Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™ Webinar: Clinical Updates from SITC 2019

Tuesday, February 4, 2020

2:00-3:00 p.m. EST

Webinar Agenda

2:00-2:05 p.m. EST Overview: Welcome and Introductions

2:05-2:40 p.m. EST Presentation

2:40-2:55 p.m. EST Question and Answer Session

2:55-3:00 p.m. EST Closing Remarks

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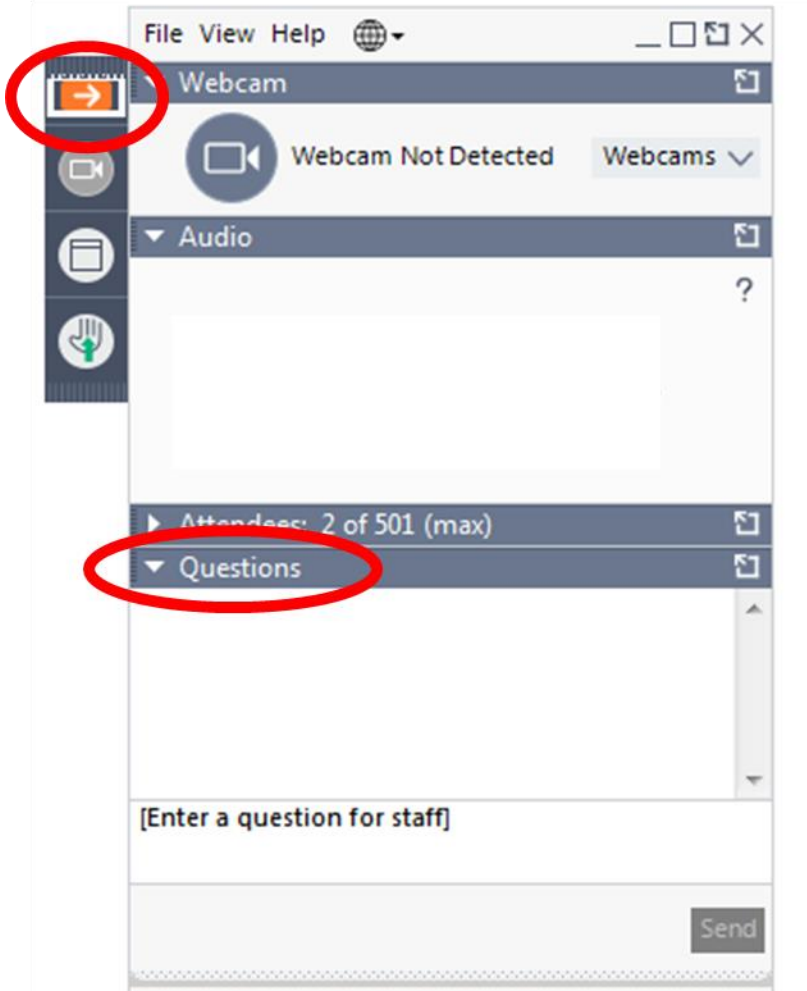
How to Submit Questions

Computer



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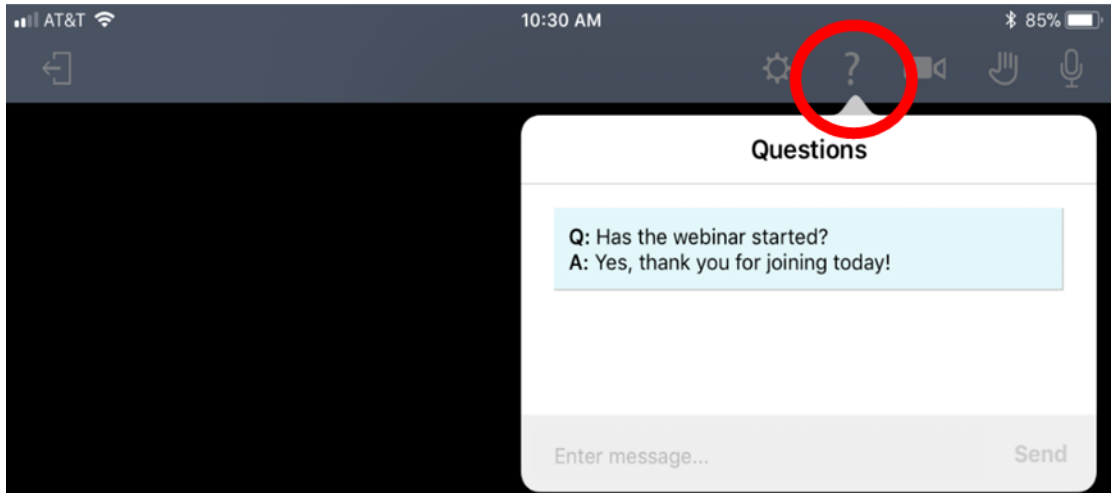


Webinar Faculty

Sanjiv Agarwala, MD
Temple University

Igor Puzanov, MD, MSCI, FACP
Roswell Park Comprehensive Cancer Center

Anil Shanker, PhD
Meharry Medical College

Learning objectives

Upon completion of this webinar, participants will be able to:

- Describe the latest advances in clinical cancer immunotherapy, involving treatments such as cellular therapies, T cell engagers, and checkpoint inhibitors
- Discuss the rationale for intratumoral immunotherapies and current clinical advances in this area
- Identify rational combination immunotherapy treatments based upon each agent's mechanism-of-action

Outline

- Cellular therapies and T cell engagers
- Checkpoint-targeted therapies
- Intratumoral therapies
- Other agents

Cellular therapies/T cell engagers

Final results from a phase 2 study using off-the-shelf activated natural killer (aNK) cells in combination with N-803, an IL-15 superagonist, in patients with metastatic Merkel cell carcinoma (MCC)

Shailender Bhatia[1,2], Candice D. Church[1], Kelly G. Paulson[1,2], Robert H. Pierce[2], Paul Nghiem[1,2], John H. Lee[3], Bridget M. Adcock[3], Patrick Soon-Shiong[3], Sunandana Chandra[4]

[1]University of Washington, Seattle, WA

[2]Fred Hutchinson Cancer Research Center, Seattle, WA

[3]NantKwest, Inc, and ImmunityBio, Inc, Culver City, CA

[4]Northwestern University Feinberg School of Medicine, Chicago, IL

QUILT-3.009 study design

Enrollment: 7 patients total (Initial target N = 24)

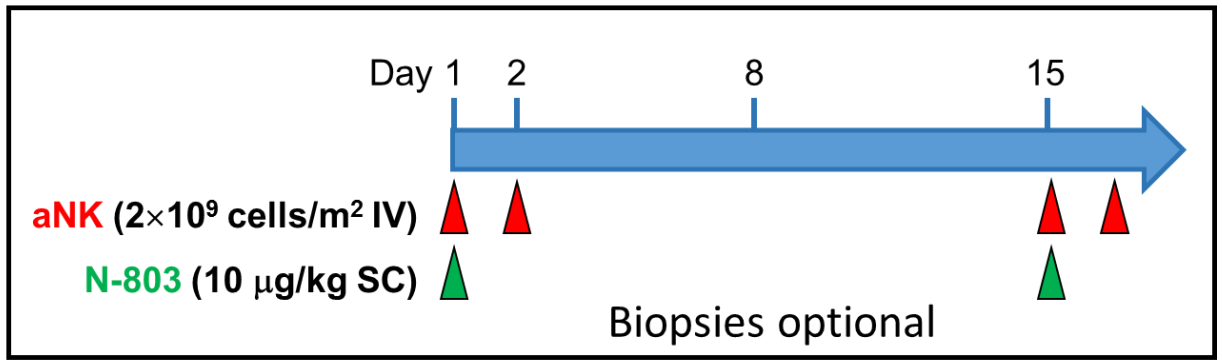
3 patients received aNK monotherapy

4 patients received aNK + N-803

Trial was discontinued prematurely:

- **Proof-of-concept met** with convincing signal of safety and efficacy
- Logistical **challenges with on-site expansion** of aNK cells

2 week treatment cycles:



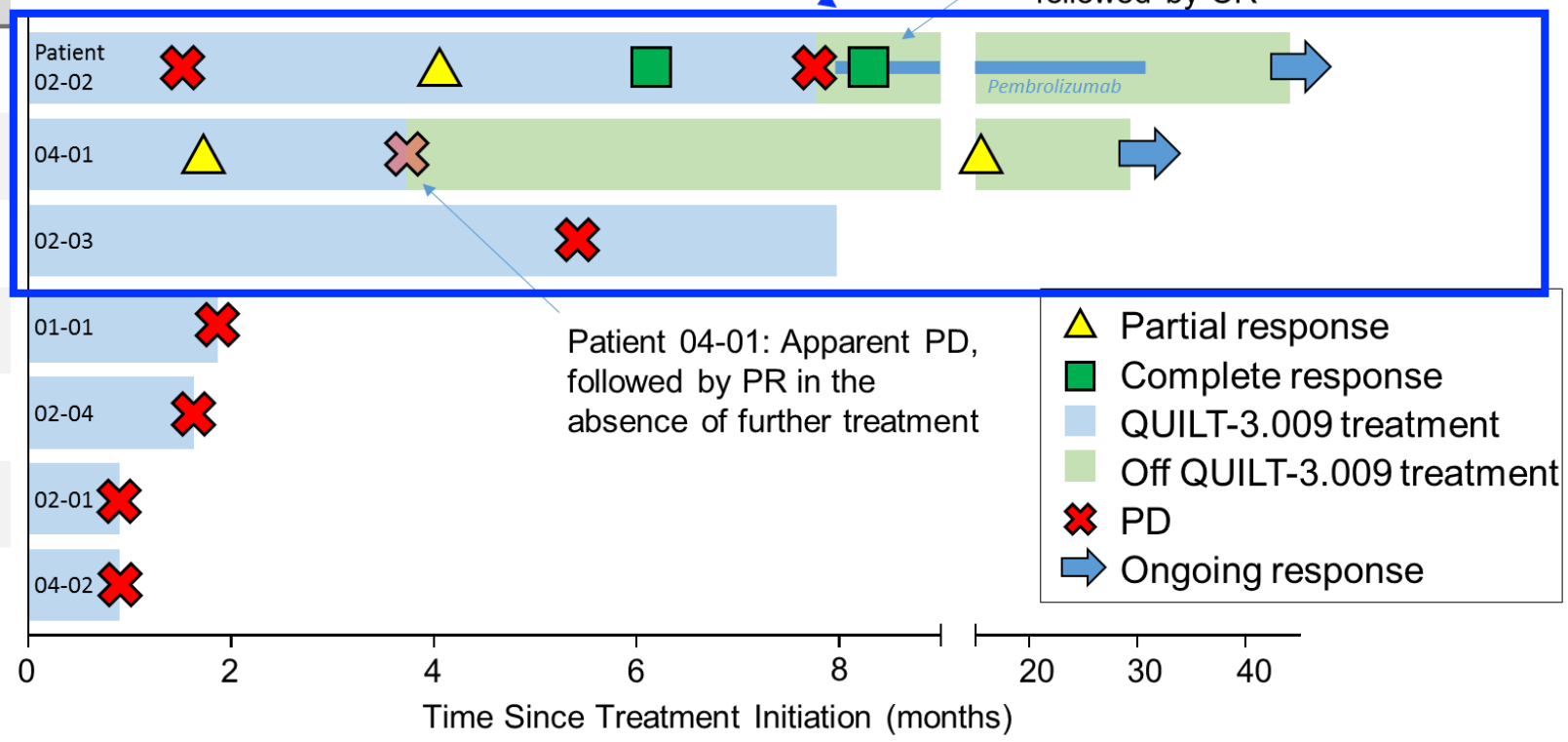
Bhatia, SITC 2019.

QUILT-3.009 Results

ORR for QUILT-3.009: 29% (2/7)
- 1 radiologic CR
- 1 PR

One patient also had SD (5.5 months)

Sex	Age	Prev Ther	Prev ICI
M	81	4	Pem
M	61	3	Nivo
F	60	2	Pem
M	76	0	-
M	61	12	Pem
M	75	3	Pem
M	63	3	Pem



Bhatia, SITC 2019.

Phase 1 dose escalation study of PRS-343, a HER2/4-1BB bispecific molecule, in patients with HER2+ malignancies

Sarina Piha-Paul[1], Johanna Bendell[2], Anthony Tolcher[3], Sara Hurvitz[4], Amita Patnaik[5], Anuradha Krishnamurthy[6], Rachna Shroff[7], Paula Pohlmann[8], Noah Hahn[9], Markus Zettl[10], Jian Mei[10], Kayti Aviano[10], Manuela Duerr[10], Rushdia Yusuf[10], Louis A Matis[10], Shane Olwill[10], Ingmar Bruns[10], Geoffrey Ku[11]

[1]The University of Texas MD Anderson Cancer Center, Texas
[2]Sarah Cannon Research Institute, LLC, Tennessee
[3]NEXT Oncology, Texas
[4]University of California Los Angeles Jonsson Comprehensive Cancer Center, California
[5]South Texas Accelerated Research Therapeutics, Texas
[6]University of Pittsburgh Medical Center, Pennsylvania
[7]University of Arizona Cancer Center, Arizona
[8]Georgetown University Hospital, Washington DC
[9]Sydney Kimmel Cancer Center at Johns Hopkins, Maryland
[10]Pieris Pharmaceuticals, Inc., Massachusetts
[11]Memorial Sloan Kettering Cancer Center, New York

PRS-343 Study design

Primary Objectives

- Characterize safety profile
- Identify MTD or RP2D

Secondary Objectives

- Characterize PK profile
- Investigate dosing schedule
- Assess potential immunogenicity and PD effects
- Investigate efficacy

Active schedules

Schedule 1: Q3W dosing on Day 1

Schedule 2 : Q2W dosing on Days 1, 15

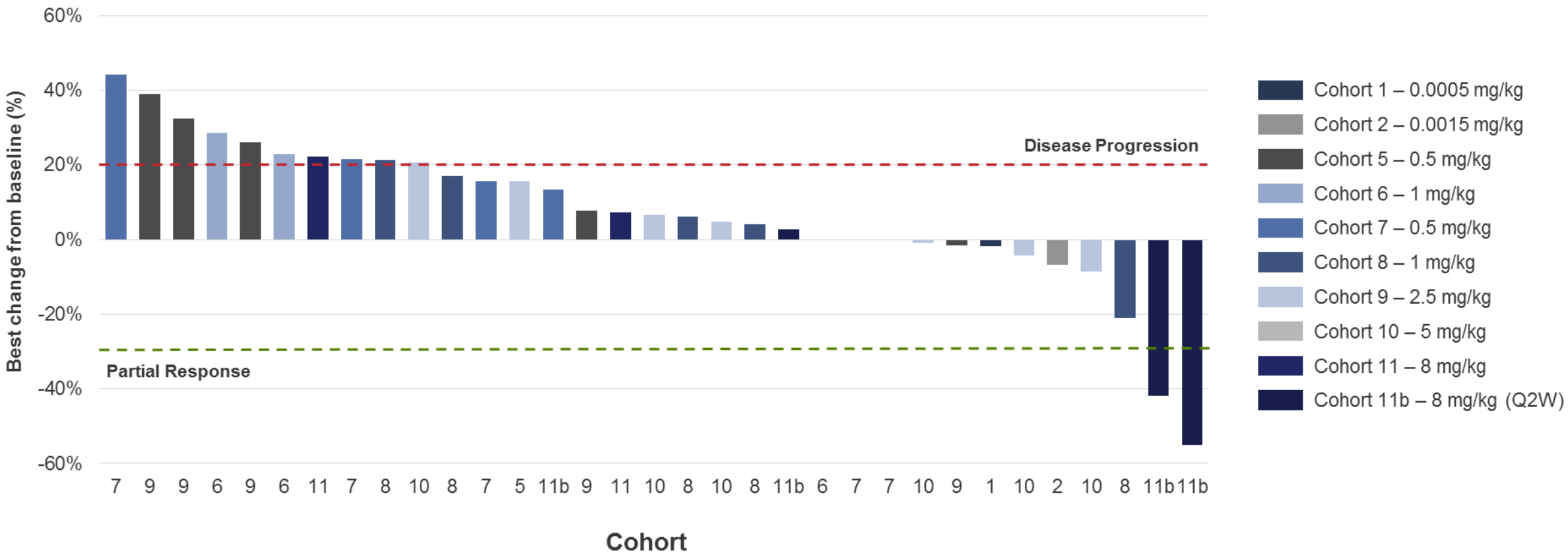
Data cut-off: 23-Oct-19 for subjects up to Cohort 11b; additional cohorts enrolling

Current Enrollment

Dose Level	No. Patients	Dose (mg/kg)
1	1	0.0005 (Q3W)
2	1	0.0015
3	1	0.005
4	2	0.015
5	2	0.05
6	5	0.15
7	7	0.5
8	6	1
9	6	2.5
10	9	5
11	7	8
11b	6	8 (Q2W)
Total	53	

Piha-Paul, SITC 2019.

PRS-343 Results



Piha-Paul, SITC 2019.

Cellular therapies – conclusions and implications

- The field is moving beyond only T cell therapies
- Treatment of solid tumors is still a work in progress
- Logistical challenges of cell therapies will need to be addressed before their widespread clinical use

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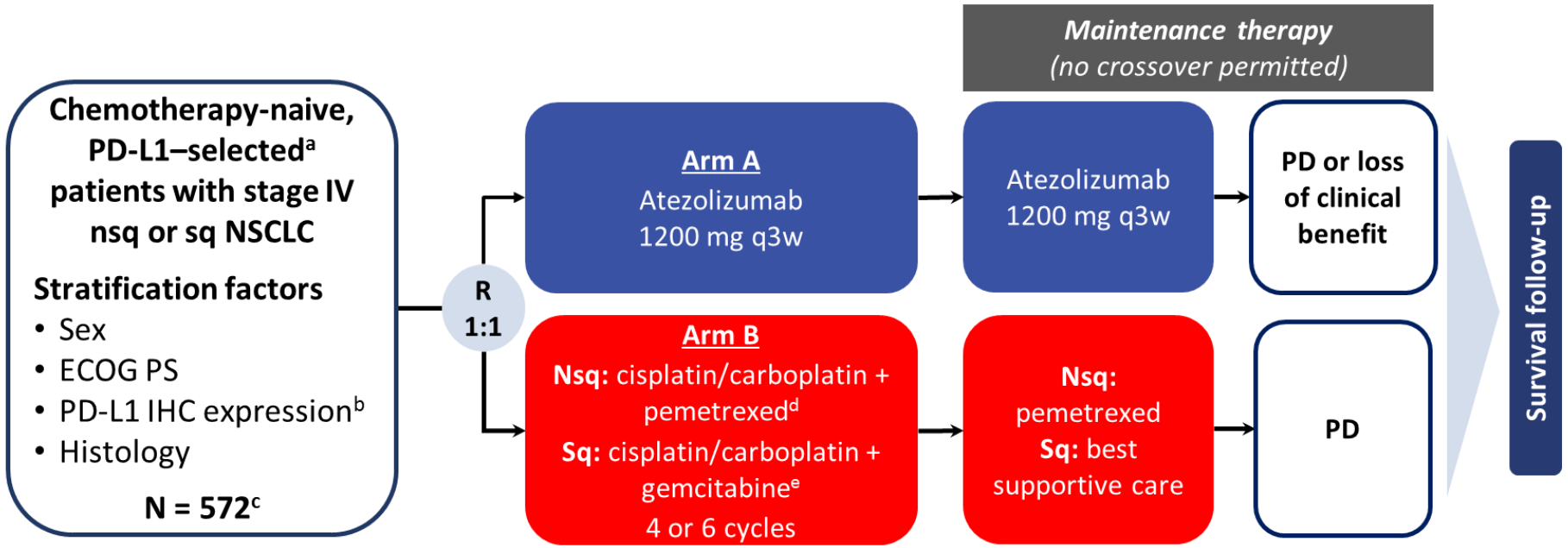
Immune checkpoint inhibitors

IMpower110: Interim overall survival analysis of a phase III study of atezolizumab monotherapy vs platinum-based chemotherapy as first-line treatment in PD-L1-selected NSCLC

Roy S Herbst,[1] Filippo De Marinis,[2] Giuseppe Giaccone,[3] Niels Reinmuth,[4] Alain Vergnenegre,[5] Carlos Henrique Barrios,[6] Masahiro Morise,[7] Enriqueta Felip,[8] Zoran Andric,[9] Sarayut Geater,[10] Mustafa Özgüroğlu,[11] Simonetta Mocci,[12] Mark McCleland,[12] Ida Enquist,[12] Kim Komatsubara,[12] Yu Deng,[12] Hiroshi Kuriki,[12] Xiaohui Wen,[12] Jacek Jassem,[13] David R Spigel[14]

[1]Yale School of Medicine, New Haven, CT, USA; [2]European Institute of Oncology, Milan, Italy; [3]Weill Cornell Medical Center, New York, NY, USA; [4]Asklepios Lung Clinic, Munich-Gauting, Germany; [5]Limoges University Hospital, Limoges, France; [6]Centro de Pesquisa Clínica, Hospital São Lucas, PUCRS, Porto Alegre, Brazil; [7]Nagoya University Graduate School of Medicine, Aichi, Japan; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]Clinical Hospital Center Bezanijska Kosa, Belgrade, Serbia; [10]Prince of Songkla University - Hat Yai, Songkhla, Thailand; [11]Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; [12]Genentech, Inc, South San Francisco, CA, USA; [13]Medical University of Gdańsk, Gdańsk, Poland; [14]Sarah Cannon Research Institute, Nashville, TN, USA

IMpower110 study design



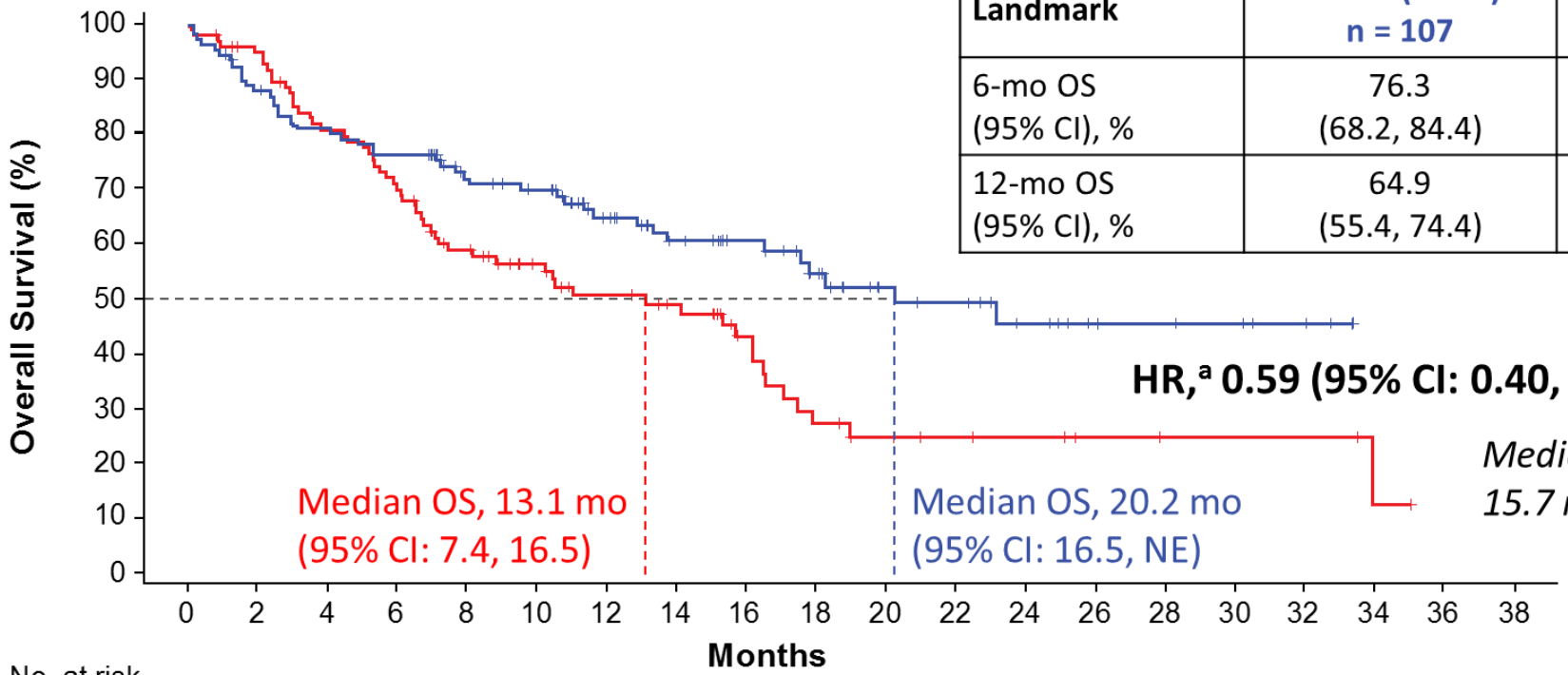
- Primary endpoint: OS in WT population[f]
- Key secondary endpoints: investigator-assessed PFS, ORR and DOR (per RECIST 1.1)

IC, tumor-infiltrating immune cells; IHC, immunohistochemistry; nsq, non-squamous; sq, squamous; TC, tumor cells; WT, wild-type.
[a] PD-L1 expression (VENTANA SP142 IHC assay) ≥ 1% on TC or IC. [b] TC1/2/3 and any IC vs TC0 and IC1/2/3. [c] 554 patients in the WT population. [d] Cisplatin 75 mg/m^2 or carboplatin area under the curve (AUC) 6 + pemetrexed 500 mg/m^2 IV q3w. [e] Cisplatin 75 mg/m^2 + gemcitabine 1250 mg/m^2 or carboplatin AUC 5 + gemcitabine 1000 mg/m^2 IV q3w. [f] WT population excludes patients with *EGFR*+ and/or *ALK*+ NSCLC.

Herbst, SITC 2019.

IMpower110 Results – TC3 or IC3 WT

Landmark	Arm A (atezo) n = 107	Arm B (chemo) n = 98
6-mo OS (95% CI), %	76.3 (68.2, 84.4)	70.1 (60.8, 79.4)
12-mo OS (95% CI), %	64.9 (55.4, 74.4)	50.6 (40.0, 61.3)



No. at risk

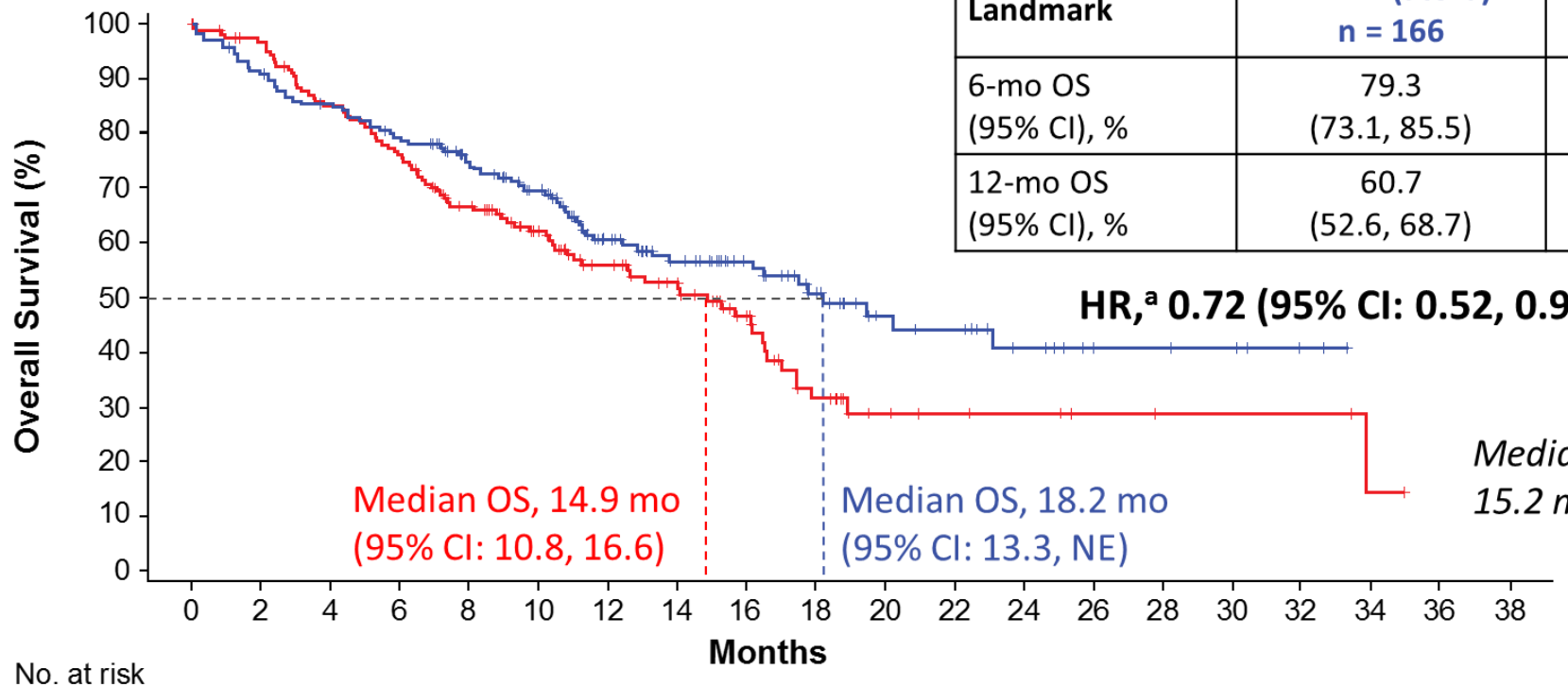
Atezolizumab	107	94	85	80	66	61	48	40	34	25	18	16	11	7	6	5	2
Chemotherapy	98	89	75	65	50	40	33	28	19	12	9	7	6	4	3	3	3	1

NE, not estimable. [a] Stratified. [b] Stratified log-rank.
Data cutoff: September 10, 2018.

Herbst, SITC 2019.

IMpower110 Results – TC2/3 or IC2/3 WT

Landmark	Arm A (atezo) n = 166	Arm B (chemo) n = 162
6-mo OS (95% CI), %	79.3 (73.1, 85.5)	76.1 (69.3, 82.8)
12-mo OS (95% CI), %	60.7 (52.6, 68.7)	56.0 (47.7, 64.3)



HR,[a] 0.72 (95% CI: 0.52, 0.99); *P* = 0.0416[b,c]

Median follow-up, 15.2 mo (range, 0-35)

No. at risk

Atezolizumab	166	151	139	128	108	92	66	54	42	30	19	17	11	7	6	5	2
Chemotherapy	162	150	131	117	95	75	57	46	32	17	9	7	6	4	3	3	3	1

[a] Stratified. [b] Stratified log-rank. [c] Not crossing the pre-specified alpha boundary.
Data cutoff: September 10, 2018.

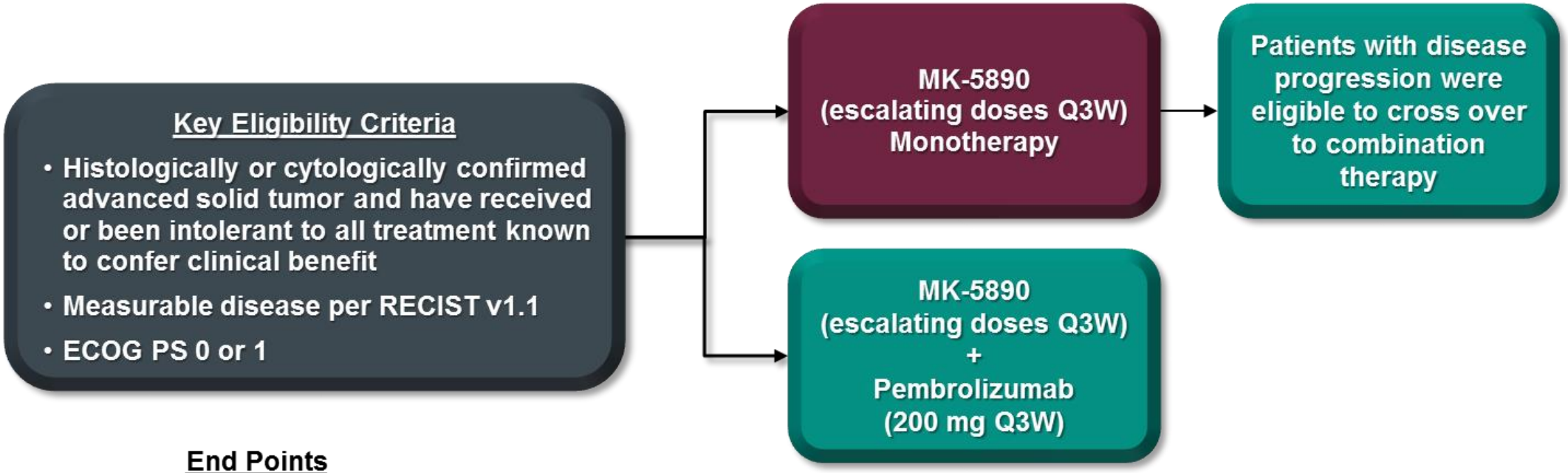
Herbst, SITC 2019.

Phase 1 study of a CD27 agonist antibody as monotherapy and in combination with pembrolizumab in patients with advanced solid tumors

Ronnie Shapira-Frommer,[1] Marloes G. J. van Dongen,[2] Konstantin Dobrenkov,[3] Elliot Chartash,[3] Fang Liu,[3] Claire Li,[3] Richard Wnek,[3] Manish R. Patel[4]

[1]Oncology Institute, Sheba Medical Center, Ramat-Gan, Israel;
[2]Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands;
[3]Merck & Co., Inc., Kenilworth, NJ, USA;
[4]Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, USA

MK-5890 Study Design

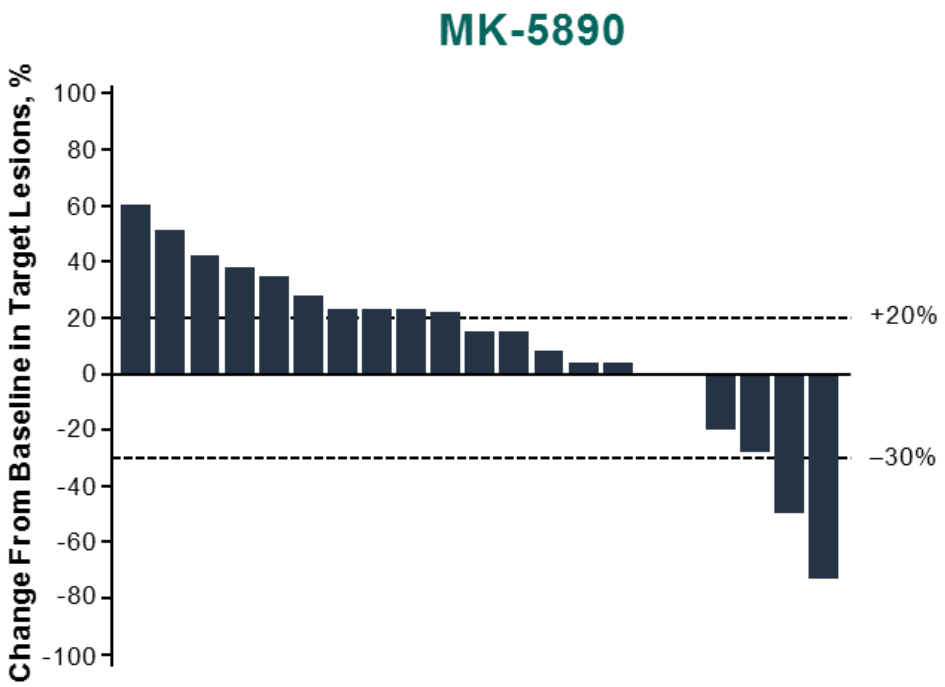


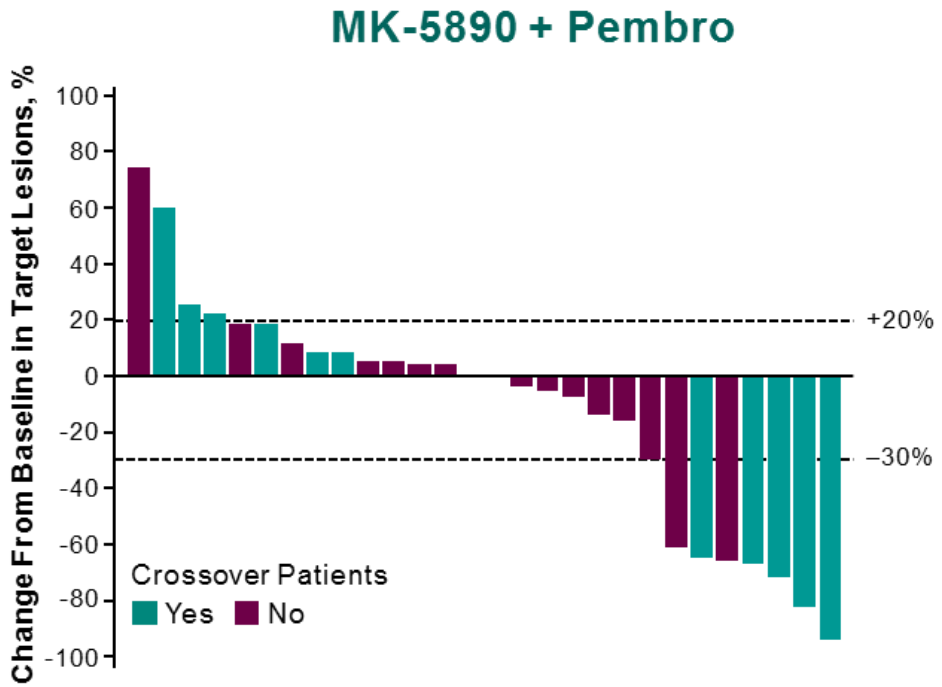
End Points

- Safety and tolerability (primary)
- ORR by investigator per RECIST v1.1
- PK/PD
- Blood- and/or tumor-derived molecular biomarkers (genomic, metabolic, and/or proteomic)

Shapira-Frommer, SITC 2019.

MK-5890 Results





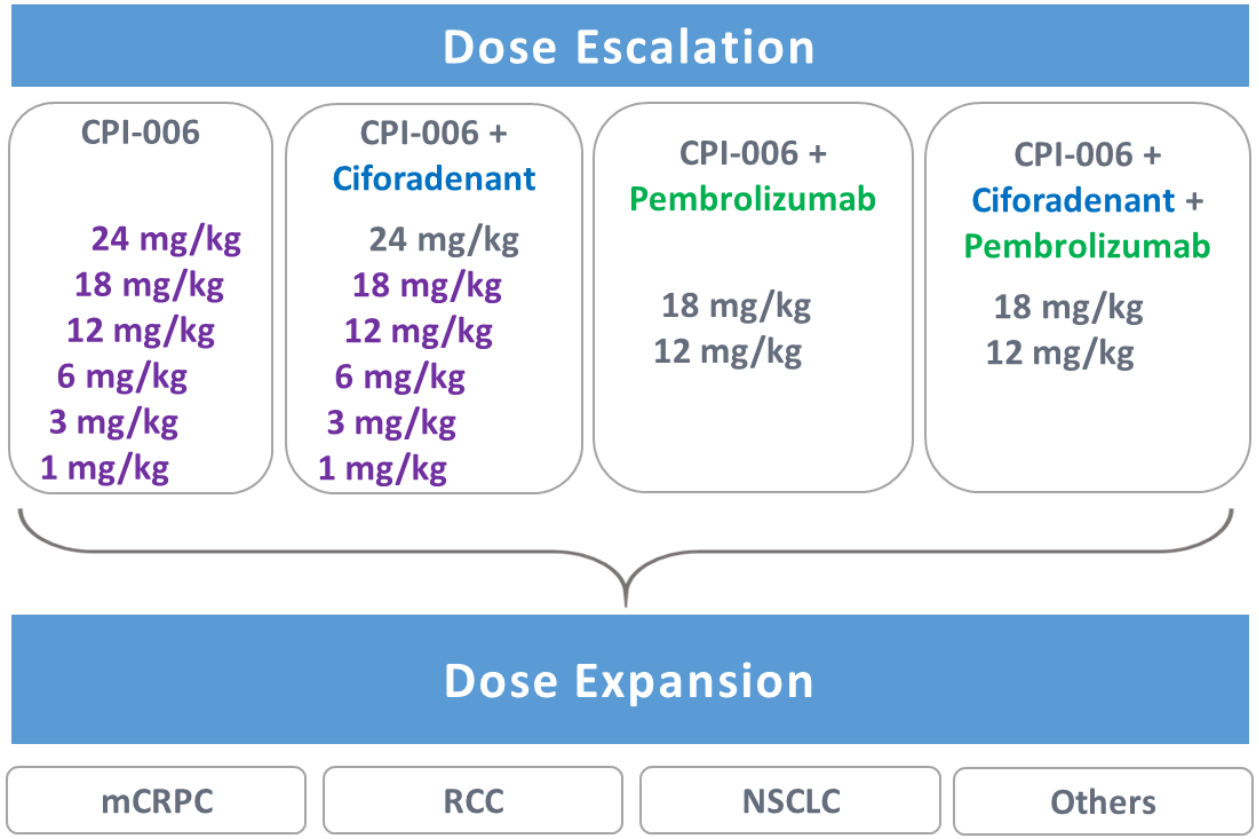
Database cutoff date: May 30, 2019.
[a]Based on investigator assessment per RECIST v1.1; all patients had ≥1 post-baseline target lesion measurement.

Shapira-Frommer, SITC 2019.

Immunobiology and clinical activity of CPI-006, an anti-CD73 antibody with immunomodulating properties in a phase 1/1b trial in advanced cancers

Luke JJ, Merchan J, Harshman LC, Marron T, Powderly J, Barve M, LoRusso P, Johnson M, Hotson A, Gittelman R, Munneke B, Buggy J, Willingham S, Piccione E, Mobasher M, Miller R

CPI-006 Study Design



Doses explored to date & planned doses

Design
- Phase 1/1b dose escalation/dose expansion in disease specific cohorts
- CPI-006 every 3 weeks; fixed dose of ciforadenant

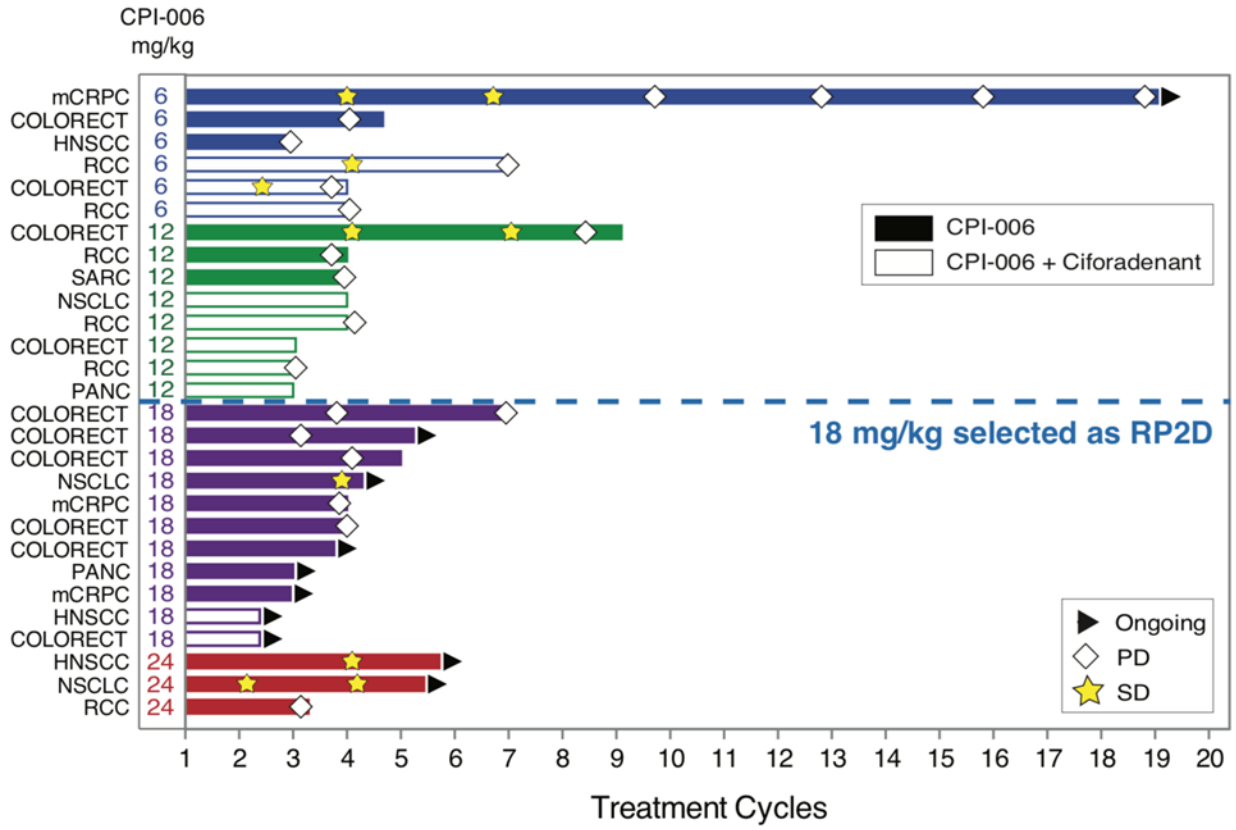
Eligibility
- Cancers progressed on 1-5 prior therapies
- CD73 expression: required in expansion, not in dose escalation
- Adenosine gene signature not used to select patients

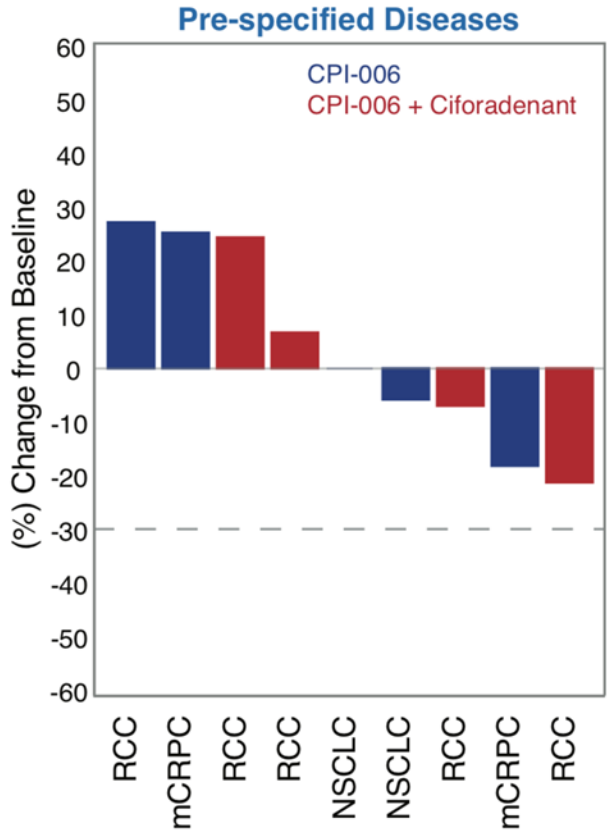
Objectives
- Primary: Safety and tolerability
- Secondary: PK/PD, efficacy, biomarkers

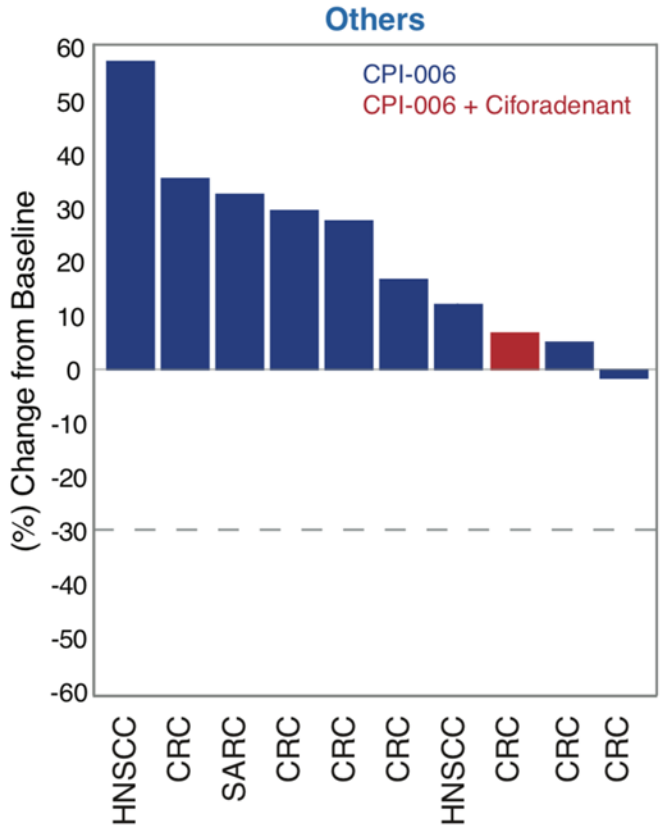
Biomarker Assessments
- Tumor markers, cytokines, etc.

Luke, SITC 2019.

CPI-006 Results







- Response assessments in patients receiving ≥ 6 mg/kg dose

Luke, SITC 2019.

Single agent anti-tumor activity in PD-1 refractory NSCLC: phase 1 data from the first-in-human trial of NC318, a Siglec-15-targeted antibody

Anthony Tolcher, Omid Hamid, Jeffrey Weber, Patricia LoRusso, Kathryn Shantz, Kevin N. Heller, and Martin Gutierrez

NC318 Study Design

Phase 1: Dose Escalation

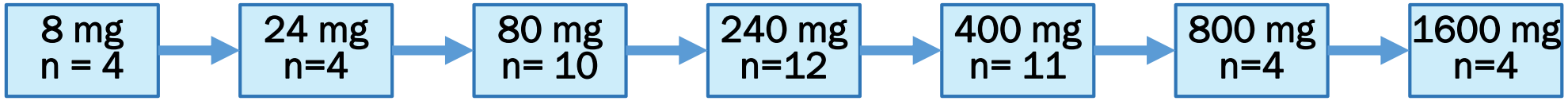
OBJECTIVES: Safety and Tolerability of NC318

3+3 Design

- Subjects dosed every 2 weeks
- DLT period 28 days
- Additional subjects enrolled for biopsies

Eligibility:

- Men/Women ≥ 18 y/o, and PS<2
- Advanced/metastatic solid tumors (all comers)
- Refractory/intolerant to standard of care

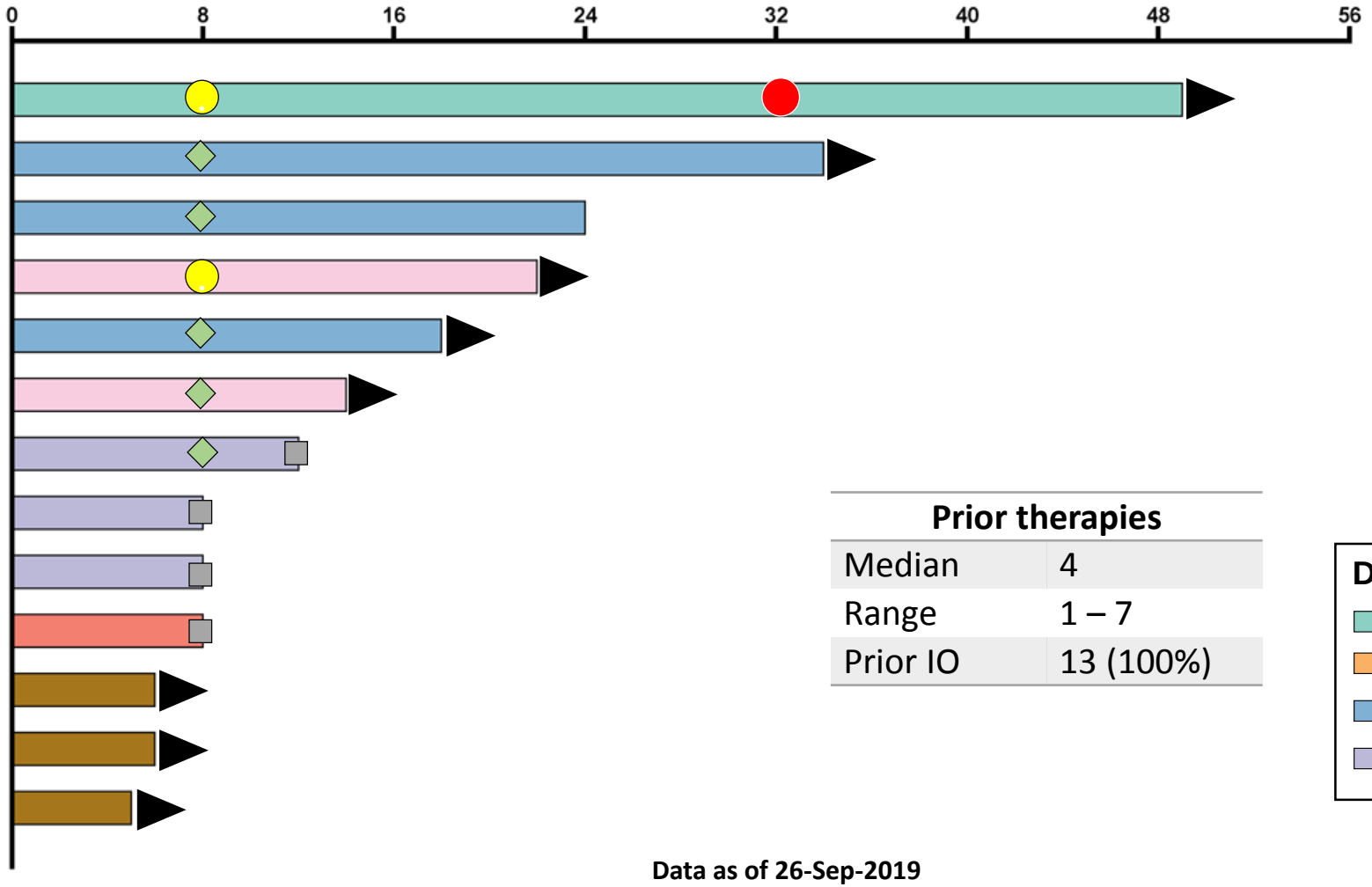


1600 mg cohort added after no DLTs observed through 800 mg cohort

Data as of 26-Sep-2019

Clinical trial information: NCT03665285

NC318 Results



Clinical Benefit[1]	NSCLC (n = 13)[2]
CR	1
PR	1
SD >16 weeks	3

[2]n = 10 efficacy evaluable population

Prior therapies	
Median	4
Range	1 – 7
Prior IO	13 (100%)

Dose Level
- 8 mg
- 24 mg
- 80 mg
- 240 mg
- 400 mg
- 800 mg
- 1600 mg

Best Response
- CR Start
- PR Start
- SD Start
- PD
- Treatment ongoing

Data as of 26-Sep-2019

Checkpoints – conclusions and implications

- Moving beyond PD-1 and CTLA-4 pathways
- Combination treatments showing promise – but always need to consider potential toxicity of combinations
- Appropriate sequencing of therapies is still an outstanding question

Society for Immunotherapy of Cancer

Intratumoral Therapies

Flt3L-primed *in situ* vaccine

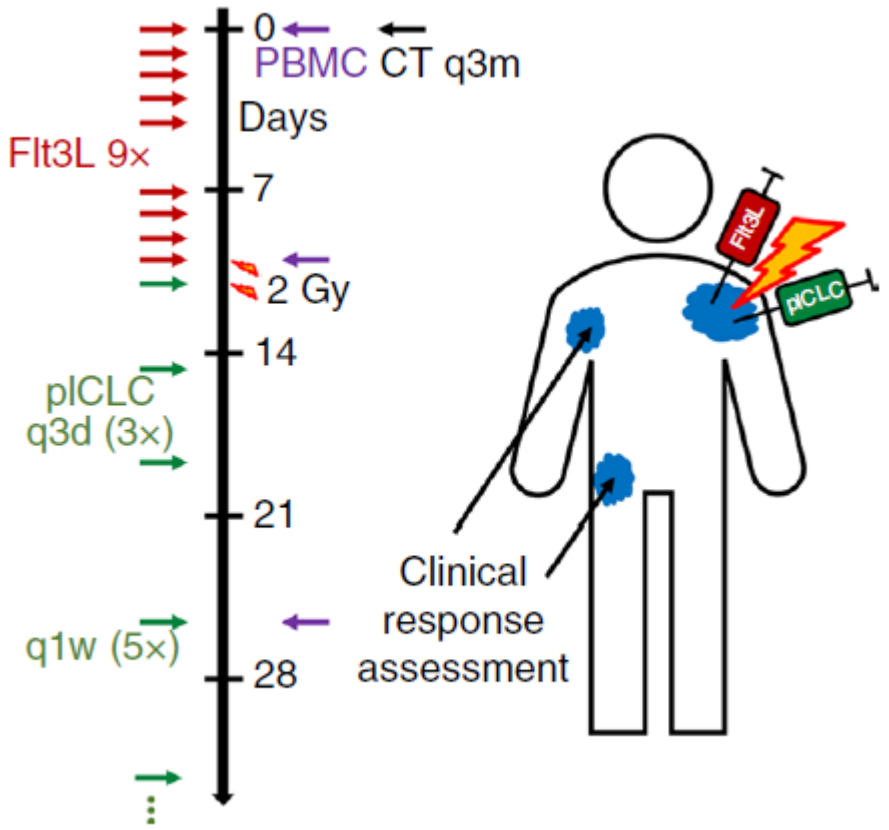
Joshua Brody, MD

Mount Sinai School of Medicine

Presented during pre-conference program: Workshop on Intratumoral Immunomodulation

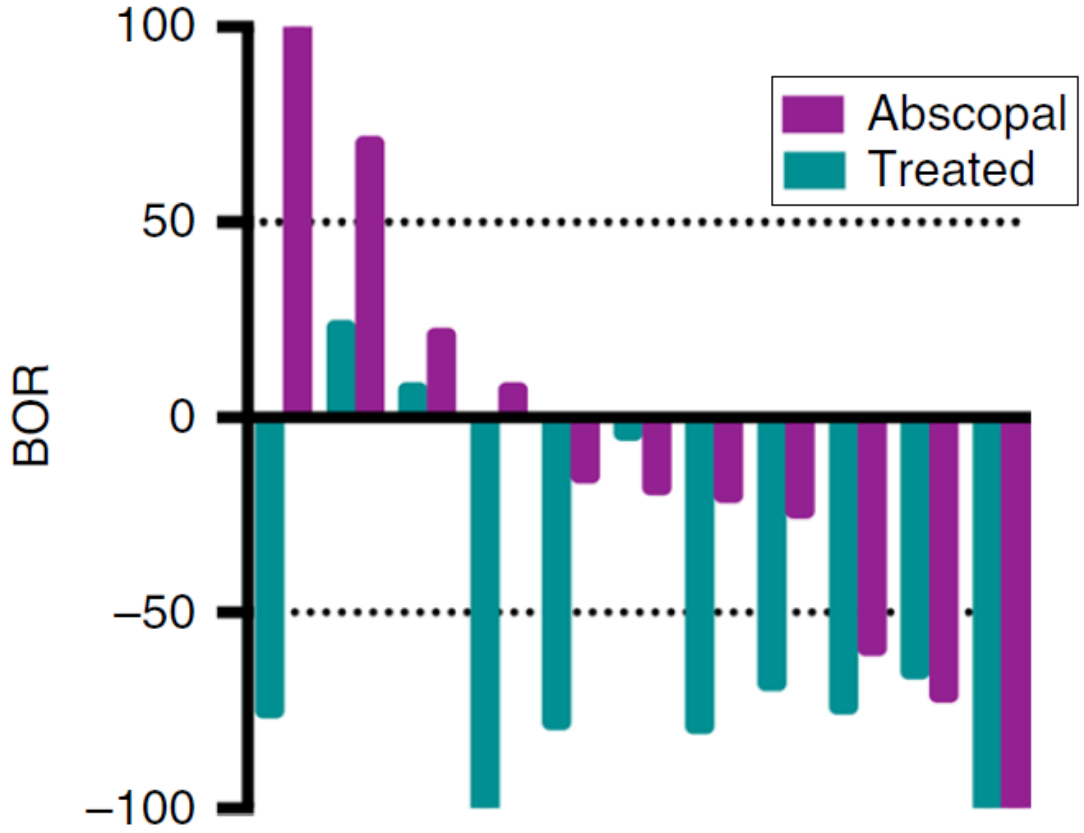
In situ vaccination - rationale

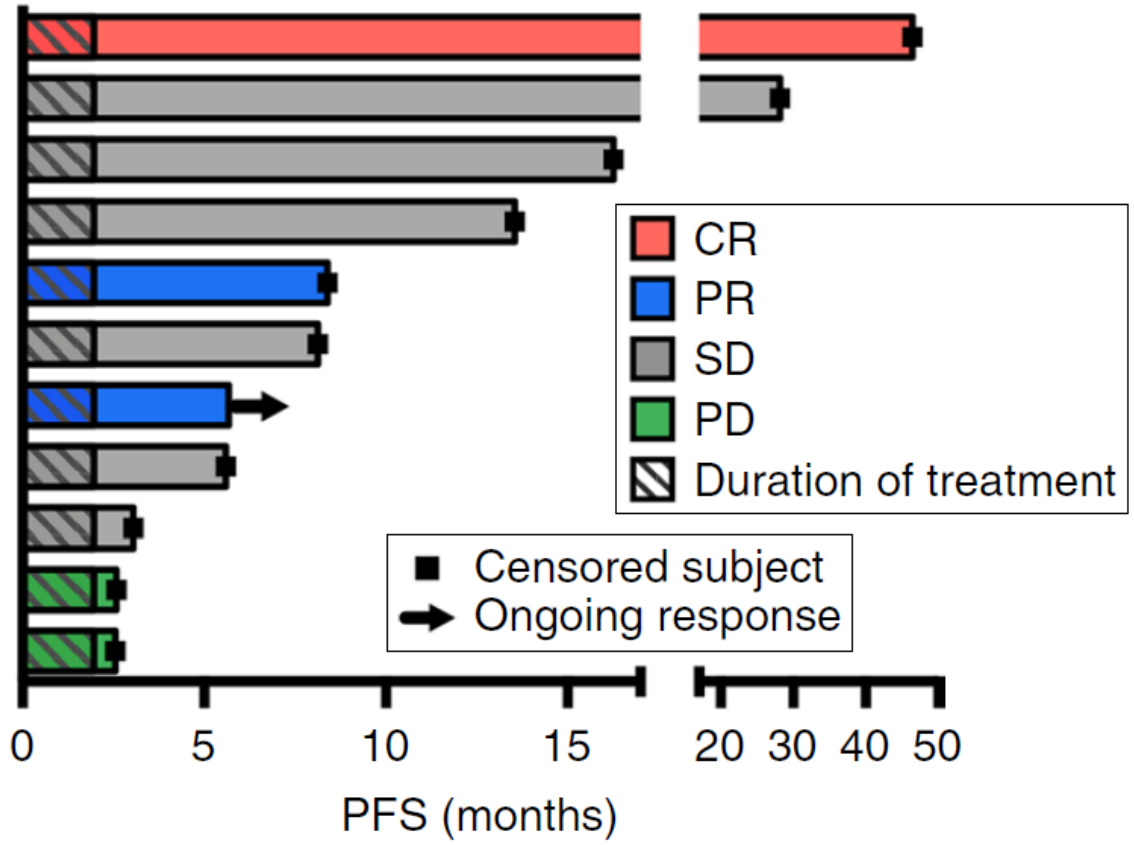
1. Intratumoral Flt3L administration recruits DC to the tumor
2. Low-dose radiotherapy to release tumor antigens
3. Intratumoral poly-ICLC administration activates tumor-antigen loaded DC



Hammerich, Nat Med 2019.
Brody, SITC 2019.

In situ vaccination - results





Hammerich, Nat Med 2019.
Brody, SITC 2019.

Durable responses in anti-PD-1 refractory melanoma following intratumoral injection of Toll-like receptor 9 (TLR9) agonist CMP-001, in combination with pembrolizumab

On Behalf of the CMP-001-001 Study Team:

Mohammed Milhem, Yousef Zakharia, Diwakar Davar, Elizabeth Buchbinder, Theresa Medina, Adil Daud, Antoni Ribas, Jiaxin Niu, Geoffrey Gibney, Kim Margolin, Anthony J. Olszanski, Interjit Mehmi, Takami Sato, Montaser Shaheen, Aaron Morris, David Mauro, Katie Campbell, Riyue Bao, George Weiner, Jason J. Luke, Arthur M. Krieg and John M. Kirkwood

CMP-001 Study Design

Key Elements of Study Design

- 3+3 Dose Escalation (1, 3, 5, 7.5, 10mg; n=44) / Expansion (5, 10mg; n=100, ongoing)
- CMP-001 intratumoral/pembrolizumab IV

Two schedules of escalation with CMP-001 evaluated:

Weekly x 7 → then Q3 weeks until discontinuation

Weekly x 2 → then Q3 weeks until discontinuation

- Q12 week scans. RECIST v1.1 assessment per investigator
- Parallel Monotherapy Cohort (n=24, ongoing)

Two different formulations of CMP-001 were used during the trial:

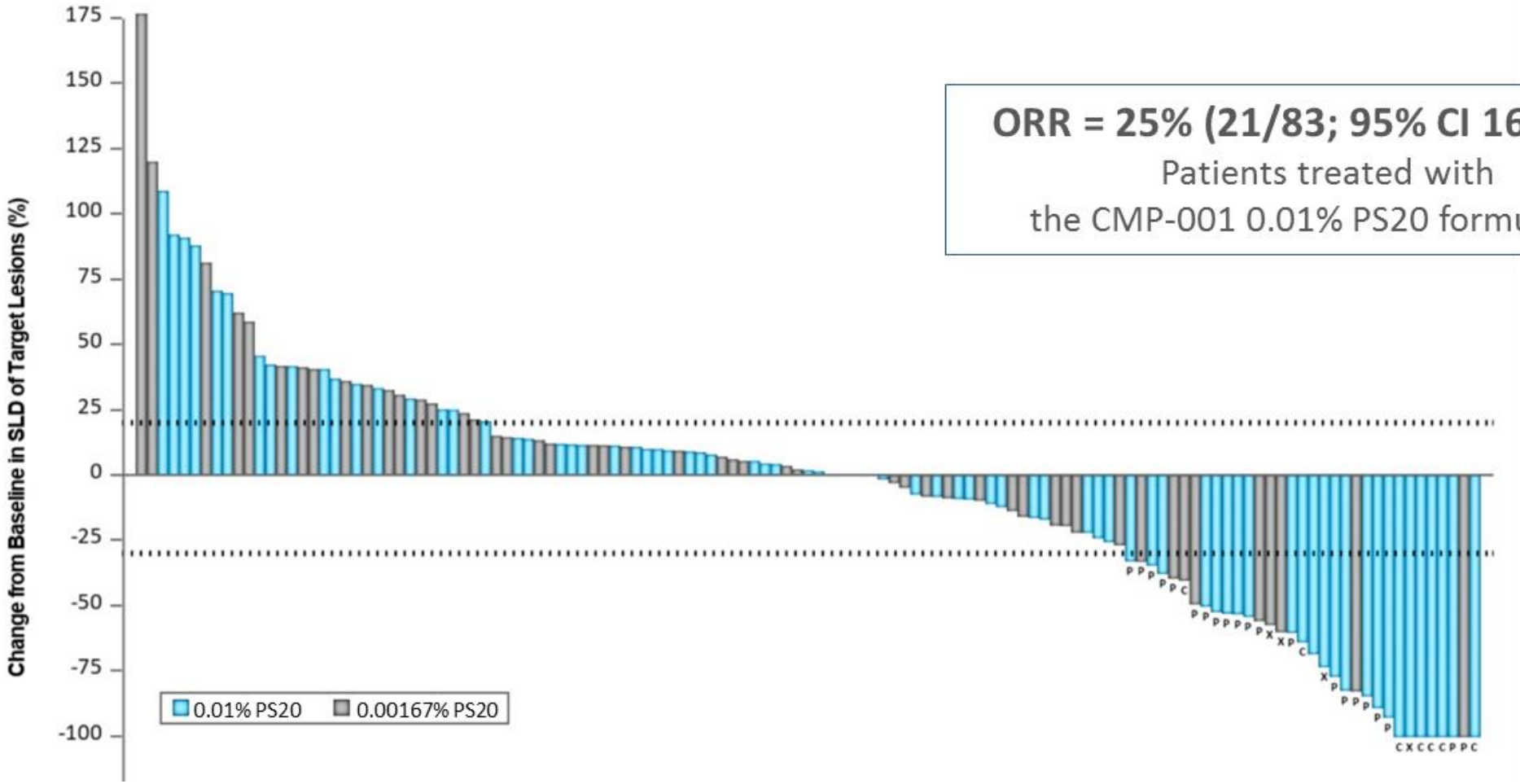
1. 0.01% polysorbate 20 (PS20), n=83 including the 44 dose escalation patients, and 39 expansion patients
2. 0.00167% PS20 (n=61 expansion patients)

Study Objectives

- Safety
- Dose and schedule selection
- Anti-tumor activity
- Pharmacodynamics

Milhem, SITC 2019.

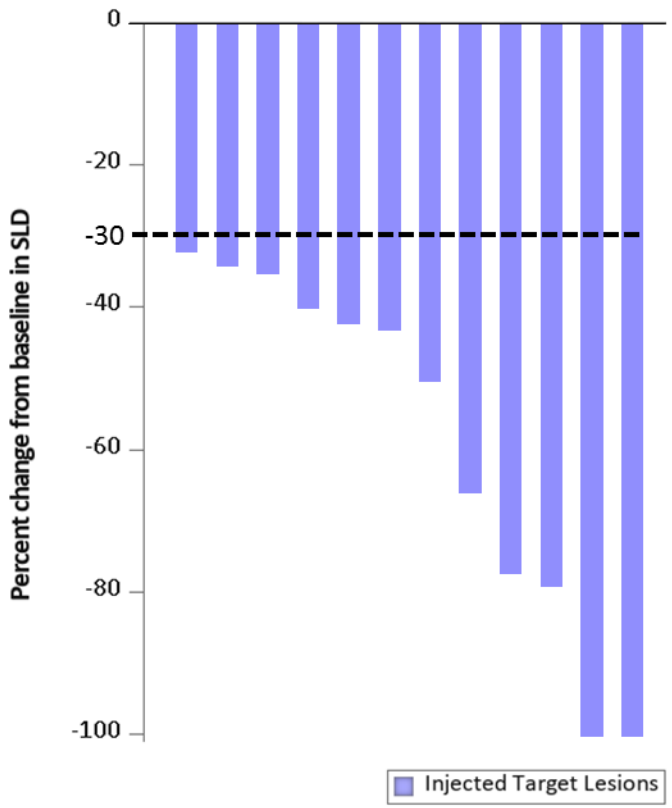
CMP-001 Results



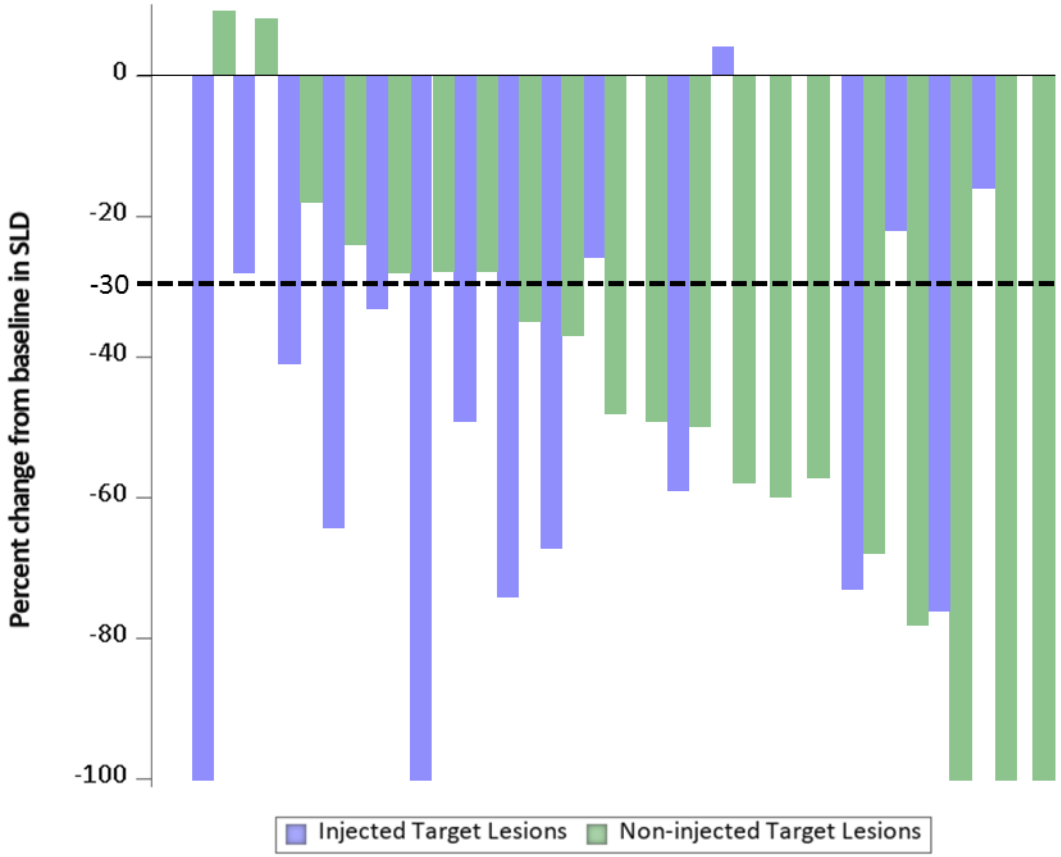
ORR = 25% (21/83; 95% CI 16%-36%)
Patients treated with
the CMP-001 0.01% PS20 formulation

Milhem, SITC 2019.

CMP-001 Results



Patients with injected target lesions only (N=12)



Patients with non-injected target lesions (N=20)

Milhem, SITC 2019.

Intratumoral therapies – conclusions and implications

- While locally administered, intratumoral therapies may enhance systemic effects
- May help alleviate some toxicity concerns from systemic administration
- Potential issues may include dosing, unique regulatory considerations

Other agents

Clinical activity of BEMPEG plus NIVO in previously untreated patients with metastatic melanoma: Updated results from the phase 1/2 PIVOT-02 study

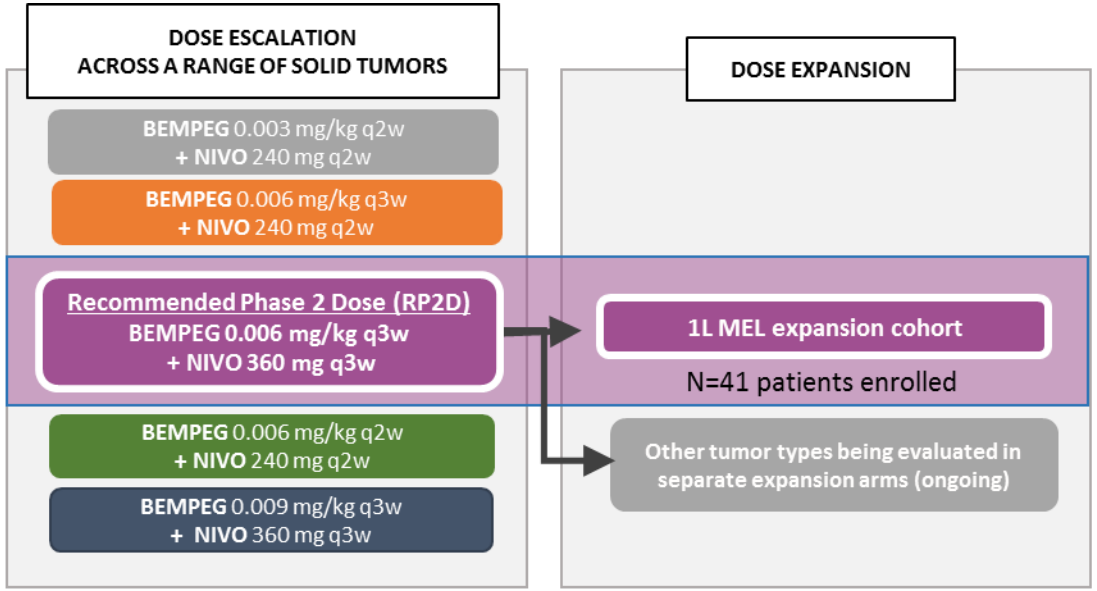
Adi Diab[1], Igor Puzanov[2], Michele Maio[3], Brendan Curti[4], Mehmet Bilen[5], Karl Lewis[6], Scott Tykodi[7], Gregory Daniels[8], Alexander Spira[9], Chantale Bernatchez[1], Salah Eddine Bentebibel[1], Michael Wong[1], James Larkin[10], Ewa Kalinka-Warzocha[11], Sunny Xie[12], Sue Currie[12], Ute Hoch[12], Wei Lin[12], Mary Tagliaferri[12], Stina Singel[12], Mario Sznol[13], Michael Hurwitz[13]

[1]MD Anderson Cancer Center, [2]Roswell Park Comprehensive Cancer Center, [3]Azienda Ospedaliera Universitaria Senese, [4]Providence Portland Medical Center, [5]Emory University Hospital, [6]University of Colorado, Denver, [7]Seattle Cancer Care Alliance, [8]University of California, San Diego, [9]Virginia Cancer Specialists, [10]The Royal Marsden, [11]Instytut Medyczny Santa Familia, [12]Nektar Therapeutics, [13]Yale School of Medicine

PIVOT-02 Study Design

Key MEL Inclusion Criteria

- 1L Metastatic Melanoma (with known BRAF status)
- IO naïve
- Measurable disease per RECIST v1.1
- ECOG PS 0-1



Primary endpoints:

- Safety and tolerability
- ORR per RECIST assessed every 8 weeks*
- Efficacy evaluable per protocol defined as patients with ≥ 1 post baseline scan

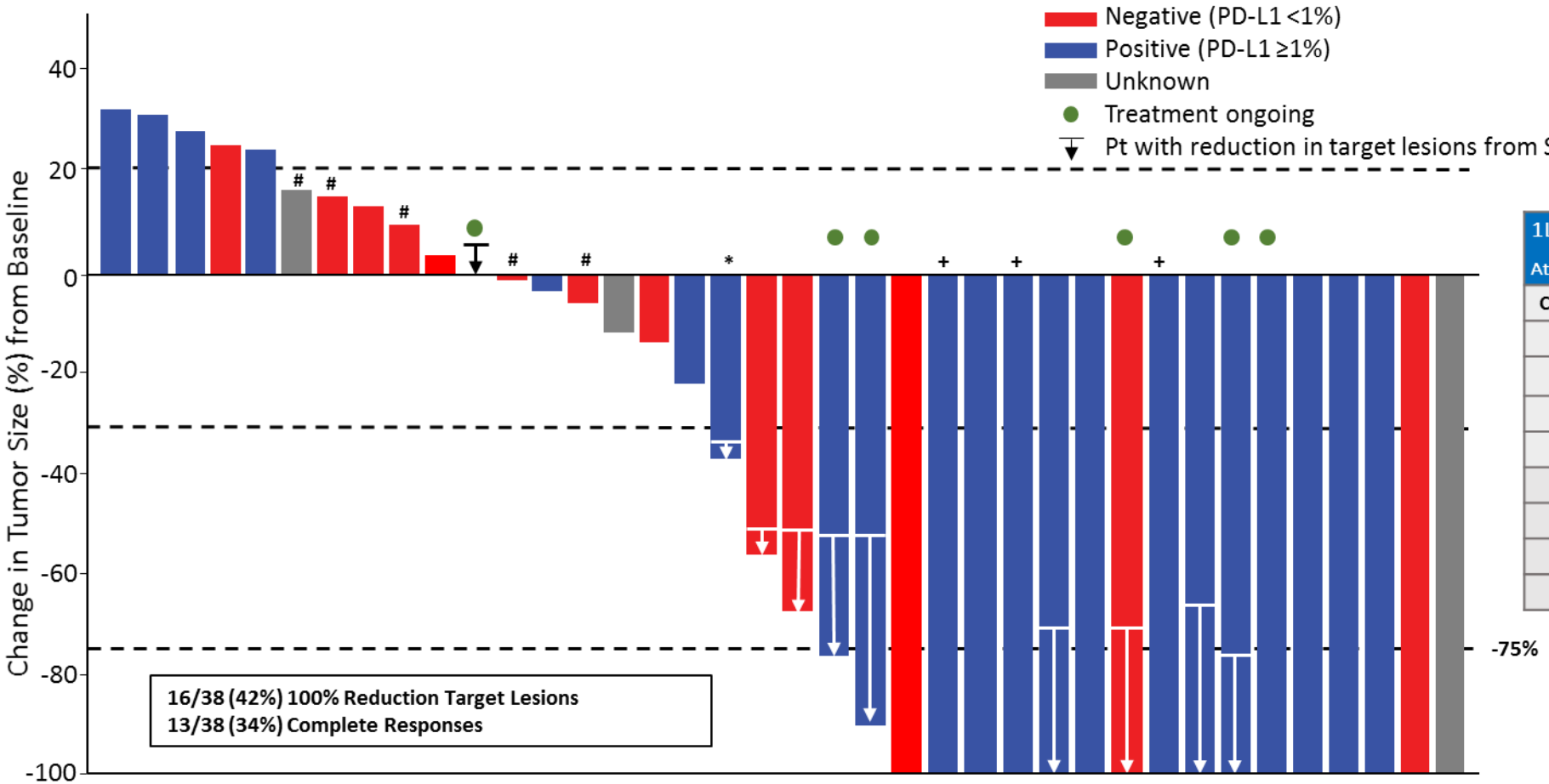
Secondary and exploratory endpoints:

- Duration of response, OS, PFS, clinical benefit rate, PK
- Biomarker analyses in blood and tumor

- 41 MEL patients enrolled and received at least one dose of BEMPEG plus NIVO
- As of Sept 25, 2019, 38 patients were efficacy evaluable defined as patients with ≥1 post-baseline scan (3 patients discontinued prior to first scan due to an unrelated TEAE [n=1] and patient decision [n=2])

Diab, SITC 2019.

PIVOT-02 Results



1L Melanoma (n=38 Efficacy Evaluable) At Median Time of 18.6 months of Follow-up:	Overall Response Rate
Confirmed ORR (CR+PR)	20 (53%)
CR	13 (34%)
PD-L1 negative (n=13)	5 (39%)
PD-L1 positive (n=22)	14 (64%)
PD-L1 unknown (n=3)	1 (33%)
LDH > ULN (n=11)	5 (45%)
Liver metastases (n=10)	5 (50%)
Median Time to Response (months)	2.0
Median Time to CR (months)	7.9

Data Cutoff Date: 25SEP2019. Response evaluable population includes patients who have measurable disease (per RECIST 1.1) at baseline and also have at least one post-baseline assessment of tumor response and (for Parts 2 and 4) meet eligibility criteria are response evaluable. All objective responses are confirmed. #Best overall response is PD due to non-target lesion progression or presence of new lesion; *Best overall response is SD; +Best overall response is PR. CR for target lesion, non-target lesion still present.

Diab, SITC 2019.

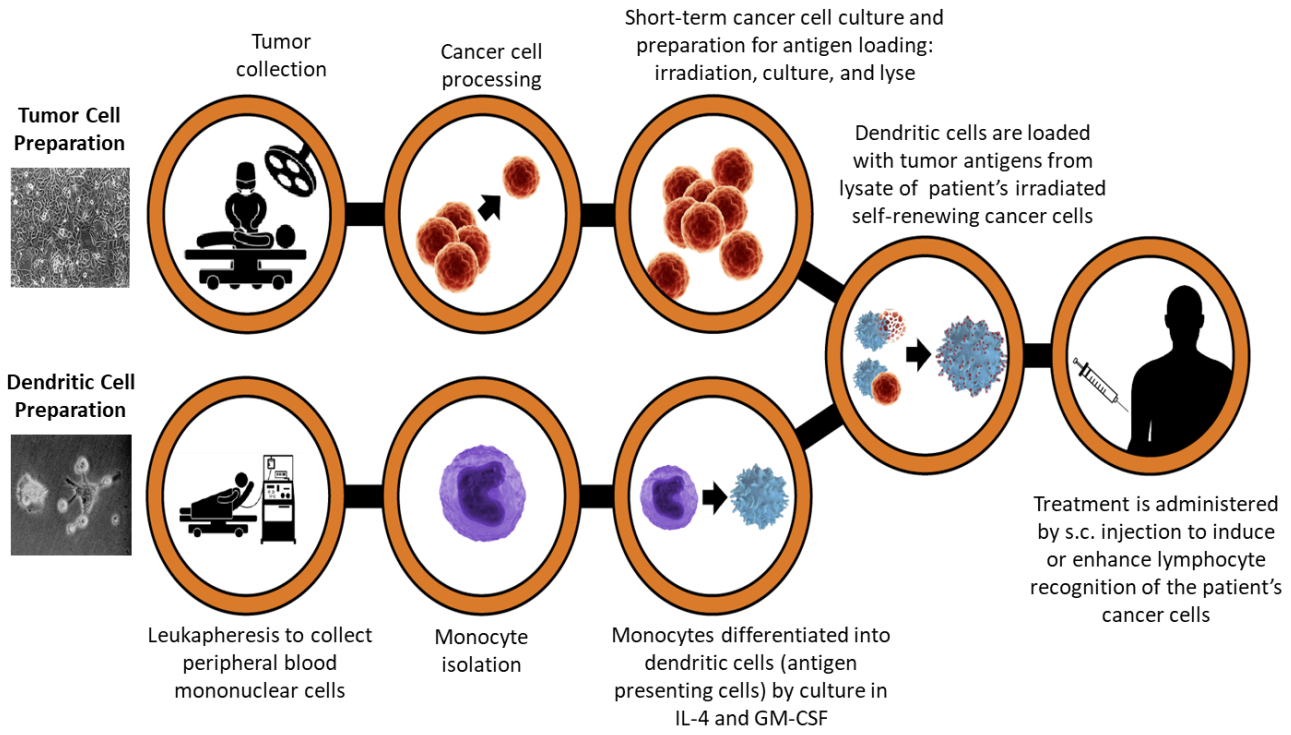
Phase II trial of therapeutic vaccine consisting of autologous dendritic cells loaded with autologous tumor cell antigens from self-renewing cancer cells in patients with newly diagnosed glioblastoma

Daniela A. Bota,[1] David E. Piccioni,[2] Renato V. LaRocca,[3] Christopher M. Duma [4] Santosh Kesari,[4,5] Jose A. Carrillo,[5] Robert D. Aiken[6], Robert O'Donnell,[7] Thomas H. Taylor,[1] Candace Hsieh,[8] Gabriel I. Nistor,[8] and Robert O. Dillman[8]

[1]University of California Irvine, Irvine, CA; [2]University of California San Diego, San Diego, CA; [3]Norton Cancer Center, Louisville, KT; [4]Hoag Hospital, Newport Beach, CA; [6]John Wayne Cancer Institute, Santa Monica, CA; [5]Rutgers University, New Brunswick, NJ; [7]University of California Davis, Sacramento, CA; [8]AIVITA Biomedical, Inc., Irvine, CA

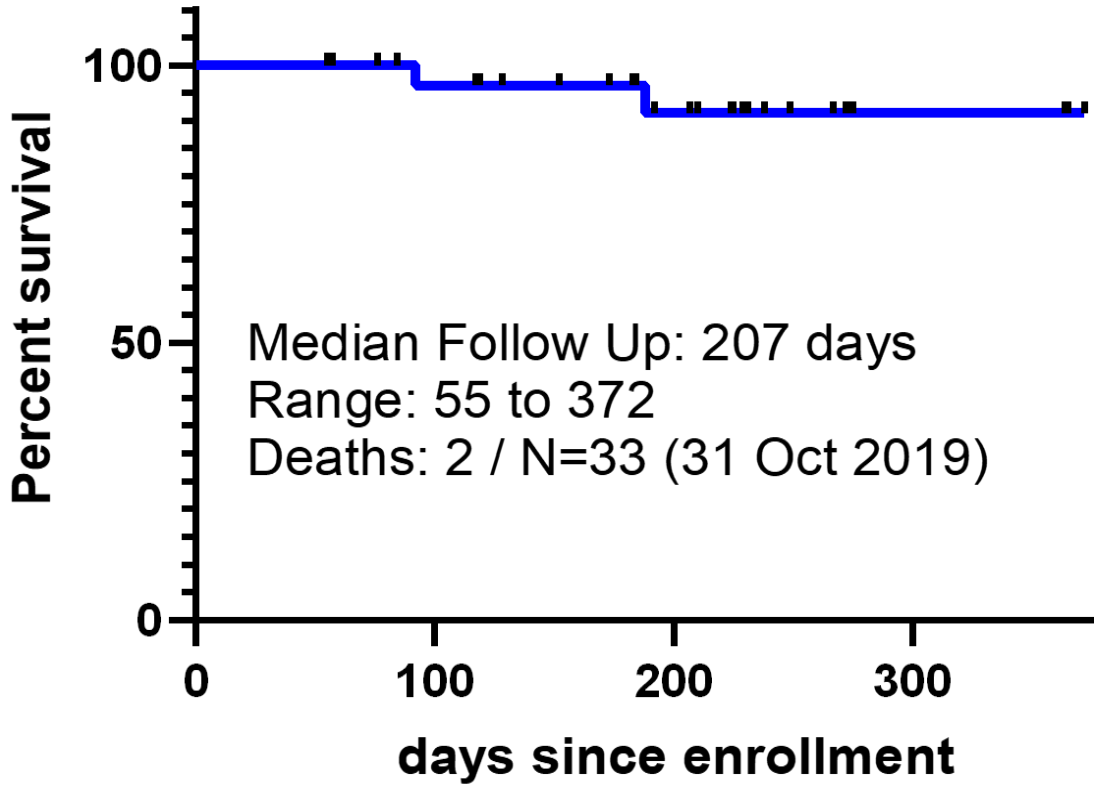
Study design

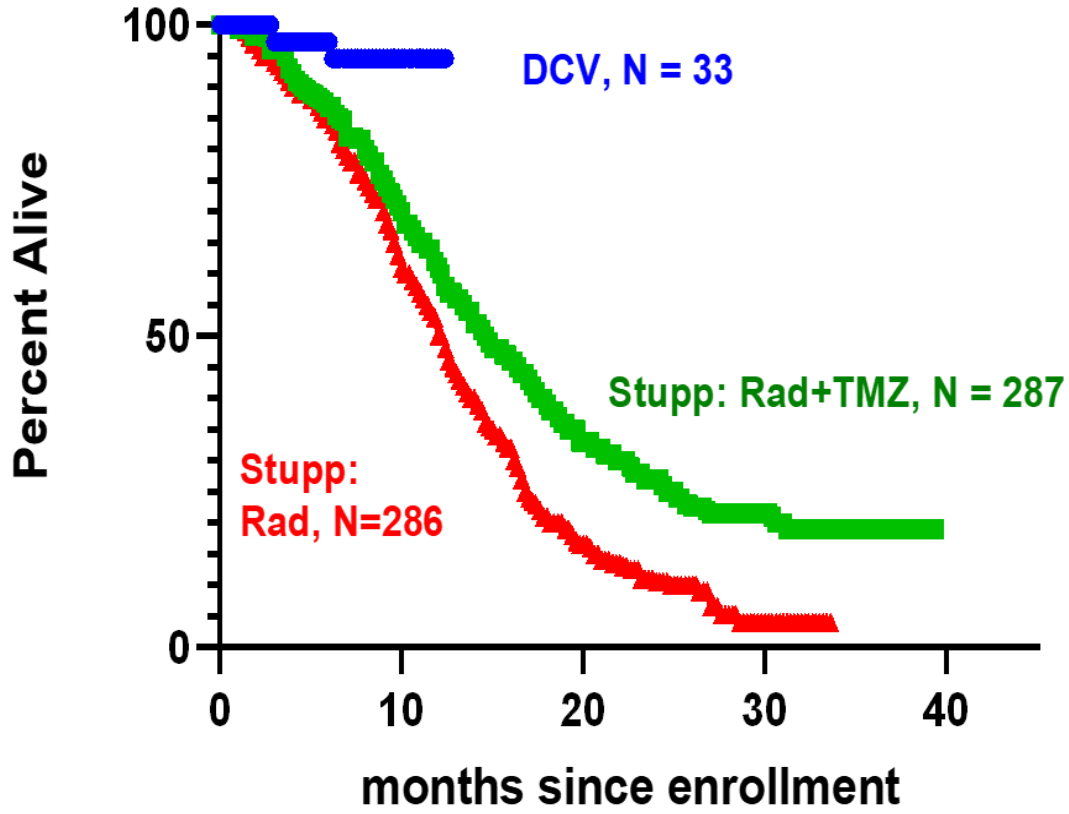
- DCV s.c. weekly x 3, starting after recovery from chemoradiation
- Adjuvant TMZ or other standard therapy while giving monthly DCV injections (weeks 8, 12, 16, 20, and 24)
- Treatment continued through radiologic progression



Bota, SITC 2019.

Results





Bota, SITC 2019.

Other agents –conclusions and implications

- Novel approaches to immunomodulation are demonstrating promise both alone and in combination with more traditional therapies
- Personalized vs. off-the-shelf options: benefits and drawbacks for each

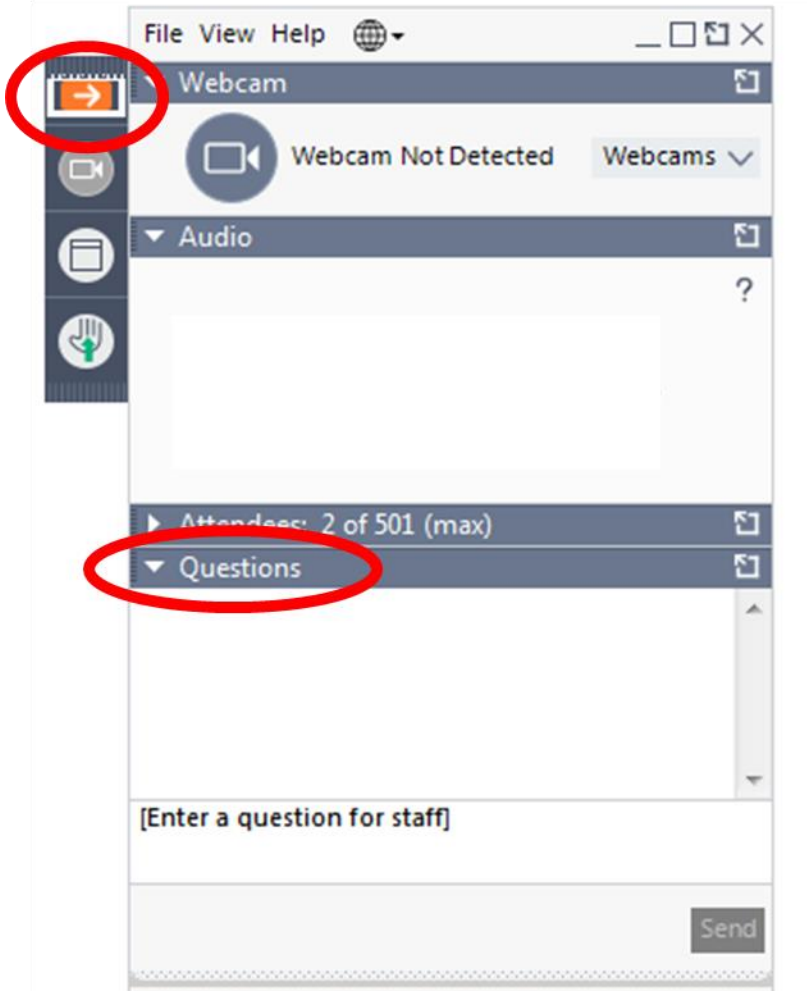
SITC 2019 trends and conclusions

- Novel approaches being tested in clinical trials – but which ones will have clinical impact?
- Combination treatments show enhanced responses, but often with additional toxicity
- Clinical and preclinical studies are leading to a greater understanding of the immune system and anti-cancer responses

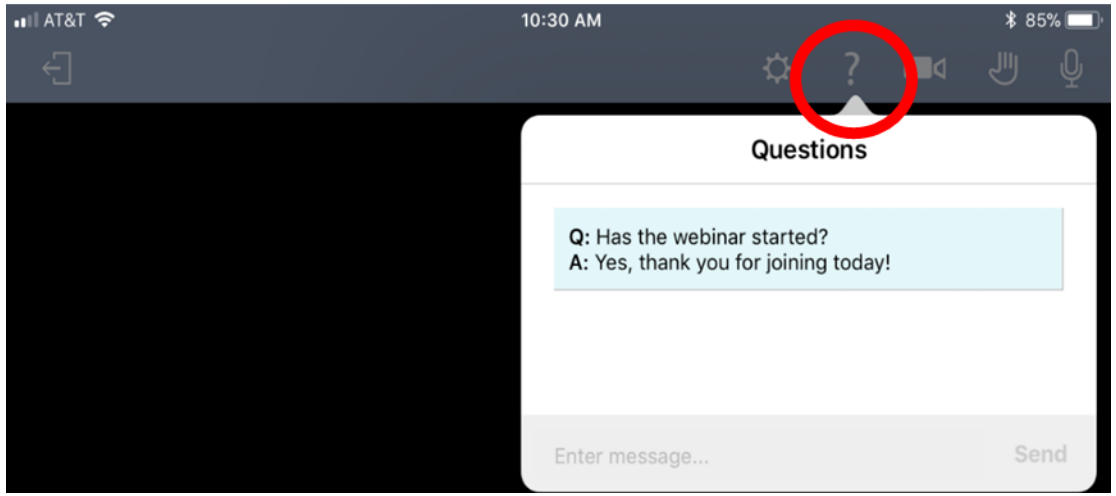
Society for Immunotherapy of Cancer

How to Submit Questions

Computer



Mobile Phone



Upcoming Advances in Cancer Immunotherapy™ Webinar:

Clinical Updates from ESMO Congress 2019

Friday, February 28, 2020, 1:00-2:00 p.m. EST

Faculty:

Hossein Borghaei, MD – *Fox Chase Cancer Center*

Amanda Kirane, MD – *UC Davis Comprehensive Cancer Center*

Brian Rini, MD – *Vanderbilt University Medical Center*

To register visit sitcancer.org/acionline

Other SITC Resources

Continuing Education Credits

- Continuing Education Credits are offered for Physicians, PA's, NP's, RN's and Pharmacists
- You will receive an email following the webinar with instructions on how to claim credit
- Questions and comments: connectED@sitcancer.org

Thank you for attending the webinar!

Jointly provided by Postgraduate Institute for Medicine and the Society for Immunotherapy of Cancer

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