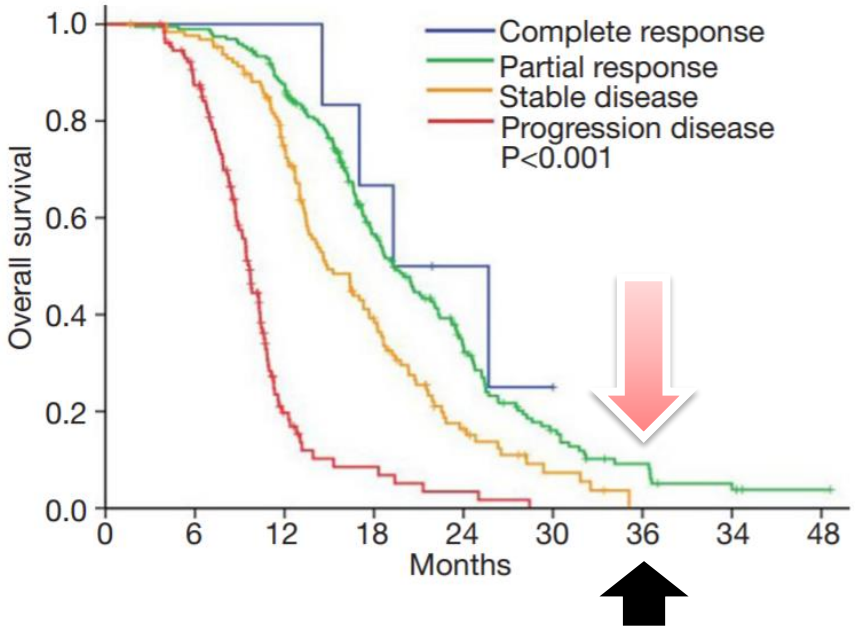
Depletion of Tregs by anti-CTLA4

3

Activation of Cytotoxic Cells & Immune Destruction of Cancer Cells

CHIMIO vs IMMUNO / ORR vs OS

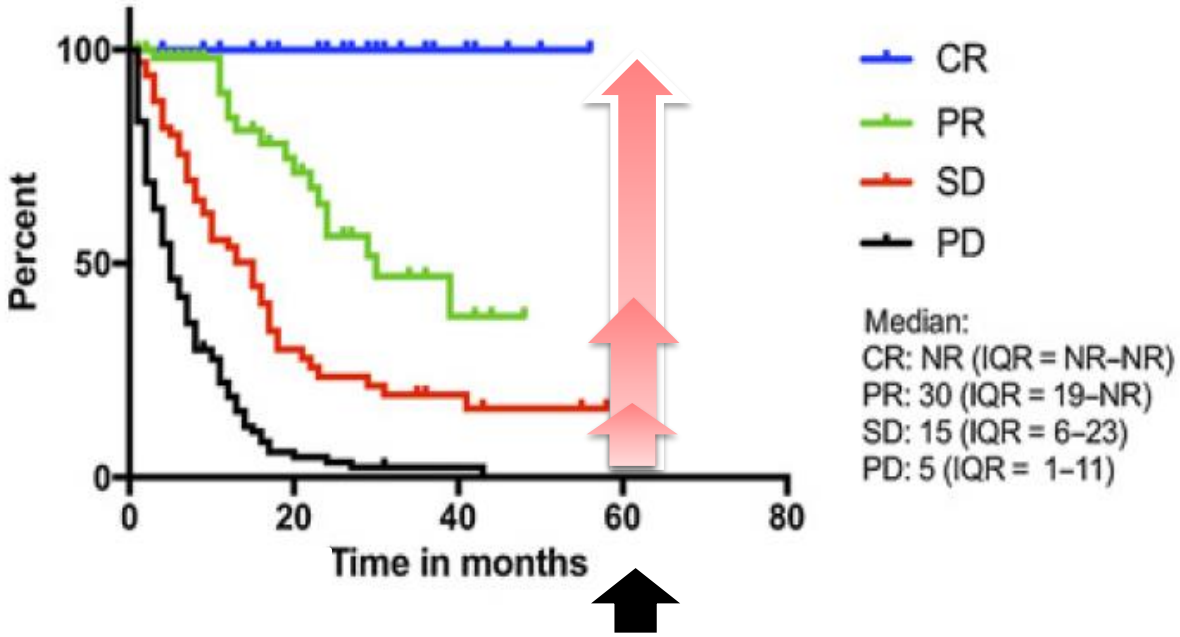
CHIMIOTHERAPIES



3 ans

Chen Y, et al. Outcomes of concurrent chemoradiotherapy versus chemotherapy alone for esophageal squamous cell cancer patients presenting with oligometastases. J Thorac Dis Vol 11, No 4 (April 2019) J Thorac Dis 2019.

IMMUNOTHERAPIES

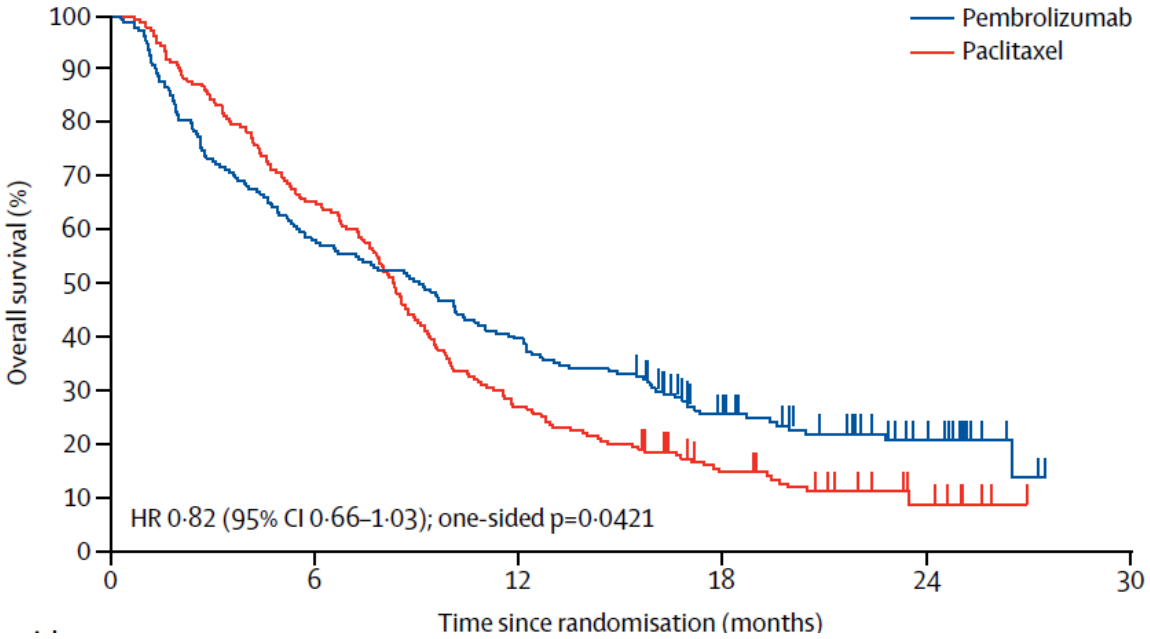


5 ans

Gauci M-L, et al. Long-Term Survival in Patients Responding to Anti-PD-1/PD-L1 Therapy and Disease Outcome upon Treatment Discontinuation. Clin Cancer Res 2019;25:946–56.

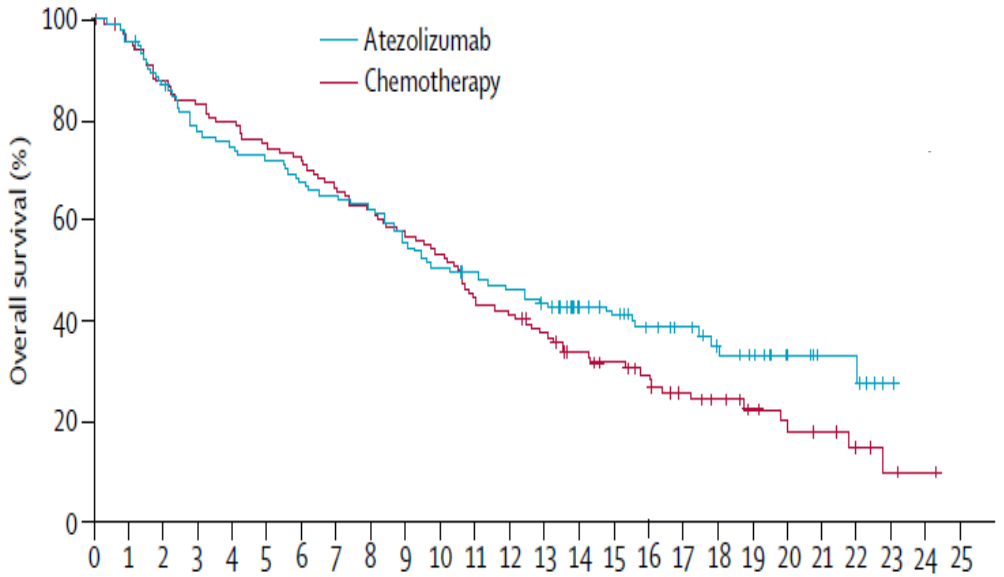
How to read survival curves in the IO era ?

Pembro Gastric



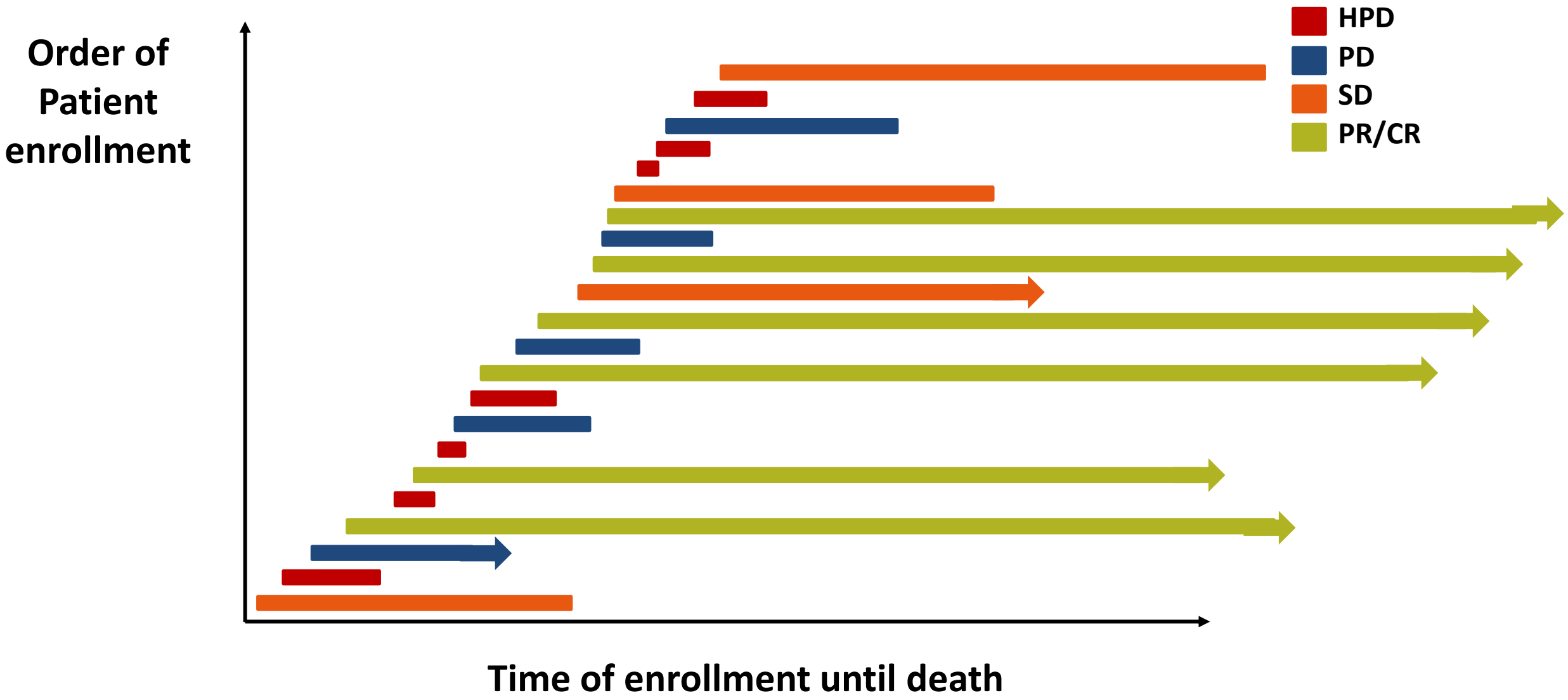
Shitara K, et al. Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): a randomised, open-label, controlled, phase 3 trial. Lancet 2018;392:123–33.

Atezo Bladder

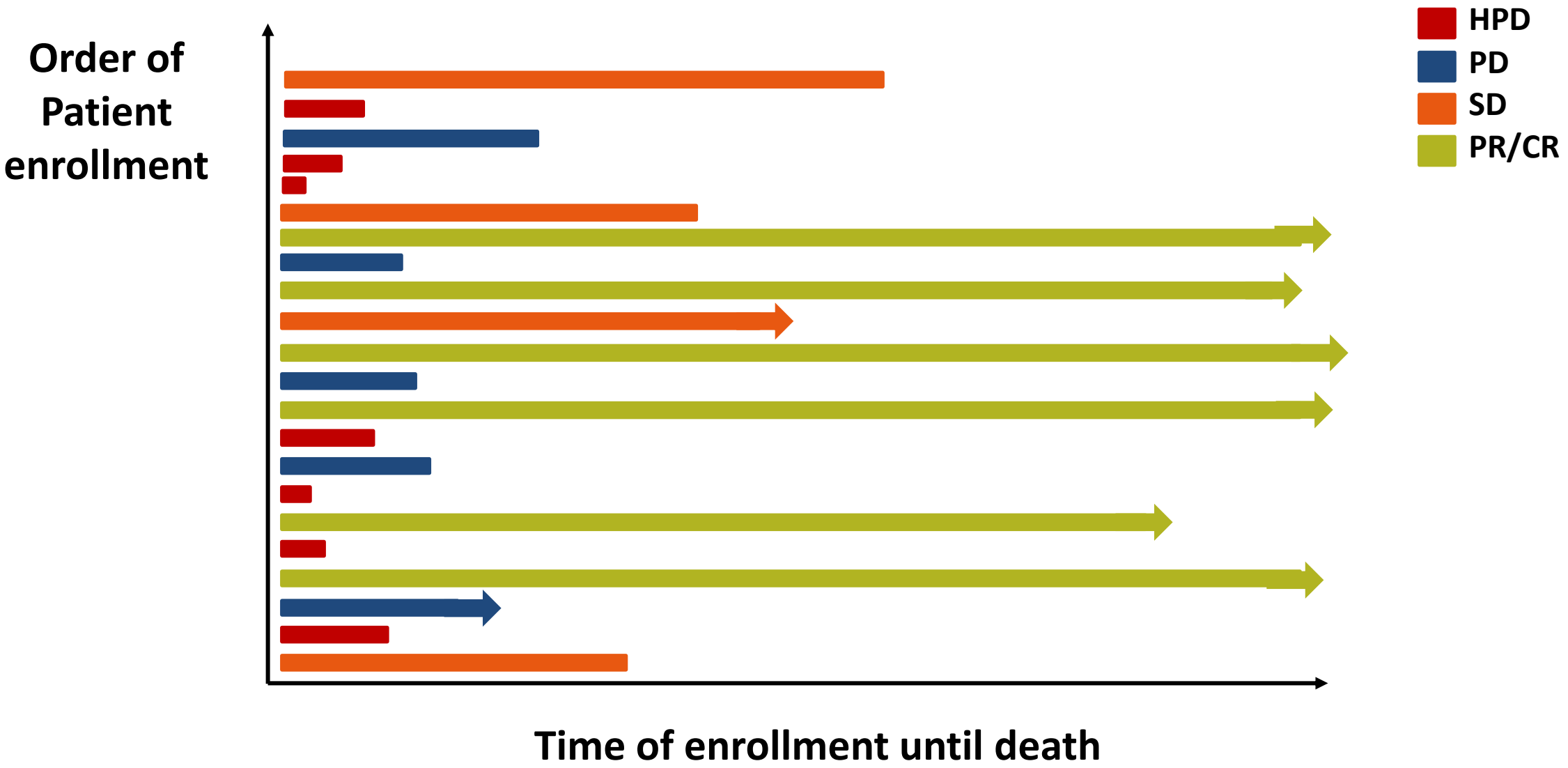


Powles T, et al. Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. Lancet 2018;391:748–57.

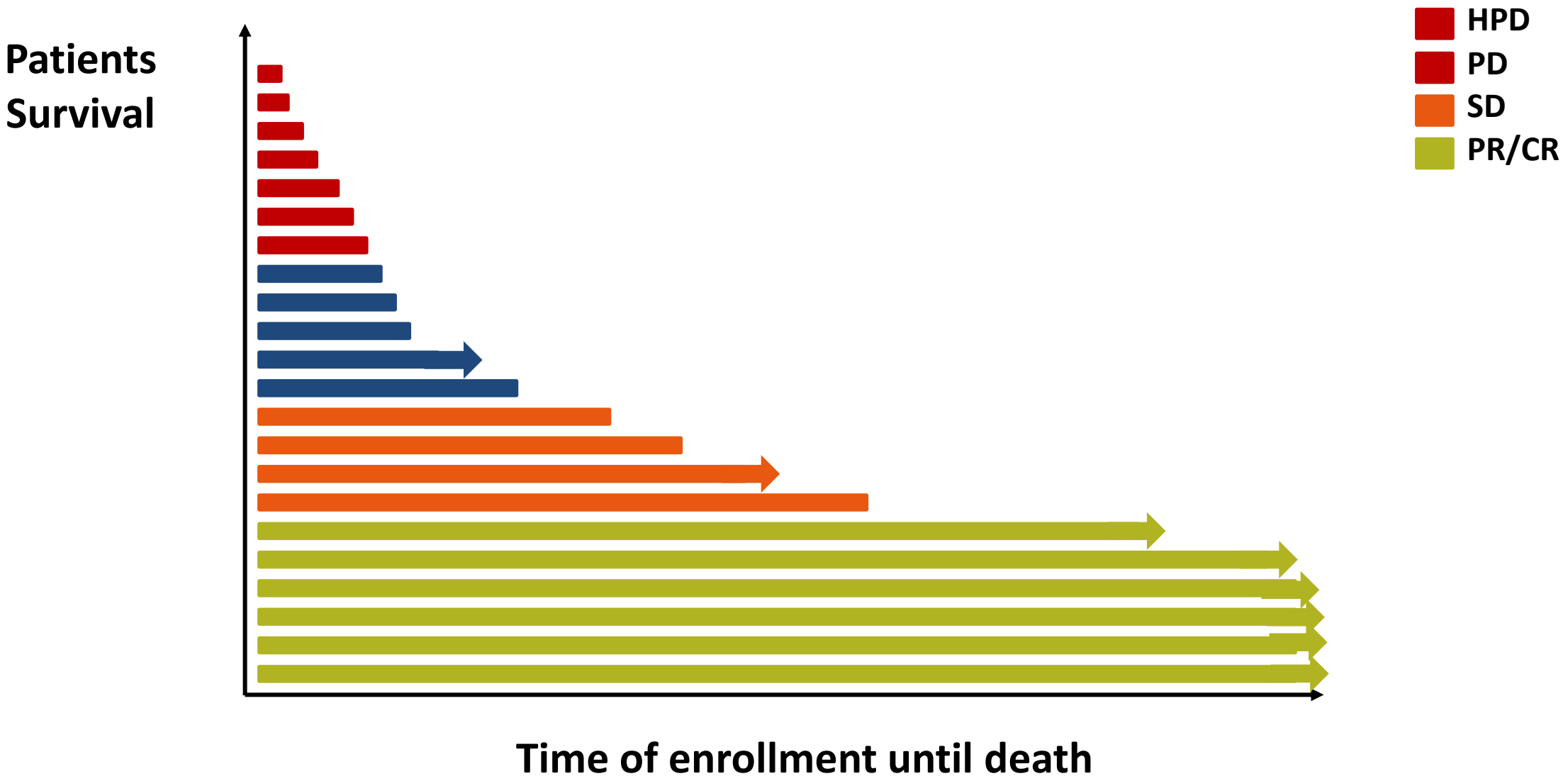
How to read a Kaplan Meier Curve



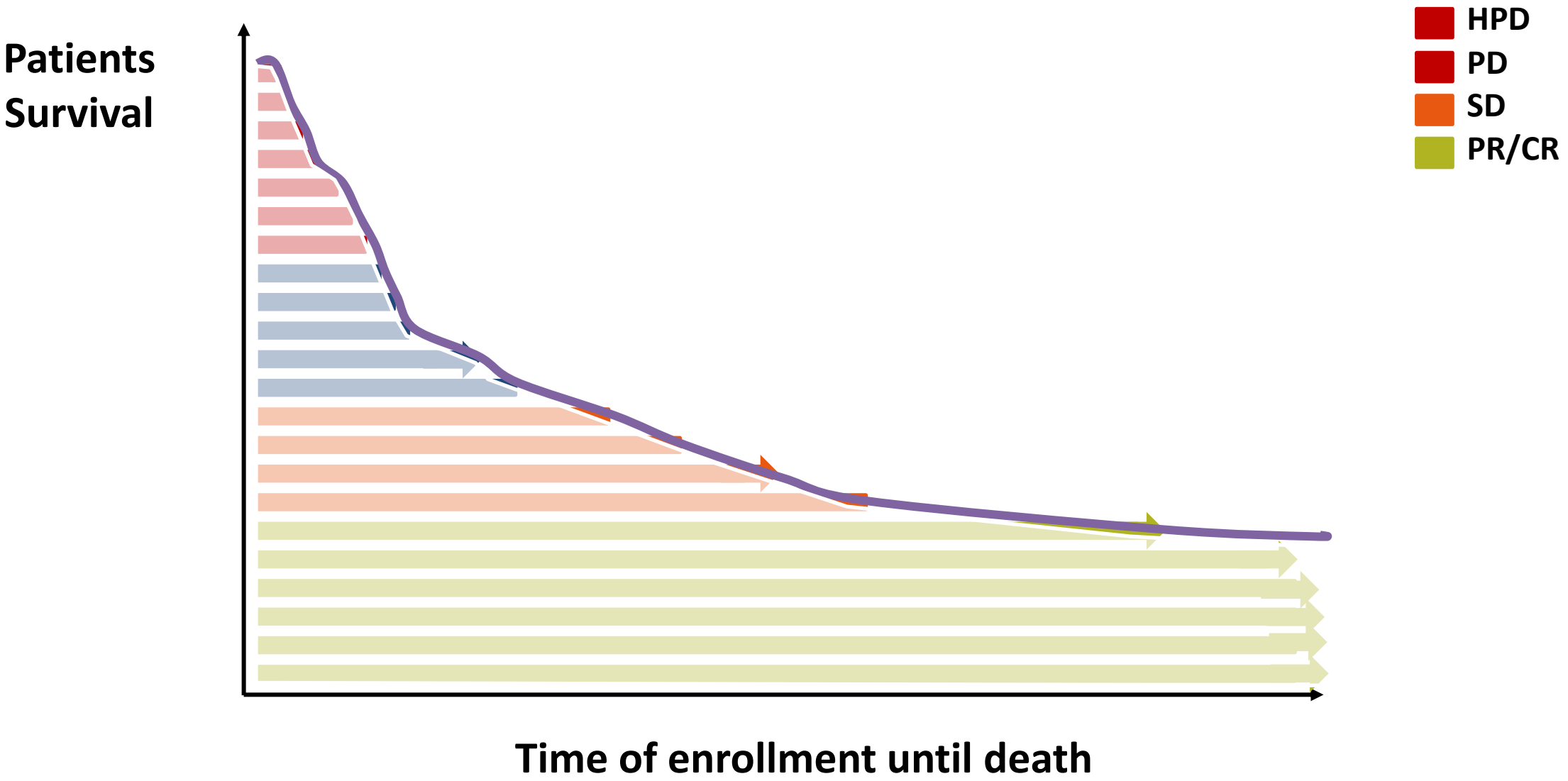
How to read a Kaplan Meier Curve



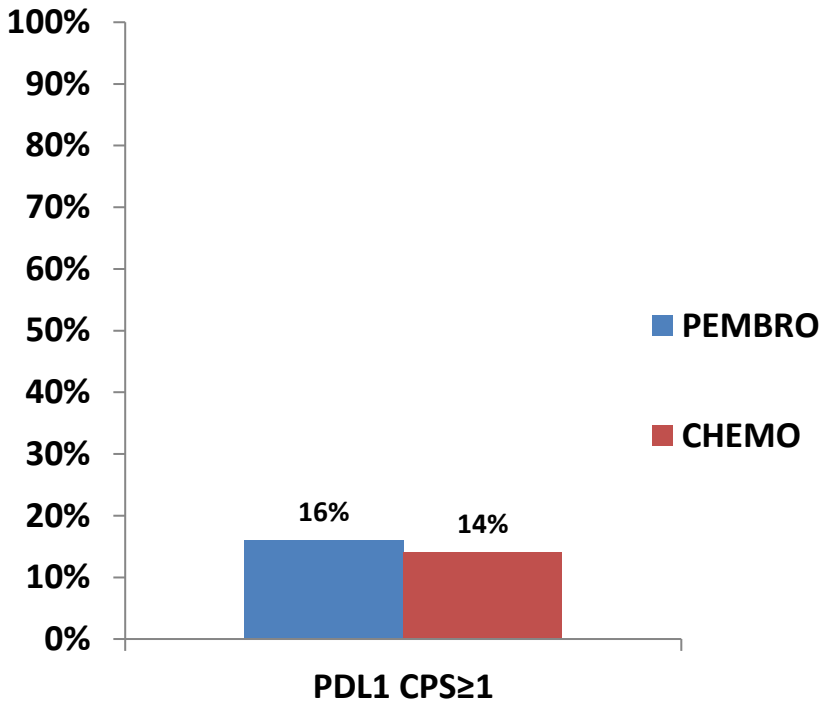
How to read a Kaplan Meier Curve

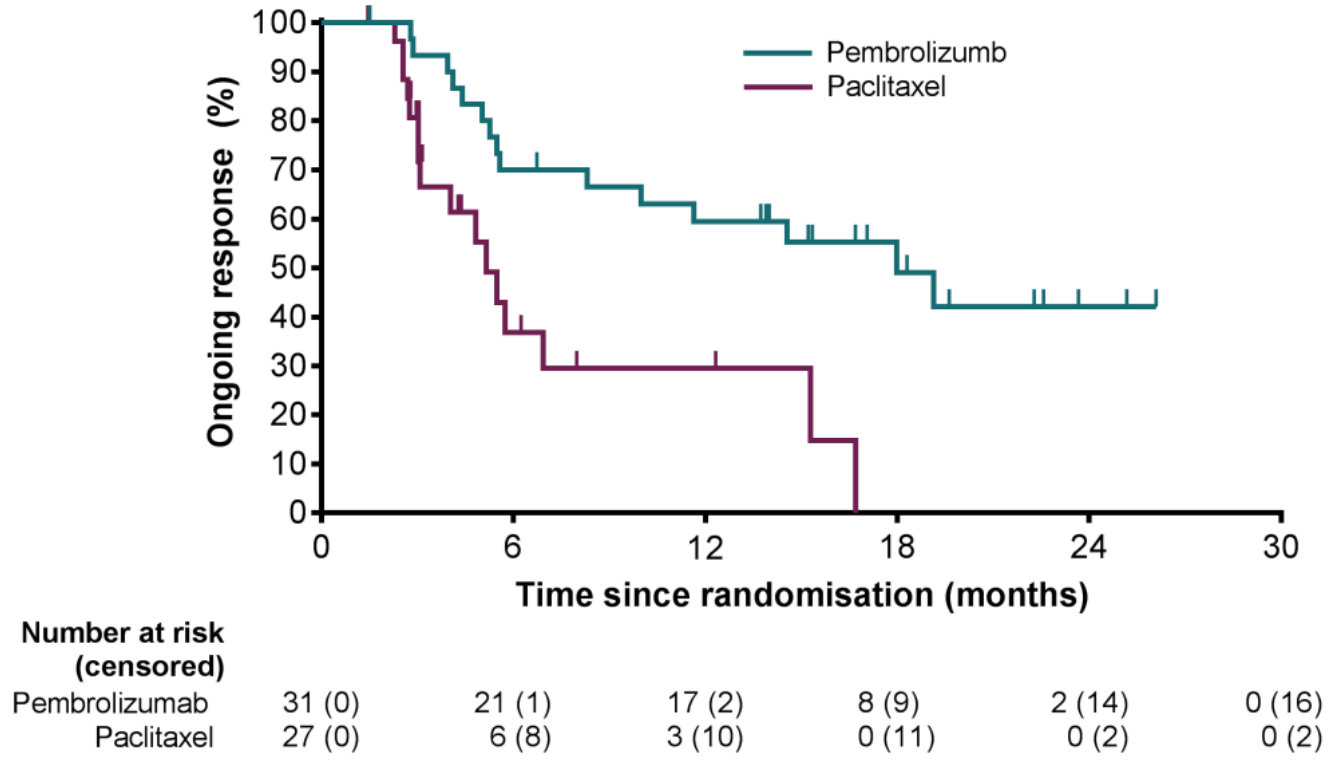


How to read a Kaplan Meier Curve



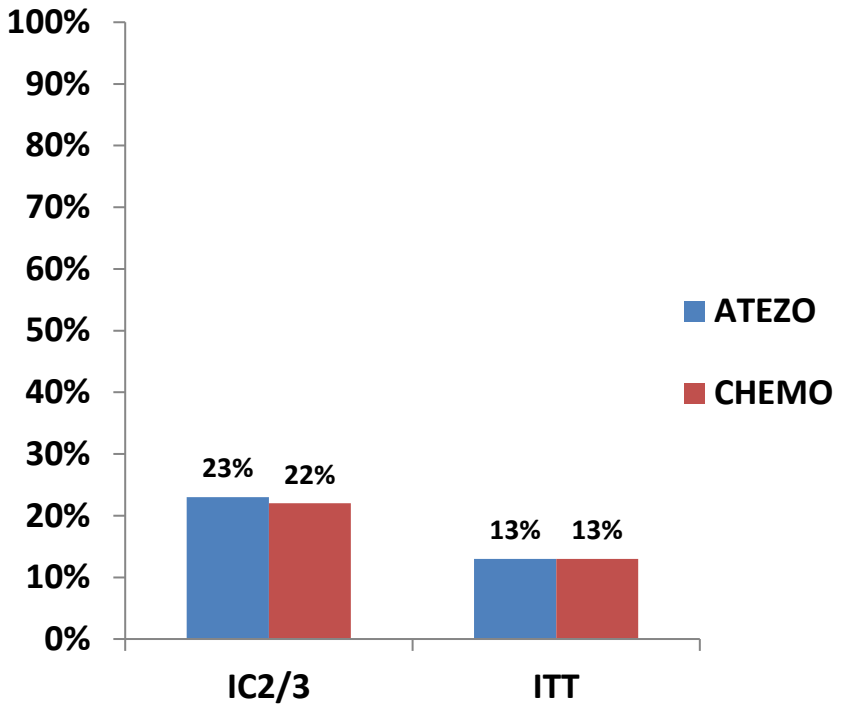
ORR vs DOR: pembro gastric

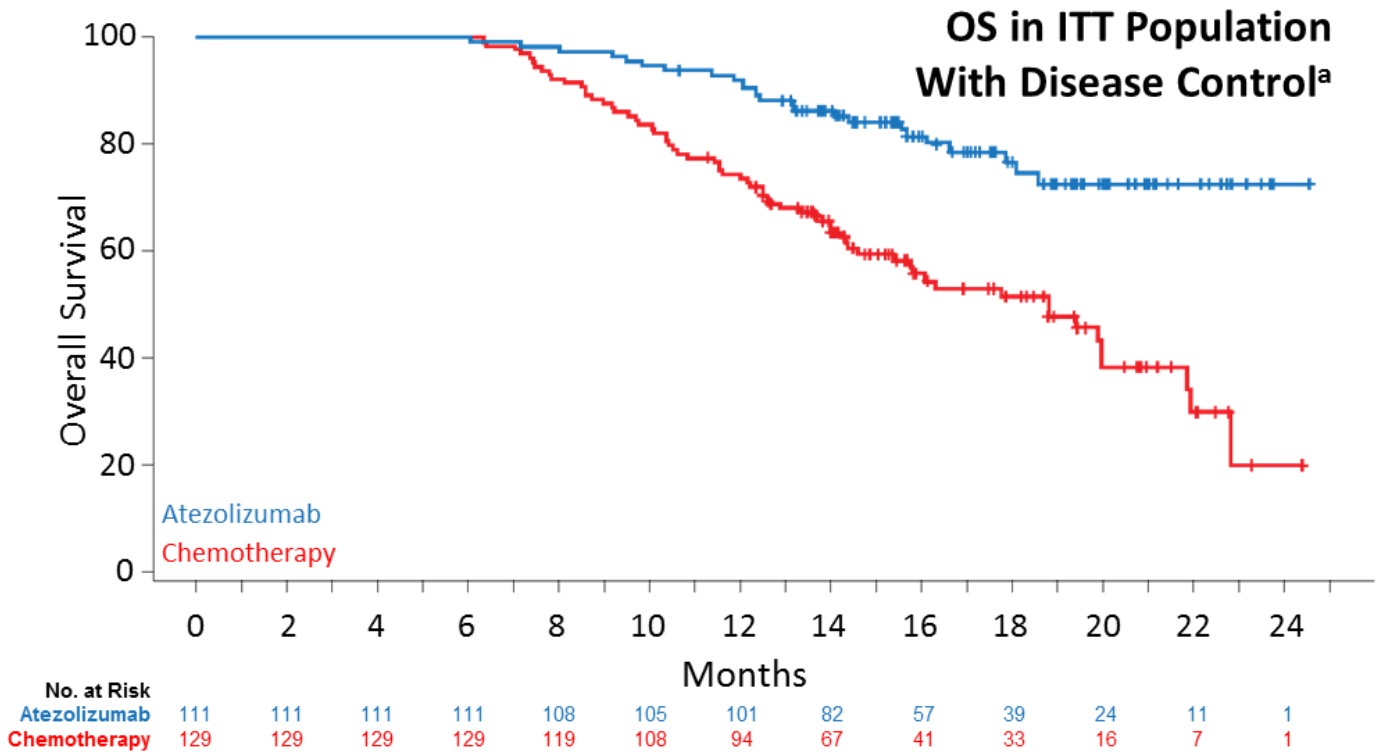




Shitara K, et al. Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): a randomised, open-label, controlled, phase 3 trial. Lancet 2018;392:123–33.

ORR vs DOR: atezo bladder

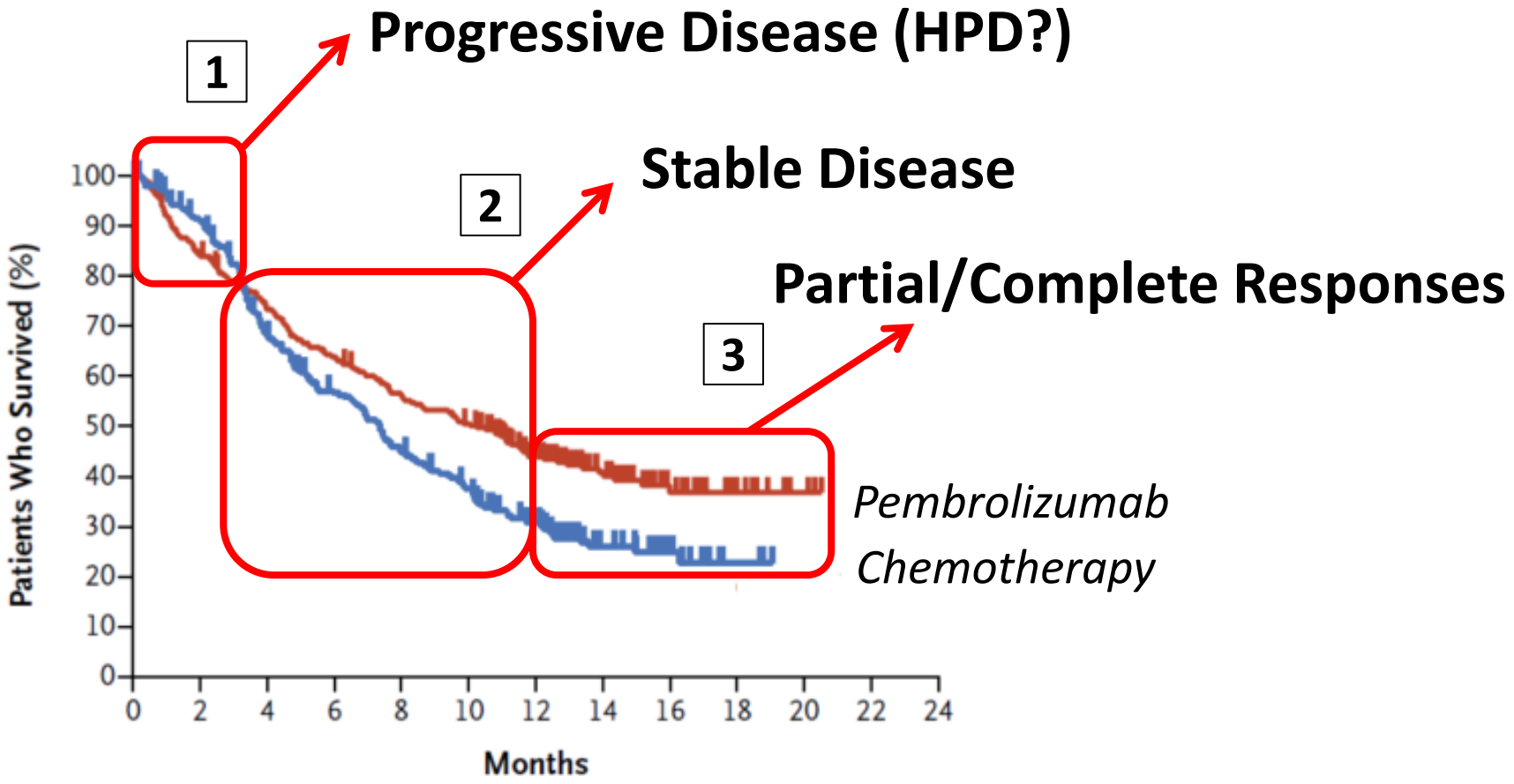




Powles T, et al. EAS 2017, IMvigor211.

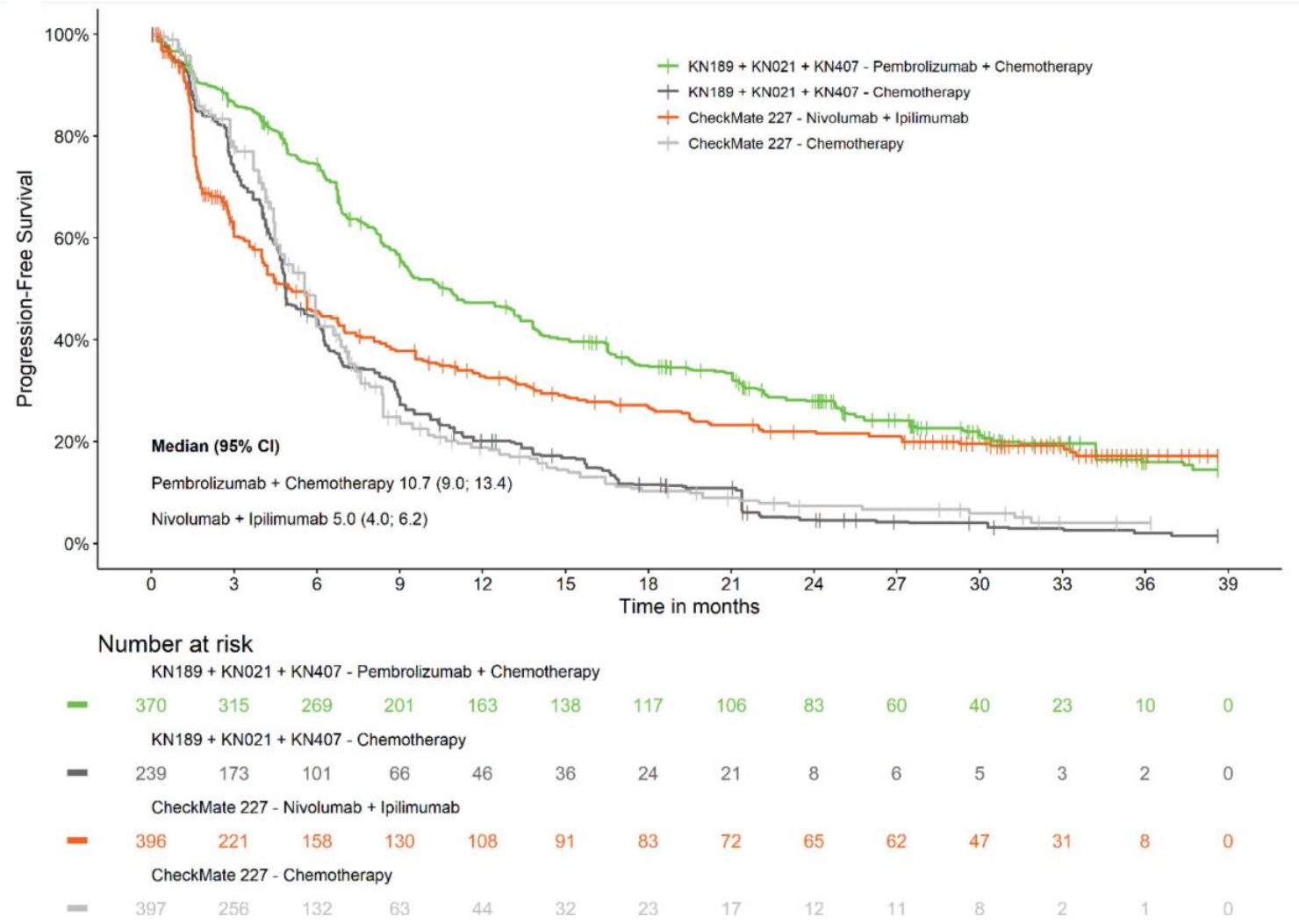
How to read survival curves in the IO era ?

Pembro Bladder



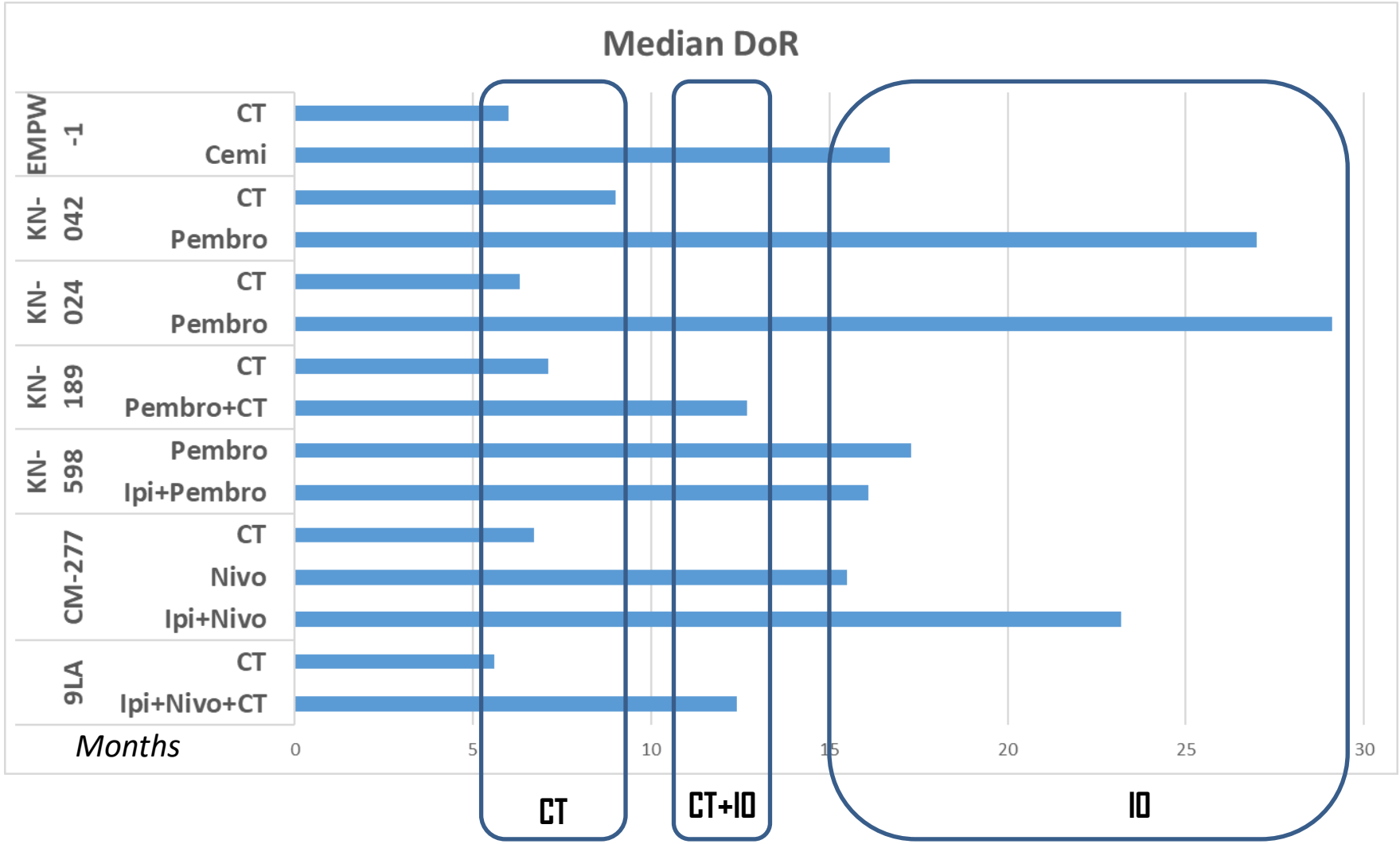
NEJM 2017; 376(11):1015–1026.

The Therapy Dilemna of 2025 in NSCLC

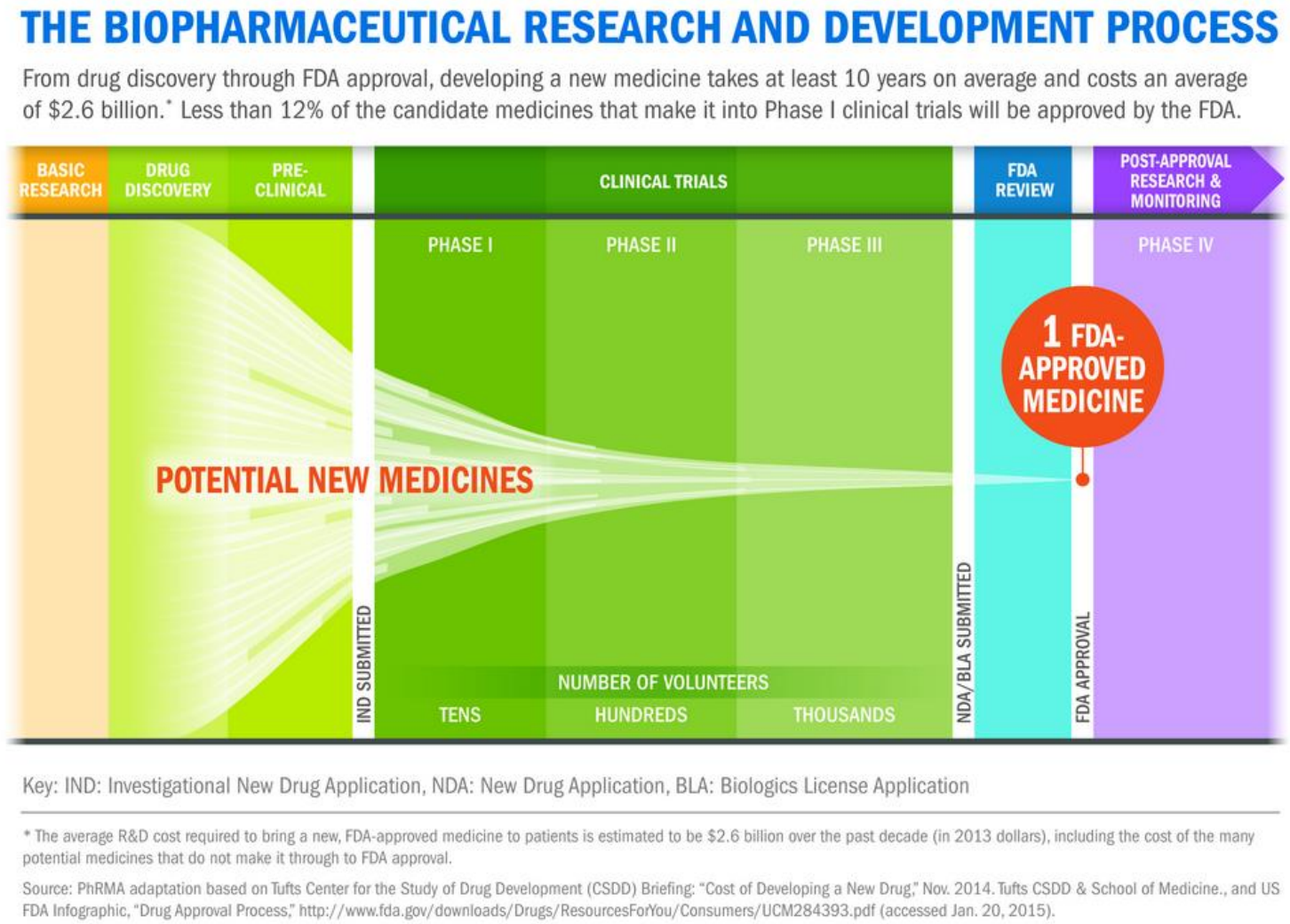


Halmos B, et al. A Matching-Adjusted Indirect Comparison of Pembrolizumab + Chemotherapy vs. Nivolumab + Ipilimumab as First-Line Therapies in Patients with PD-L1 TPS ≥1% Metastatic NSCLC. Cancers 2020;12(12):3648.

Median Duration of Responses in NSCLC: Chemo is Toxic for White Blood Cells (!)



THE FAILURE RATE OF DRUG DEVELOPMENT IN ONCOLOGY IS > 95%

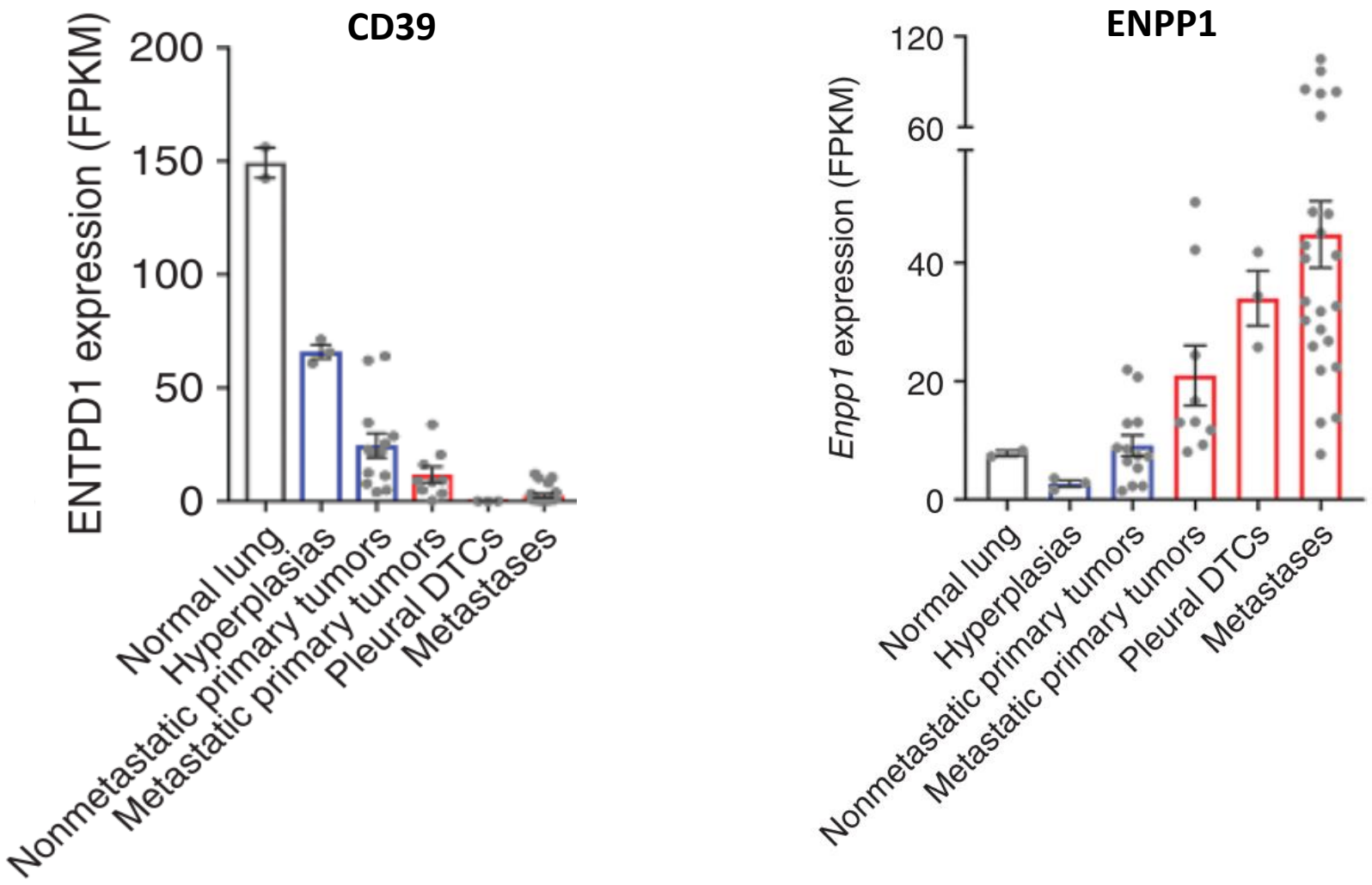


Biotechnology Innovation Organization (BIO) report, "Clinical Development Success Rates 2006-2015", 2016.
https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf

Current Assumptions in Oncology Drug Development are Flawed

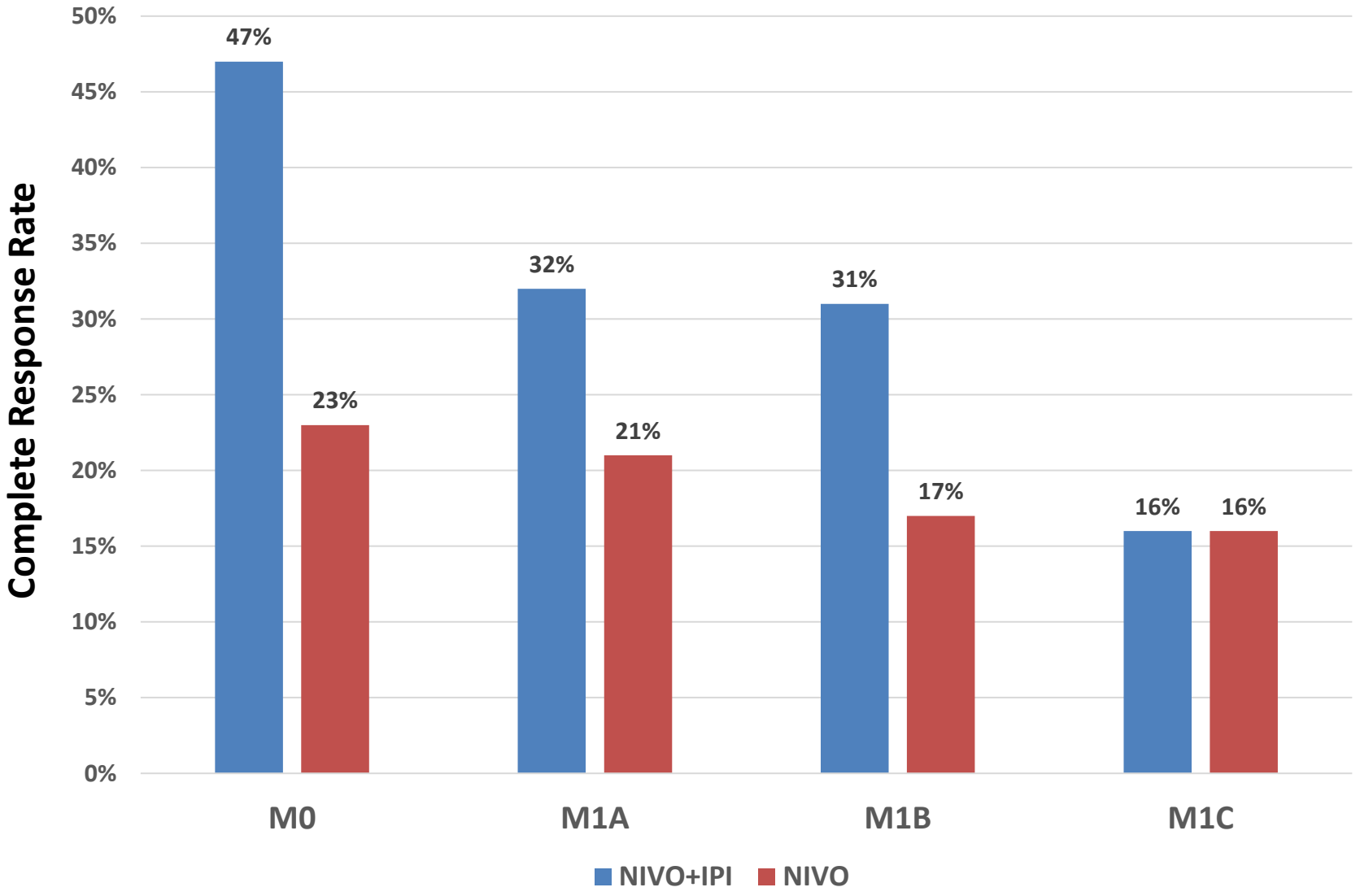
Assumptions		Reality
« Therapy Efficacy Depends on Pathology»	→	« Therapy Efficacy Relies on Tumor Biology»
« All Patients in a Given Indication are Equal »	→	« Huge Interindividual Variability »
« What Fails in Advanced Stages will not work in Early Stages »	→	« Cancer Biology Evolves over Time »

Localised Cancer ≠ Metastatic Cancers



Duran, M.A., et al. (2021). Cancer Discov. 11, 1212–1227.

Immunotherapy Efficacy can be Stage Dependent



CheckMate 066, 067, 069

Robert, C. et al. 1082MO 5-year characterization of complete responses in patients with advanced melanoma who received nivolumab plus ipilimumab (NIVO+IPI) or NIVO alone. Ann. Oncol. ***31****, S734–S735 (2020).*

ALSO AFTER ROBUST SCIENTIFIC PRECLINICAL DEVELOPMENT, DRUG DEVELOPERS SHOOT IN THE DARK WHEN TREATING PATIENTS

PRE-CLINICAL DRUG DEVELOPMENT

PHASE I FIRST IN HUMAN TRIALS

Why?

Because Current Biomarker Assays Have Long Turn Around Times

IHC

1.Fixation
2.Embedding
3.Sectioning
4.Deparaffinization/rehydration
5.Antigen retrieval
6.Blocking
7.Primary Ab incubation
8.Detection
9.Staining
10.Mounting
11.Scanning
12.Scoring

RNA-Seq & WES

1.Sample preparation
2.Library preparation
3.Library QC
4.RNA extraction +/- cDNA synthesis
5.Sequencing
6.Data cleaning, pre-processing & QC
7.Data analysis
8.Data Interpretation

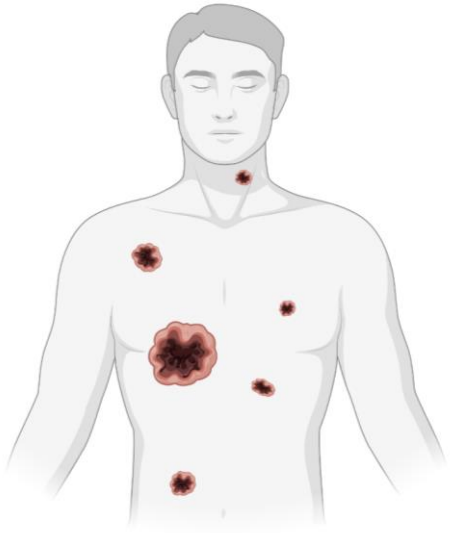
WEEKS / MONTHS

PRACTICAL CONSTRAINTS OF CLINICAL CANCER RESEARCH HINDER OUR ABILITY TO SELECT FOR THE APPROPRIATE PATIENTS

Consent Signature

3-4 weeks

C1D1



CT-Scan
Blood
Tumor Biopsy

Too Late !

Processing of Samples

Shipping to CRO

Weeks/Months

Results

CONVENTIONAL CLINICAL RESEARCH TOOLS DO NOT ADDRESS KEY QUESTIONS:

TARGET EXPRESSION? – TARGET SATURATION? – TARGET ENGAGEMENT?

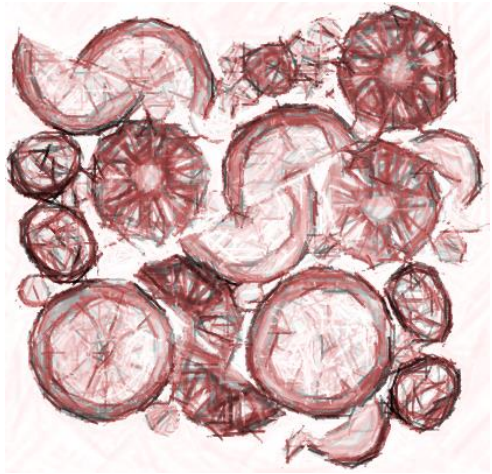
Fixed Tissue

Frozen Tissue

Semi-quantitative
Spatial Scoring

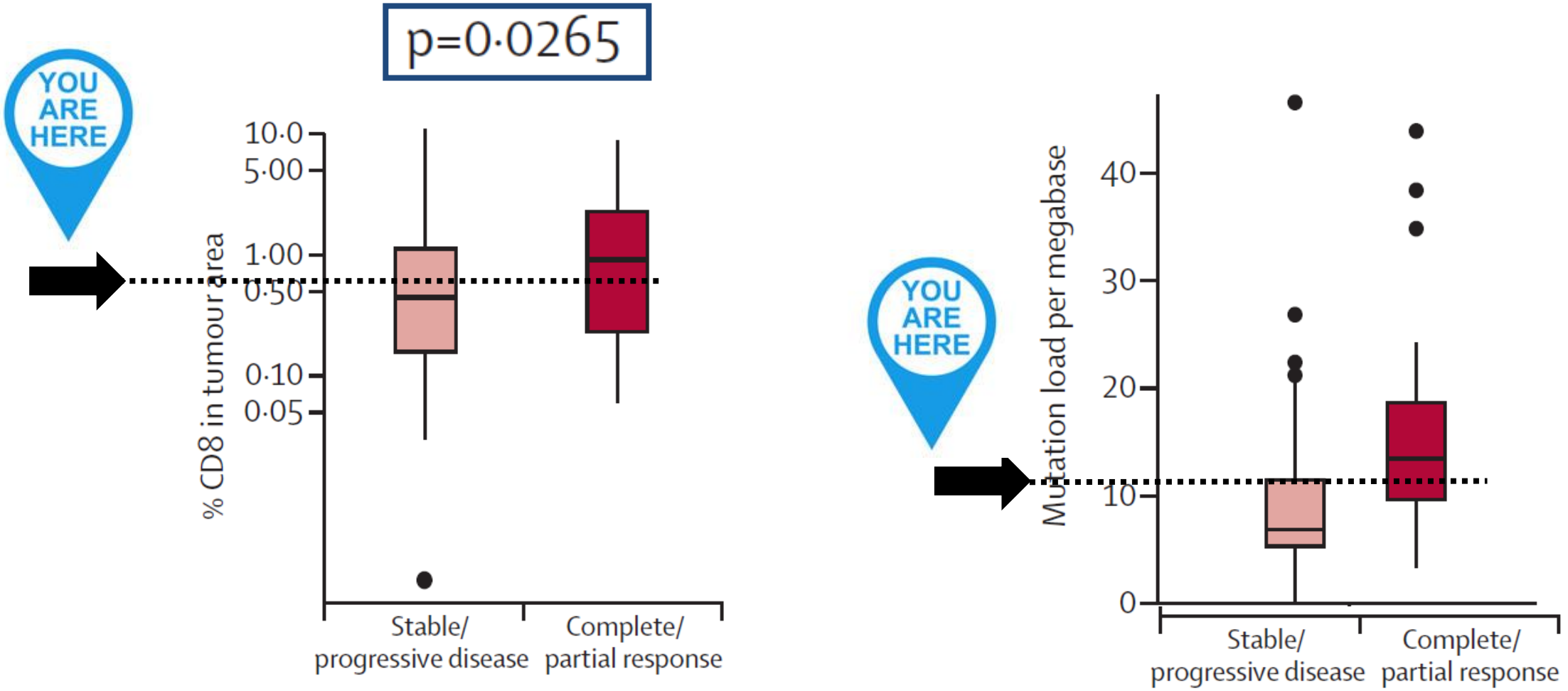
Deconvolution

IHC



DNA/RNA Seq

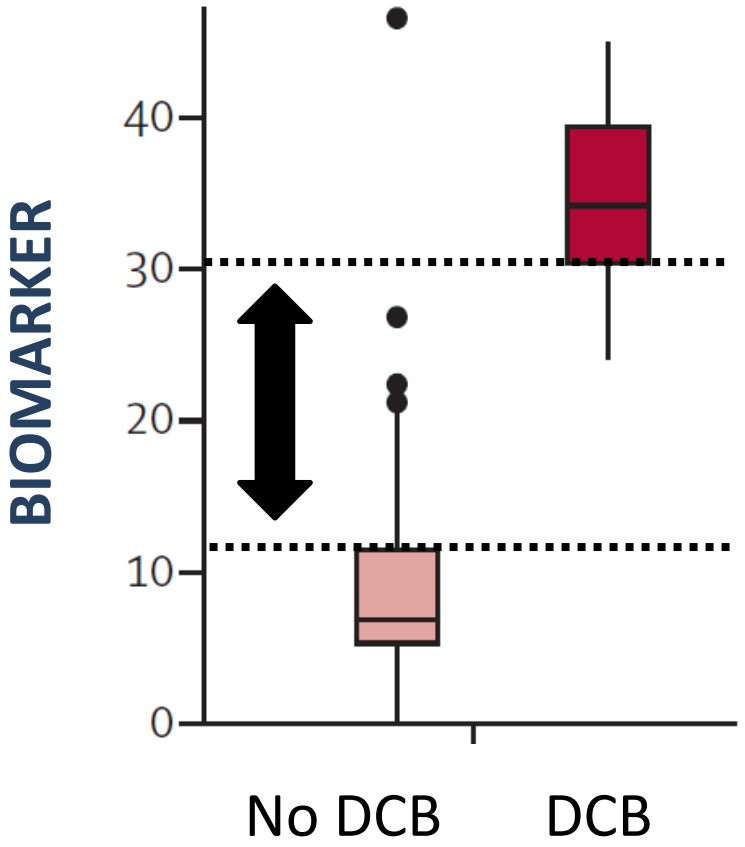
Current Biomarkers: Statistically vs Clinically Significant



Rosenberg JE, et al. Lancet 2016; 387(10031):1909–1920.

We need Biomarkers with Strong Predictive Values

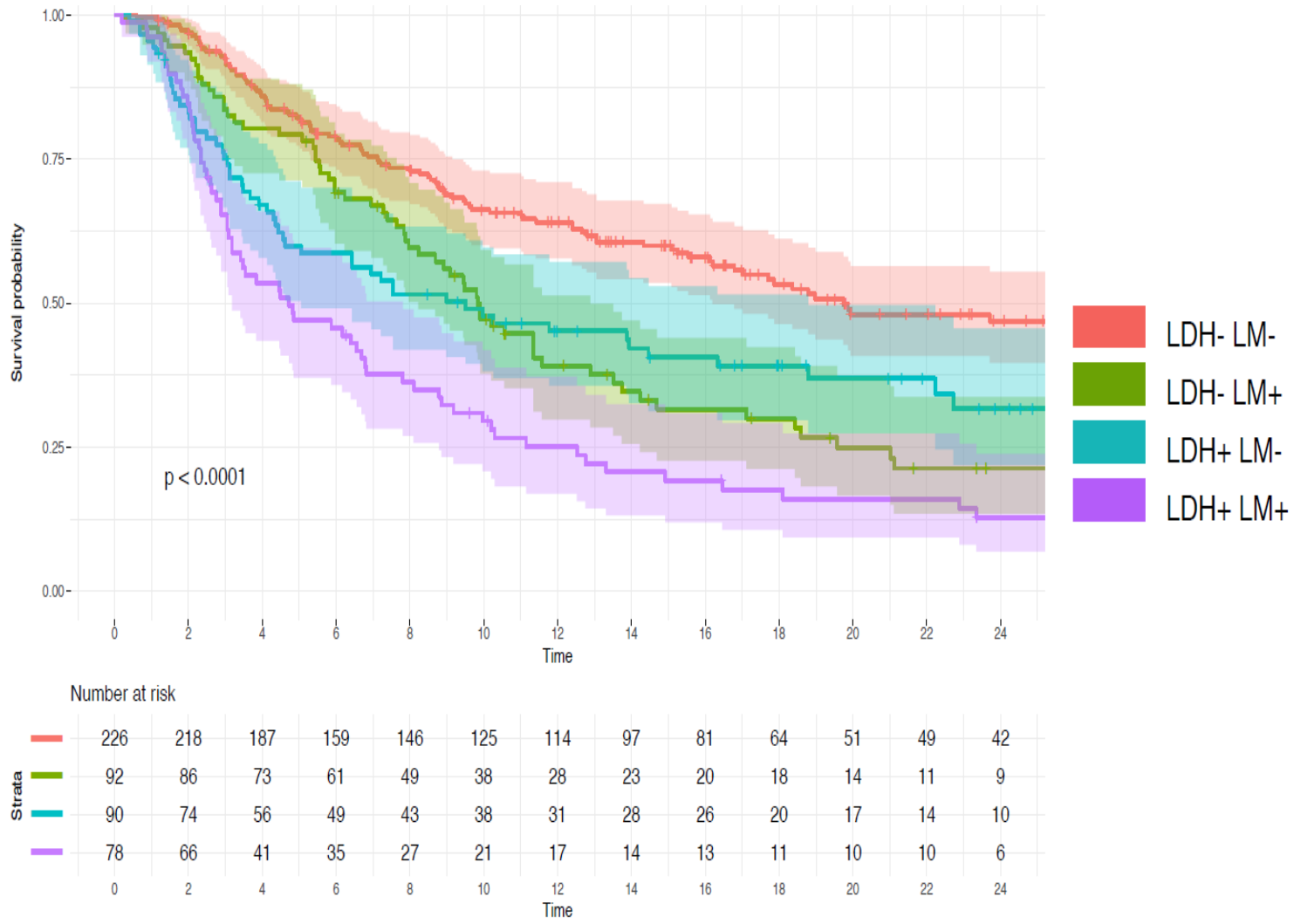
Small Overlap of Data



Biomarkers with Good Predictive Values

	DCB	No DCB	
BIOMARKER +	% TRUE POSITIVE (TP)	% FALSE POSITIVE (FP)	→ POSITIVE PREDICTIVE VALUE (PPV)
BIOMARKER -	% FALSE NEGATIVE (FN)	% TRUE NEGATIVE (TN)	→ NEGATIVE PREDICTIVE VALUE (NPV)
	→ SENSITIVITY	→ SPECIFICITY	

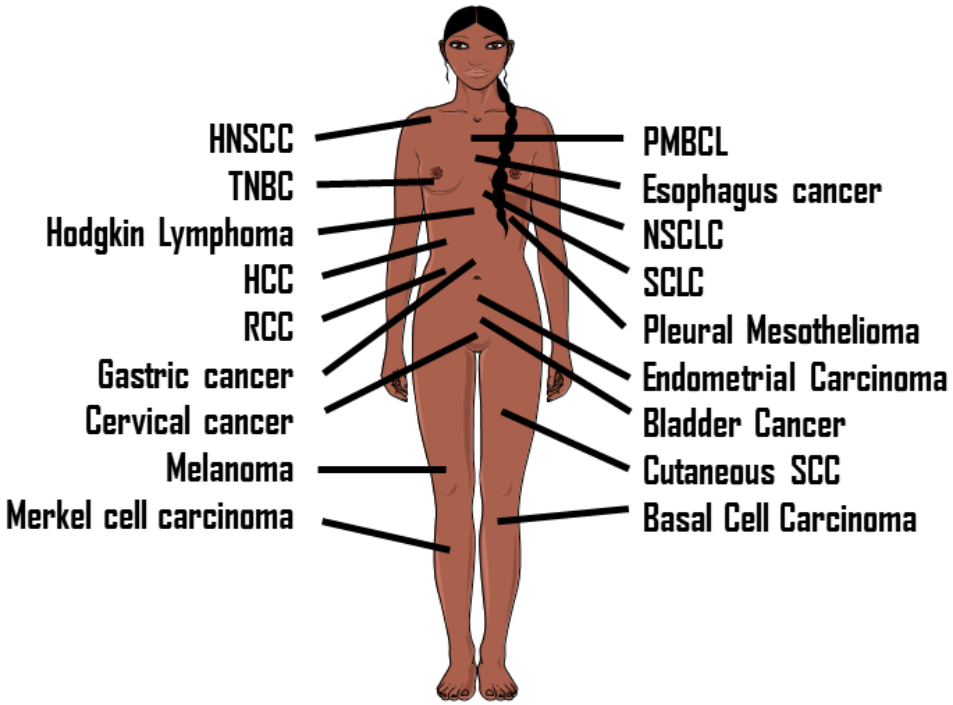
All Patients in a Given Indication are not Equivalent: LDH & Liver Mets



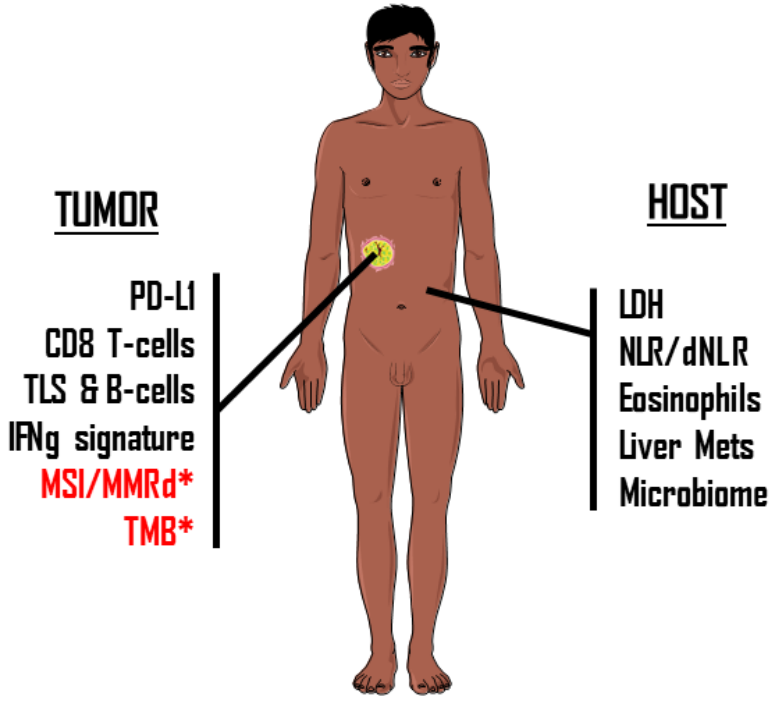
Dercle L. et al. (2022). High serum LDH and liver metastases are the dominant predictors of primary cancer resistance to anti-PD(L)1 immunotherapy. Eur. J. Cancer *177*, 80–93.

Biology (not Histology) Drives the Efficacy of Cancer Immunotherapies

Histology Based Approvals for Immunotherapy



Histology Independent Biomarkers Driving Efficacy of Immunotherapies

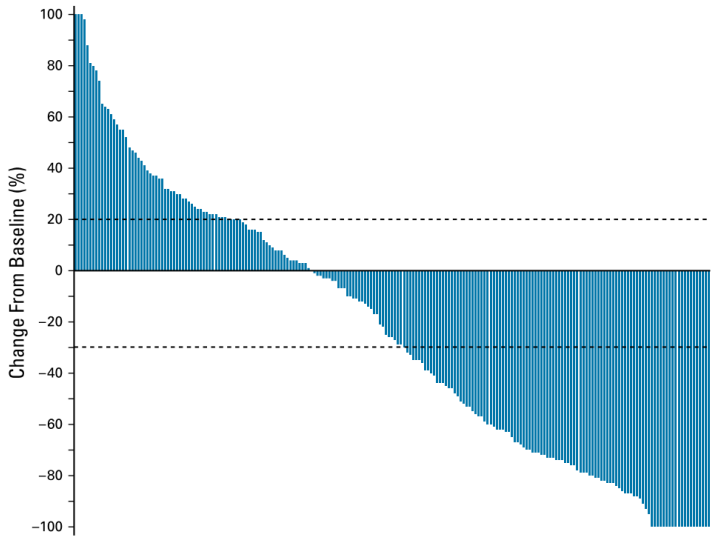


*Approved by the FDA but not by the EMA

Bonvalet et al. Cancer immunotherapy efficacy is driven by tumour biology, not by its histology. Impact on drug development and approvals. Eur. J. Cancer 162, 130–132. (2022).

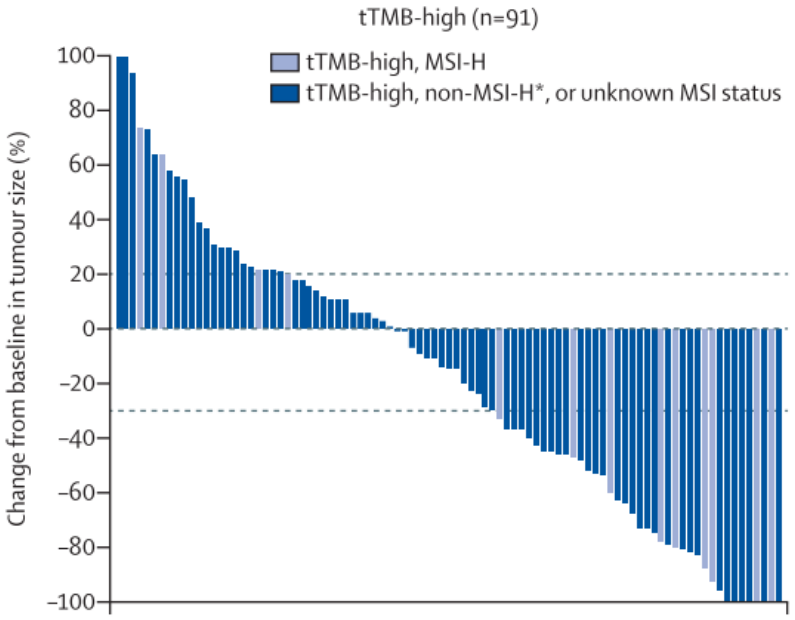
Tumor Agnostic Indications Are Becoming a Clinical Reality

MSI-H



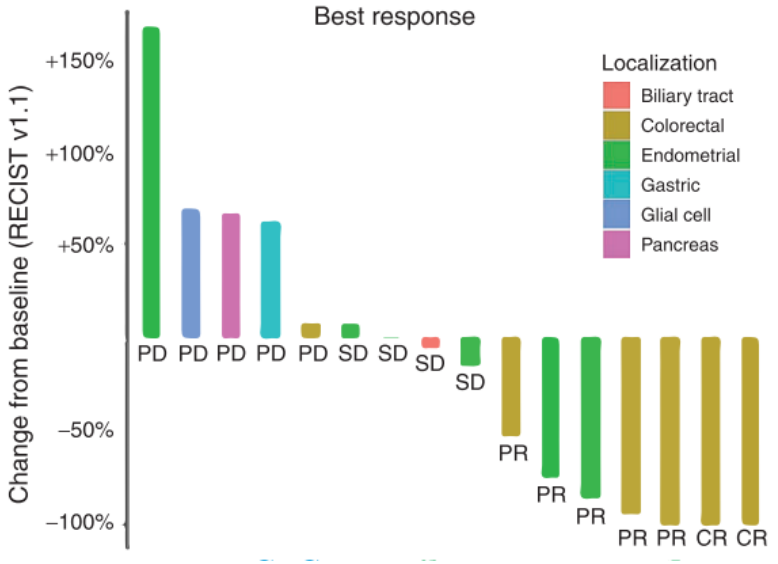
Marabelle, A., et al. (2020). J. Clin. Oncol. 38, 1–10.

TMB-H



Marabelle, A.,et al. (2020). Lancet Oncol. 21, 1353–1365.

POLEd

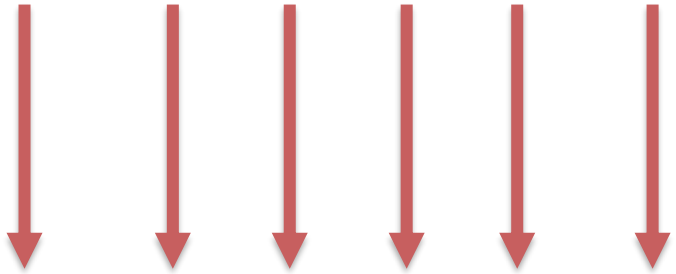


Rousseau, B., et al. (2022). Cancer Discov. 12, 1435–1448.

Increase Cancer Treatment Efficacy by providing Patients with Therapies based on Biology rather than Histology

Current Standard of Care

Histology: NSCLC CRC RCC HCC MM CRPC

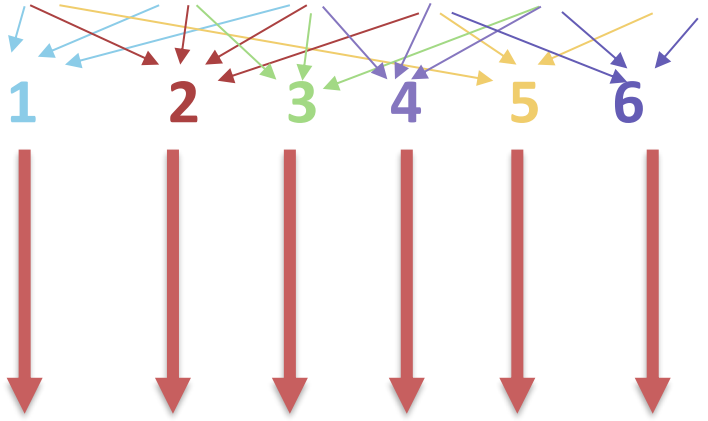


Treatment: A B C D E F

Future

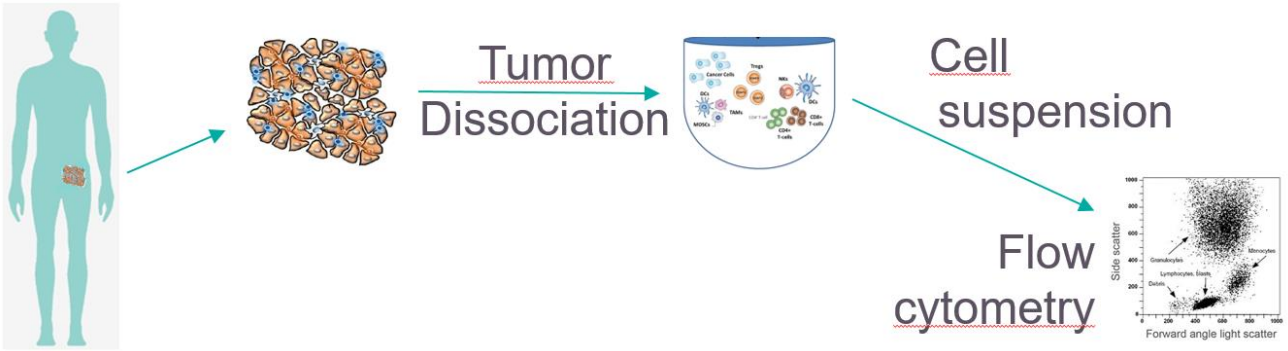
Histology: NSCLC CRC RCC HCC MM CRPC

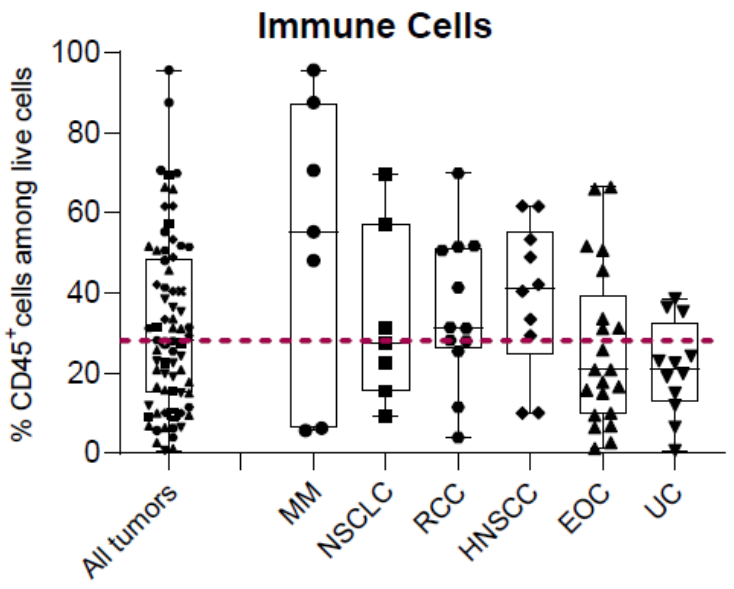
Biology:

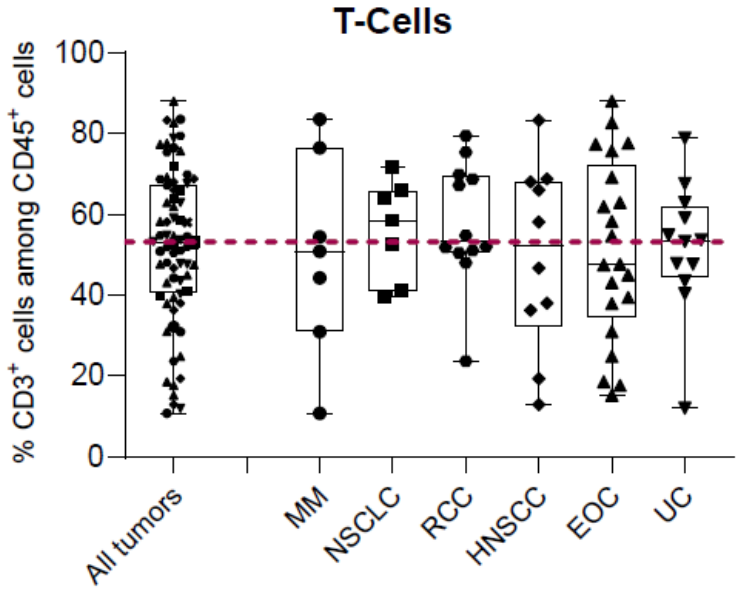


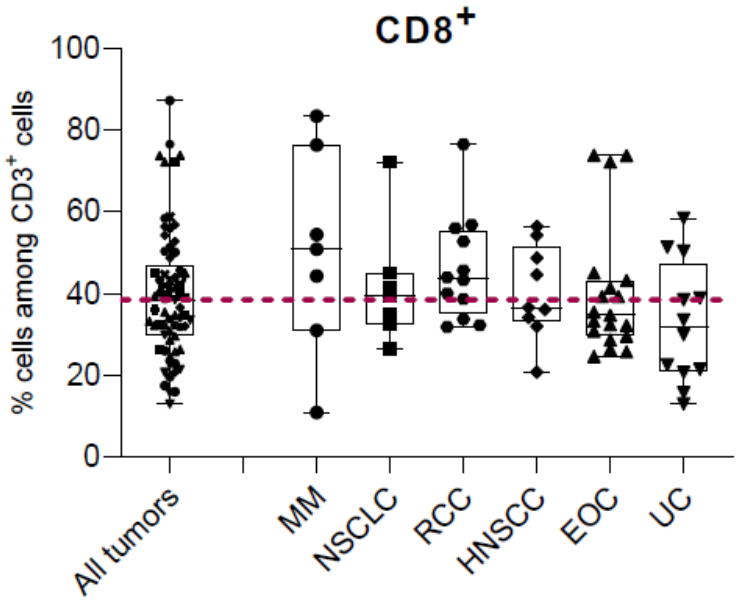
Treatment: A B C D E F

Histology does not Inform on Tumor Immune Infiltrates



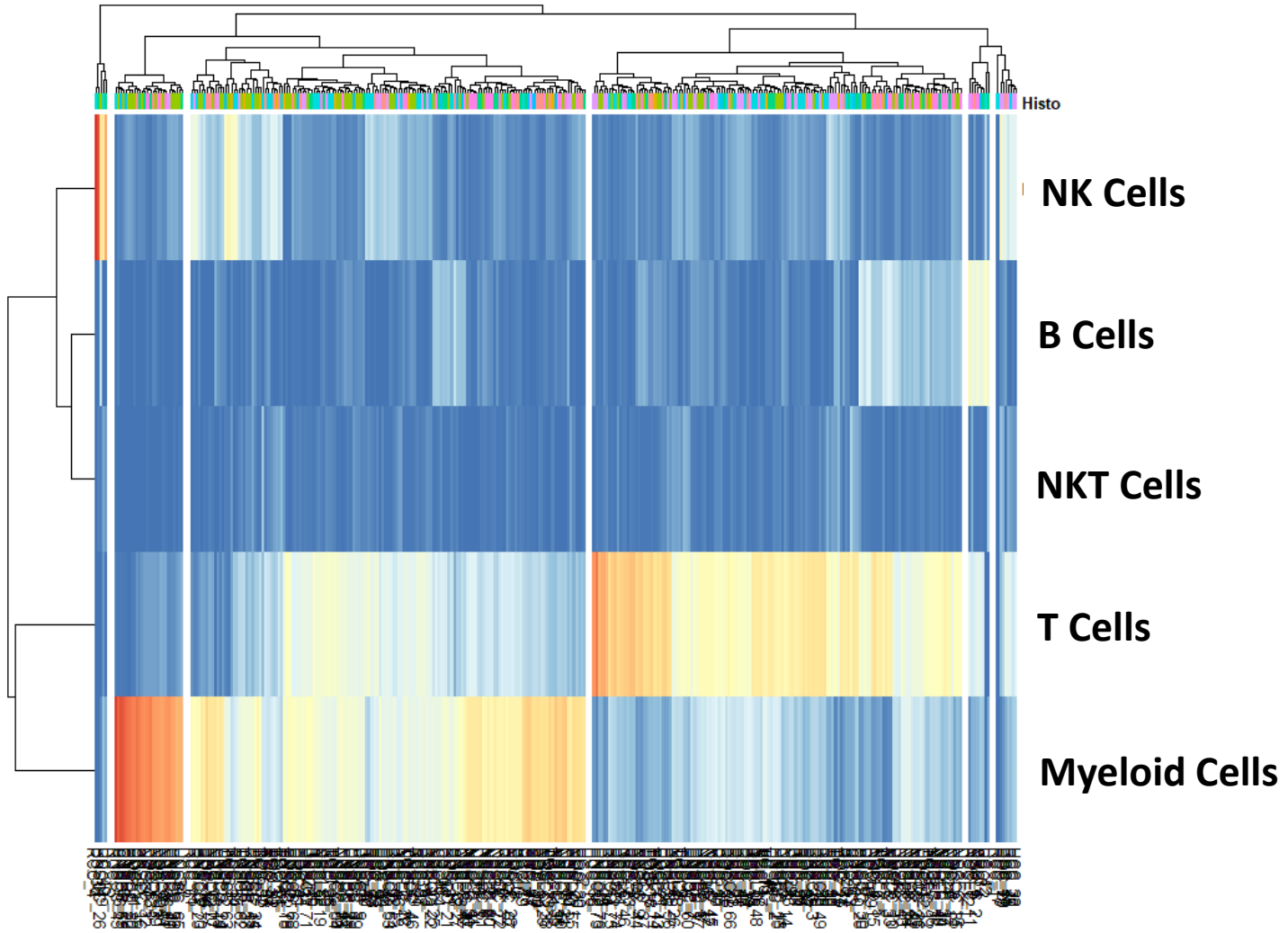






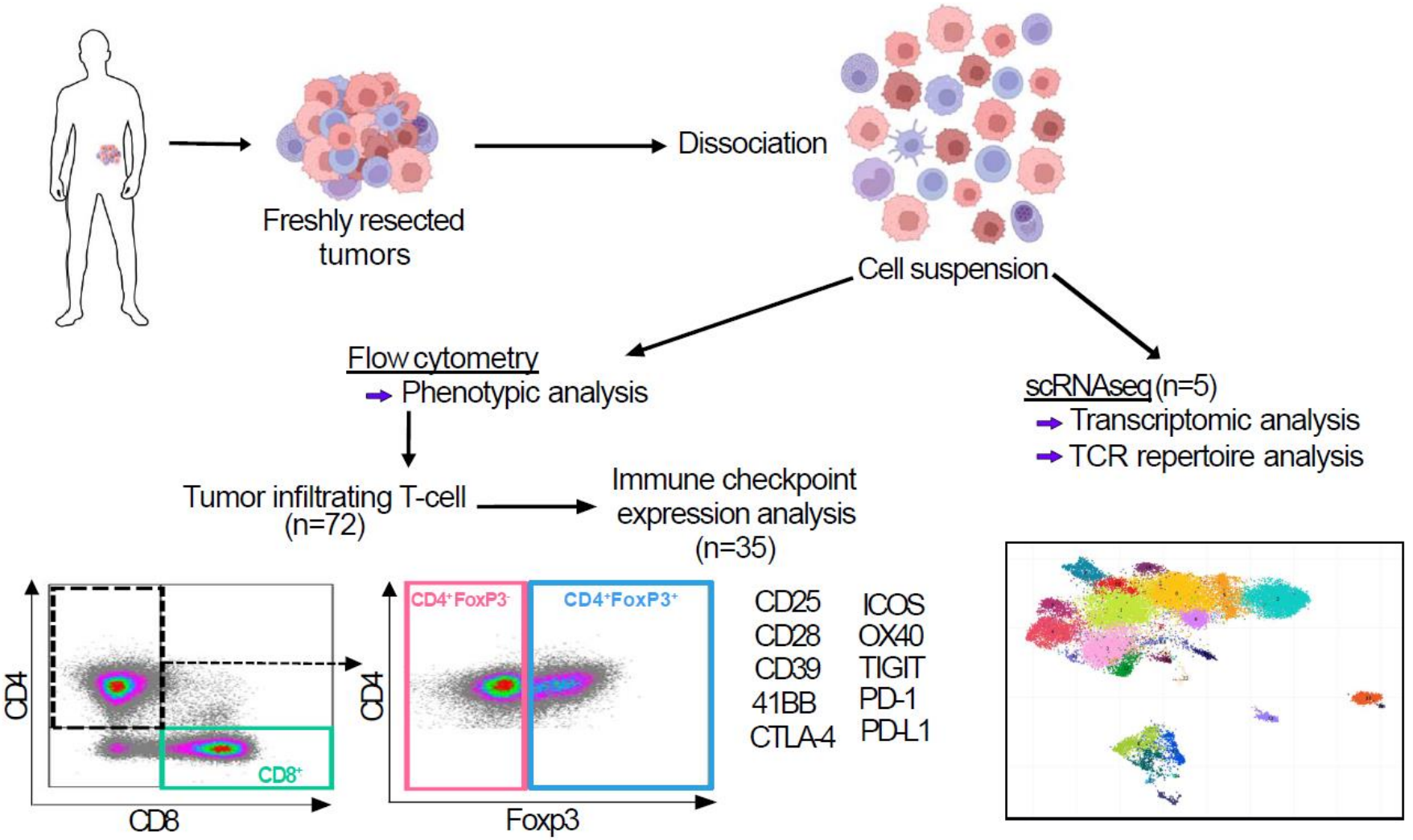
Bredel, D., et al. (2023). J. Exp. Clin. Cancer Res. *42*, 333.

But Common Immune Contextures are found across Indications



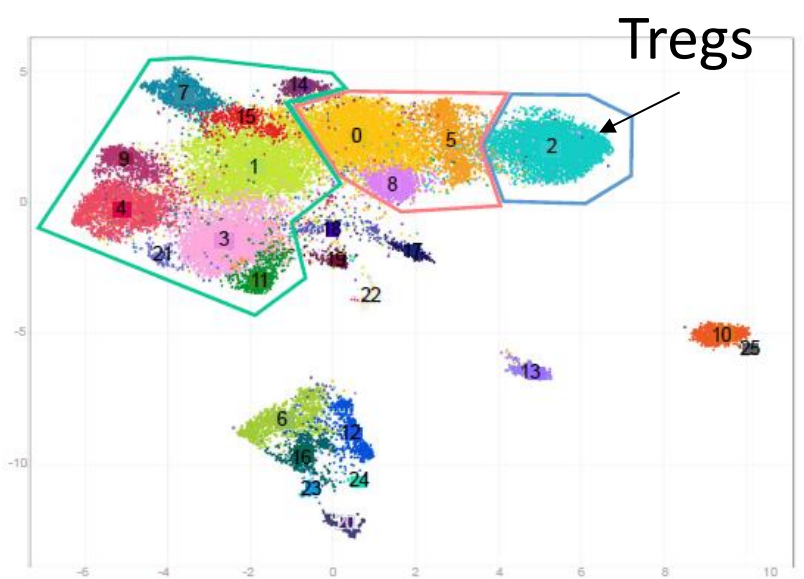
Bonvalet et al. Subset of Immune Cells in 300+ Human Cancers (Flow Cytometry). Unpublished Data.

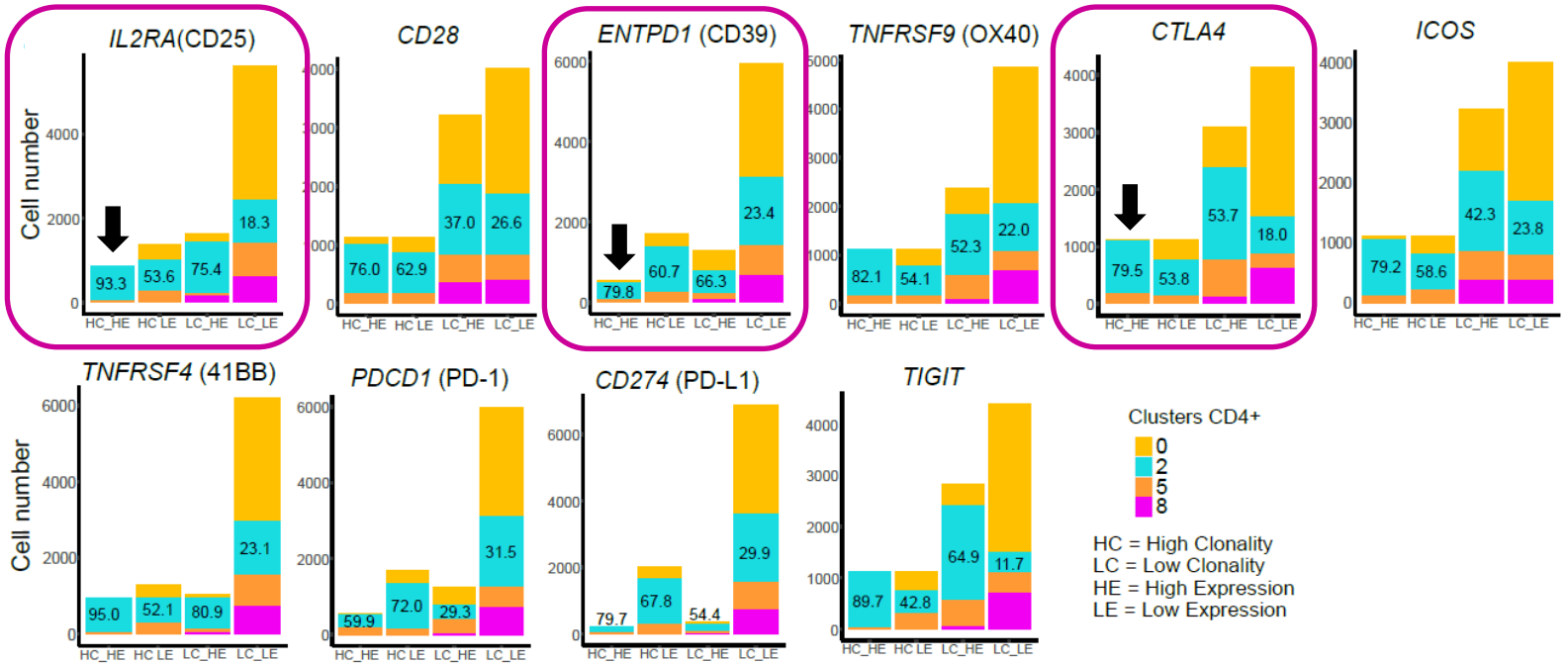
Immune Checkpoints Expression in Human Cancers

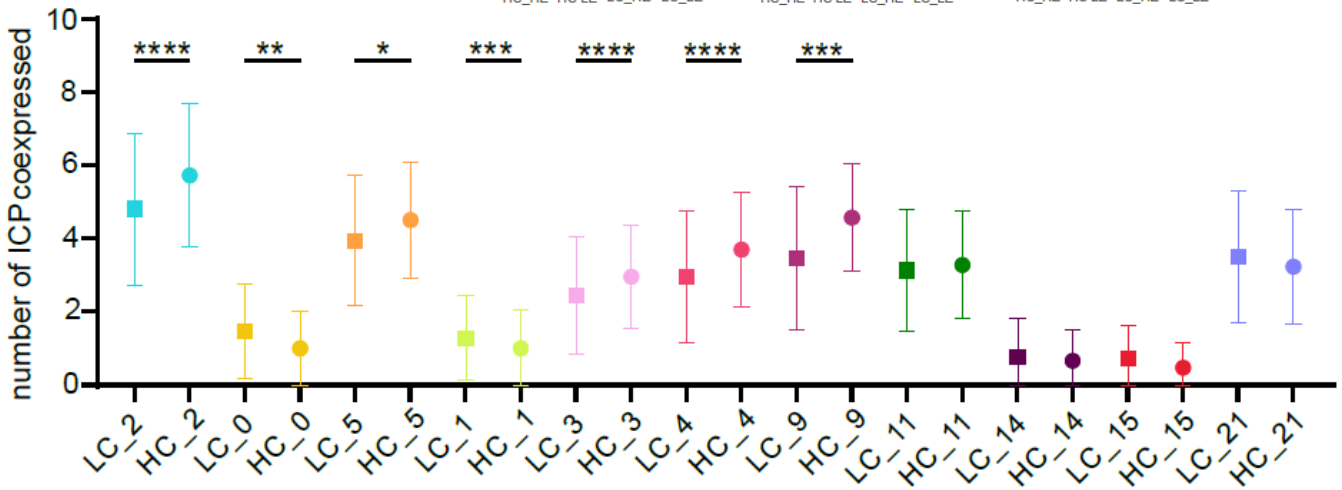


Cancer types: MM (n=7), NSCLC (n=9), RCC (n=12), HNSCC (n=11), EOC (n=22), UC (n=12), HCC (n=2), NET (n=1), Thyr (n=1)

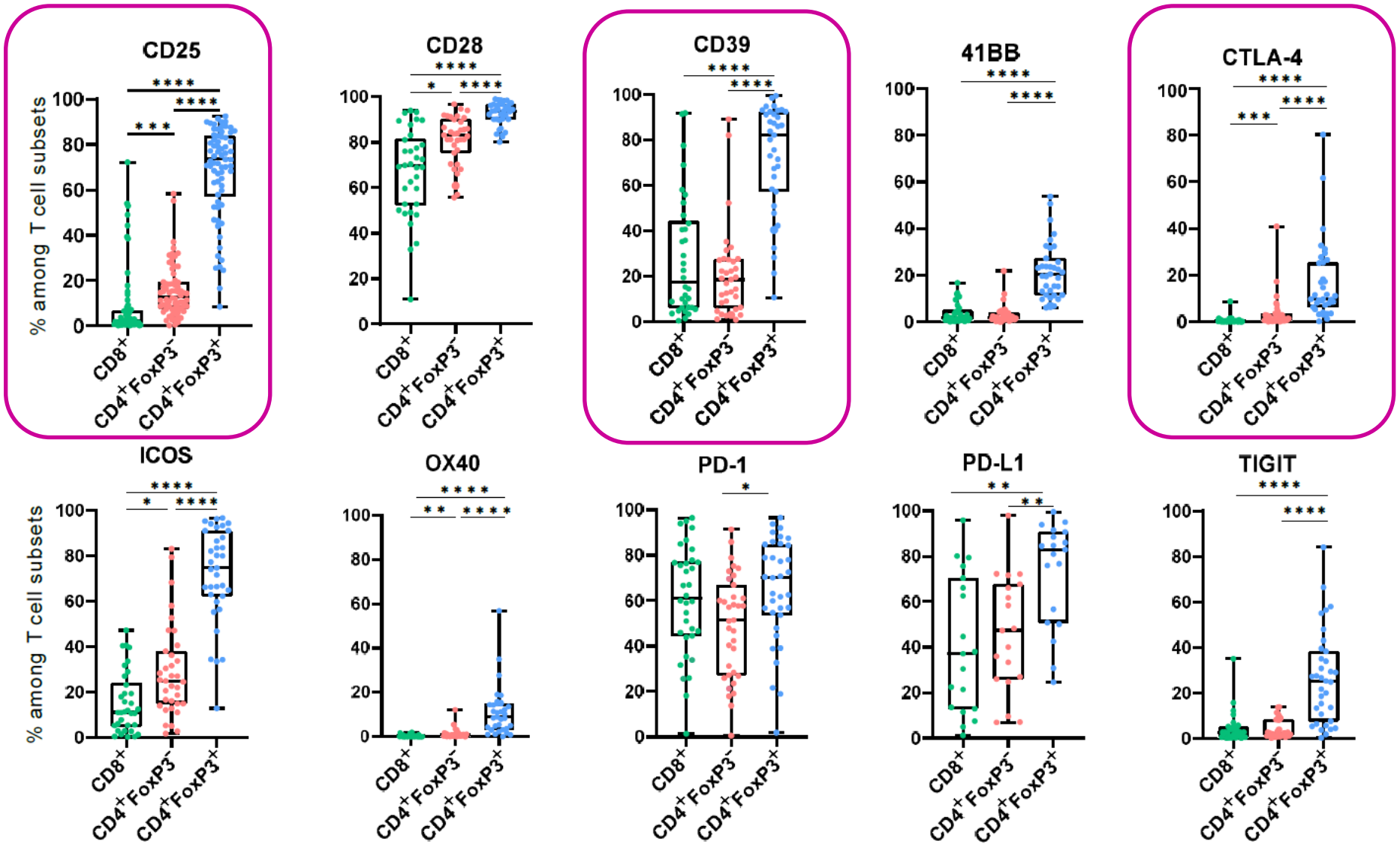
Single Cell RNA & TCR Seq:
Intratumoral CD25+CD39+ Tregs are Clonally Expanded





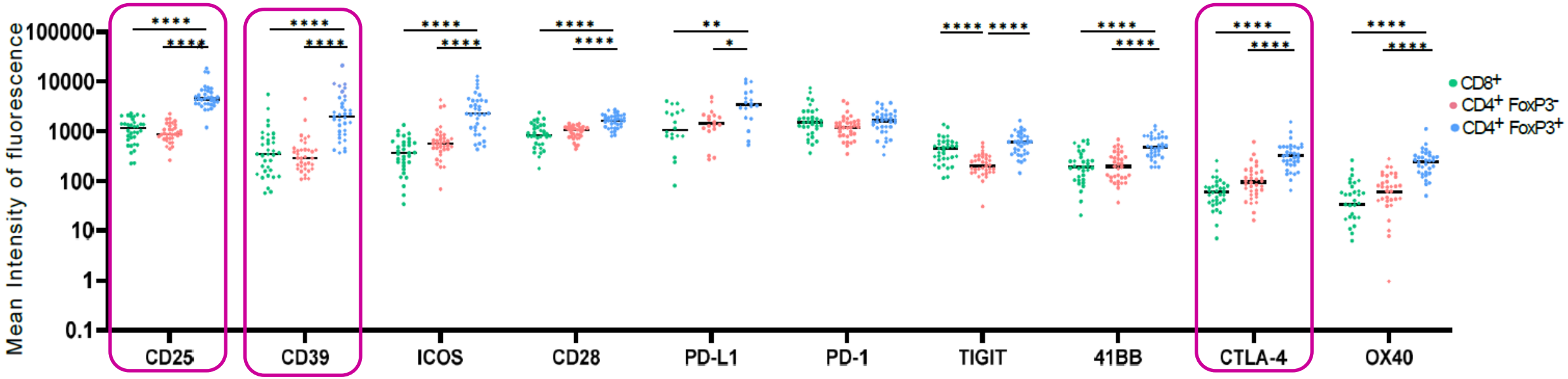


Intratumoral Human Tregs are CD25+CD39+CTLA4+ (%)



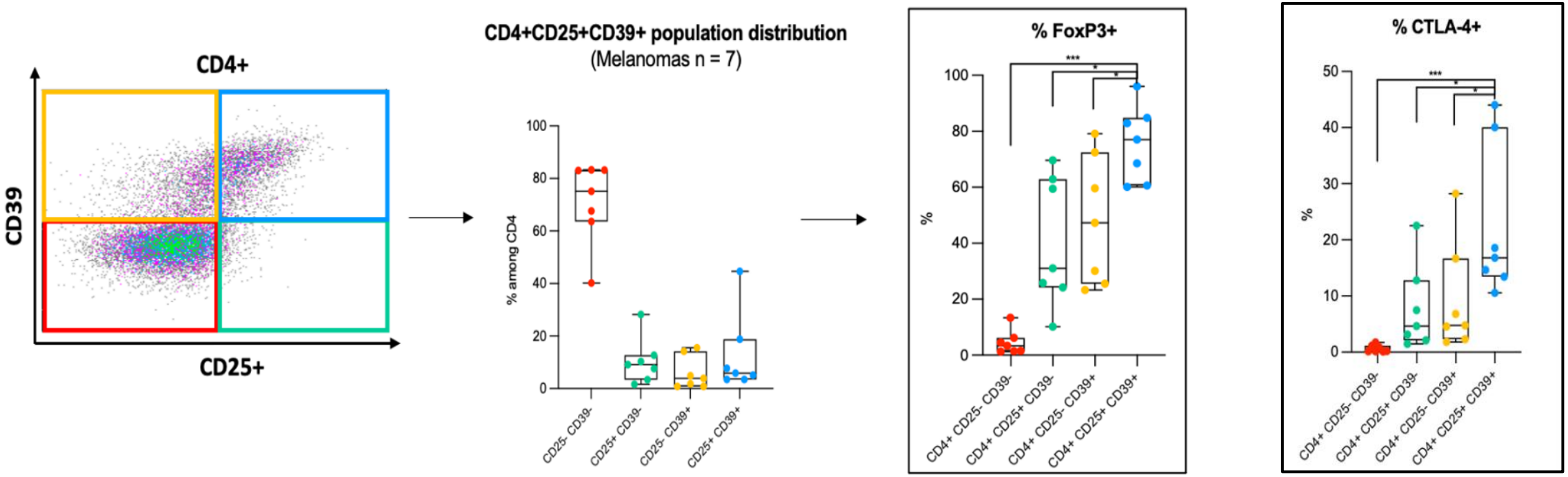
Bredel, D., et al. (2023). J. Exp. Clin. Cancer Res. *42*, 333.

Intratumoral Human Tregs are CD25+CD39+CTLA4+ (MFI)

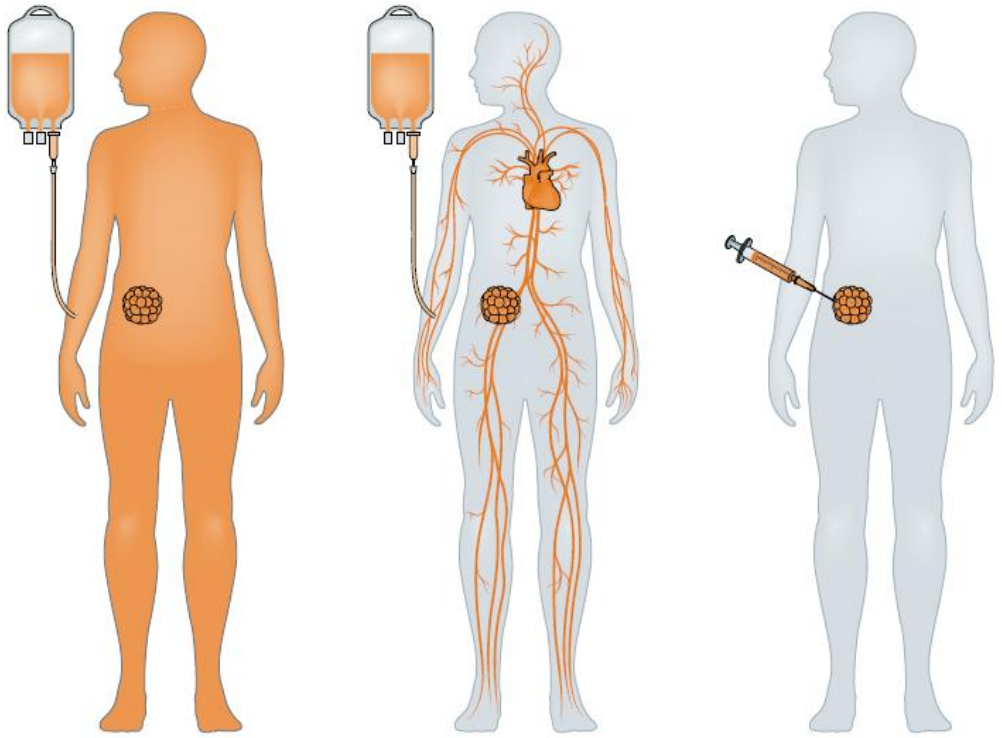


Bredel, D., et al. (2023). J. Exp. Clin. Cancer Res. *42*, 333.

Intratumoral Clonally Expanding Tregs are CTLA4+ in Melanoma



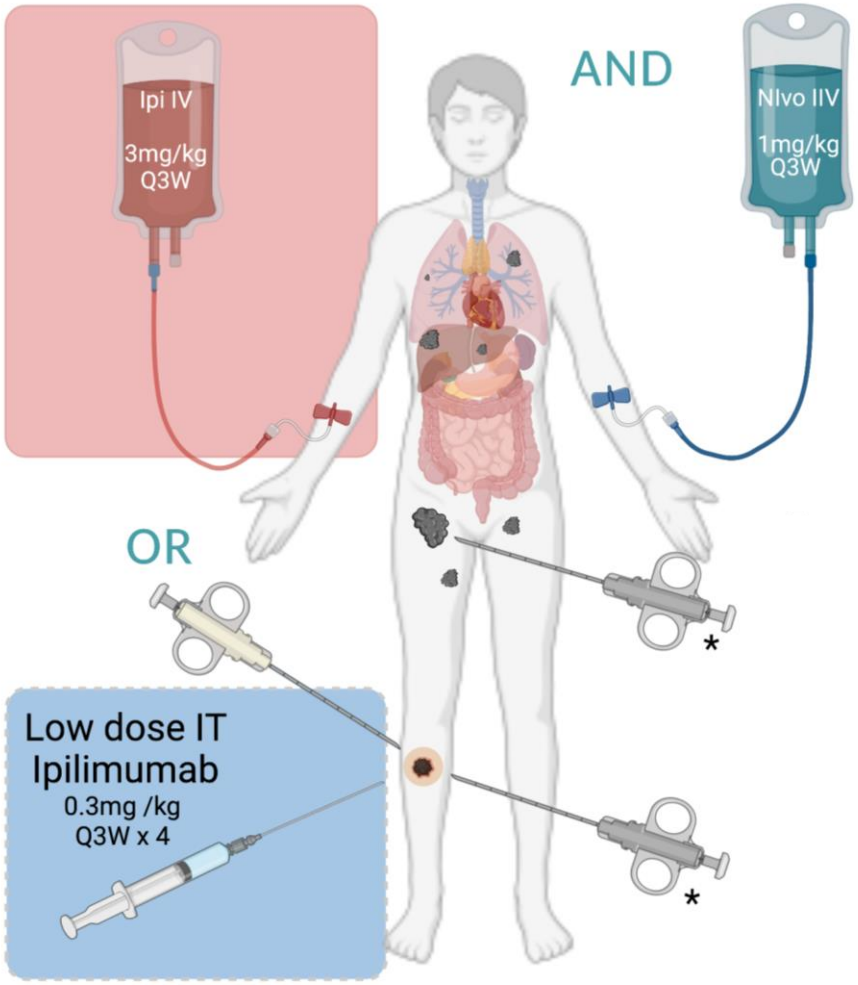
Intratumoral (IT) vs Intravenous (IV) delivery of Cancer Immunotherapies



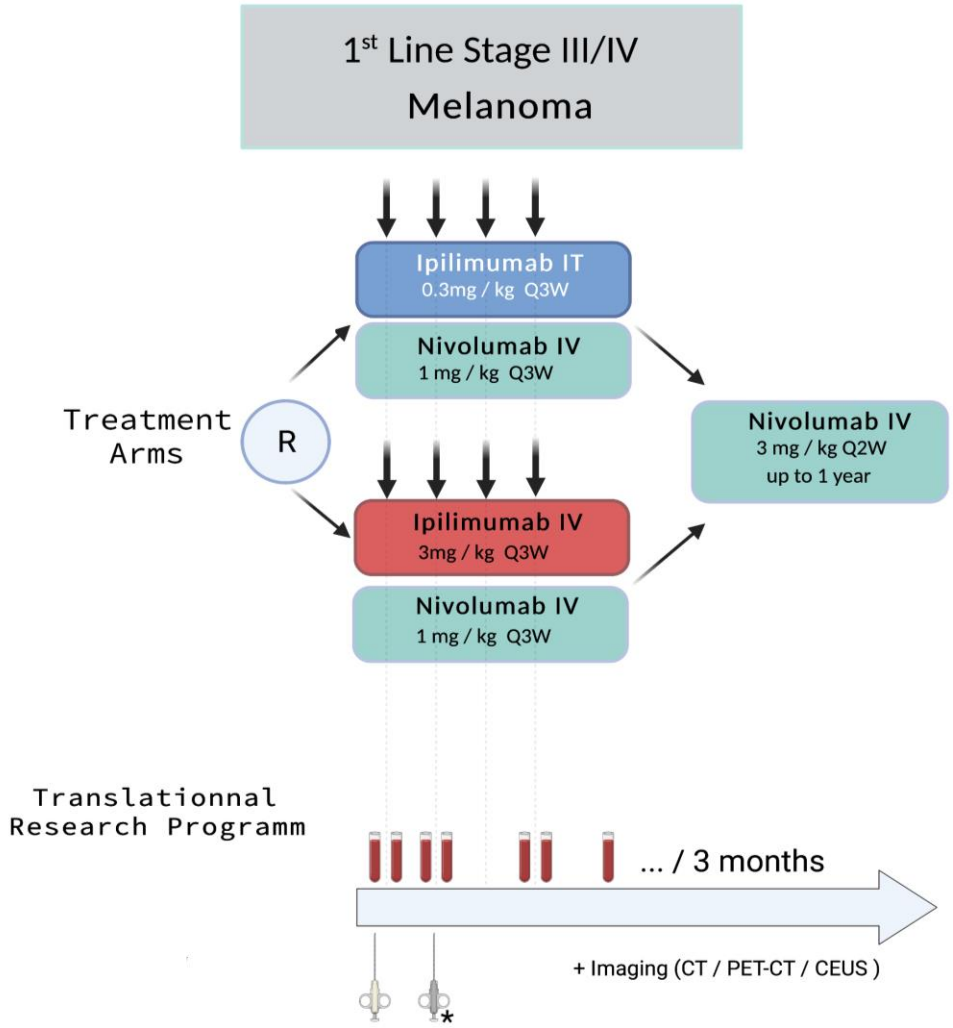
	Systemic	Tumour-targeted	Intratumoural
Advantages	Practical	Practical	• High therapeutic index • Low toxicity
Disadvantages	• Low therapeutic index • High toxicity	On-target, off-tumour toxicity	Technical

Melero I, Castanon E, Alvarez M, Champiat S, Marabelle A. Intratumoural administration and tumour tissue targeting of cancer immunotherapies. Nat Rev Clin Oncol. 2021;18:558–76.

NIVIPIT (NCT02857569) : Trial Design



* For the IT arm **both** Injeacted and non injected tumors were biopsierd prior to cycle 2

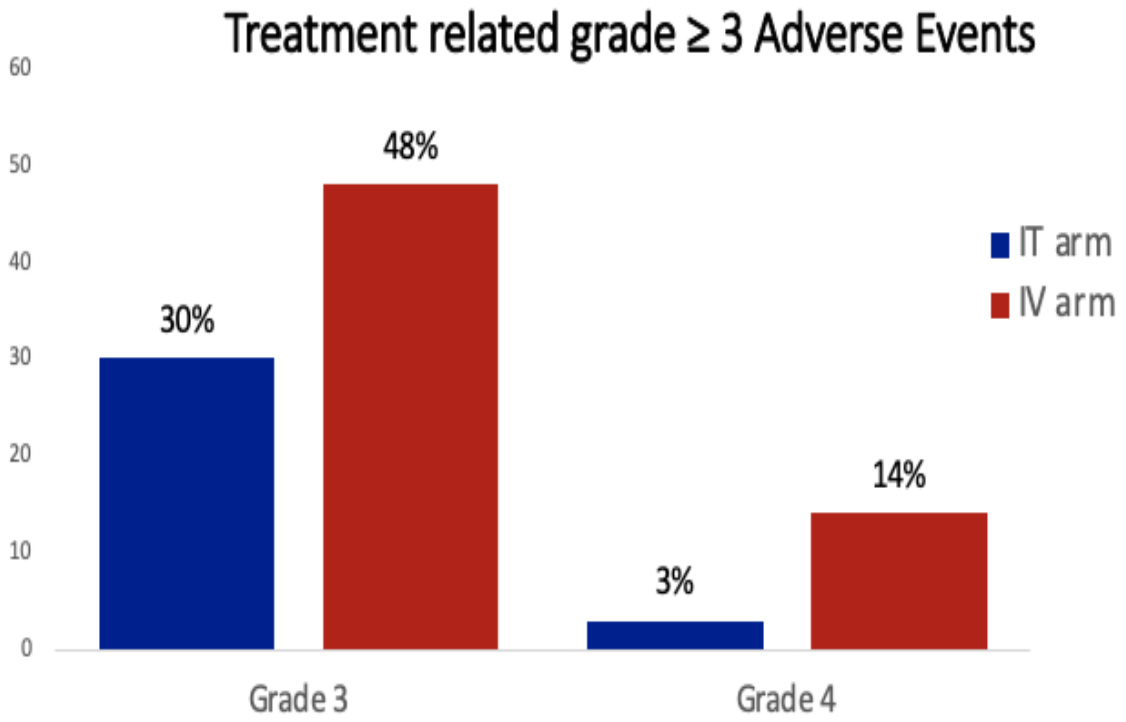


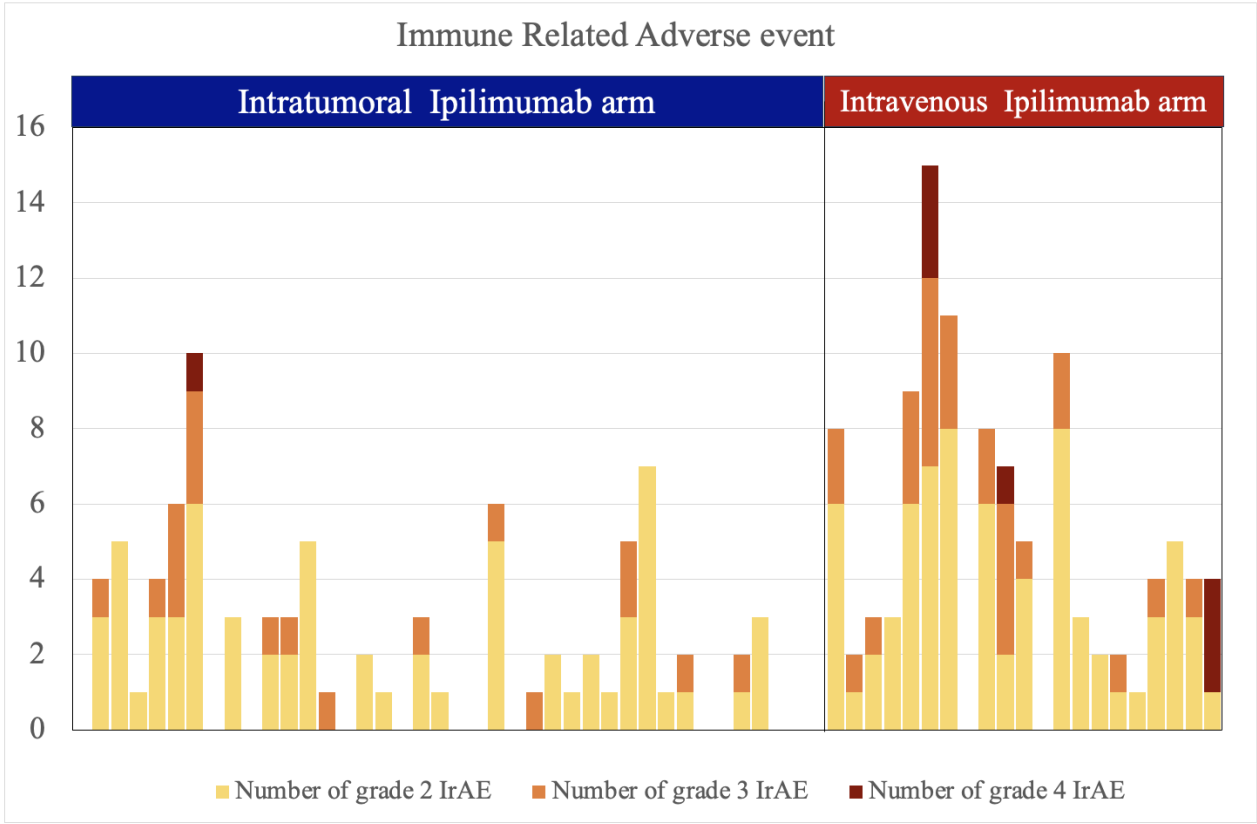
NIVIPIT : Safety (Primary Endpoint)

Time	Incidence Rate IT ARM	Incidence Rate IV ARM
6 months	22.6% [12.4 ; 37.6]	57.1% [36.5 ; 75.5]
12 months	33% [22.6 ; 54.2]	60.9% [40.9 ; 79.2]

Primary endpoint : **POSITIVE** trial

(<30% grade ≥3 treatment related AE @ 6 months)

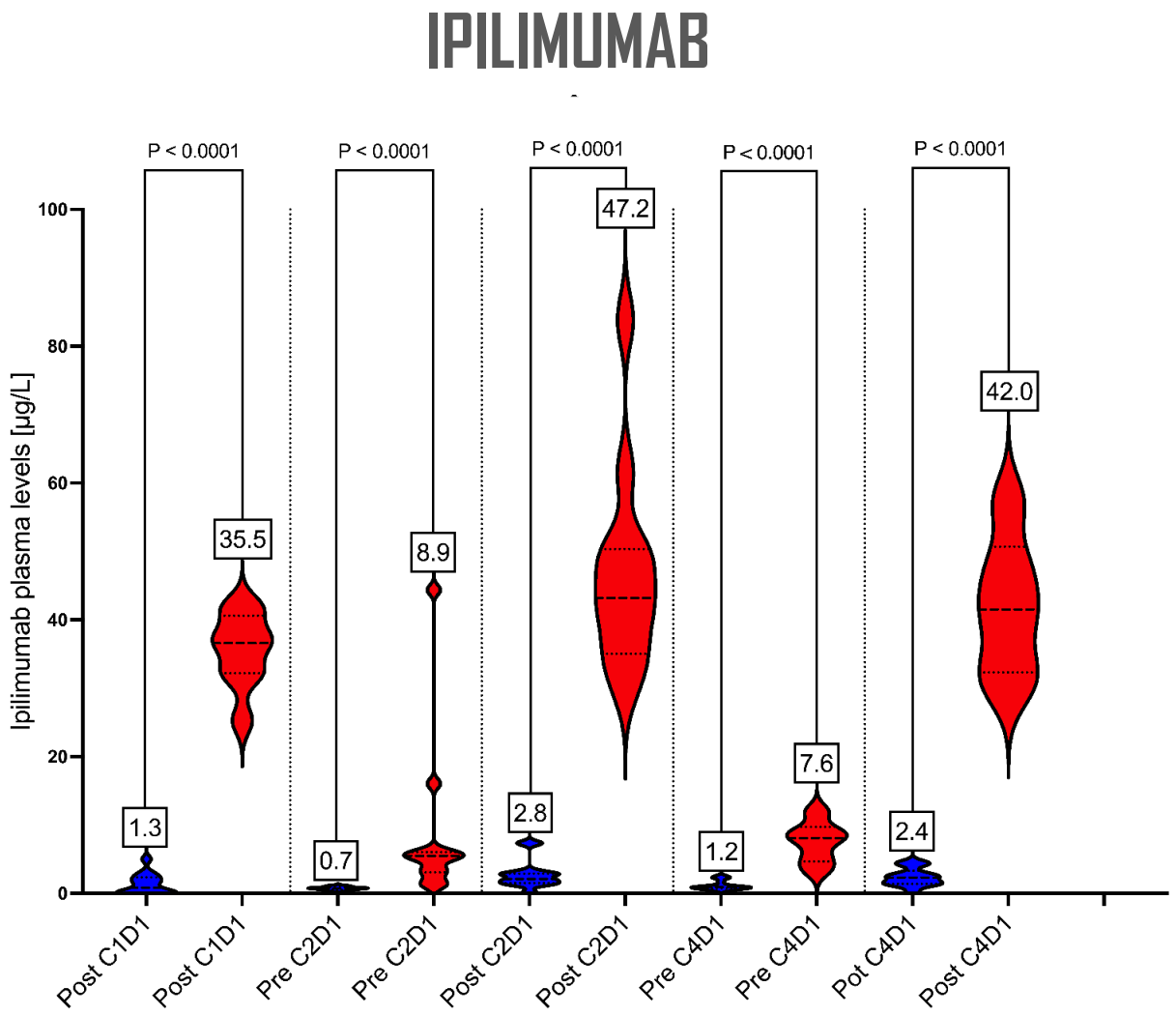




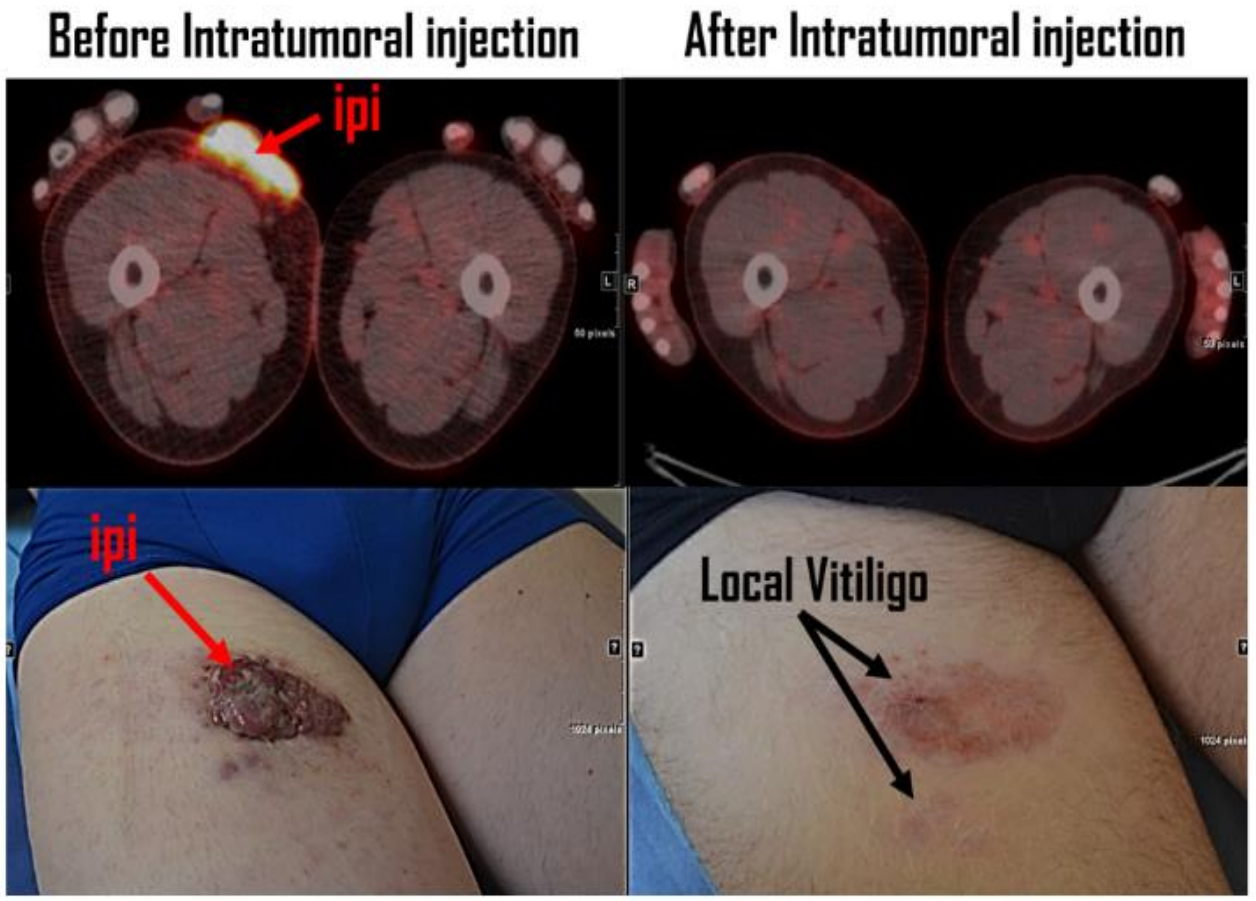
PK: Low Systemic Exposure upon Ipi IT

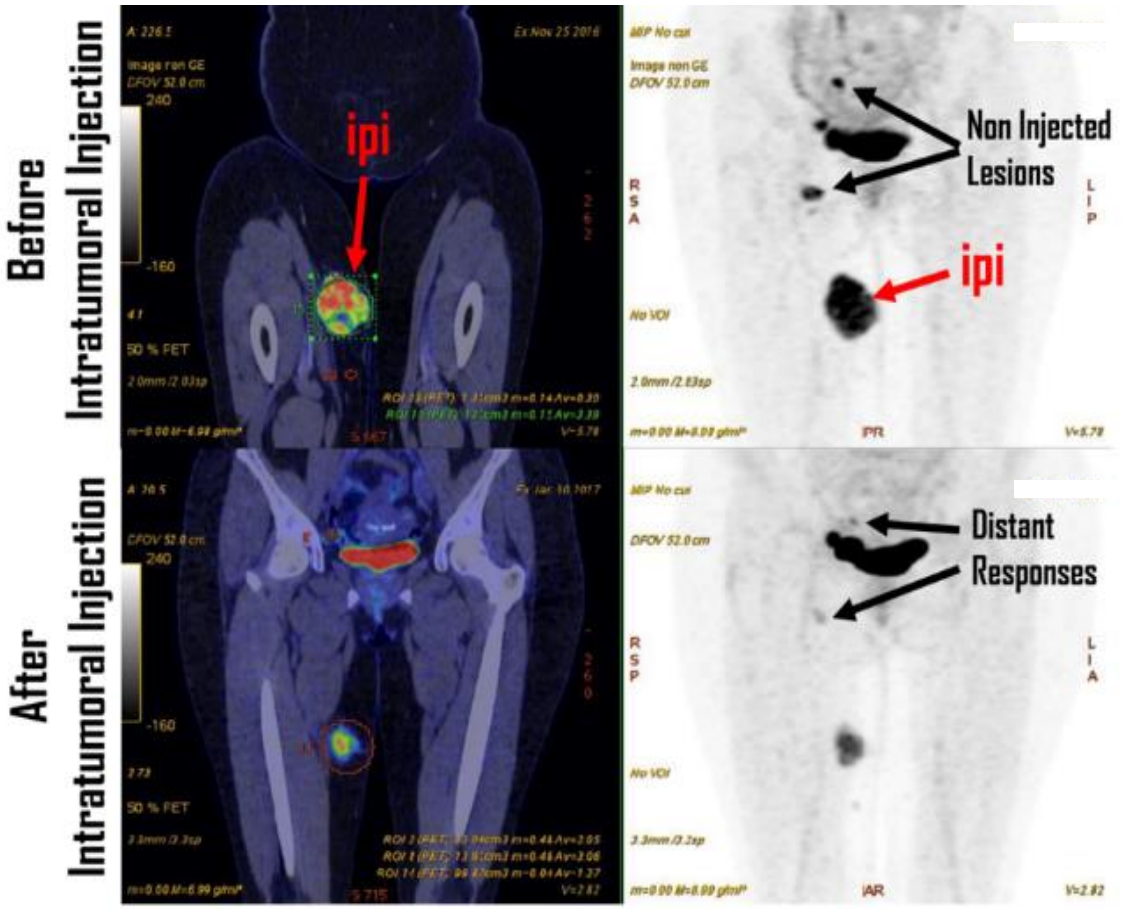
Serum PK

30x less
anti-CTLA4 exposure



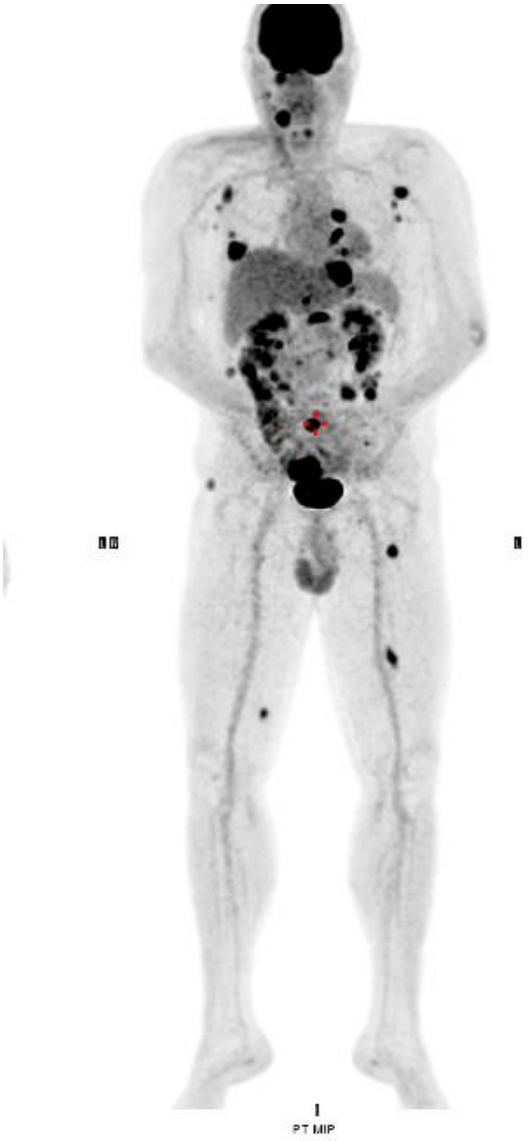
Illustrative Case #1: Skin Lesion Injected

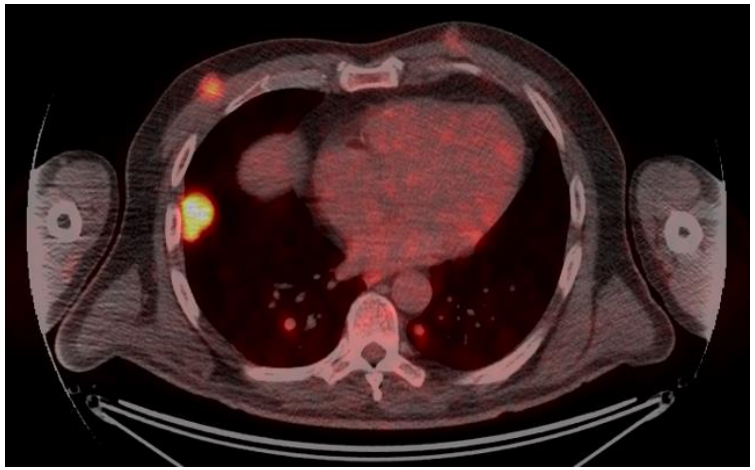


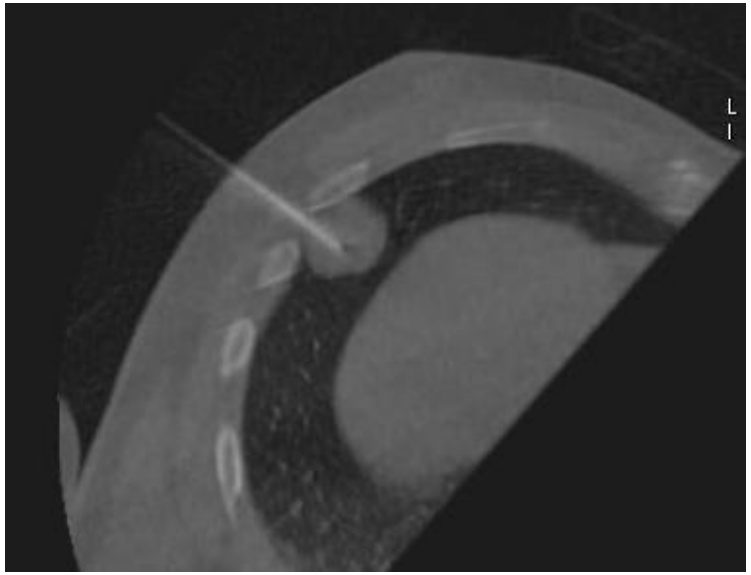


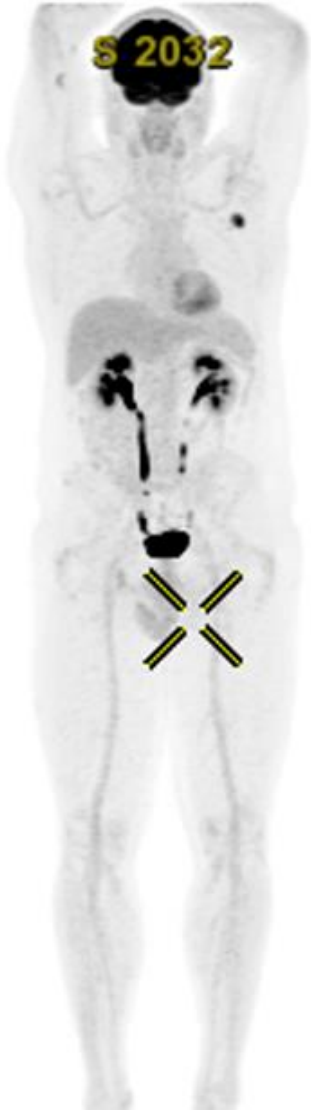
Illustrative Case #2: Lung Lesion Injected

50 y-o patient, Chest melanoma, Stage IV

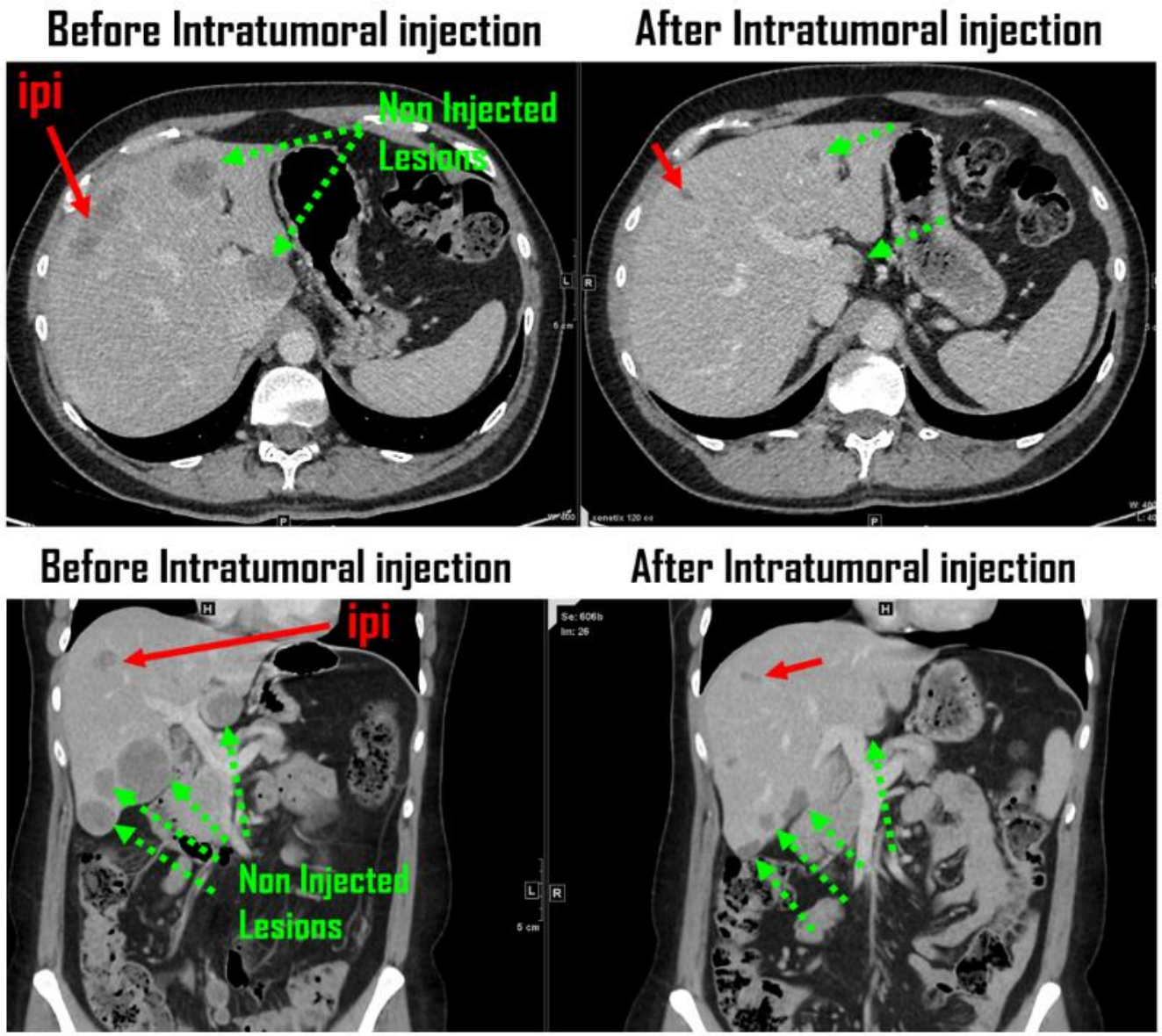




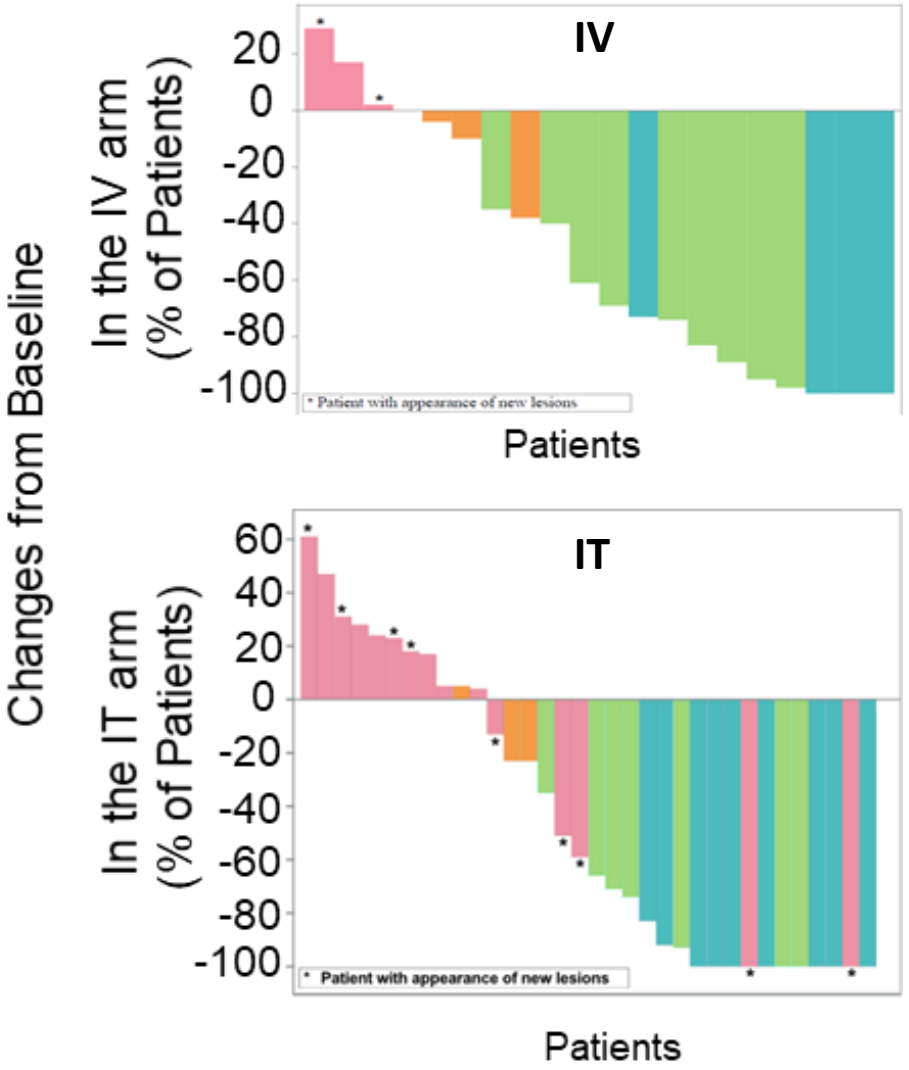




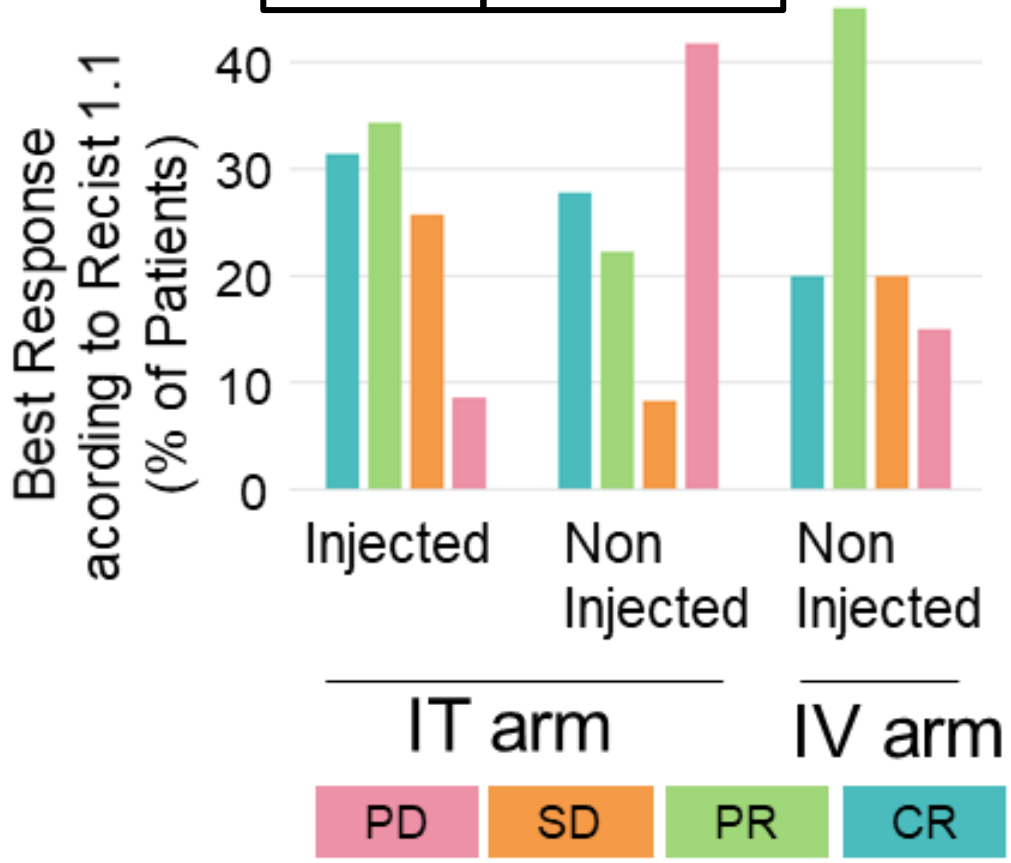
Illustrative Case #3: Liver Lesion Injected



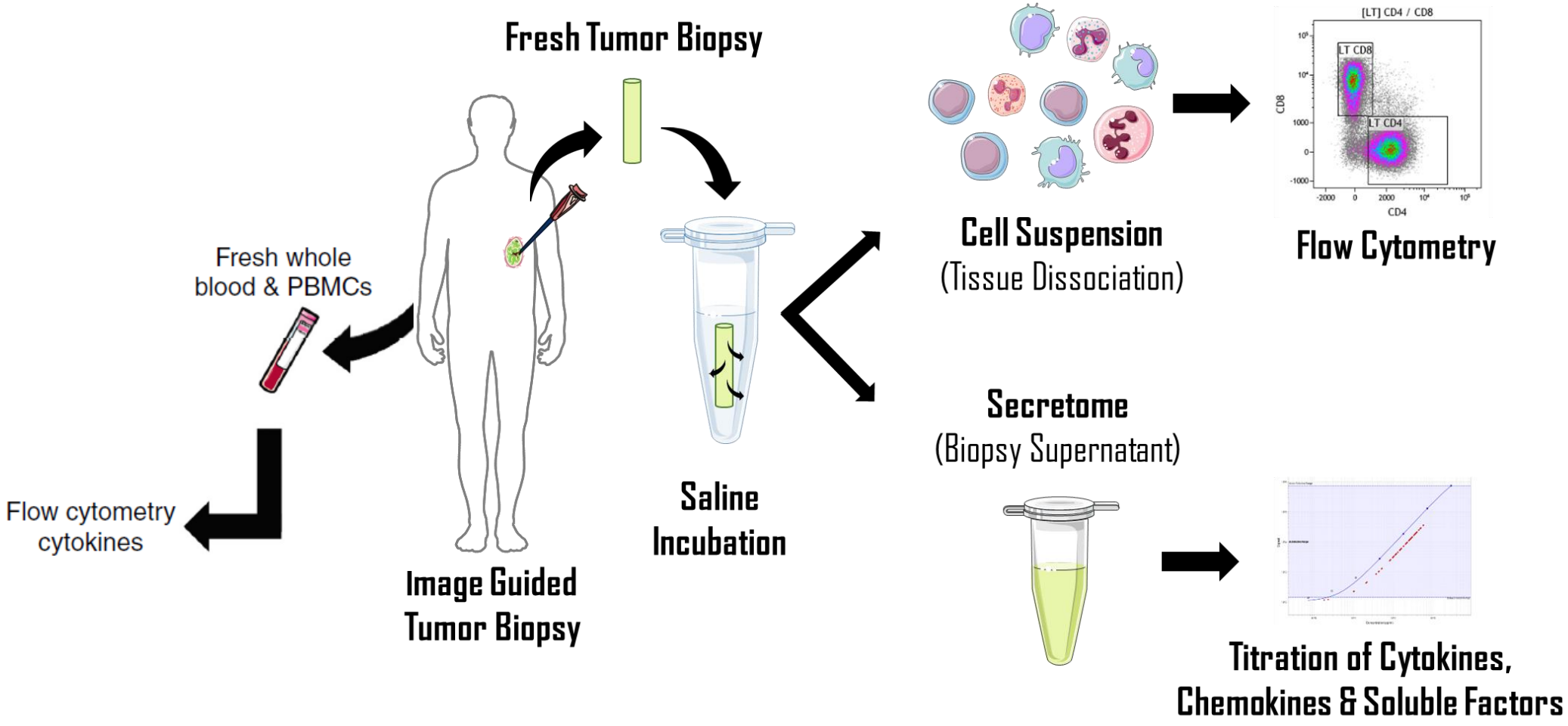
NIVIPIT : Best Overall Response (RECIST 1.1)



ORR Injected Lesions = 65.7%	ORR Non Injected Lesions = 50%	ORR IV arm = 65%



Implementation of Fresh Material Explorations in Clinical Trials

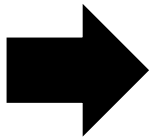


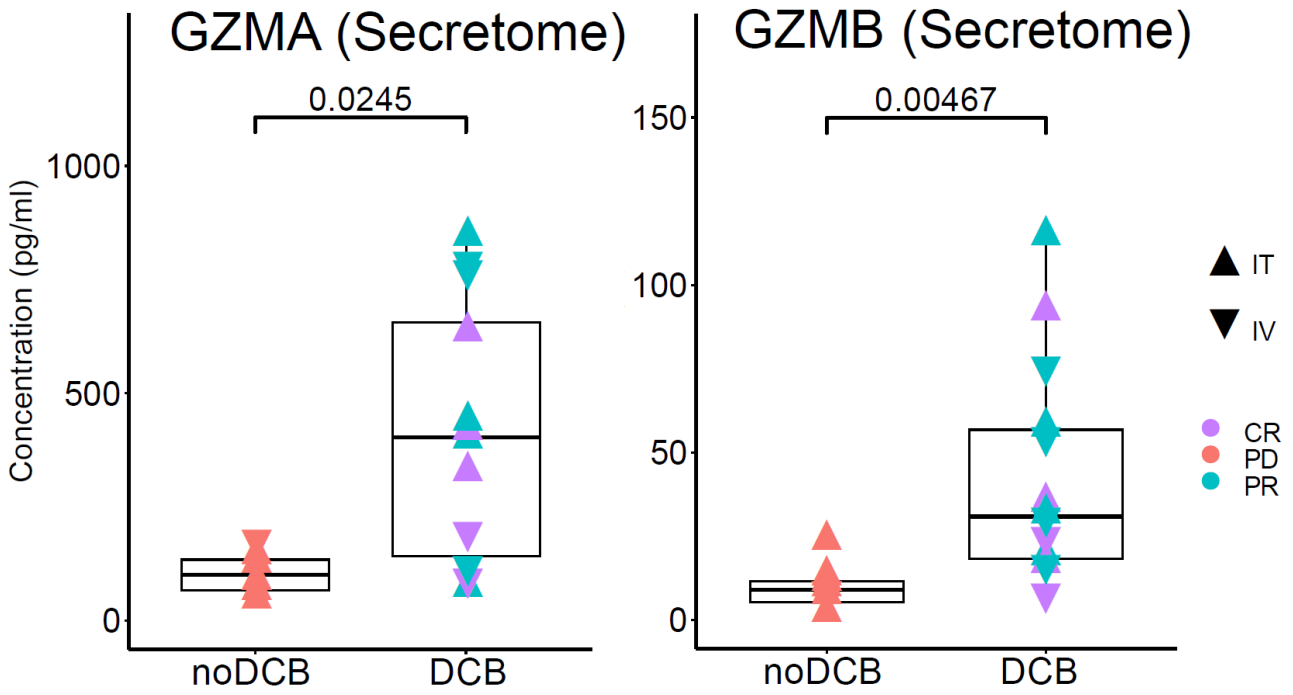
Fresh Material: Sensitive, Specific & *Same Day Data !*

Novel Predictive Biomarkers at Baseline: Gz in Secretome

Tumor

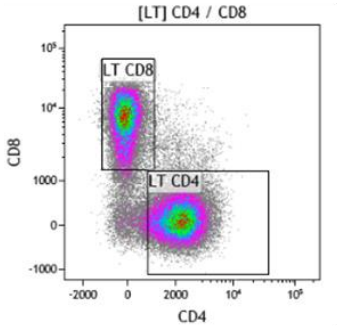
Secretome
(Biopsy Supernatant)





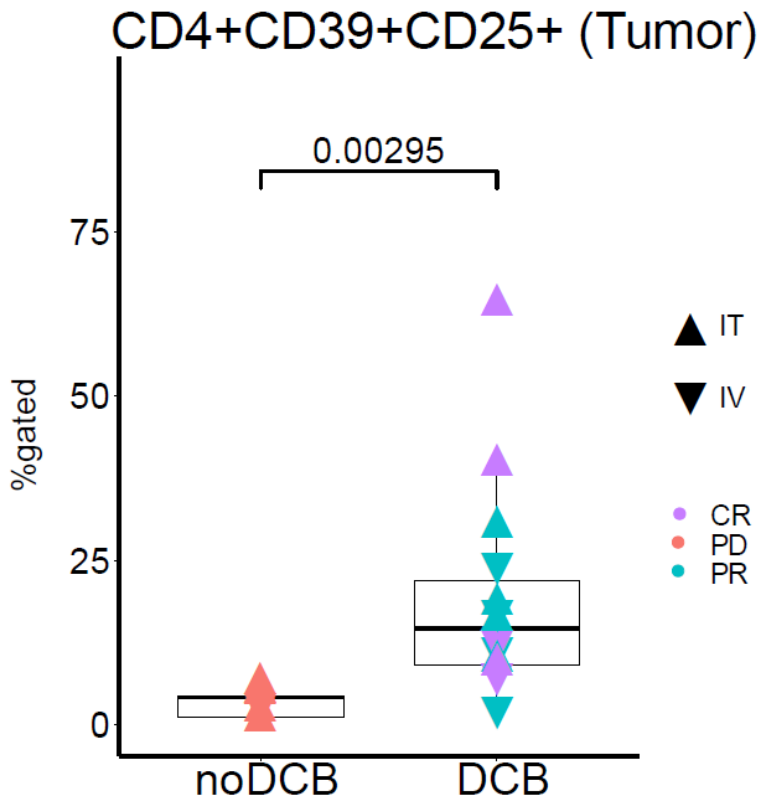
Unexpected Predictive Biomarkers at Baseline: Tregs

Tumor



Flow Cytometry

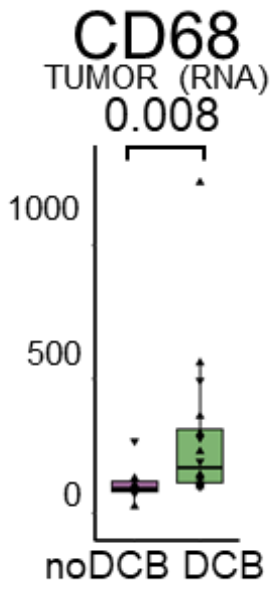
FACS

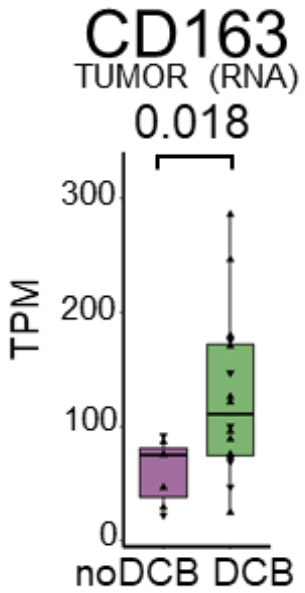


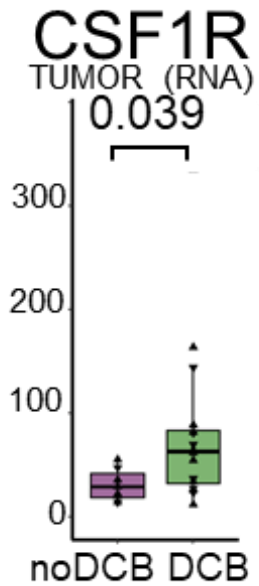
Unexpected Predictive Biomarkers at Baseline: M2 FcgR+ Macrophages

Tumor

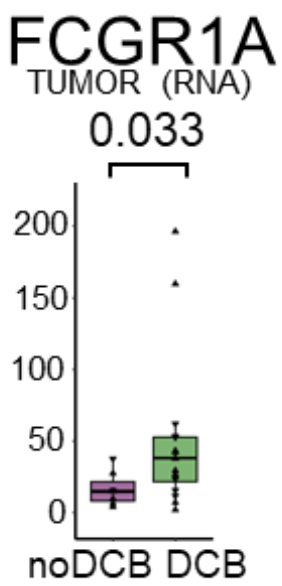
More M2 Markers RNA at Baseline in DCB

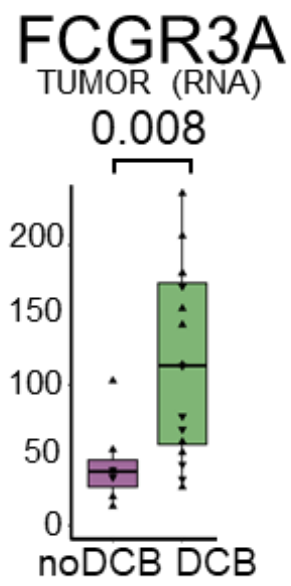


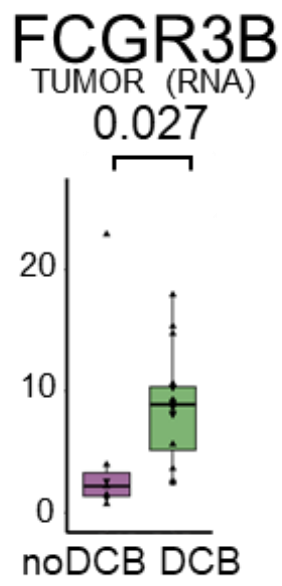




More FcgR at Baseline in DCB

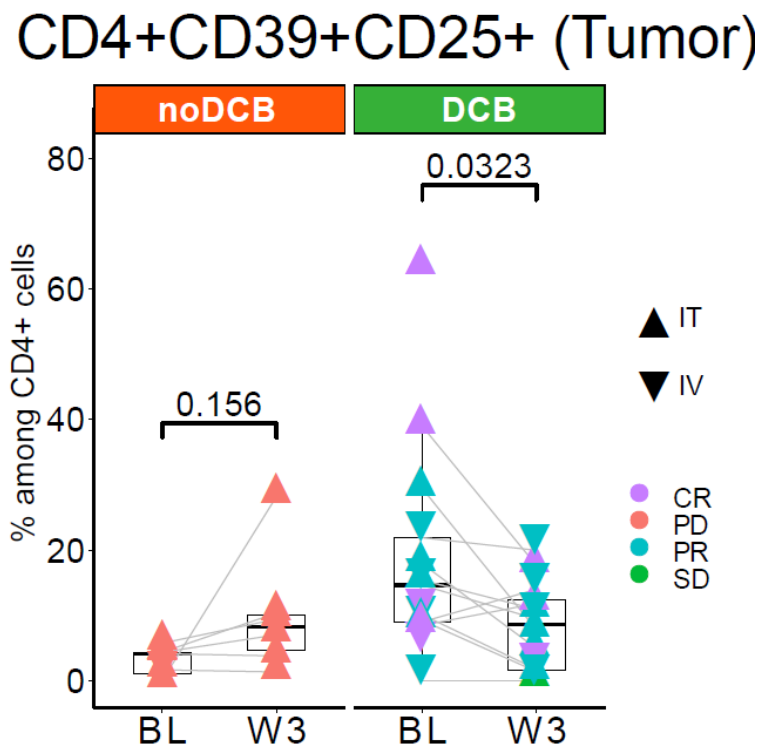




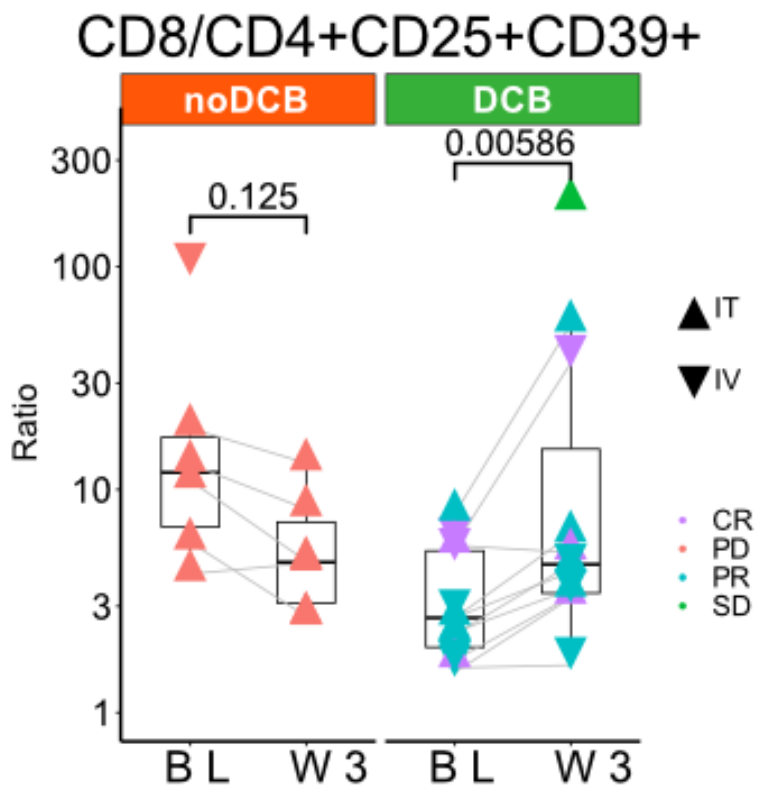


Decrease of Activated Tregs upon Treatment

Depletion of Tregs



Increased CD8+/Treg Ratio



Intratumoral anti-CTLA4

Feasible
Great Safety
Excellent local efficacy
Demonstrates added value of anti-CTLA4

Fresh Tumor Biopsy Analysis provides better predictive Biomarkers:

- **CD4+CD39+CD25+**
- **Granzyme A et B**

Proof of Mechanism:

- **Only patients with intratumoral Tregs & ongoing anti-tumor immunity respond to treatment**
- **Treg depletion upon treatment**

Direct application for patients:

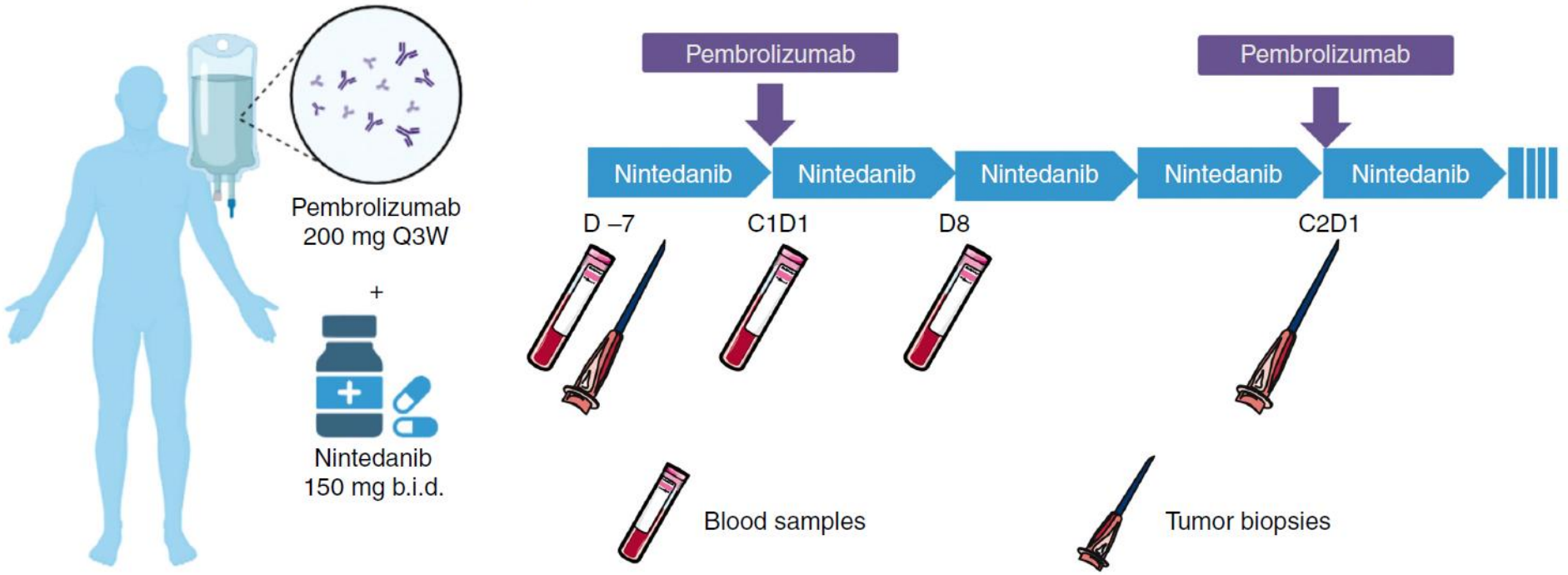
- with **oligometastatic disease** *(non eligible for IV combo)*
- With localized disease in the **neo-adjuvant** setting

Direct implication for science:

- Anti-PD1 + Anti-CTLA4 efficacy requires an **ongoing intratumoral immuno-editing** process

Pembrolizumab + Nintedanib (PEMBIB) Trial (NCT02856425)

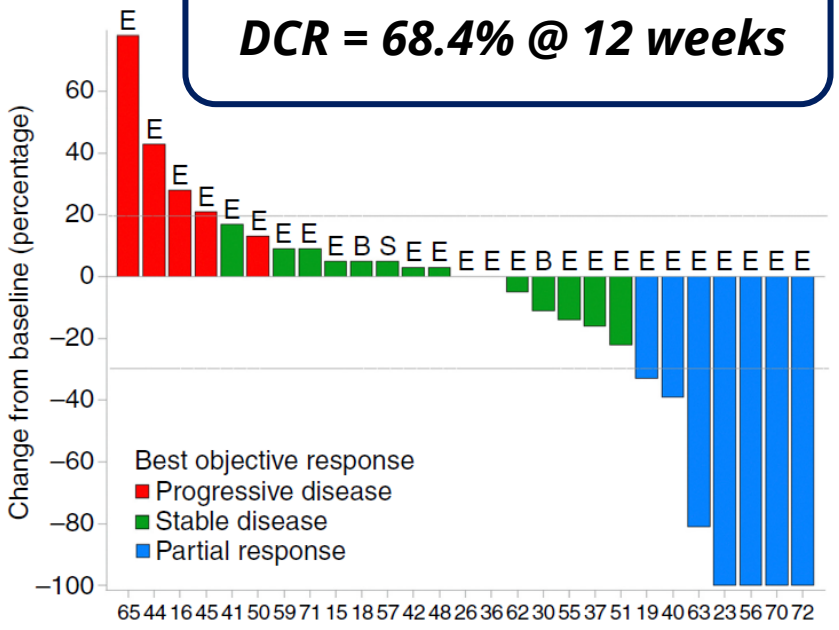
- Multi-Center Multi-Arm Phase 1b Basket trial
- Mesothelioma cohort = 30 patients



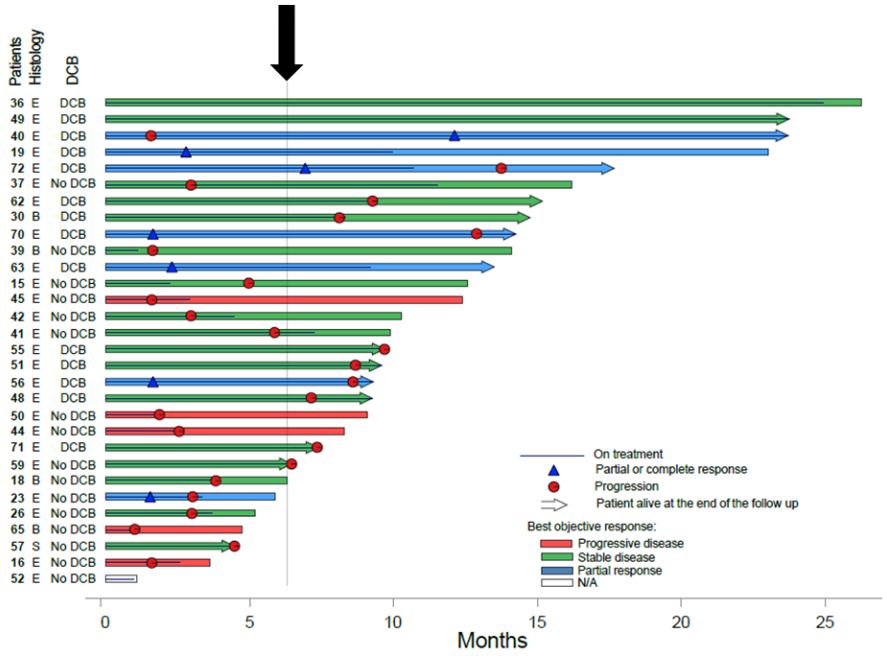
Danlos, F.-X., et al. (2023). Genomic Instability and Protumoral Inflammation Are Associated with Primary Resistance to Anti-PD-1 + Antiangiogenesis in Malignant Pleural Mesothelioma. Cancer Discov. 13, 858–879.

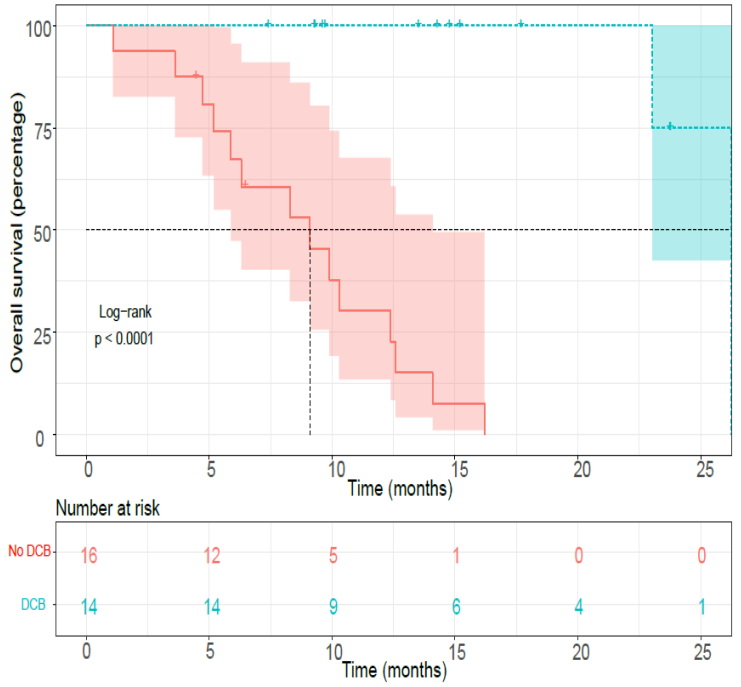
PEMBIB Efficacy (RECIST1.1)

BORR = 24%
DCR = 68.4% @ 12 weeks



DCB = Durable Clinical Benefit
(CR, PR & SD @ 6 months)

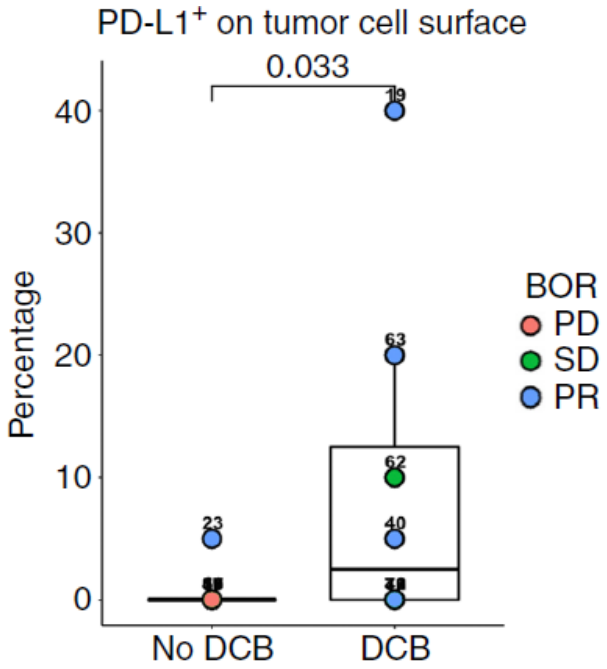




Danlos, F.-X., et al. (2023). Genomic Instability and Protumoral Inflammation Are Associated with Primary Resistance to Anti-PD-1 + Antiangiogenesis in Malignant Pleural Mesothelioma. Cancer Discov. 13, 858–879.

PD-L1 IHC on FFPE vs CD8+ T-cells by FACS on Fresh Tumors in Mesothelioma with DCB at Baseline

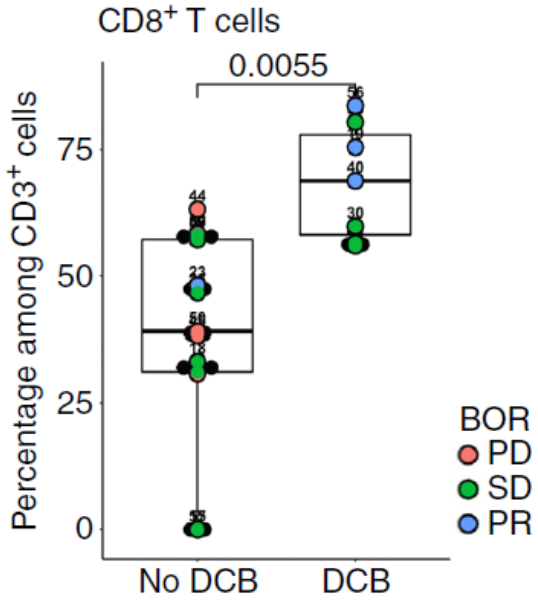
FFPE Baseline Tumor Biopsies



IHC (sp263)

➔ Turn around time = **Days / Weeks**

Fresh Baseline Tumor Biopsies



Flow Cytometry

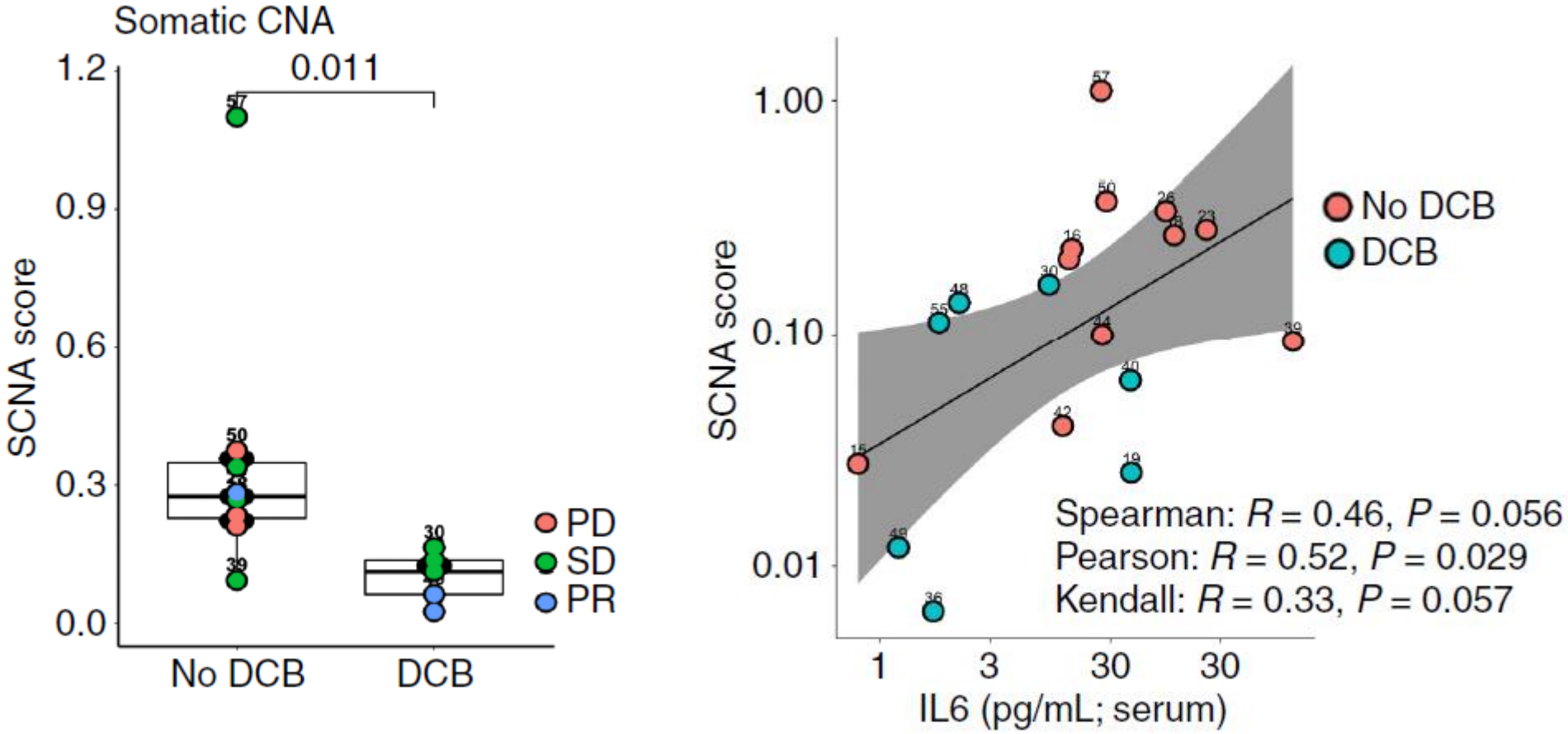
➔ Turn around time = **Hours**

Danlos, F.-X., et al. (2023). Cancer Discov. 13, 858–879.

Genomic Instability leads to Pro-Tumoral Inflammation

WES Baseline Tumor Biopsies

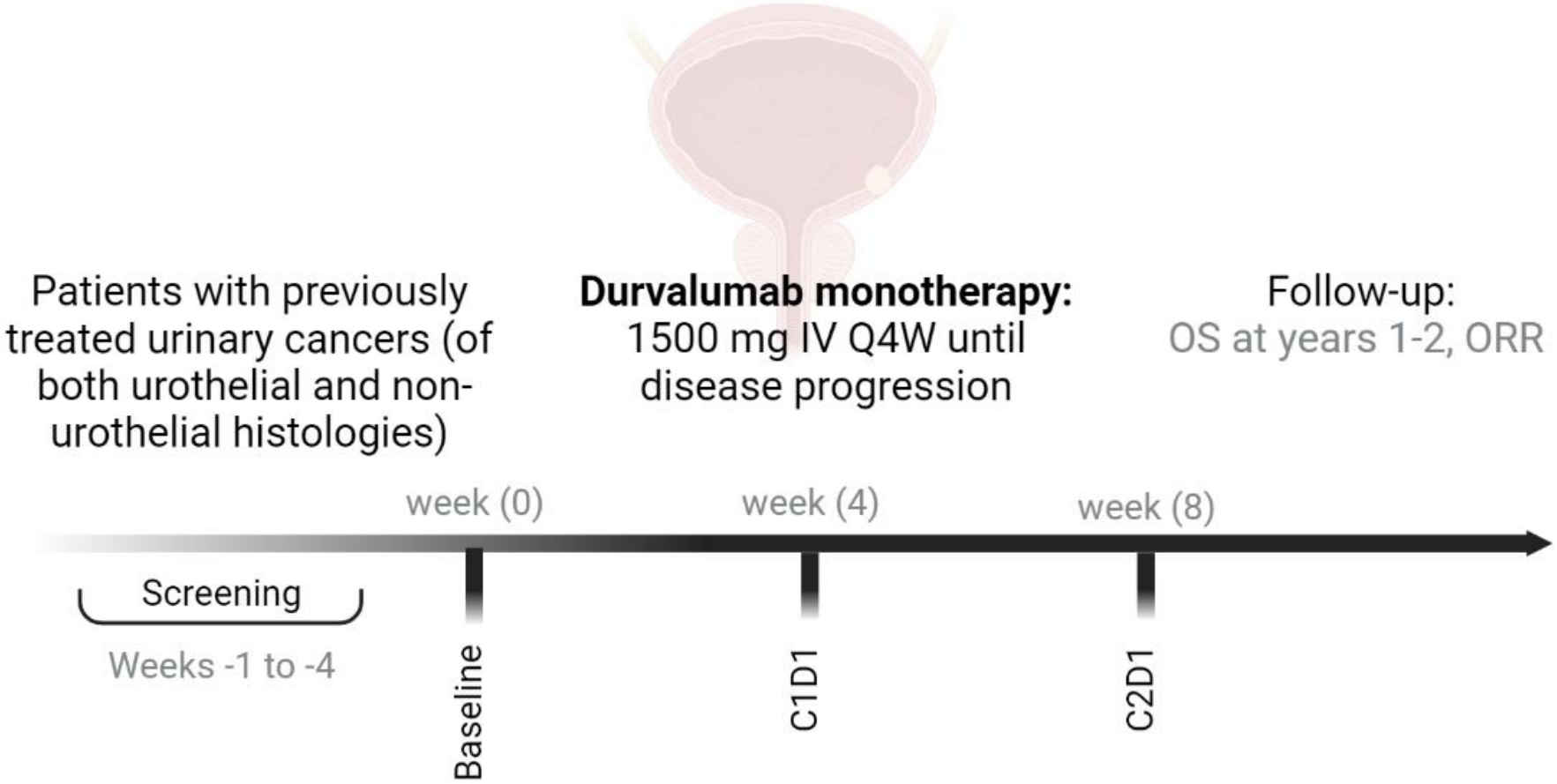
Blood Plasma



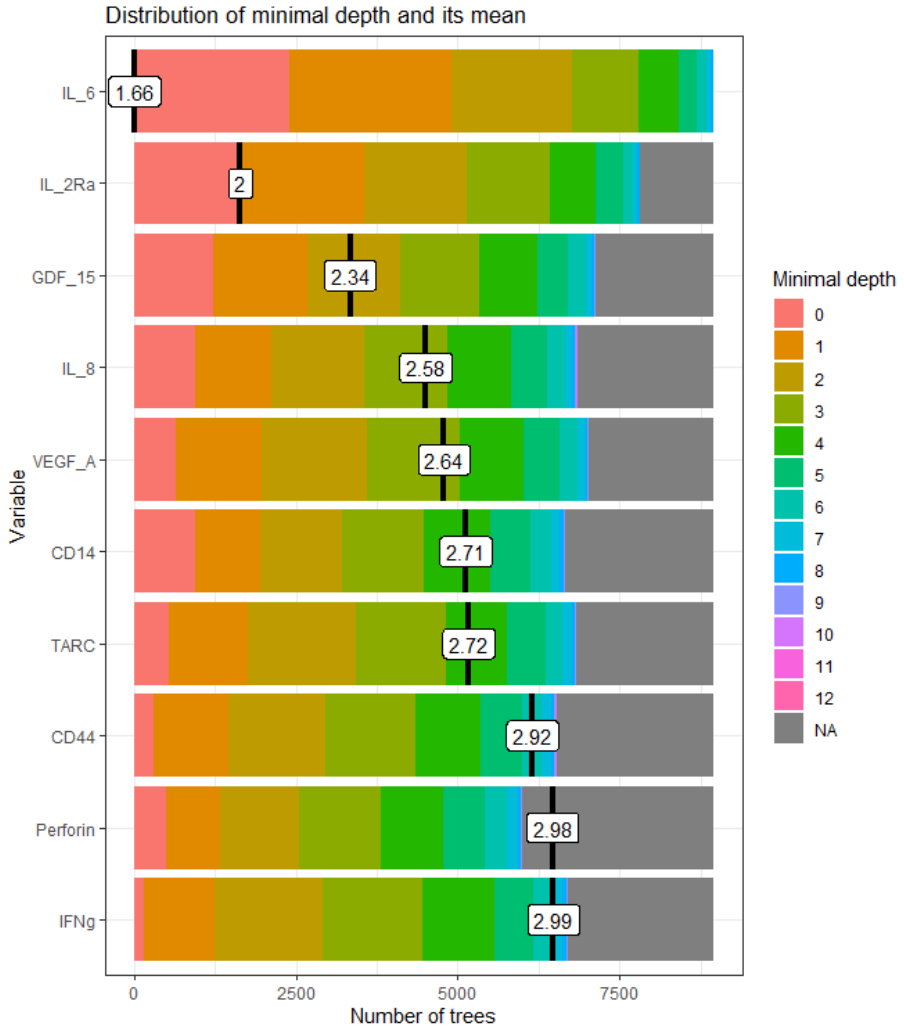
➔ *Plasma can inform on the Tumor Biology*

Danlos, F.-X., et al. (2023). Cancer Discov. 13, 858–879.

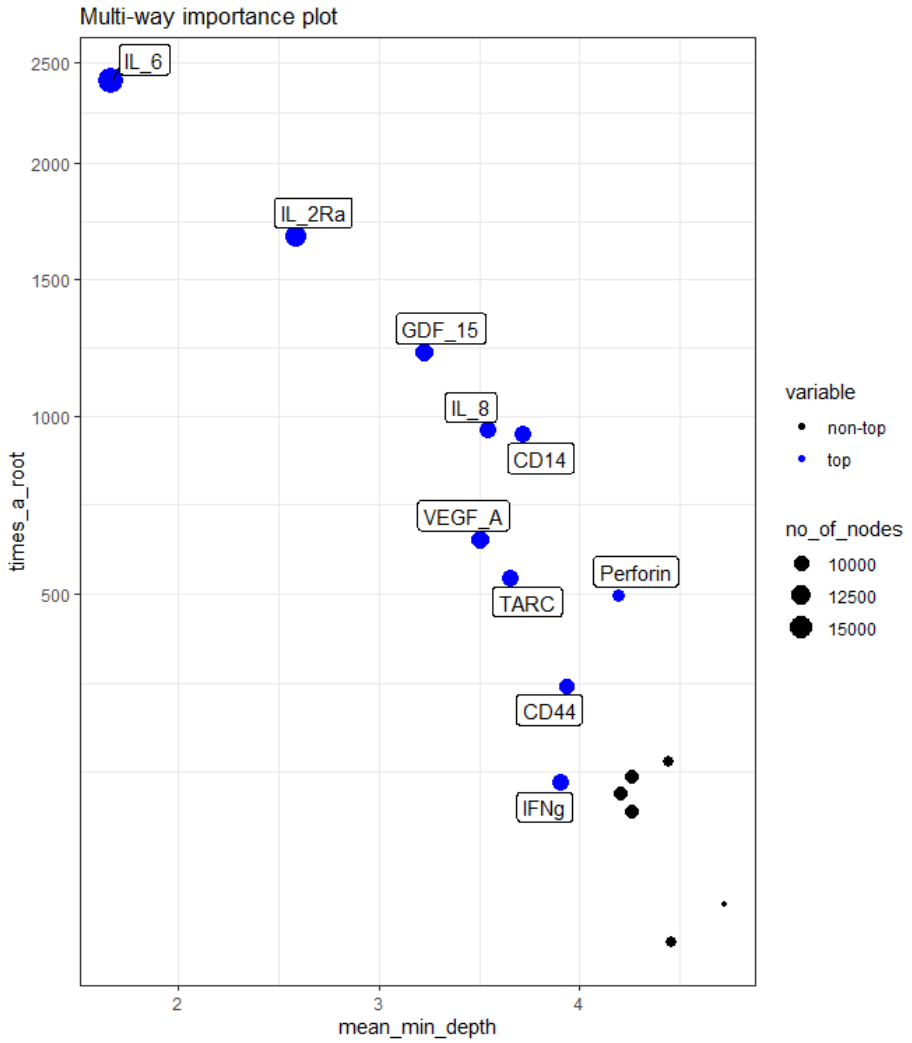
STRONG/IOPREDI Trial



Baseline Plasma Factors Associated with Resistance

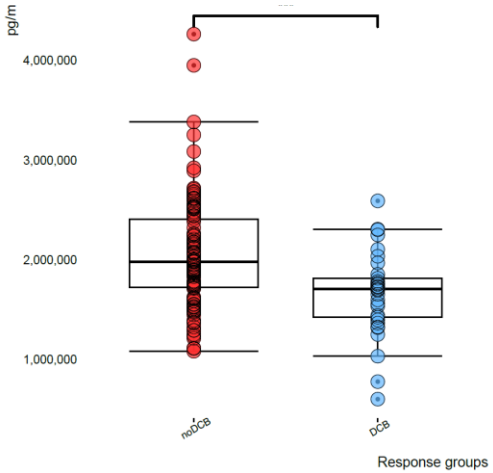


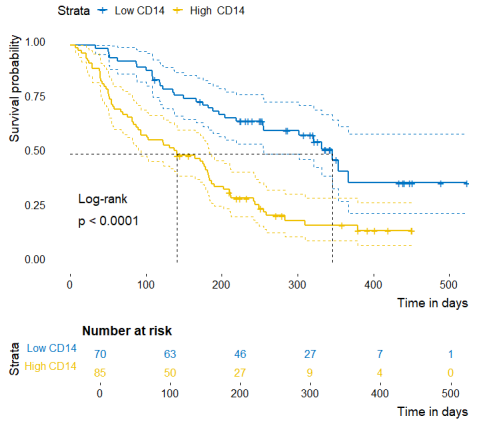
- N(discovery)=36
- N(Validation)=120
- N(pooled)=156

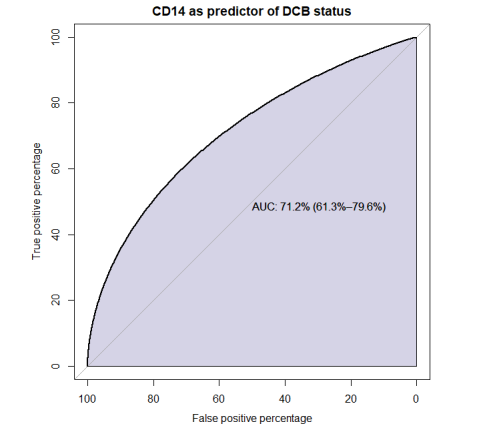


Al Shatti et al. Unpublished Data.

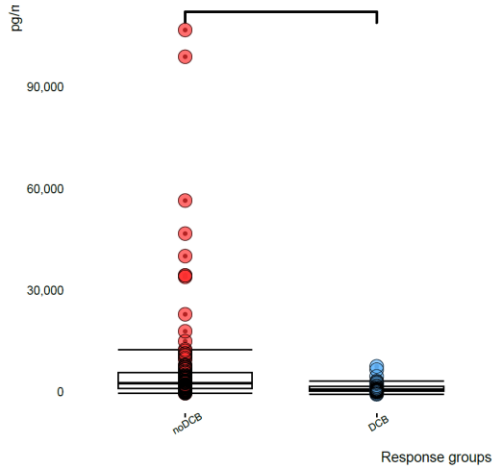
sCD14

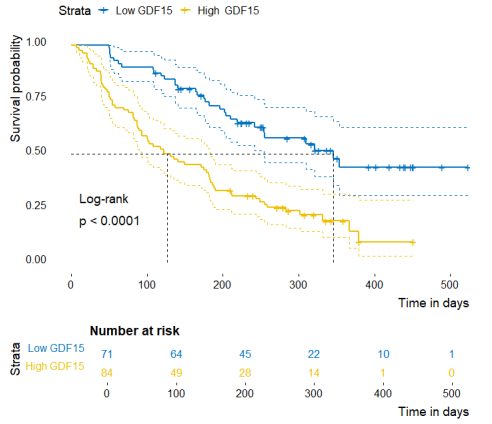


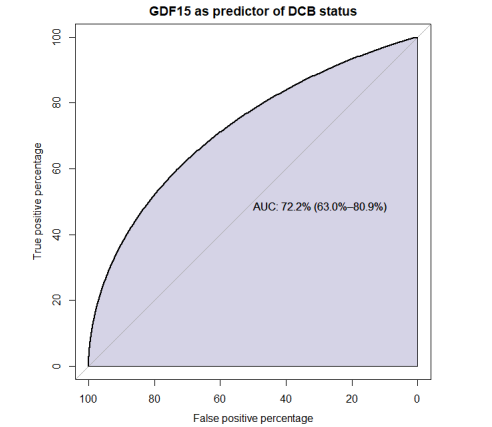




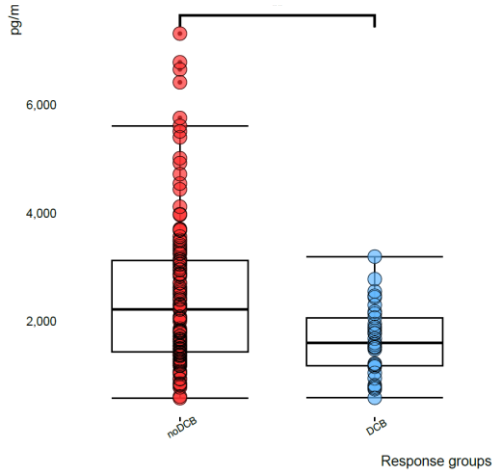
GDF15

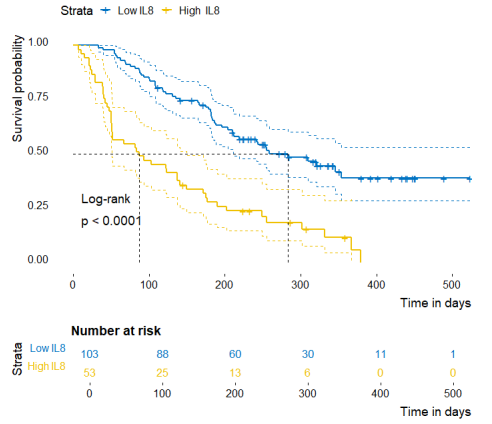


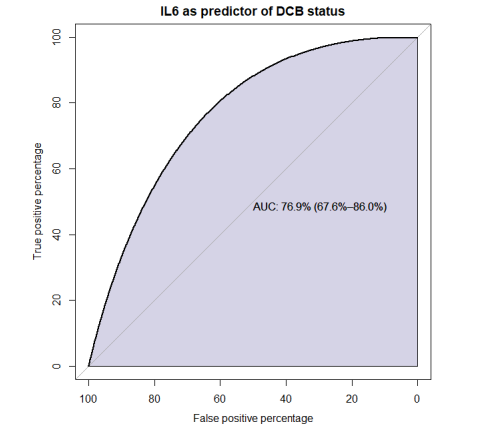




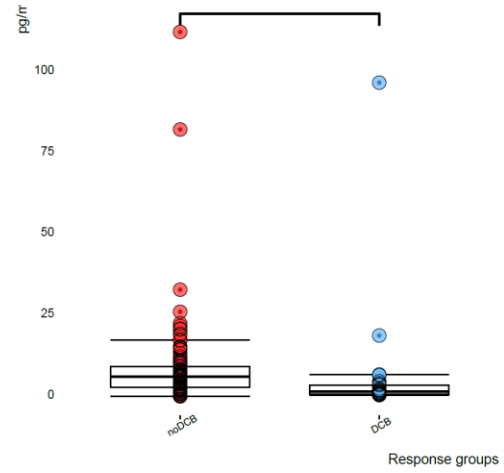
sCD25

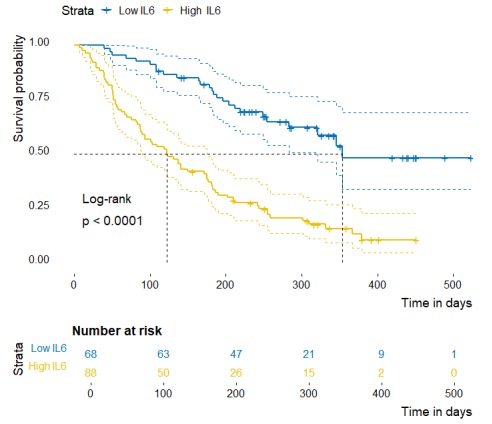


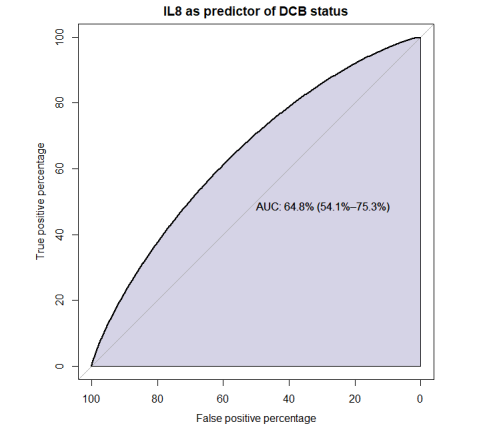




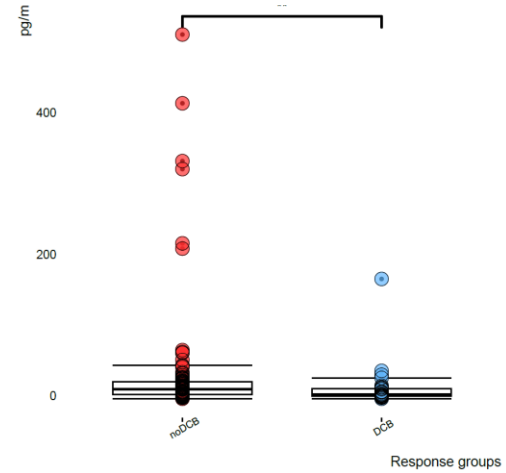
IL6

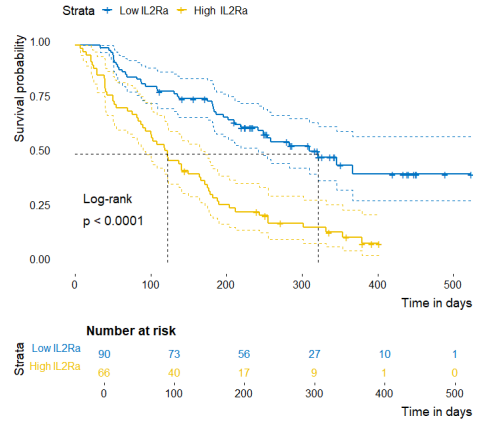


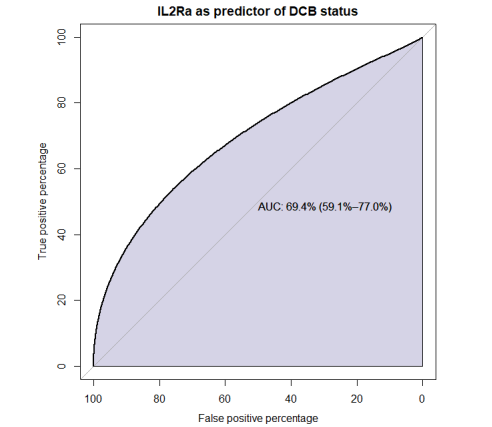




IL8

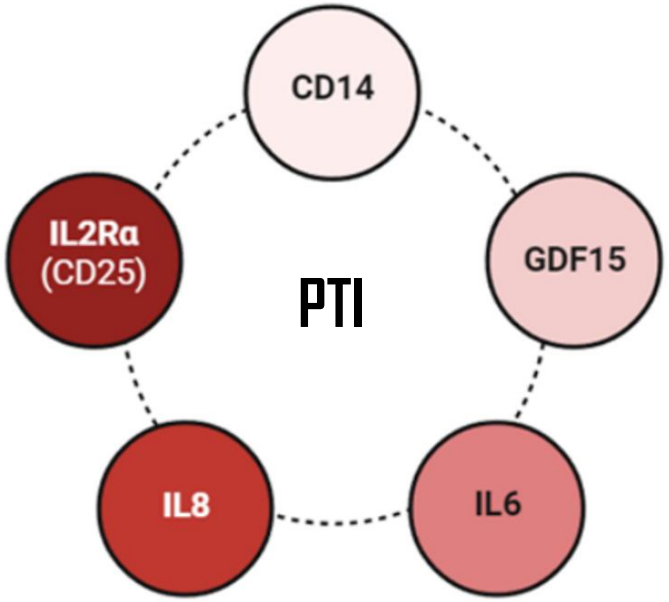






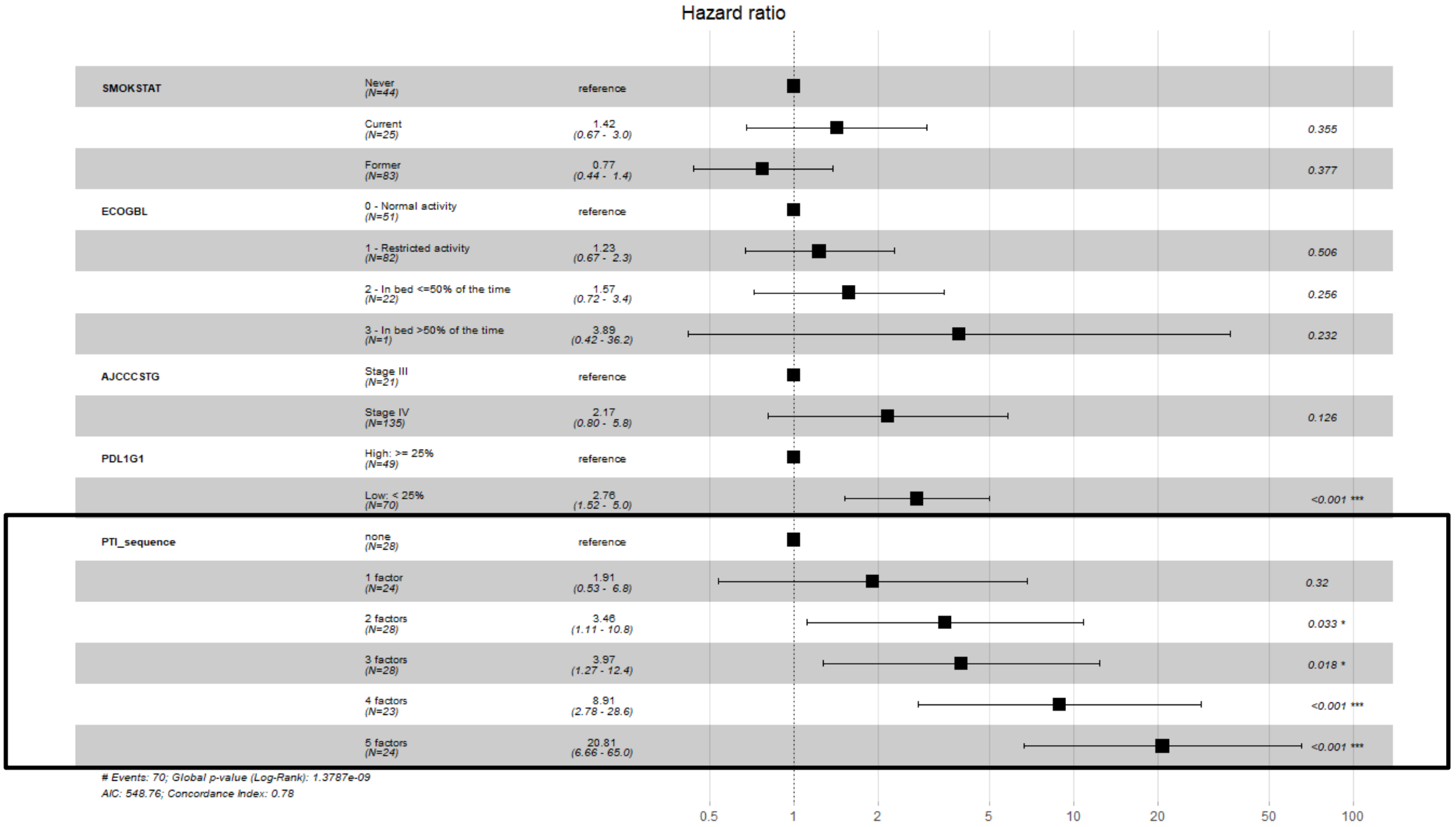
Pro-Tumoral Inflammation (PTI) Score

Paving the Way for Patient Stratification

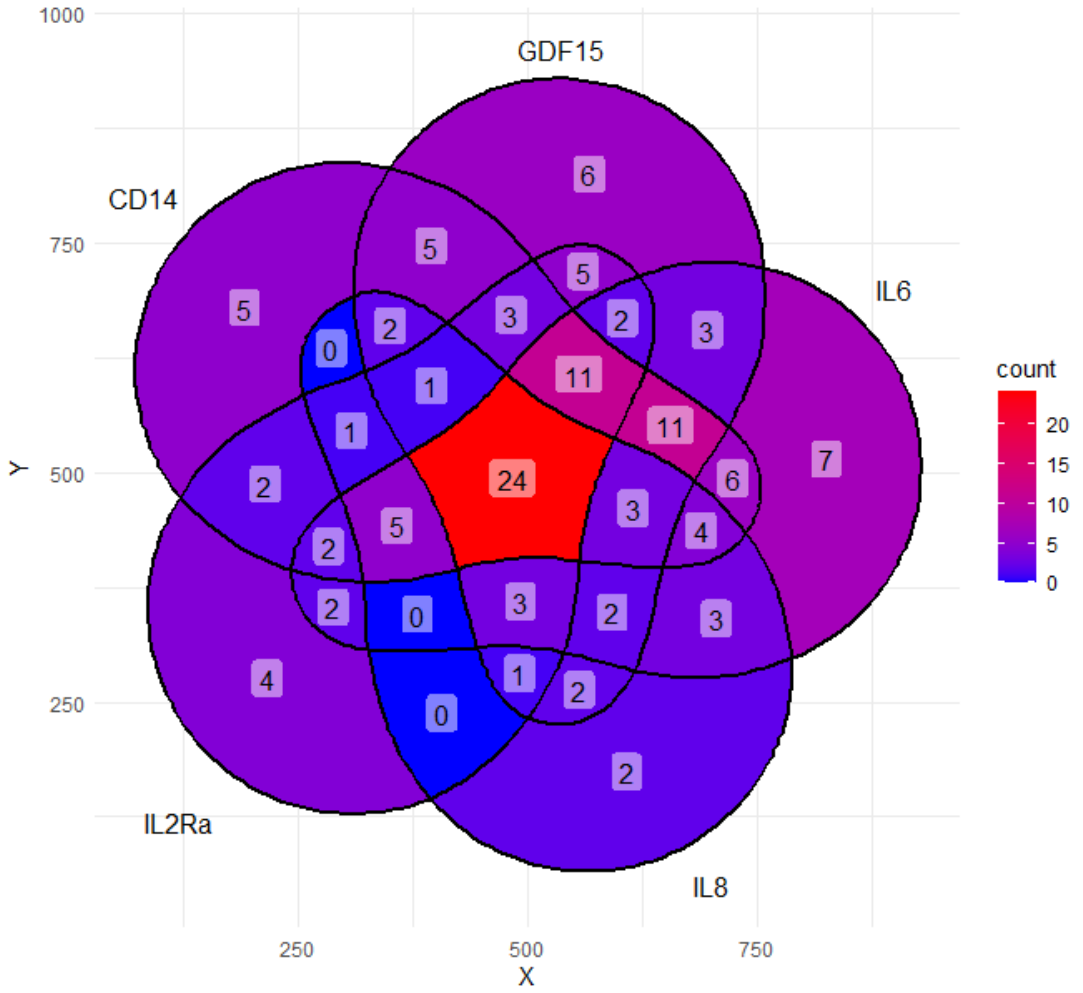


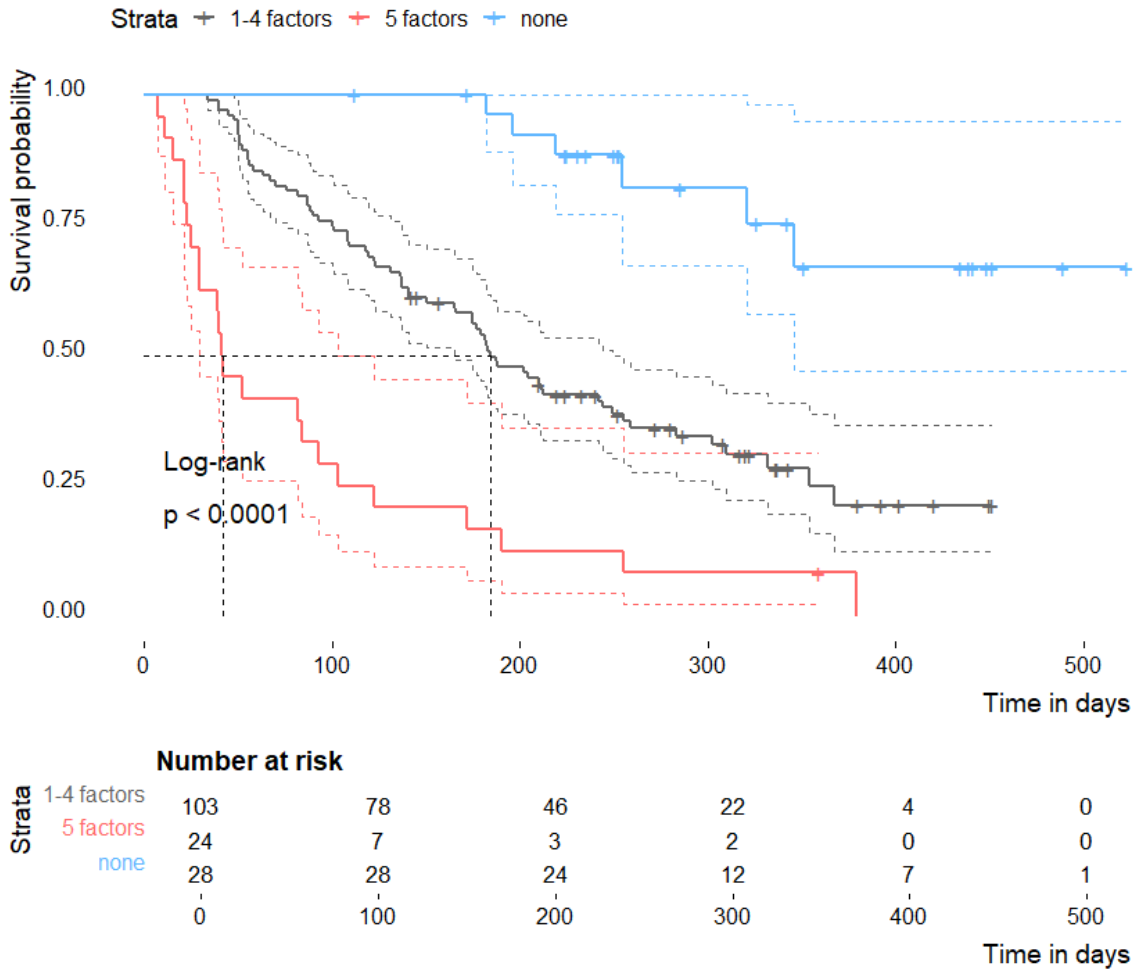
Al Shatti et al. Unpublished Data.

Pro-Tumoral Inflammation (PTI) Score



Pro-Tumoral Inflammation (PTI) Score

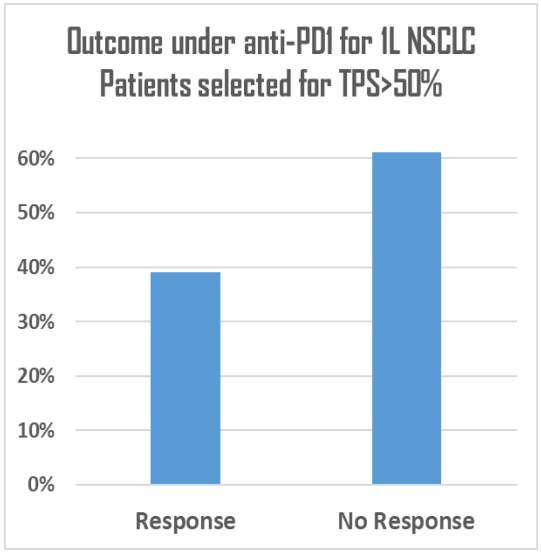




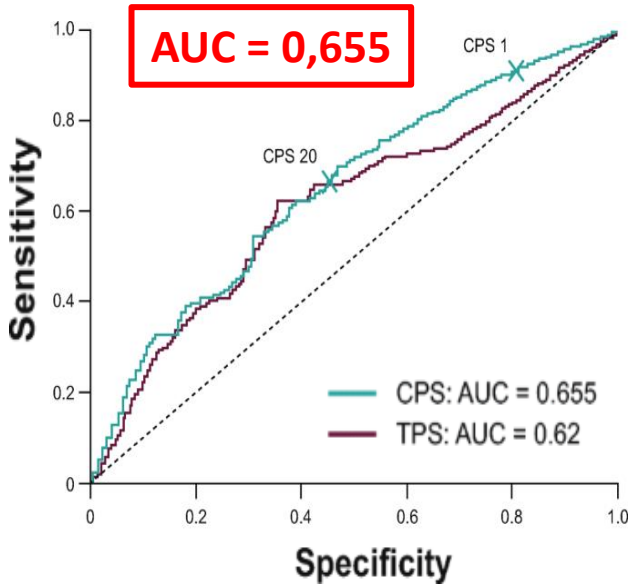
Al Shatti et al. Unpublished Data.

What if Soluble Biomarkers Become Better ?

PD-L1 IHC

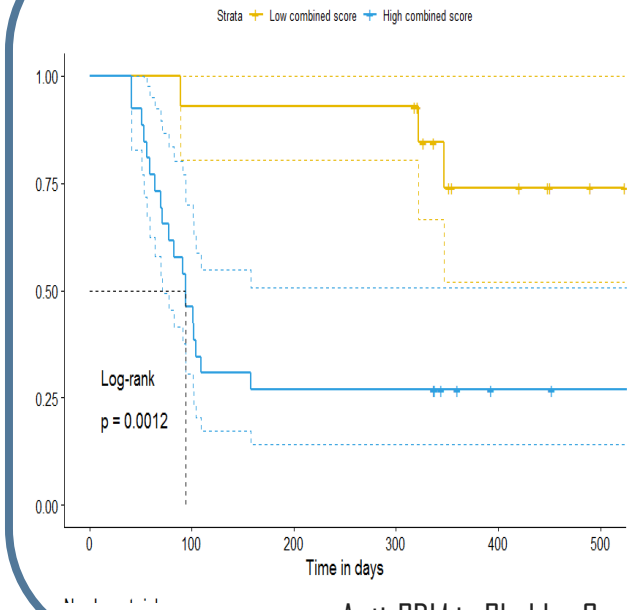


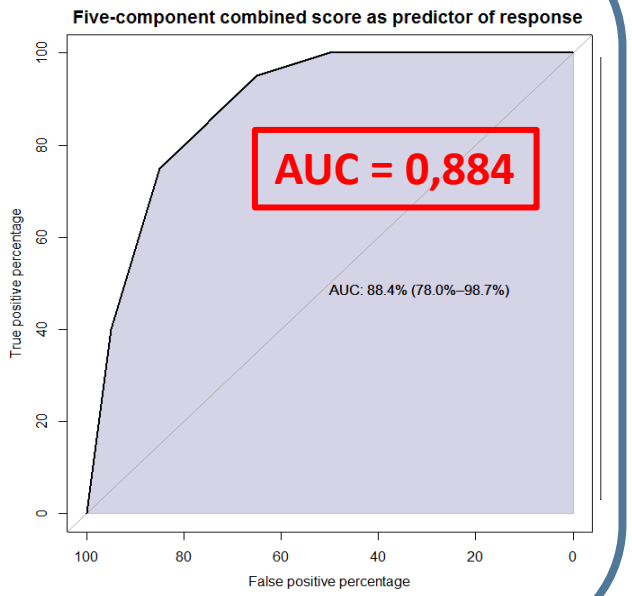
Lancet. 2019 May 4;393(10183):1819-1830.



AAPS J. 2020 Nov 22;23(1):5.

PTI Score

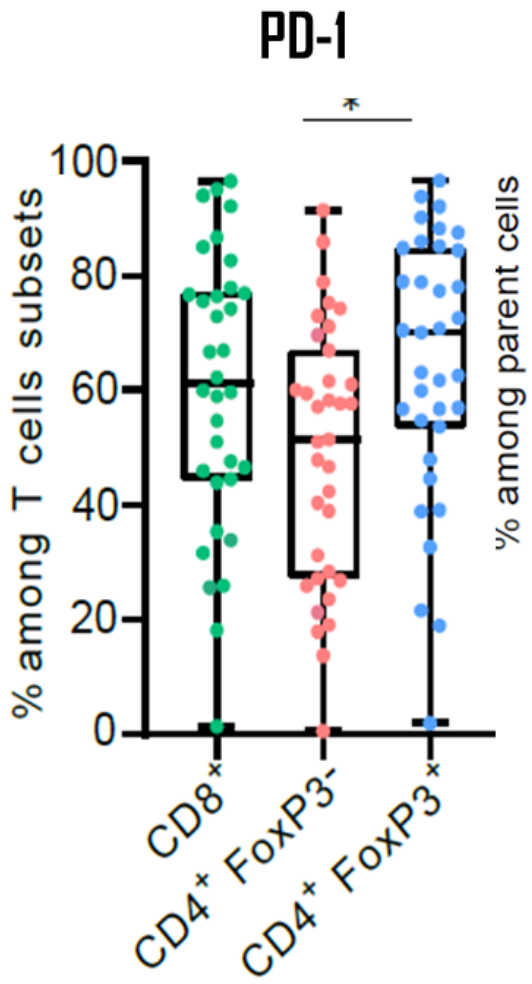




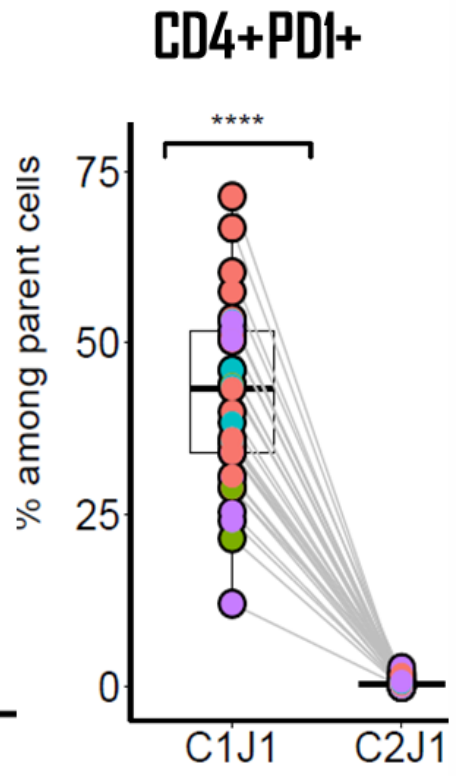
Anti-PDL1 in Bladder Cancers – Unpublished Data

Fresh Material Provides Answers to Critical Drug Development Questions

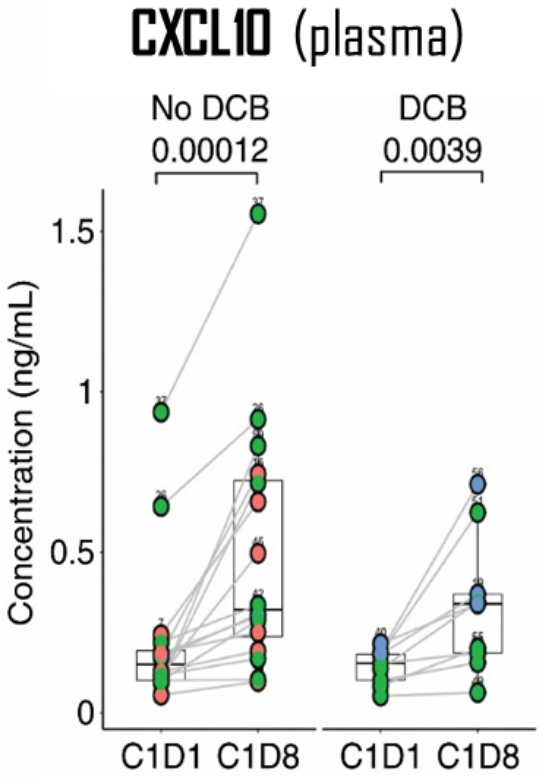
TARGET EXPRESSION



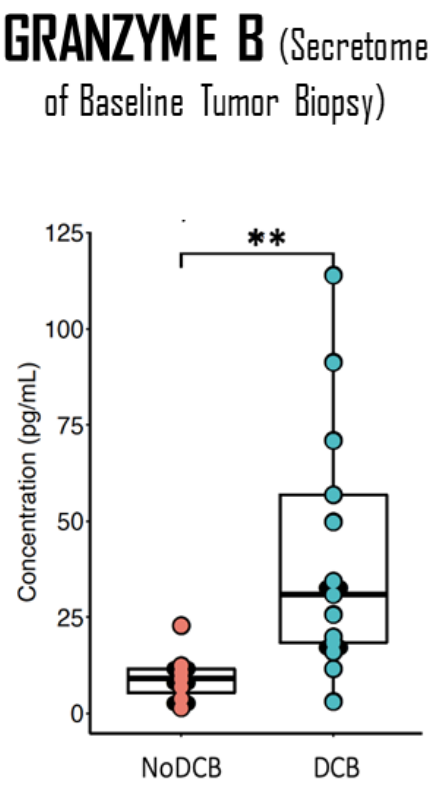
TARGET SATURATION



TARGET ENGAGEMENT



PREDICTIVE BIOMARKERS



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Société Française d'Immuno-Thérapie du Cancer

REMISSION

Rapid Evaluation of Molecular & Immune Status for Stratified Immunotherapies in ONcology

Recherche Hospitalo-Universitaire en santé (RHU) 2023

Pr Aurélien Marabelle

Soutenu par GOUVERNEMENT Liberté Égalité Fraternité

FRANCE 2030

unicancer

veracyte

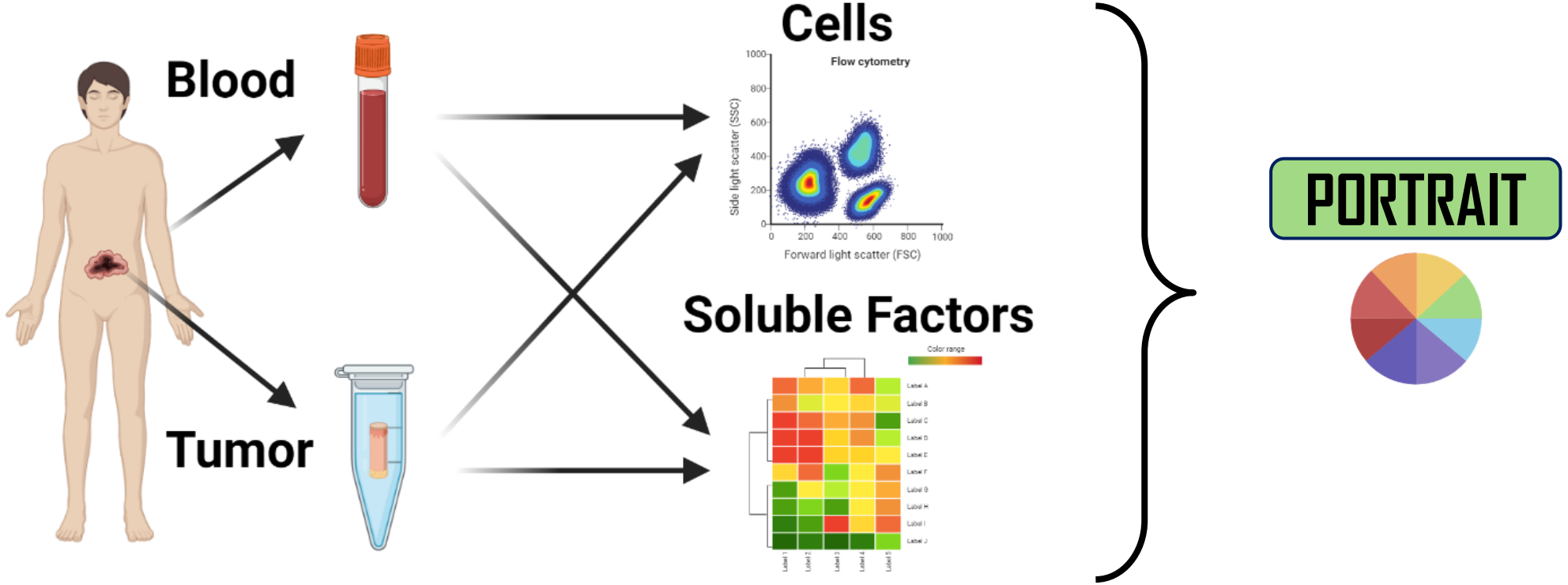
HiFiBiO THERAPEUTICS

ImCheck therapeutics

PegaOne

PORTRAIT Pre-Screening Study :

Profile in **O**nco-immunology for a **R**apid **T**reatment **R**esearch **A**dapted to your **I**mmunity and your **T**umor

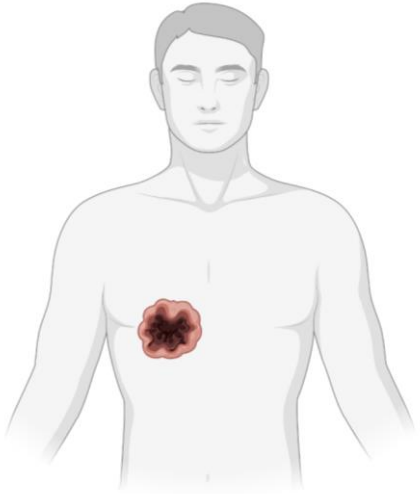


Work with Fresh Material: ***Turn around time within Days***

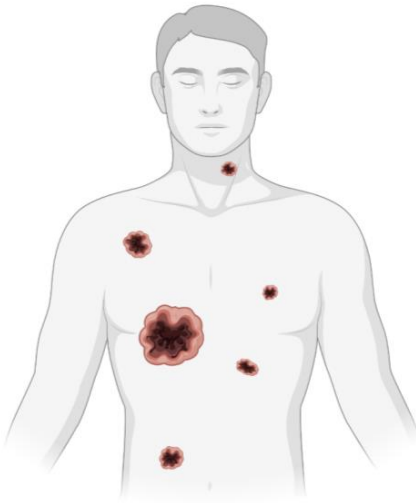
Overnight Shipping in One Central Lab: ***Robust Biomarkers***

Cancer Patient Oriented in Dedicated Cohorts according to their Immune PORTRAIT

Localized Cancer



Metastatic Cancer



PORTRAIT

TARGET EXPRESSION

Treatment Orientation

NEOREM

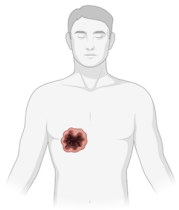
Master Protocol

METAREM

Master Protocol

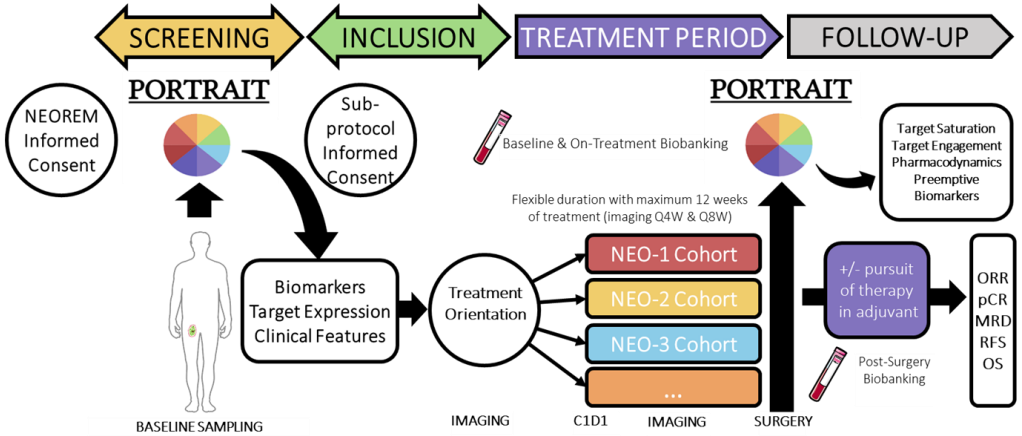
REMISSION

Localized Cancer

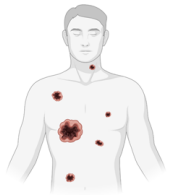


NEOREM

Master Protocol

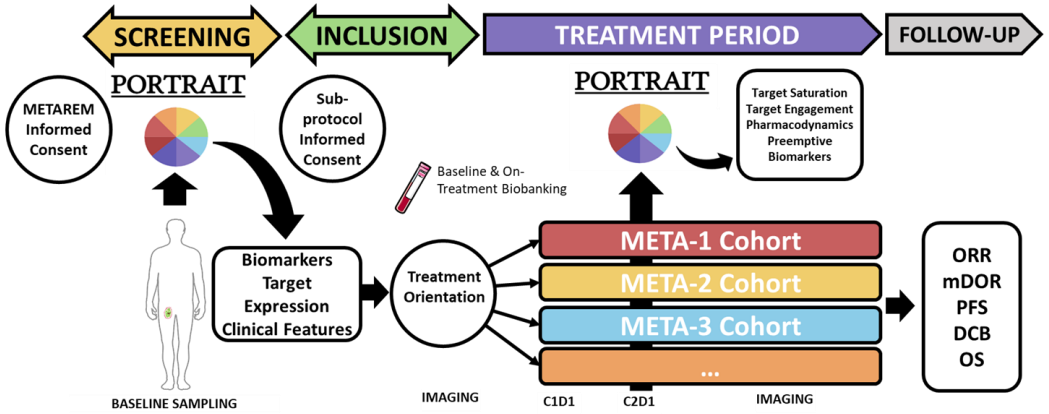


Metastatic Cancer



METAREM

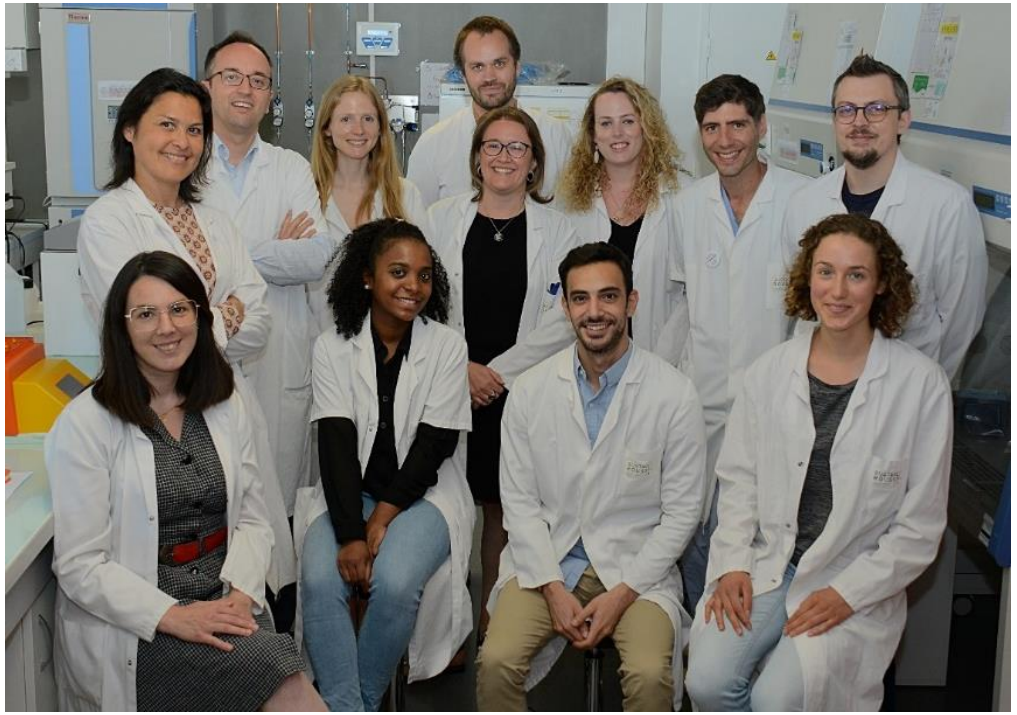
Master Protocol



- > Multi-Center, Nationwide
- > Academic Sponsor unicancer RECHERCHE
- > Phase 2 Master Protocols
- > Cohorts of 50 patients
- > Simon 2 stage Design
- > Including Conventional Biobanking

Laboratoire de Recherche Translationnelle en Immunothérapie

CIC BIOTHERIS: Biotherapies for Anti-Tumor *In Situ* Immunization



Devenez Membres de la FITC !

www.fitcancer.fr