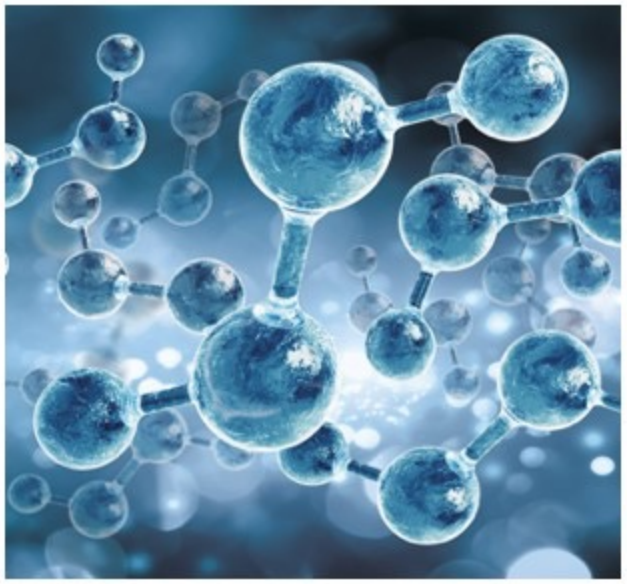
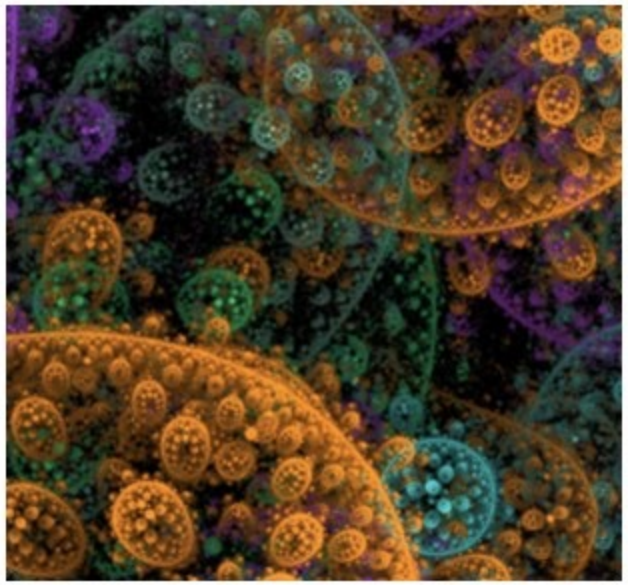
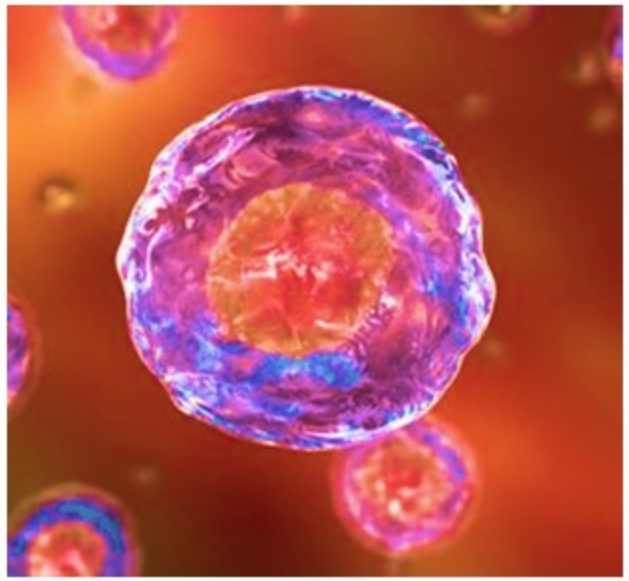
Galecto



Galecto KOL Event

GB1211: A Potential Treatment For Non-Small Cell Lung Cancer

NOVEMBER, 2021

Forward-looking statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding Galecto, Inc.'s (the "Company") strategy, future operations, future financial position, projected costs, prospects, plans, and objectives, are forward-looking statements. Such forward-looking statements include statements about the GALACTIC-1 trial, plans for continuing to enroll patients, working with investigators and regulatory authorities, the timing of completing enrollment and the initial unblinded data readout, GB0139's potential (including the effectiveness of the 3 mg dose), plans for clinical development and potential to market, as well as Galecto's product candidates and pipeline. The words ''anticipate,'' ''believe,'' ''continue,'' ''could,'' ''estimate,'' ''expect,'' ''intend,'' ''may,'' ''plan,'' ''potential,'' ''predict,'' ''project,'' ''target,'' ''should,'' ''would,'' and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. For such statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. The Company may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Factors that could cause actual results to differ materially from such statements include, without limitation: our ability to modify the GALACTIC-1 trial protocol for GB0139 to the satisfaction of the FDA and other regulatory agencies; our ability to continue to enroll patients and complete the GALACTIC-1 trial with fewer dosage groups; the risk that FDA or other regulatory agencies impose a clinical hold on the GALACTIC-1 trial; that drug development is expensive, time consuming, uncertain and susceptible to change, interruption, delay or termination; the duration and severity of the ongoing coronavirus disease (COVID-19) pandemic, including but not limited to the impact on our clinical and other operations, the operations of our suppliers, others and the capital markets, which in each case remains uncertain; that the timing and outcome of research, development and regulatory review and feedback is uncertain; our need to raise additional capital to advance all of our programs; the amount of our future losses is uncertain and could cause our stock price to fluctuate or decline; top-line data may not accurately reflect the complete results of a particle study or trial; results of clinical trials and other studies are subject to different interpretation and may not be predictive of future results; new data or results may be unexpected or unfavorable; our drug candidates may not advance in development or be approved for marketing; clinical trial and other studies may not proceed at the time or in the manner expected or at all; enrolling patients in our ongoing and intended clinical trials is competitive and challenging; clinical and nonclinical data is voluminous and detailed, and regulatory agencies may interpret or weigh the importance of data differently and reach different conclusions than we or others, request additional information, have additional recommendations or change their guidance or requirements; data and information related to our program may not meet regulatory requirements or otherwise be sufficient for further development at all or on our projected timeline; and other risks related to developing, seeking regulatory approval of and commercializing drugs, including regulatory, manufacturing, supply and marketing issues and drug availability. Additional factors that could cause results to differ materially from those stated or implied by our forward-looking statements are disclosed in our Securities and Exchange Commission (SEC) filings, including our most recent Annual Report on Form 10-K, filed with the SEC on March 29, 2021, under the headings "Risk Factors." In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so.

Investment Highlights

Clinical stage biotechnology company committed to the development of novel small molecule therapeutics for the treatment of fibrosis, inflammation & cancer

- Small molecule fibrosis inhibitors targeting Galectin-3 & lysyl oxidase-like 2 (LOXL2)
- Lead asset GB0139: a potentially first-in-class with FDA and EMA orphan drug designation (ODD)

Deep pipeline with meaningful upcoming catalysts

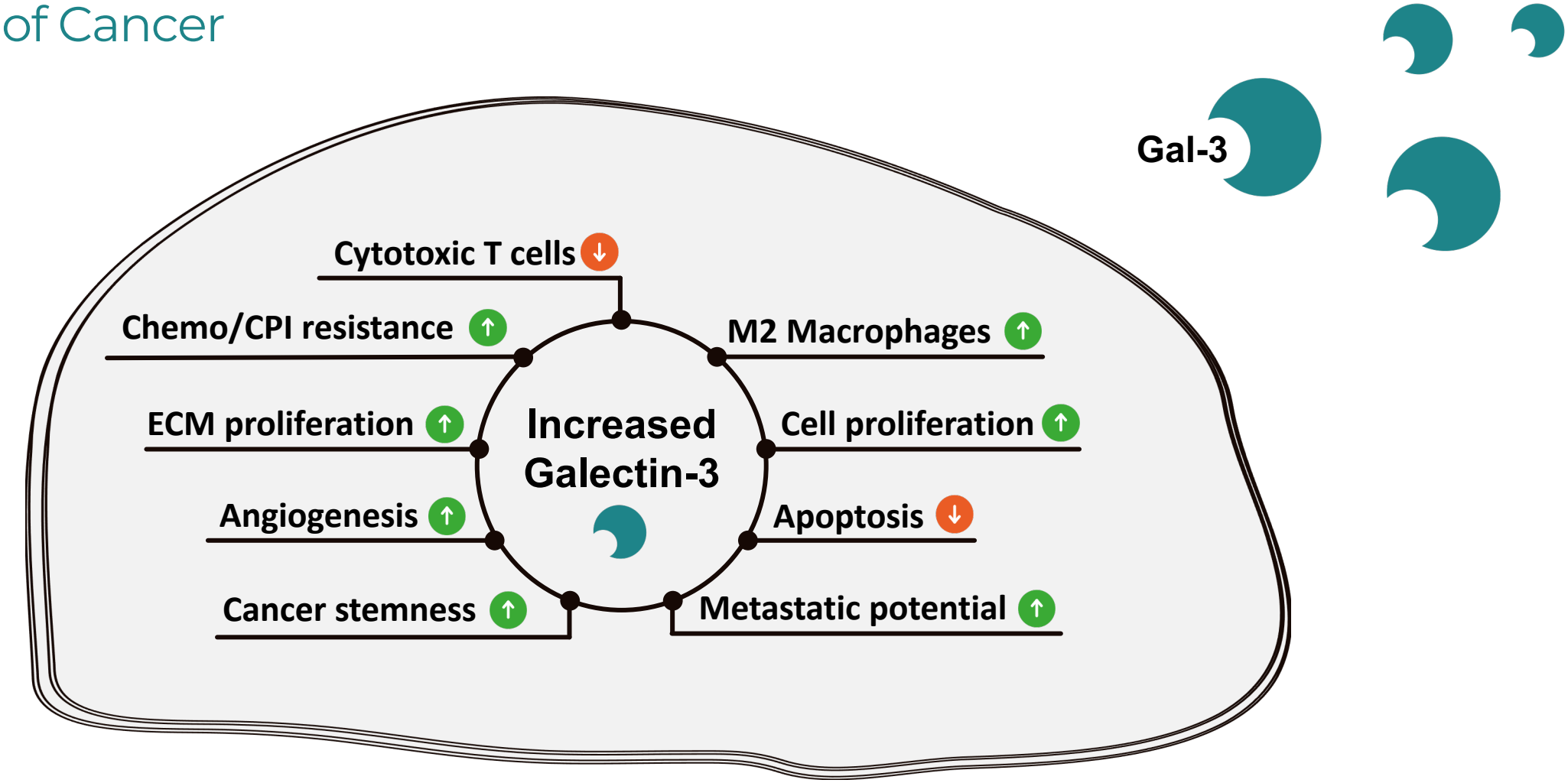
- Phase 2 trials in IPF, myelofibrosis, & liver cirrhosis ongoing
- Phase 2 study in NSCLC to be initiated in next 6 months – Collaboration with Roche

Cash balance at September 30, 2021 of ~$128M, funded into 2H 2024

Deep Pipeline of Assets Targeting Fibrosis and Cancer

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Steps	Planned Readout
GB0139	Idiopathic Pulmonary Fibrosis	**GALACTIC-1** (Inhaled Galectin-3 inhibitor)				Complete Phase 2b Enrollment	Mid-2023
GB2064	Fibrotic Indications (Initially in Myelofibrosis)	**MYLOX-1** (Oral LOXL2 inhibitor)				Complete Phase 2a Enrollment	2H 2022
GB1211	Oncology (Initially in NSCLC)	**GALLANT-1** (Oral Galectin-3 inhibitor)				Phase 2a Start	Mid-2023
GB1211	Fibrotic Indications (Initially in Liver Cirrhosis)	**GULLIVER-2** (Oral Galectin-3 inhibitor)				Complete Phase 1b Enrollment/ Phase 2a Start	2H 2022

Increased Levels of Tumor Galectin-3 Significantly Drives the Hallmarks of Cancer



Adapted from:
Ebrahim et al (2014); Ann Transl Med;2(9):88
Farhad et al (2018); Oncoimmunology;7(6):e1434467
Vuong et al (2019); Cancer Res;79;1480

GB1211:
A Potential Treatment For Non-Small Cell Lung Cancer

Agenda:

- The Immunotherapy Revolution by Professor Alexander M.M. Eggermont, MD, PhD
  - Chief Scientific Officer at the Princess Máxima Center for Pediatric Oncology
  - Professor of Immunotherapy at the University Medical Center Utrecht, the Netherlands
- Galectin-3-mediated regulation of the tumor microenvironment by Dr. Will Redmond
  - Immune Monitoring Laboratory, Earle A. Chiles Research Institute, Providence Cancer Institute
- GB1211: A Potential Treatment For Non-Small Cell Lung Cancer by Professor Tariq Sethi
  - Galecto co-founder, Professor Emeritus, King's College London
- Q&A

The Immunotherapy Revolution: Lessons from Melanoma

Alexander M.M. Eggermont, MD, PhD
Professor Clincal&Translational Immunotherapy
University Medical Center Utrecht
Chief Scientific Officer
Princess Maxima Center for Pediatric Oncology
Utrecht, Netherlands
Emeritus Professor, Surgical Oncology
Erasmus University Rotterdam, NL
& Paris-Saclay University, France

Disclosure information

Alexander Eggermont

I have the following financial relationships over the last 3 years to disclose:

Consultant honoraria for: Agenus, Biocad, BioInvent, BioNTech, Bristol Myers Squibb, CatalYm, Dash Therapeutics, Ellipses, Galecto, GSK, IO Biotech, ISA Pharmaceuticals, Merck&Co, Merck Sharpe Dohme, Nektar, Novartis, Pfizer, Regeneron, RiverD, Sairopa, Sellas, SkylineDx, TigaTx, TTxDiscovery

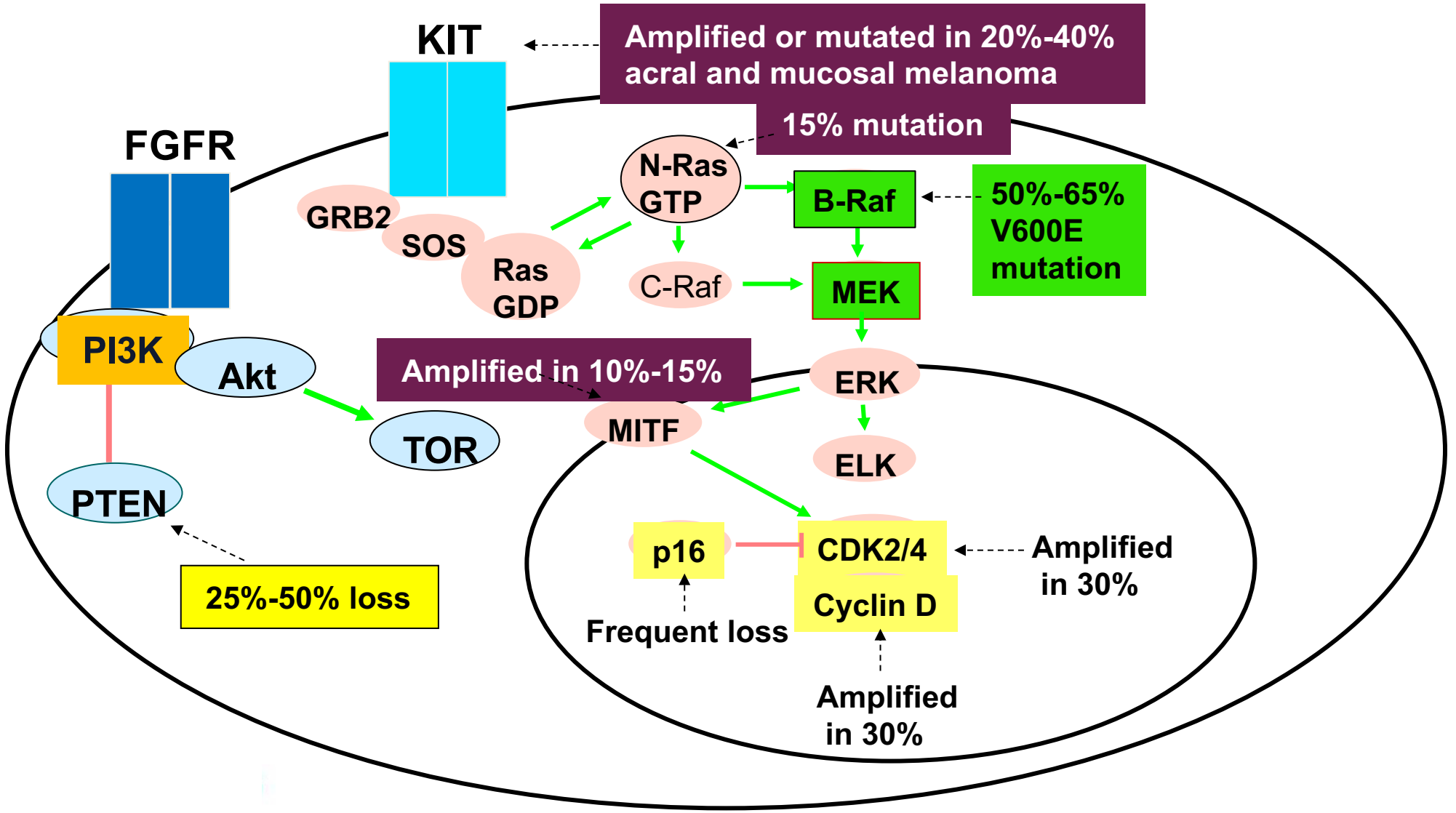
Speaker engagements: Biocad, BMS, Merck/MSD, Novartis, SkylineDx

THE MELANOMA PARADIGM

MUTATION DRIVEN DRUG DEVELOPMENT

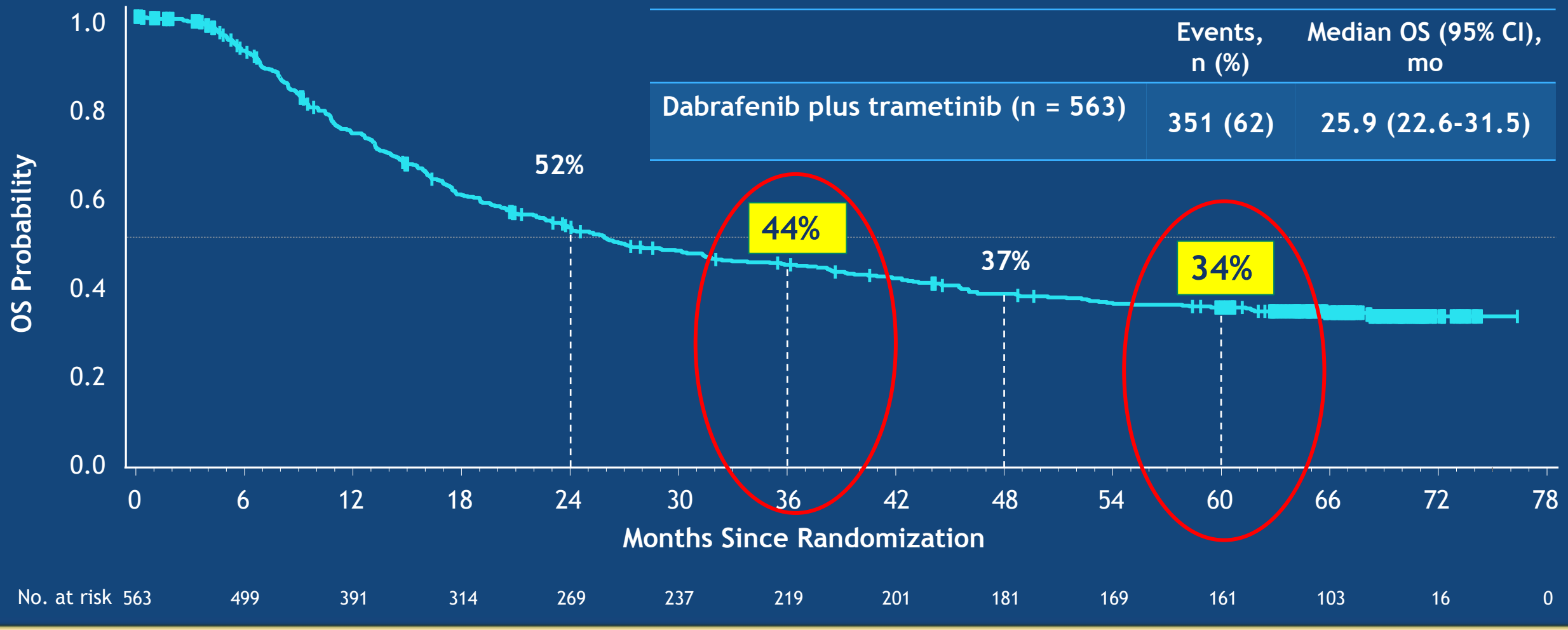
INNOVATIVE IMMUNOMODULATION

BRAF + MEK Inhibitors Combo



Adapted from Sosman, *Curr. Oncol. Rep.* 11, 405 (2009)

Dabrafenib Plus Trametinib: 3Yr 44% and 5-Yr 34% OS



	Events, n (%)	Median OS (95% CI), mo
Dabrafenib plus trametinib (n = 563)	351 (62)	25.9 (22.6-31.5)

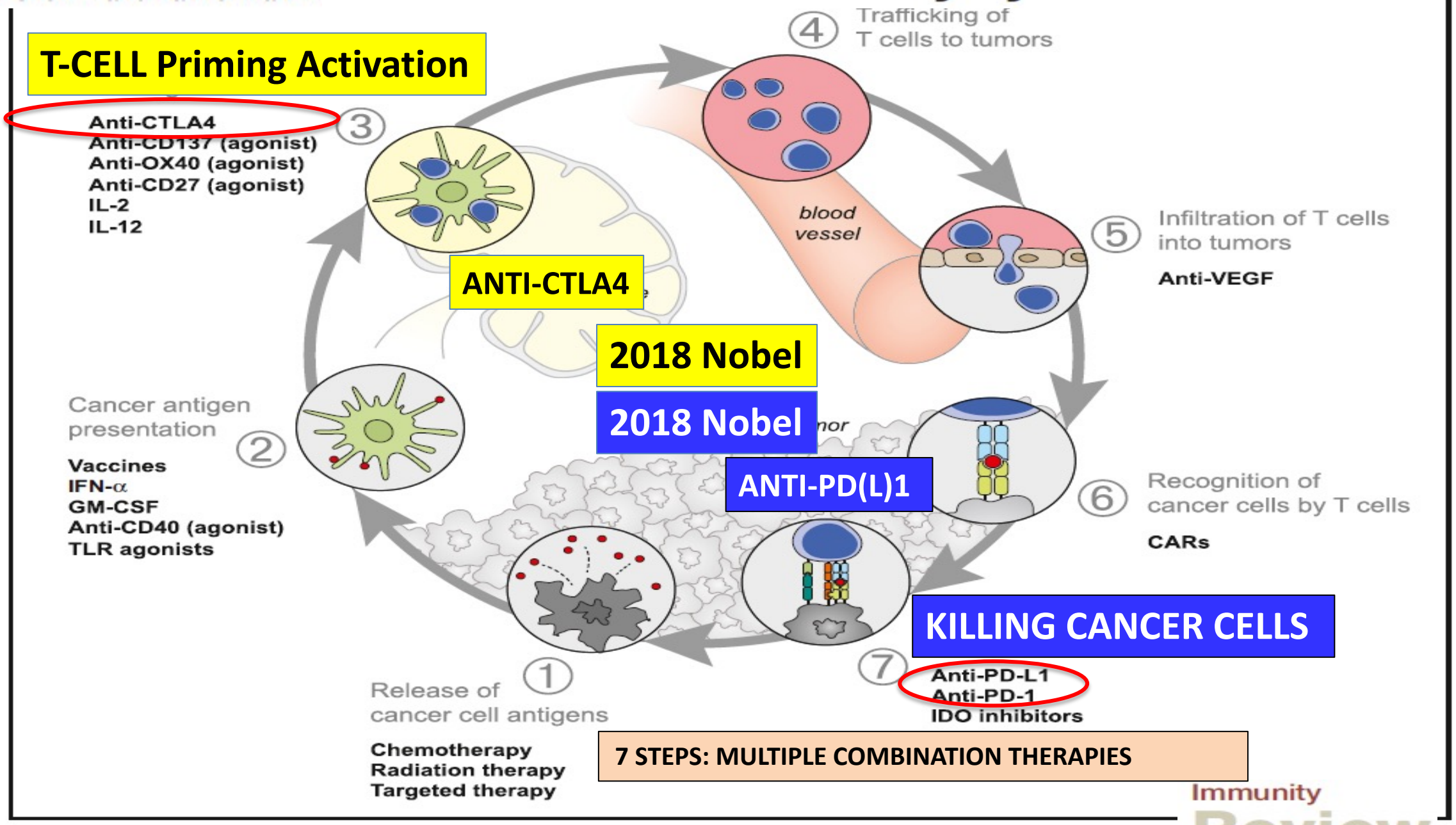
THE MELANOMA PARADIGM

MUTATION DRIVEN DRUG DEVELOPMENT

INNOVATIVE IMMUNOMODULATION

Daniel S. Chen[1,3] and Ira Mellman[2,3,]

The Cancer-Immunity Cycle



Immunity Review

Figure 3. Therapies that Might Affect the Cancer-Immunity Cycle

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Phase I Keynote-001 :
3 yr 52% and 5 yr 41% survival
Pembrolizumab in advanced melanoma

Pooled Analysis of Long-Term Survival Data From Phase II and Phase III Trials of Ipilimumab in Unresectable or Metastatic Melanoma

Dirk Schadendorf, F. Stephen Hodi, Caroline Robert, Jeffrey S. Weber, Kim Margolin, Omid Hamid, Debra Patt, Tai-Tsang Chen, David M. Berman, and Jedd D. Wolchok

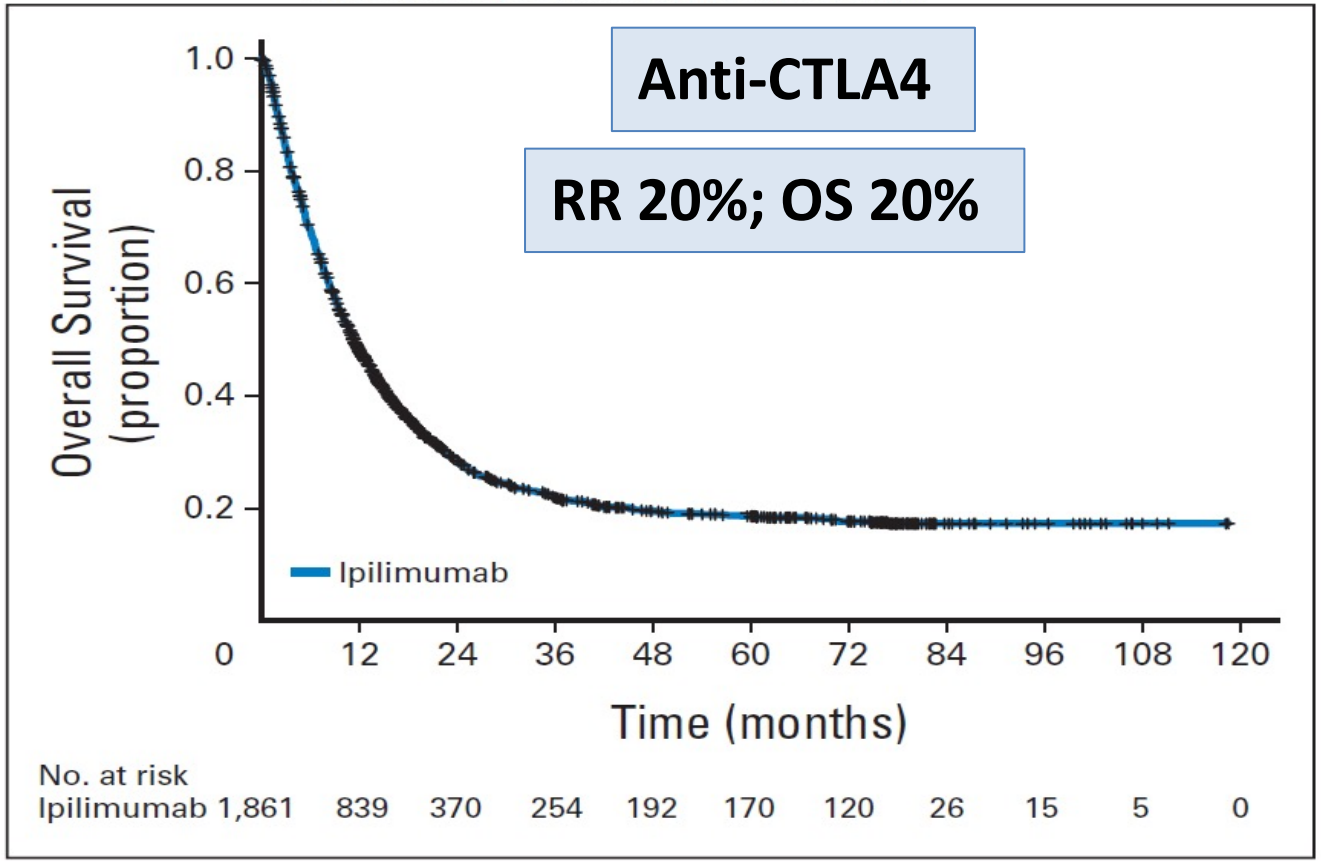
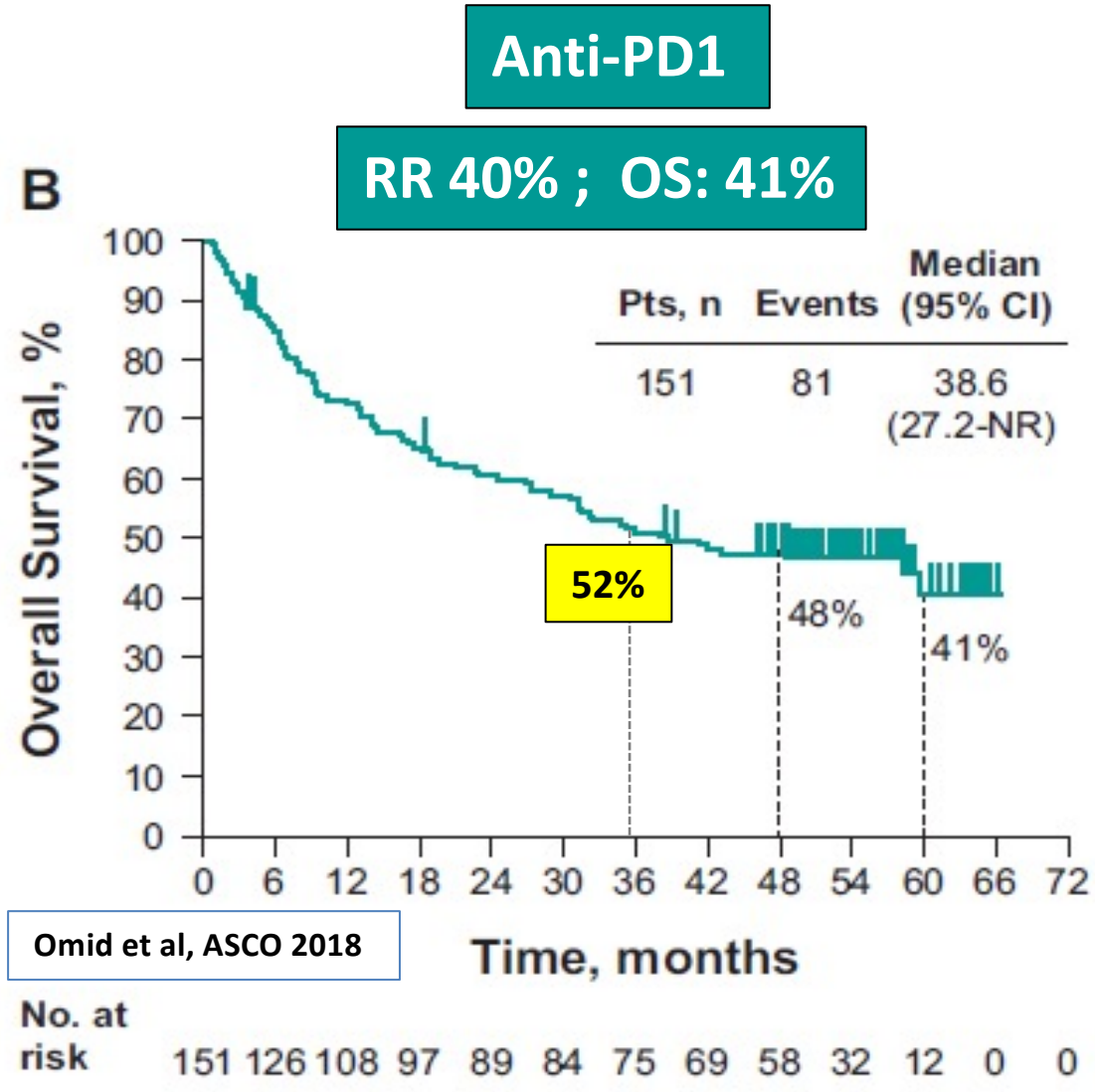


Fig 1. Primary analysis of pooled overall survival (OS) data. Individual patient data were pooled from 10 prospective trials and two retrospective, observational studies of ipilimumab in metastatic melanoma (n = 1,861). Median OS was 11.4 months (95% CI, 10.7 to 12.1 months) with a 3-year survival rate of 22% (95% CI, 20% to 24%). Crosses indicate censored patients.

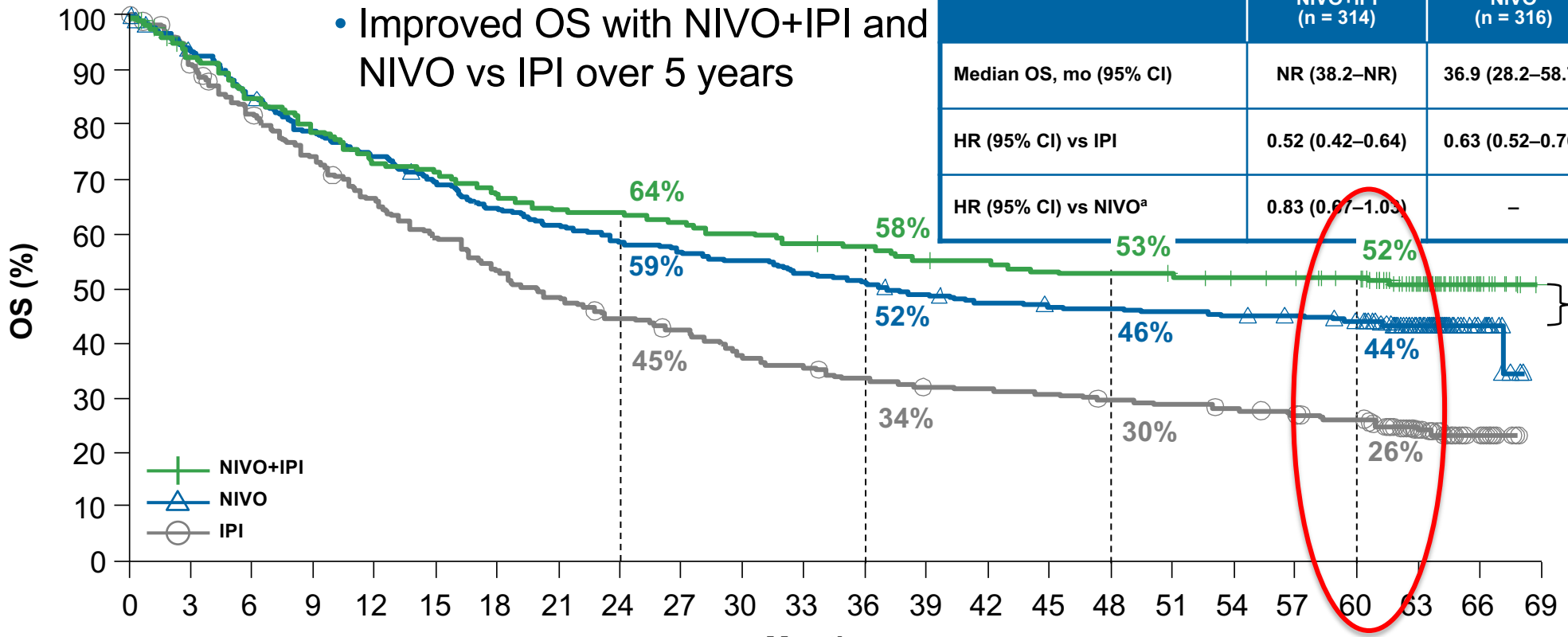


Omid et al, ASCO 2018

NIVO + IPI: 5 Year Overall Survival

- Improved OS with NIVO+IPI and NIVO vs IPI over 5 years

	NIVO+IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Median OS, mo (95% CI)	NR (38.2–NR)	36.9 (28.2–58.7)	19.9 (16.8–24.6)
HR (95% CI) vs IPI	0.52 (0.42–0.64)	0.63 (0.52–0.76)	–
HR (95% CI) vs NIVO[a]	0.83 (0.67–1.03)	–	–



No. at risk

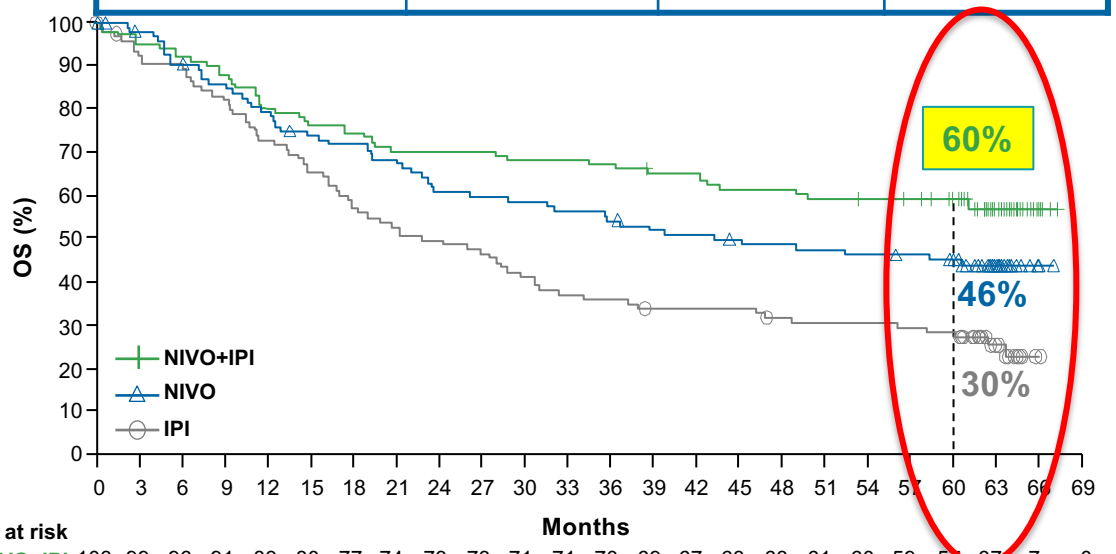
NIVO+IPI	314	292	265	248	227	222	210	201	199	193	187	181	179	172	169	164	163	159	157	155	150	92	14	0
NIVO	316	292	266	245	231	214	201	191	181	175	171	164	158	150	145	142	141	139	137	135	130	78	14	0
IPI	315	285	253	227	203	181	163	148	135	128	113	107	100	95	94	91	87	84	81	77	73	36	12	0

[a]Descriptive analysis. 1. Larkin J, et al. Oral presentation at the AACR Annual Meeting; April 1–5, 2017; Washington DC, USA. Abstract CT075; 2. Wolchok JD, et al. *N Engl J Med* 2017;377:1345–1356; 2. Hodi FS, et al. *Lancet Oncol* 2018;19:1480–1492.

OS in Patients With *BRAF*-Mutant and Wild-Type Tumors

BRAF Mutant

	NIVO+IPI (n = 103)	NIVO (n = 98)	IPI (n = 100)
Median, mo (95% CI)	NR (50.7–NR)	45.5 (26.4–NR)	24.6 (17.9–31.0)
HR (95% CI) vs IPI	0.44 (0.30–0.64)	0.63 (0.44–0.90)	–
HR (95% CI) vs NIVO[a]	0.70 (0.46–1.05)	–	–



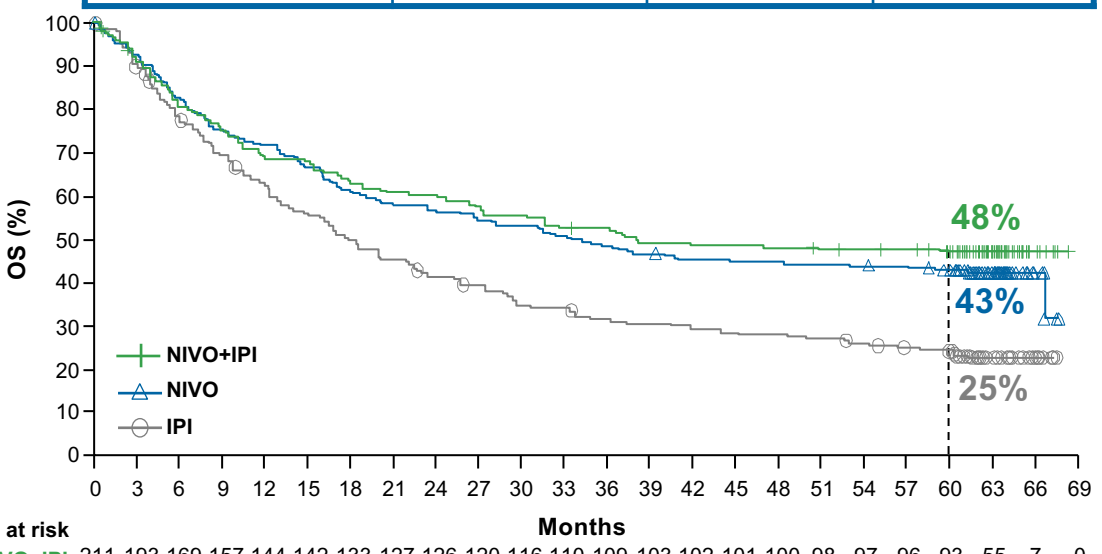
No at risk

NIVO+IPI	103	99	96	91	83	80	77	74	73	73	71	71	70	69	67	63	63	61	60	59	57	37	7	0
NIVO	98	93	86	81	75	69	67	64	57	56	55	53	52	48	47	45	44	43	42	41	40	27	4	0
IPI	100	91	88	81	71	64	58	53	49	47	41	37	36	33	33	33	30	29	29	28	27	13	2	0

- 5-year PFS rates of 38% (NIVO+IPI), 22% (NIVO), and 11% (IPI)

BRAF Wild-Type

	NIVO+IPI (n = 211)	NIVO (n = 218)	IPI (n = 215)
Median, mo (95% CI)	39.1 (27.5–NR)	34.4 (24.1–59.2)	18.5 (14.1–22.7)
HR (95% CI) vs IPI	0.57 (0.45–0.73)	0.64 (0.50–0.81)	–
HR (95% CI) vs NIVO[a]	0.89 (0.69–1.15)	–	–



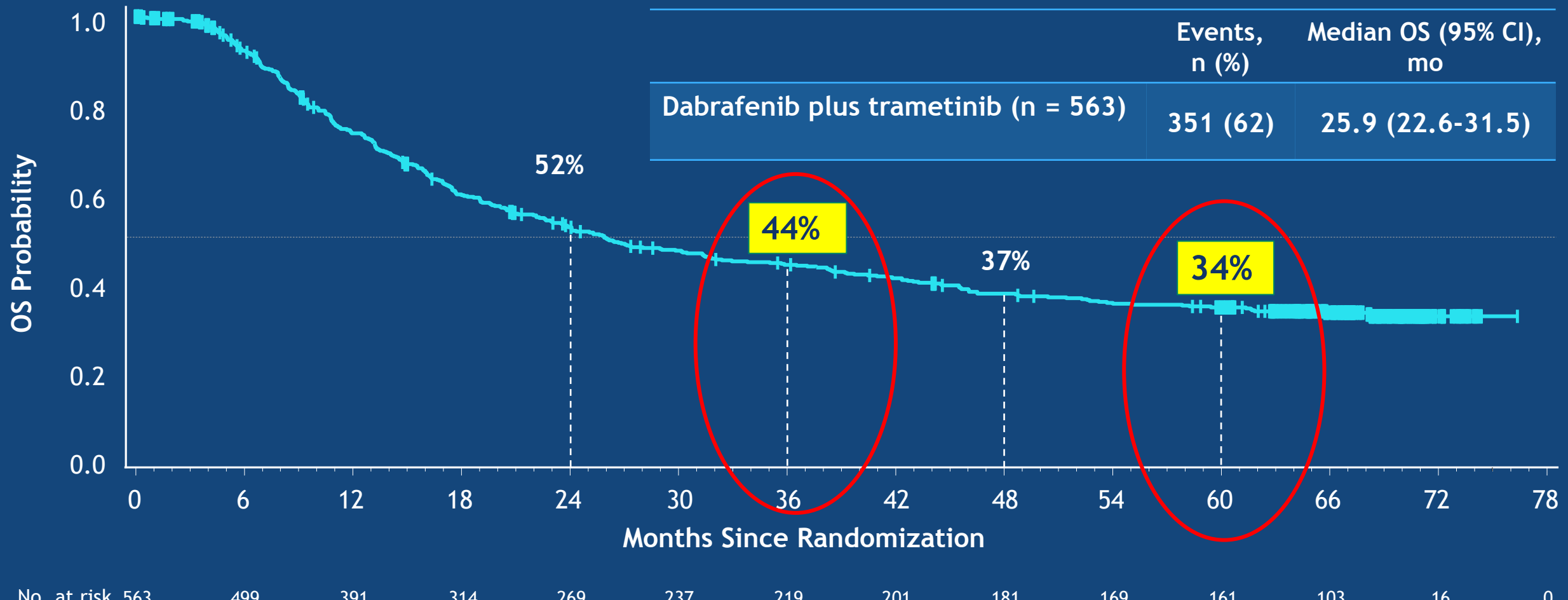
No. at risk

NIVO+IPI	211	193	169	157	144	142	133	127	126	120	116	110	109	103	102	101	100	98	97	96	93	55	7	0
NIVO	218	199	180	164	156	145	134	127	124	119	116	111	106	102	98	97	97	96	95	94	90	51	10	0
IPI	215	194	165	146	132	117	105	95	86	81	72	70	64	62	61	58	57	55	52	49	46	23	10	0

- 5-year PFS rates of 35% (NIVO+IPI), 32% (NIVO), and 7% (IPI)

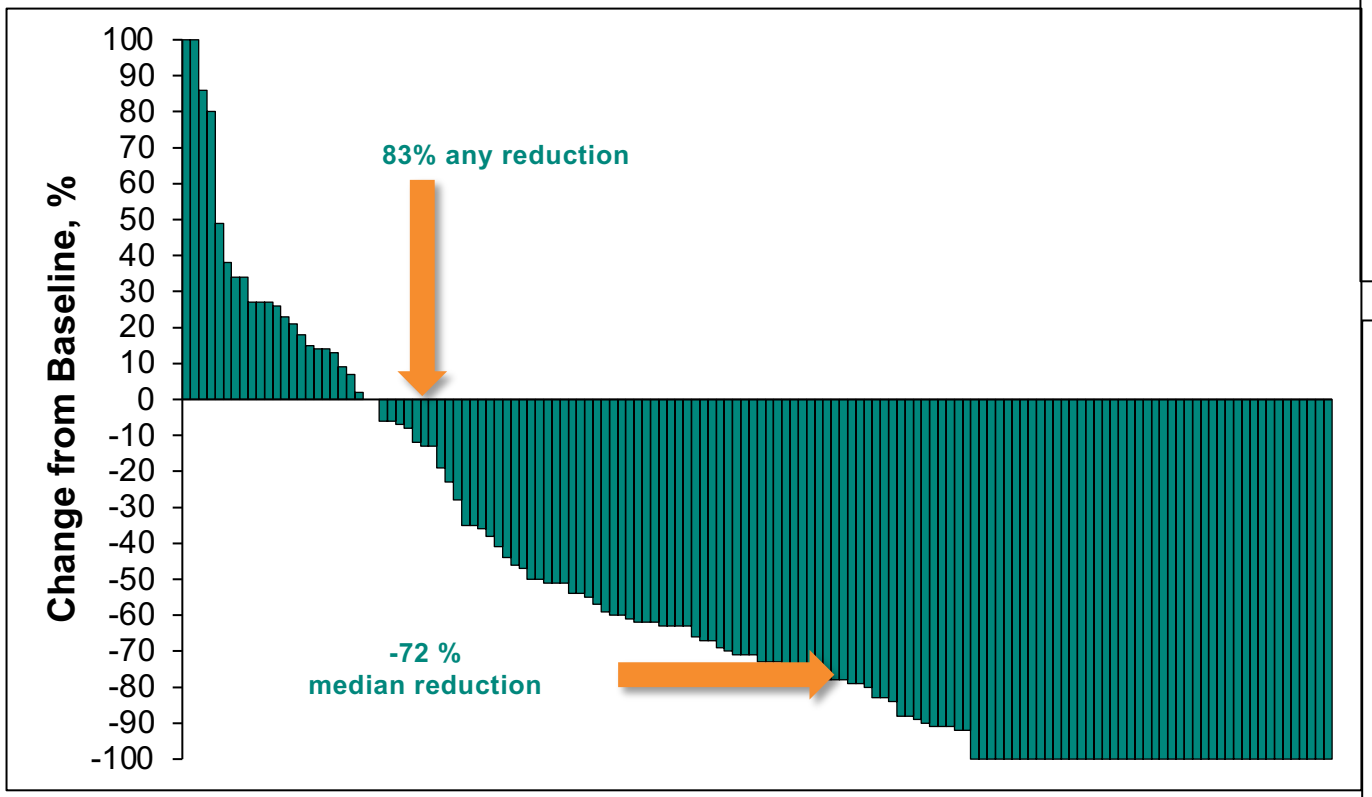
[a]Descriptive analysis. 1. Larkin J, et al. Oral presentation at the AACR Annual Meeting; April 1–5, 2017; Washington DC, USA. Abstract CT075; 2. Wolchok JD, et al. *N Engl J Med* 2017;377:1345–1356; 2. Hodi FS, et al. *Lancet Oncol* 2018;19:1480–1492.

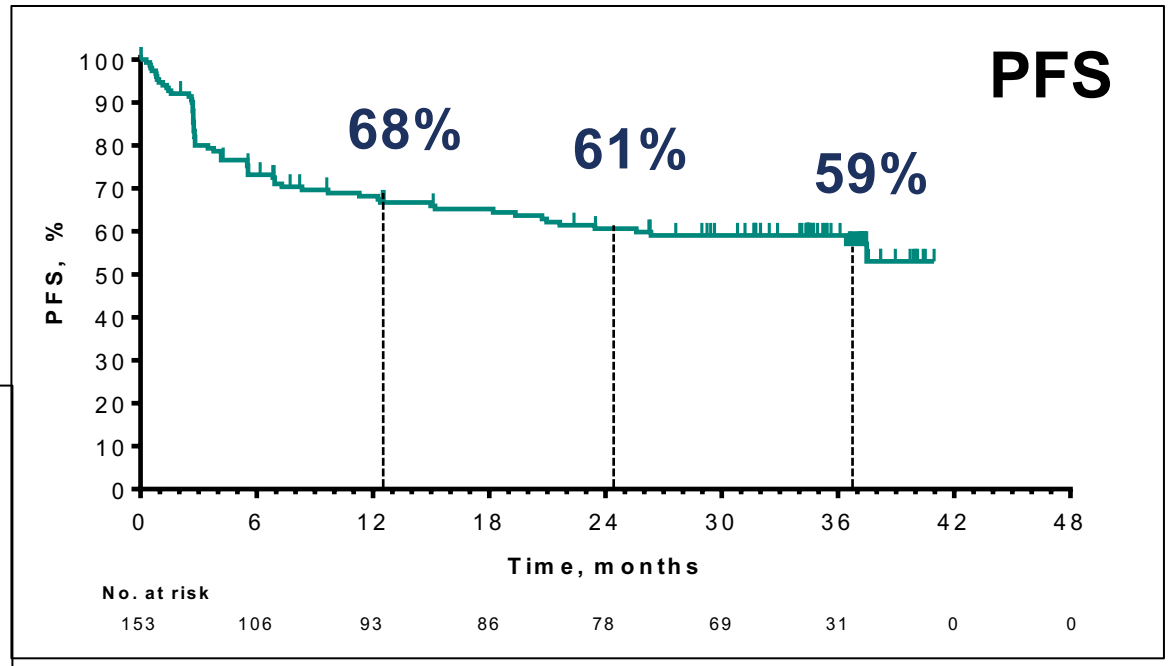
Dabrafenib Plus Trametinib: 3Yr 44% and 5-Yr 34% OS

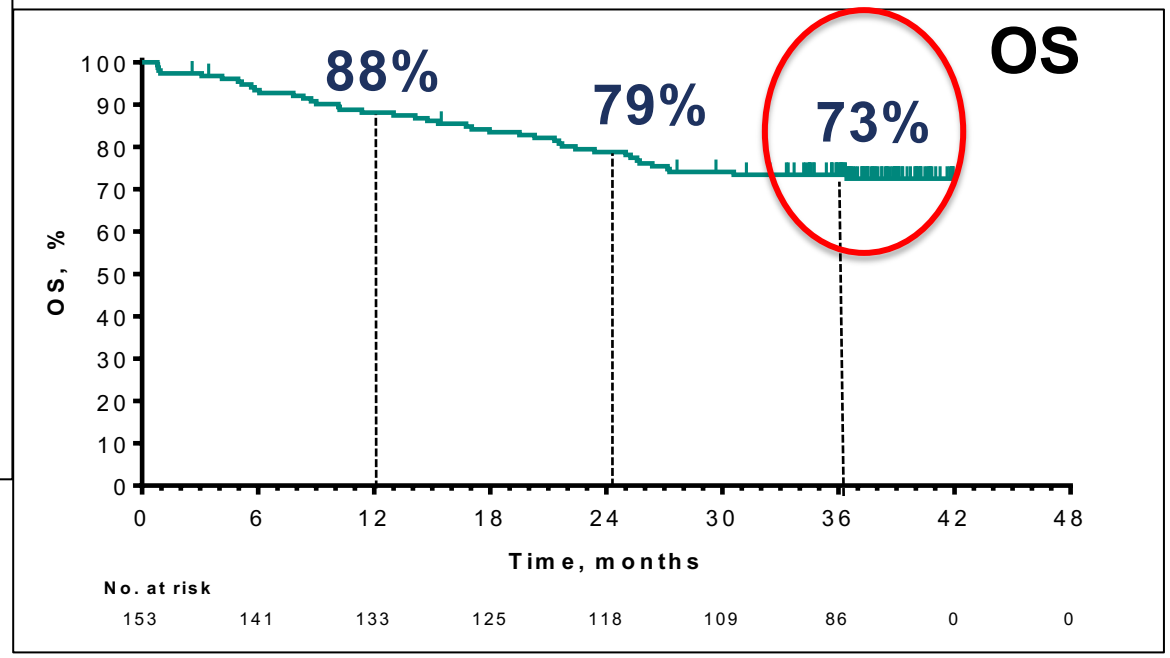


	Events, n (%)	Median OS (95% CI), mo
Dabrafenib plus trametinib (n = 563)	351 (62)	25.9 (22.6-31.5)

KEYNOTE-029 3YR DATA
Pembro + Ipilimumab 1mg

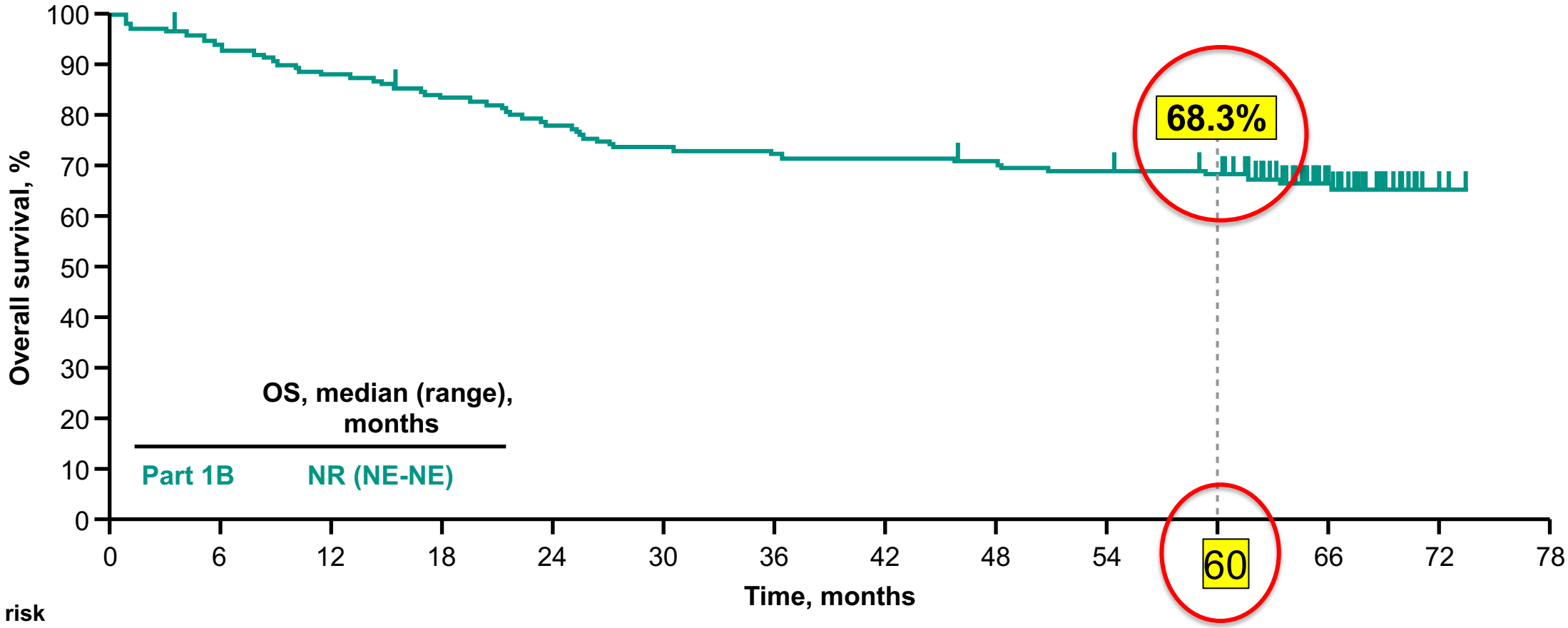






Long GV et al ESMO 2018..

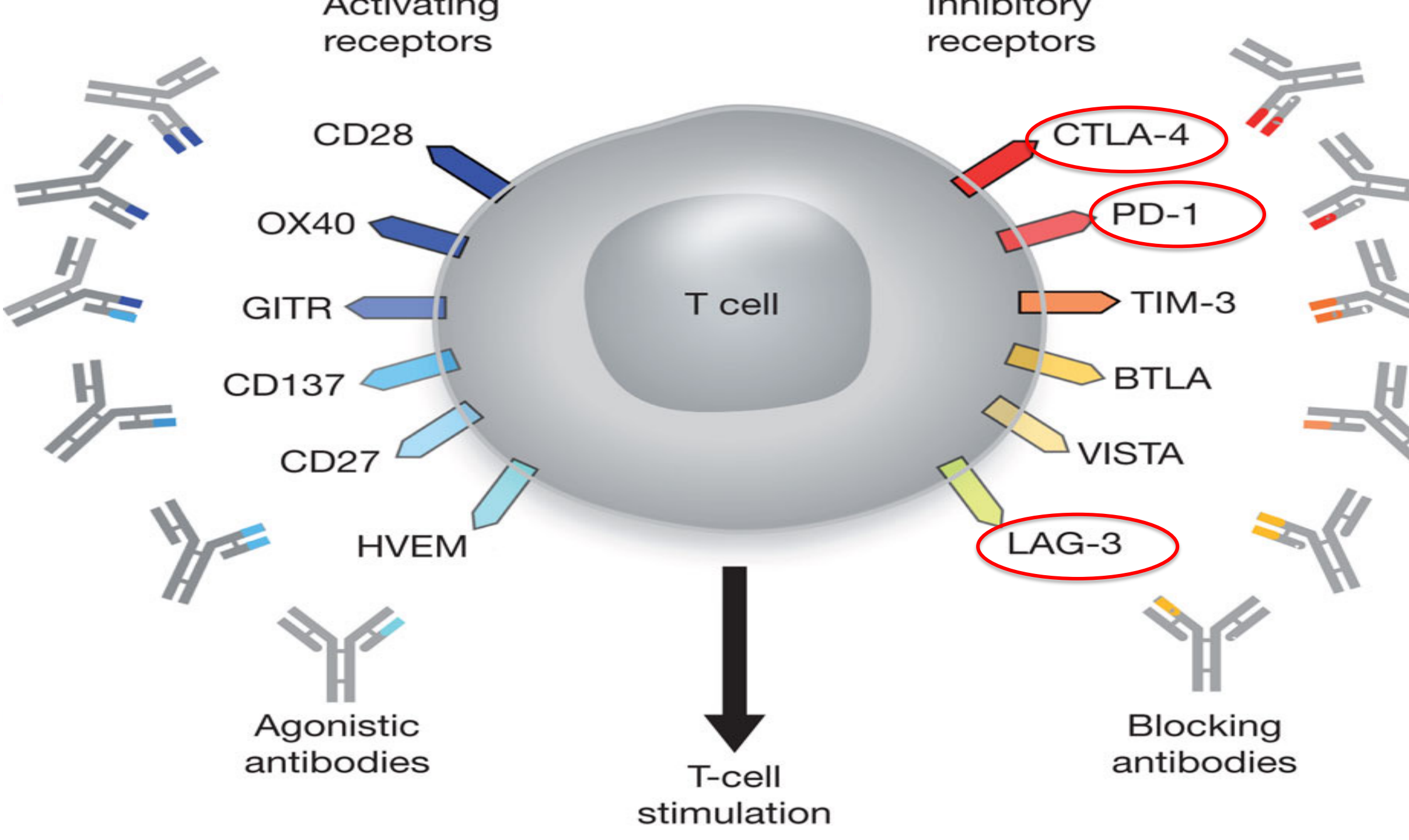
KEYNOTE-029: Overall Survival @ 5yrs
PEMBRO + IPI 1MG



No. at risk													
Pembro + Ipi 1 mg/kg	153	142	134	126	118	111	109	108	106	103	100	54	3	0

Database cut-off: April 1, 2021. **presented by GEORGINA LONG SMR 2021**

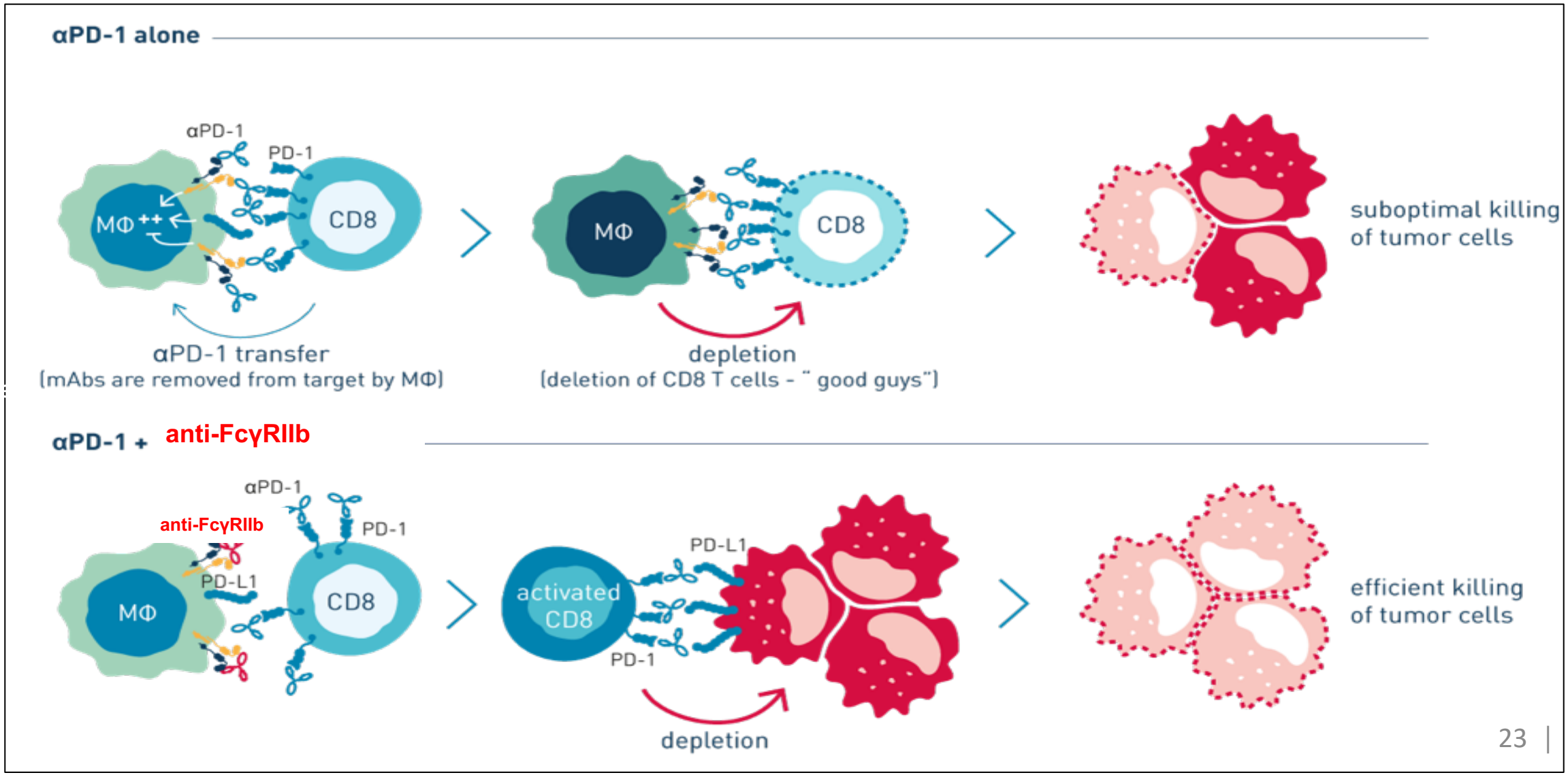
Soooo hard to break the anti-PD1 ceiling


Activating receptors
Inhibitory receptors
CD28
OX40
GITR
CD137
CD27
HVEM
T cell
CTLA-4
PD-1
TIM-3
BTLA
VISTA
LAG-3
Agonistic antibodies
T-cell stimulation
Blocking antibodies

IMMUNE SYSTEM BLOCKED AT MULTIPLE LEVELS (1-2-3)

- 1) **CTL PRIMING**
  - e.g. CTLA4 …… - **Unblock: anti-CTLA4**
- 2) **CTL EFFECTOR Function**
  - e.g. PD-1 / PDL-1…… - **Unblock: anti-PD1/anti-PDL1**
- 3) **MACROPHAGES in Tumor Infiltrate (TAM)**
  - **e.g. Macrophages; MDSC - Unblock:**
    - **anti-IFNcγR2 Mabs: avoid anti-PD1 neutralization**
    - **Fc-modulation of ICI : optimize ICI (e.g. LaLa mut: Prolgolimab)**
    - **anti-CD47 + anti-SIRPα**
    - **M2-M1 repolarization agents (CCR5; CCR5/CCR2)**
    - **M2-M1 repolarization by Galectin-3 inhibition/depletion**

Unblocking Macrophages by anti-FcγRIIb: continued CD8 effector activity



Macrophage Checkpoint Blockage SIRPα

Antibody Therapeutics, 2020, Vol. 3, No. 2 80–94
doi:10.1093/abt/tbaa006
Advance Access Publication on 18 April 2020

Review Article

Macrophage checkpoint blockade: results from initial clinical trials, binding analyses, and CD47-SIRPα structure–function

AbdelAziz R. Jalil[1,2,†], Jason C. Andrechak[2,3,†] and Dennis E. Discher[2,3,*]

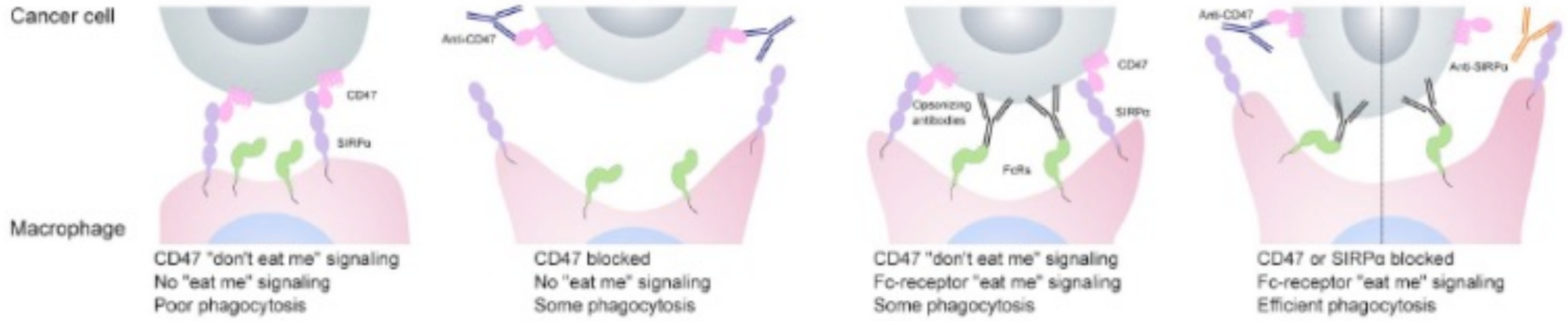
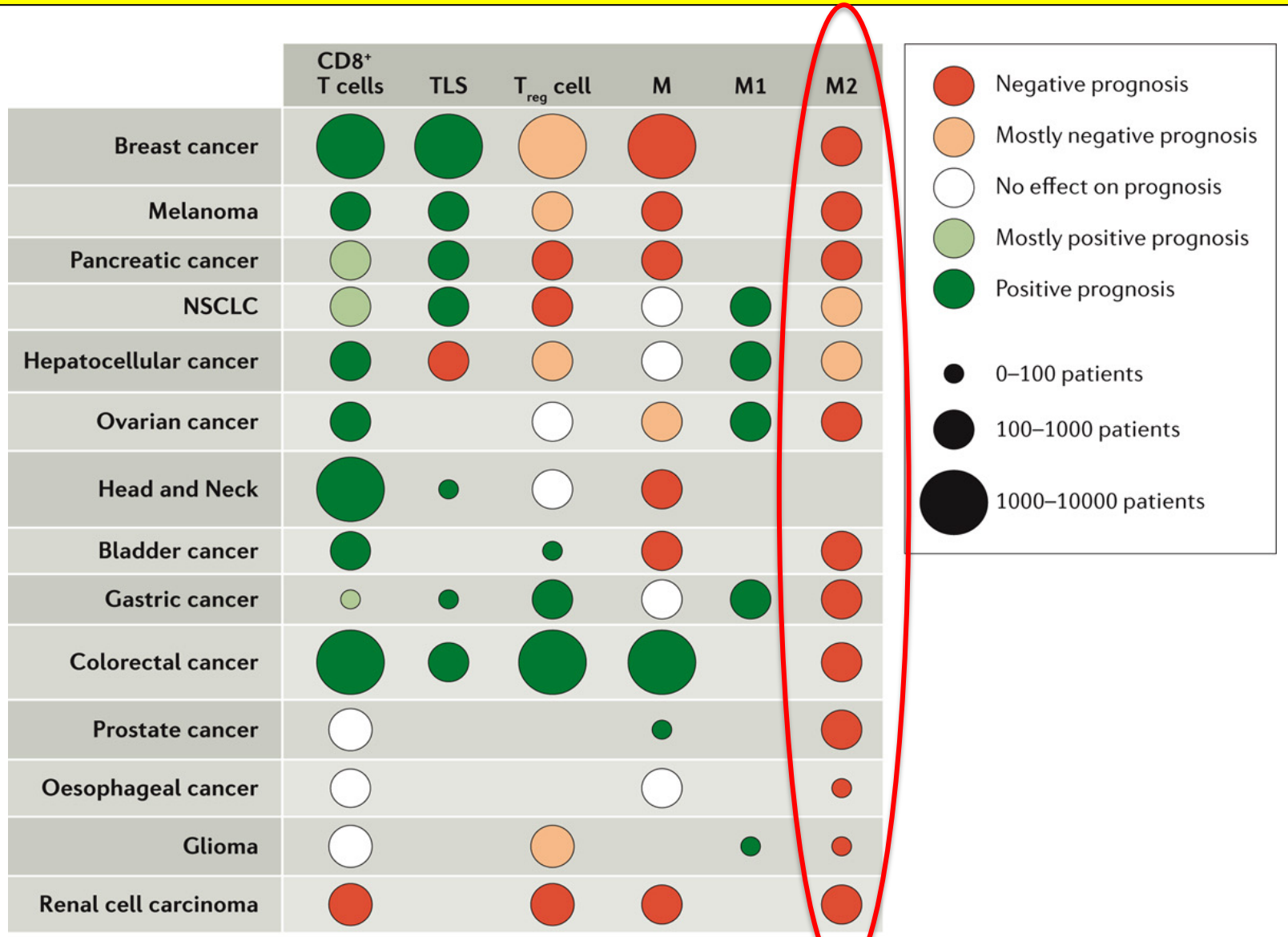


Figure 1. Phagocytosis is maximized by inhibiting CD47 on 'self' cells (the target) or SIRPα on macrophages in combination with antibodies that opsonize the target. CD47 binding to SIRPα signals "don't eat me" to the macrophage (leftmost). Neither antibody blockade of CD47-SIRPα nor antibody opsonization of a target is sufficient to make target engulfment efficient (middle two), whereas the combination maximizes phagocytosis (rightmost).

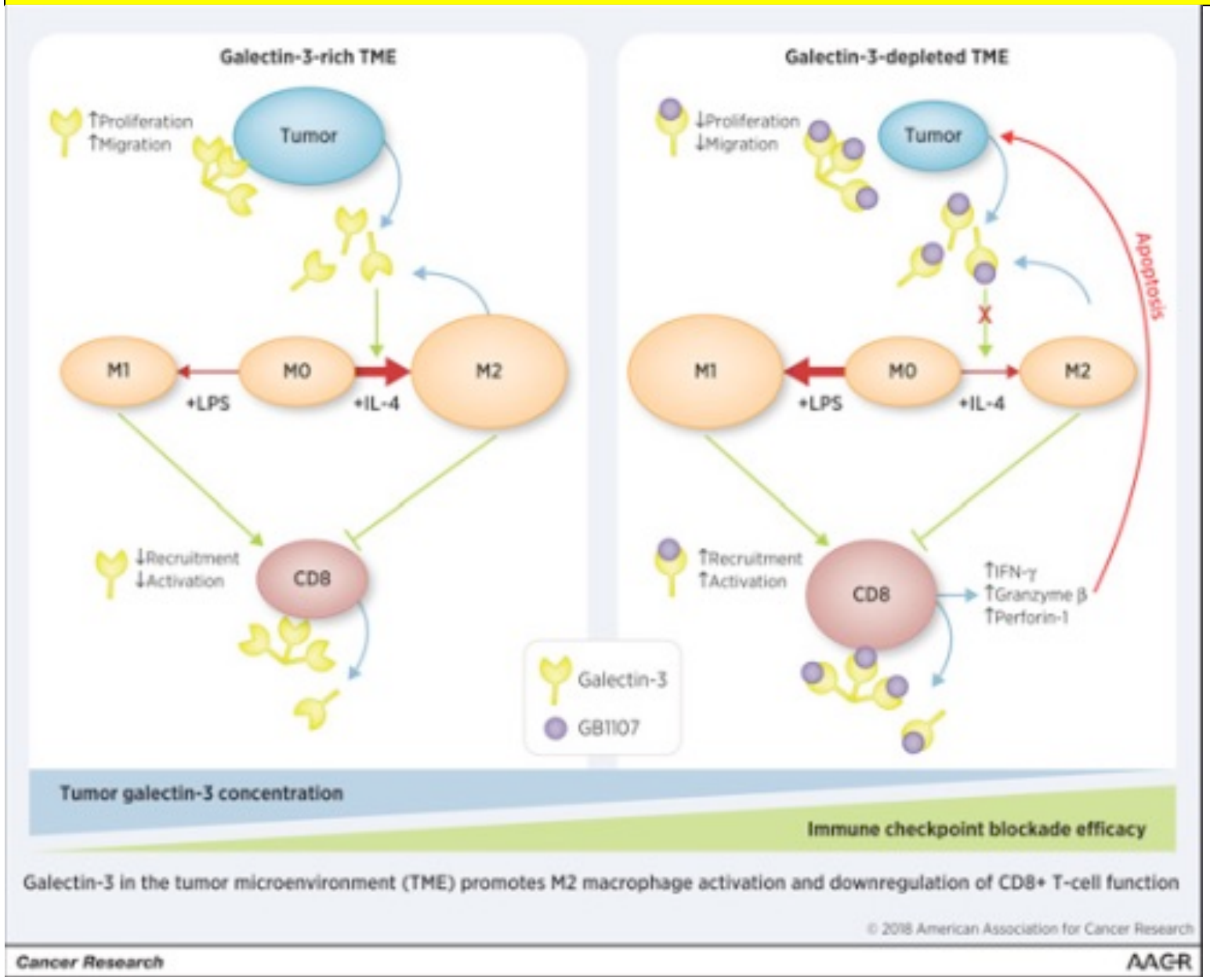
M2 Macrophages : Immunosuppression / Bad Prognosis



WH Fridman et al, 2018

Nature Reviews | Clinical Oncology

Galectin-3 inhibition/depletion and M2-M1 (re)Polerization

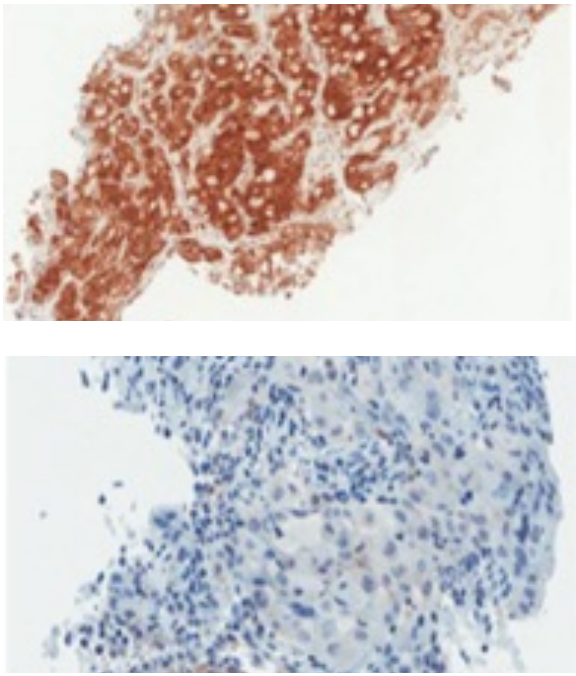


Cancer Research 2019;79:1480-1492

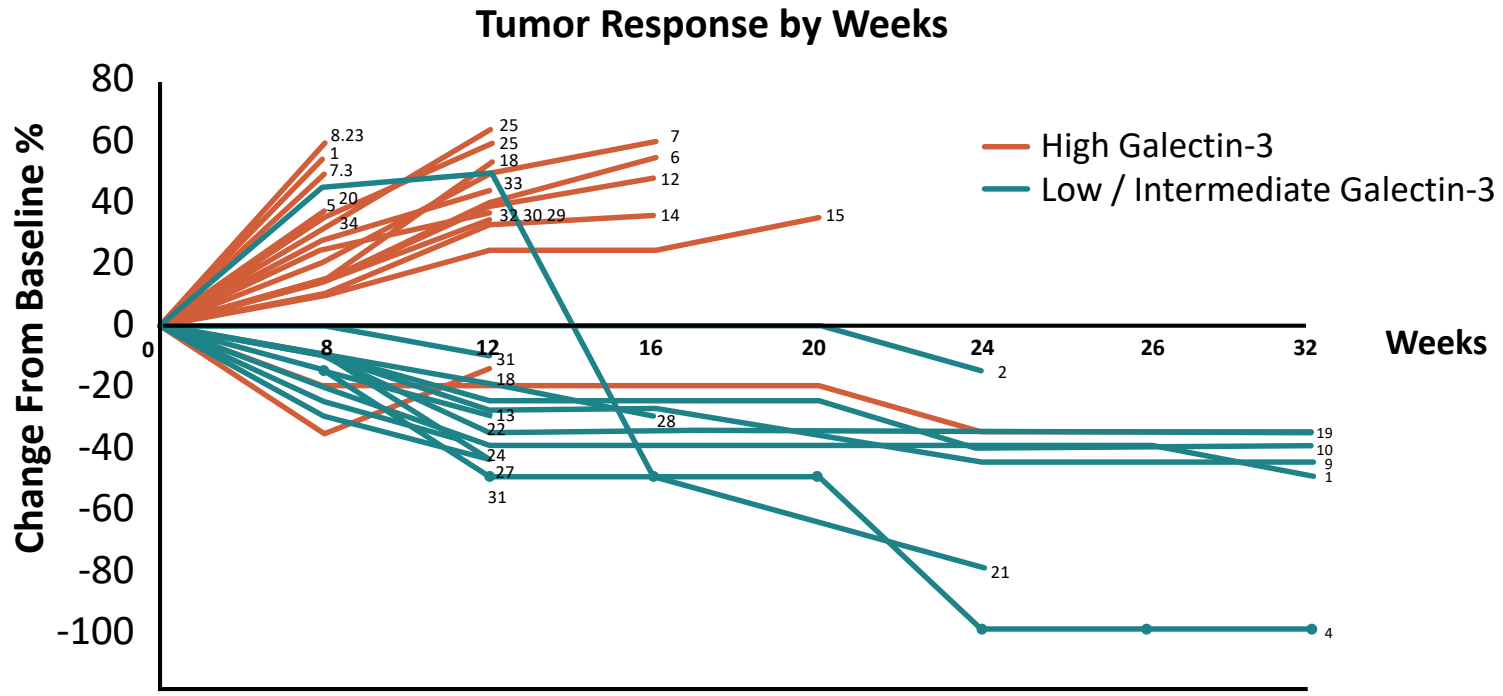
An Orally Active Galectin-3 Antagonist Inhibits Lung Adenocarcinoma Growth and Augments Response to PD-L1 Blockade

Lynda Vuong2, Eleni Kouverianou1, Claire M. Rooney2, Brian J.McHugh1, Sarah E.M. Howie1, Christopher D. Gregory1, Stuart J. Forbes3, Neil C. Henderson1, Fredrik R. Zetterberg4, Ulf J. Nilsson5, Hakon Leffler6, Paul Ford4, Anders Pedersen4, Lise Gravelle4, Susan Tantawi4, Hans Schambye4, Tariq Sethi2, and Alison C. MacKinnon1

Galectin-3 Expression Predicts Response to Pembrolizumab in NSCLC



Galectin-3 expression in NSCLC biopsies

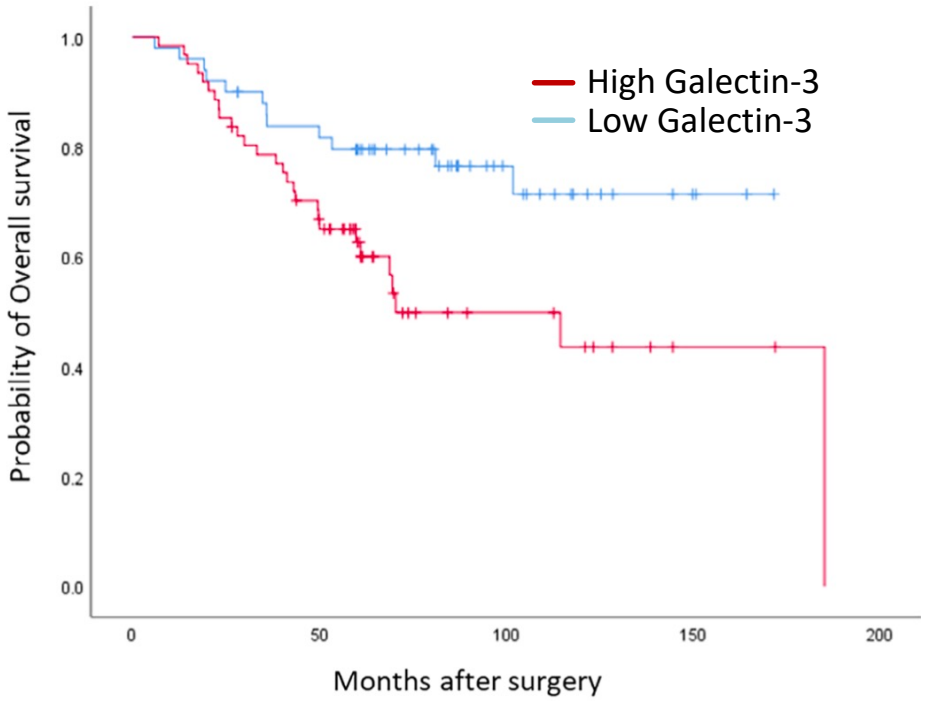


34 patients with PD-L1 +ve NSCLC stage IV received pembrolizumab (200 mg IV @ 3 wks)

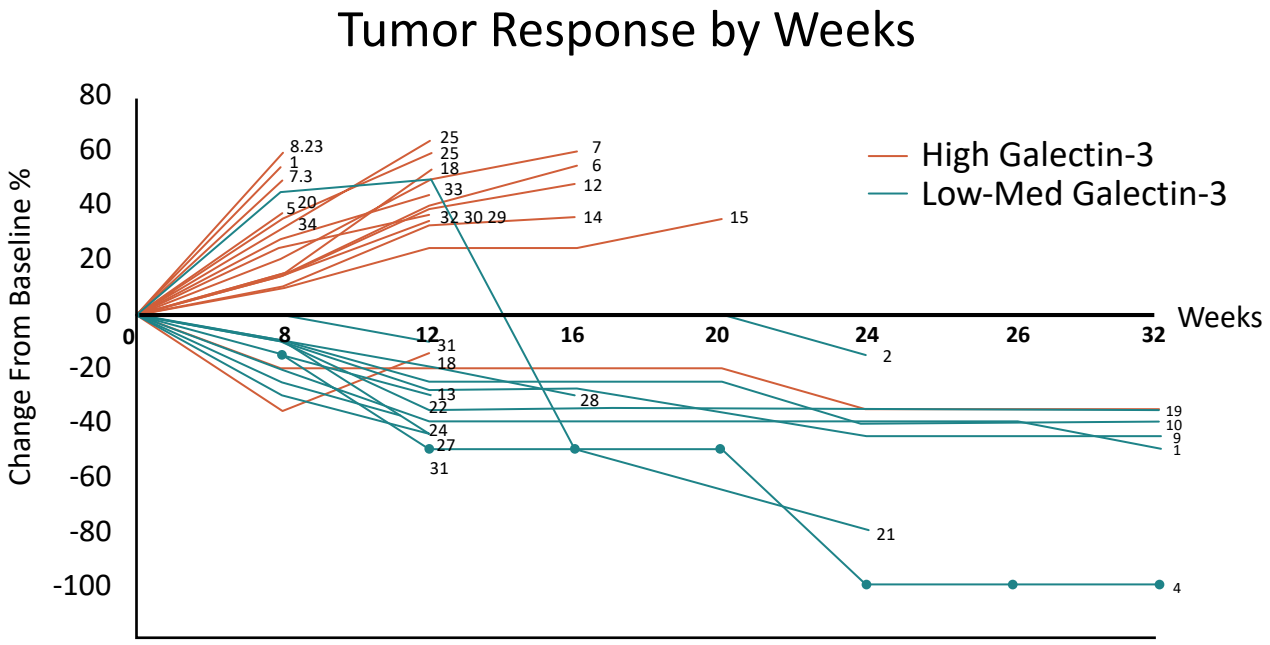
- Tumor resistance to pembrolizumab strongly correlated with high galectin-3 expression in NSCLC
- A clinical response was seen in tumors with a negative, low or intermediate galectin-3 expression

Capalbo et al. (*2019); Int J Mol Sci;20.*

Galectin-3 Expression Linked to the Poor Survival and low CPI Response Rate in NSCLC



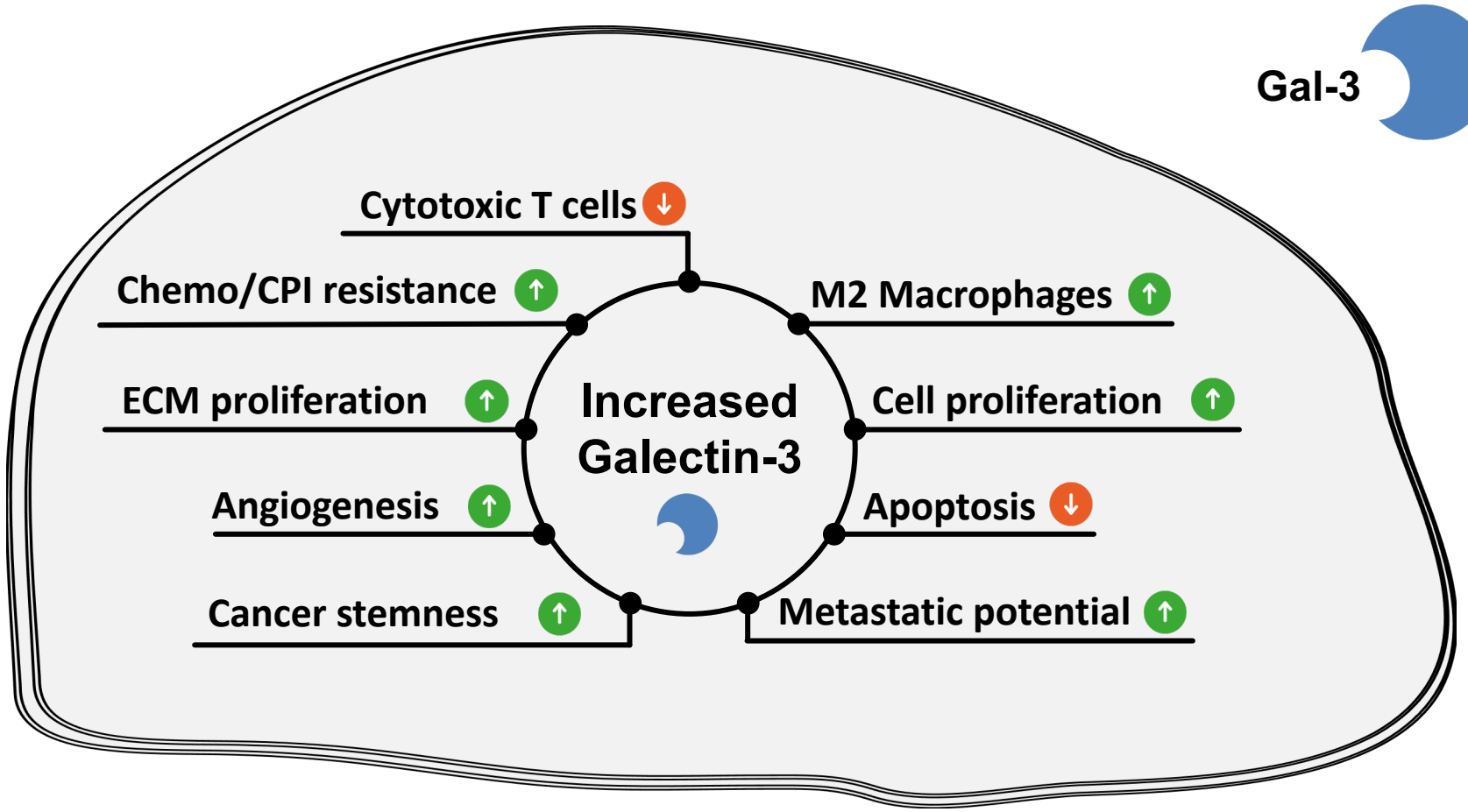
Kusuhara et al (2021); Thorac Cancer;12:1570–1578



34 patients with PD-L1 +ve NSCLC stage IV received pembrolizumab (200 mg IV @ 3 wks)

Capalbo et al (*2019); Int J Mol Sci; 20*

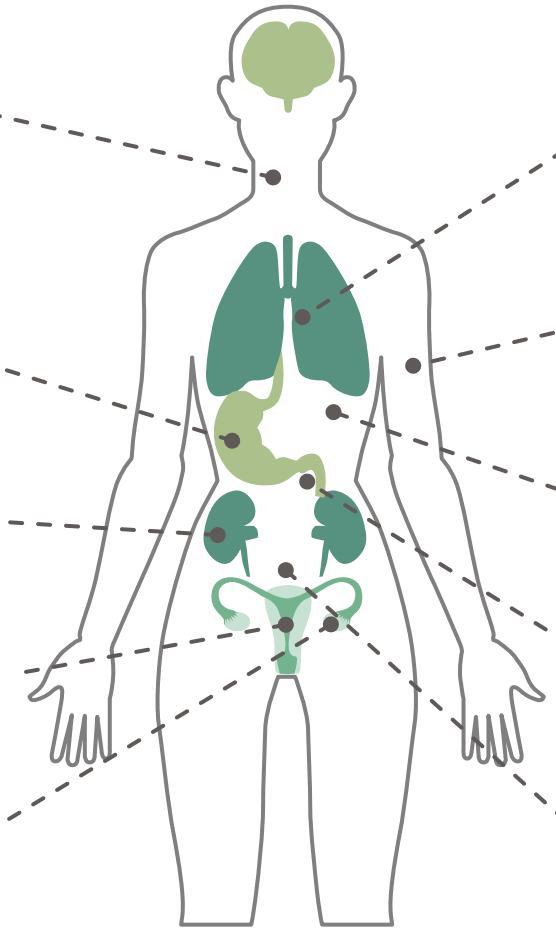
Increased Levels of Tumor Galectin-3 Significantly Drives the Hallmarks of Cancer



Adapted from:
Ebrahim et al (2014); Ann Transl Med;2(9):88
Farhad et al (2018); Oncoimmunology;7(6):e1434467
Vuong et al (2019); Cancer Res;79;1480

Galectin-3 in the Tumor Microenvironment - Examples

Galectin-3 modulates tumor growth and immunosuppression in the tumor microenvironment



Head and Neck Cancer
Cell proliferation, anti-apoptosis, immune escape

Gastric Cancer
Enhances gastric cell motility and mediates metastasis

Renal Cell Cancer
Anti-apoptosis, resistance to chemotherapy

Cervical Cancer
Mediates resistance to chemotherapy

Ovarian Cancer
Mediates resistance to chemotherapy

Lung Cancer
Tumor growth, metastasis, immune suppression, predicts response to CPI therapy

Melanoma
Increased growth, progression, angiogenesis and metastasis

Hepatocellular Carcinoma
Tumor progression, vascular invasion and metastasis

Pancreatic Cancer
Tumor progression and tumor evasion

Bladder Cancer
Increases malignant potential

Adapted from
Ebrahim et al, Ann Transl Med 2014;2(9):88
Dubé-Delarosbil et al, Cell Mol Life Sci (2018);75:1215
Kindt et al, Int. J Mol Sci (2017); 18, 2745
Song et al, Br J Cancer (2020);123:1521

IMMUNE SYSTEM BLOCKED AT MULTIPLE LEVELS (4)

- 1) CTL PRIMING
  - e.g. CTLA4 ……. Unblock: anti-CTLA4
- 2) CTL EFFECTOR Function
  - e.g. PD-1 / PDL-1…… Unblock: anti-PD1/anti-PDL1
- 3) MACROPHAGES in Tumor Infiltrate (TAM)
  - e.g. Macrophages; MDSC Unblock: - anti-FcIFNγR2
    - Fc of ICI modulation: optimize ICI / overcome resistance (prolgolimab)
    - anti-CD47 + anti-SIRPα
    - M2-M1 repolarization agents (CCR5; CCR5/CCR2) (Galactin-3 depletion)
- 4) **VARIOUS IMMUNE ESCAPE MECHANISMS**
  - e.g.:
    - **JAK1/2 mutations and loss Gamma-IFN pathways**
    - **B2M mutations, Loss MHC Class I molecules, Loss Recognition**
    - **ß-cathenin pathway activation : immune exclusion**
    - **TOX and T-cell exhaustion**

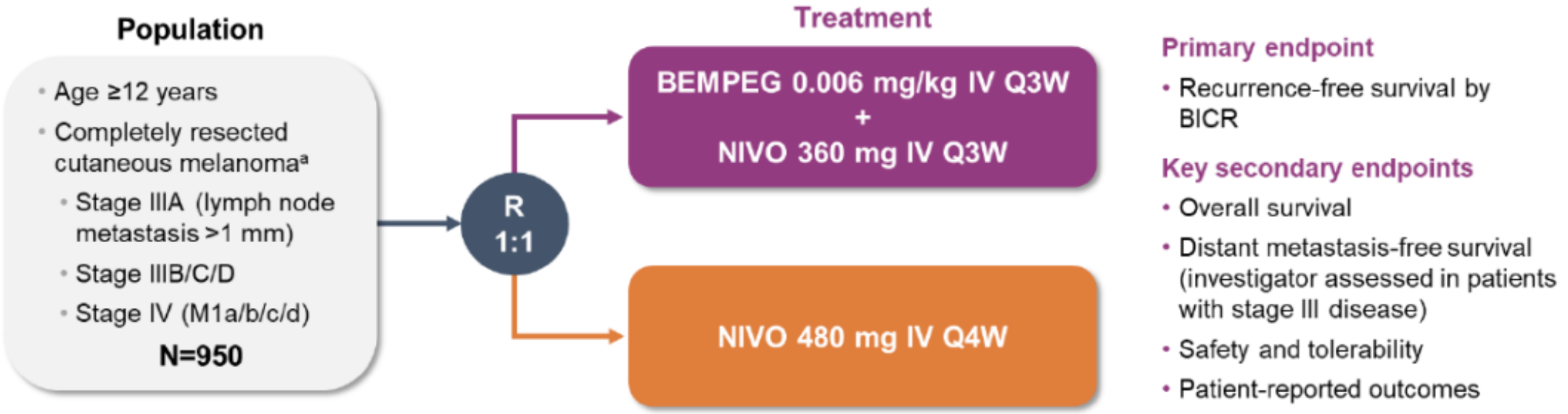
Smarter Cytokines ?

Prevent Treg Tsunami

PIVOT-12: A phase 3 randomized study of adjuvant bempegaldesleukin (BEMPEG) plus nivolumab (NIVO) versus NIVO in completely resected cutaneous melanoma at high risk for recurrence

Alexander Eggermont[1*], Paolo Ascierto[2], Nikhil I. Khushalani[3], Dirk Schadendorf[4], Genevieve Boland[5], Adi Diab[6], Jeffrey Weber[7], Karl Lewis[8], Daniel Johnson[9], Georgina V. Long[10], Sue Currie[11], Mann Muhsin[11], Mary Tagliaferri[11], Matteo Carlino[12]

Figure 1. PIVOT-12 study design



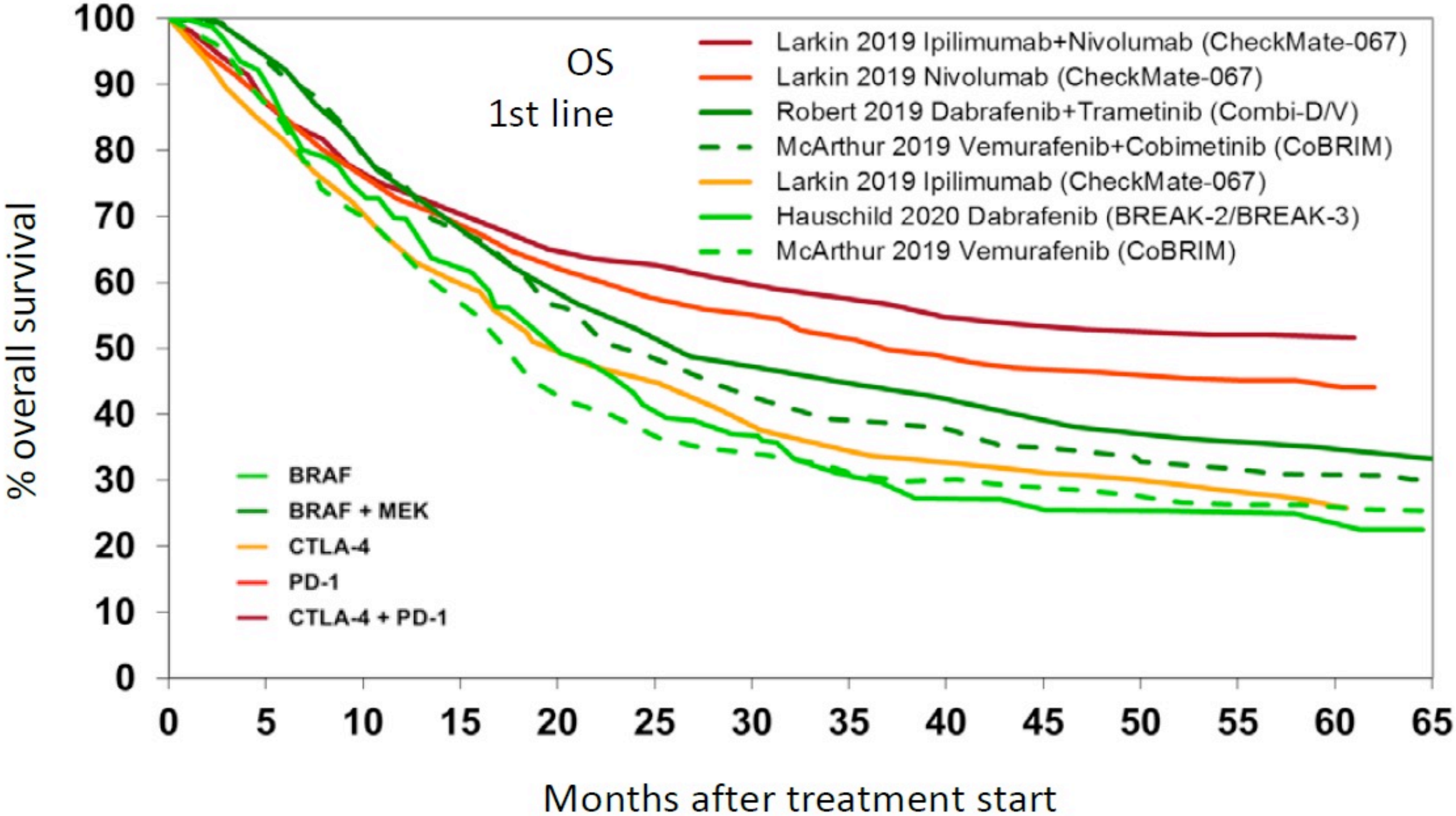
[a]By American Joint Committee on Cancer (8th edition).
BEMPEG, bempegaldesleukin (NKTR-214); BICR, blinded independent central review; IV, intravenous; NIVO, nivolumab; Q3W, every 3 weeks; Q4W, every 4 weeks.
Clinicaltrials.gov. NCT04410445.

Vaccines ?

YES, provided effector cells

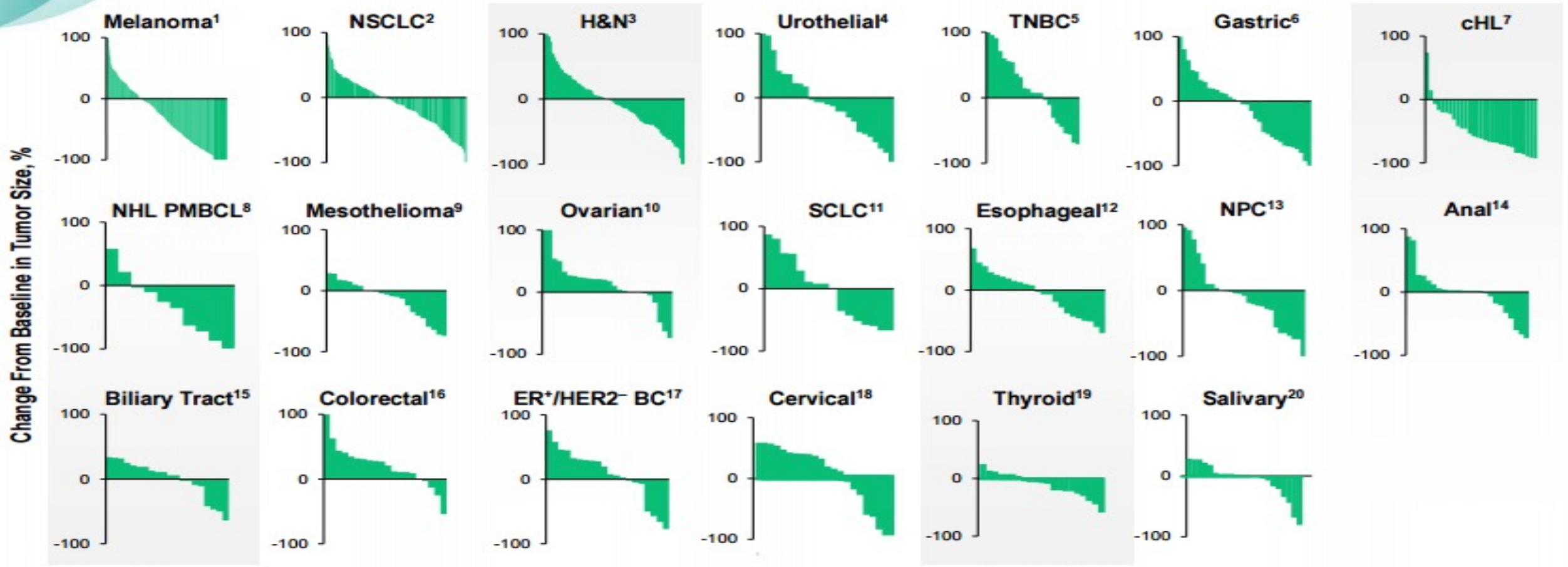
are protected

by anti-PD1



S. Ugurel et al. / European Journal of Cancer 130 (2020) 126–138

Anti-PD1 demonstrates broad antitumor activity
Approvals in > 20 tumor types



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

COMBINATION TRIALS WITH Anti-PD(L)-1

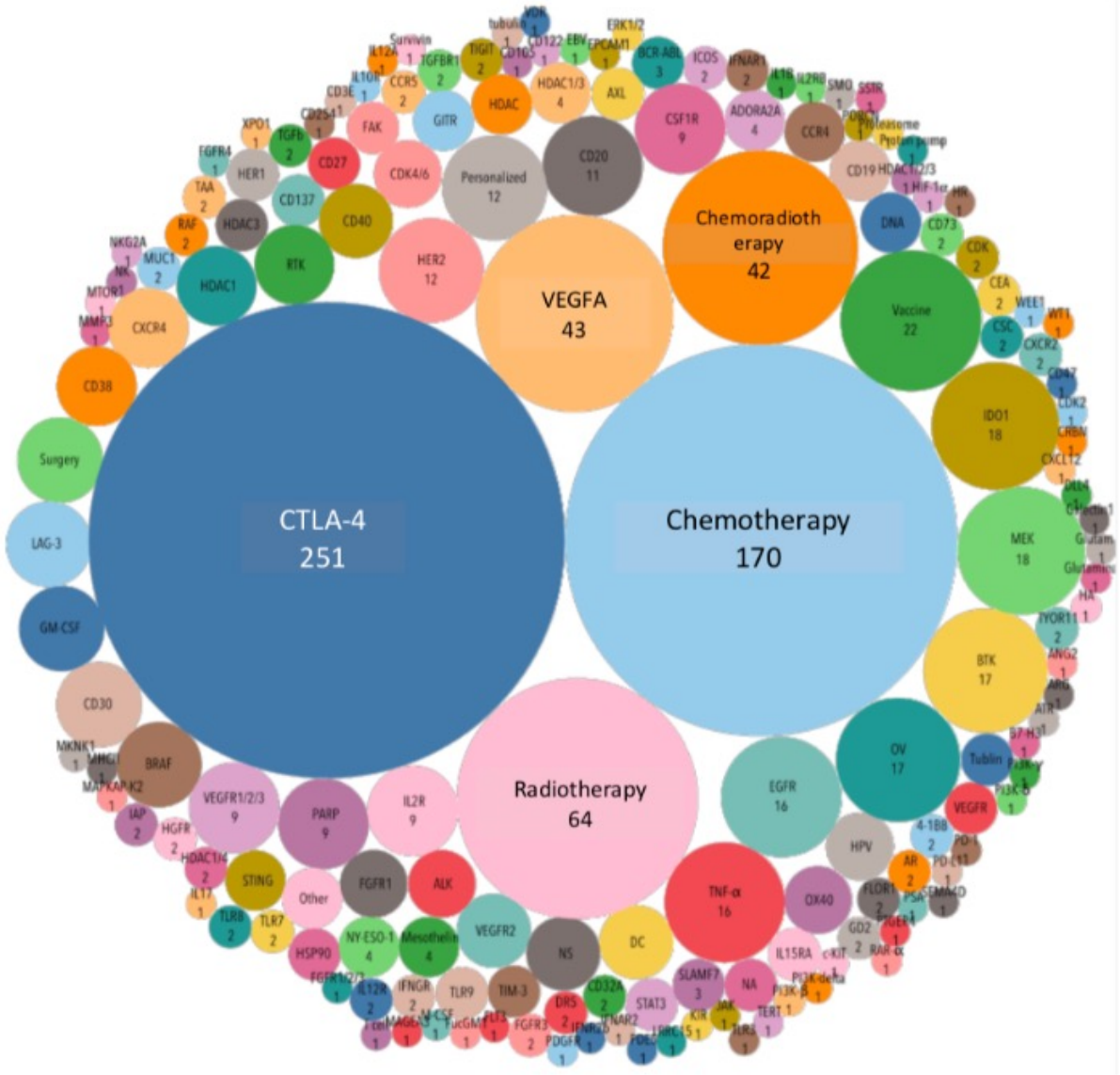
PD-1/L1 COMBO PARTNER ANALYSIS

165 DIFFERENT TARGETS ARE BEING COMBINED

Numbers of Trials Using Common Combo

Strategies:

1. Anti-CTLA-4 agents: 251
2. Chemotherapies: 170
3. Radiotherapies: 64
4. Anti-VEGFA agents: 43
5. Chemoradiotherapy combos: 42



The New Adjuvant Therapy Era results similar to those in advanced melanoma

THE OLD AND NEW ERA
Approved drugs for the adjuvant therapy of stage III melanoma

Old Era (1996–2011)

- High-Dose Interferon (IFN)-α2b (US, EU), Low-Dose IFN-α2a (EU), pegylated IFN-α2b (US)[1]

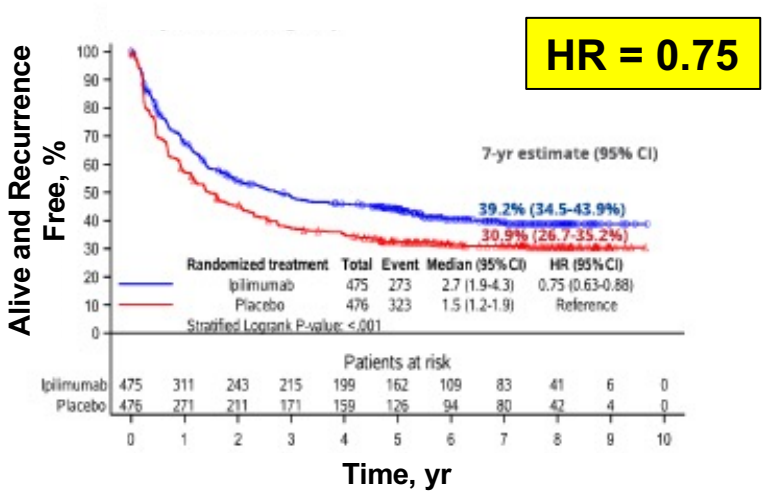
New Era (2015–2018)

		HR	Stage	FDA/EMA
Ipilimumab (US)[2,3,4]	HR_{RFS}(Ipilimumab vs. Placebo)=**0.75**		III	(2015)
Nivolumab[5,6]	HR_{RFS}(Nivolumab vs. **Ipilimumab**)=**0.65**	± 0.50	IIIB/IV	(2017)
Dabrafenib plus Trametinib[7,8]	HR_{RFS}(Dab+Tra vs. Placebo)=**0.47**	± 0.50	III	(2018)
Pembrolizumab[9,10,11]	HR_{RFS}(Pembrolizumab vs. Placebo)=**0.57**	± 0.50	III	(2018)

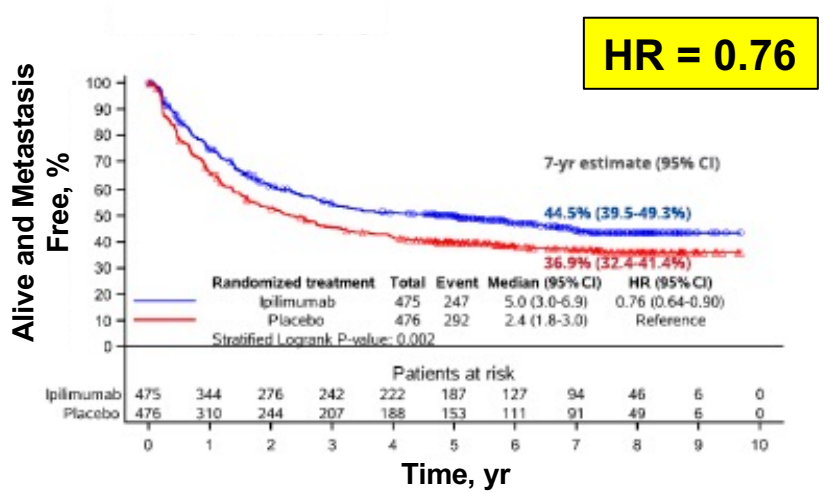
[1]Eggermont AM, et al. *Lancet* 2014;383:816-27;
[2]Eggermont AM, et al. *Lancet Oncology* 2015;16:522-30 ; [3]Eggermont AM, et al. *NEJM 2016; 375: 1845-55* [4;] Eggermont AM, et al. *Eur J Cancer 2019;119:1-10*
[5]Weber J, et al. *NEJM* 2017;377:1824-35; [6]Ascierto, PA et al. *Lancet Oncology* 2020; 21:1465-1477
[7]Long GV, et al. *NEJM* 2017;377:1813-23; [8]Dummer R et al. *NEJM* 2020;383:1139-1148
[9]Eggermont AM, et al. *NEJM* 2018;379:1879-1891; [10]Eggermont AM, et al. *JCO* 2020;38:3925-3936; [11]Eggermont AM, et al. *Lancet Oncology* 2021;22:643-654

EORTC 18071 (Ipilimumab vs Placebo) Long-Term *RFS = DMFS = OS IMPACT*[1]

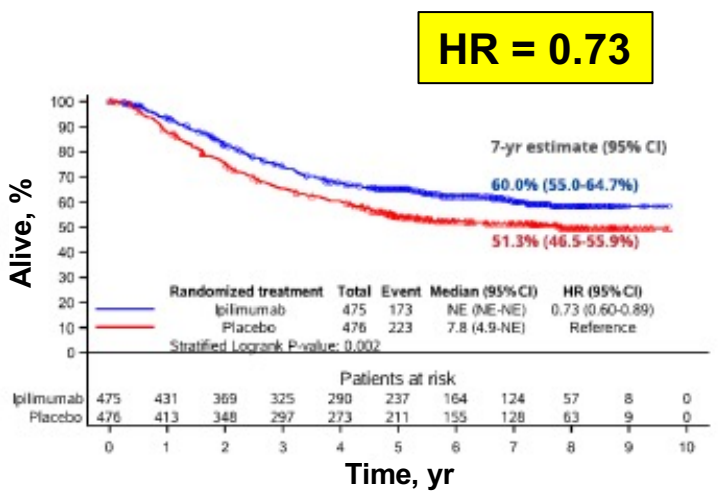
RFS by Treatment Group



DMFS by Treatment Group



OS by Treatment Group

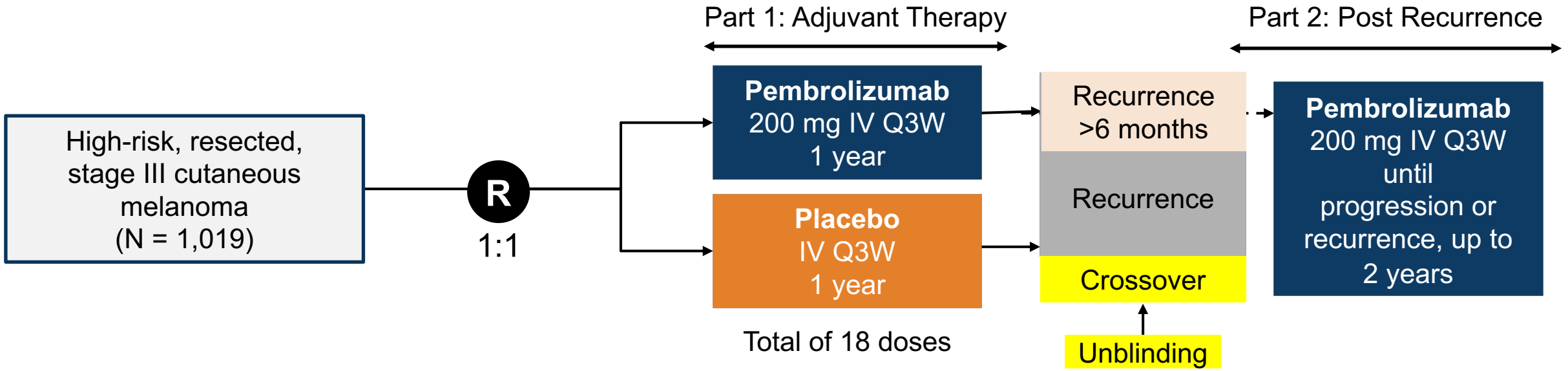


Problem:
Ipilimumab 10mg/Kg Toxicity!
54% Discontinuation for irAEs

All benefit seems achieved in first 4 doses, no proof of need for maintenance therapy

1. Eggermont AMM et al. *Eur J Cancer.* 2019;199:1-10.

EORTC 1325/KEYNOTE-054 Study Design[1]



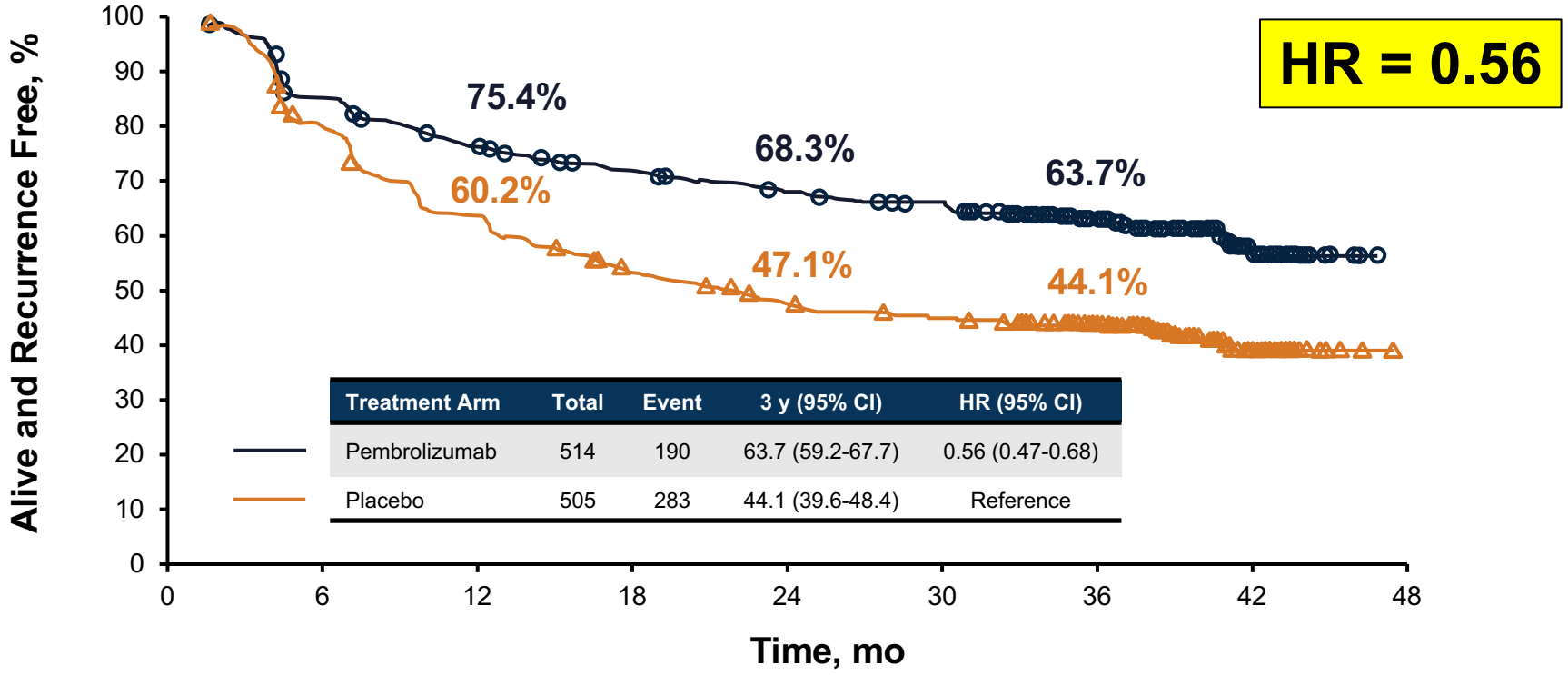
Unblinding/crossover: anti–PD-1 for all, or just as good if only for those at time of recurrence?

- **Stratification factors:** stage: IIIA (>1-mm metastasis) vs IIIB vs IIIC 1-3 positive lymph nodes vs IIIC ≥4 positive lymph nodes; region: North America, European countries, Australia/New Zealand, and other countries
- **Primary endpoints:** RFS (per investigator) in overall (ITT) population, RFS in patients with PD-L1–positive tumors
- **Secondary endpoints:** DMFS and OS in all patients and in patients with PD-L1–positive tumors, safety, and health-related quality of life

1. *Eggermont AM et al. NEJM 2018;379:1879-1891; Eggermont AM, et al. JCO 2020;38:3925-3936; Eggermont AM, et al. Lancet Oncology 2021;22:643-654*

EORTC 1325/KEYNOTE-054: New RFS Analysis @ 3yrs mFU[1]

Cutoff date (September 30, 2019): duration of follow-up = median 3 years; 473 RFS events



Treatment Arm	Total	Event	3 y (95% CI)	HR (95% CI)
Pembrolizumab	514	190	63.7 (59.2-67.7)	0.56 (0.47-0.68)
Placebo	505	283	44.1 (39.6-48.4)	Reference

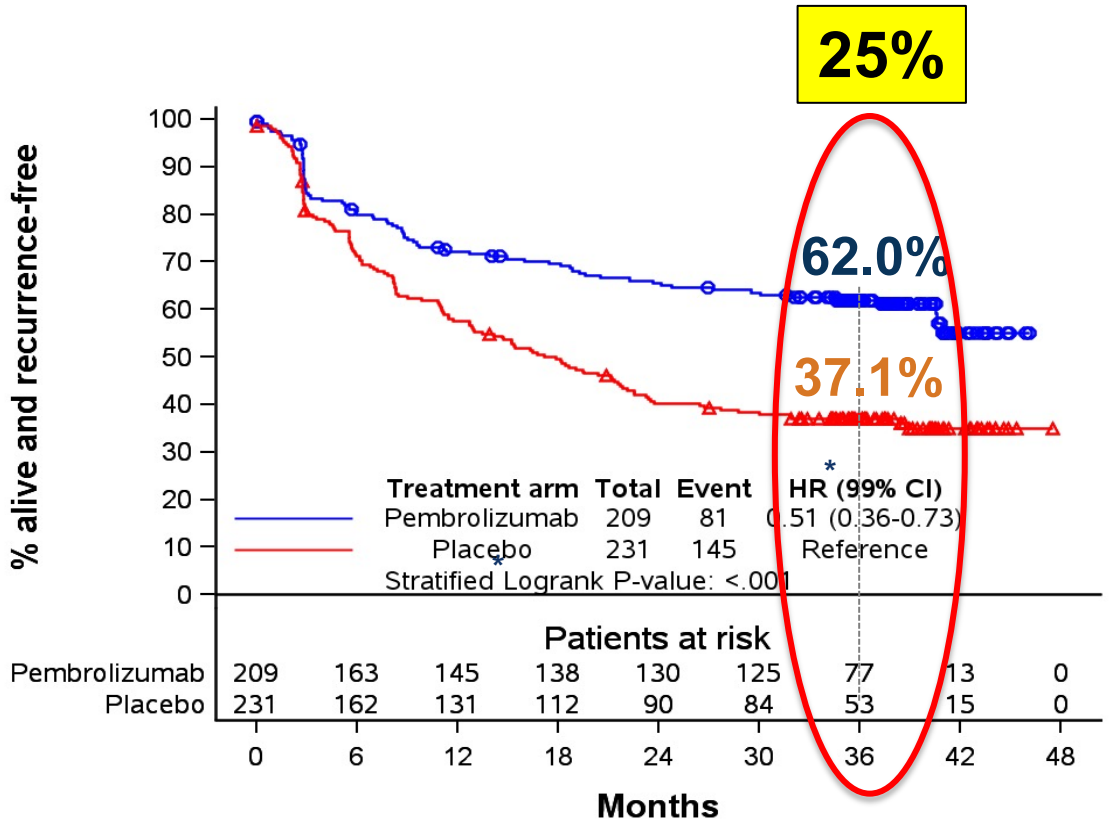
No. at Risk

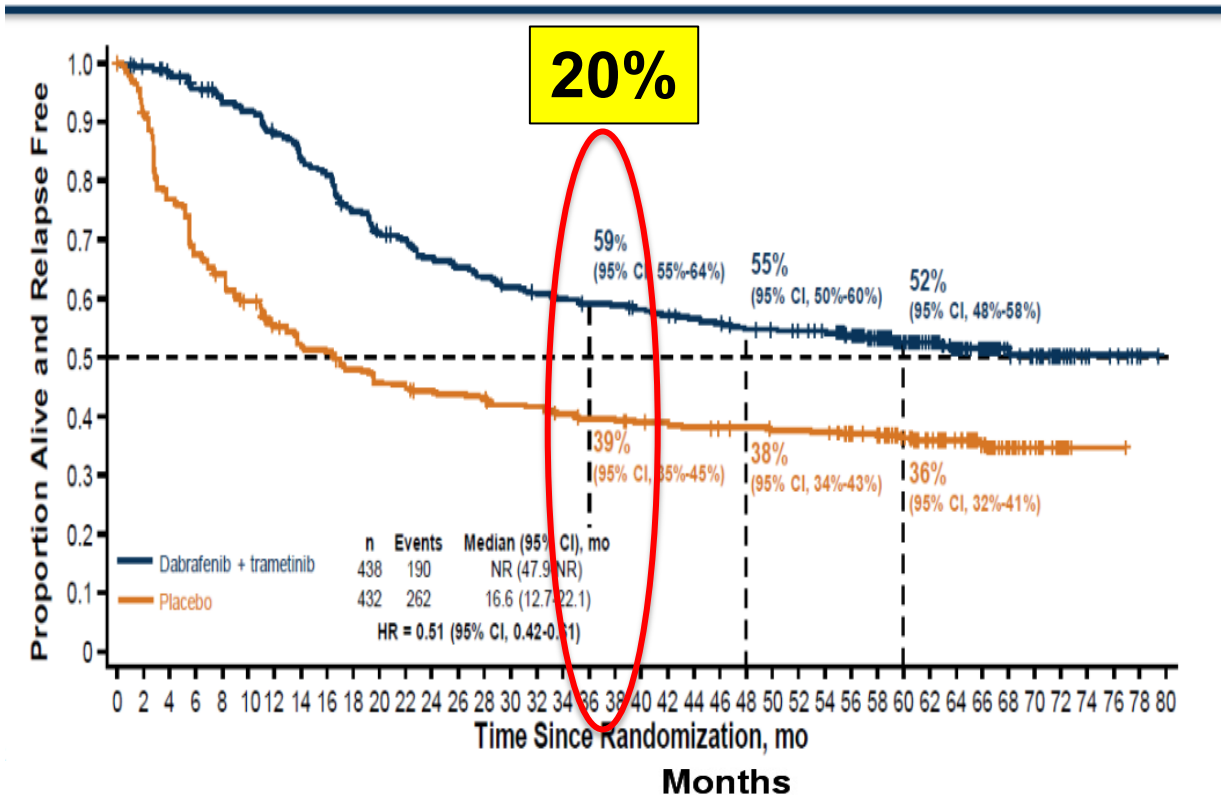
Pembrolizumab	514	412	374	351	333	314	189	29	0
Placebo	505	360	298	259	226	215	126	28	0

1. Eggermont AMM et al. *J Clin Oncol*. 2020;38:3925-3936.

RFS According to *BRAF* V600E/K Mutation Status[1]

***Pembrolizumab in BRAF* Mutated)**



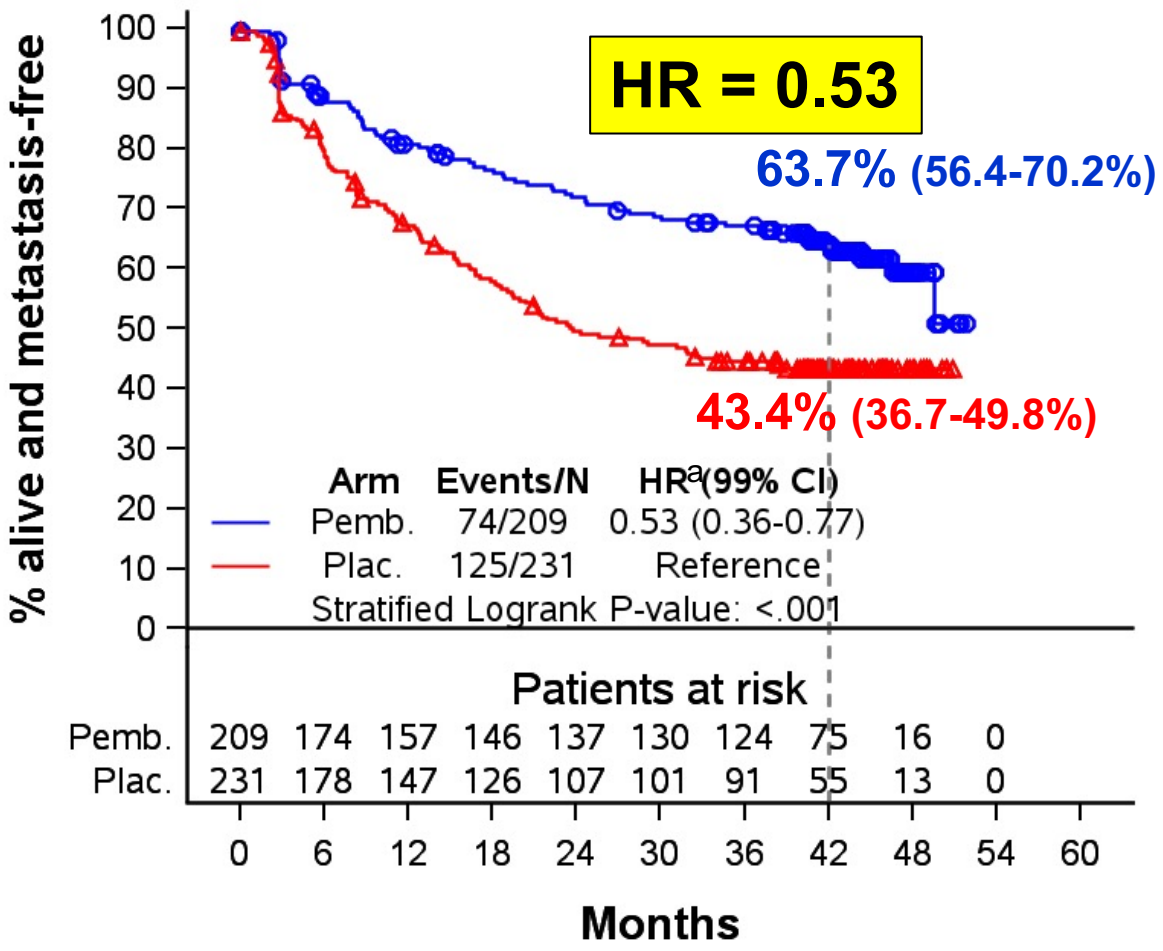


[a] Stratified by stage given at randomization.

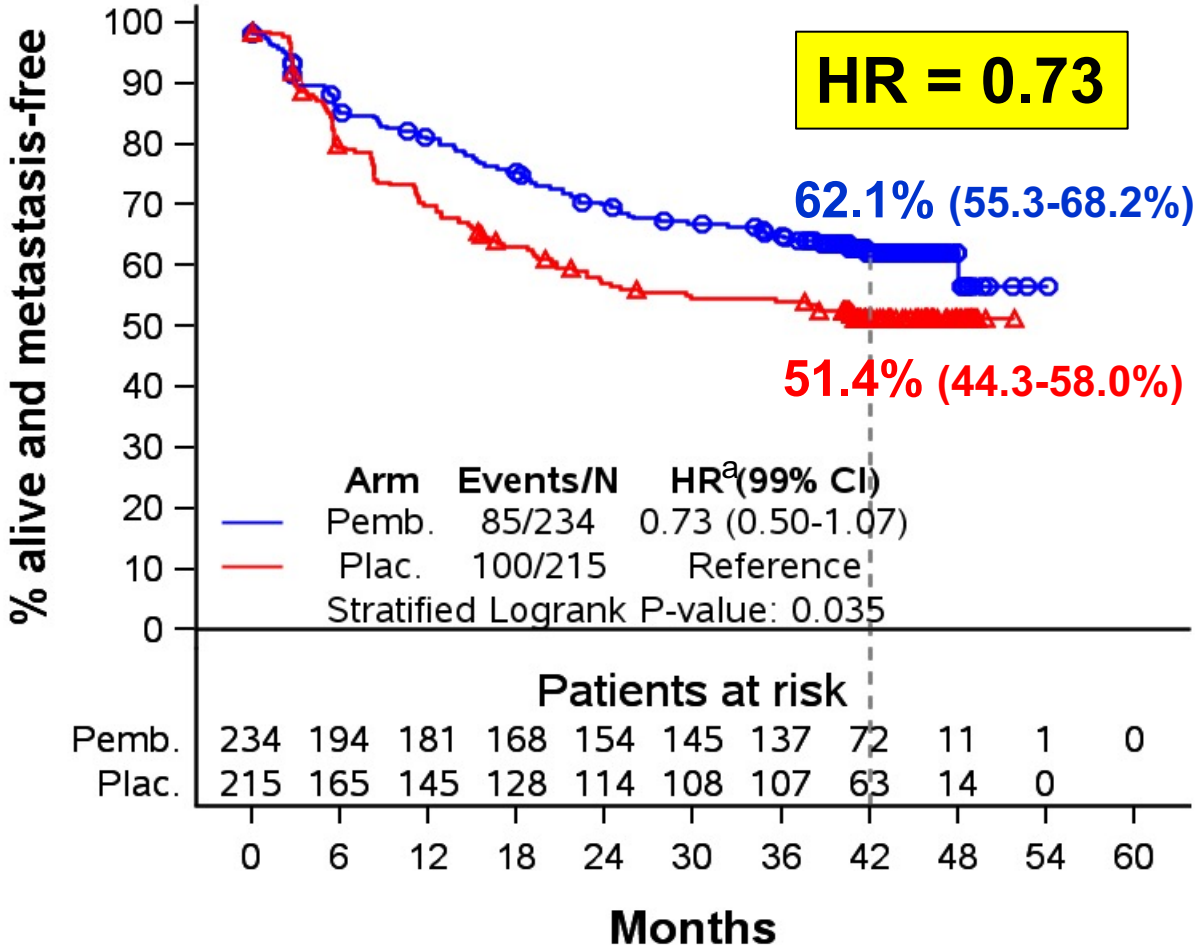
1. Eggermont AMM et al. *J Clin Oncol*. 2020;38:3925-3936.

DMFS According to *BRAF* V600E/K Mutation Status[1]

BRAF Mutated (n = 440)



BRAF WT (n = 448)



[a] Stratified by stage given at randomization.

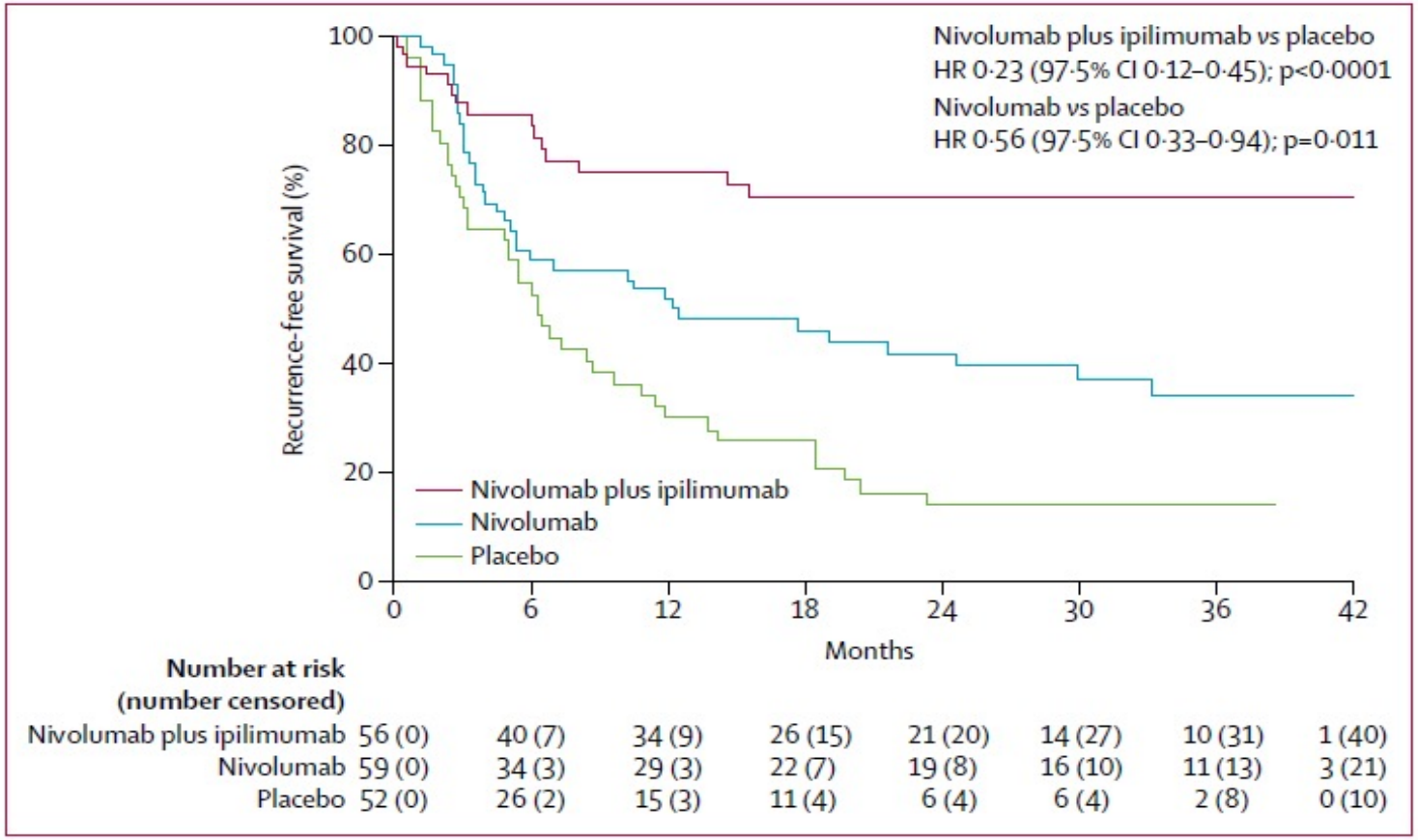
1. Eggermont AMM et al. ESMO 2020. Abstract LBA46. *Lancet Oncol.* 2021. April

CheckMate-915: Adjuvant Nivo/Ipi vs Nivo in III B/C–IV
IMMUNED : Nivo+Ipi vs Nivo vs PB in resected IV

IMMUNED TRIAL

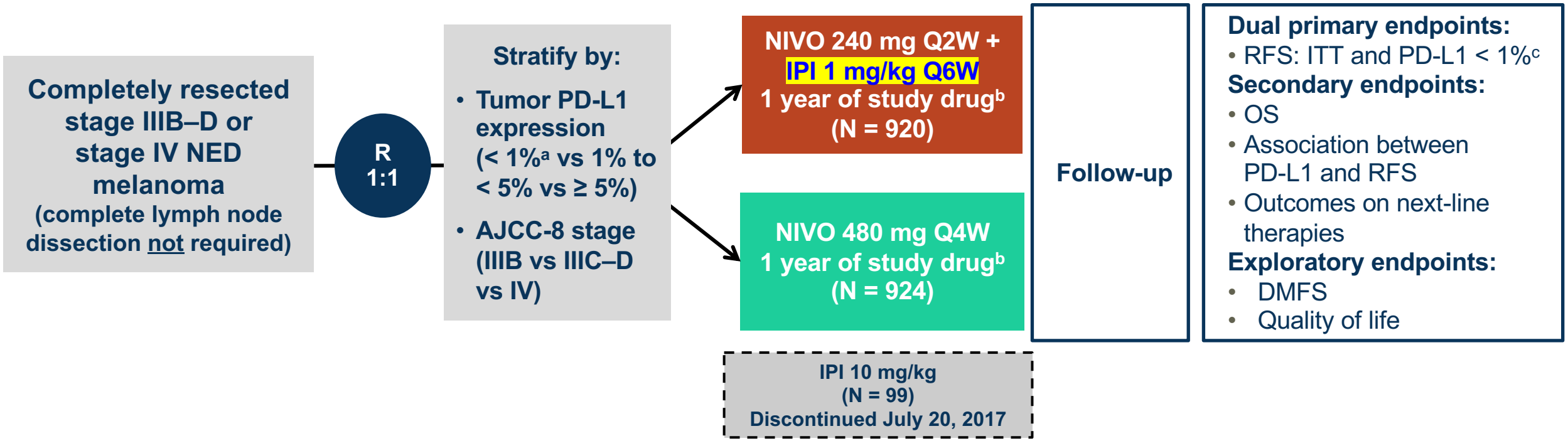
IMMUNED TRIAL (167 pts) : Positive

- **Nivo 1mg + Ipi 3mg (Q3wk)**
  vs Nivo 3mg vs Placebo[2]
- Lancet May 2020
  - Positive randomized phase II in resected stage IV[2]



1. https://clinicaltrials.gov/ct2/show/NCT03068455. 2. Zimmer L et al. *Lancet.* 2020;395:1558-1568.

CheckMate 915 study design (2000 PTS)



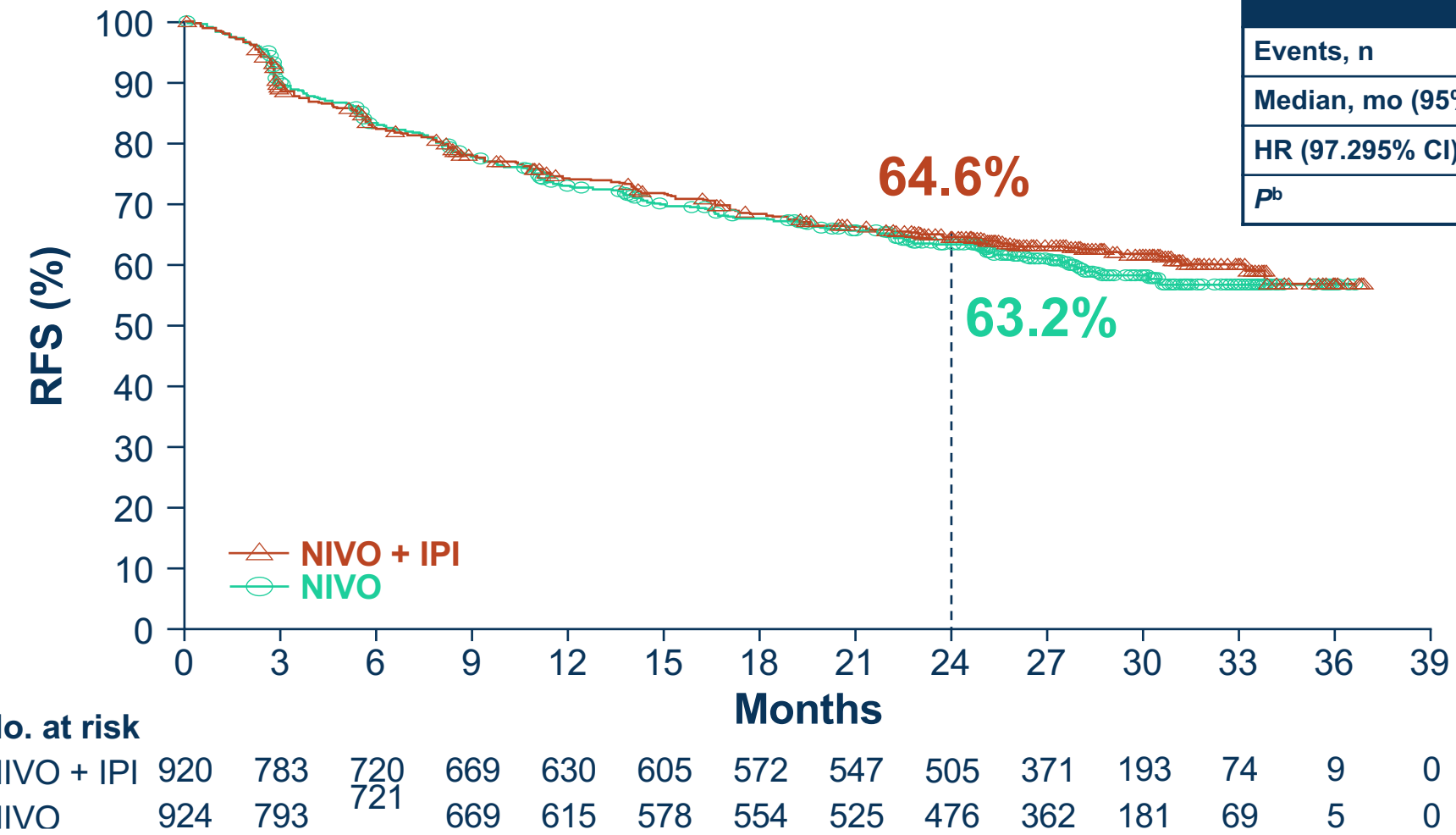
COMMENT: IPI 1 mg/kg Q6W is 6x lower dosing of IPI than 3mg/kg Q3W !!!

Moreover: No proof of benefit maintenance IPI (placing the wrong bet…..)

[a]Or indeterminate; [b]Until recurrence, unacceptable toxicity, or 1 year of treatment; [c]In November 2019, the data monitoring committee indicated that the dual primary endpoint of RFS in patients with tumor PD-L1 < 1% was not met; the study remained blinded until the ITT endpoint was evaluable. AJCC, American Joint Committee on Cancer; DMFS, distant meta free survival; NED, no evidence of disease; PD-L1, programmed death-ligand 1.

Checkmate 915
Dual primary endpoint: RFS in ITT population

	NIVO + IPI (n = 920)	NIVO (n = 924)
Events, n	327	347
Median, mo (95% CI)	NR	NR
HR (97.295% CI)[a]	0.92 (0.77–1.09)	
P[b]	0.269	



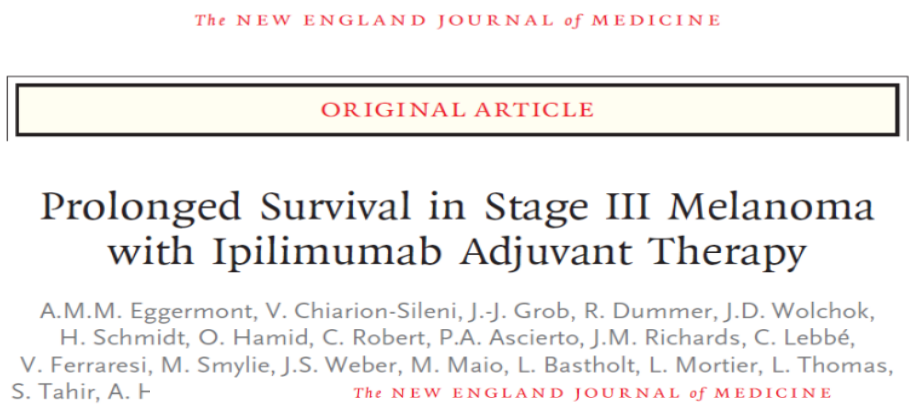
Adjuvant ICI-based Therapies

MELANOMA

- **Ipilimumab** **2015**
- **Nivolumab** **2017**
- **Pembrolizumab** **2018**

Anti-PD(L1) based: from 2019 onwards

- **RENAL CELL CANCER**
- **BLADDER CANCER**
- **NSCLC CANCER**
- **ESOPHAGEAL @ GEJ CANCER**
- **Pending:**
  - **cutSCC**
  - **Merkel Cell**
  - **MSI tumors**
  - **HCC**
  - **……**

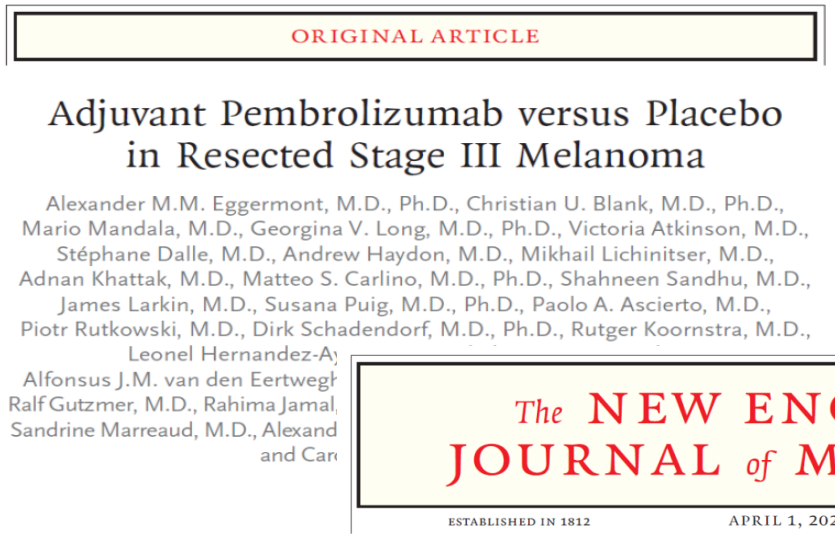

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prolonged Survival in Stage III Melanoma with Ipilimumab Adjuvant Therapy

A.M.M. Eggermont, V. Chiarion-Sileni, J.-J. Grob, R. Dummer, J.D. Wolchok, H. Schmidt, O. Hamid, C. Robert, P.A. Ascierto, J.M. Richards, C. Lebbé, V. Ferraresi, M. Smylie, J.S. Weber, M. Maio, L. Bastholt, L. Mortier, L. Thomas, S. Tahir, A. H

The NEW ENGLAND JOURNAL of MEDICINE


ORIGINAL ARTICLE

Adjuvant Pembrolizumab versus Placebo in Resected Stage III Melanoma

Alexander M.M. Eggermont, M.D., Ph.D., Christian U. Blank, M.D., Ph.D., Mario Mandala, M.D., Georgina V. Long, M.D., Ph.D., Victoria Atkinson, M.D., Stéphane Dalle, M.D., Andrew Haydon, M.D., Mikhail Lichinitser, M.D., Adnan Khattak, M.D., Matteo S. Carlino, M.D., Ph.D., Shahneen Sandhu, M.D., James Larkin, M.D., Susana Puig, M.D., Ph.D., Paolo A. Ascierto, M.D., Piotr Rutkowski, M.D., Dirk Schadendorf, M.D., Ph.D., Rutger Koornstra, M.D., Leonel Hernandez-A
Alfonsus J.M. van den Eertwegh
Ralf Gutzmer, M.D., Rahima Jamal,
Sandrine Marreaud, M.D., Alexand
and Car

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 1, 2021 VOL. 384 NO. 13

Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer

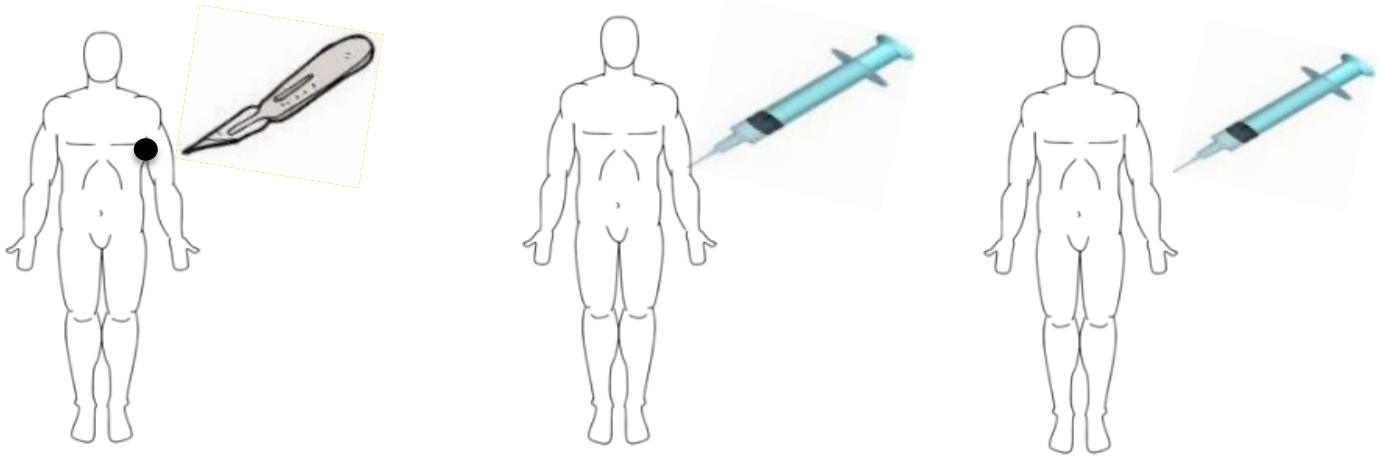
R.J. Kelly, J.A. Ajani, J. Kuzdzal, T. Zander, E. Van Cutsem, G. Piessen, G. Mendez, J. Feliciano, S. Motoyama, A. Lièvre, H. Uronis, E. Elimova, C. Grootscholten, K. Geboes, S. Zafar, S. Snow, A.H. Ko, K. Feeney, M. Schenker, P. Kocon, J. Zhang, L. Zhu, M. Lei, P. Singh, K. Kondo, J.M. Cleary, and M. Moehler, for the CheckMate 577 Investigators*

NEOADJUVANT IMMUNOTHERAPY REVOLUTION

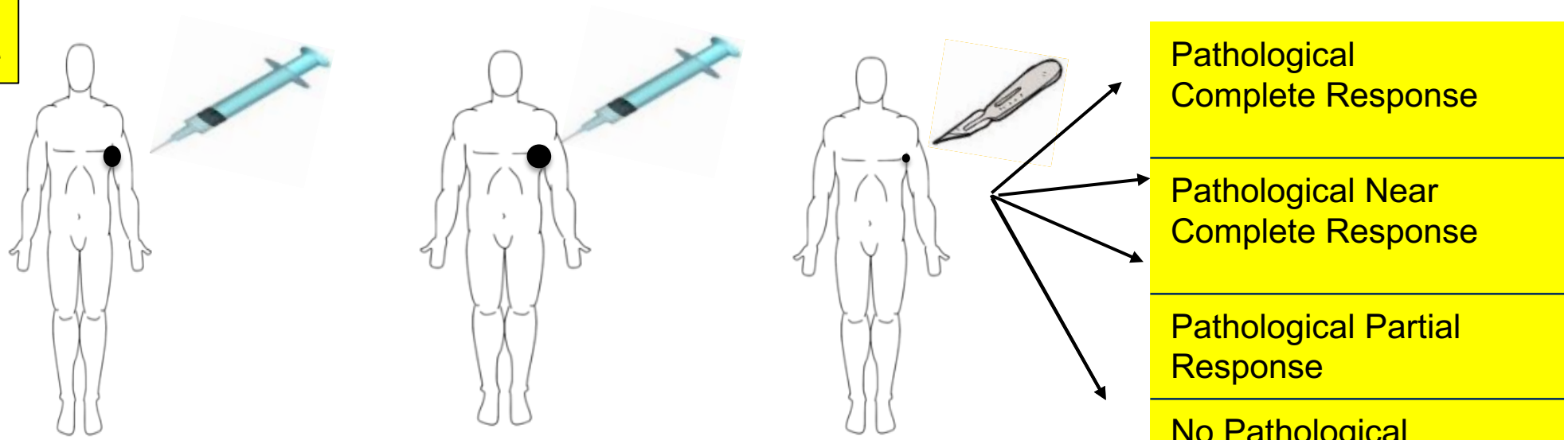
More Cures / Shorter TXs / Less Surgery

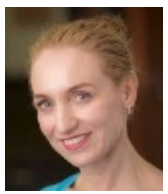
- Palpable/Macroscopic Stage III Melanoma
- Resectable Stage IV Melanoma
- MSI ColoRectal Cancer
- T3 Bladder Cancer
- Locally advanced CSCC
- Multiple other trials (Lung, H&N,GEJ,TNB,GBM)

Adjuvant



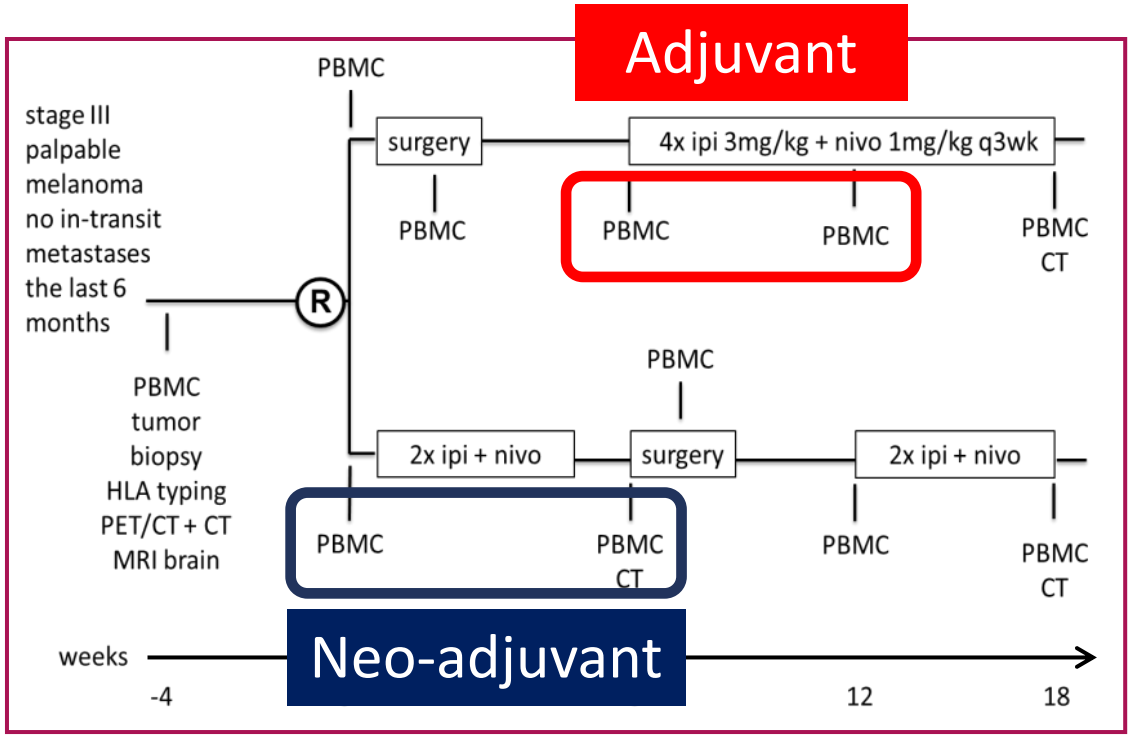
NeoAdjuvant

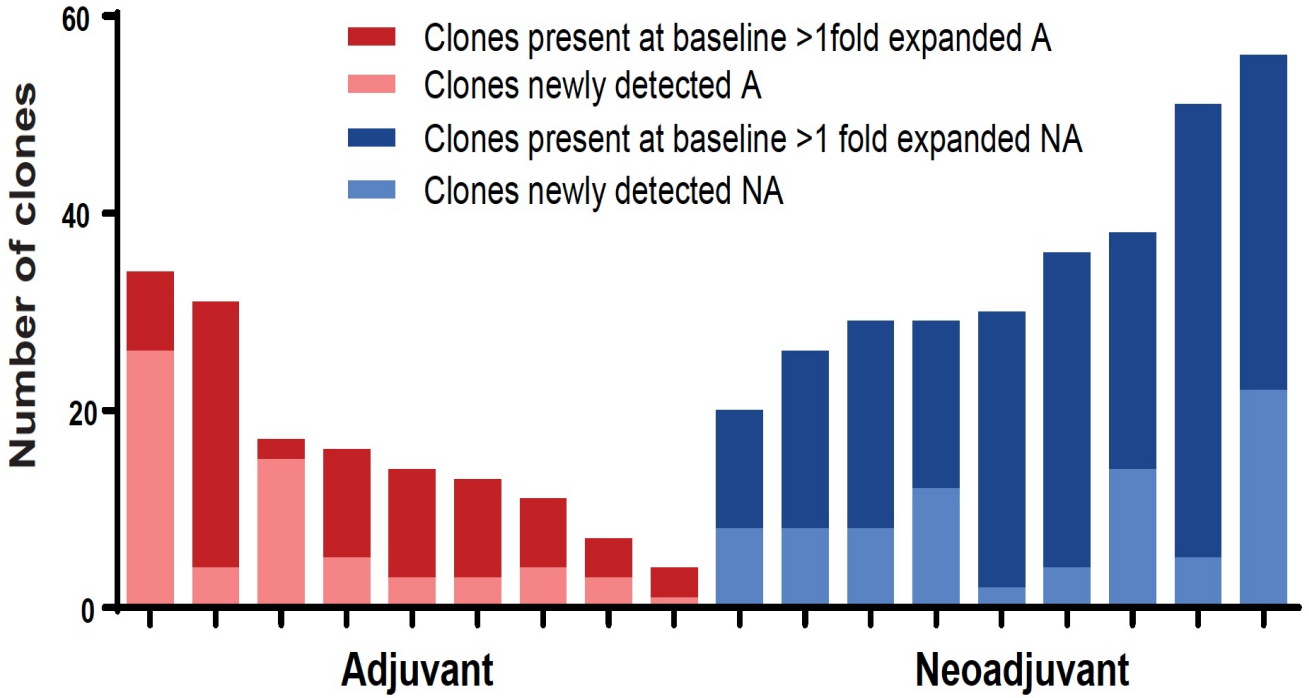




OpACIN trial –neoadjuvant versus adjuvant IPI + NIVO checkpoint inhibition

Palpable Stage III Melanoma Patients

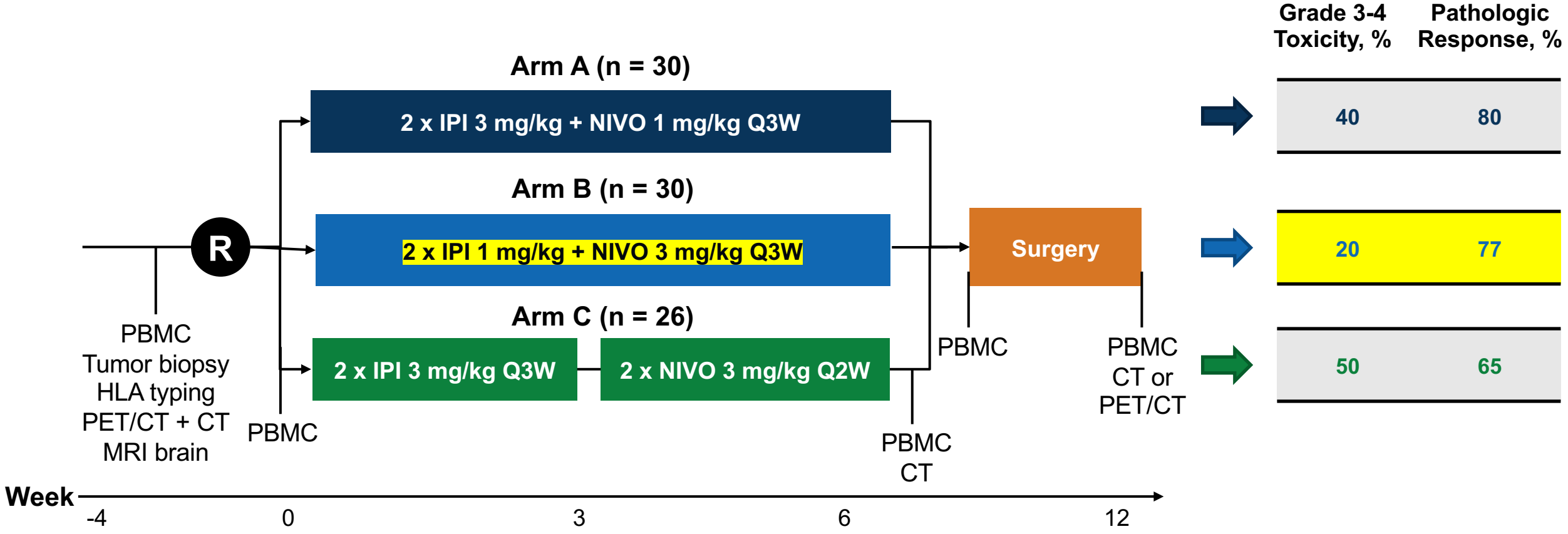




Christian BLANK &
Ton SCHUMACHER

Blank et al., Nat Med 2018

The OpACIN-neo Study Identified Neoadjuvant IPI 1 mg/kg + NIVO 3 mg/kg as the Optimal Treatment Scheme[1]

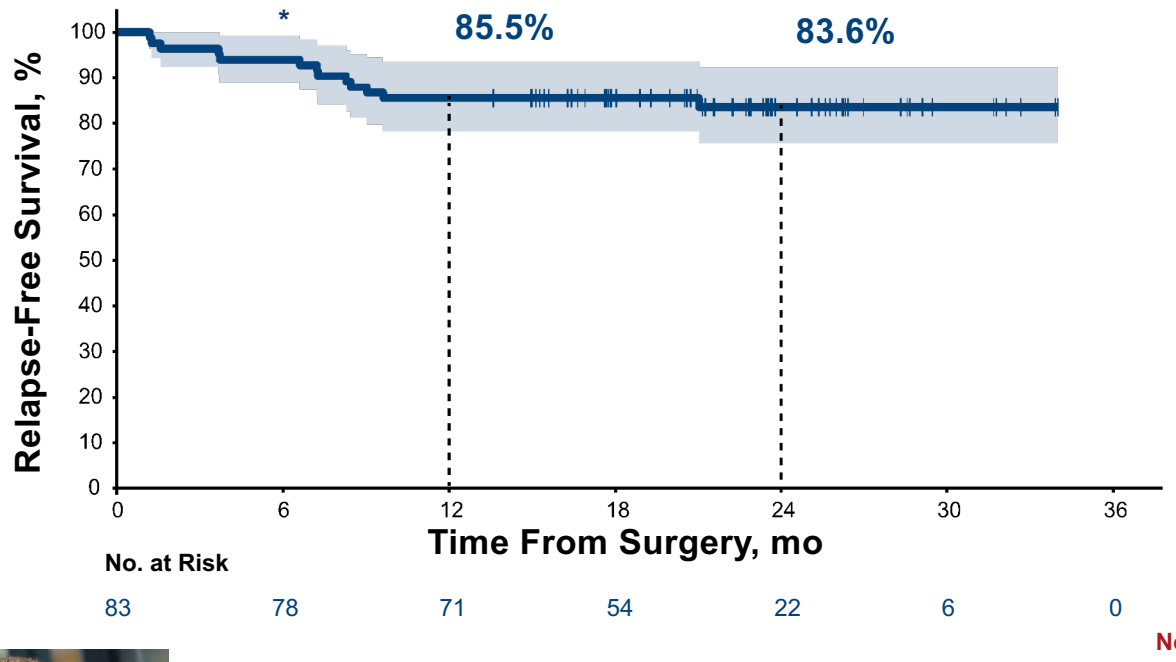


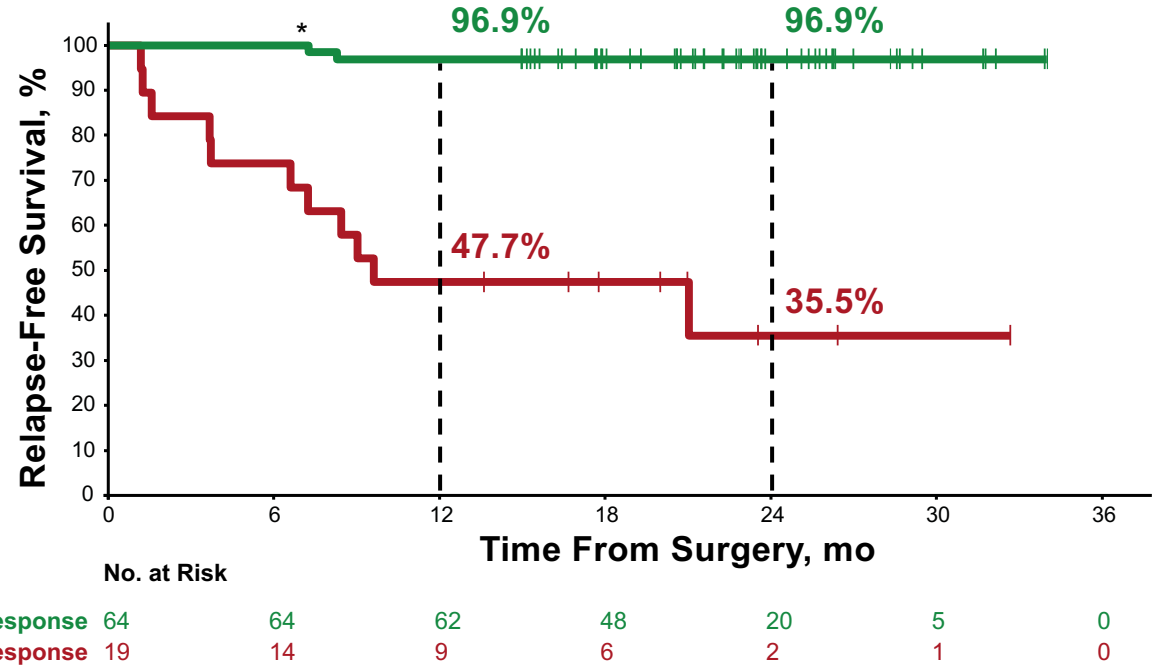
Christian BLANK

1. Rozeman EA et al. *Lancet Oncol*. 2019;20:948-960.

OpACIN-neo": RFS After 2 Years Follow-Up and Pathologic Response Predicts Outcome[1]

- OpACIN-neo: after a median follow-up of 24.6 months, only 1/64 (2%) patient with pathologic response has relapsed





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Rozeman et al., ASCO 2020
Rozeman et al., Nat Med 2021

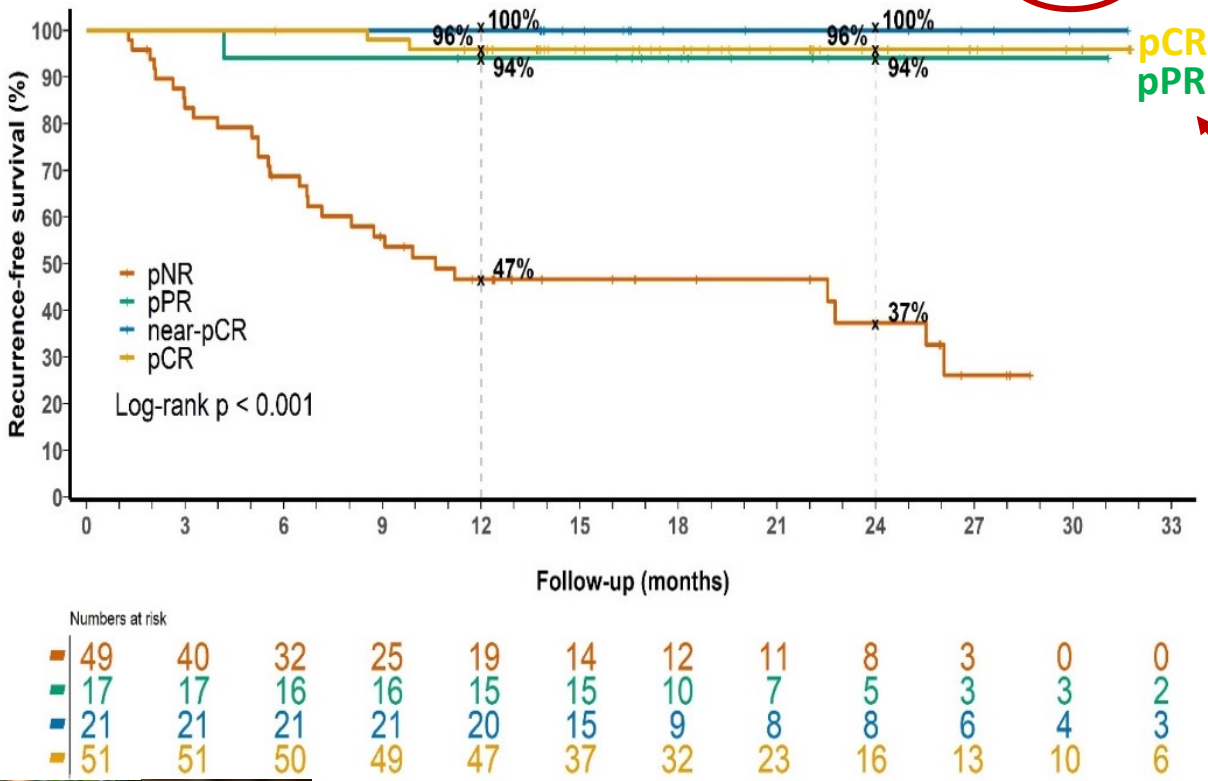
Pooled Analysis: Neoadjuvant Therapy in Stage III Melanoma

RFS by Pathological Response : SUPERIORITY IMMUNOTHERAPY

IMMUNOTHERAPY

Anti-PD1 pCR = 20%

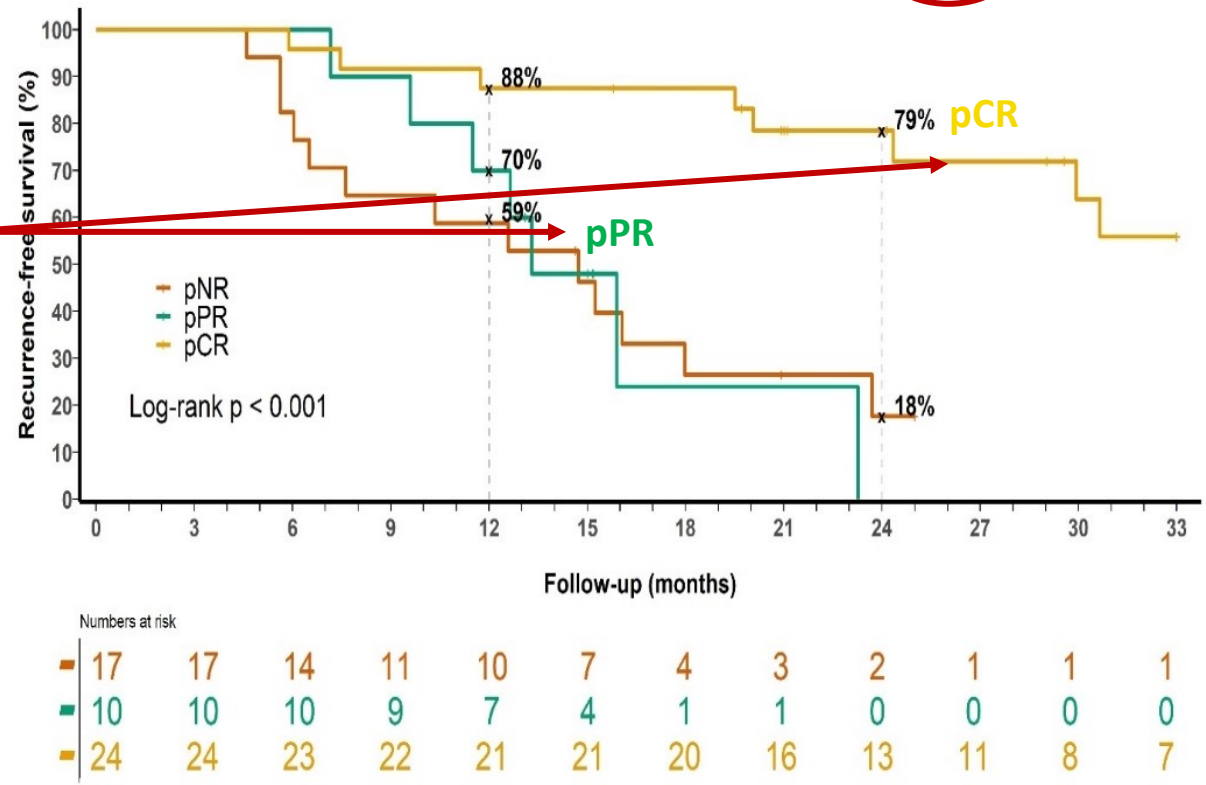
Anti-PD1 + Anti-CTLA4 pCR = 43%



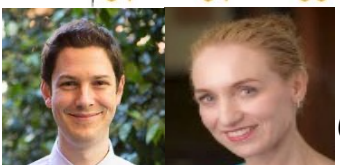
Med f/u 19.3 mo

Targeted Therapy

Dabrafenib + Trametinib pCR = 47%



Med f/u 25.9 mo



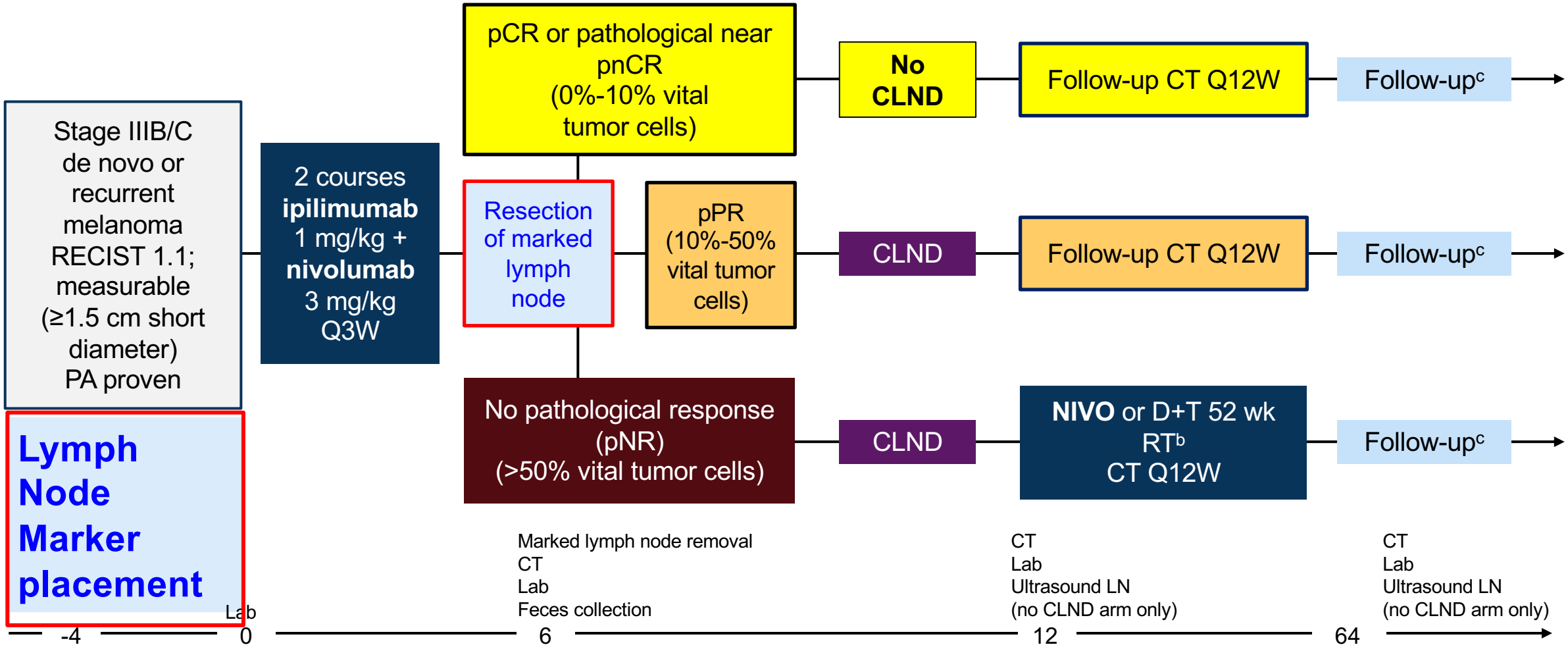
@ProfGLongMIA

Alexander Menzies et al Nat Med 2021

ASCO 2020: PRADO (The First 99 Patients)[1]

NEOADJUVANT IPI+NIVO TO REDUCE TLND RATES

Personalized Response-Driven Adjuvant Therapy After Combination of Ipilimumab and Nivolumab in Stage IIIB/C Melanoma



[a] BRAF + MEK inhibition in *BRAF* V600E/K patients is allowed according to patient's and treating physician's decision when available. [b] Adjuvant radiotherapy according to patient's and physician's decision. [c] According to institute's standard.

1. Blank CU et al. ASCO 2020. Abstract 10002.

Objectives and Results of PRADO Extension Cohort[1]

- PRADO **confirms path response rate and safety** with ipilimumab 1 mg/kg + nivolumab 3 mg/kg
  - **Pathologic response rate: 71%**
  - **Grade 3-4 irAE rate: 22% in the first 12 weeks**

- **TLND was omitted in 59 (60%) patients!**

Christian BLANK

1. Blank CU et al. ASCO 2020. Abstract 10002.

Neo-Adjuvant IO in BLADDER Cancer

Neoadjuvant immunotherapy for muscle invasive urothelial bladder carcinoma: will it change current standards?

Alex Renner, Mauricio Burotto, Jose Miguel Valdes, Juan Carlos Roman and Annerleim Walton-Diaz

Therapeutic Advances in Urology 13

Table 1. Overview of drug activity in the neoadjuvant setting for UC.

Study	Drug	Design	Patients	cTNM stage	cT2 (%)	cN+ (%)	pCR (%)	AE G3–4 (%)
PURE-01[17]	Pembrolizumab	Prospective phase II	50	T2-T3 N0-1 M0	42	4	41	6
ABACUS[18]	Atezolizumab	Prospective phase II	95	T2-T4 N0 M0	74	0	31	11
NABUCCO[19]	Nivolumab + Ipilimumab	Prospective phase II	24	T2-4a N1-3 M0	N/A	42	46	55
HCRN GU14-188[20]	GC + Pembrolizumab	Prospective phase Ib/II	43	T2-T4a N0 M0	43	0	44	30
BLASST-1[21]	GC + Nivolumab	Prospective Phase II	41	T2-T4a N0-1 M0	90	3	49	20
SWOG 8710 (INT-0080)[15]	MVAC	Prospective phase III	153	T2-T4a N0 M0	40	0	38	72
Zargar *et al.*[16]	MVAC	Retrospective	183	T2-T4a N0 M0	50	0	25	N/A
Zargar *et al.*[16]	GC	Retrospective	602	T2-T4a N0 M0	69	0	24	N/A

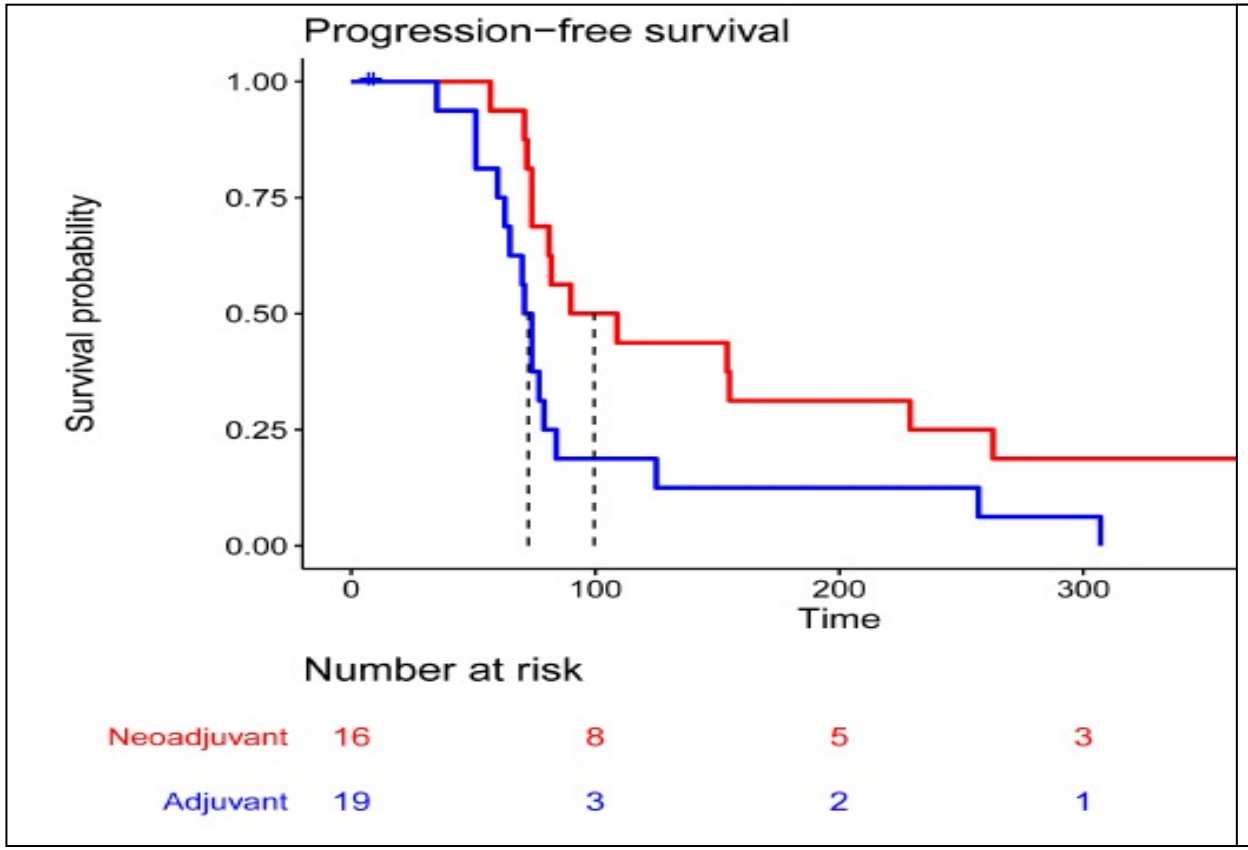
AE, adverse events; GC, gemcitabine plus cisplatin; MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin; N/A, not available; TMN, tumour, node, metastasis; UC, urothelial carcinoma.

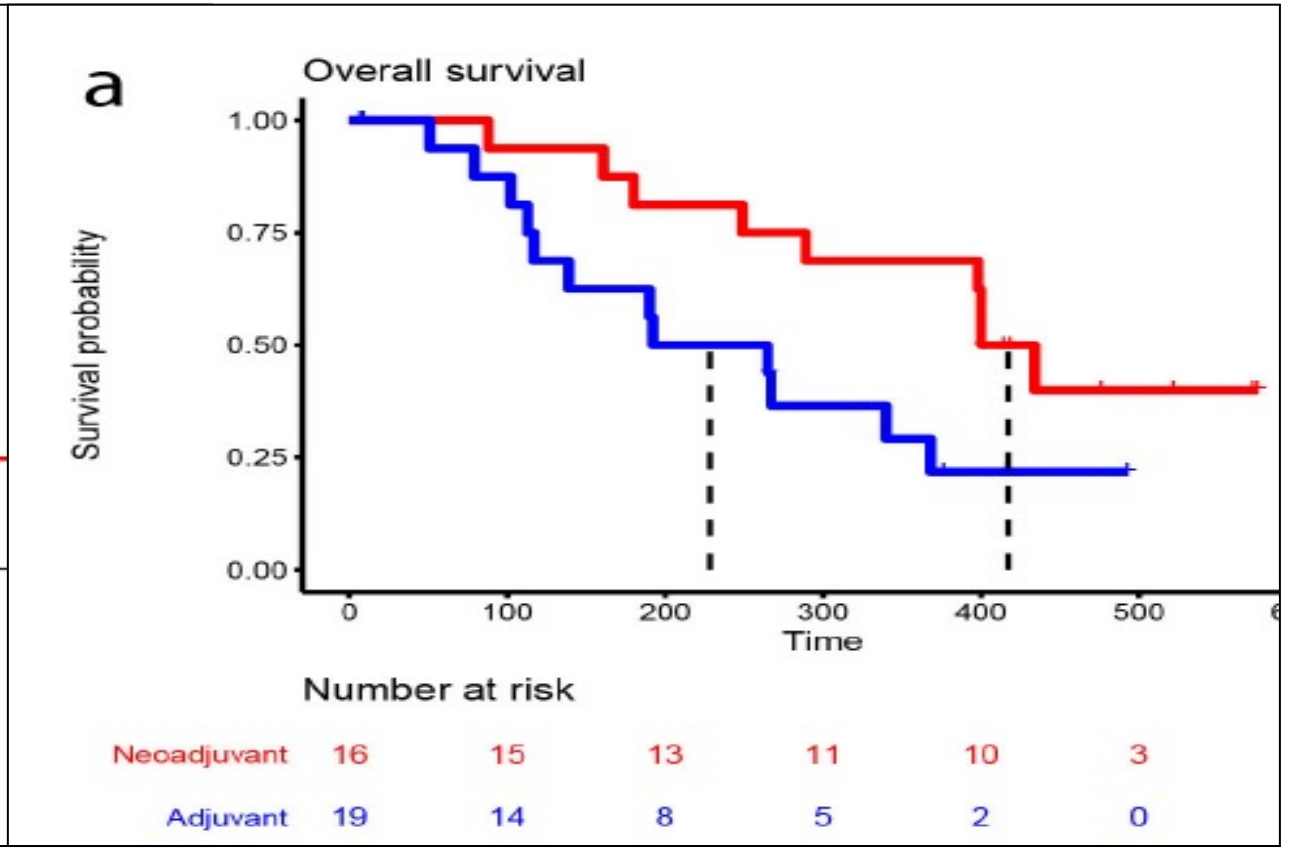
Neo-Adjuvant IO in COLORECTAL MSI

19/20 pCR for MSI CRC!
(Haanen et al. *Nature Medicine.* 2020)

In Future in case of pCR:
NO more (rectal) surgery, but endoscopy + MRI !

Impact of Only 1 Dose Neo-Adjuvant Anti-PD1 for Recurrent GBM





Median PFS: 72.5 – 99.5 days
HR: 0.43; P2 =0.03

Median OS: 228.5 days – 417 days
HR: 0.39; P2 = 0.04

NEOADJUVANT IMMUNOTHERAPY WILL BE #1 TOPIC IN THE NEXT 5 YEARS: *More Cures—Less Surgery!*

MELANOMA palpable lymph nodes

- Nivolumab 3 + ipilimumab 1: 70% pathologic CR!
- **No more TLND in >50%** of patients with palpable nodes in 5 years

BLADDER CANCER

- 40-50% pCR for T3 bladder cancers: wait and see
- **Reduction cystectomies**

MSI COLORECTAL CANCER

- **19/20 pCR for MSI CRC! (Haanen et al. *Nature Medicine.* 2020)**
- **In Future in case of pCR: NO more (rectal) surgery, but endoscopy + MRI**

LUNG, HEAD and NECK, ESOPHAGEAL and GASTRIC, BREAST, GBM

Galectin-3 depletion is potentially a transversal potentiator across multiple indications

- **OPPORTUNITIES**

- **LUNG** in 1st Line: Atezolizumab vs Atezo+GAL-3inh
- **Gastric/GEJ** in 1st Line) Pembro = Pembr+chemo in 1L and so field is open for Pembro vs Pembro+GAL-3inh
- **Neoadjuvant Strategies: Colorectal liver mets, H&N, etc**
- **No toxicity means**: opportunities **TRIPLE IMMUNOCOMBO**
  - Melanoma, cSCC, Bladder etc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dkfz.
GERMAN CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

Thank You

Galectin-3-mediated regulation of the tumor microenvironment

William L. Redmond, PhD
Member and Director, Immune Monitoring Laboratory
Earle A. Chiles Research Institute, Providence Cancer Institute
@ChilesResearch @wwredmond4 *finishcancer.org*

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Disclosures

- Research grants
  - Bristol-Myers Squibb, Nektar Therapeutics, GlaxoSmithKline, Aeglea Biotherapeutics, Shimadzu, MiNA Therapeutics, Veana Therapeutics, OncoSec, Inhibrx, Galectin Therapeutics, Calibr, Turn Bio, CanWell Pharma
- Advisory boards/Consulting
  - Vesselon, Nektar Therapeutics, Galecto
- Licensing fees
  - Galectin Therapeutics

EARLE A. CHILES RESEARCH INSTITUTE

Outline

- Overview of galectins
- Galectin-3 (Gal-3) expression and function within the TME
- Therapeutic targeting of Gal-3
- Conclusions

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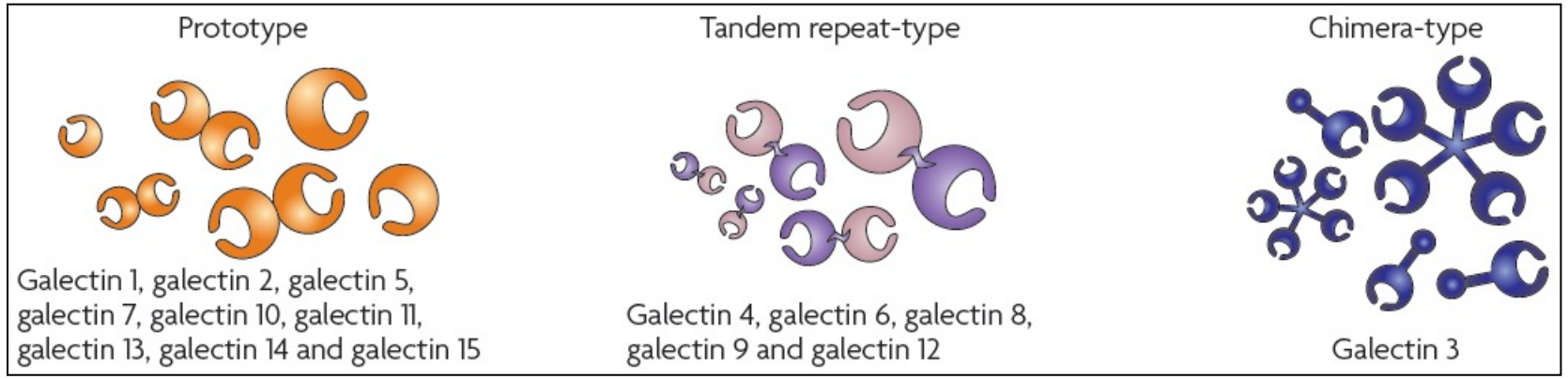
Galectins

- Members of the lectin family of glycan binding proteins
  - C-type lectins (mannose receptor, DEC-205, DC-SIGN, etc.)
  - Siglecs
  - Galectins
    - Carbohydrate binding proteins containing a shared carbohydrate recognition domain (CRD)
    - Affinity for N-acetyllactosamine-expressing proteins



Rabinovich G, *Nat Rev Immunol,* 2009

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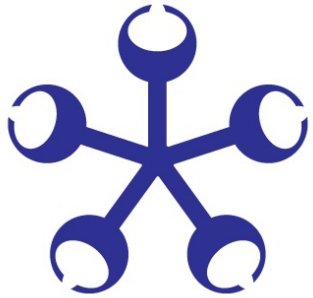
Galectin-3 (Gal-3)

- Structurally unique among the galectins
  - Forms oligomers through N-terminal domain
  - Oligomerization promotes receptor clustering, lattice formation, and intercellular interactions
- Expressed in numerous cells
- Involved in physiological and pathological processes: cell adhesion, cell activation, chemoattraction, cell cycle, apoptosis, cell growth, and differentiation

Gal-3 monomer



Gal-3 pentamer

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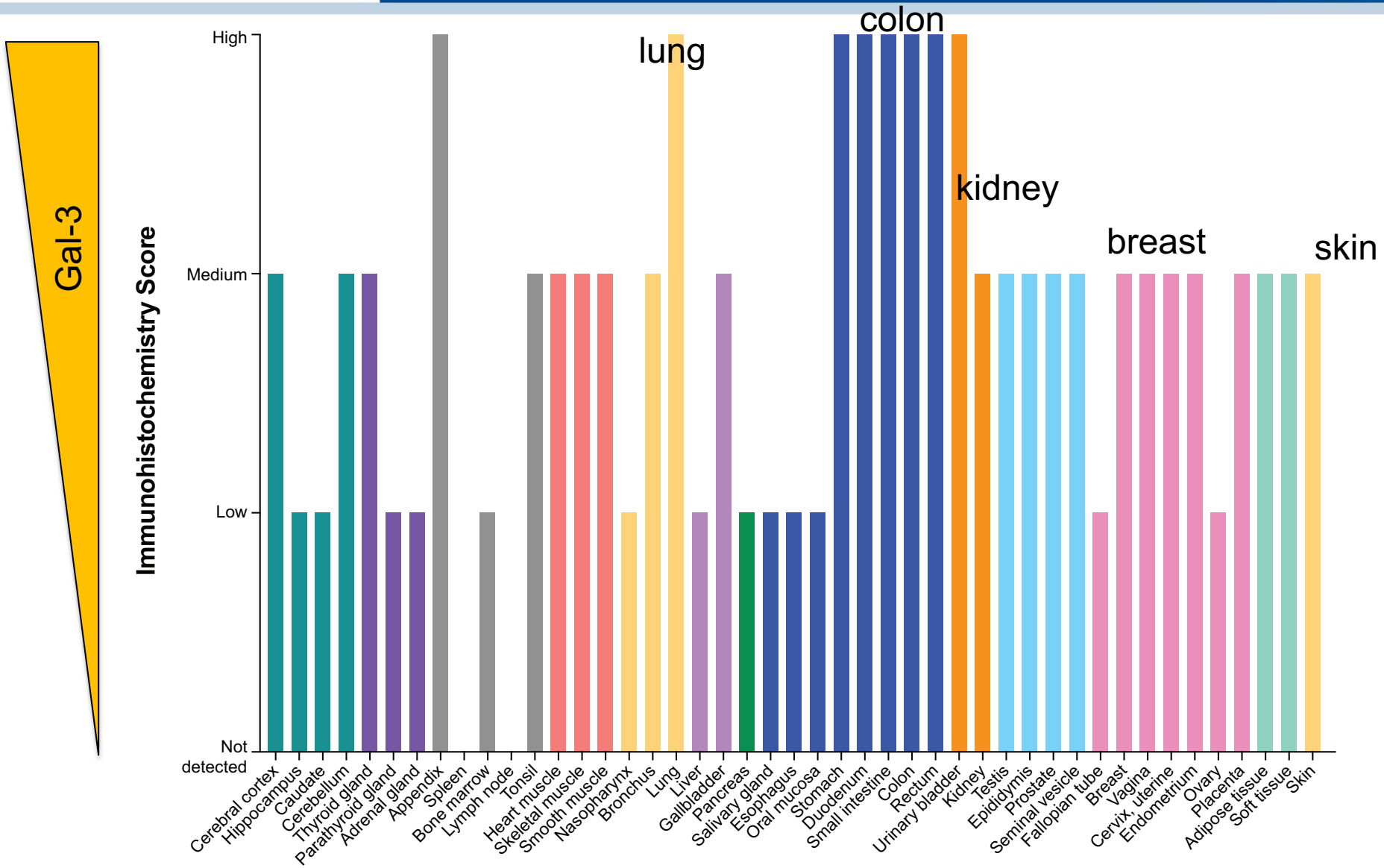
Gal-3 expression (protein)



Farhad M, *OncoImmunol,* 2018

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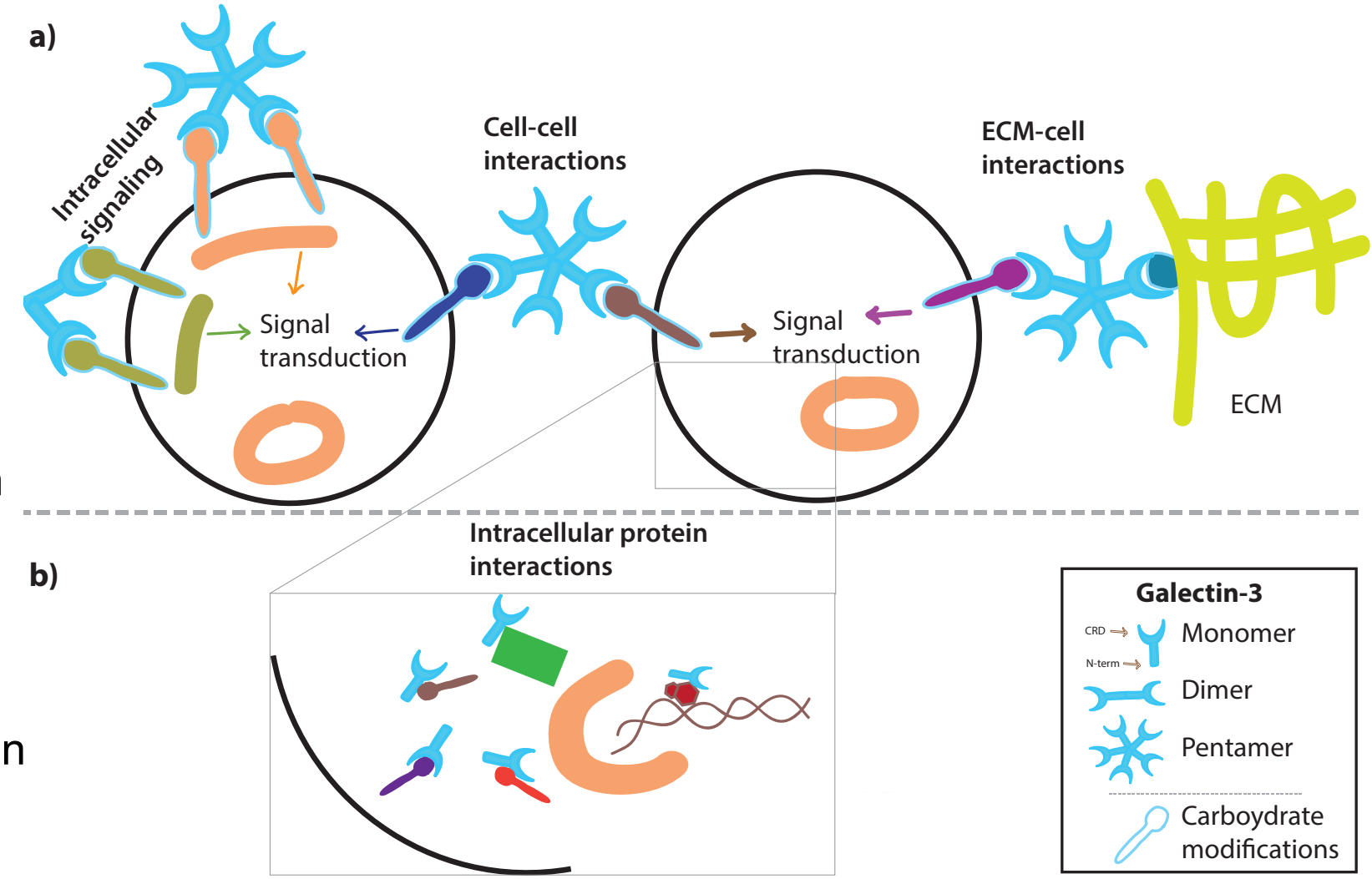
Extracellular vs. intracellular Gal-3

- Cellular location is important for the function of Gal-3
  - –Extracellular
    - Can be secreted (MOA unknown)
    - Cell-cell interactions / adhesion
  - –Intracellular
    - Nucleus and cytoplasm
    - Inhibits apoptosis
    - Regulates cell cycle progression and proliferation



Farhad M, *OncoImmunol,* 2018

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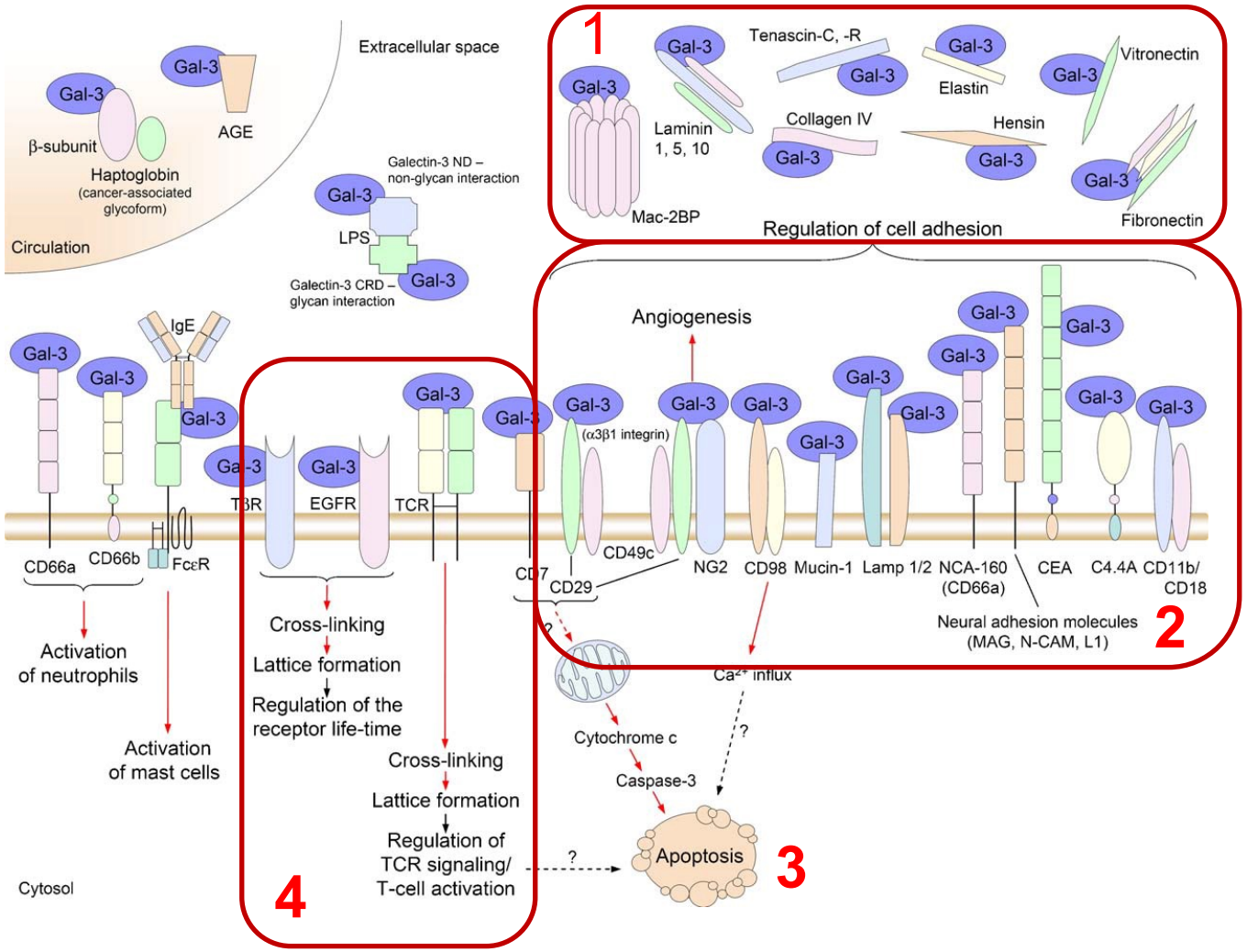
Extracellular Gal-3

1. Binds ECM components
2. Regulates cell adhesion
3. Promote apoptosis
4. Induces receptor cross-linking and lattice formation



Dumic J *et al.*, *Biochem Biophys Acta*, 2006

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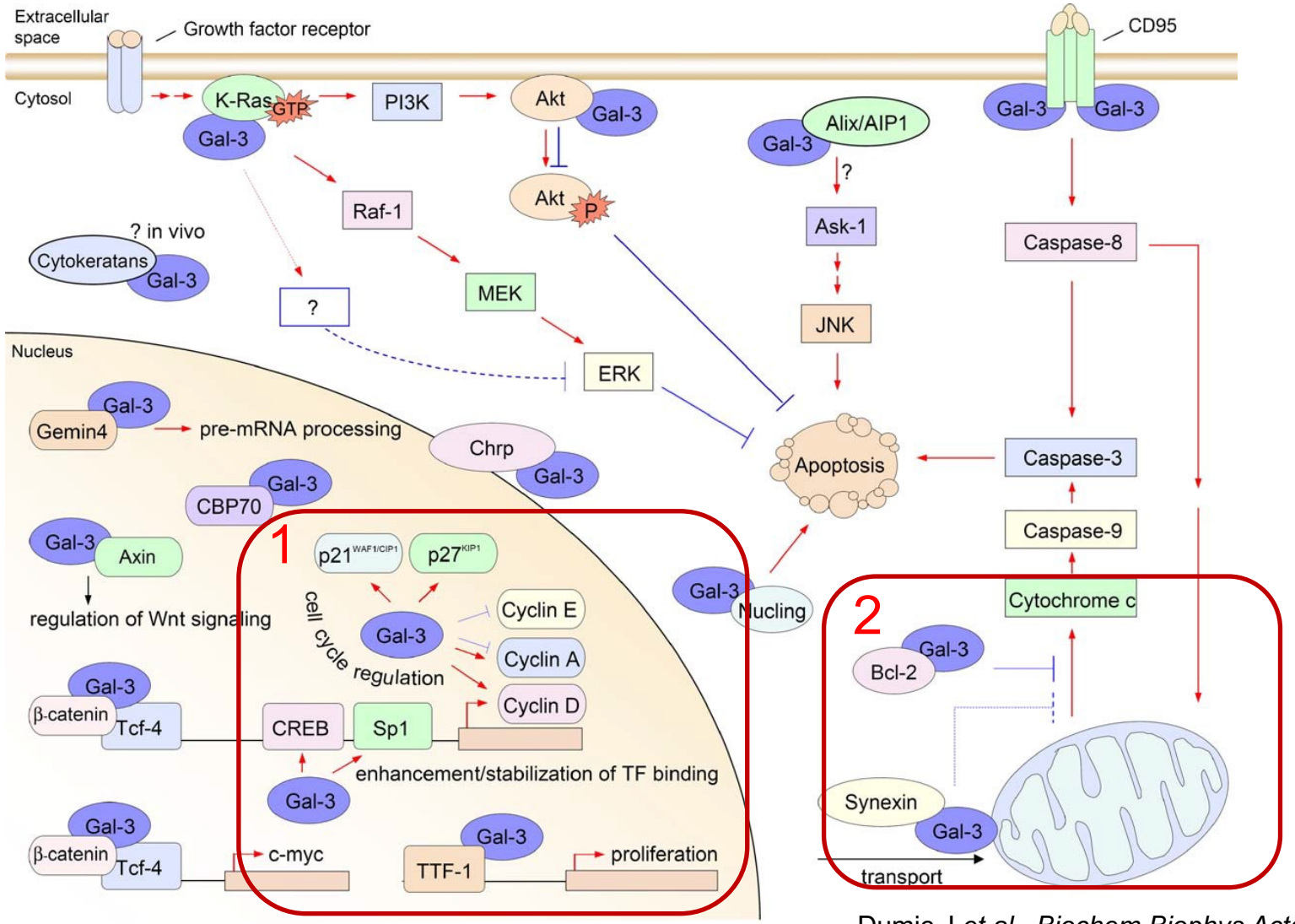
Intracellular Gal-3

1. Regulates cell cycle progression and proliferation
2. Inhibits apoptosis
3. Mediated through protein-protein interactions, not carbohydrate binding



Dumic J *et al.*, *Biochem Biophys Acta*, 2006

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Outline

- Overview of galectins
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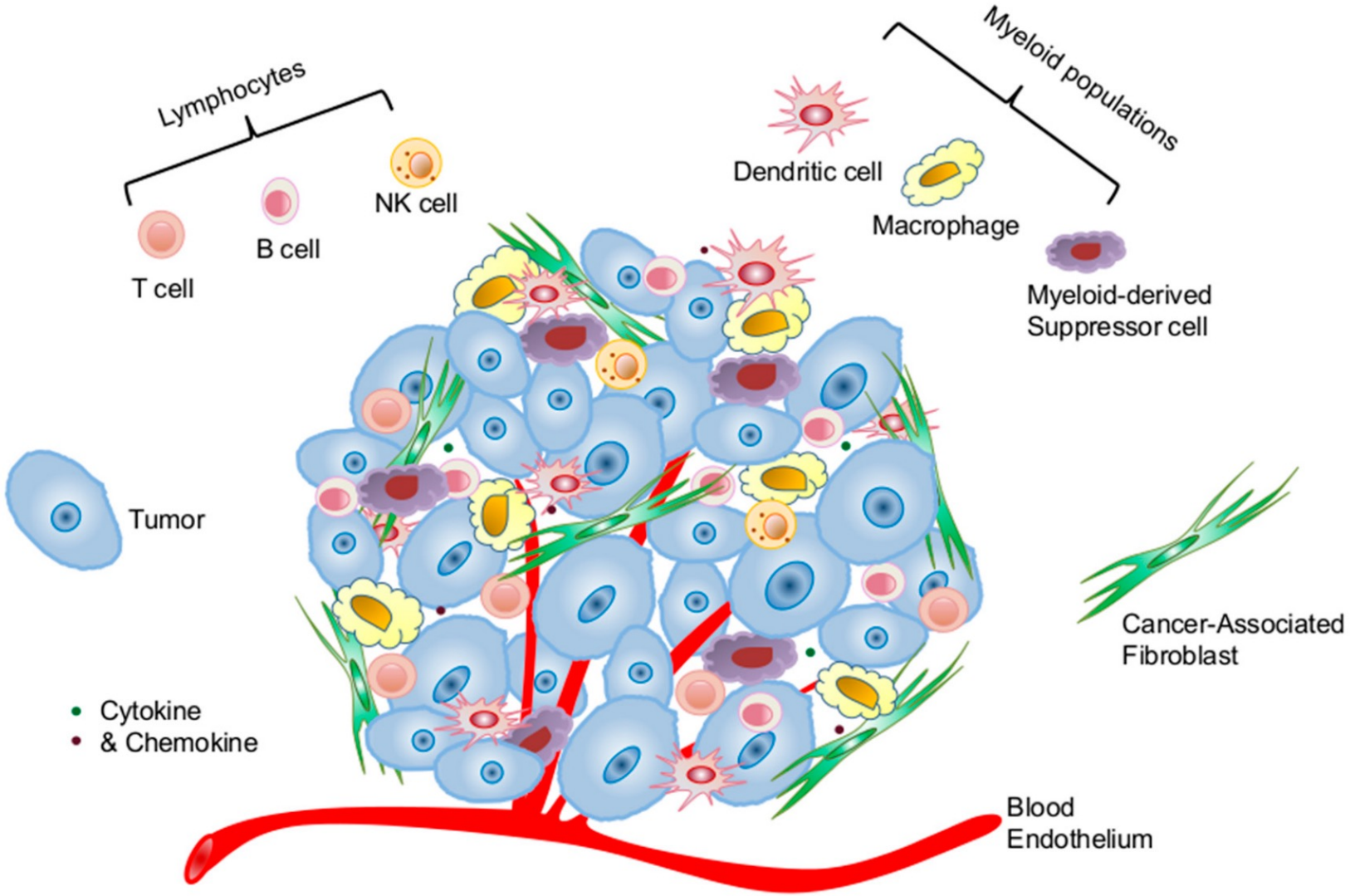
Tumor microenvironment (TME)

- TME is complex!
- …and has a major impact on the efficacy of therapy
- Stroma, hypoxia, MDSC, TGF-β, cytokines, chemokines, etc.
- **What is the impact of Gal-3 in the TME?**



Cui Y, *Int J Mol Sci,* 2016

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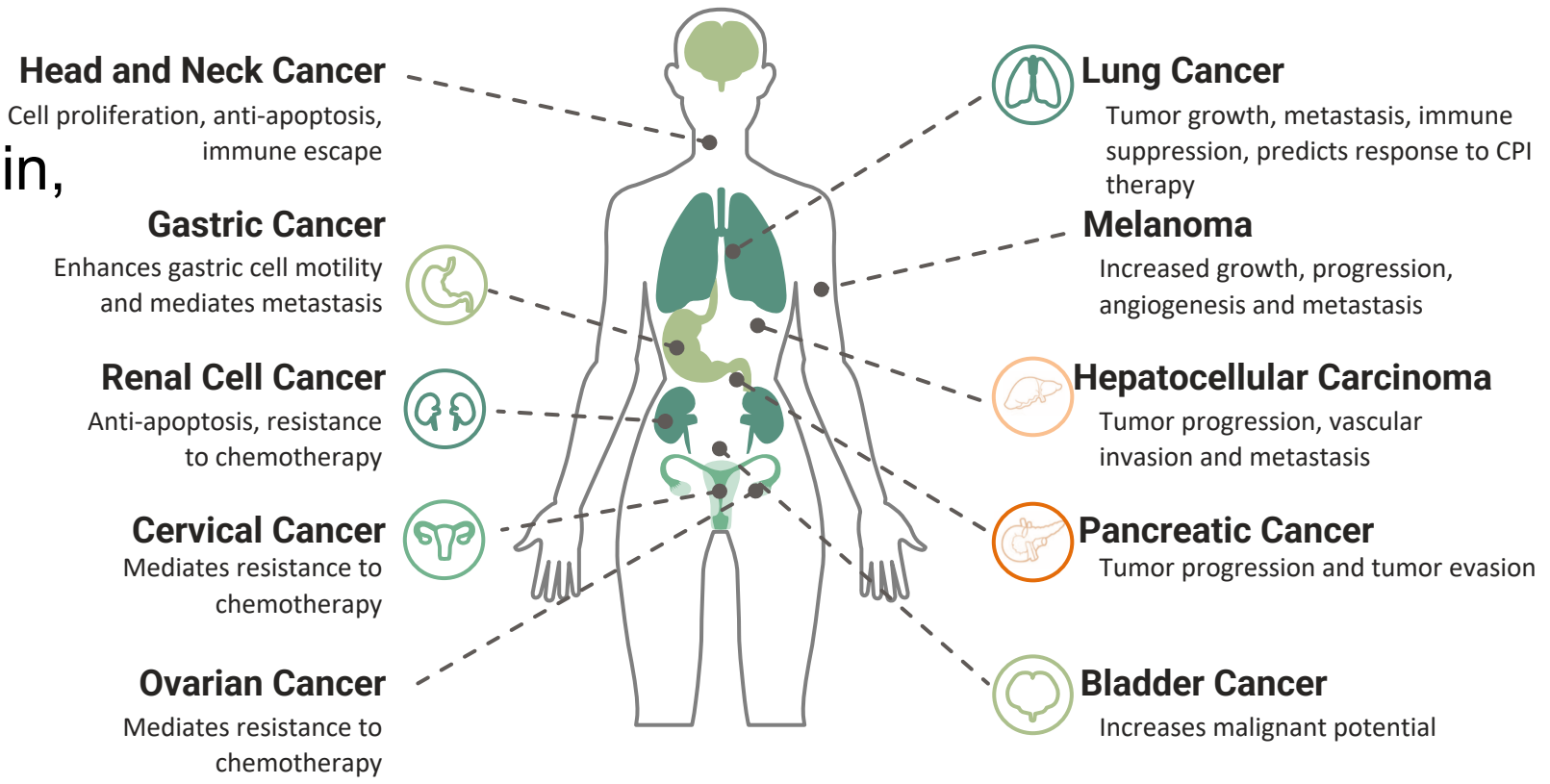
Gal-3 in human cancer

- Expressed in numerous cancer types
  - –Lung, melanoma, colon, brain, pancreatic, breast, prostate, thyroid, colorectal, etc.
- Expression generally correlates with disease progression
  - –Lung, pancreatic, colon, melanoma, etc.
  - –Typically increased in metastatic lesions



Adapted from Ebrahim et al, *Ann Transl Med,* 2014

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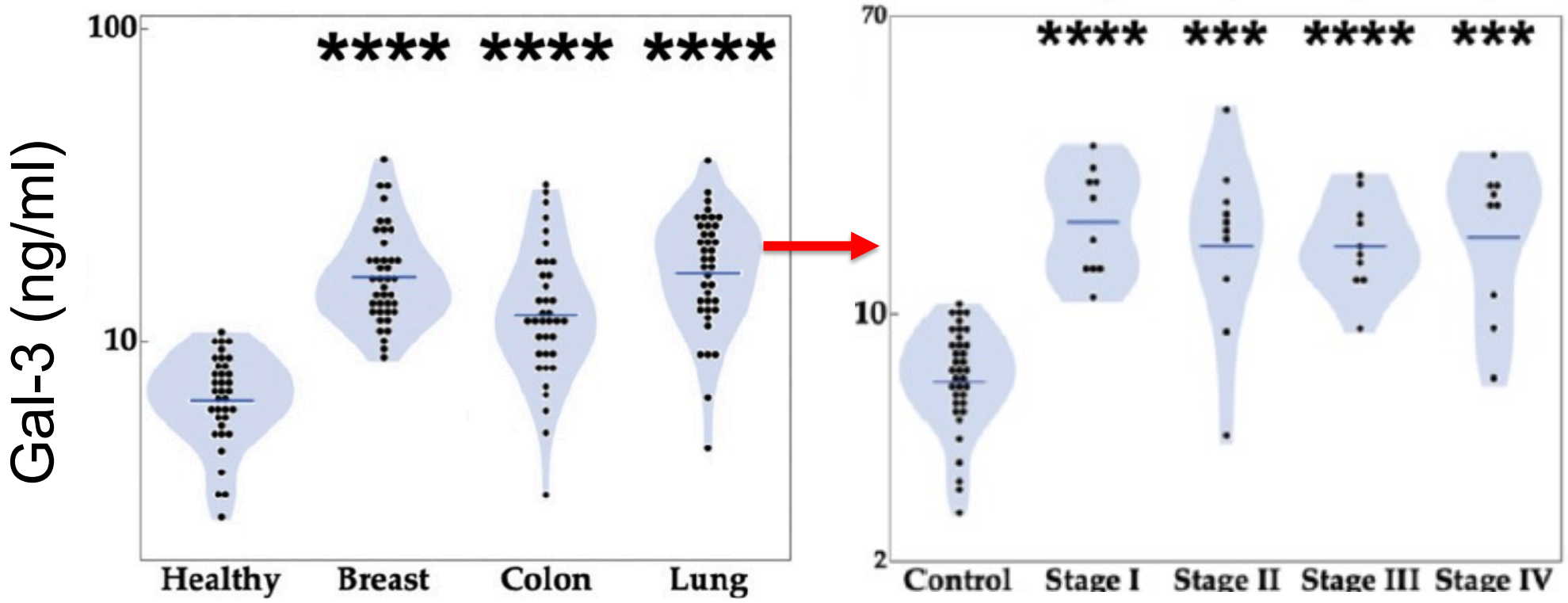
Gal-3 in human cancer



Blair B *et al.*, *Cancers*, 2021

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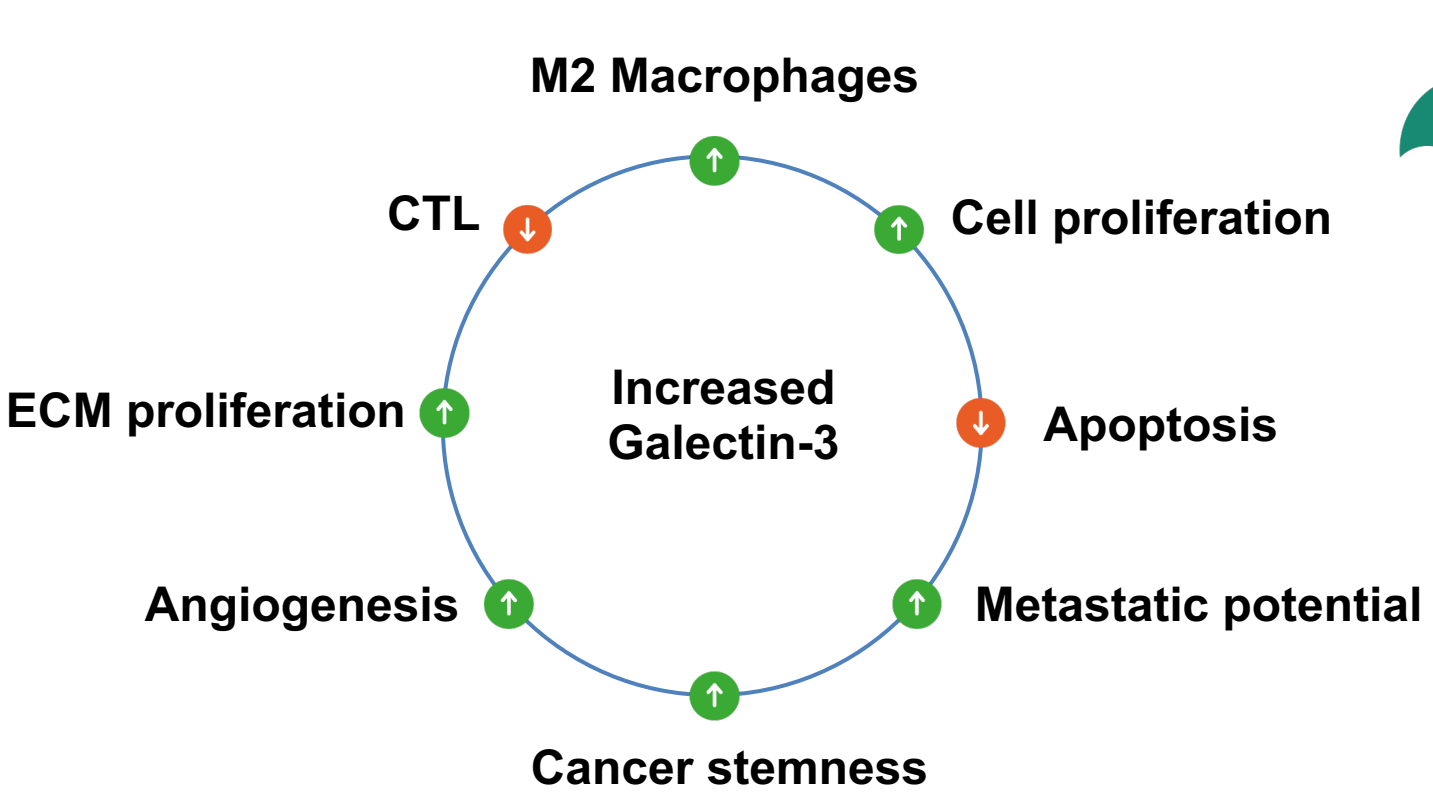
Increased Gal-3 may significantly contribute to the hallmarks of cancer



Ebrahim *et al.*, *Ann Transl Med*, 2014
Farhad M *et al.*, *OncoImmunol,* 2018
Vuong L *et al.*, *Can Res*, 2019

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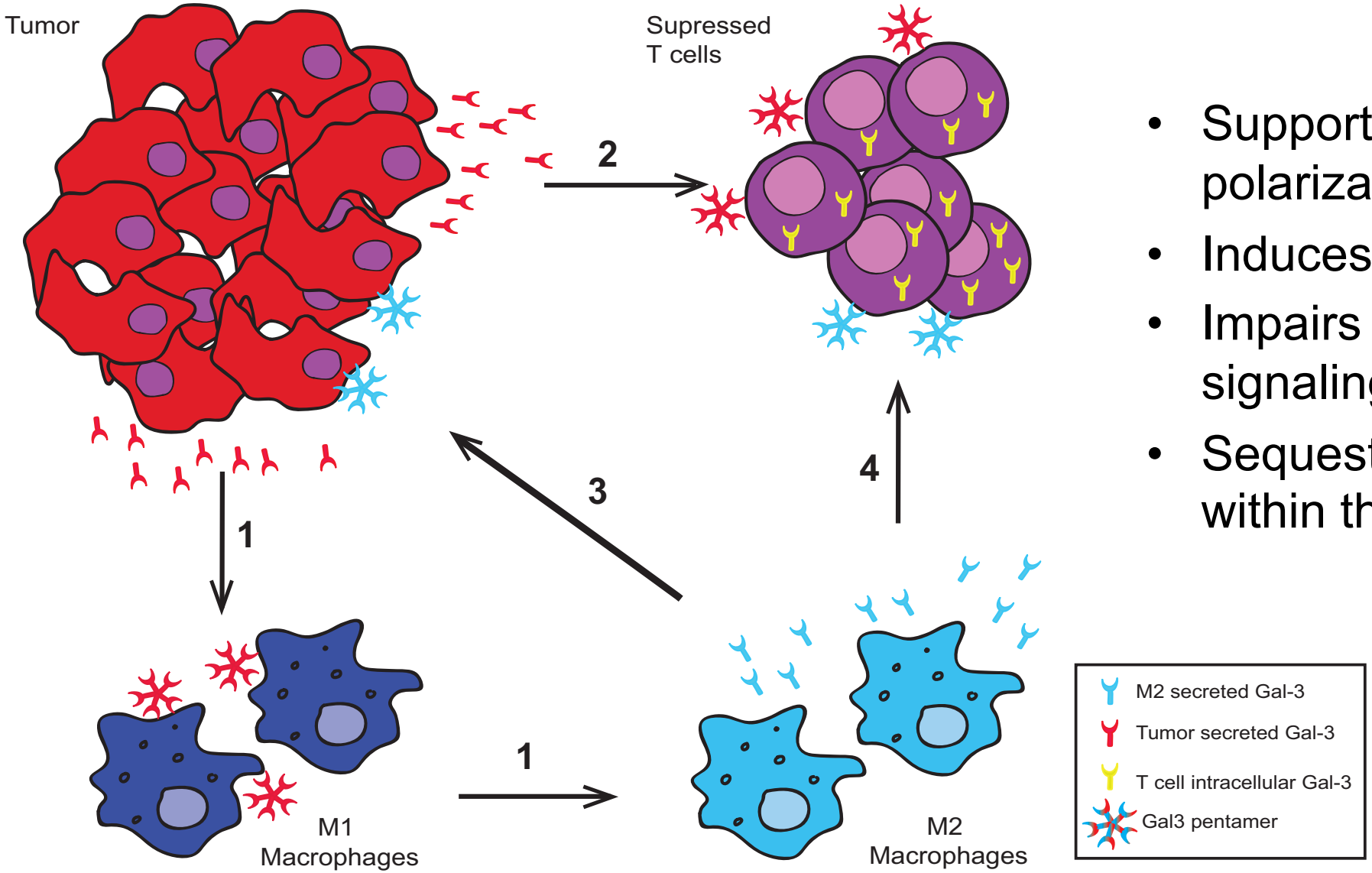
Immune suppressive effects of Gal-3



- Supports M2 macrophage polarization
- Induces T cell apoptosis
- Impairs TCR clustering + signaling
- Sequesters cytokines (IFN-γ) within the TME

Farhad M *et al.*, *OncoImmunol,* 2018

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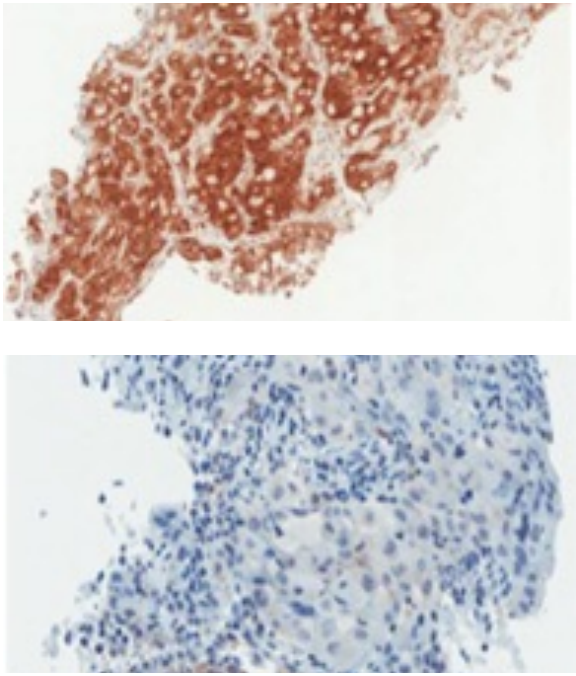
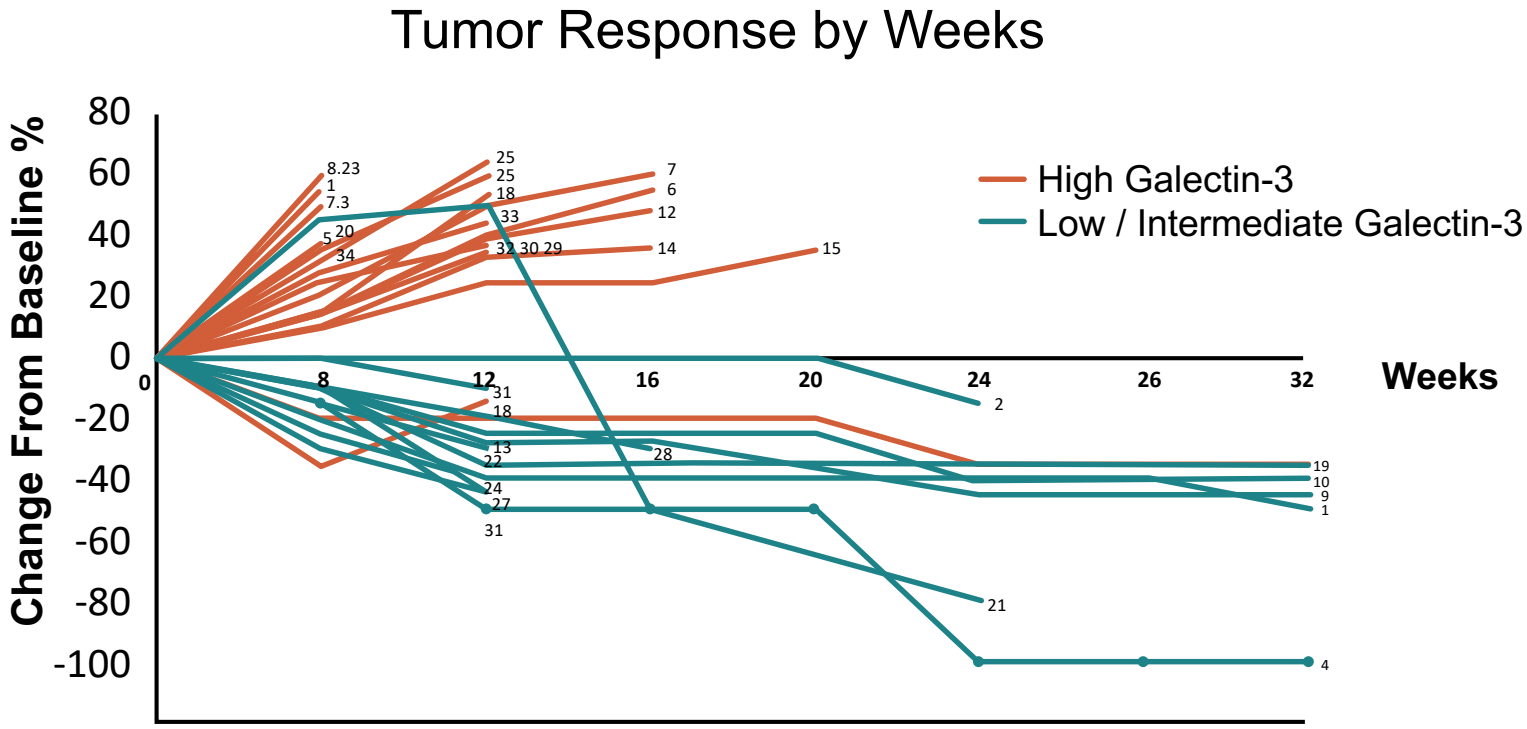
Galectin-3 expression predicts response to pembrolizumab in NSCLC



- **Galectin-3 in NSCLC**



- **34 patients with PD-L1+ NSCLC (stage IV) received pembro (200 mg IV @ 3 wks)**

- Tumor resistance to anti-PD-1 (pembro) strongly correlated with high Gal-3 in NSCLC
- Clinical responses were seen in tumors with negative, low, or intermediate Gal-3

Capalbo et al., *Int J Mol Sci,* 2019

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Outline

- Overview of galectins
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- Therapeutic targeting of Gal-3

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Gal-3 inhibitors

- Various approaches including complex carbohydrates, peptides, small molecule inhibitors, mAbs, etc.

Inhibitors	Cancer model	Effect	Clinical trial				REF.
			Status	Intervention	Conditions	Phase	
Modified citrus pectin (MCP)	SKOV-3 human ovarian cancer; HT-29 and HCT116 human colon cancer; human prostate cancer.	Inhibiting inflammation; Mediating chemoresistance; Inhibiting invasion and migration.	Completed ($n = 60$)	Dietary Supplement: PectaSol-C Modified Citrus Pectin (MCP)	Prostatic Neoplasms	Phase II (NCT01681823)	[148–150]
GR-MD-02 (belapectin)	4T-1 breast cancer model	Reducing lung metastases; Decreasing in functional tumor vasculature.	Completed ($n = 8$)	Biological: 1, 2, 4, 8 mg/kg GR-MD-02 Biological: Ipilimumab	Metastatic Melanoma	Phase I (NCT02117362)	[151]
			Recruiting ($n = 22$)	Drug: GR-MD-02 Drug: Pembrolizumab	Melanoma, Non-Small Cell Lung Cancer, Squamous Cell, Carcinoma of the Head and Neck	Phase I (NCT02575404)	
GCS-100	Acute myeloid leukemia; U266 and RPMI 8226 myeloma cells.	Inducing apoptosis; Inducing cell cycle arrest.	Completed ($n = 12$)	GCS-100	Chronic Lymphocytic Leukemia	Phase II (NCT00514696)	[152,153]
			Terminated	Drug: GCS-100 Drug: Bortezomib/ Dexamethasone	Multiple Myeloma	Phase I (NCT00609817)	
			Withdrawn	Drug: GCS-100 Drug: Etoposide; Dexamethasone	Diffuse Large B-cell Lymphoma	Phase I/II (NCT00776802)	
G3-C12	PC-3 tumor-bearing nude mice.	Inhibiting tumor growth; inducing apoptosis; synergic effect with chemotherapy.	–	–	–	–	[154,155]
GB1107	Human lung A549 adenocarcinoma xenografts.	Reducing lung adenocarcinoma growth and metastasis.	–	–	–	–	[156]
Ginseng-derived pectin (i.g. RG-1-4, WGPA-UD)	HT-29 human colon cancer.	Inhibiting cell adhesion and aggregation; inhibiting gal-3 binding to T cell.	–	–	–	–	[84,140]
2- or 6-de-sulfated *N*-acetylated heparin derivatives	SW620 human colon cancer; ACA19+ human melanoma.	Inhibiting cell adhesion; inhibiting of gal-3-mediated metastasis; inhibiting angiogenesis.	–	–	–	–	[156]

Jin QY *et al.*, *Life Sci*, 2021

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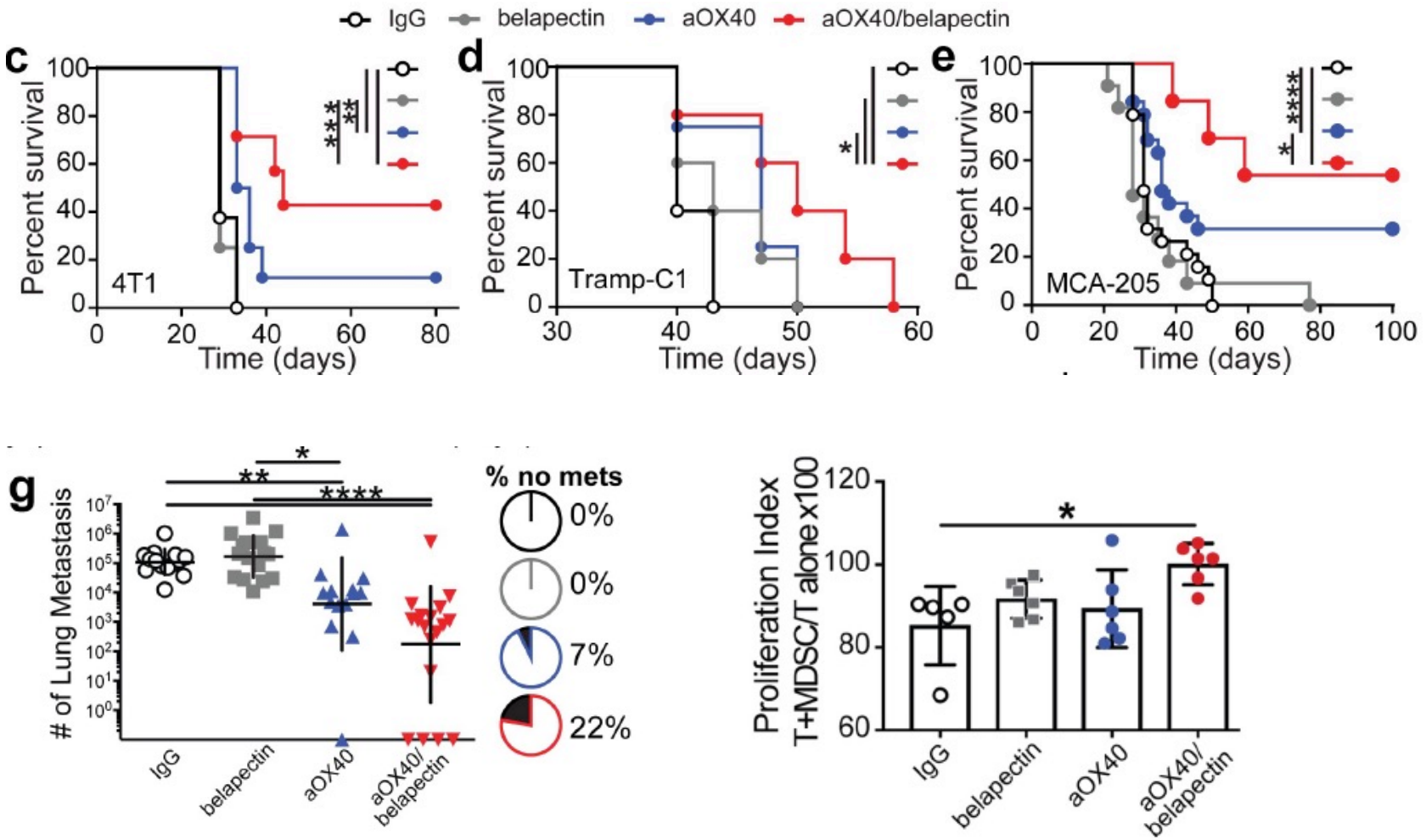
Gal-3 blockade plus agonist anti-OX40 therapy augments anti-tumor immunity

- Gal-3 inhibitor + aOX40 enhanced survival
  - T cell-dependent
- Reduced metastasis
- Abrogated MDSC-mediated suppression



Sturgill E *et al.*, *OncoImmunol*, 2021

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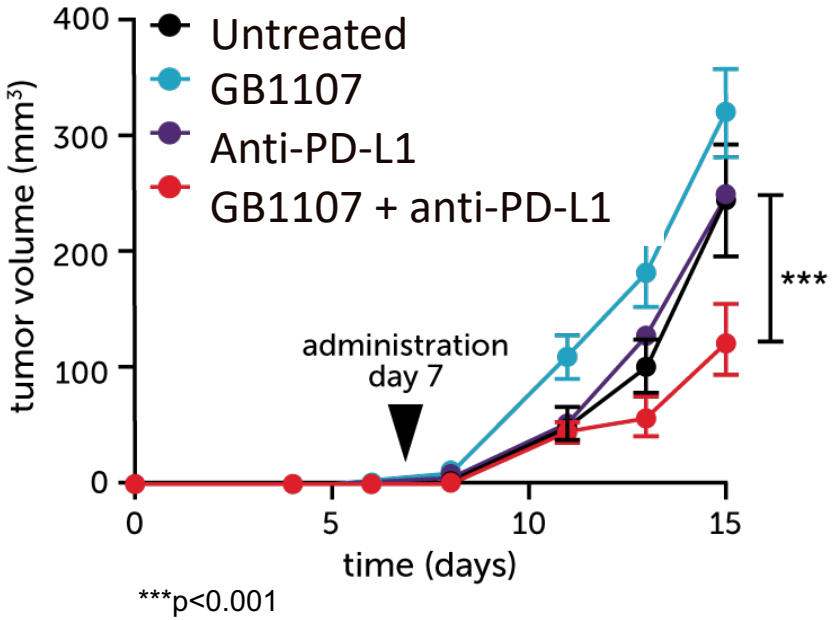
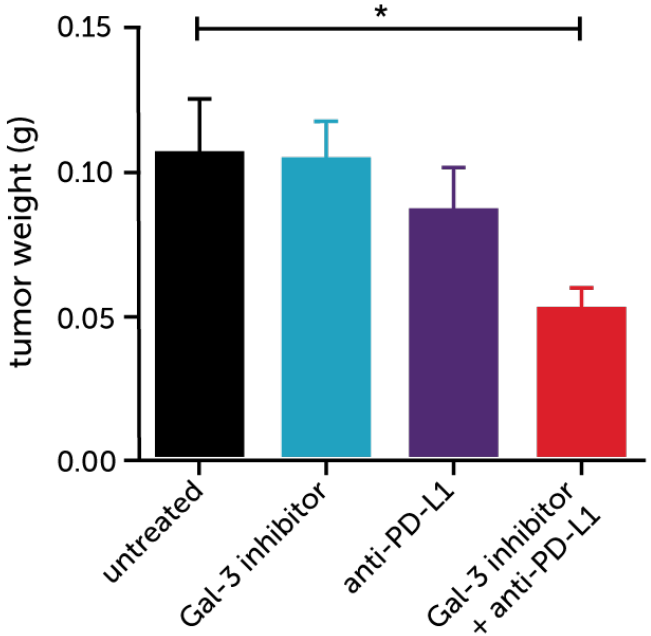
GB1107 increases the efficacy of anti-PD-L1 to reduce lung cancer growth

Lewis Lung Carcinoma Syngeneic Model



***p<0.001



*p<0.05

Vuong L *et al.*, *Can Res*, 2019

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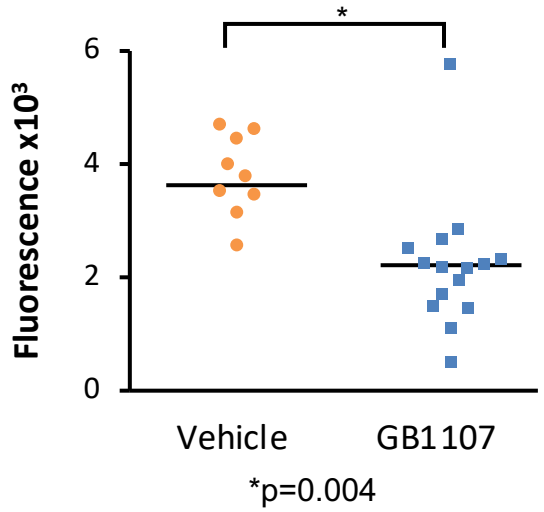
GB1107 reduces M2 polarization and increases CD8$^+$ T-cell infiltration

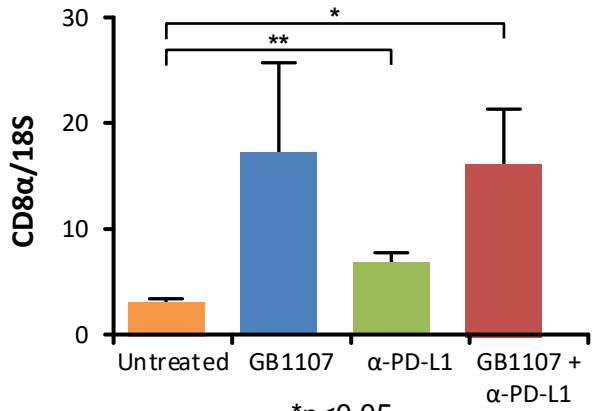
LLC tumor-bearing mice

CD206 M2-like TAM



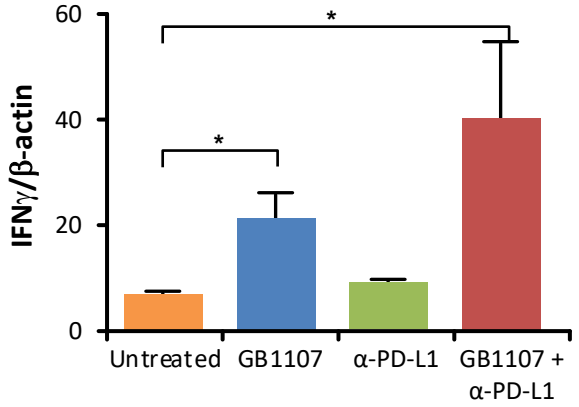
*p=0.004

CD8α



*p<0.05
**p<0.01

IFN-γ



*p<0.05

- GB1107 reduces M2-like TAMs
- GB1107 increases recruitment of CD8$^+$ T cells
- GB1107 increases IFN-γ and PD-1 expression both associated with increased response to checkpoint inhibitors
- GB1107 reduced expression of Gal-3 and mesenchymal markers TGF-β, VEGF and αSMA in the TME

Vuong L *et al.*, *Can Res*, 2019

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Conclusions

- Gal-3 is a novel regulator of the TME
  - –Suppresses T cell activation / survival
  - –Sequester cytokines within the TME
  - –Promotes M2 macrophage polarization
- Gal-3 is overexpressed in many cancer types, including NSCLC
  - –Associated with reduced response to PD-1 blockade in NSCLC
- Combined Gal-3 inhibition plus immunotherapy has potent efficacy in preclinical models
- Supports further clinical development of Gal-3 inhibitors + checkpoint blockade or T cell agonists

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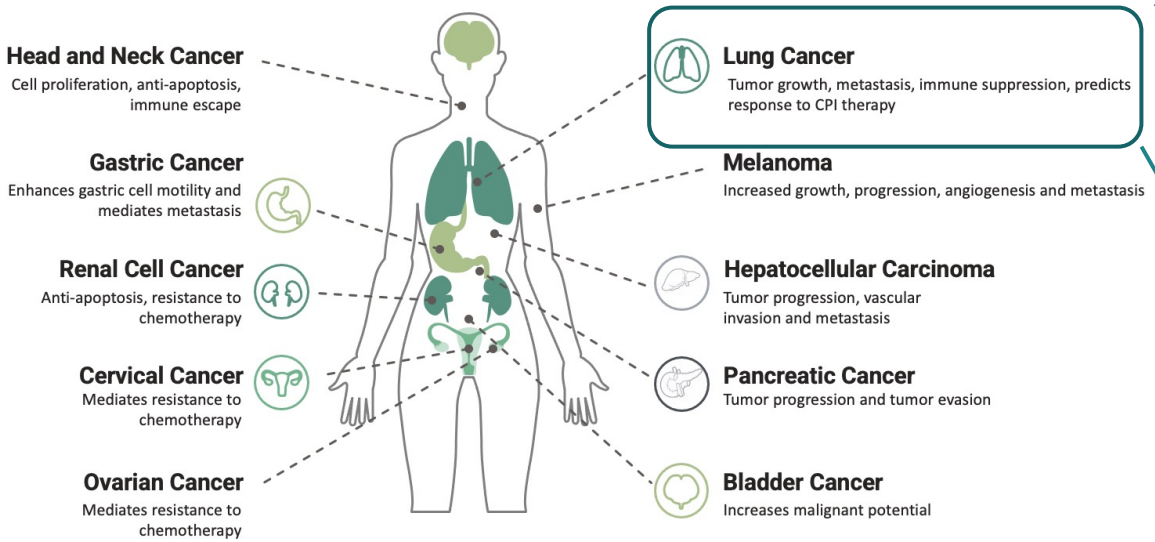
Galecto has Chosen Non-Small Cell Lung Cancer as First Development Target

NSCLC represents a significant unmet medical need with a strong rationale for anti-Galectin-3 therapy



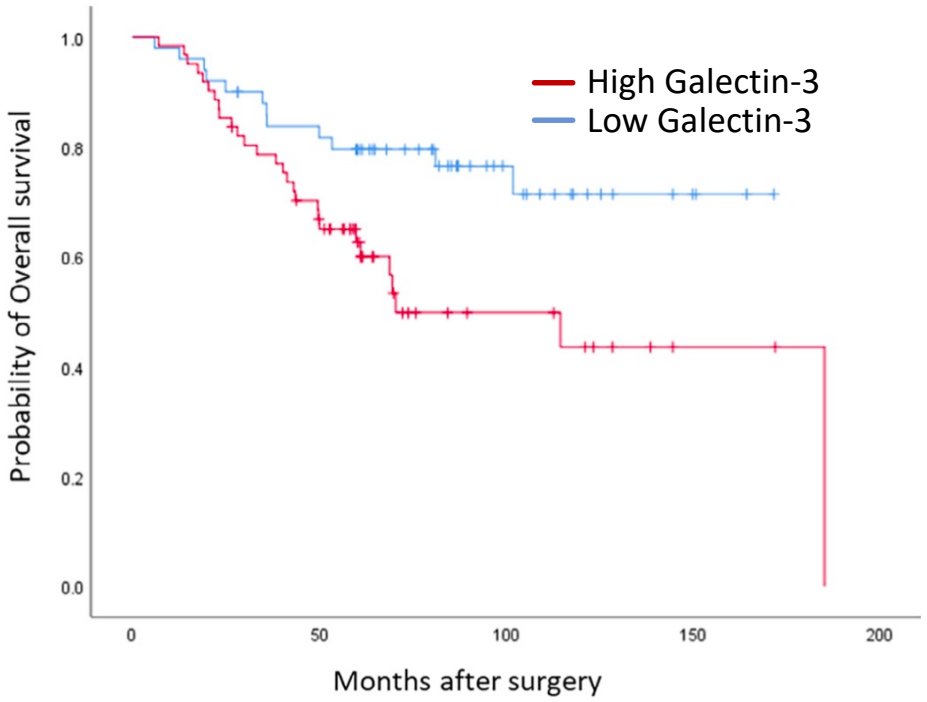
- **High unmet need**
  - Lung cancer is 2nd most common cancer and leading cause of cancer death
    - More than 130.000 death/year in US
    - 1.59 million death/year globally
  - NSCLC has a poor prognosis – 5-year survival <25%
    - Metastatic NSCLC: 5-year survival rate < 7%
  - Billion-dollar market opportunity

- **Galectin-3 is a promising target** that
  - Predicts overall poor survival
  - Predicts response to CPI therapy

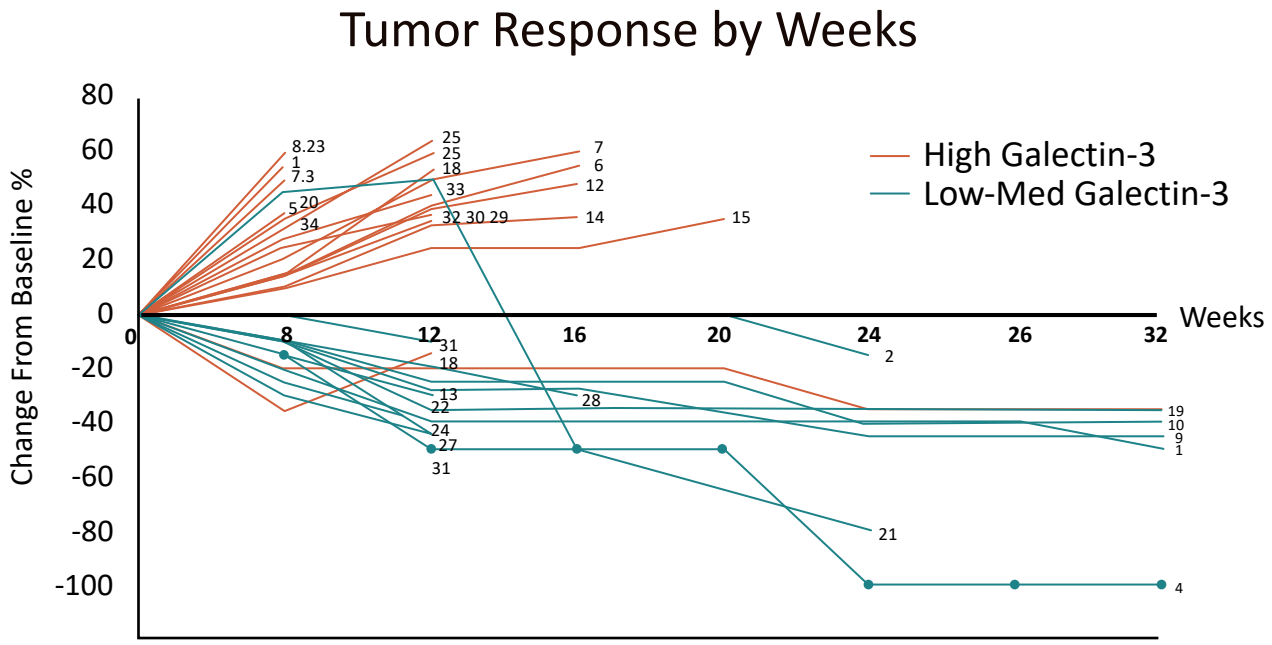
- **CPI therapy for treatment of NSCLC is well established**
  - However, 40-60% of patients don't respond to therapy
  - Gal-3 inhibitors show:
    - Anti-tumor effects
    - T cell activation – LAG3 blockade
    - Macrophage polarizations
    - Increased apoptosis

ASCO: Cancer.net (01-2021)
Ebrahim et al (2014); Ann Transl Med;2(9):88
Kuou et al (2015); Cancer Immunol Res;3: 412
Ou et al (2021); Ther Adv Med Oncol;13: 1
Capalbo et al. (*2019); Int. J. Mol. Sci.;20*
Vuong et al (2019); Cancer Res;79: 1480

Galectin-3 Expression Linked to the Poor Survival and low CPI Response Rate in NSCLC



Kusuhara et al (2021); Thorac Cancer;12:1570–1578

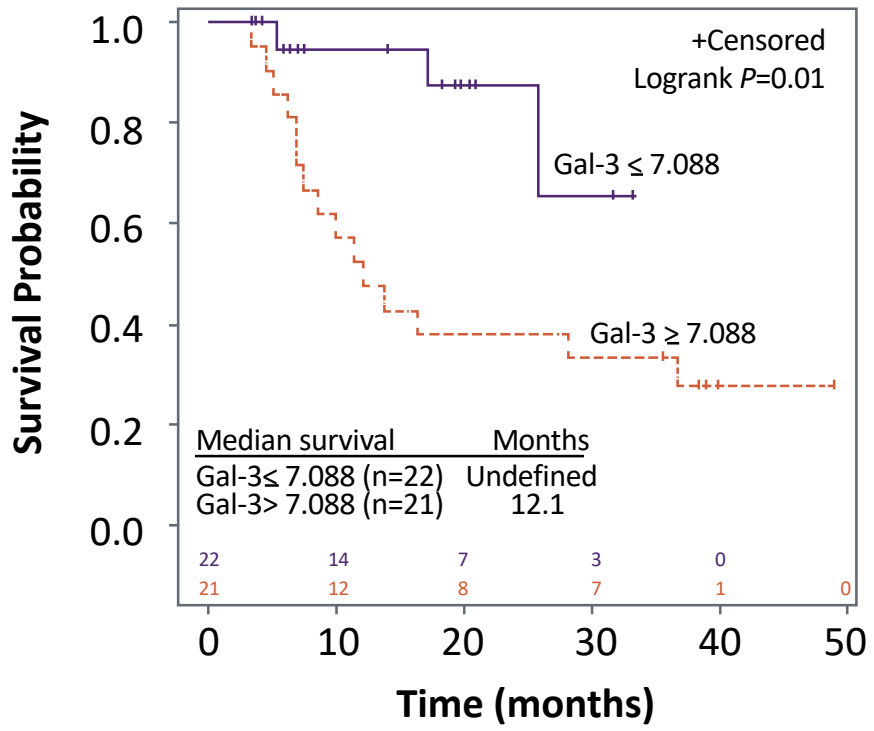


34 patients with PD-L1 +ve NSCLC stage IV received pembrolizumab (200 mg IV @ 3 wks)

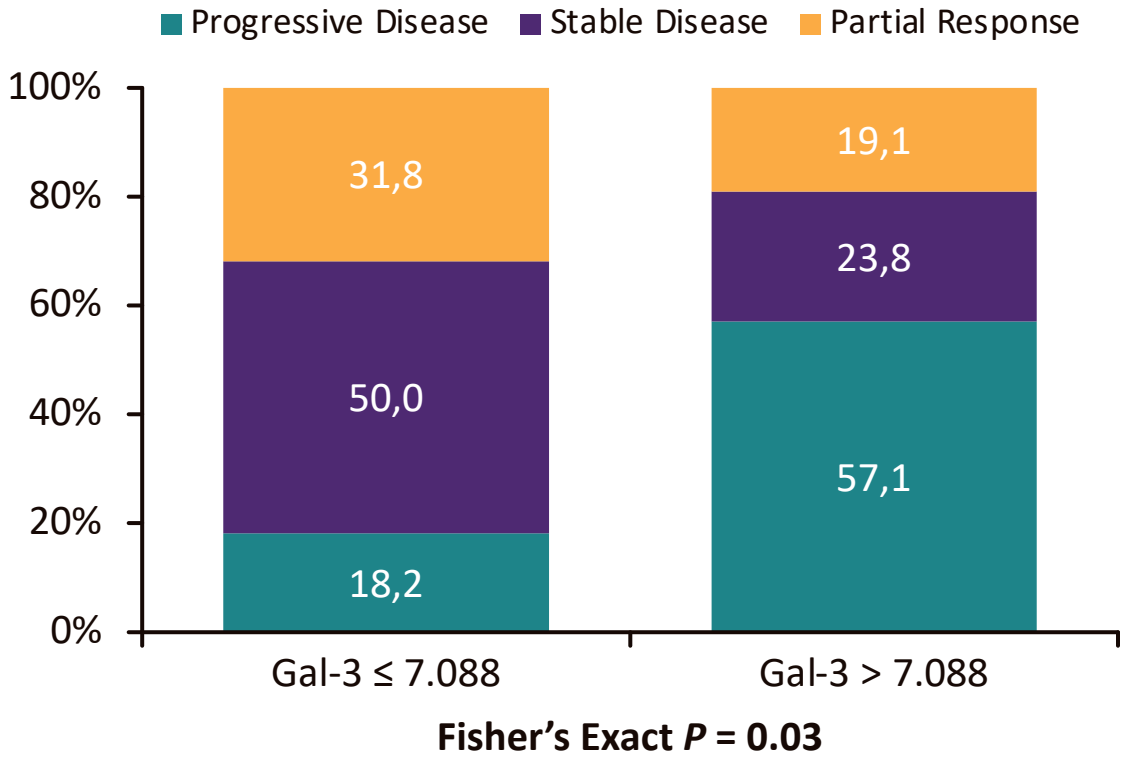
Capalbo et al (*2019); Int J Mol Sci; 20*

Pre-treatment Serum Galectin-3 is Associated With Clinical Outcomes in PD-1 blockade Treated Melanoma Patients

Kaplan-Meier Survival Curves based on pre-treatment Gal-3 levels



Response to PD-1 blockade based on pre-treatment Gal-3 levels



- Melanoma patients with high pre-treatment serum Galectin-3 had poor survival and disease response compared to patients with low serum Galectin-3 following PD-1 blockade with Nivolumab or Pembrolizumab

Xinqi Wu et al;. *Oncoimmunology* 2018, VOL. 7, NO. 7, e1440930

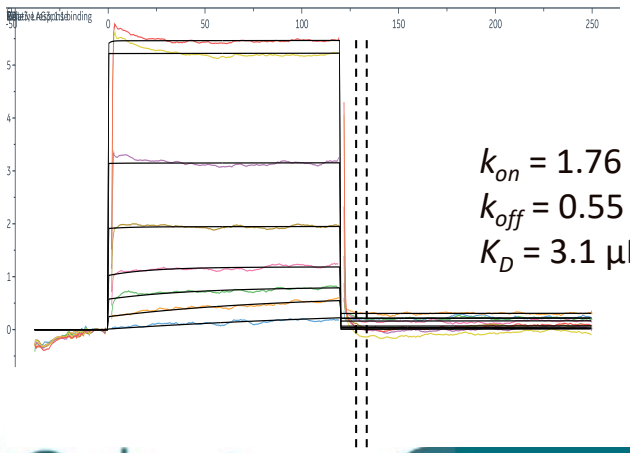
Reasons to Believe

GB1211 drives immune stimulation and increased response to to anti PD-1 immunotherapy

- Decreased Galectin-3 signature strongly correlated with NSCLC increased responsiveness to anti PD-1 immunotherapy
- Increased proliferating T-cell infiltration and interferon gamma (IFNγ)-related signatures (indicative of increased adaptive anti-tumor responses) strongly correlate with increased responsiveness to anti PD-1 immunotherapy
- Eftilagimod a (soluble LAG-3 protein) in combination with pembrolizumab shows encouraging antitumor activity in 1st line advanced NSCLC patients. Targetting LAG-3/Galectin-3 has been shown to overcome immunosuppression in multiple myeloma

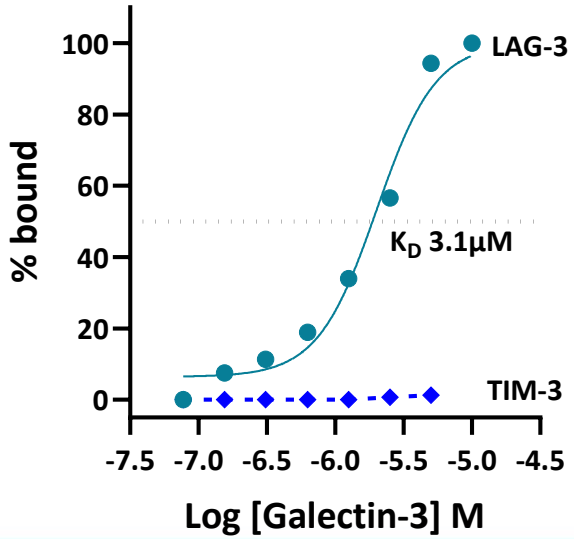
Galectin-3 Kinetics Mode

Steady state measurement at 3 s prior to dissociation captured over a 5 s period

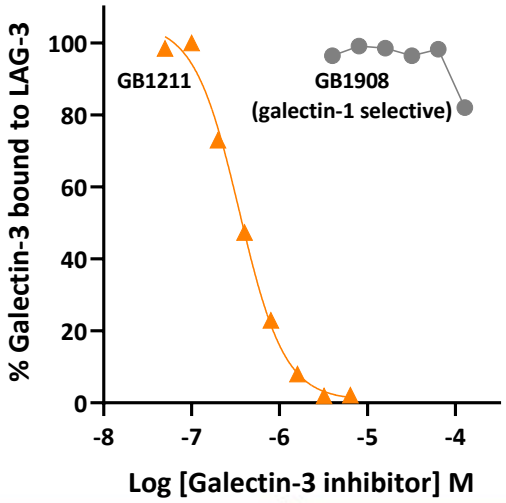


k_{on} = 1.76 x 10^5
k_{off} = 0.55
K_D = 3.1 µM

Galectin-3 Steady State Binding

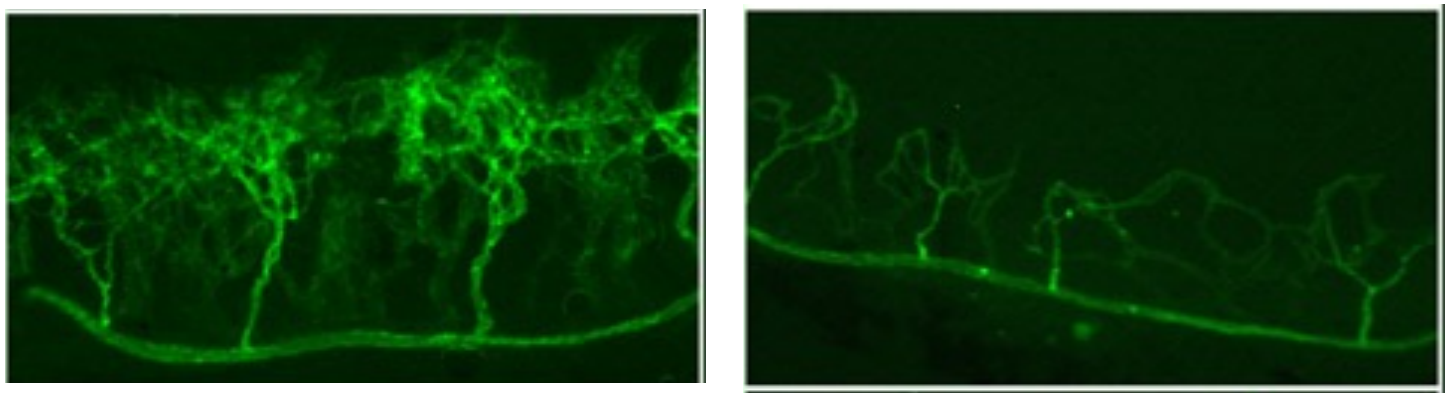


Binding of Galectin-3 to LAG-3 is CRD Binding Site-mediated



GB1211 has direct anti-cancer activity

- Galectin-3 inhibition blocks VEGF and neovascularization

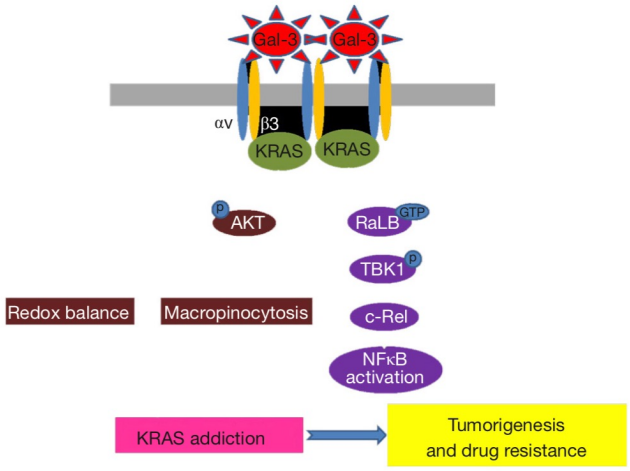


Control **Galectin-3 inhibition**

Naggia Makker et al., 2000.
Markowska et al. 2010).
Dos Santos 2017
Chen et al., 2017

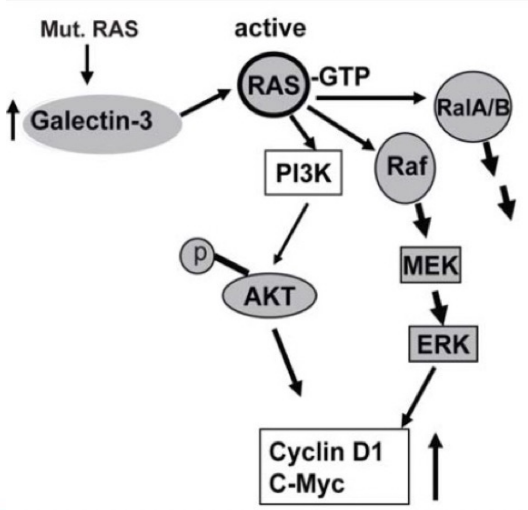
- Galectin-3 inhibition blocks activated mutant Ras signalling

The molecular basis for integrin αvβ3 mediated KRAS addiction to Galectin-3 in KRAS Mutant Cancers



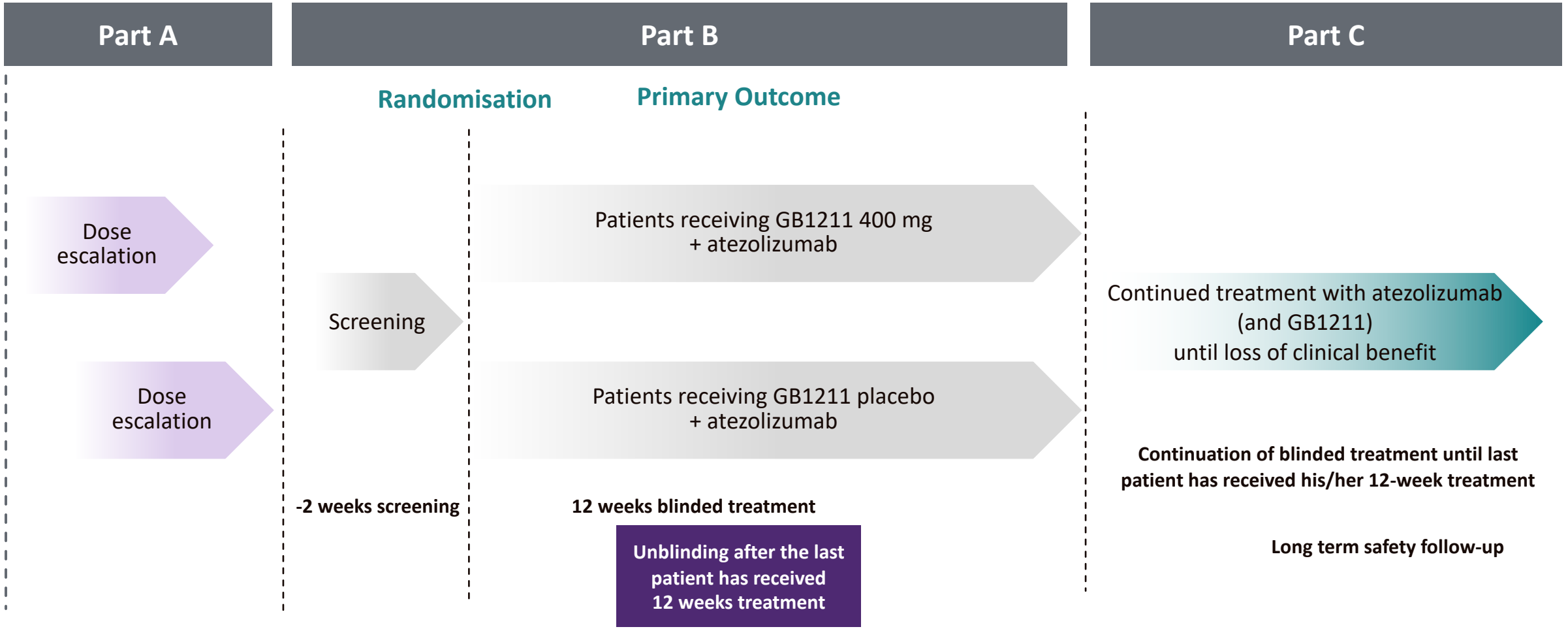
Seguin et al 2017

Galectin-3 binds and Activates RAS signalling



Protocol Design – Part B and C

Primary efficacy measure is tumor shrinkage



Galecto Oncology Opportunities

Myelofibrosis study with GB2064 ongoing

Galectin-3 plays central role for the hallmarks of cancer and is linked to poor survival for many solid tumors

Galectin-3 is a negative regulator of immune cell functions and drives low CPI response rate

GB1211 is a specific oral galectin-3 inhibitor ready for phase 2

- Anti-tumor effects in preclinical models
- Well-tolerated and no observed adverse safety or drug interaction signals

Galecto collaborates with Roche on upcoming NSCLC first line trial with GB1211

- Randomized, placebo-controlled trial in combination with Tecentriq®
- Planned initiation H1-22 with readout mid 2023

This marks Galecto's first entry into the solid tumor space