Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Bespoke Therapy

Personalizing Clinical Trials to Benefit Patients

Omid Hamid MD

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The Angeles Clinic and Research Institute

A Cedars-Sinai Affiliate

#LearnACI

Omid Hamid, MD, has a financial interest/relationship or affiliation in the form of:

Contracted Research For Institution:
Arcus; Aduro;Akeso; Amgen; Bioatla; BMS; CytomX; Exelixis; Roche Genentech; GSK; Immunocore; Idera; Incyte; Iovance; Merck; Moderna; Merck-Serono; NextCure; Novartis; Pfizer; Sanofi Regeneron; Seagen;Taiga; Torque; Zelluna

Speakers Bureau participant with:
BMS; Novartis; Pfizer; Sanofi Regeneron

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Aduro; Alkermeres; Akeso; Amgen; Beigene; Bioatla; BMS; Roche Genentech; Gigagen;GSK; Immunocore; Idera; Incyte; Janssen; Merck; NextCure; Novartis; Partner Therapeutics; Pfizer; Sanofi Regeneron; Seagen; Tempus; Zelluna

Omid Hamid, MD, does intend to discuss either non-FDA-approved or investigational use for the following products/devices: pembrolizumab as adjuvant therapy in high-risk stage II melanoma; various combination strategies with checkpoint inhibitors and vaccine-based approaches/targeted agents.

- Consultative Physician Team
- HLA type
- BRAF Status
- Next Generation Sequencing
- Predictive Markers

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Find a study (all fields optional)

Status

- ○ Recruiting and not yet recruiting studies
- ● All studies

Condition or disease (For example: breast cancer)

Other terms (For example: NCT number, drug name, investigator name)

Country

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Click to edit Master title style

Find Your Expertise

Physician Champions

Physician Enforcer

PATIENT
Sample, Jane

TUMOR TYPE
Lung adenocarcinoma

REPORT DATE
01 Jan 2018

GRF#
XXXXXXX

ABOUT THETEST FoundationOne®CDx is a next-generation sequencing (NGS) based assay that identifies genomic findings within hundreds of cancer-related genes

PATIENT

DISEASE Lung adenocarcinoma
NAME Not Given
DATE OF BIRTH Not Given
SEX Female
MEDICAL RECORD # Not Given

PHYSICIAN

ORDERING PHYSICIAN Not Given
MEDICAL FACILITY Not Given
ADDITIONAL RECIPIENT Not Given
MEDICAL FACILITY ID Not Given
PATHOLOGIST Not Given

SPECIMEN

SPECIMEN SITE Not Given
SPECIMEN ID Not Given
SPECIMEN TYPE Not Given
DATE OF COLLECTION Not Given
SPECIMEN RECEIVED Not Given

Biomarker Findings

Tumor Mutational Burden - TMB-Intermediate (11 Muts/Mb)

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

EGFR amplification, L858R
PTCH1 T416S
CDKN2A/B loss
RBM10 Q494*
TP53 R267P

7 Disease relevant genes with no reportable alterations: *KRAS, ALK, BRAF, MET, RET, ERBB2, ROS1*

14 Therapies with Clinical Benefit
0 Therapies with Lack of Response
18 Clinical Trials

BIOMARKER FINDINGS	THERAPIES WITH CLINICAL BENEFIT (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL BENEFIT (IN OTHER TUMOR TYPE)
Tumor Mutational Burden - TMB-Intermediate (11 Muts/Mb)	Drug name Drug name Drug name Drug name	Drug name
9 Trials see p. 14		
Microsatellite status - MS-Stable	No therapies or clinical trials. see Biomarker Findings section	

GENOMIC FINDINGS	THERAPIES WITH CLINICAL BENEFIT (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL BENEFIT (IN OTHER TUMOR TYPE)
***EGFR* -** amplification, L858R	Drug name Drug name Drug name Drug name	Drug name Drug name Drug name
4 Trials see p. 16		
***PTCH1* -** T416S	None	Drug name Drug name
5 Trials see p. 17		

GENOMIC FINDINGS WITH NO REPORTABLE THERAPEUTIC OR CLINICAL TRIALS OPTIONS

For more information regarding biological and clinical significance, including prognostic, diagnostic, germline, and potential chemosensitivity implications, see the Genomic Findings section.

CDKN2A/B - loss p.5
RBM10 - Q494* p.5
TP53 - R267P p.6

NOTE: Genomic alterations detected may be associated with activity of certain approved therapies; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Therapies and the clinical trials listed in this report may not be complete and exhaustive. Neither the therapeutic agents nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type. This report should be regarded and used as a supplementary source of information and not as the single basis for the making of a therapy decision. All treatment decisions remain the full and final responsibility of the treating physician and physicians should refer to approved prescribing information for all therapies.

Therapies contained in this report may have been approved by the US FDA.

Whats your type ?

Diagnosis
Metastatic melanoma

Accession No.
TL-22-W4D9HBTS

xT

Sex
Male

Physician
Michelle Offner

Institution
The Angeles Clinic and Research Institute - Los Angeles
202238546

TEMPUS | xT
648 gene panel

Tumor specimen:
Axilla, right
The American British Cowdray Hospital - Pathology B-11214-21, 5
Collected 10/6/2021
Received 1/29/2022
Tumor Percentage: 70%

Normal specimen:
Blood
Collected 10/19/2021
Received 10/21/2021

GENOMIC VARIANTS

Potentially Actionable		Variant Allele Fraction
TERT	c.-146C>T Variant - Promoter mutation	65.3%
NRAS	p.G13D Missense variant (exon 2) - GOF	38.2%

Biologically Relevant

NF1	p.W1685* Stop gain - LOF	76.7%
TP53	p.Q375* Stop gain - LOF	67.0%
ARID2	p.W264* Stop gain - LOF	46.5%
PTPRT	p.R1226* Stop gain - LOF	27.7%
ARID2	p.Q68* Stop gain - LOF	25.0%

Germline - Pathogenic / Likely Pathogenic

A matched normal sample is being sequenced and updated results will be reported upon completion.

Pertinent Negatives

No pathogenic single nucleotide variants, indels, or copy number changes found in:

BRAF KIT

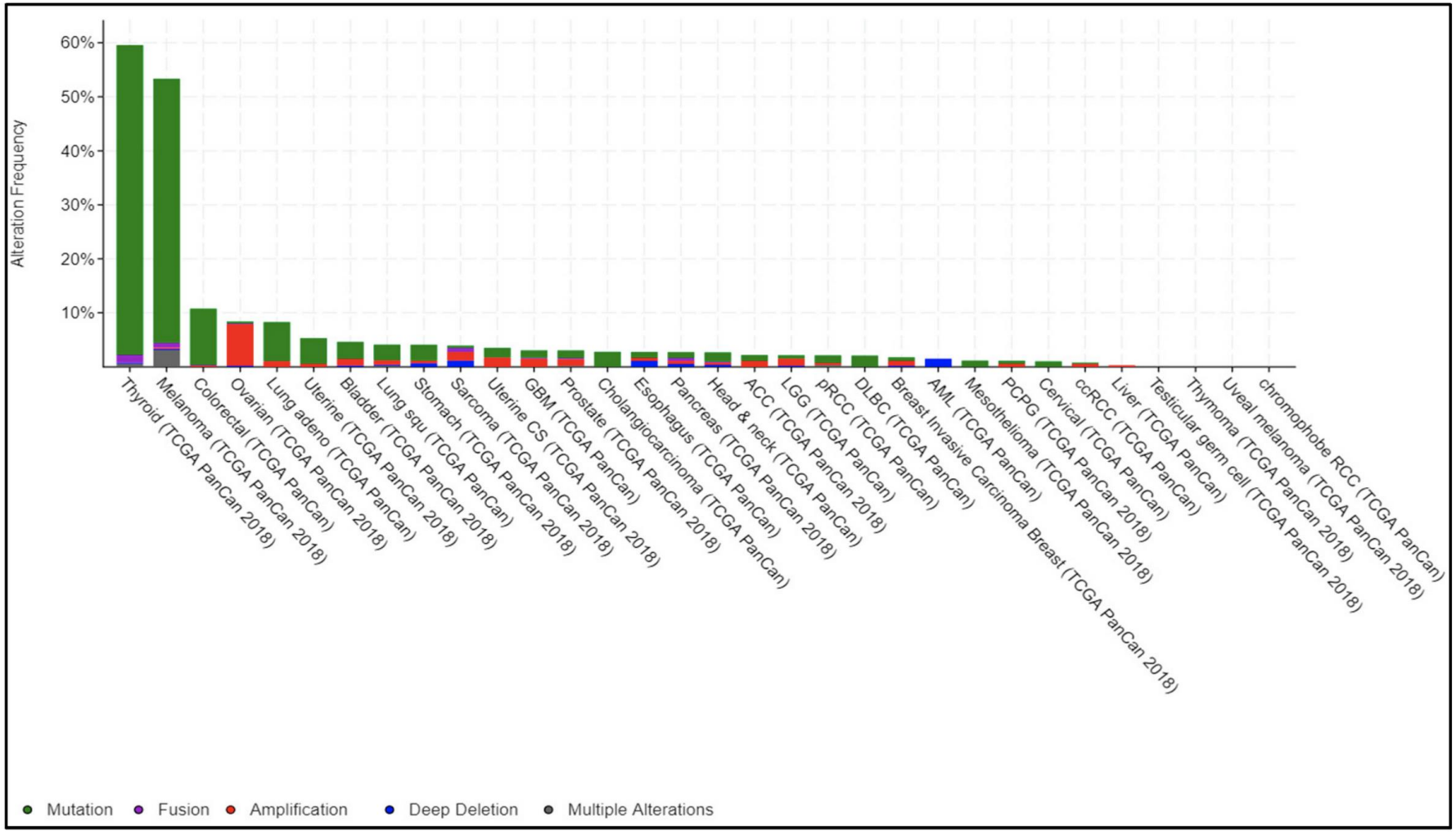
IMMUNOTHERAPY MARKERS

Tumor Mutational Burden
21.6 m/MB 96th percentile

Microsatellite Instability Status
Stable Equivocal High

FDA-APPROVED THERAPIES, CURRENT DIAGNOSIS

Anti-PD-1 MAb	**Pembrolizumab**	High TMB Consensus, Solid Tumors: FDA



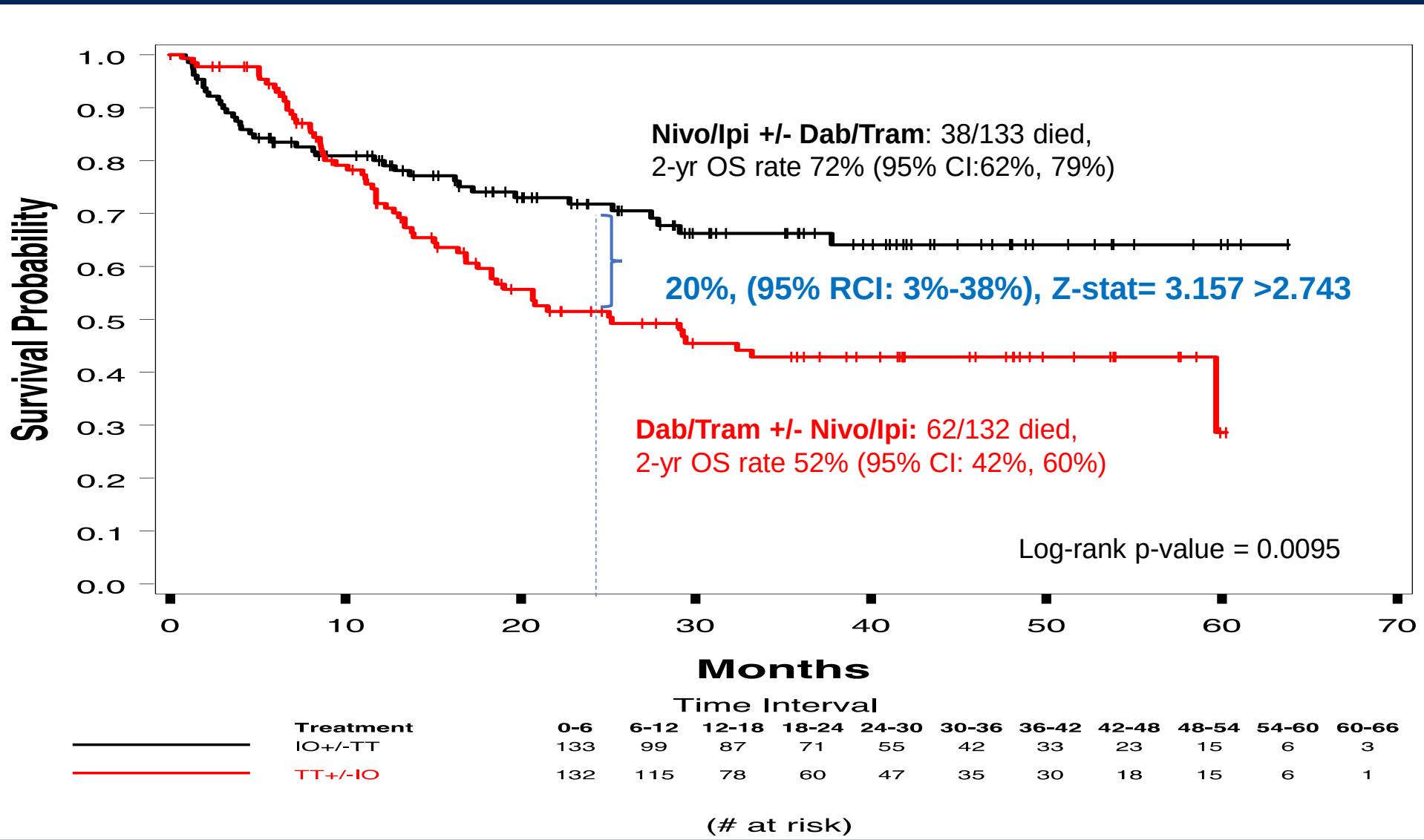
ASCO® Plenary Series

DREAMseq (Doublet, Randomized Evaluation in Advanced Melanoma Sequencing) a Phase III Trial: ECOG-ACRIN EA6134

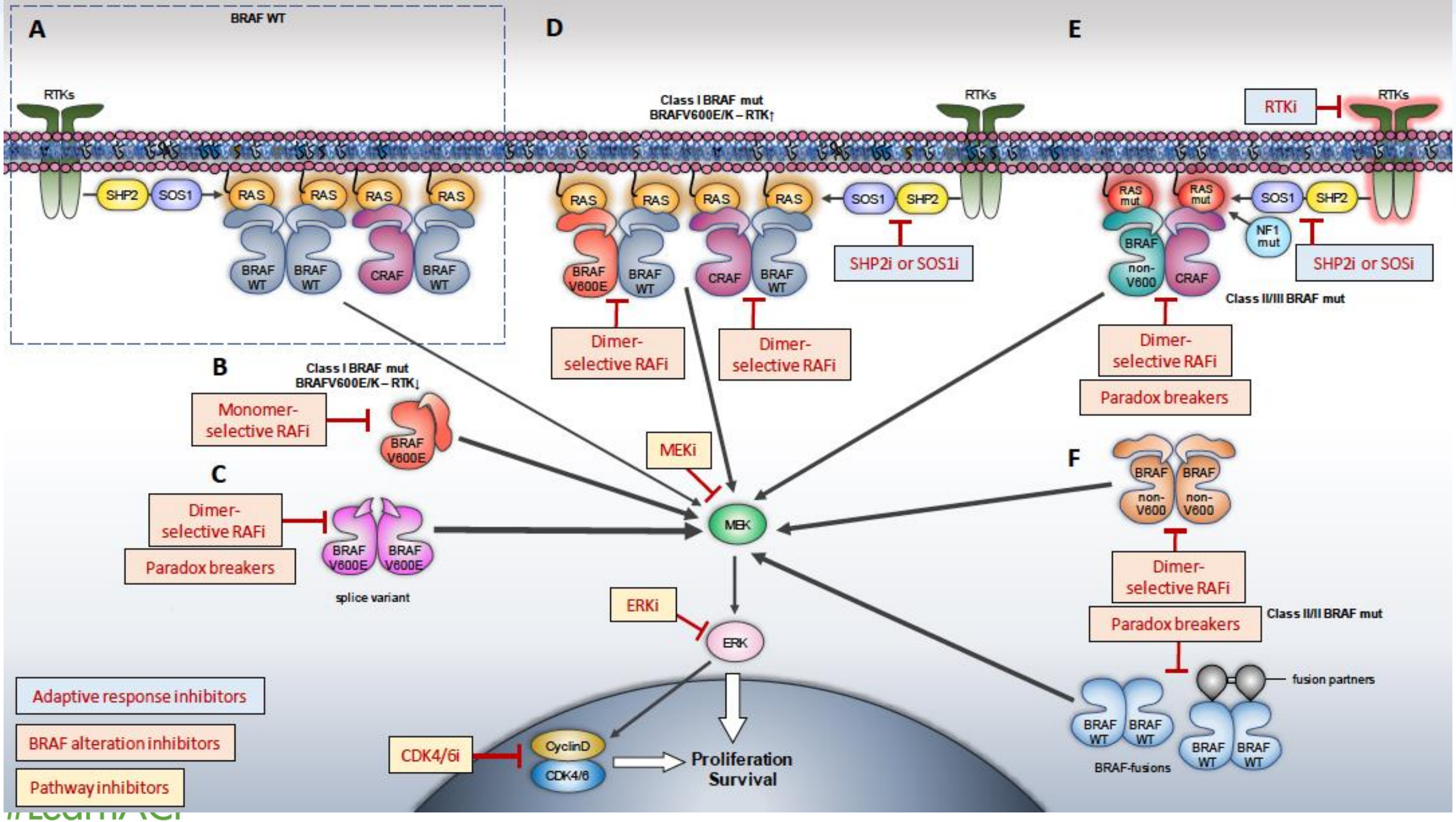
Michael B. Atkins[1], Sandra Lee[2], Bartosz Chmielowski[3], Antoni Ribas[3], Ahmad A. Tarhini[4], Thach-Giao Truong[5], Diwakar Davar[6], Mark O'Rourke[7], Brendan D. Curti[8], Joanna M. Brell[9], Kari L. Kendra[10], Alexandra P. Ikeguchi[11], Jedd D. Wolchok[12], John M. Kirkwood[6]

[1]Georgetown Lombardi Comprehensive Cancer Center, Washington DC; [2]Dana-Farber Cancer Institute, Boston MA; [3]Jonsson Comprehensive Cancer Center University of California Los Angeles, Los Angeles CA; [4]H. Lee Moffitt Cancer Center and Research Institute, Tampa FL; [5]Kaiser Permanente Northern California, Vallejo CA; [6]Pittsburgh Cancer Institute, Pittsburgh PA; [7]Greenville Health System Cancer Institute, Greenville SC; [8]Providence Cancer Institute, Portland OR; [9]MetroHealth Medical Center, Cleveland OH; [10]Ohio State University Comprehensive Cancer Center, Columbus OH; [11]University of Oklahoma Medical Center, Oklahoma City OK; [12]Memorial Sloan Kettering Cancer Center, New York NY

Overall Survival (OS): Step 1 +/- Step 2



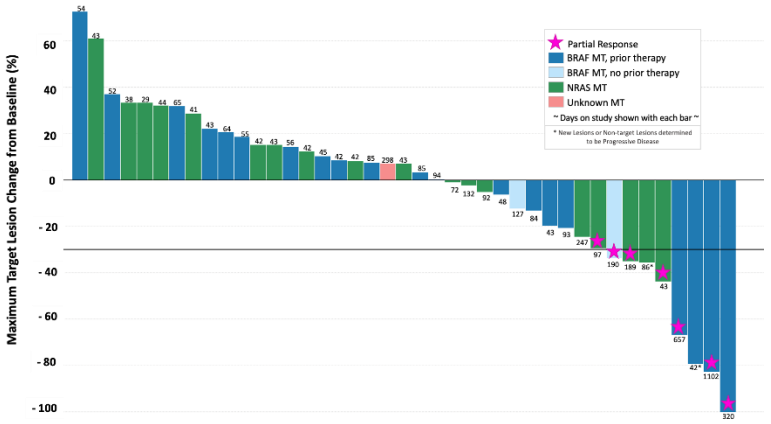
PRESENTED BY: Michael B. Atkins, MD



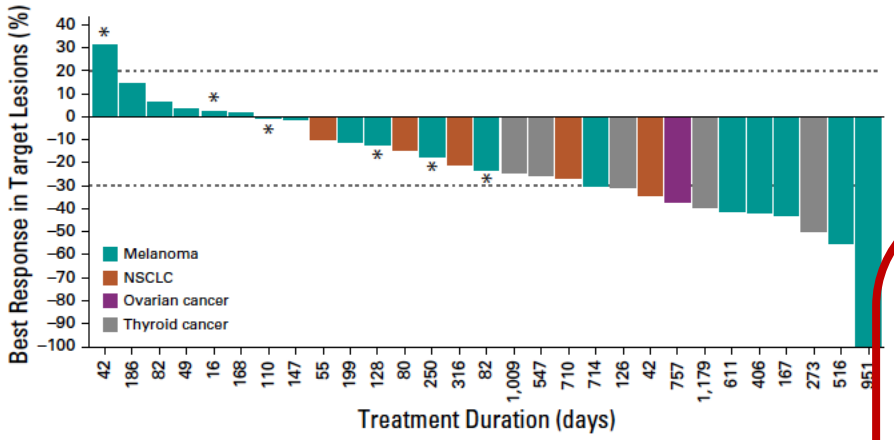
Poulikakos, Sullivan, Yaeger. Submitted 2022.

Emerging Data With BRAF Dimer, ERK, MEK, Various Combos

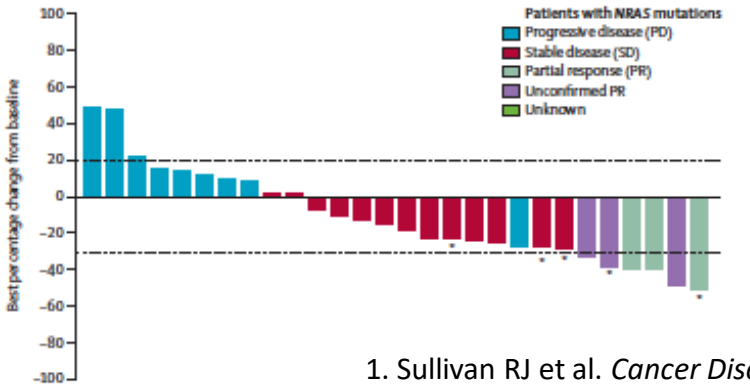
ERKi[1]

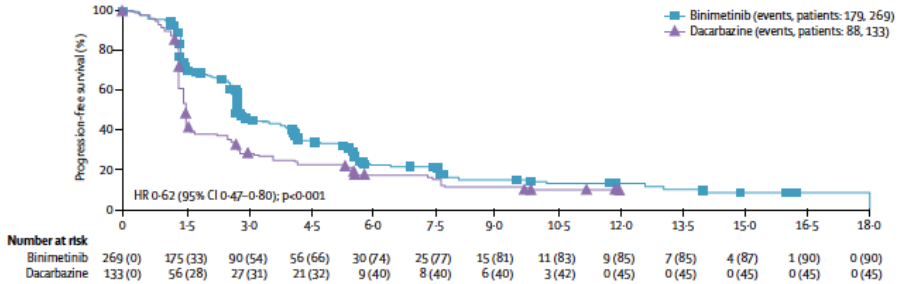


RAF dimer i[2]

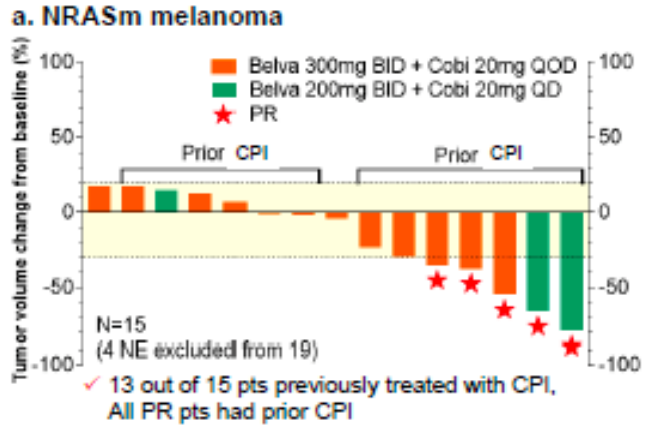


MEKi[3,4]





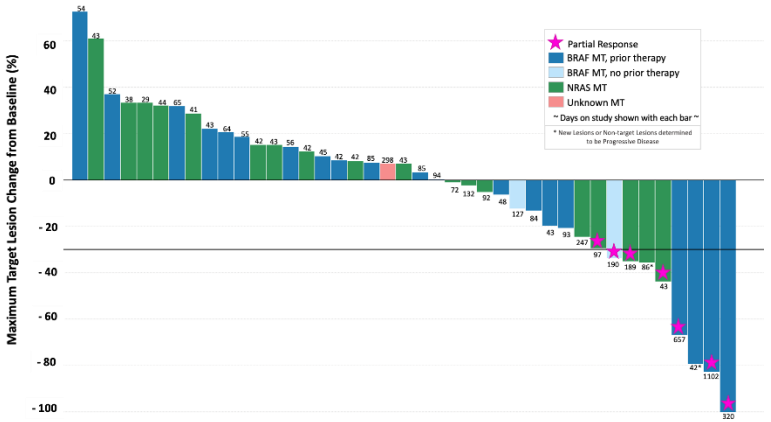
RAF dimer I + MEKi[5]



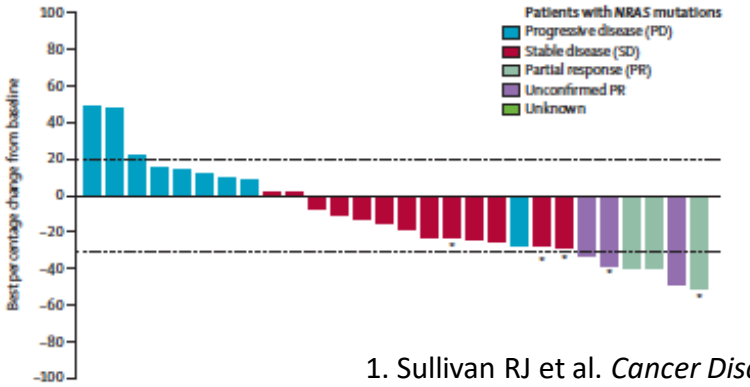
1. Sullivan RJ et al. *Cancer Discov.* 2018;8(2):184-195; 2. Desai J et al. *J Clin Oncol.* 2020;38(19):2140-2150; 3. Ascierto PA et al. *Lancet Oncol.* 2013;14(3):249-256; 4. Dummer R et al. *Lancet Oncol.* 2017;18(4):435-445; 5. Kim TW et al. ESMO 2021. Abstract 529P.

Emerging Data With BRAF Dimer, ERK, MEK, Various Combos

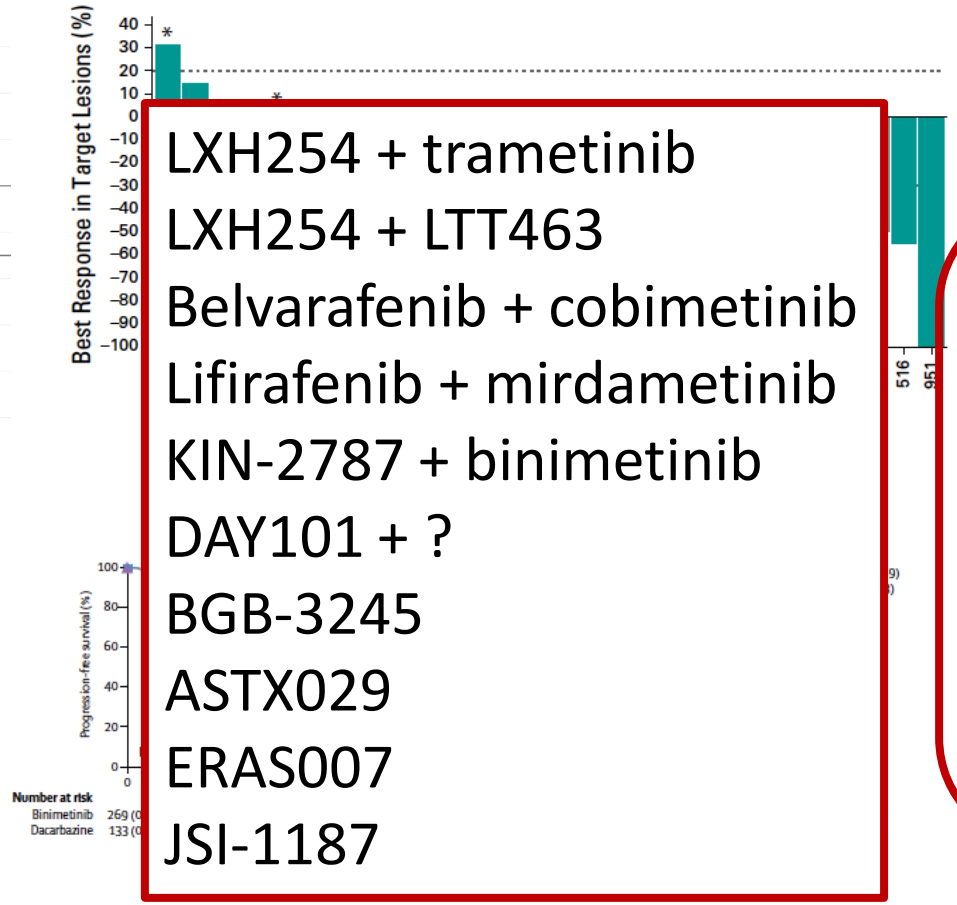
ERKi[1]



MEKi[3,4]

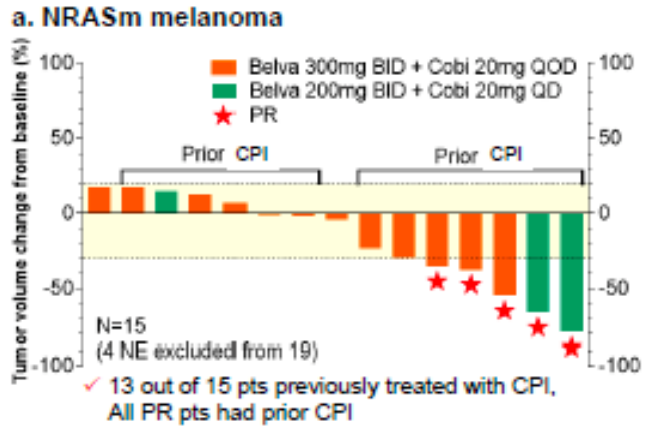


RAF dimer i[2]



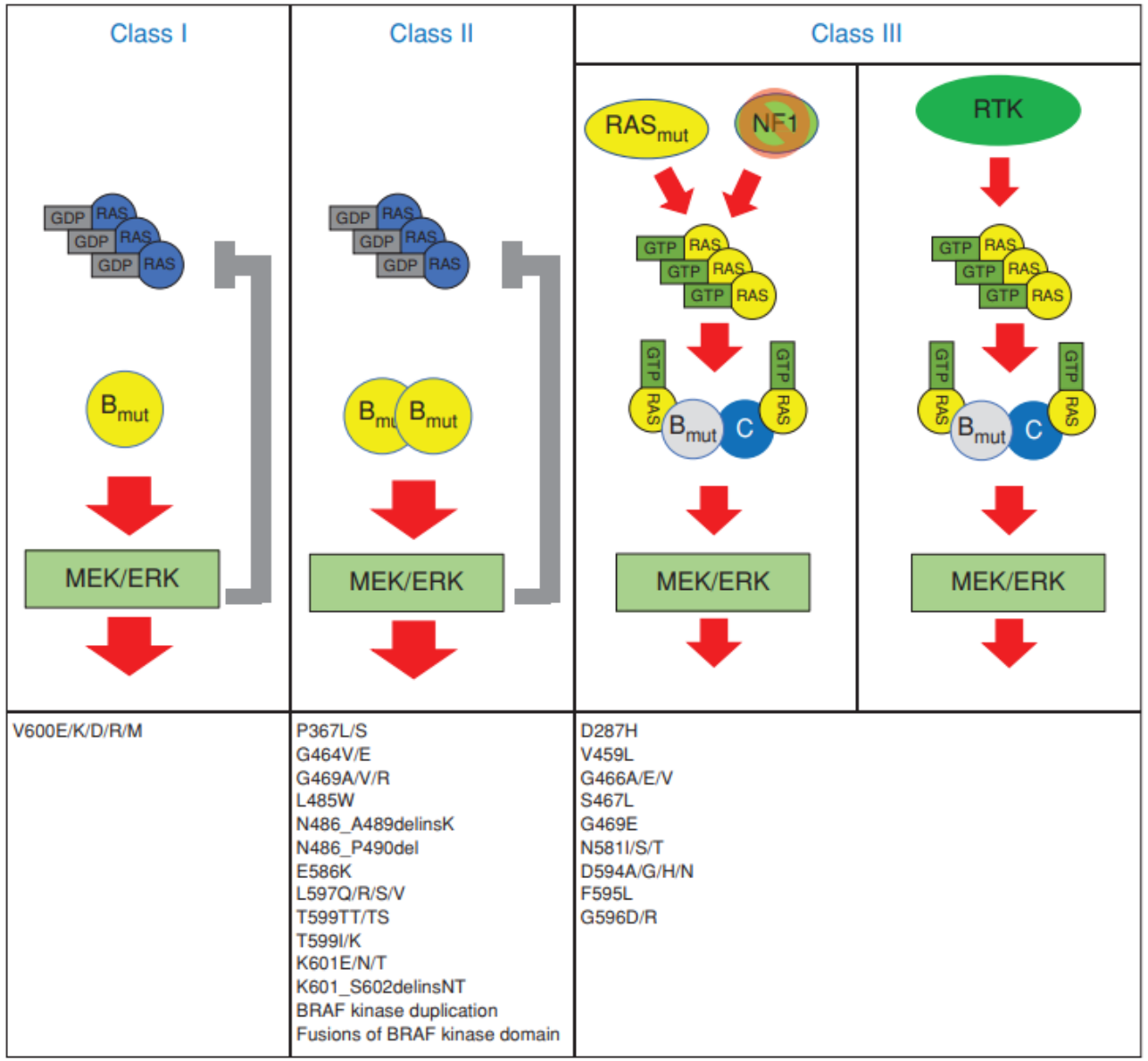
- LXH254 + trametinib
- LXH254 + LTT463
- Belvarafenib + cobimetinib
- Lifirafenib + mirdametinib
- KIN-2787 + binimetinib
- DAY101 + ?
- BGB-3245
- ASTX029
- ERAS007
- JSI-1187

RAF dimer I + MEKi[5]



1. Sullivan RJ et al. *Cancer Discov.* 2018;8(2):184-195; 2. Desai J et al. *J Clin Oncol.* 2020;38(19):2140-2150; 3. Ascierto PA et al. *Lancet Oncol.* 2013;14(3):249-256; 4. Dummer R et al. *Lancet Oncol.* 2017;18(4):435-445; 5. Kim TW et al. ESMO 2021. Abstract 529P.

Targeting Less Common BRAF Mutations



Class I	Class II	Class III
V600E/K/D/R/M	P367L/S G464V/E G469A/V/R L485W N486_A489delinsK N486_P490del E586K L597Q/R/S/V T599TT/TS T599I/K K601E/N/T K601_S602delinsNT BRAF kinase duplication Fusions of BRAF kinase domain	D287H V459L G466A/E/V S467L G469E N581I/S/T D594A/G/H/N F595L G596D/R

Yaeger R et al. *Cancer Discovery.* 2019;9(3):329-341.

Improving First Line Therapy

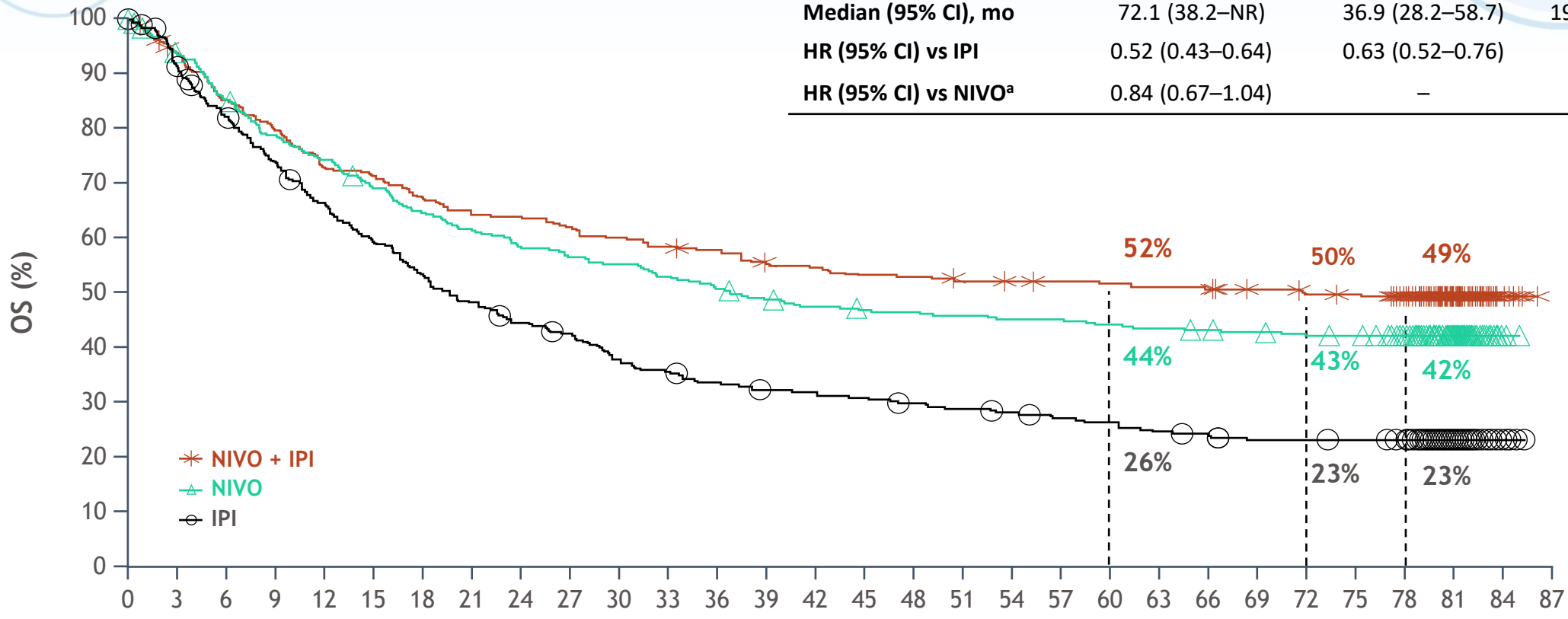
Combinations CTLA4 and PD1

LAG -3

Others……

CheckMate 067: 6.5-year Overall survival

	NIVO + IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Median (95% CI), mo	72.1 (38.2–NR)	36.9 (28.2–58.7)	19.9 (16.8–24.6)
HR (95% CI) vs IPI	0.52 (0.43–0.64)	0.63 (0.52–0.76)	–
HR (95% CI) vs NIVO[a]	0.84 (0.67–1.04)	–	–



No. at risk

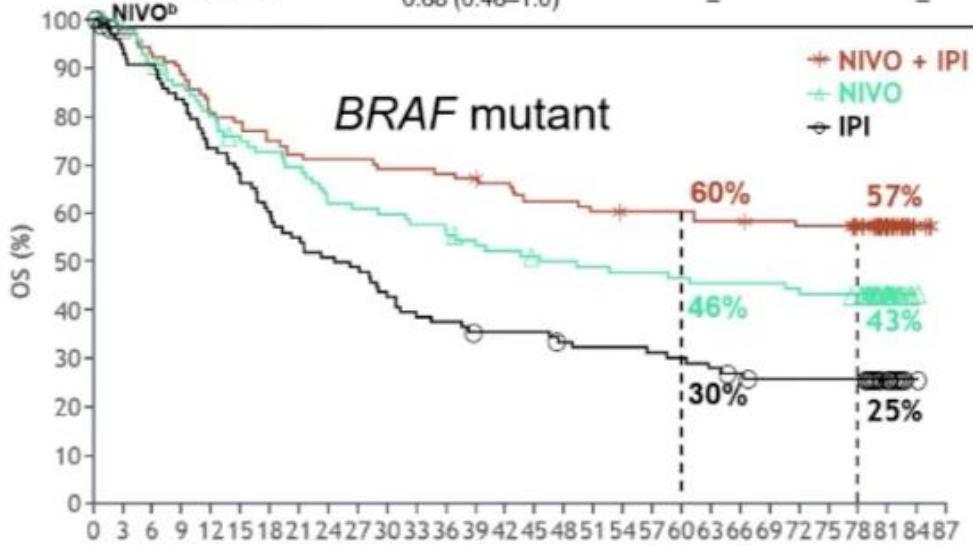
NIVO + IPI	314	292	265	248	227	222	210	201	199	193	187	181	179	172	169	164	163	159	158	157	156	154	153	150	147	145	138	66	10	0
NIVO	316	292	266	245	231	214	201	191	181	175	171	164	158	150	145	142	141	139	137	137	134	132	130	128	126	124	117	59	3	0
IPI	315	285	253	227	203	181	163	148	135	128	113	107	100	95	94	91	87	84	81	77	75	70	68	64	64	63	61	32	7	0

Wolchok JD et al. ASCO 2021. Abstract 9506.

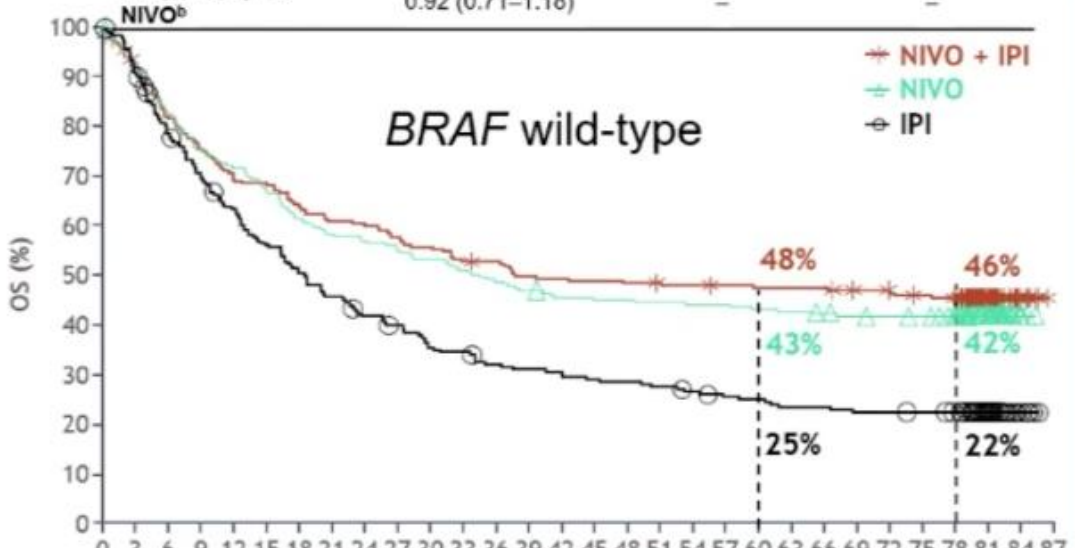
[a]Descriptive analysis.

Retrospective subset analysis: OS
CTLA-4 contributes efficacy only in BRAF mutant patients

	NIVO + IPI (n = 103)	NIVO (n = 98)	IPI (n = 100)
Median (95% CI), mo	NR (50.7–NR)	45.5 (26.4–NR)	24.6 (17.9–31.0)
HR (95% CI) vs IPI	0.43 (0.30–0.60)	0.63 (0.44–0.90)	–
HR (95% CI) vs NIVO[b]	0.68 (0.46–1.0)	–	–



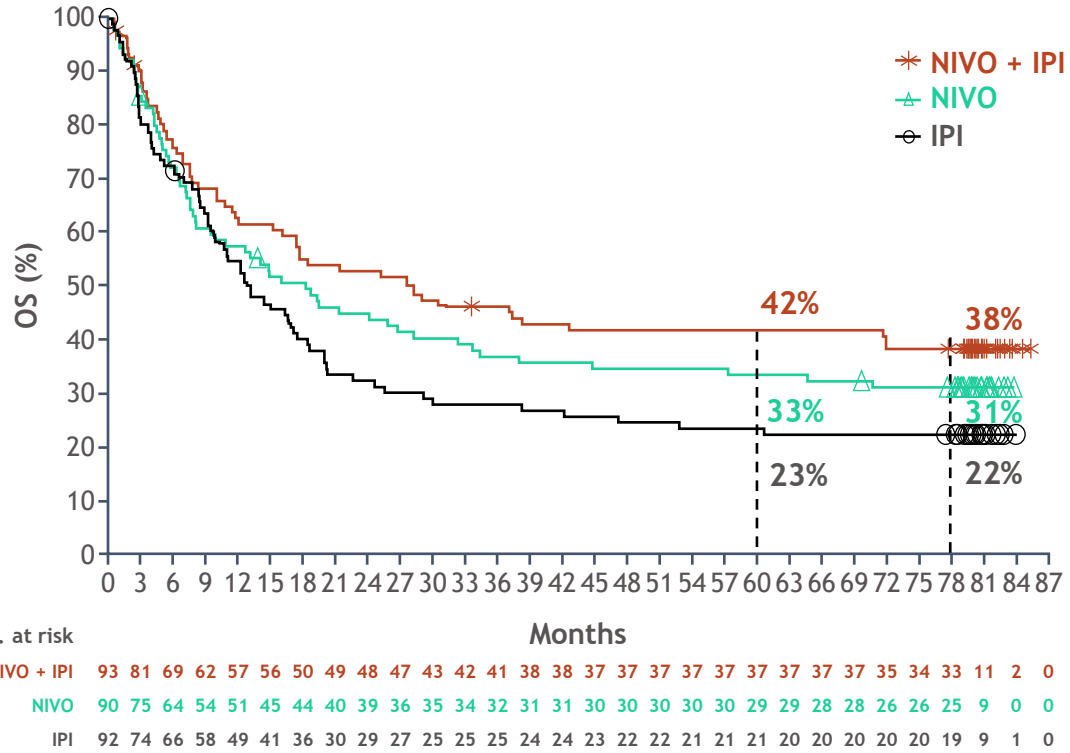
	NIVO + IPI (n = 211)	NIVO (n = 218)	IPI (n = 215)
Median (95% CI), mo	39.1 (27.5–NR)	34.4 (24.1–59.2)	18.5 (14.1–22.7)
HR (95% CI) vs IPI	0.58 (0.45–0.74)	0.63 (0.50–0.80)	–
HR (95% CI) vs NIVO[b]	0.92 (0.71–1.18)	–	–



Wolchok JD et al. ASCO 2021. Abstract 9506.

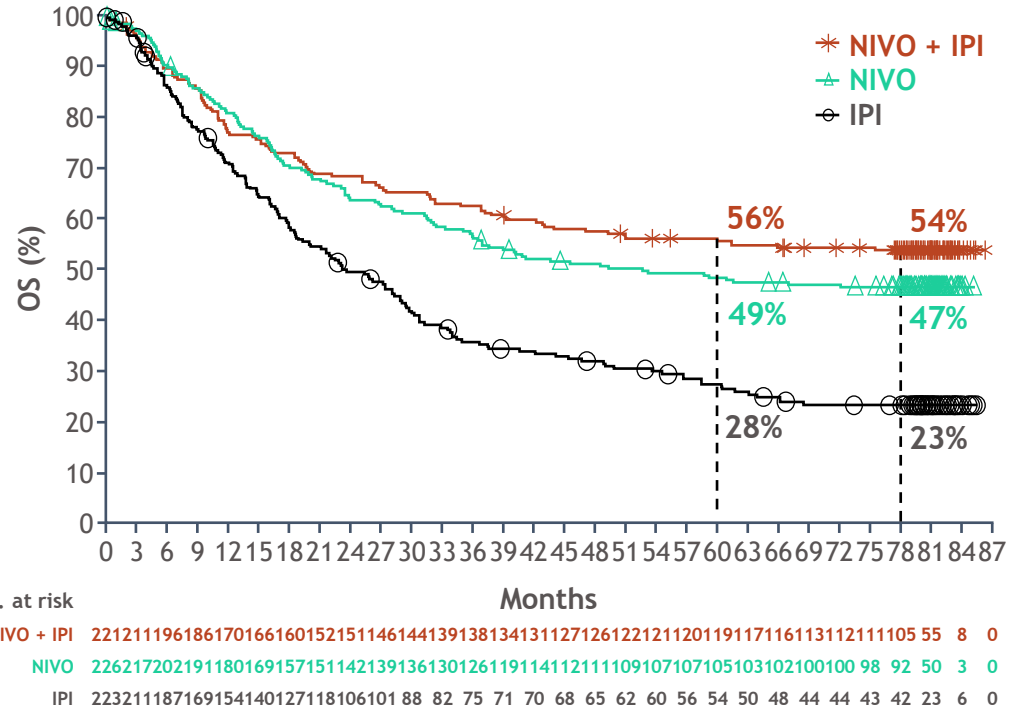
OS by presence of baseline liver metastases

	NIVO + IPI (n = 93)	NIVO (n = 90)	IPI (n = 92)
Median (95% CI), mo	28.2 (15.2–71.9)	18.2 (8.1–32.3)	13.1 (9.6–18.4)
HR (95% CI) vs IPI	0.66 (0.46–0.93)	0.81 (0.58–1.14)	–
HR (95% CI) vs NIVO[a]	0.81 (0.56–1.16)	–	–



With liver metastases

	NIVO + IPI (n = 221)	NIVO (n = 226)	IPI (n = 223)
Median (95% CI), mo	NR (50.7–NR)	52.7 (36.0–NR)	23.5 (18.6–29.4)
HR (95% CI) vs IPI	0.47 (0.37–0.60)	0.56 (0.44–0.71)	–
HR (95% CI) vs NIVO[a]	0.84 (0.64–1.09)	–	–



Without liver metastases

Wolchok JD et al. ASCO 2021. Abstract 9506.

[a]Descriptive analysis.

2021 ESMO congress

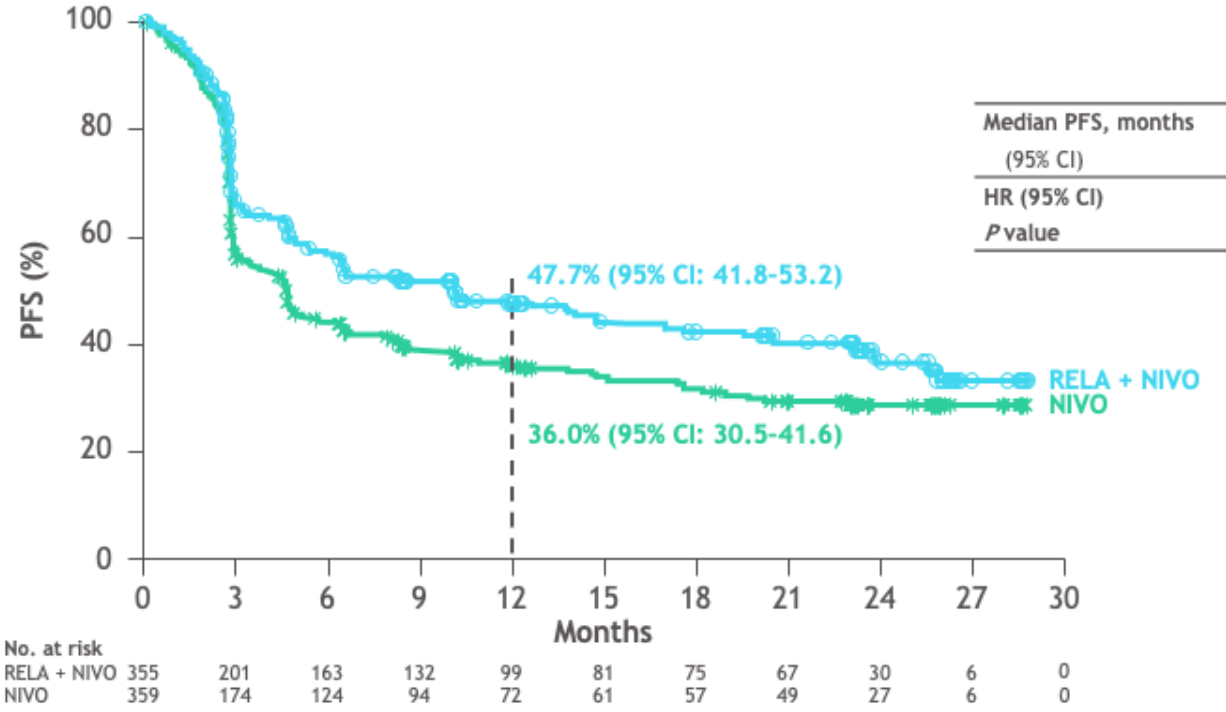
Relatlimab (RELA) + nivolumab (NIVO) versus NIVO in previously untreated metastatic or unresectable melanoma: Additional efficacy in RELATIVITY-047

F. Stephen Hodi,[1] Hussein A. Tawbi,[2] Evan J. Luis Matamala,[6,7] Erika Castillo Gutiérrez,[8] Juliana Janoski De Menezes,[12] Stéphane Dal Toms,[16] Karin Jonczak,[16] Anne Marie Sobiesk

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]The University Institute for Cancer Immunotherapy, Johns Hopkins Sidney Kimme Essen, Germany; [5]Istituto Nazionale Tumori Fondazione "G. Pasca Lopez Perez, Santiago, Chile; [7]Department of Oncology, Instituto [9]Maria Sklodowska-Curie National Research Institute of Oncology, Greece; [11]University of Michigan, Ann Arbor, MI, USA; [12]Hospital N Research Center of Lyon, Pierre-Bénite, France; [14]Hospital Clinic France; [16]Bristol Myers Squibb, Princeton, NJ, USA; [17]Melanoma In Hospitals, Sydney, Australia.

Hodi FS e

RELATIVITY 047 demonstrated superior PFS benefit by BICR for RELA + NIVO FDC vs NIVO



	RELA + NIVO (n = 355)	NIVO (n = 359)
Median PFS, months	10.12	4.63
(95% CI)	(6.37-15.74)	(3.38-5.62)
HR (95% CI)	0.75 (0.62-0.92)	
P value	0.0055	

CI, confidence interval; HR, hazard ratio.
All randomized patients. Statistical model for HR and *P* value: stratified Cox proportional hazard model and stratified log-rank test. Stratified by LAG-3 (≥ 1% vs < 1%), *BRAF* (mutation positive vs mutation wild-type), AJCC M stage (M0/M1any[0] vs M1any[1]). PD-L1 was removed from stratification because it led to subgroups with < 10 patients.

Hodi FS et al. ESMO 2021. Abstract 1036O.

Physician Educator

Serum IL-6 and CRP Are Prognostic Factors in Melanoma Patients Receiving Single Agent and Combination Checkpoint Inhibition

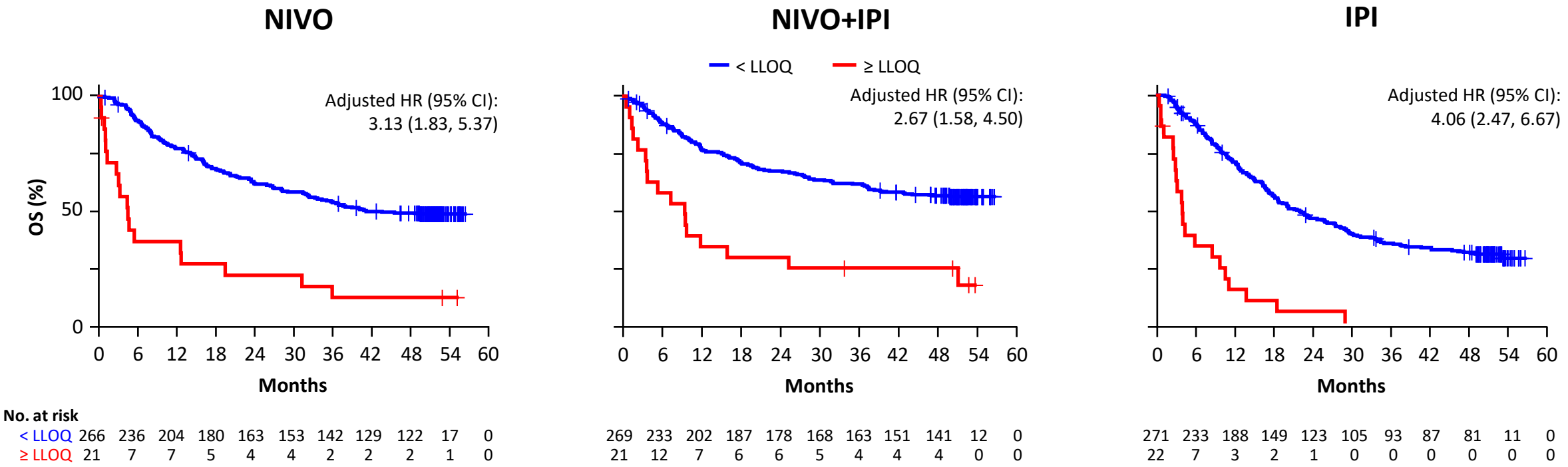
Jeffrey Weber,[1] F. Stephen Hodi,[2] Hao Tang,[3] Lauren Hippeli,[3] Xiaozhong Qian,[3] Megan Wind-Rotolo,[3] James Larkin,[4] Jedd Wolchok,[5] Mario Sznol,[6] Caroline Robert,[7] David Woods,[1] Melinda Vassallo,[1] Andressa Laino[1]

[1]NYU Perlmutter Cancer Center, New York, NY, USA; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Bristol-Myers Squibb, Princeton, NJ, USA; [4]Royal Marsden Hospital, London, UK; [5]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [6]Yale University Medical Center, New Haven, CT, USA; [7]Gustave Roussy, Paris, France

Weber JS et al. ASCO 2019. Abstract 100.

PRESENTED BY: J Weber; Jeffrey.Weber@nyulangone.org

CheckMate 067: Association of Baseline IL-6 Levels With OS Across Treatment Arms



High IL-6 levels were associated with shorter OS

IL-6 LLOQ: 11 pg/mL.
HR adjusted for ECOG, *BRAF*, M stage, and baseline LDH.

Weber JS et al. ASCO 2019. Abstract 100.

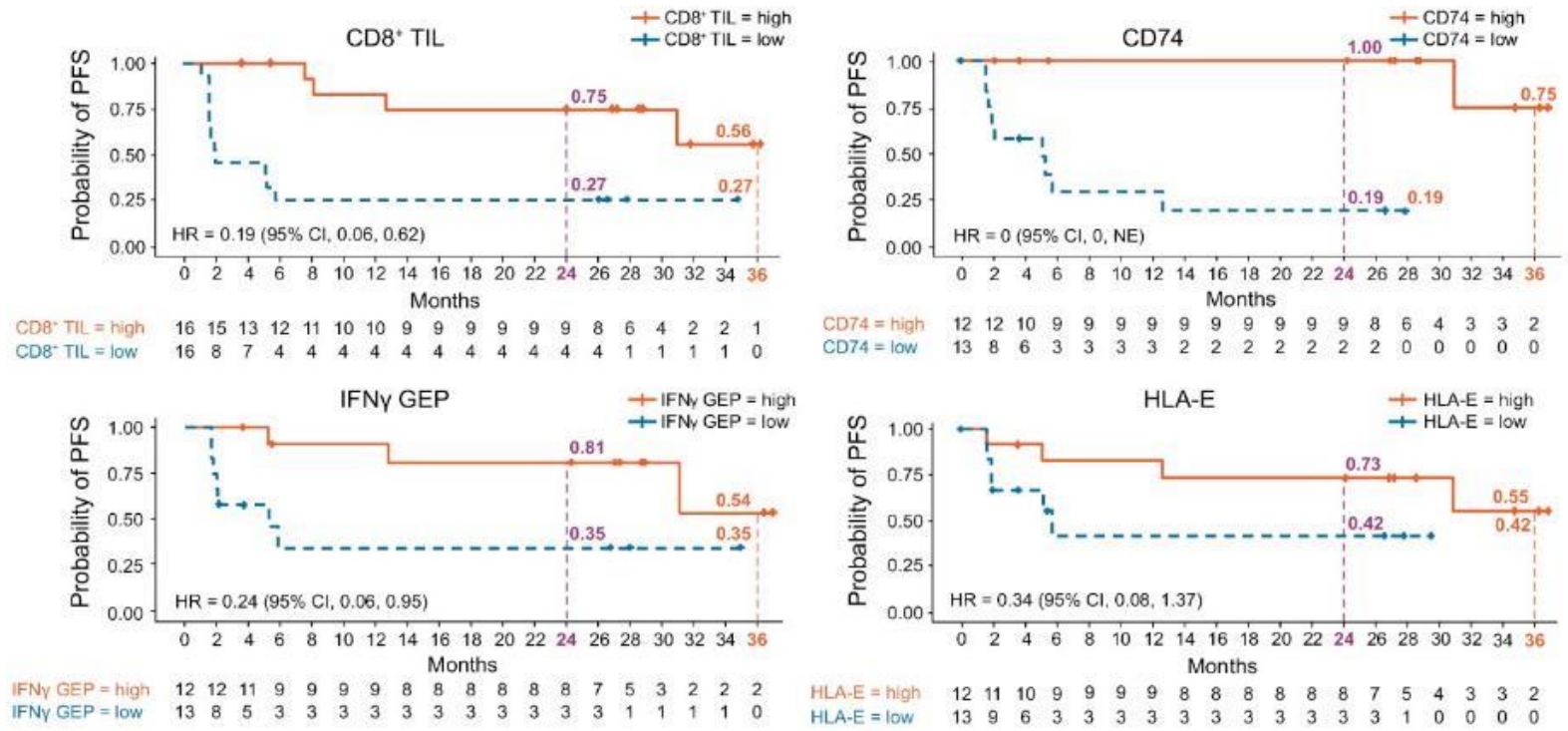
PRESENTED BY: J Weber; Jeffrey.Weber@nyulangone.org

Relationship Between Baseline Biomarkers and Response

Baseline tumor biomarkers were associated with longer PFS*†

- High **CD8+ TIL**, high **IFN-γ GEP**, high **CD74**, and high **HLA-E** in baseline tumor biopsies were associated with a longer PFS

Relationship between selected baseline tumor biomarkers and PFS



Diab A et al. *J Clin Oncol.* 2021;39(26):2914-2925.

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Second Line Options

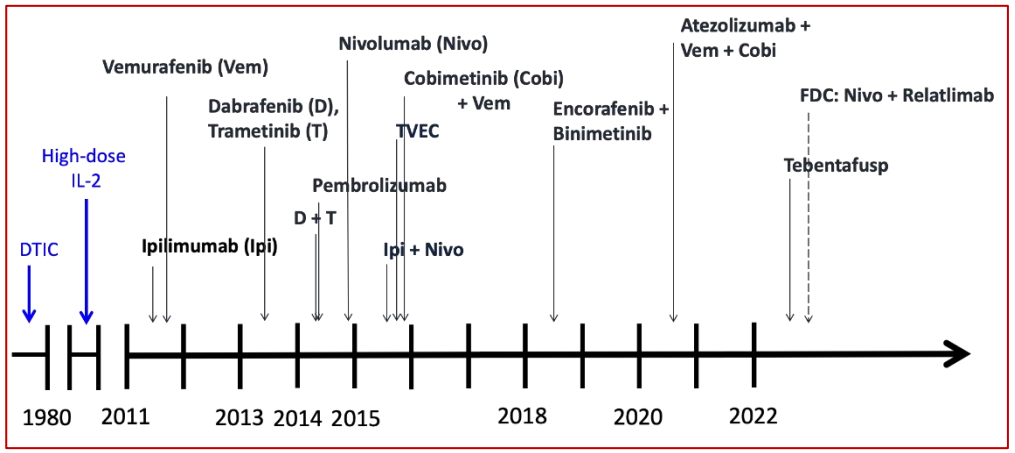
Combinations CTLA4 and PD1

LAG -3

Others……

Unmet Needs in Advanced Disease

Nearly all the presented and published data is in front-line setting and in patients with cutaneous melanoma



2nd/3rd line therapy after anti-CTLA-4 plus or after anti-PD-1

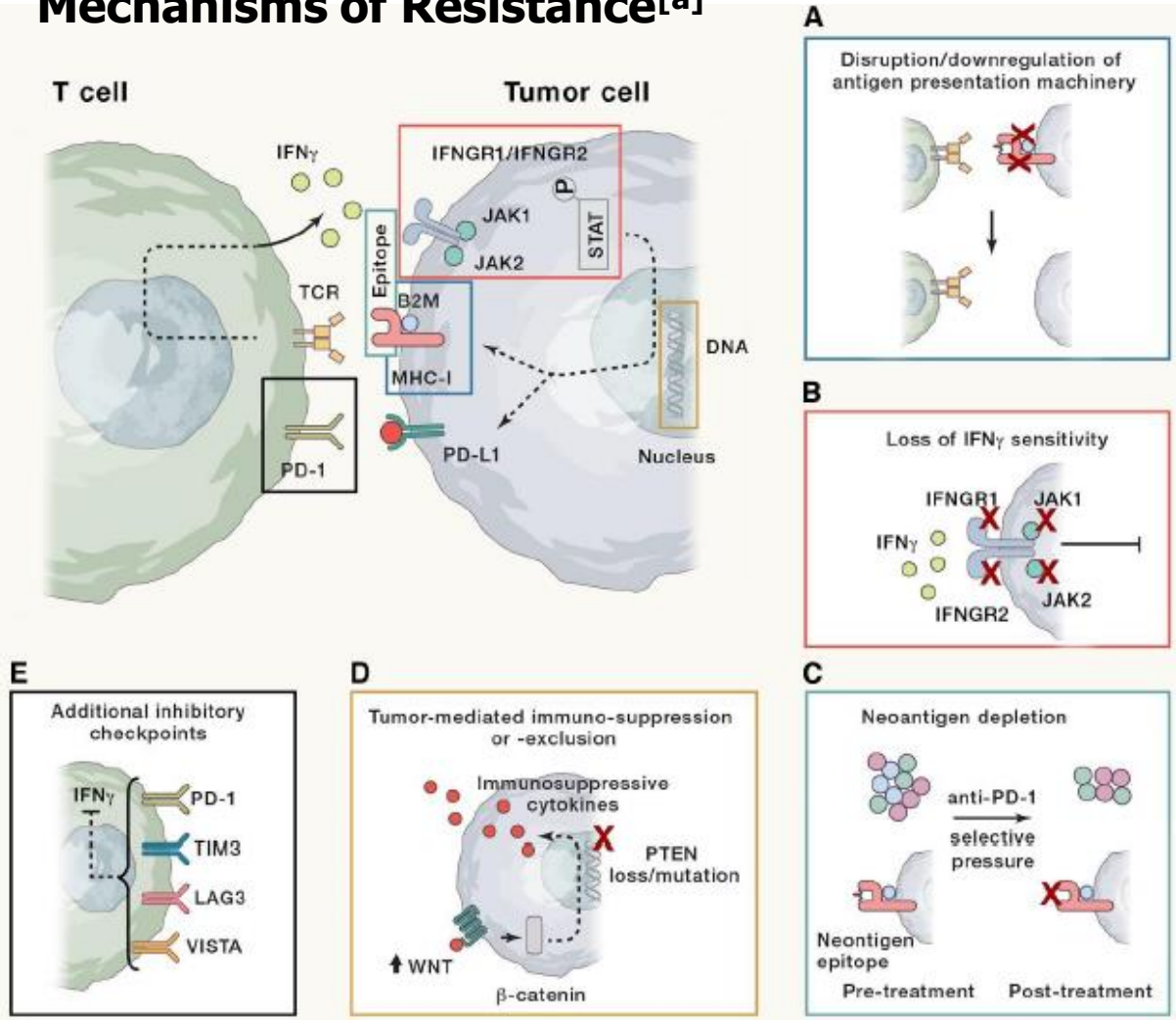
Adoptive cell therapy

Feces?

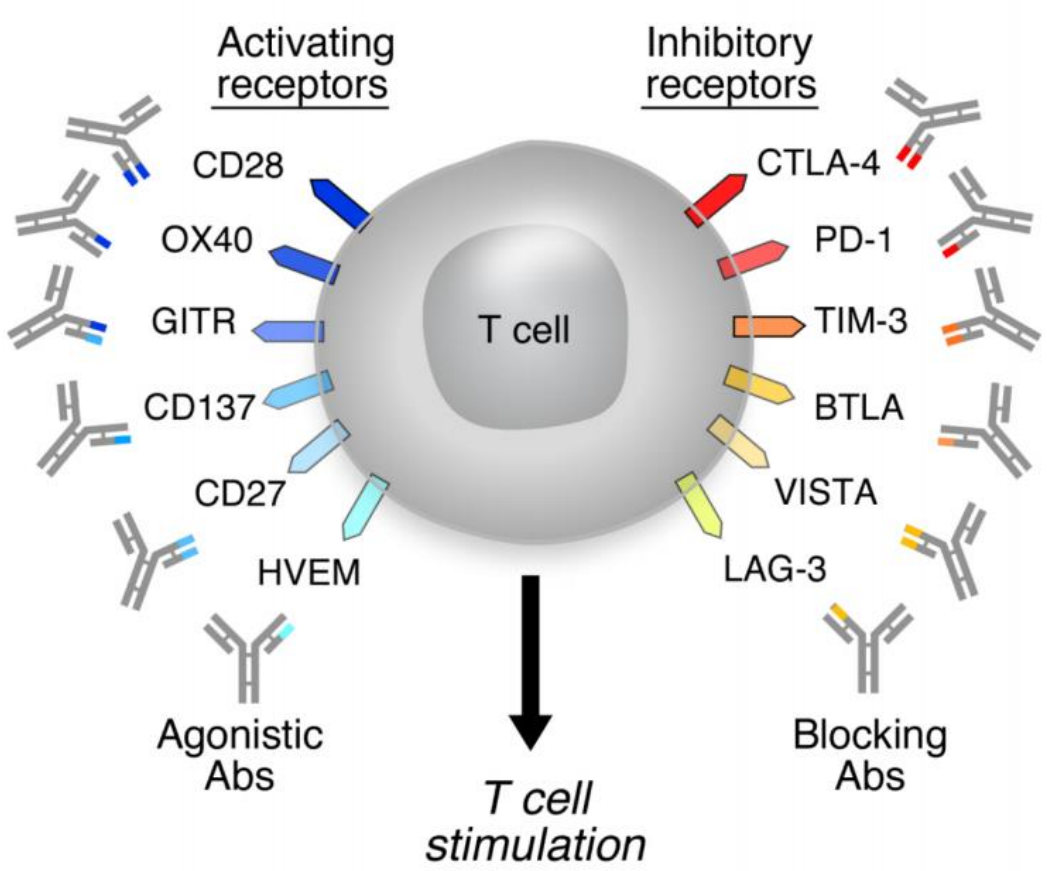
Clinical trials in the post-PD-1 setting

T Cell-Tumor Interactions: Loci for Proposed Acquired Resistance

Mechanisms of Resistance[a]



Activating Receptors/Costimulatory Molecules

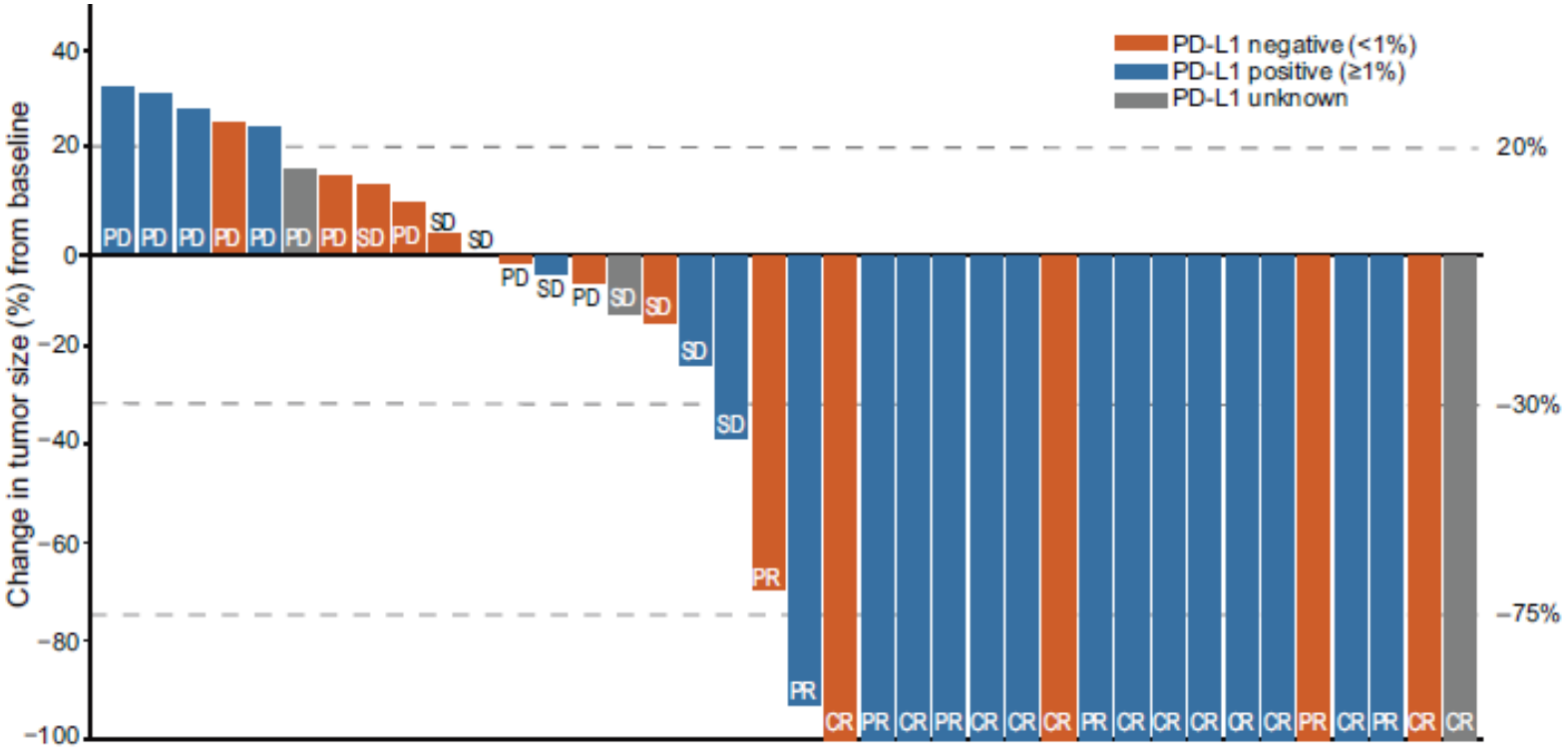


a. Schoenfeld AJ, et al. *Cancer Cell*. 2020;37:443-455; b. Mellman I, et al. *Nature*. 2011;480:480-489.

PIVOT-02 1L Melanoma: Best Overall Response by Independent Radiology

- **Median duration of follow-up: 29.0 months** (IQR: 15.7–32.3 months)
- **Confirmed ORR** by BICR: **52.6%** (95% CI: 35.8–69.0; n=20/38)
  - **CR rate: 34.2%** (n=13/38)
  - **90%** (18/20) of responding patients achieved 100% reduction in target lesions from baseline
- **Median time to response:**
  - First response: **2.0 months** (range: 1.5–4.1 months)
  - CR: **7.9 months** (range: 1.5–15.2 months)

Waterfall plot showing the maximum change in tumor size with BEMPEG plus NIVO (n=38)



Data cut-off: September 1, 2020.

Response-evaluable population includes eligible patients with measurable disease (per RECIST v1.1) at baseline and at least one post-baseline assessment of tumor response. All objective responses are confirmed.

BEMPEG, bempegaldesleukin; CR, complete response; NIVO, nivolumab; PD, progressive disease (due to non-target lesion progression or presence of new lesion); PD-L1, programmed death-ligand 1; PR, partial response (complete response for target lesion; non-target lesion still present); RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease.

Diab A et al. *J Clin Oncol.* 2021;39(26):2914-2925.

Lenva

Lenvatinib Plus Pembrolizumab For Patients With Advanced Melanoma and Confirmed Progression on a PD-1 or PD-L1 Inhibitor: Updated Findings of LEAP-004

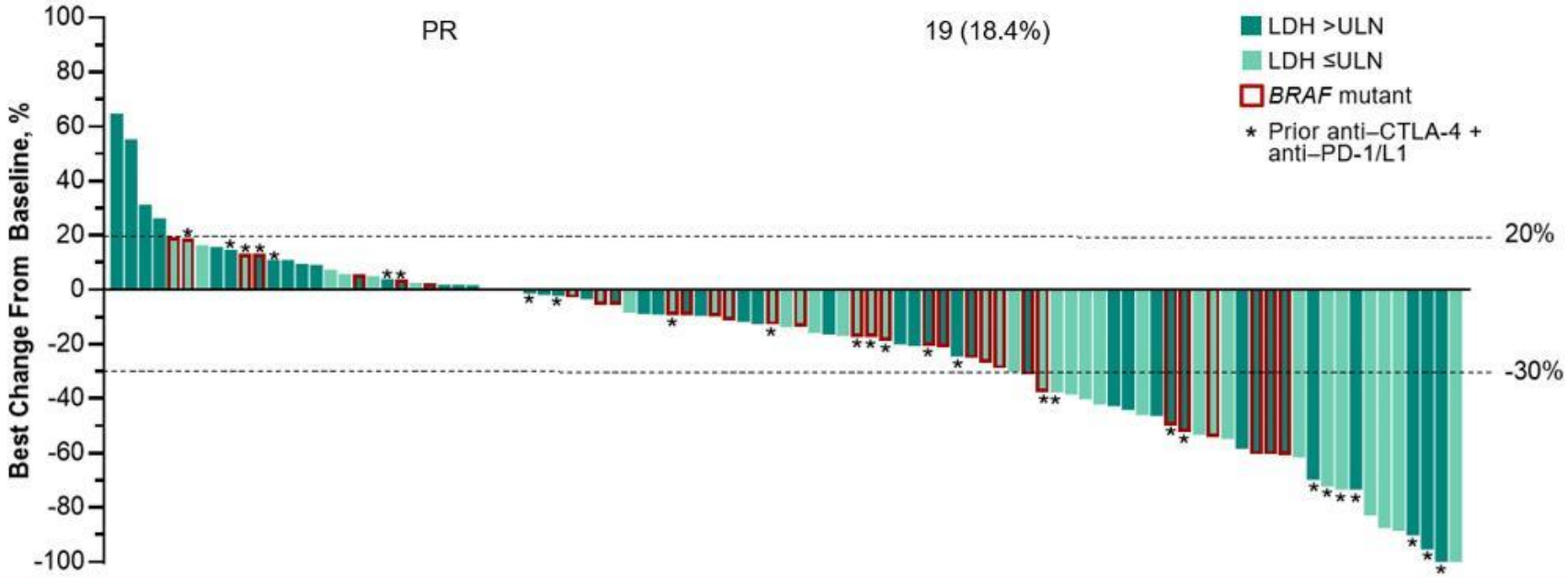
Ana Arance,[1] Luis de la Cruz Merino,[2] Teresa M. Petrella,[3] Rahima Jamal,[4] Lars Ny,[5] Ana Carneiro,[6] Alfonso Berrocal,[7] Ivan Márquez-Rodas,[8] Anna Spreafico,[9] Victoria Atkinson,[10] Fernanda Costa Svedman,[11] Andrew Mant,[12] Alan D. Smith,[13] Ke Chen,[14] Scott J. Diede,[14] Clemens Krepler,[14] Georgina V. Long[15]

[1]Hospital Clinic Barcelona, Barcelona, Spain; [2]Hospital Universitario Virgen Macarena, Seville, Spain; [3]Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [4]Centre hospitalier de l'Université de Montréal, Montréal, QC, Canada; [5]University of Gothenburg and Sahlgrenska University Hospital, Gothenburg, Sweden; [6]Skåne University Hospital and Lund University, Lund, Sweden; [7]Hospital General Universitario de Valencia, Valencia, Spain; [8]Hospital General Universitario Gregorio Marañón and CIBERONC, Madrid, Spain; [9]Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada; [10]Princess Alexandra Hospital, University of Queensland, Brisbane, QLD, Australia; [11]Karolinska University Hospital, Stockholm, Sweden; [12]Eastern Health, Monash University, Melbourne, VIC, Australia; [13]Eisai Ltd., Hatfield, United Kingdom; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]Melanoma Institute Australia, University of Sydney, and Royal North Shore and Mater Hospitals, Sydney, NSW, Australia

Arance A et al. ASCO 2021. Abstract 9504.

Responses in patients with prior anti-PD1 and combination PD1-CTLA4

	Total Population N = 103
ORR, % (95% CI)	**21.4% (13.9-30.5)**
DCR, % (95% CI)	66.0% (56.0-75.1)
Best overall response, n (%)	
CR	3 (2.9%)
PR	19 (18.4%)



Arance A et al. ASCO 2021. Abstract 9504.

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Novel Immune Mechanisms

Bispecific Antibodies

Adoptive T Cell Therapy

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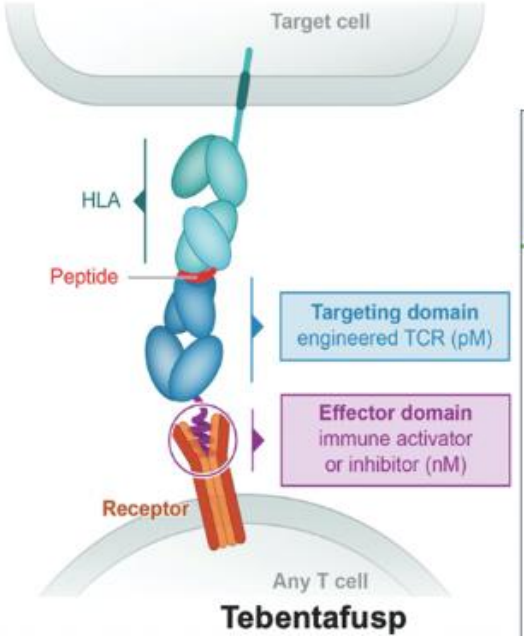
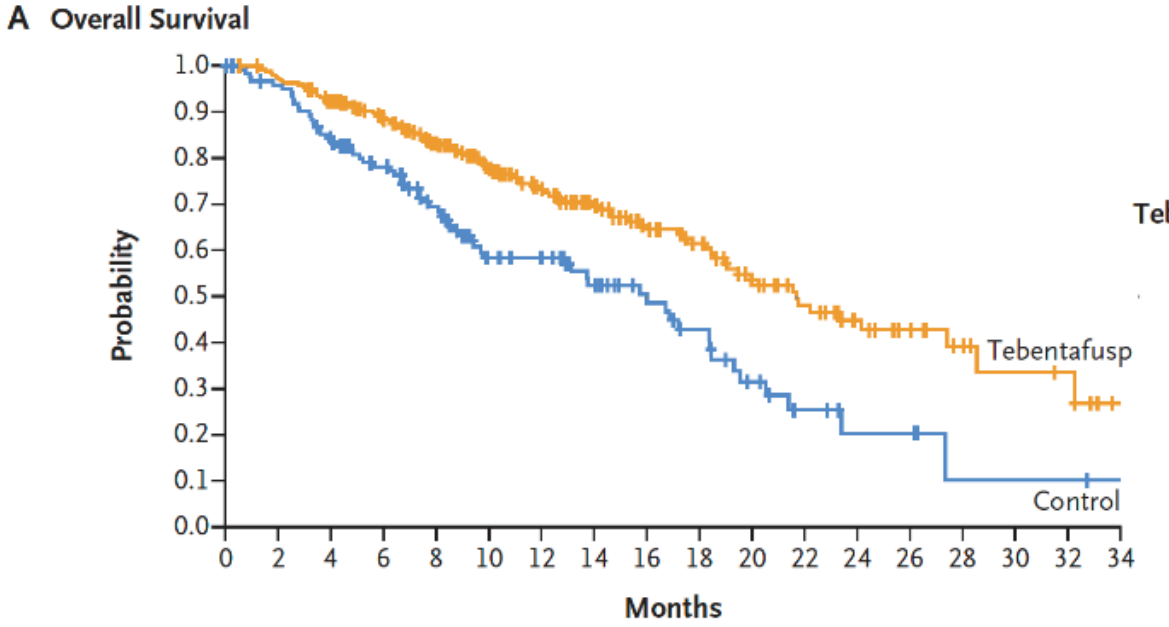
Immune Mobilizing T Cell Receptor Against Cancer (ImmTAC)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE



Overall Survival Benefit with Tebentafusp in Metastatic Uveal Melanoma



	Median Overall Survival (95% CI) *mo*
Tebentafusp	21.7 (18.6–28.6)
Control	16.0 (9.7–18.4)

Stratified hazard ratio for death, 0.51 (95% CI, 0.37–0.71)

No. at Risk																	
Tebentafusp	252	242	221	197	167	132	109	90	71	59	44	33	22	17	9	6	5	0
Control	126	116	100	86	69	48	43	34	27	20	12	7	4	4	1	1	1	0

Nathan P et al. *N Engl J Med.* 2021;385:1196-1206.

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Results from Phase Ib study of tebentafusp (tebe) in combination with durvalumab (durva) and/or tremelimumab (treme) in metastatic cutaneous melanoma

Authors: O. Hamid[1], J. C. Hassel[2], A.N. Shoushtari[3], F. Meier[4], T. Bauer[5], A. Salama[6], J. Kirkwood[7], P. Ascierto[8], P. Lorigan[9], C. Mauch[10], M. Orloff[11], J. Evans[12], R. Edukulla[13], C. Holland[13], S.E. Abdullah[13], R. Mundy[13], M. Middleton[14]

[1]The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, CA, United States; [2]Heidelberg University Hospital, Heidelberg, Germany; [3]Memorial Sloan-Kettering Cancer Center, New York, NY, United States; [4]University Hospital Carl Gustav, Dresden, Germany; [5]Tenesse Oncology, Nashville, TN, United States; [6]Duke University, Durham, NC, United States; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, United States; [8]IRCCS National Cancer Institute Pascale Foundation, Naples, Italy; [9]The Christie NHS Foundation Trust, Manchester, United Kingdom; [10]University Hospital of Cologne, Cologne, Germany; [11]Thomas Jefferson University Hospitals; Philadelphia, PA, United States; [12]Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; [13]Immunocore, Abingdon, United Kingdom; [14]University of Oxford, Oxford, United Kingdom

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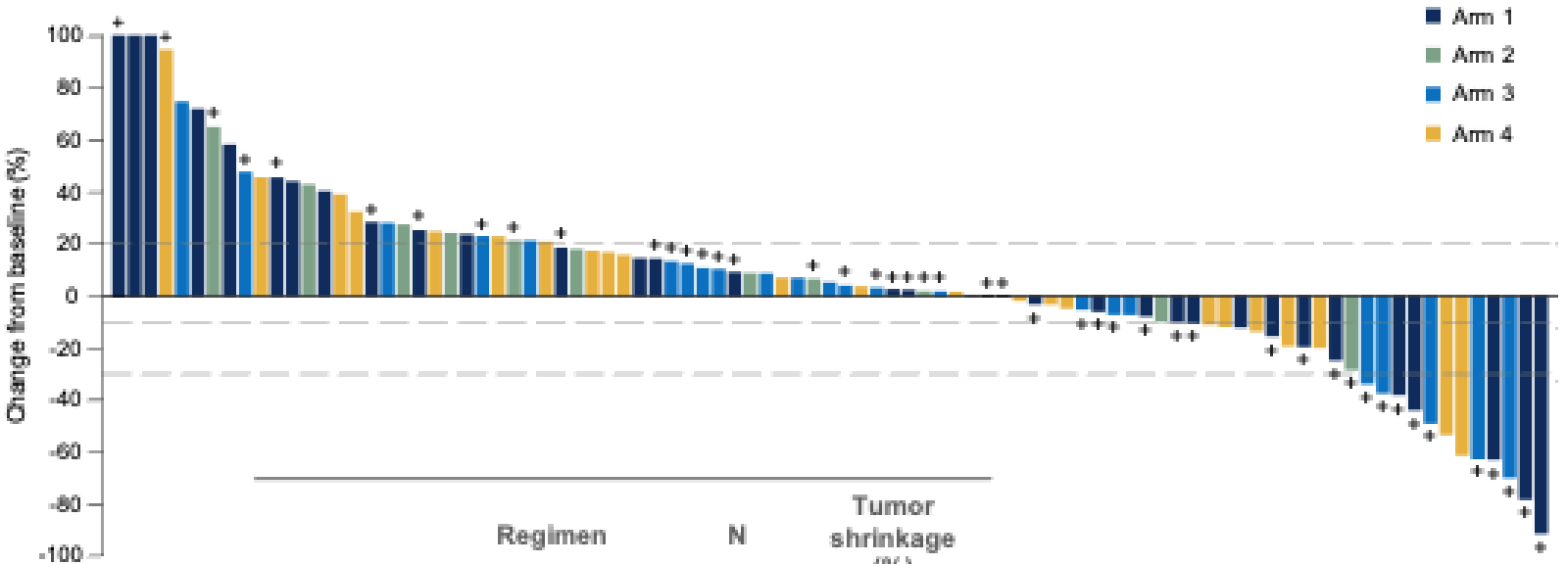
Results

Figure 3a – % change from baseline in tumor size of patients who received prior anti-PD(L)1 therapy, by arm of study



- 6% had a confirmed RECIST PR; median duration of response 20 months (95% CI: 6-NR)
- 37% had any tumor shrinkage as best change

	Regimen	N	Tumor shrinkage (%)
Arm 1	Tebe + durva (D)	32	44%
Arm 2	Tebe + treme (T)	11	18%
Arm 3	Tebe +D+T	25	32%
Arm 4	Tebe alone	23	44%

* Patients evaluable for response (N=91); Tumor shrinkage at any time prior to subsequent therapy
+ indicates patients with ≥12 mo survival

2021 ASCO® ANNUAL MEETING

Lifileucel (LN-144), a Cryopreserved Autologous Tumor Infiltrating Lymphocyte (TIL) Therapy in Patients with Advanced Melanoma: Evaluation of Impact of Prior Anti–PD-1 Therapy

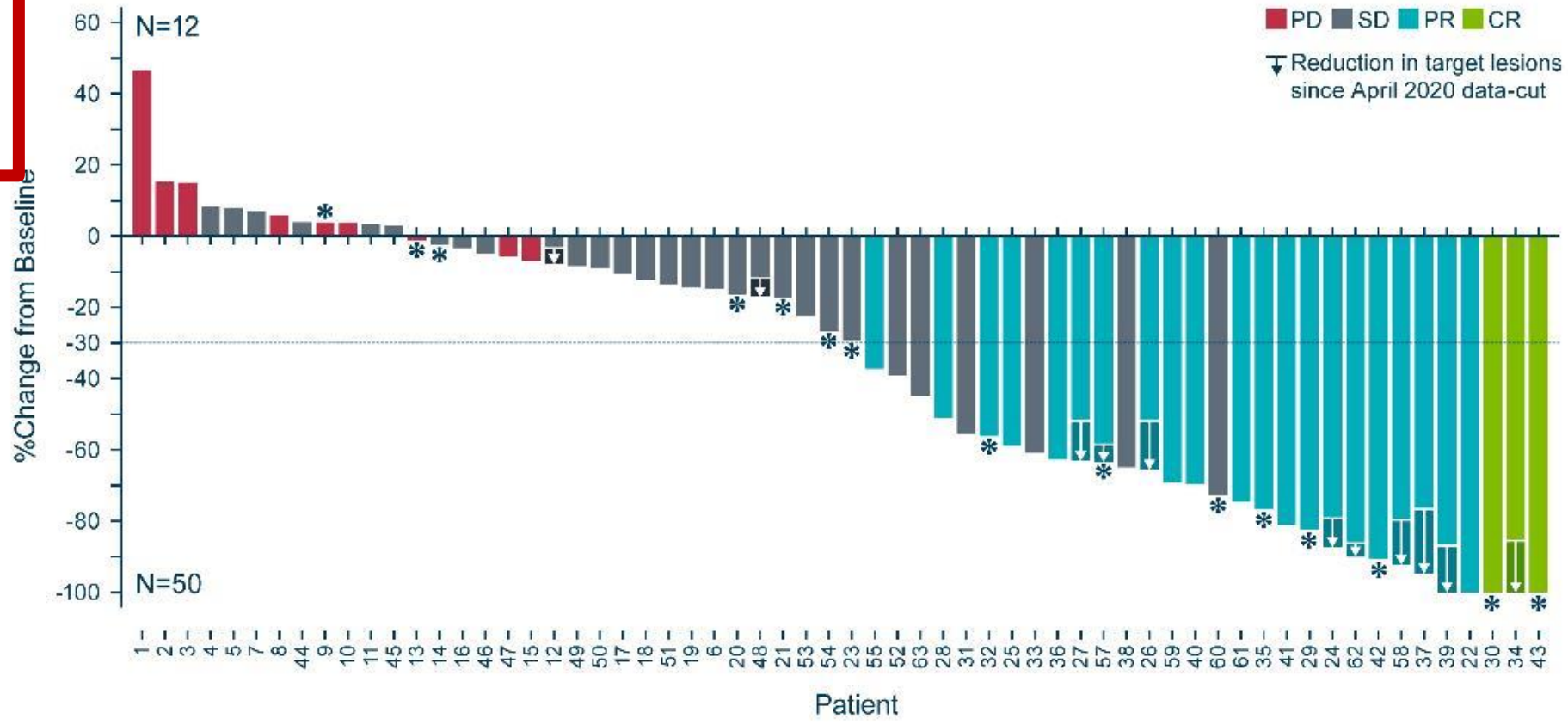
James M. G. Larkin,[1] Amod Sarnaik,[2] Jason Alan Chesney,[3] Nikhil I. Khushalani,[2] John M. Kirkwood,[4] Jeffrey S. Weber,[5] Karl D. Lewis,[6] Theresa Michelle Medina,[6] Harriet M. Kluger,[7] Sajeve Samuel Thomas,[8] Evidio Domingo-Musibay,[9] Judit Oláh,[10] Eric D. Whitman,[11] Salvador Martin-Algarra,[12] Philippa Gail Corrie,[13] Jose Lutzky,[14] Wen Shi,[15] Renee Xiao Wu,[15] Maria Fardis,[15] Omid Hamid[16]

[1]The Royal Marsden Hospital NHS Foundation Trust, London, UK

Larkin J et al. ASCO 2021. Abstract 9505.

Best Overall Response

- 81% (50/62) of patients had a reduction in tumor burden
- 11 patients (17.7%) had further SOD reduction since April 2020 datacut

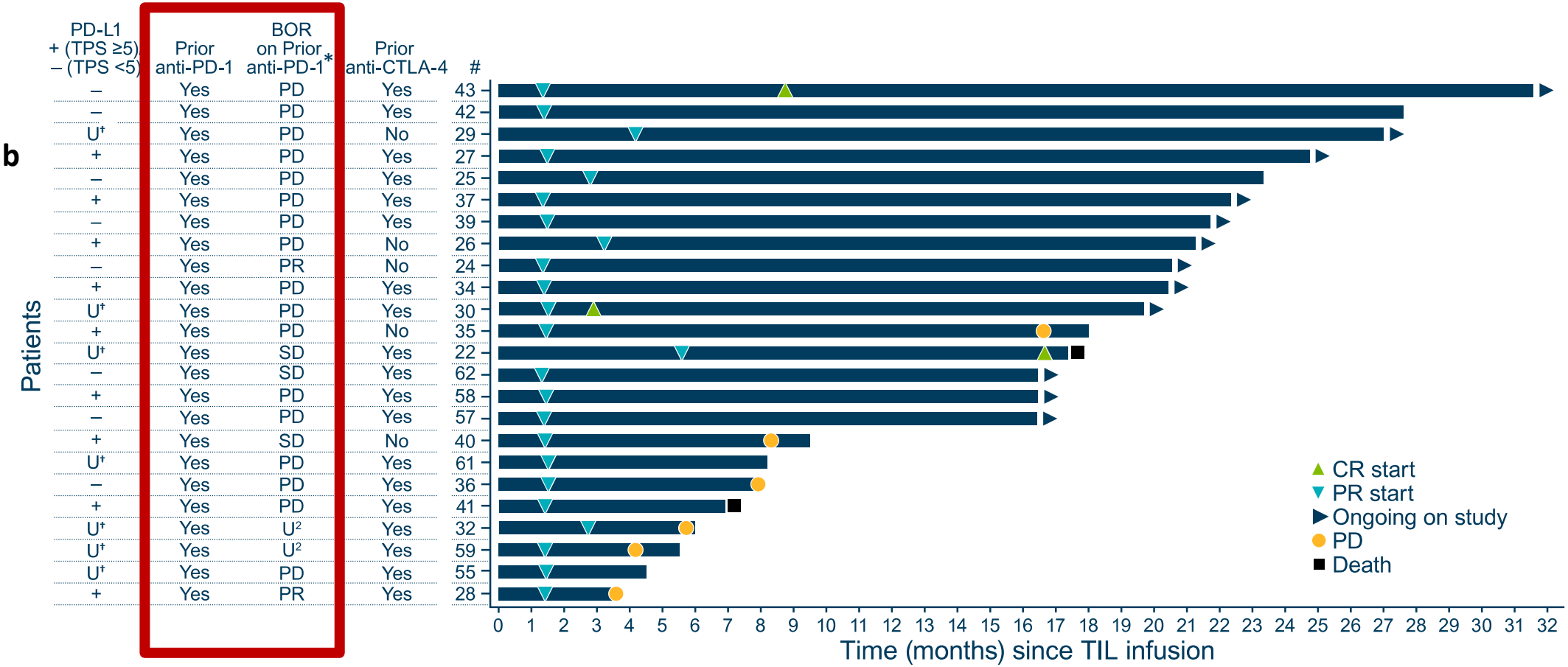


NEKTAR

Larkin J et al. ASCO 2021. Abstract 9505.

Time and Duration of Response for Evaluable Patients (PR or Better)

79% of responders had received prior ipilimumab

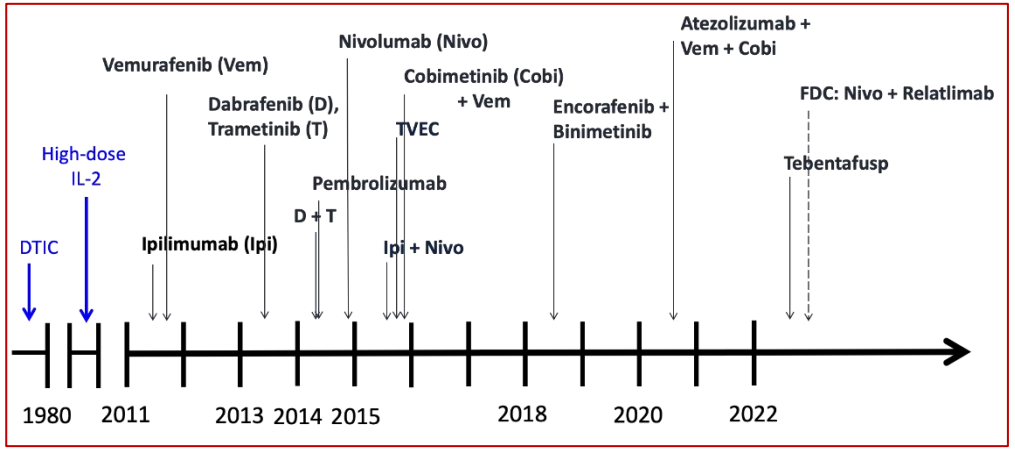


***BOR is best overall response on prior anti-PD-1 immunotherapy**
†U: unknown

Sarnaik AA et al. ASCO 2020. Abstract 10006.

Major Unmet Needs in Advanced Disease

Nearly all the presented and published data is in front-line setting and in patients with cutaneous melanoma

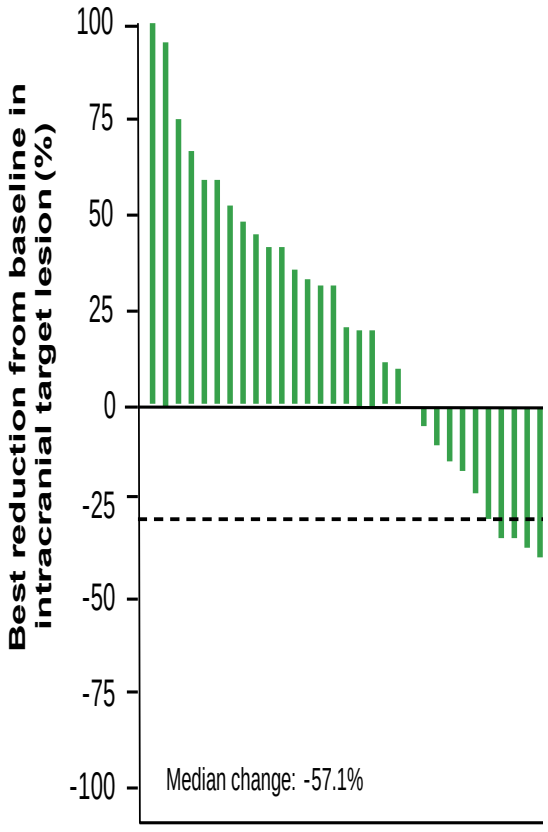


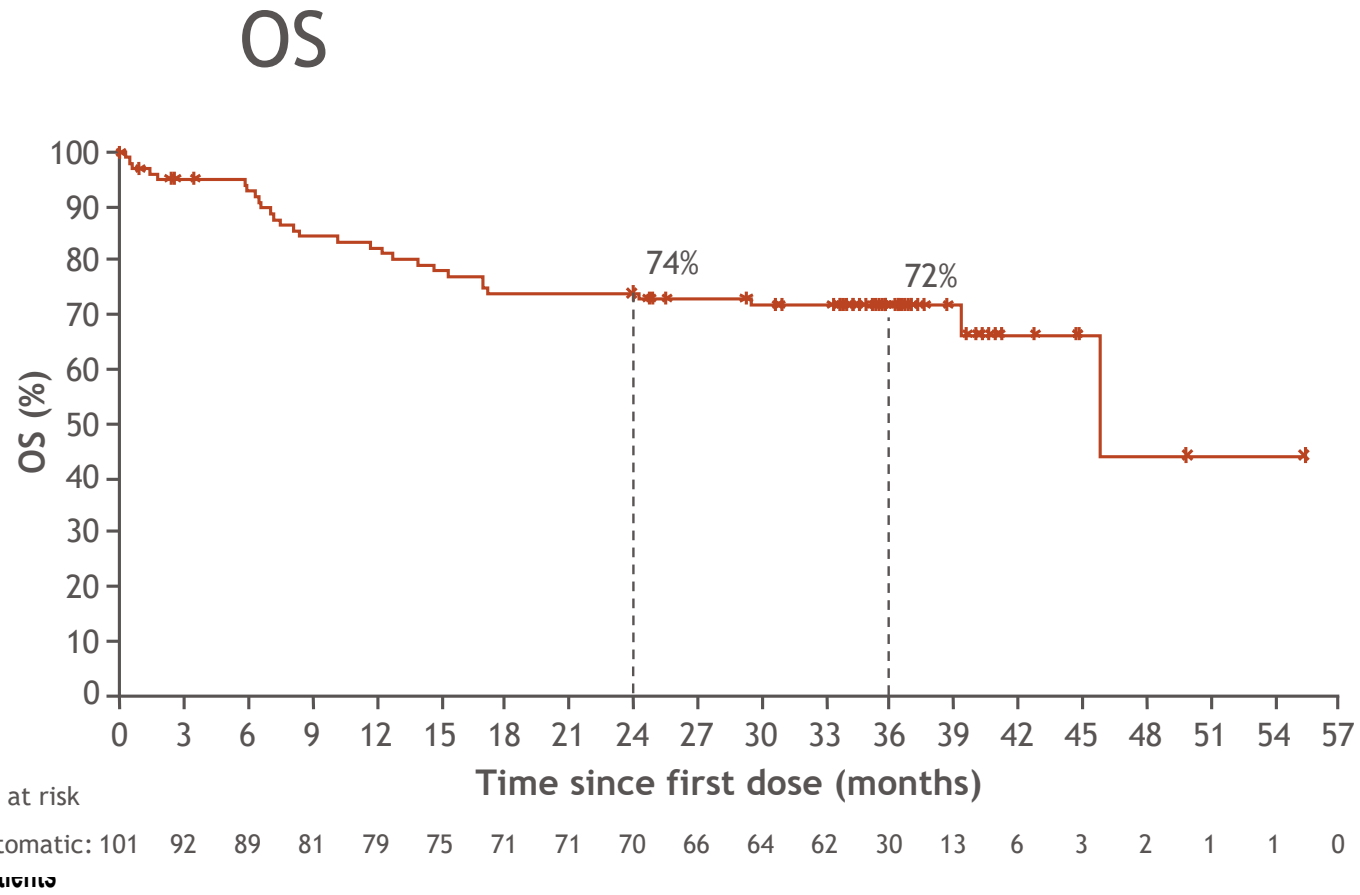
- Uveal Melanoma
- Mucosal/Acral Melanoma
- CNS Metastases

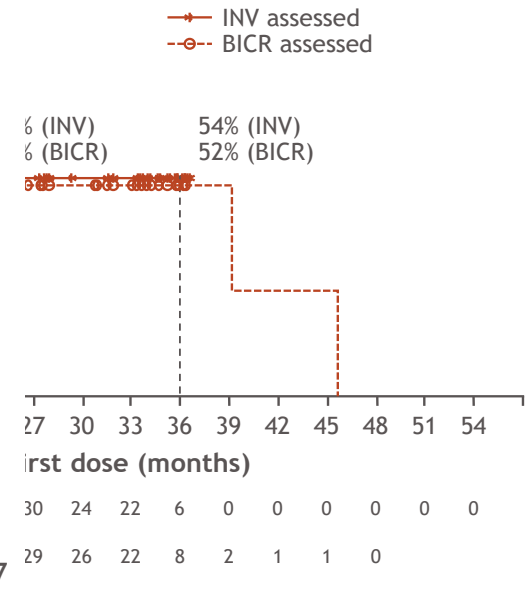
BRAIN METS in Melanoma

CheckMate 204- Ipi+nivo in Melanoma Brain Metastases

Intracranial Response and PFS- Asymptomatic Patients





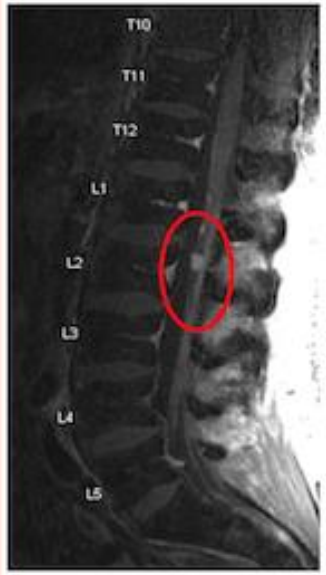


Tawbi, H. et al, N Engl J Med. 2018 Aug 23;379(8):722-730; Tawbi, H. et al, Neuro Oncol. 2021 Apr 21.

ABSTRACT 9519: Intrathecal (IT) and intravenous (IV) nivolumab (N) for metastatic melanoma (MM) patients (pts) with leptomeningeal disease (LMD)

Ida John[1], Alexandra P. Foster[1], Cara L. Haymaker[2], Roland L. Bassett Jr.[3], J. Jack Lee, Michelle L. Rohlfs[1], Jessie Richard[1], Masood Iqbal[1], Ian E. McCutcheon[4], Sherise D. Ferguson[4], Amy B. Heimberger[4], Barbara J. O'Brien[5], Sudhakar Tummala[5], Nandita Guha- Thakurta[6], Matthew Debnam[6], Elizabeth M. Burton[1], Hussein A. Tawbi[1], Michael A. Davies[1], Isabella C. Glitza Oliva[1]
The University of Texas MD Anderson Cancer Center, Houston, TX- [1]Department of Melanoma Medical Oncology, [2] Translational Molecular Pathology, [3]Department of Biostatistics, [4]Department of Neurosurgery, [5] Department of Neuro-Oncology,[6]Department of Neuroradiology

Intrathecal Nivolumab Phase I: Conclusions



06/2018

First-in-human study of intrathecal anti-PD1

Evaluation of 4 IT Nivolumab doses (5 mg, 10 mg, 20 mg, 50 mg)

Dose escalation completed: 50mg = recommended IT Nivo dose

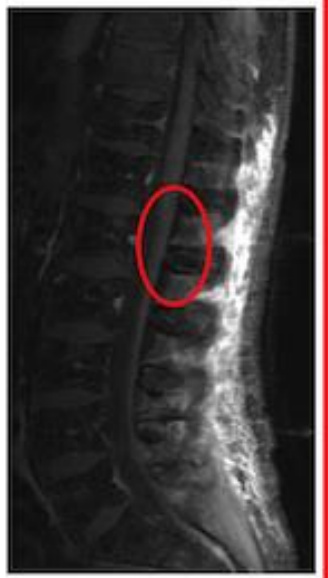
No significant toxicities observed

23 metastatic melanoma patients treated (currently 5 additional pts enrolled)

Largest prospective clinical trial to date in melanoma patients with LMD

Evidence of clinical activity- Median OS 4.9 months

6 months OS: 47%- 12 months OS 35%



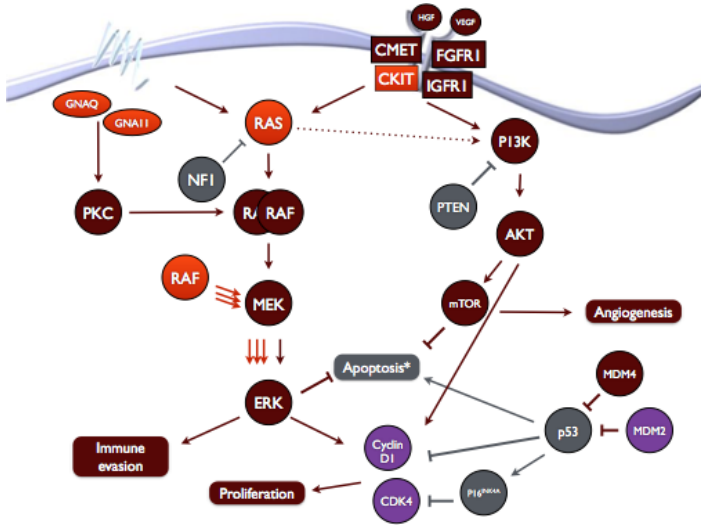
04/2020
50 cycles later

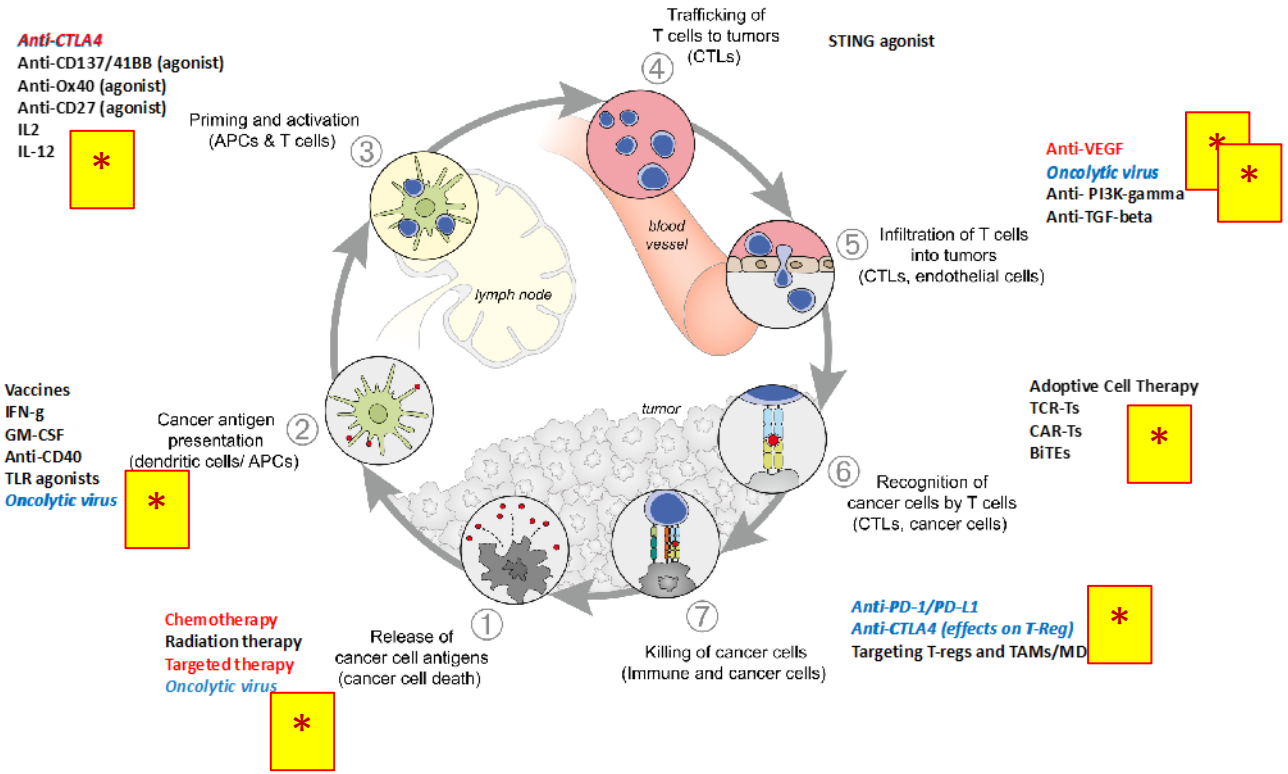
Unusual responder: demonstration of clinical and radiographic response in patient with PD1- refractory disease

Concluding Thoughts

New targeted therapy strategies are emerging to treat BRAF, NRAS, and other oncogene driven populations in melanoma

Unmet needs remain in advanced disease; particularly for those who have progressed after PD-1 and CTLA-4 inhibition





A number of combinations and strategies are ongoing to define the benefit of therapy in this population

Find an Interpreter

Checkpoints within tumor	**CTLA-4, LAG3**, TIM3, TIGIT, B7-H3, B7-H4, PD-1H (Vista), CD200, CEACAM1, **KIR**
MDSC/TAMS	**HDACi**, MER-TKi, CCR2i, CSF-1Ri, CD40, CKITi, ibrutinib, Anti-CD47 ('Don't Eat Me Signals'), SIGLECs, chemotherapy
Treg	Anti-CCR4, **anti–CTLA-4, anti-CD25**
Inhibitory Cytokines	Antibodies and small molecule inhibitors of TGF-beta or its receptors
Hypoxia/Adenosine	**Adenosine 2AR inhibitors** Anti-CD39, anti-CD73
Metabolic Inhibitors and Prostaglandins	**IDO inhibitors**, Cox2 inhibitors, modulators of tumor/T-cell glucose consumption (PPAR-alpha inhibitors)
Barriers to T-cell infiltration	**Anti-VEGF**, anti–SEMA-4D, anti–CTLA-4

Thanks to Mario Sznol

Conclusions

- Improved survival
- Many new pathways
- New standards in first line
- Second-line options expanding
- Brain metastasis options
- Clinical trials, clinical trials, clinical trials. . .

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The Angeles Clinic
AND RESEARCH INSTITUTE
A CEDARS-SINAI AFFILIATE

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TRANSFORMING CANCER

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