MacroGenics®

Developing
Breakthrough Biologics,
Life-changing Medicines

ASCO 2020 Conference Call: MGD013 & MGC018

May 29, 2020

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Investigational Agents

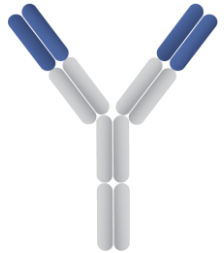
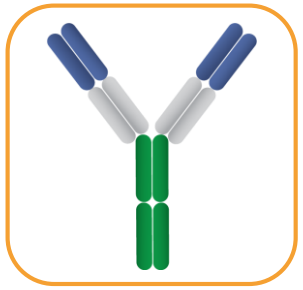
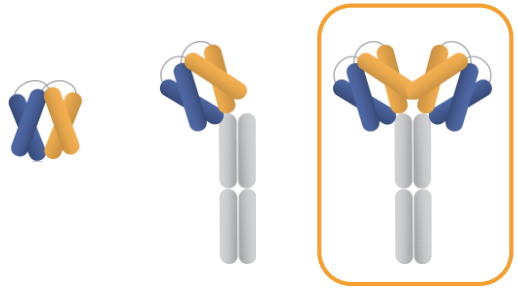
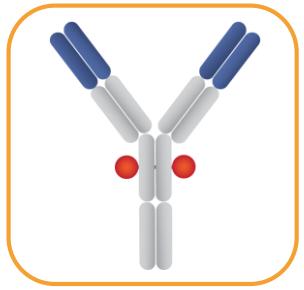
All Company product candidates described or mentioned herein are investigational and have not yet been approved for marketing by any regulatory authority.

ASCO 2020 Conference Call Agenda

Topic	Presenter
Introduction	**Scott Koenig, M.D., Ph.D.** President & Chief Executive Officer
MGD013: Bispecific DART® Molecule Binding PD-1 and LAG-3 *A Phase 1, First-in-Human, Open-Label, Dose Escalation Study in Patients with Unresectable or Metastatic Neoplasms*	**Jason Luke, M.D., FACP** UPMC Hillman Cancer Center, Pittsburgh, PA
MGC018: Anti-B7-H3 Antibody-Drug Conjugate *Preliminary Dose Escalation Results from a Phase 1/2, First-in-Human Study in Patients with Advanced Solid Tumors*	**John Powderly, M.D., CPI** Carolina BioOncology, Huntersville, NC
Prostate Cancer – Treatment Paradigm	**Emmanuel Antonarakis, M.D.** Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD
Q&A	

Engineering Antibodies to Engage Immune System Against Cancer

- Seven immuno-oncology product candidates in clinical development
- Complementary immune mechanisms provide potential for combination

Antibody	Fc-Engineered Antibody	DART® Molecules	Antibody-Drug Conjugate
			
• retifanlimab (anti-PD-1)*	• **margetuximab (anti-HER2)** • enoblituzumab (anti-B7-H3)	• flotetuzumab (CD123 × CD3) • **MGD013 (PD-1 × LAG-3)** • MGD019 (PD-1 × CTLA-4)	• **MGC018 (anti-B7-H3 ADC)****
	• Enhance Fc-mediated activity, including ADCC • Promote innate and adaptive immunity • Combine with checkpoint inhibitors to augment activity	• Tailored half-life and avidity/valency • Broad range of modalities: – Redirect T-cell killing – Co-blockade of multiple checkpoint molecules	• Deliver potent anti-tumor payload • Leverage third-party payload and linker technologies

**Licensed to Incyte; MacroGenics retains rights to develop its pipeline assets in combination w/retifanlimab (MGA012) and to manufacture a portion of global clinical and commercial supply needs.*
***MGC018 is an antibody-drug conjugate (ADC) based on a duocarmycin payload with a cleavable peptide linker that was licensed from Byondis (formerly Synthon Biopharmaceuticals).*

A Phase 1, First-in-Human, Open-Label, Dose Escalation Study of MGD013, a Bispecific DART® Molecule Binding PD-1 and LAG-3 in Patients with Unresectable or Metastatic Neoplasms

Jason J. Luke,[1] Manish R. Patel,[2] Erika Hamilton,[3] Bartosz Chmielowski,[4] Susanna Ulahannan,[5] Hedy Kindler,[6] Shakeela Bahadur,[7] Philip Clingan,[8] Girish Mallesara,[9] Andrew Weickhardt,[10] Scott Currence,[11] Linzhi Xu,[11] Sanjeev Kaul,[12] Francine Chen,[11] Paul A. Moore,[11] Ezio Bonvini,[11] Bradley J. Sumrow,[11] George Blumenschein[13]

[1]UPMC Hillman Cancer Center, Pittsburgh, PA; [2]Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL; [3]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [4]Division of Hematology & Medical Oncology, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA; [5]SCRI Nashville/OUHSC Oklahoma City, Oklahoma City, OK; [6]Division of Hematology/Oncology, Department of Medicine, University of Chicago, Chicago, IL; [7]Banner MD Anderson Cancer Center, Gilbert, AZ; [8]Southern Medical Day Care Centre, Wollongong, NSW, Australia; [9]Calvary Mater Newcastle Hospital, Waratah, NSW, Australia; [10]Austin Health, Olivia Newton-John Cancer Research Institute, Heidelberg, Victoria, Australia; [11]MacroGenics, Inc., Rockville, MD; [12]Bio-ClinPharm Consulting, LLC. Cranbury, NJ; [13]Department of Thoracic Head & Neck Medical Oncology, Division of Cancer Medicine, MD Anderson Cancer Center, Houston, TX.

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: Jason J. Luke, MD, FACP @jasonlukemd

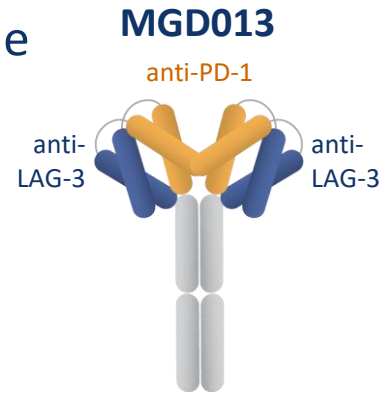
Presenter Disclosure Information

Jason J. Luke, MD, FACP

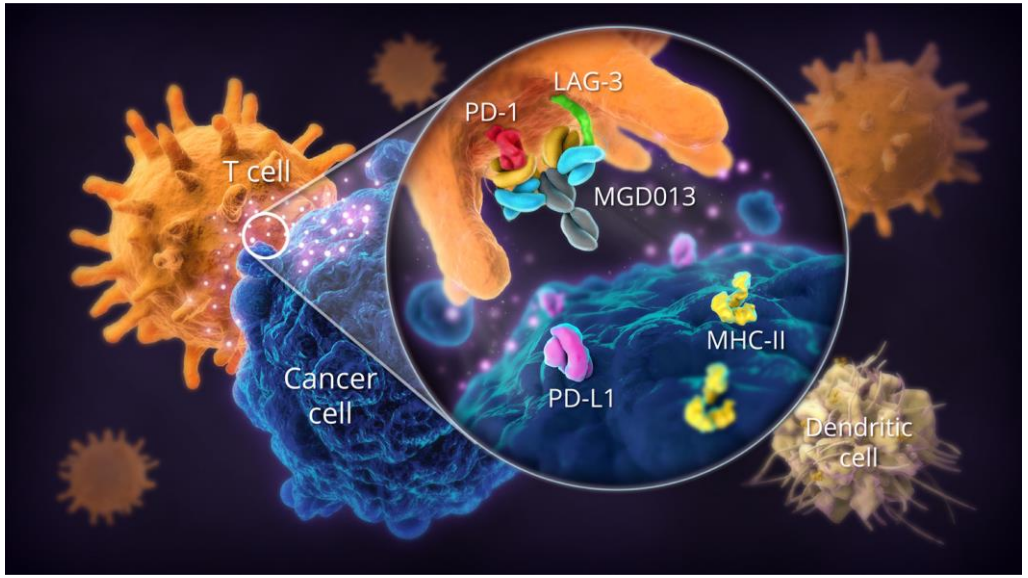
- Data and Safety Monitoring Board: TTC Oncology
- Scientific Advisory Board: 7 Hills, Actym, Alphamab Oncology, Kanaph, Mavu (now part of AbbVie), Onc.AI, Pyxis, Springbank, Tempest
- Consultancy: Abbvie, Akrevia, Algios, Array, Astellas, Bayer, Bristol-Myers Squibb, Eisai, EMD Serono, Ideaya, Incyte, Janssen, Merck, Mersana, Novartis, PTx, RefleXion, Regeneron, Silicon, Tesaro, Vividion
- Research Support: (all to institution for clinical trials unless noted) AbbVie, Agios (IIT), Array (IIT), Astellas, Bristol-Myers Squibb, CheckMate (SRA), Compugen, Corvus, EMD Serono, Evelo (SRA), Five Prime, FLX Bio, Genentech, Immatics, Immunocore, Incyte, Leap, MedImmune, MacroGenics, Necktar, Novartis, Palleon (SRA), Merck, Springbank, Tesaro, Tizona, Xencor
- Travel: Akrevia, Bayer, Bristol-Myers Squibb, EMD Serono, Incyte, Janssen, Merck, Mersana, Novartis, Pyxis, RefleXion
- Patents (both provisional): Serial #15/612,657 (Cancer Immunotherapy), PCT/US18/36052 (Microbiome Biomarkers for Anti-PD-1/PD-L1 Responsiveness: Diagnostic, Prognostic and Therapeutic Uses Thereof)

Rationale for Dual Targeting of PD-1 and LAG-3

- Checkpoint molecules are leveraged by tumors or APCs to evade the immune system
- PD-1 and LAG-3 receptors are expressed on “exhausted” T-cells
  - Interactions with corresponding ligands negates anti-tumor T cell activity
- Synergy of anti-PD-1 + anti-LAG-3 mAbs in animal tumor models
  - Combination trials of anti-PD-1 plus anti-LAG-3 are ongoing
- MGD013, an investigational DART protein, targets PD-1 and LAG-3 with a single molecule
  - Greater synergistic T-cell activation (IFN-γ) with MGD013 compared with combination of individual constituents
- DART bispecific platform:
  - Stable diabody format
  - Multiple configurations & applications

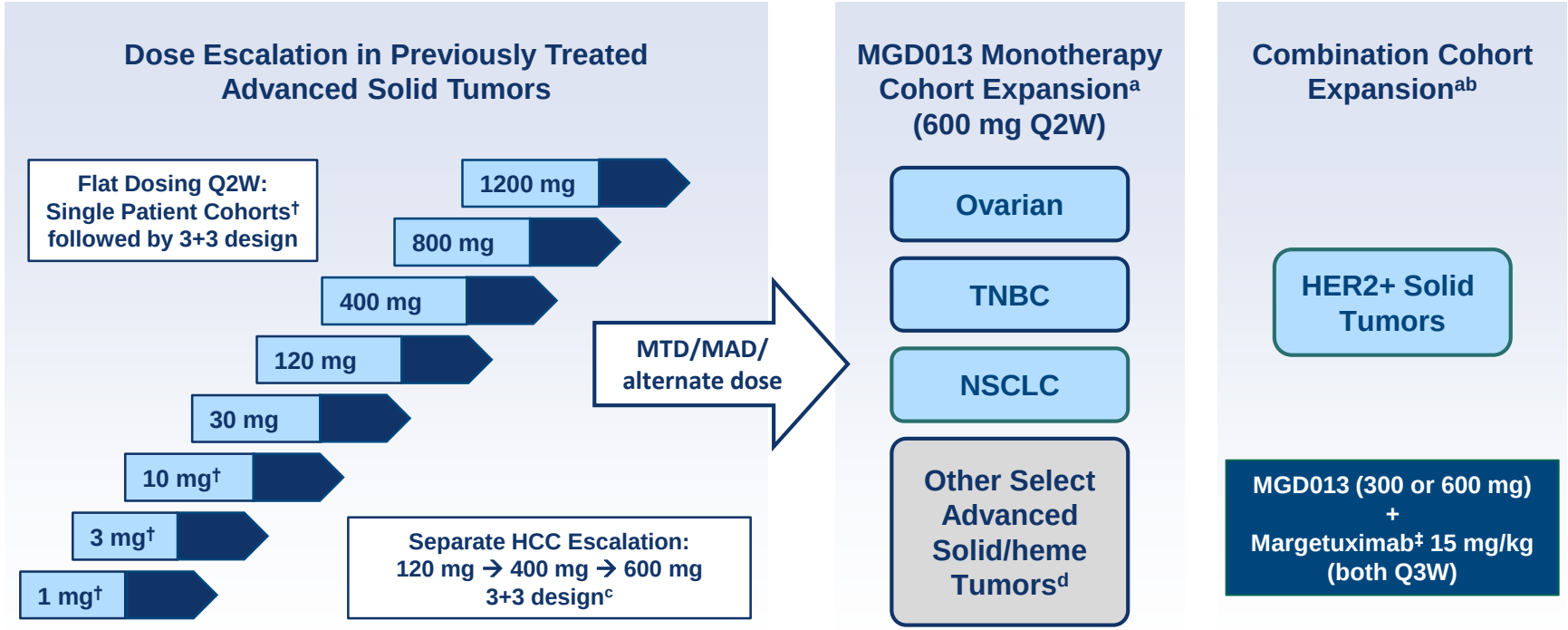


PD-1 × LAG-3
Tetravalent Bispecific
DART Molecule



MGD013 Phase 1 Trial Design

- **Primary objectives:**
  - Safety, tolerability
  - DLTs, MTD, MAD
  - Alternate dose
- **Secondary objectives:**
  - Pharmacokinetics
  - Immunogenicity
  - Preliminary activity
- **Exploratory PD objectives:**
  - Receptor/ligand expression
  - Serum biomarkers
  - Gene expression profiling



DLT = dose-limiting toxicity; MAD = maximum administered dose; MTD = maximum tolerated dose; IHC = immunohistochemistry; Q2W = every 2 weeks. ClinicalTrials.gov identifier: NCT03219268. ‡ Margetuximab is an investigational Fc-optimized mAb targeting HER2. [a] Monotherapy and combination expansion cohorts are ongoing. [b] Combination cohort involved a one-step dose escalation followed by expansion. [c] Separate hepatocellular carcinoma (HCC) 3+3 dose escalation initiated after corresponding dose levels cleared in primary Dose Escalation. [d] Other expansion cohorts enrolling patients with SCCHN, SCLC, HCC, cholangiocarcinoma, cervical cancer, gastric/gastroesophageal junction carcinoma, and DLBCL. Data cutoff: April 25, 2020.

Baseline Demographics

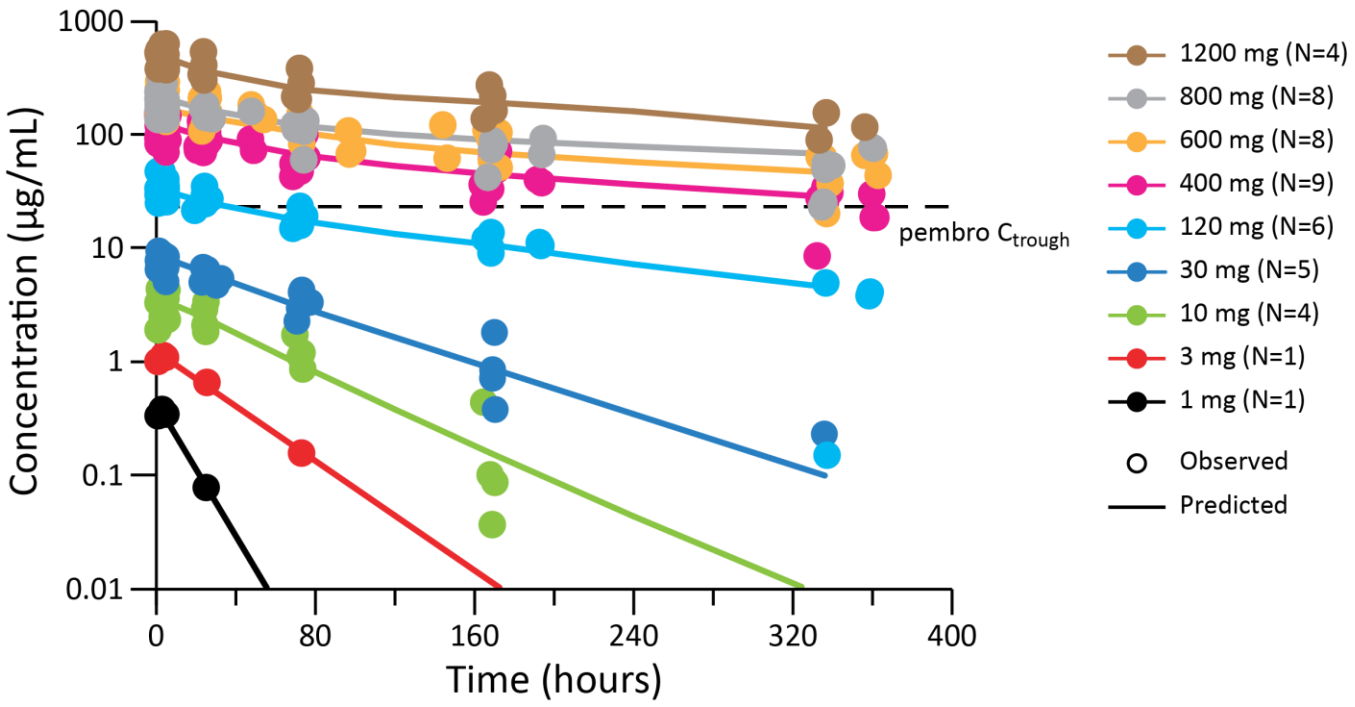
	Dose Escalation 1 -1200 mg Q2W (n=53)	Monotherapy Cohort Expansion 600 mg Q2W (n=205)	Combination Cohort Expansion MGD013 + Margetuximab (n=21)
Median age (range), years	64 (24, 84)	60 (27, 84)	62 (29, 83)
Gender, n (%)			
Male	32 (60.4)	74 (36.1)	7 (33.3)
Female	21 (39.6)	131 (63.9)	14 (66.7)
ECOG PS, n (%)			
0	22 (41.5)	60 (29.3)	12 (57.1)
1	31 (58.5)	145 (70.7)	9 (42.9)
Median prior lines of therapy (range)	2 (1, 9)	2 (1, 9)[a]	2 (1, 7)
Prior Checkpoint Inhibitor			
Yes	23 (43.4)	55 (26.8)	1 (4.8)
No	30 (56.6)	139 (67.8)	20 (95.2)

[a] Monotherapy Cohort Expansion median prior lines of therapy derived from n=200 patients (5 patients without this information available). Data cutoff: April, 25, 2020.

Pharmacokinetics and Receptor Occupancy

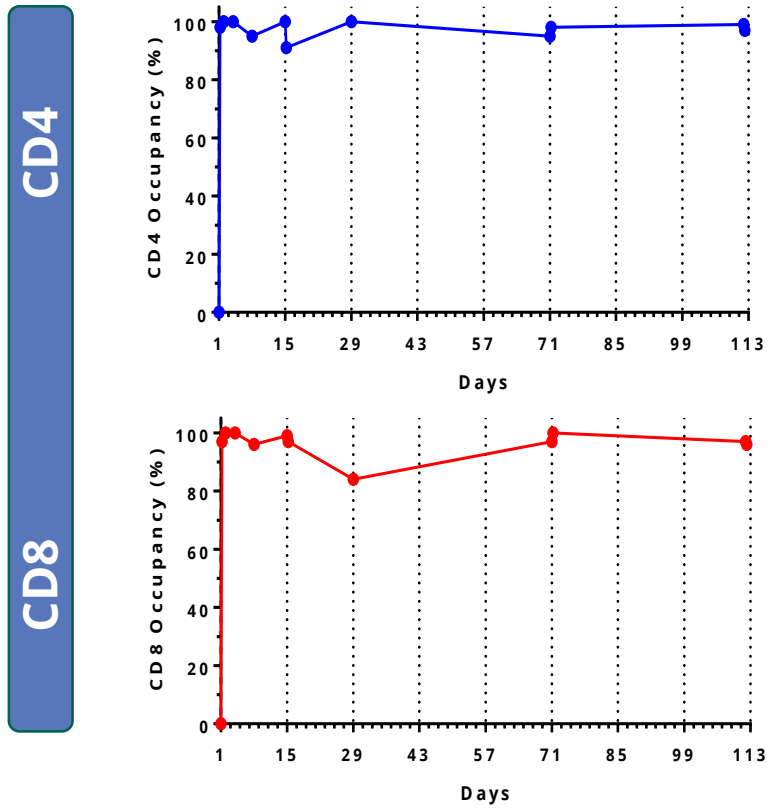
Linear PK (400-1200 mg dose range) and sustained receptor occupancy (≥120 mg)

Pharmacokinetics (1-1200 mg)



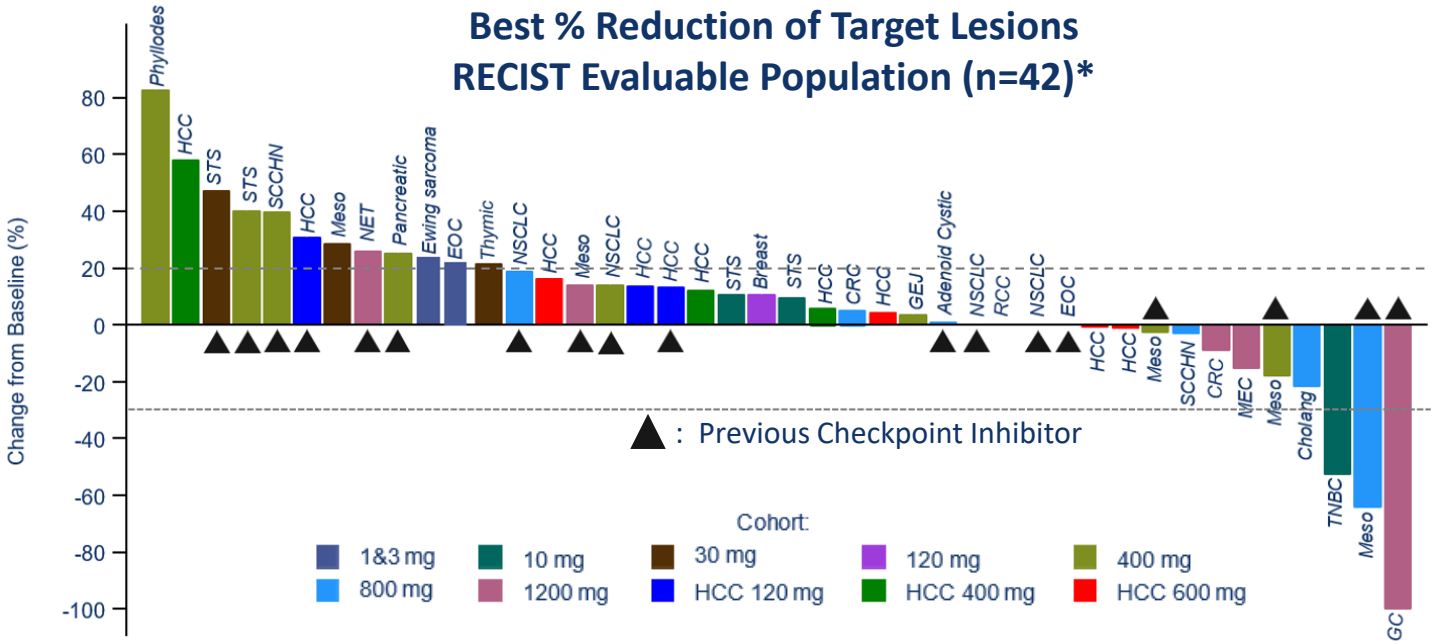
Estimated $t_{1/2}$ = 274 hours (~11 days)

Receptor (PD-1) Occupancy (120 mg Q2W)



pembro c_{trough} = published serum trough concentration of pembrolizumab at 2 mg/kg Q3W (23.6 µg/mL)
[CDER, KEYTRUDA (pembrolizumab) Clinical Pharmacology and Biopharmaceutics Review(s). 2014]

MGD013 Dose Escalation: Results



* Based on patients with baseline and post-treatment tumor measurements. Data cutoff: April, 25, 2020

Immune-Related Adverse Events of Special Interest (AESIs)

	No. (%) of Patients	
	All Grades (N=53)	≥ Grade 3 (N=53)
Rash	7 (13.2)	1 (1.9)
Hypothyroidism	6 (11.3)	0
Immune-mediated hepatitis	2 (3.8)	2 (3.8)
Pancreatitis	1 (1.9)	1 (1.9)
Colitis	1 (1.9)	1 (1.9)
Adrenal insufficiency	1 (1.9)	1 (1.9)
Hyperthyroidism	1 (1.9)	0

Confirmed Partial Responses (n=1, each):

- TNBC (10 mg)
- Mesothelioma (800 mg)
- Gastric Cancer (1200 mg)

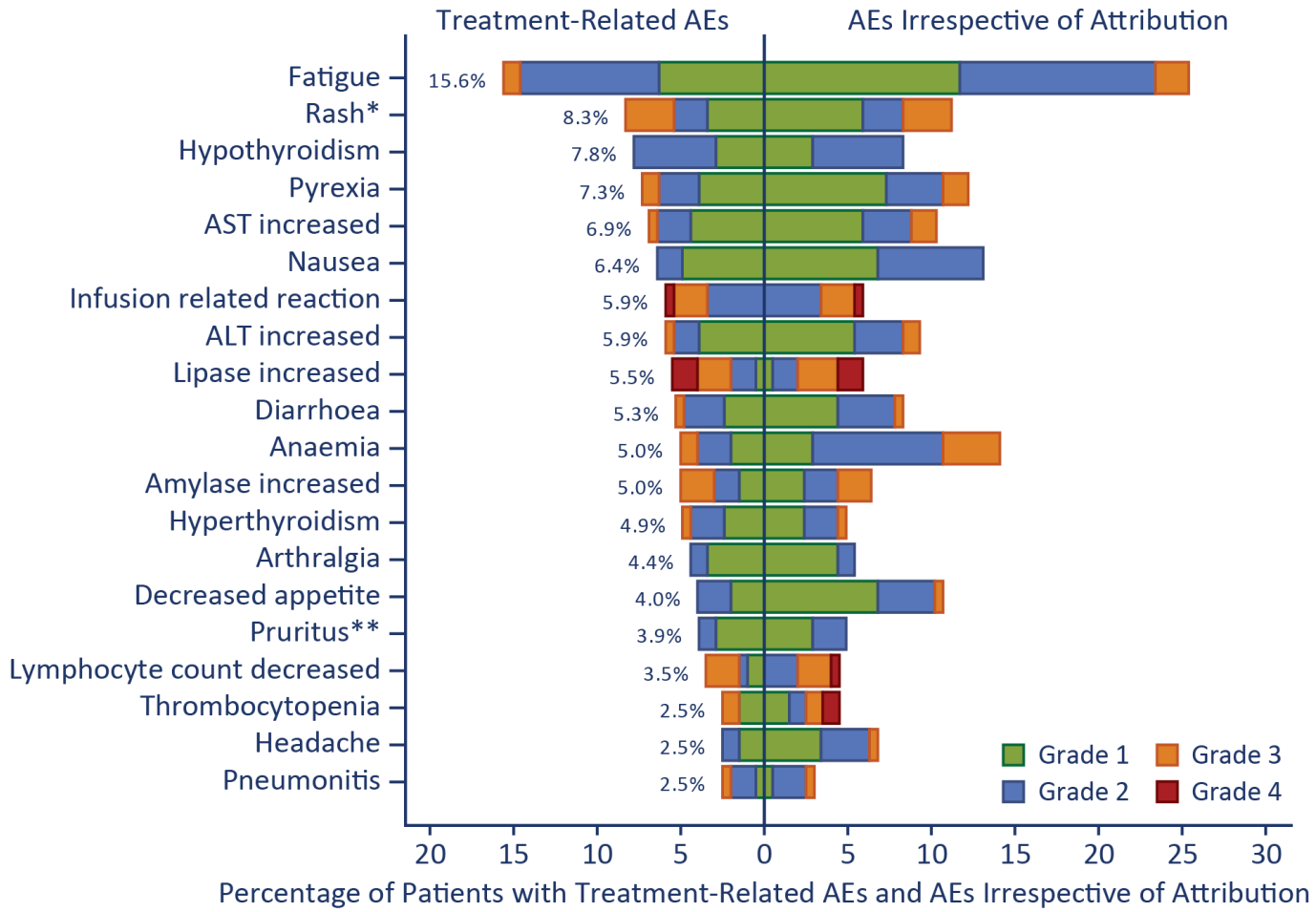
} **Refractory to anti-PD-1 treatment**

- 18 patients with SD as best overall response (DCR = 48.8%)

- Well-tolerated with manageable irAEs
- Safety consistent with anti-PD-(L)1 toxicity profile
- MTD not exceeded or defined at up to 1200 mg Q2W
- Dose limiting toxicities:
  - Immune-mediated hepatitis (1200 mg – primary dose escalation); resolved without sequelae
  - Lipase increase with radiographic evidence of pancreatitis (600 mg – HCC escalation); dose level subsequently cleared

MGD013 Monotherapy Cohort Expansion: Safety

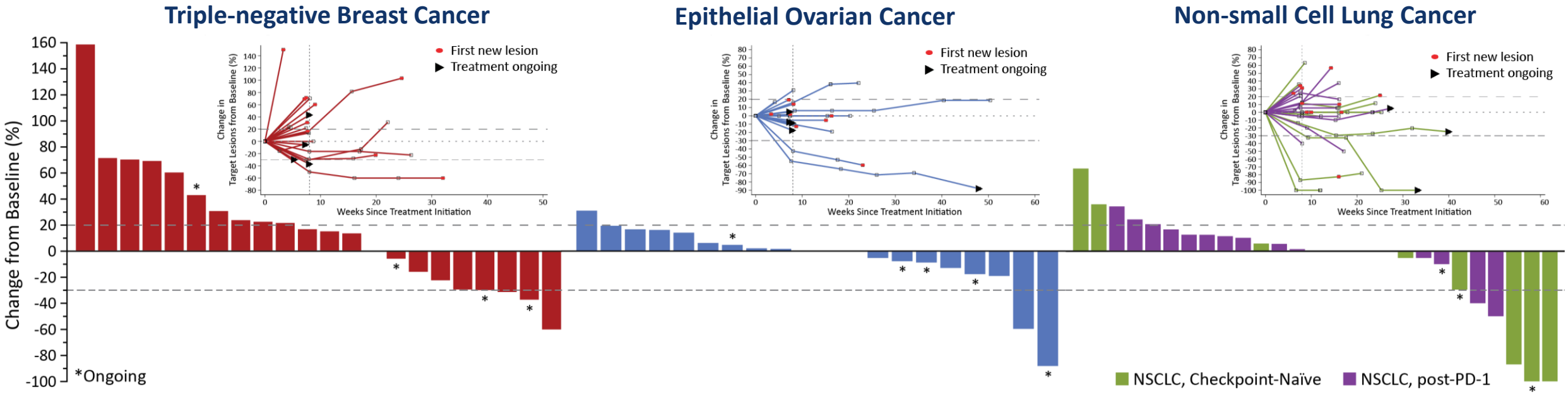
Overall AE Totals	No. (%) of Patients	
	All Grades (N=205)	≥ Grade 3 (N=205)
AE (irrespective of causality)	178 (86.8)	86 (42.0)
Treatment-related AE	118 (57.6)	37 (18.0)[a]
SAE (irrespective of causality)	63 (30.7)	47 (22.9)
Treatment-related SAE	18 (8.8)	11 (5.4)
AE leading to discontinuation	18 (8.8)	16 (7.8)
AESIs in ≥ 2 Patients		
Rash	17 (8.3)	6 (2.9)
Hypothyroidism	16 (7.8)	0 (0.0)
IRR or CRS	13 (6.3)	5 (2.4)
Diarrhoea	11 (5.4)	1 (0.5)
Lipase increased	11 (5.4)	7 (3.4)
Hyperthyroidism	10 (4.9)	1 (0.5)
Arthralgia	9 (4.4)	0 (0.0)
Pneumonitis	4 (2.0)	1 (0.5)
Myalgia	4 (2.0)	0 (0.0)
Peripheral neuropathy	3 (1.5)	1 (0.5)
Hepatitis	3 (1.5)	2 (1.0)
Adrenal insufficiency	2 (1.0)	0 (0.0)



* Includes MedDRA Preferred Terms of *Rash* and *Maculopapular Rash*. ** Includes MedDRA Preferred Terms of *Pruritus* and *Generalized Pruritus*.
[a] Grade 4 drug-related AEs include: lipase increased (n=3), neutrophil count decreased, and IRR (n=1, each). No Grade 5 TRAEs have been reported.
AESI = adverse events of special interest. Data cutoff: April, 25, 2020.

MGD013 Monotherapy Cohort Expansion: Activity

Anti-tumor activity observed in multiple tumor types



	TNBC	EOC	NSCLC, CPI-Naïve	NSCLC, post-PD-1
Evaluable Patients	23	23	14	15
ORR (Confirmed)	4.3% (1/23)	8.7% (2/23)	14.3% (2/14)	0% (0/15)
ORR (Confirmed + Unconfirmed)	17.4% (4/23)	8.7% (2/23)	21.4% (3/14)	13.3% (2/15)
SD	34.8% (8/23)	43.5% (10/23)	50.0% (7/14)	53.3% (8/15)
DCR	39.1% (9/23)	52.2% (12/23)	64.3% (9/14)	53.3% (8/15)

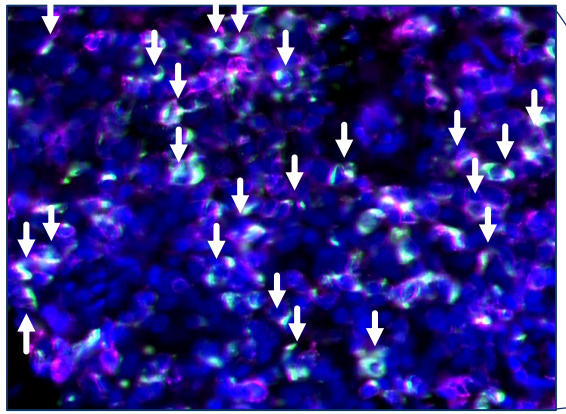
Data cutoff: April, 25, 2020

Complete Response after Single MGD013 Administration

27-year-old male with DLBCL progressive disease after CAR-T cell therapy

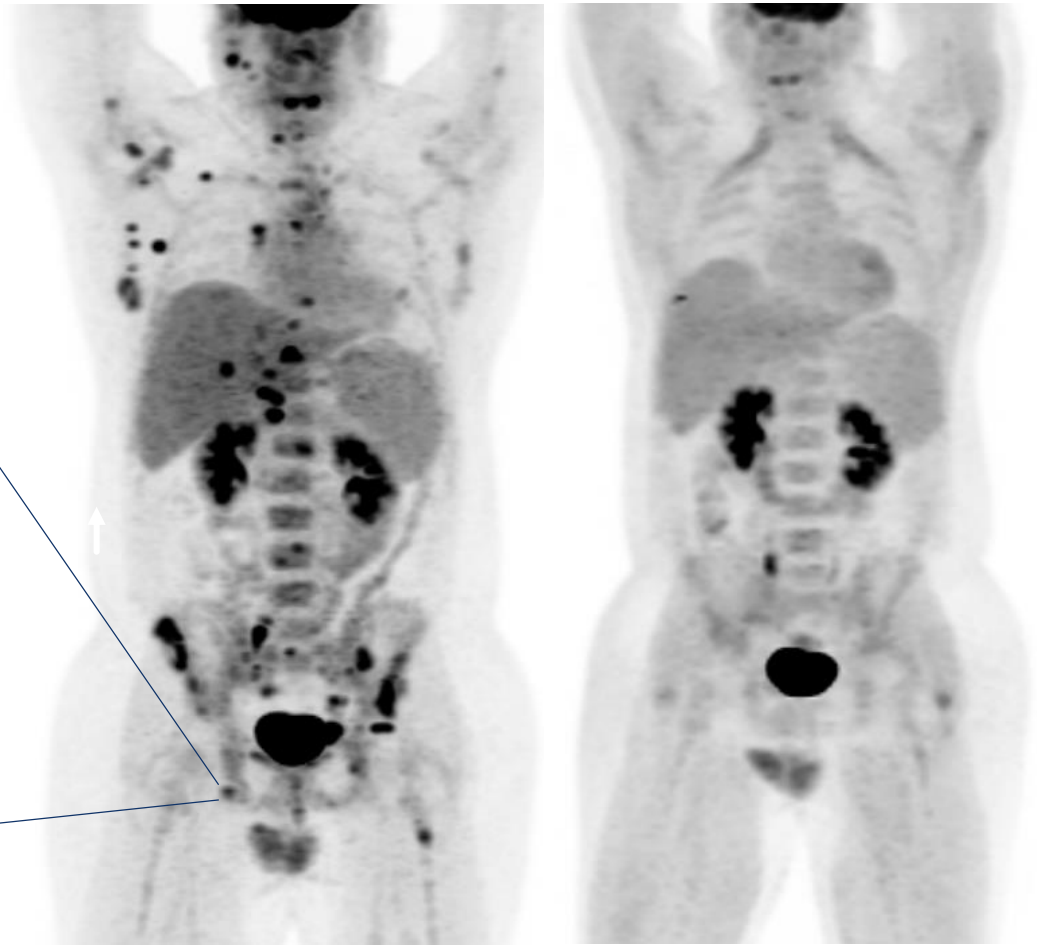
- Relapsed subsequent to DA-R-EPOCH and JCAR017
- Pre-treatment biopsy: High levels of LAG-3 & PD-L1
- Received MGD013, 600 mg x 1
- Admitted on Day 11 for management of Grade 2 CRS
- CR on Day 24 (per Lugano classification)
- No evidence of CAR-T in circulation
- Allogeneic SCT performed
- Currently in remission:
  - 11 months post-MGD013
  - 9 months post-transplant

PD-1/LAG-3 Co-expression



PD-1 (magenta) and LAG-3 (green) co-localized staining

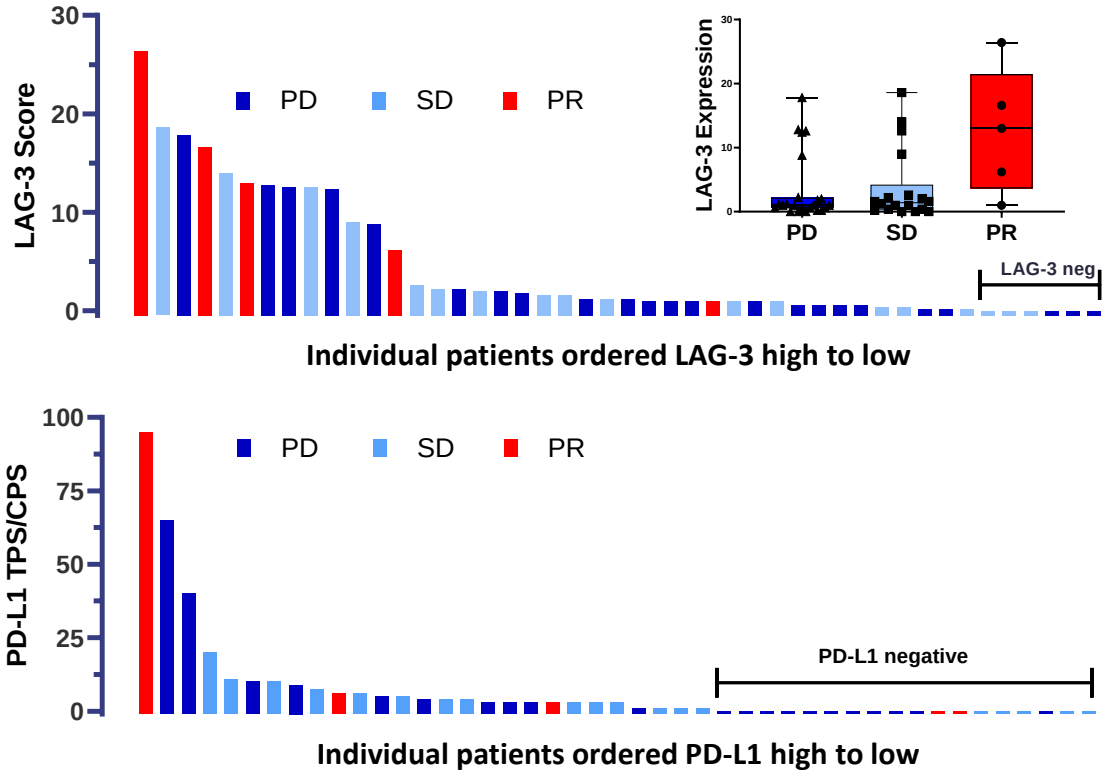
Screening | **MGD013 Complete Response - Day 24**



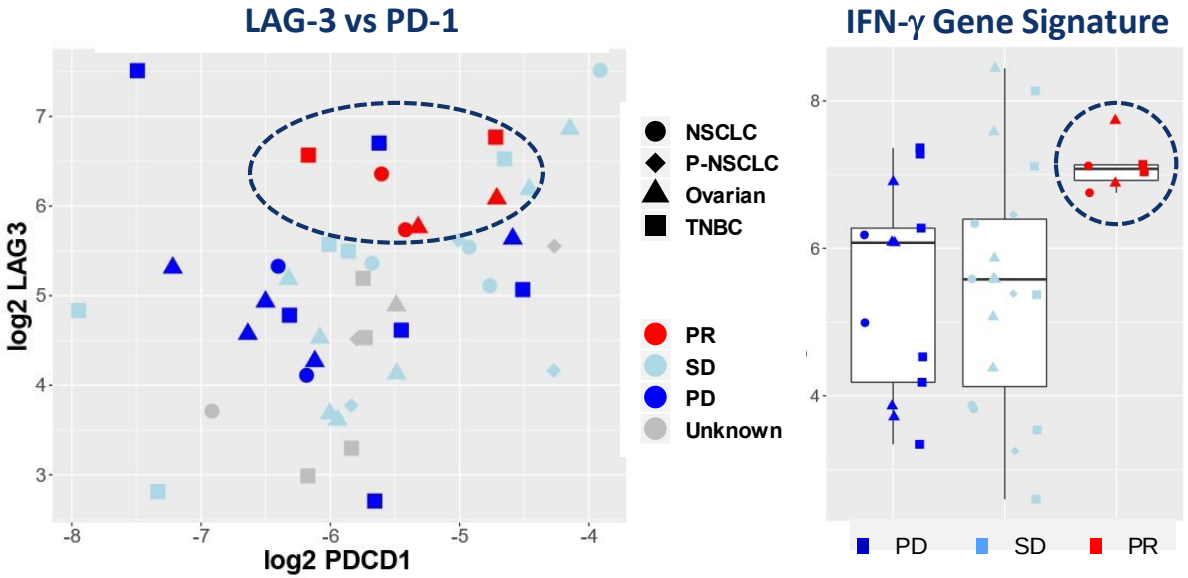
Objective Responses Associated with LAG-3 Expression

Inflammatory interferon-γ signature elevated in patients with clinical response

Retrospective IHC Analyses



Transcript Profiling (Baseline Tumor Biopsy)



Objective responses associated with high baseline LAG-3/PD-1 expression and IFN-γ gene signature (CXCL9, CXCL10, CXC11, STAT1)

Archival biopsies from TNBC, EOC, and NSCLC expansion cohorts analyzed for LAG-3 (N=46) or PD-L1 (N = 45) by IHC. LAG-3 score was determined by calculating mean value of LAG-3+ cells per 40x field across 5 LAG-3+ hot spots (Chen et al., e15086 ASCO 2020). PD-L1 expression was determined per Agilent PD-L1 (22C3) pharmDx kit; TPS (NSCLC) was calculated as per interpretation manual and CPS (EOC, TNBC) calculated as follows: number of PD-L1 + cells (tumor and immune)/total number of viable tumor cells x 100. CPS <1 or TPS <1% was considered negative.

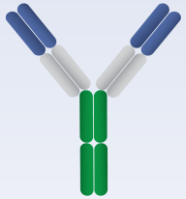
The NanoString PanCancer IO 360™ assay was used to interrogate gene expression, including the abundance of 14 immune cell types and 32 immuno-oncology signatures from archival biopsies from EOC (N= 14) NSCLC (N= 25) and TNBC (N=13) expansion cohorts

Can Tumors Be Made More Responsive to PD-1 × LAG-3 Intervention?

Enhancing effector-cell activation via Fc-engineered mAb

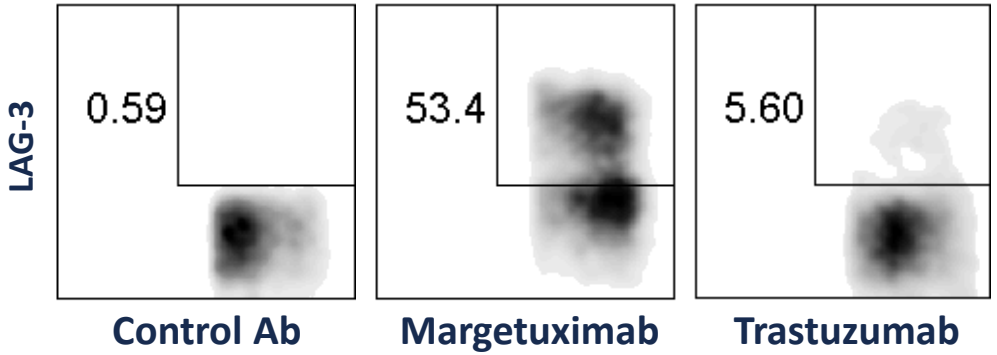
Margetuximab

Investigational Fc-engineered anti-HER2 mAb



- Same anti-HER2 properties as trastuzumab
- Enhanced Fc-mediated effector function[a]
- Superior PFS to trastuzumab in clinical study
  - SOPHIA: Head-to-head Phase 3 study in mBC[b]
- Anti-tumor activity in advanced gastric cancer
  - In combination with anti-PD-1[c]

Margetuximab Enhances LAG-3 Expression by NK Cells

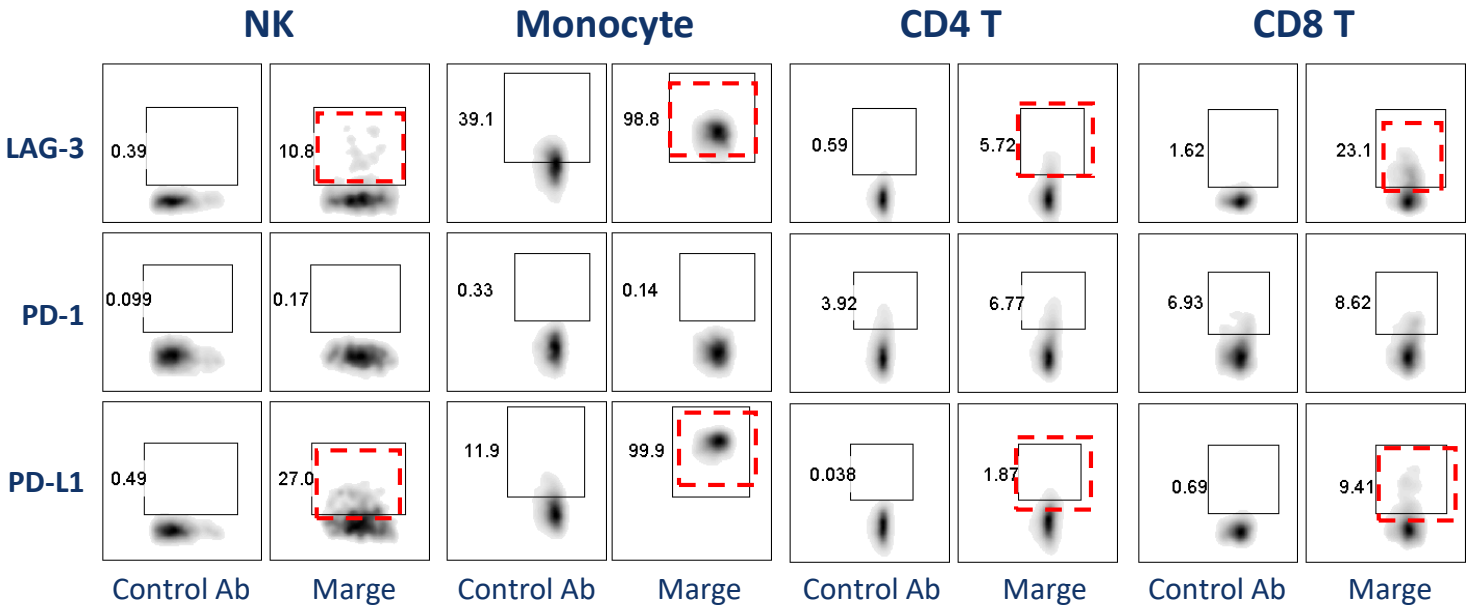


[a] Nordstrom, et al., 2011 *Breast Cancer Research,* 13: R123
[b] Rugo, et al., *ASCO 2019*, Chicago, IL
[c] Catenacci, et al., ASCO GI 2019, San Francisco, CA | Catenacci et al. 2020 *Lancet Oncology*, in press

Human PBMC (Donor # 859) + N87 (HER2+) gastric cancer cells; E:T = 10:1; (IL-2, 20 U/mL)
Control Ab 50ng/mL, margetuximab/trastuzumab, 5ng/mL;. FACS analyses (72h) on $CD3^{-}CD56^{+}$-gated NK cells

Fc-engineered mAb *plus* PD-1 x LAG-3 DART: Combinatorial Biology

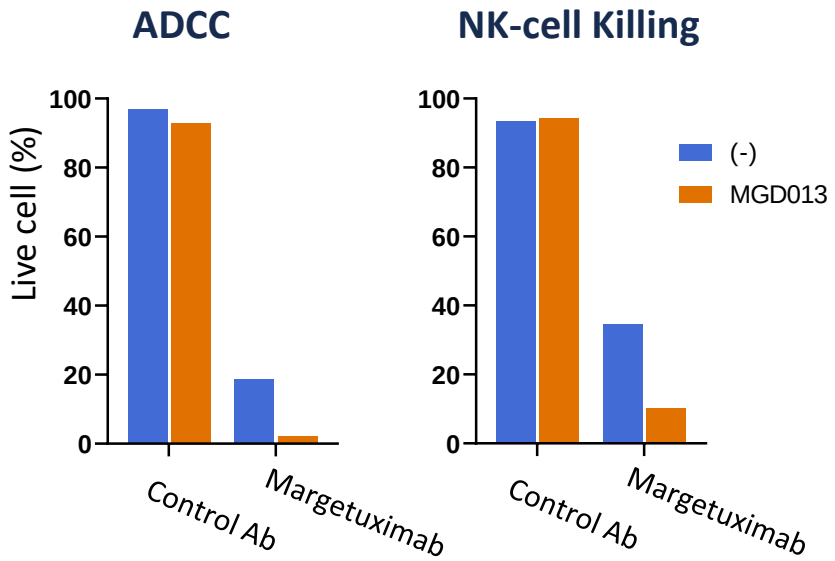
Fc-engineered Margetuximab Up-regulates LAG-3/PD-L1 Expression



Upregulation of LAG-3 and PD-L1 on NK, monocytes and T cells

Human PBMC (Donor # 731) + N87 (HER2+) gastric cancer cells; E:T = 15:1 +/- margetuximab (no supplementary IL-2)

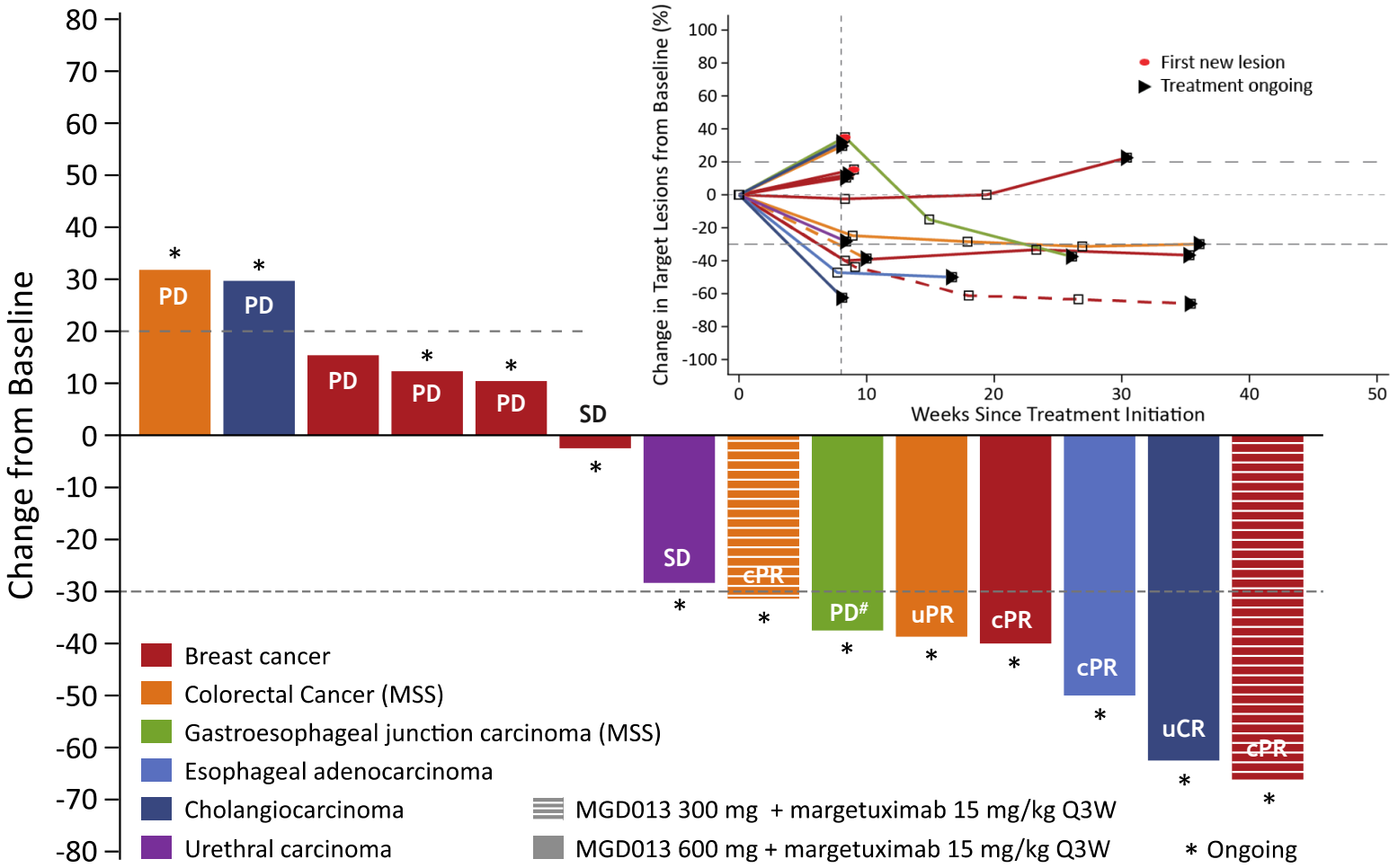
PD-1 x LAG-3 (MGD013) Enhances Lytic Activity of Immune Cells Primed by Fc-engineered mAb (Margetuximab)



ADCC (target: margetuximab opsonized N87, E:T=10) and NK-cell killing (target: K562, E:T=10) mediated by immune cells activated for 6 days by margetuximab +/- MGD013 in the presence of N87 tumor cells.

Fc-engineered αHER2 *plus* PD-1 × LAG-3 DART (Margetuximab *plus* MGD013)

Preliminary results in patients with relapsed/refractory HER2+ solid tumors



GEJ pt with apparent pseudo-progression (PD per RECIST), now with 37.5% reduction in target lesions (iPR per iRECIST).

- ORR = 42.9% (6/14 evaluable pts)
  - Includes unconfirmed objective responses
- Well-tolerated
  - Responding patients remain on therapy

Baseline PD-L1 & LAG-3 in # of Responding Patients (N = 6)

PD-L1 CPS:	< 1	1	TBD
N	4	1	1

LAG-3 Score:	< 5	5-15	TBD/NE
N	3	1	2

Durable Response in Patient Receiving MGD013 *plus* Margetuximab

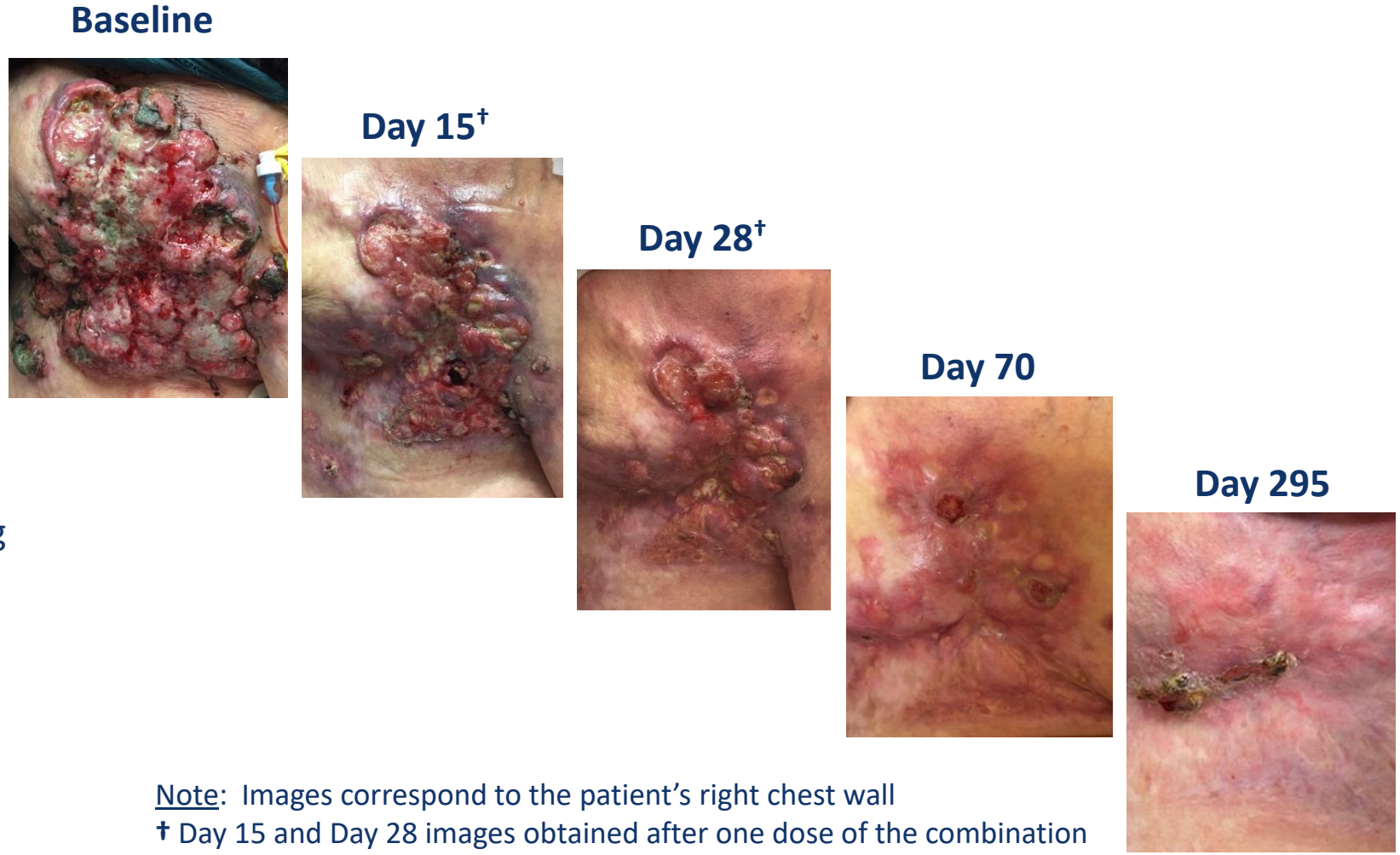
Resolution of chest wall disease with confirmed PR of overall tumor burden

Metastatic HER2+ breast cancer in 67-year-old female

- **Previously progressed on**:
  - 1L pertuzumab/trastuzumab/anastrozole
  - 2L TDM1/anastrozole
  - 3L TDM1

Baseline tumor burden:

- Right breast, liver and lymph nodes
  - PD-L1 CPS: <1; LAG-3 score: 0.8
- Patient remains on treatment in Cycle 15 with improved clinical status and ongoing partial response
  - 1st tumor assessment: -46%
  - 2nd tumor assessment: -61%
  - 3rd tumor assessment: -65%
  - 4th tumor assessment: -66%



Note: Images correspond to the patient's right chest wall
† Day 15 and Day 28 images obtained after one dose of the combination

MGD013 (PD-1 × LAG-3 DART Molecule): Conclusions

First-in-class bispecific checkpoint inhibitor

- Designed to independently or coordinately block PD-1 and LAG-3
- Well tolerated at doses up to 1200 mg Q2W
- RP2D: 600 mg Q2W or Q3W
- Safety profile consistent with anti-PD-1 monotherapy

Encouraging monotherapy activity in multiple tumor types

- Baseline LAG-3 expression & IFN-γ signature associated with objective response

Compelling preliminary combinatorial activity with margetuximab (Fc-engineered mAb)

- >40% ORR observed in low PD-L1-expressing, relapsed/refractory $HER2^{+}$ tumors
  - Compares favorably to low historical response rates to anti-HER2 ± CPI

Evaluation of MGD013 as monotherapy and in combination with Fc-engineered mAbs (incl. margetuximab) is ongoing

Investigators

Australia

Philip Clingan
Anthony Joshua
Girish Mallesara
Andrew Weickhardt

Bulgaria

Nadezhda Miteva
Krasimir Nikolov
Krasimir Oreshkov

Poland

Monika Dlugosz-Danecka
Iwona Lugowska
Rodryg Ramlau
Monika Tomaszewska-Kiecana
Lucjan Wyrwicz

Spain

Analia Azaro Pedrazzoli
Javier Cortes Castan
Maria Jose De Miguel Luken

Thailand

Chaiyut Charoentum
Arunee Dechapunkul
Virote Sriuranpong

Ukraine

Igor Bondarenko
Yevhen Hotko
Anna Kryzhanivska
Andriy Kurochkin
Halyna Pylypenko
Serhii Shevnia

United States of America

Charu Aggarwal
Shakeela Bahadur
George Blumenschein
Bartosz Chmielowski
Anthony El-Khoueiry
Lipika Goyal
Erika Hamilton
Hedy Kindler
Jason Luke
Robin Norris
Manish Patel
Cesar Santa-Maria
Susanna Ulahannan
Jie Wang

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Thank you to the patients and their families who participated or continue to participate in this study.

MGC018: Phase 1 Dose Escalation (Initial Results)

John Powderly, M.D., CPI

Founder & CEO, Carolina BioOncology, Huntersville, NC

Preliminary Dose Escalation Results from a Phase 1/2, First-in-Human Study of MGC018 (Anti-B7-H3 Antibody-Drug Conjugate) in Patients with Advanced Solid Tumors

John Powderly[1], Sekwon Jang[2], Juniper Scribner[3], Deryk Loo[3], Chet Bohac[3], Alexander Spira[4], Manish Sharma[5]

[1]Carolina BioOncology, Huntersville, NC; [2]Inova Schar Cancer Institute Fairfax, VA; [3]MacroGenics, Inc., Rockville, MD; [4]Virginia Cancer Specialists, Fairfax, VA; [5]START Midwest, Grand Rapids, MI

From the Poster Presented at the 2020 ASCO Annual Meeting (ASCO20 Virtual Scientific Program, May 29–31, 2020) by John Powderly, M.D.

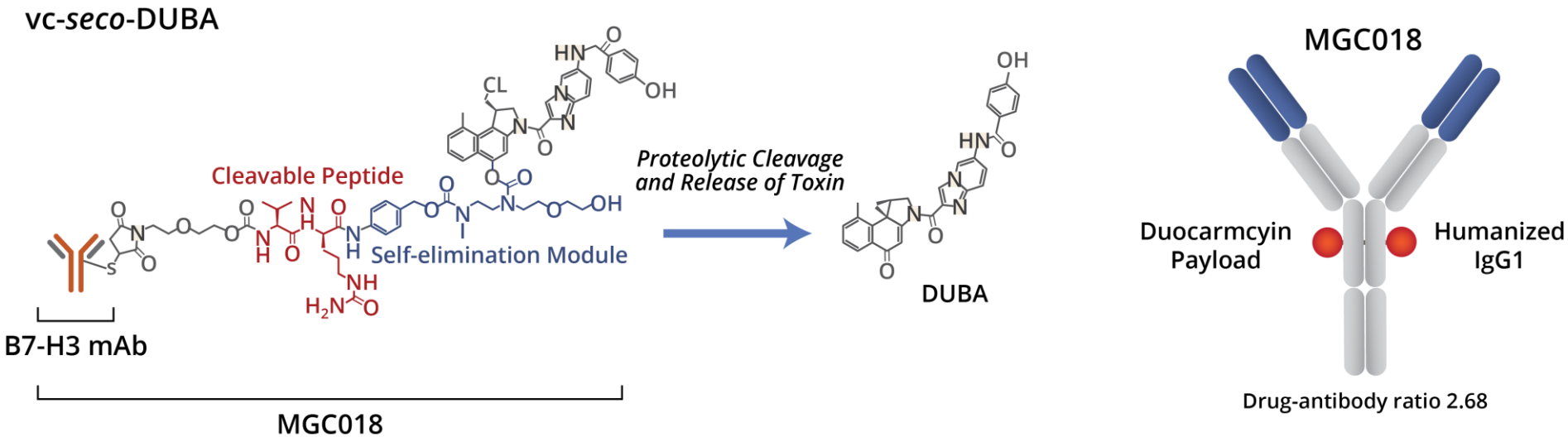
High B7-H3 Expression Levels in Solid Tumors

Potential Indications:	IHC Summary of >1,400 Tumor Tissue Samples Screened			
	B7-H3 Positive[(a)]		2+ or Above	
Head and Neck Cancer	19/19	100%	19/19	100%
Kidney Cancer	77/78	99%	75/78	96%
Glioblastoma	65/66	98%	63/66	95%
Thyroid Cancer	34/35	97%	33/35	94%
Mesothelioma	41/44	93%	39/44	89%
Melanoma	132/146	90%	94/146	64%
Prostate Cancer	88/99	89%	51/99	52%
Pancreas Cancer	69/78	88%	45/78	58%
Bladder Cancer	134/156	86%	123/156	79%
Lung Cancer	324/379	85%	300/379	79%
Breast Cancer	189/249	76%	156/249	63%
Ovarian Cancer	59/79	75%	36/79	46%

(a) B7-H3 positivity reflects any grade staining via fixed tumor microarray; B7-H3 is expressed on tumor cells and tumor vasculature.

From the Poster Presented at the 2020 ASCO Annual Meeting (ASCO20 Virtual Scientific Program, May 29–31, 2020) by John Powderly, M.D.

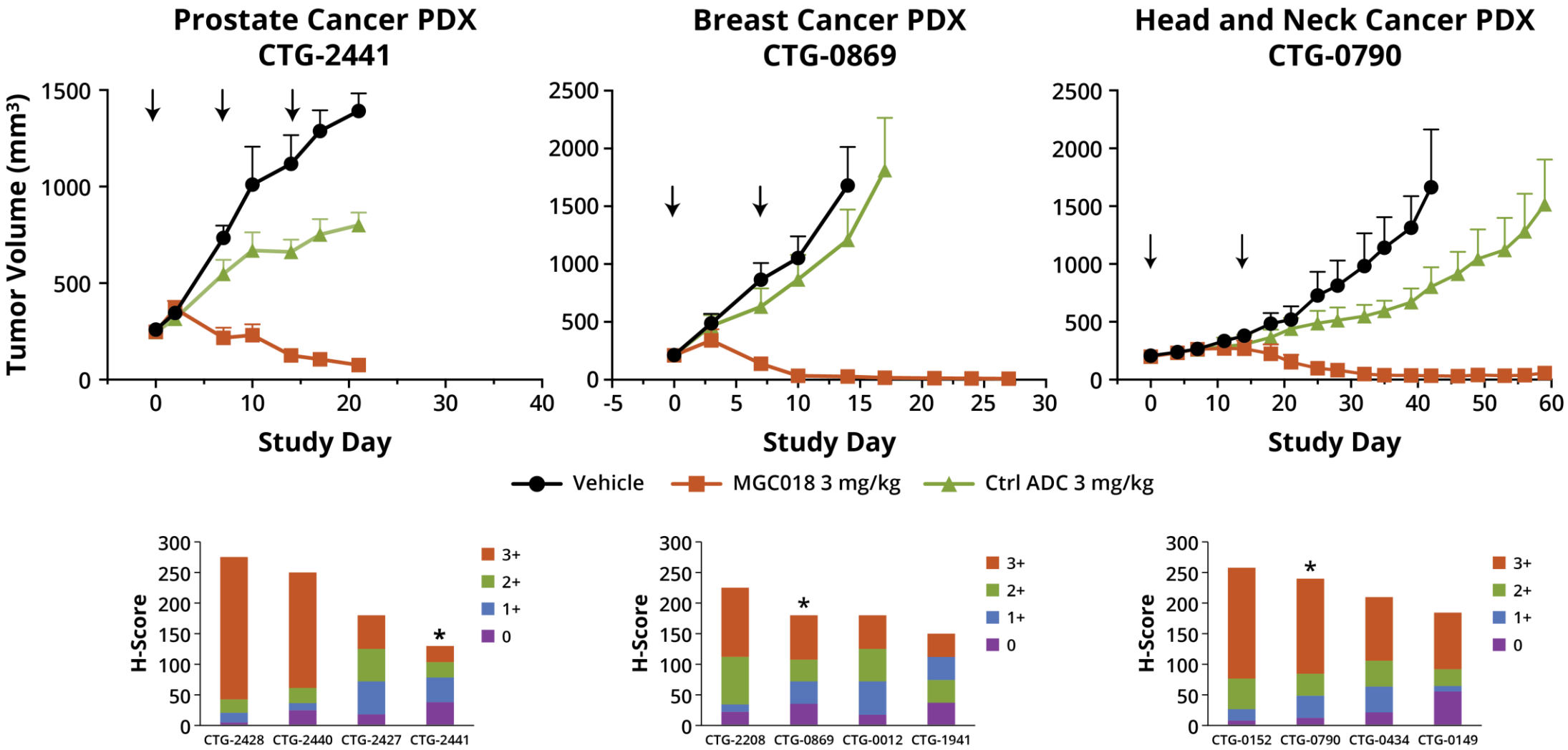
MGC018 Antibody-Drug Conjugate with Duocarmycin-based Linker Payload



- MGC018 is an anti-B7-H3 antibody-drug conjugate (ADC) with a duocarmycin payload
- vc-seco-DUocarmycin-hydroxyBenzamide Azaindole (DUBA) is a fully synthetic DNA alkylating agent
- DUBA cytotoxic activity is cell-cycle independent
- DUBA retains potency in multidrug-resistant cell lines
- Cleavable peptide linker – facilitates bystander effect
- Induces immunogenic cell death in preclinical models

DUBA Linker Payload provided and conjugated by *Byondis*.

Anti-Tumor Activity of MGC018 in Human Cancer PDX Models



Staining with goat anti-B7-H3 polyclonal Ab R&D Systems, Inc.

From the Poster Presented at the 2020 ASCO Annual Meeting (ASCO20 Virtual Scientific Program, May 29–31, 2020) by John Powderly, M.D.

Rationale for Targeting B7-H3 with MGC018 ADC

- B7-H3 is highly expressed in multiple solid tumors, with limited expression in normal tissue
- B7-H3 may play immune suppressive and tumor-autonomous roles that favor cancer growth
- In addition to tumor cells, B7-H3 is expressed by vascular endothelium and stroma in tumor microenvironment
- MGC018 is a novel ADC that delivers a potent duocarmycin payload
- Duocarmycin DNA-targeted activity is directed to both dividing and non-dividing cells

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MGC018 Phase 1 Study Design and Objectives

- Evaluates safety, dose-limiting toxicities and maximum tolerated dose in dose escalation 3+3+3 design
- Dosed intravenously every 21 days (q3w)
- Six dose escalation cohorts planned (0.5 to 5.0 mg/kg)
- Tumor response by investigator per RECIST v1.1 evaluated every 6 weeks for 1st 4 cycles, every 12 weeks thereafter
- Cohort expansion will enroll at RP2D to assess safety and tumor response

Primary Objective

- Safety and maximum tolerated dose (or maximum administered dose)

Secondary Objectives

- PK and immunogenicity
- Antitumor activity

MGC018 Phase 1 Study Key Eligibility Criteria

Inclusion

- Patients with histologically proven, relapsed or refractory, unresectable locally advanced or metastatic solid tumors of any histology
- Patients for whom no therapy with demonstrated clinical benefit is available
- Tumor tissue available to evaluate B7-H3 IHC (B7-H3 expression not required for eligibility)

Exclusion

- Abnormal laboratory parameters (hematologic, renal, and/or liver function)
- Untreated or symptomatic central nervous system metastasis
- Treatment with any systemic chemotherapy within 3 weeks (radiotherapy within 2 weeks)
- Clinically significant cardiovascular or pulmonary disease

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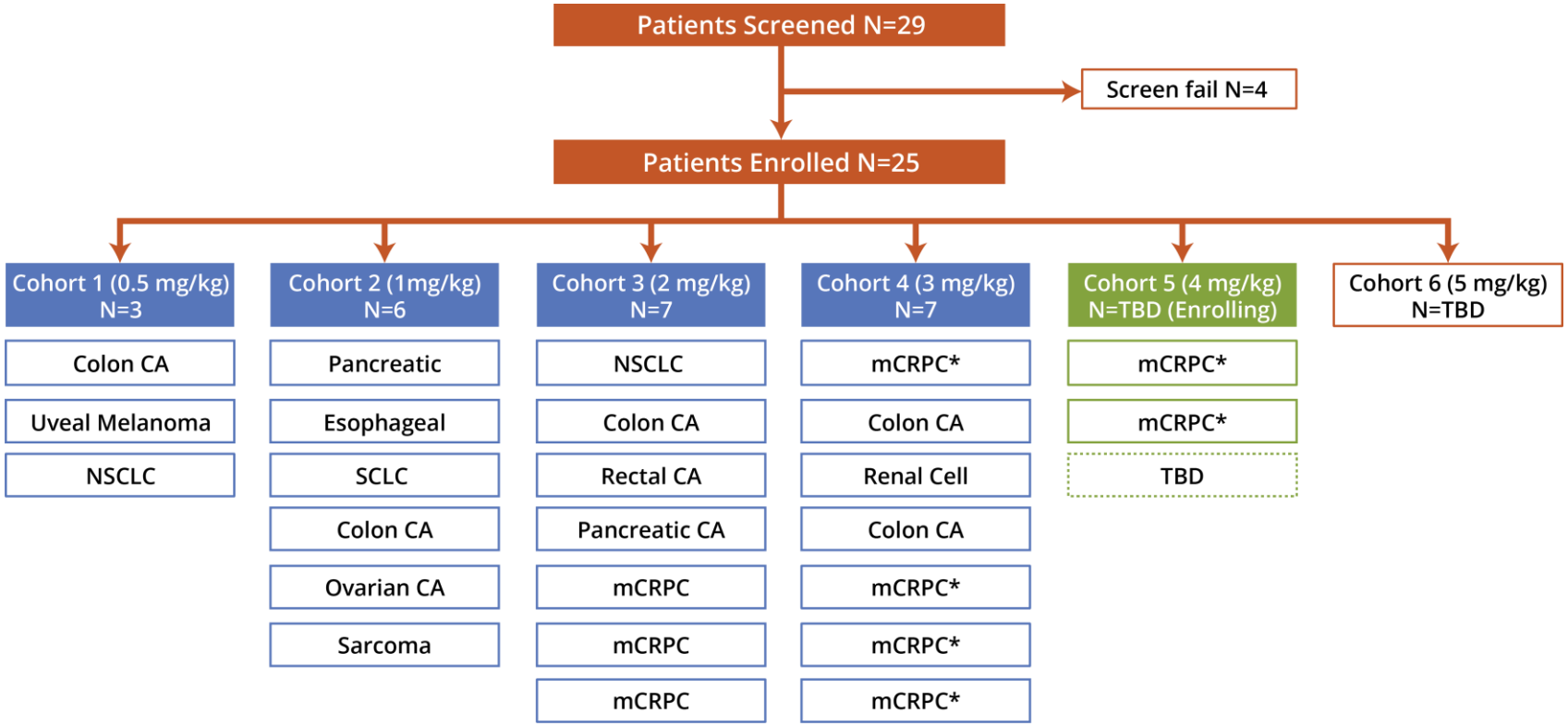
Enrollment Status



- 25 Patients enrolled as of 06 May 2020
- 23 Patients included in safety and efficacy assessment of Cohorts 1–4
- 18 Patients (1 with metastatic castration-resistant prostate cancer [mCRPC]) with measurable disease evaluated per RECIST v1.1
- 6 Patients with mCRPC with bone only disease

*On study

Safety Summary: Related Adverse Events ≥ 10%, All Grades

Cytopenias, nausea/vomiting, fatigue, and skin disorders were most common

System Organ Class Preferred Term	0.5 mg/kg (N=3)	1.0 mg/kg (N=6)	2.0 mg/kg (N=7)	3.0 mg/kg (N=7)	All (N=23)
AT LEAST ONE EVENT	3 (100)	4 (66.7)	7 (100)	7 (100)	21 (91.3)
Blood and lymphatic system disorders	0	1 (16.7)	2 (28.6)	3 (42.9)	6 (26.1)
Neutropenia	0	1 (16.7)	2 (28.6)	3 (42.9)	6 (26.1)
Lymphopenia	0	0	1 (14.3)	2 (28.6)	3 (13.0)
Gastrointestinal disorders	0	4 (66.7)	2 (28.6)	2 (28.6)	8 (34.8)
Nausea	0	2 (33.3)	2 (28.6)	1 (14.3)	5 (21.7)
Vomiting	0	1 (16.7)	2 (28.6)	1 (14.3)	4 (17.4)
General disorders and administration site conditions	2 (66.7)	2 (33.3)	2 (28.6)	5 (71.4)	11 (47.8)
Fatigue	1 (33.3)	1 (16.7)	2 (28.6)	4 (57.1)	8 (34.8)
Chills	1 (33.3)	1 (16.7)	2 (28.6)	1 (14.3)	5 (21.7)
Pyrexia	1 (33.3)	0	2 (28.6)	0	3 (13.0)
Injury, poisoning and procedural complications	0	0	2 (28.6)	5 (71.4)	7 (30.4)
Infusion related reaction	0	0	2 (28.6)	5 (71.4)	7 (30.4)
Investigations	1 (33.3)	3 (50.0)	4 (57.1)	4 (57.1)	12 (52.2)
Neutrophil count decreased	0	1 (16.7)	1 (14.3)	3 (42.9)	5 (21.7)
Lymphocyte count decreased	0	1 (16.7)	2 (28.6)	1 (14.3)	4 (17.4)
Platelet count decreased	0	0	1 (14.3)	2 (28.6)	3 (13.0)
Skin and subcutaneous tissue disorders	0	3 (50.0)	5 (71.4)	5 (71.4)	13 (56.5)
Skin hyperpigmentation	0	3 (50.0)	1 (14.3)	3 (42.9)	7 (30.4)
Palmar-plantar erythrodysaesthesia syndrome	0	0	3 (42.9)	2 (28.6)	5 (21.7)
Pruritus	0	1 (16.7)	1 (14.3)	2 (28.6)	4 (17.4)
Rash maculo-papular	0	0	2 (28.6)	1 (14.3)	3 (13.0)

[1]Includes events with causality ratings of 'Possible', 'Probable' or 'Definite'. [2]Subjects are counted once for each Preferred Term reported.
(Note: 1 pt at 1.0 mg/kg and 3.0 mg/kg experienced angioedema; both AEs were Grade 2 and resolved to baseline.)

Safety Summary: Grade ≥3 Related Adverse Events

Cytopenias and skin disorders were most common

System Organ Class Preferred Term	0.5 mg/kg (N=3)	1.0 mg/kg (N=6)	2.0 mg/kg (N=7)	3.0 mg/kg (N=7)	All (N=23)
AT LEAST ONE EVENT	2 (66.7)	2 (33.3)	7 (100)	3 (42.9)	14 (60.9)
Blood and lymphatic system disorders	0	0	2 (28.6)	2 (28.6)	4 (17.4)
Neutropenia	0	0	2 (28.6)	2 (28.6)	4 (17.4)
Lymphopenia	0	0	1 (14.3)	1 (14.3)	2 (8.7)
Gastrointestinal disorders	0	1 (16.7)	0	0	1 (4.3)
Gastrointestinal inflammation	0	1 (16.7)	0	0	1 (4.3)
Investigations	1 (33.3)	2 (33.3)	4 (57.1)	2 (28.6)	9 (39.1)
Lymphocyte count decreased	0	1 (16.7)	2 (28.6)	1 (14.3)	4 (17.4)
Blood alkaline phosphatase increased	0	0	1 (14.3)	1 (14.3)	2 (8.7)
Neutrophil count decreased	0	1 (16.7)	1 (14.3)	0	2 (8.7)
Platelet count decreased	0	0	1 (14.3)	1 (14.3)	2 (8.7)
Lipase increased	1 (33.3)	0	0	0	1 (4.3)
White blood cell count decreased	0	1 (16.7)	0	0	1 (4.3)
Respiratory, thoracic and mediastinal disorders	1 (33.3)	0	0	0	1 (4.3)
Pneumonitis	1 (33.3)	0	0	0	1 (4.3)
Skin and subcutaneous tissue disorders	0	0	3 (42.9)	1 (14.3)	4 (17.4)
Palmar-plantar erythrodysaesthesia syndrome	0	0	1 (14.3)	1 (14.3)	2 (8.7)
Rash maculo-papular	0	0	2 (28.6)	0	2 (8.7)
Stasis dermatitis	0	0	1 (14.3)	0	1 (4.3)

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Overall Summary of Treatment-Emergent Adverse Events

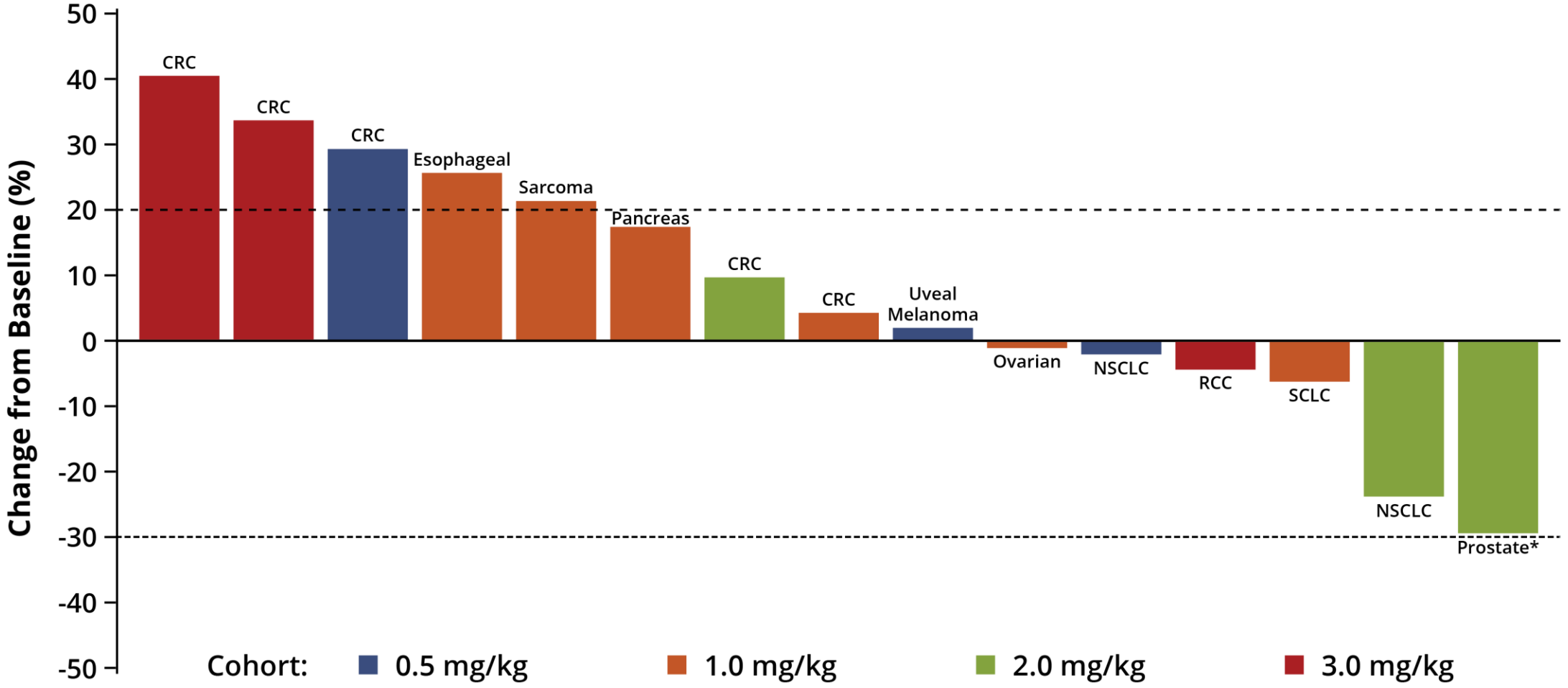
Patients Reporting at Least One Adverse Event	0.5 mg/kg (N=3)	1.0 mg/kg (N=6)	2.0 mg/kg (N=7)	3.0 mg/kg* (N=7)	All (N=23)
Adverse Event	3 (100)	6 (100)	7 (100)	7 (100)	23 (100)
Treatment-Related Adverse Event [1]	3 (100)	4 (66.7)	7 (100)	7 (100)	21 (91.3)
Adverse Event ≥ Grade 3 [2]	3 (100)	4 (66.7)	7 (100)	4 (57.1)	18 (78.3)
Treatment-Related Adverse Event ≥ Grade 3 [2]	2 (66.7)	2 (33.3)	7 (100)	3 (42.9)	14 (60.9)
Serious Adverse Event	1 (33.3)	1 (16.7)	3 (42.9)	0	5 (21.7)
Event that Resulted in Study Discontinuation	1 (33.3)	1 (16.7)	3 (42.9)	0	5 (21.7)
Event that Resulted in Drug MGC018 Withdrawal	1 (33.3)	1 (16.7)	3 (42.9)	1 (14.3)	6 (26.1)
Event that Resulted in Drug MGC018 Dose Reduction	0	0	1 (14.3)	2 (28.6)	3 (13.0)
Event that Resulted in Drug MGC018 Interrupted	1 (33.3)	0	2 (28.6)	5 (71.4)	8 (34.8)
Fatal Adverse Event (pneumonitis)	1 (33.3)	0	0	0	1 (4.3)
Adverse Event of Special Interest (AESI) – Infusion Reaction	0	0	2 (28.6)	5 (71.4)	7 (30.4)

- Three treatment-related serious adverse events occurred in three patients:
  - pneumonitis in a patient with concurrent bacterial pneumonia; non-infectious gastroenteritis; and stasis dermatitis in a patient with chronic venous insufficiency
- One DLT; Grade 4 neutropenia resolved to baseline
- No febrile neutropenia observed

[1]Includes events with causality assessments of 'Possible', 'Probable' or 'Definite'. [2]Based on CTCAE criteria version 4.0.3.
*Amendment applied to allow dose modification.

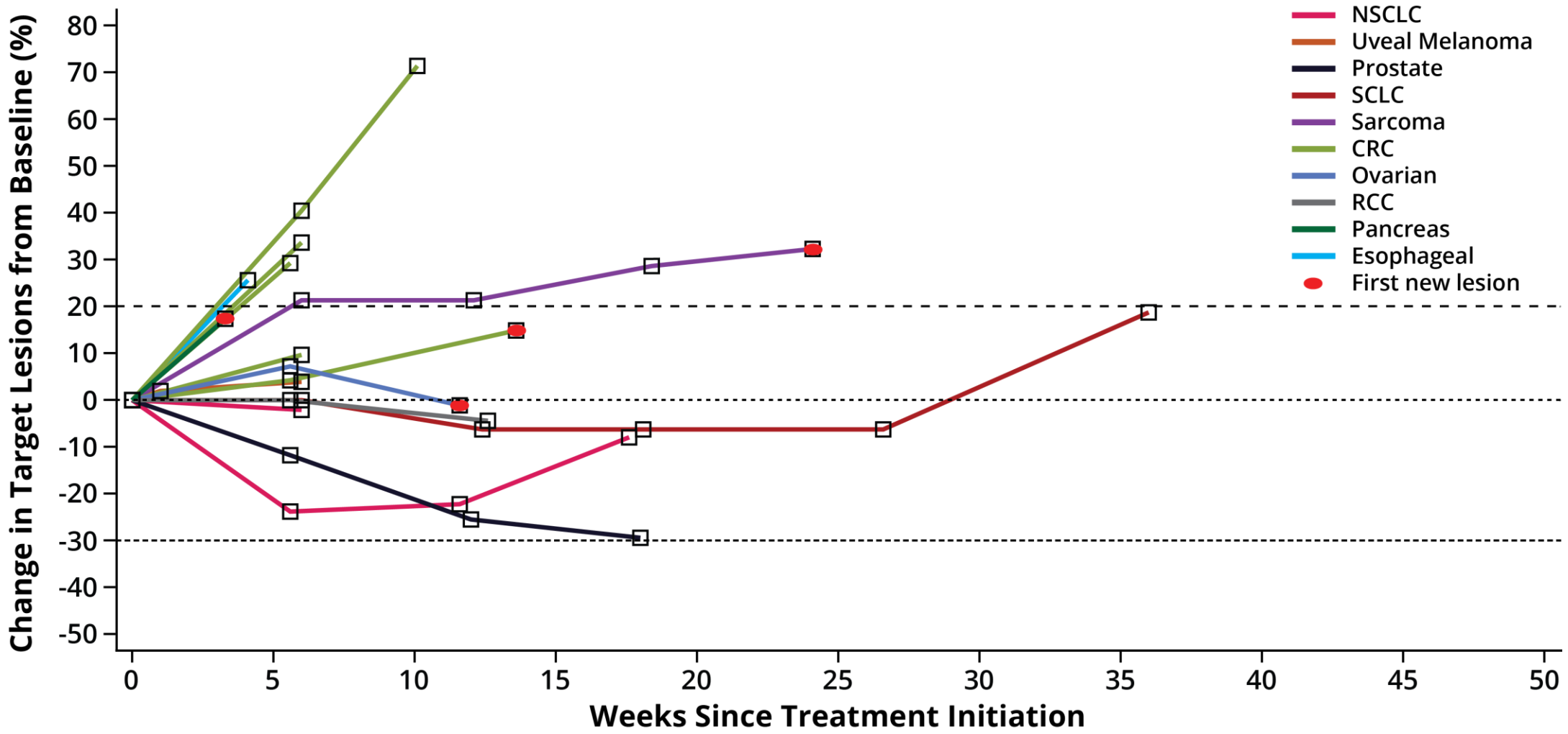
Best Percent Change of Target Lesions by MGC018 Dose Level and Tumor Type

Evaluable population[1]



[1]Patients who received at least one dose and had at least one post-baseline tumor evaluation. *mCRPC Pt #1. Data were extracted on 06MAY2020.

Percent Change of Target Lesions by Tumor Type

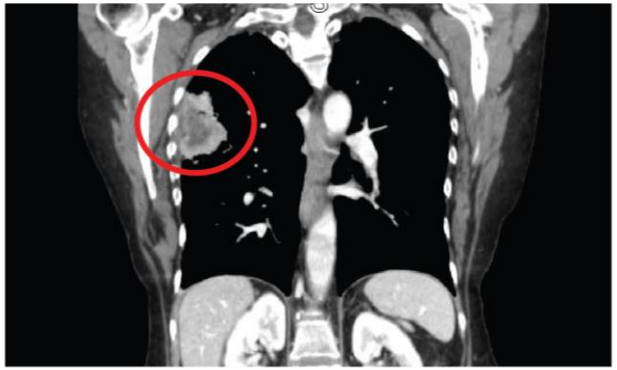


From the Poster Presented at the 2020 ASCO Annual Meeting (ASCO20 Virtual Scientific Program, May 29–31, 2020) by John Powderly, M.D.

Reduction of Pleural-based Tumor in NSCLC Patient

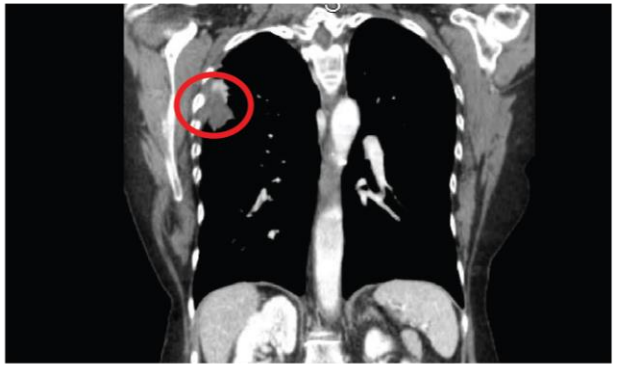
MGC018 following progression after five lines of prior therapy

Baseline (May 23, 2019)



2 Doses of MGC018 (2.0 mg/kg)
Decrease in pleural lesion read by Investigator

Week 6 (July 26, 2019)



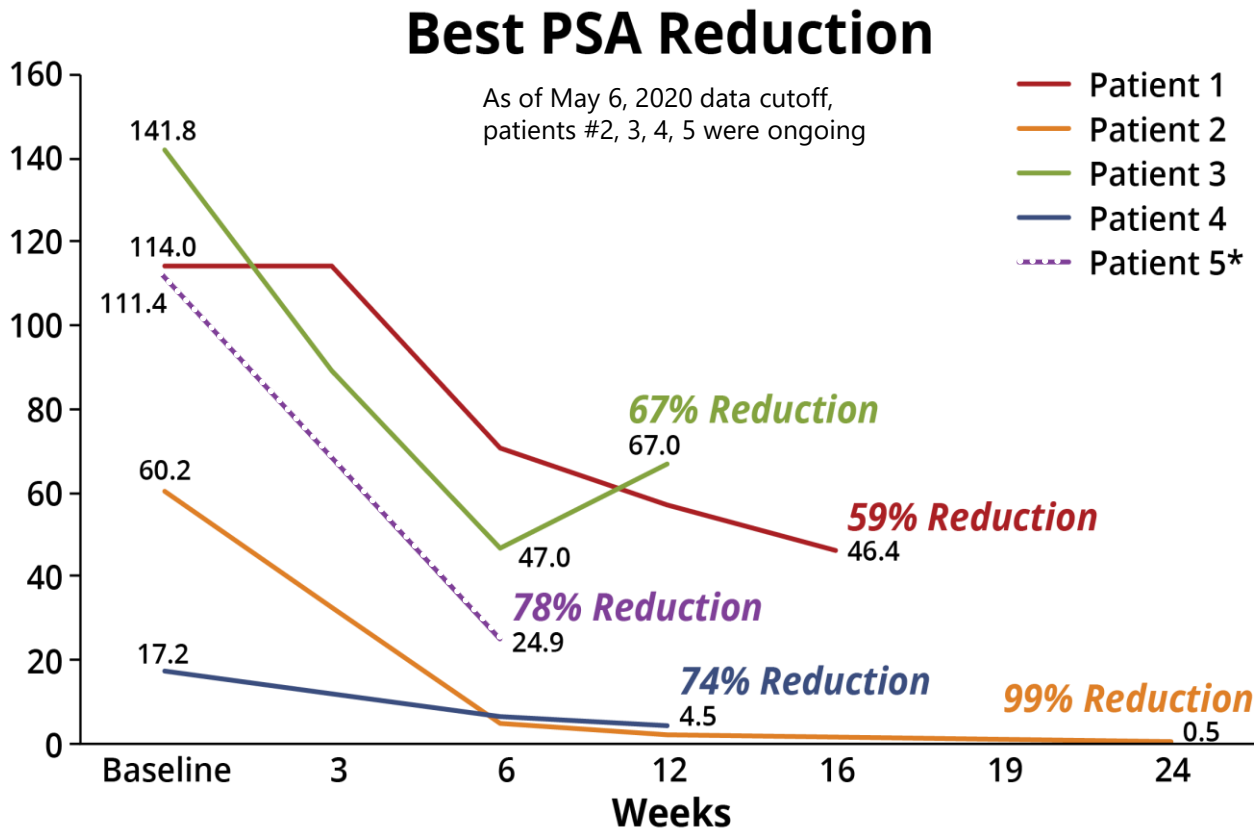
Note image not exact Anterior-Posterior slice as May 23, 2019

Line of Tx	Treatment	Cycles	Duration of Therapy (Months)	Best Response
1	Carboplatin+Paclitaxel+Bevacizumab	4	2	SD
2	Nivolumab	40	16	SD
3	MK-7162 (IDO1 inhibitor)	3	2	SD
4	APG-1252 (Bcl-2 inhibitor)	2	1	PD
5	Pembrolizumab (MK-3475)	2	1	PD
6	MGC018	2	2	SD (≈24%)

From the Poster Presented at the 2020 ASCO Annual Meeting (ASCO20 Virtual Scientific Program, May 29–31, 2020) by John Powderly, M.D.

Greater than 50% PSA Decline Following MGC018 in Heavily Pre-treated mCRPC

Patient (Dose)	Line of Therapy	Treatment	Duration of Therapy (months)	MGC018 Response
Patient #1 2 mg/kg One target lesion (lymph node), abdominal adenopathy & bone lesions	1 2 3 4 5 **6**	Docetaxel Enzalutamide Prostvac Abiraterone Nivolumab **MGC018**	4 24 5 6 6 **4**	**SD (-29%); 59% PSA Decline**
Patient #2 3 mg/kg Bone only disease	1 2 3 4 **5**	Docetaxel Abiraterone Enzalutamide Radium 223 **MGC018**	6 4 12 6 **3+**	**SD (Ongoing); 99% PSA Decline**
Patient #3 3mg/kg Bone only disease	1 2 3 4 **5**	Docetaxel Provenge Enzalutamide Abiraterone **MGC018**	8 2 6 9 **1.5+**	**SD (Ongoing); 67% PSA Decline**
Patient #4 3 mg/kg Bone only disease	1 2 **3**	Abiraterone Nivo + Rucaparib **MGC018**	Unknown Unknown **1.5+**	**SD (Ongoing); 74% PSA Decline**
Patient #5 3mg/kg Bone only disease	1 2 3 4 5 **6**	Docetaxel Provenge Enzalutamide Abiraterone Docetaxel **MGC018**	4 12 7 7 4 **1.5+**	**SD (Ongoing); 78% PSA Decline**



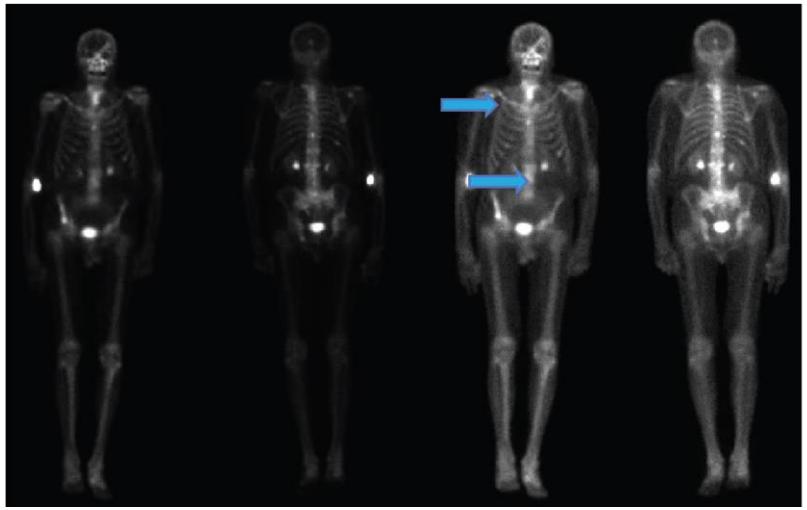
*Patient #5 data scaled for charting purposes:
Note: Baseline PSA 1,114 ng/mL dropped to 249 ng/mL at Week 6, with a further decline to 95 ng/mL at Week 12 (May 18, 2020; after the May 6, 2020 data cut-off).

From the Poster Presented at the 2020 ASCO Annual Meeting (ASCO20 Virtual Scientific Program, May 29–31, 2020) by John Powderly, M.D.

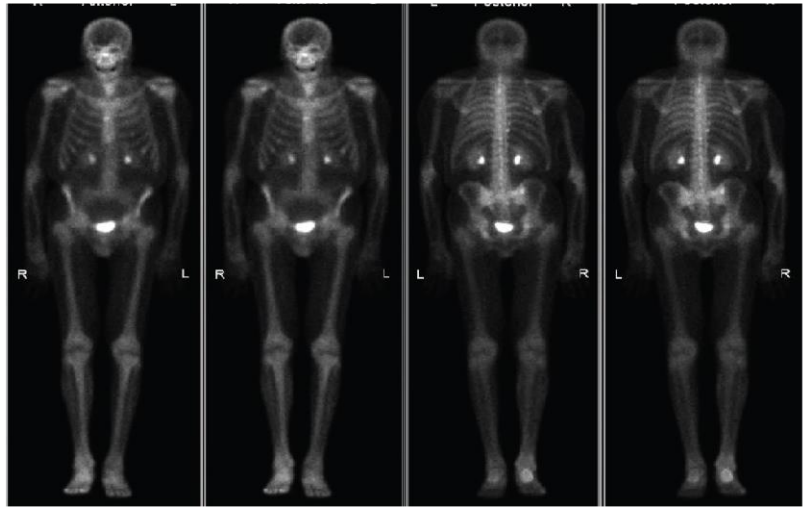
99% PSA Reduction with Substantial Improvement in Metastatic Bone Lesions

mCRPC Patient #2

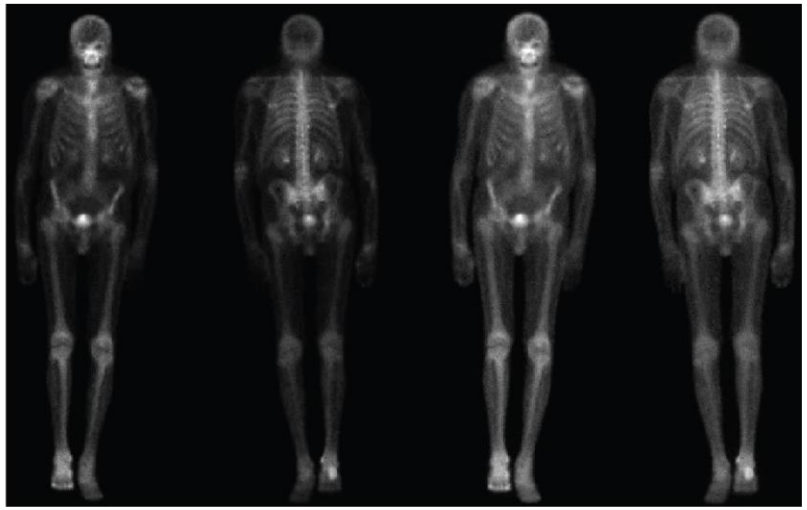
November 13, 2019



February 7, 2020



May 1, 2020



Bone lesions of thoracic/lumbar spine, ribs, sternum, and pelvis

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B7-H3 IHC Data

- 18 of 23 patients had tissue samples evaluable for B7-H3 expression
- H-score: Median 200 (range 82–279)
- Vasculature score: Median 2+ (range 0–3+)

From the Poster Presented at the 2020 ASCO Annual Meeting (ASCO20 Virtual Scientific Program, May 29–31, 2020) by John Powderly, M.D.

Conclusions

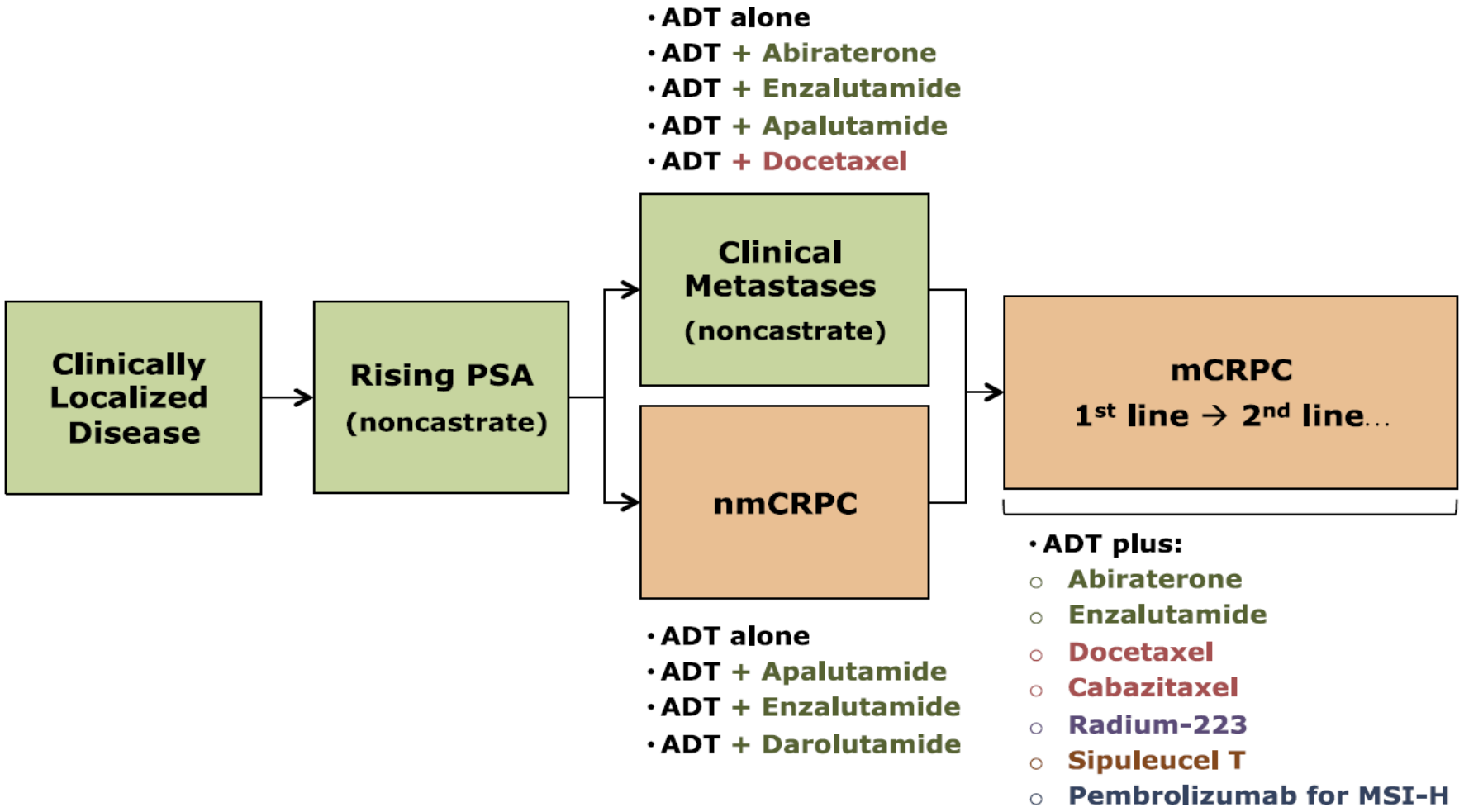
- MGC018 has an acceptable safety profile to date with manageable hematologic and skin toxicity
  - 1 DLT occurred at 2 mg/kg, resolved to baseline
- Preliminary evidence of anti-tumor activity with radiologic improvement in heavily pretreated patients:
  - NSCLC
  - mCRPC with rapid PSA reduction
- Enrollment ongoing at 4 mg/kg q3w
- Planned dose expansion in mCRPC

Prostate Cancer Current Treatment

Emmanuel Antonarakis, M.D.

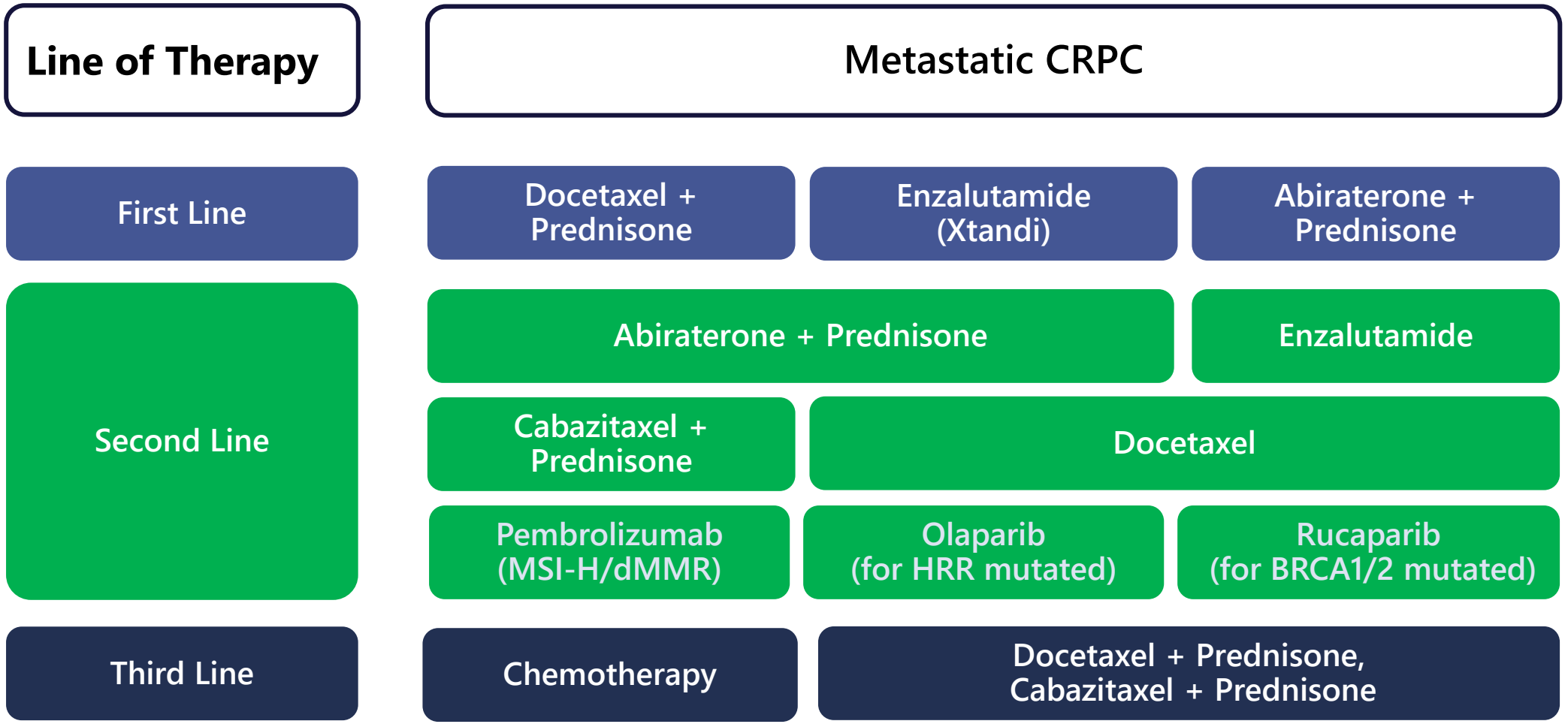
Professor of Oncology and Urology, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

Prostate Cancer Treatment Landscape



Bastos DA, Antonarakis ES. Oncotargets & Ther 2019; 12: 8769-8777.

Treatment Options for mCRPC Patients



Q&A Session

Guest Presenters:

Jason Luke, M.D.	Associate Professor of Medicine, Director of the Cancer Immunotherapeutics Center, UPMC Hillman Cancer Center
John Powderly, M.D.	Chief Executive Officer, Carolina BioOncology
Emmanuel Antonarakis, M.D.	Professor of Oncology and Urology, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

MacroGenics:

Scott Koenig, M.D., Ph.D.	President & Chief Executive Officer
Bradley Sumrow, M.D.	Clinical Research Director, MGD013 Program
Chet Bohac, PharmD, M.D.	Senior Clinical Research Director, MGC018 Program
Paul Moore, Ph.D.	Vice President, Immunology & Cell Biology