UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of report (Date of earliest event reported): May 29, 2020

MACROGENICS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware	**001-36112**	**06-1591613**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

9704 Medical Center Drive, Rockville, Maryland	**20850**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: **(301) 251-5172**

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.01 per share	MGNX	Nasdaq Global Select Market

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

[ ] Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
[ ] Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
[ ] Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
[ ] Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 **Other Events**

On May 29, 2020, at the American Society of Clinical Oncology ("ASCO") 2020 Virtual Annual Meeting, the following data were presented:

- 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. The slides used at this presentation are filed as Exhibit 99.1 to this Form 8-K.
- 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 Tumor. The slides used at this presentation are filed as Exhibit 99.2 to this Form 8-K.
- SOPHIA Analysis by Chemotherapy (Ctx) Choice: A Phase 3 (P3) Study of Margetuximab (M) + Ctx vs Trastuzumab (T) + Ctx in Patients (pts) with Pretreated HER2+ Metastatic (met) Breast Cancer (MBC). The slides used at this presentation are filed as Exhibit 99.3 to this Form 8-K.

Item 9.01 **Financial Statements and Exhibits**

(d) Exhibits.

Exhibit Number	**Description of Exhibit**
99.1	ASCO 2020 - MGD013 Phase 1
99.2	ASCO 2020 - MGC018 Phase 1
99.3	ASCO 2020 - SOPHIA by Chemotherapy

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 29, 2020

MACROGENICS, INC.

By: /s/ Jeffrey Peters
Jeffrey Peters
Vice President and General Counsel

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

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

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

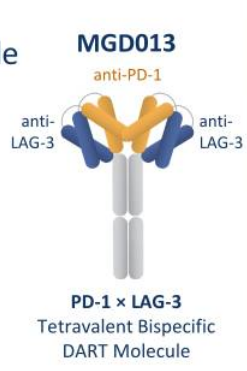
Presenter Disclosure Information

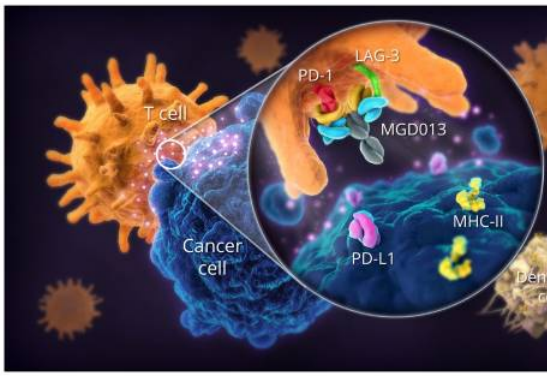
Jason J. Luke, MD, FACP

- 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, Inc 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, Bristo Squibb, CheckMate (SRA), Compugen, Corvus, EMD Serono, Evelo (SRA), Five Prime, FLX Bio, Genentech, Immat Immunocore, Incyte, Leap, MedImmune, MacroGenics, Necktar, Novartis, Palleon (SRA), Merck, Springbank, Te Tizona, Xencor
- Travel: Akrevia, Bayer, Bristol-Myers Squibb, EMD Serono, Incyte, Janssen, Merck, Mersana, Novartis, Pyxis, Ref
- Patents (both provisional): Serial #15/612,657 (Cancer Immunotherapy), PCT/US18/36052 (Microbiome Biomar Anti-PD-1/PD-L1 Responsiveness: Diagnostic, Prognostic and Therapeutic Uses Thereof)

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

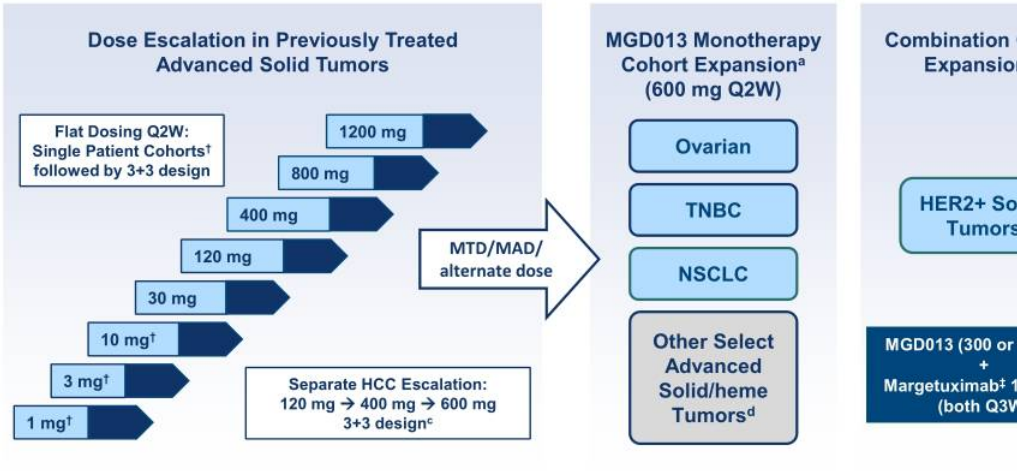
- Checkpoint molecules are leveraged by tumors or APCs to evade the immune system
- PD-1 and LAG-3 receptors are expressed on "exhausted" T-cells
  - Interactions with corresponding ligands negates anti-tumor T cell activity
- Synergy of anti-PD-1 + anti-LAG-3 mAbs in animal tumor models
  - Combination 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





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 investigatio 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 do 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 and DLBCL. Data cutoff: April 25, 2020.

Baseline Demographics

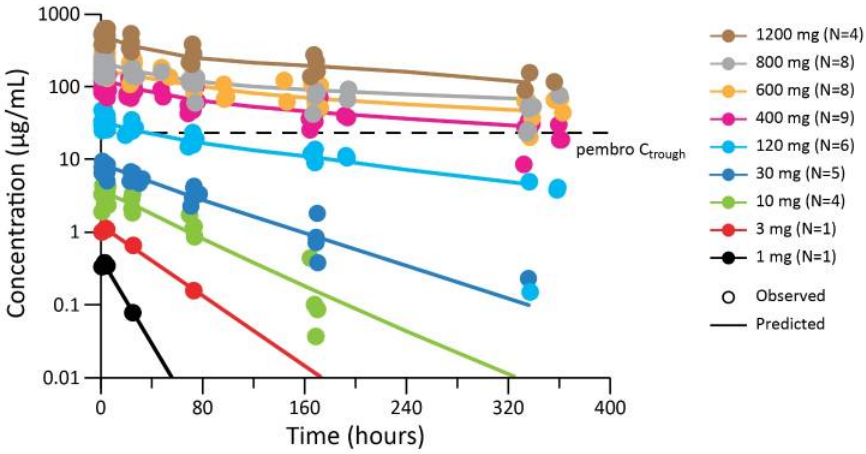
	Dose Escalation 1 -1200 mg Q2W (n=53)	Monotherapy Cohort Expansion 600 mg Q2W (n=205)	Combination Cohort Expansion MGD013 + Margetuxima (n=21)
Median age (range), years	64 (24, 84)	60 (27, 84)	62 (29, 83)
Gender, n (%)			
Male	32 (60.4)	74 (36.1)	7 (33.3)
Female	21 (39.6)	131 (63.9)	14 (66.7)
ECOG PS, 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

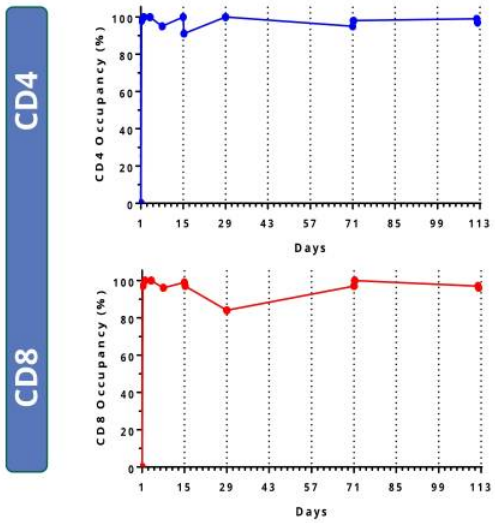
Linear PK (400-1200 mg dose range) and sustained receptor occupancy (≥120 mg)

Pharmacokinetics (1-1200 mg)



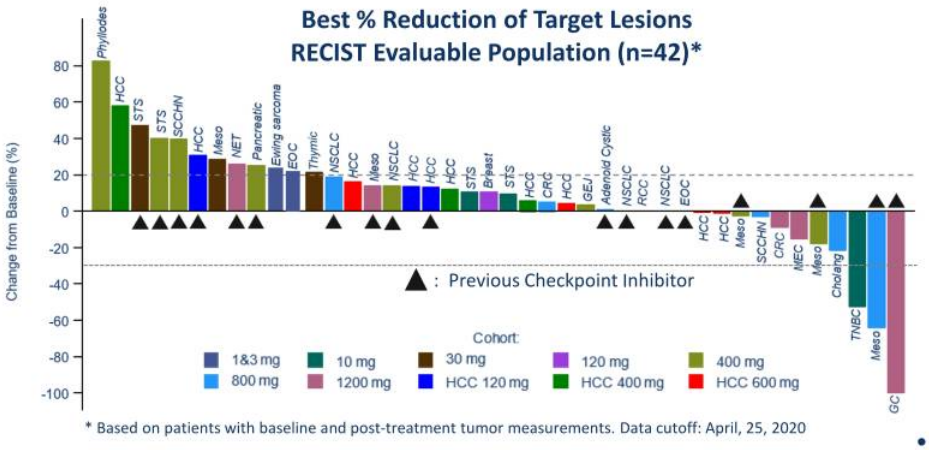
Estimated $t_{1/2}$ = 274 hours (~11 days)

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

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%)

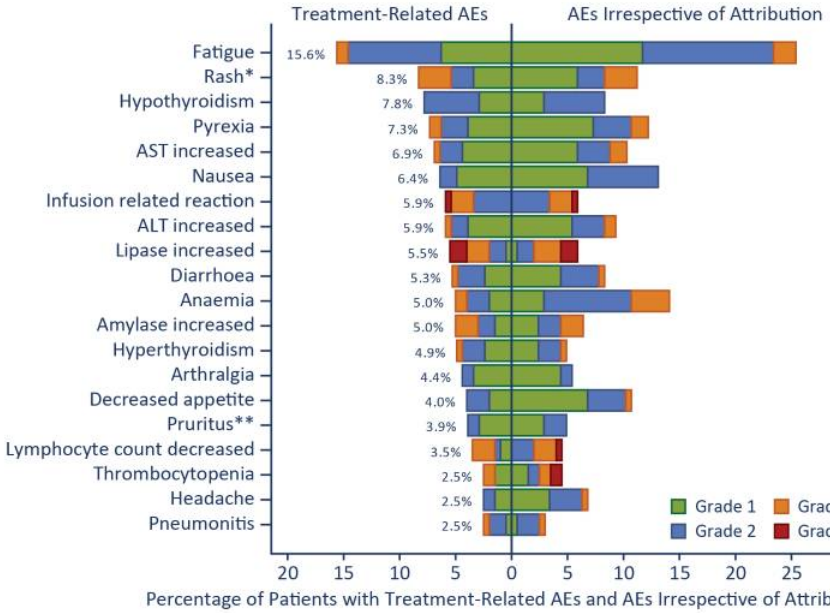
Immune-Related Adverse Events of Special Intere

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

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

MGD013 Monotherapy Cohort Expansion: Safety

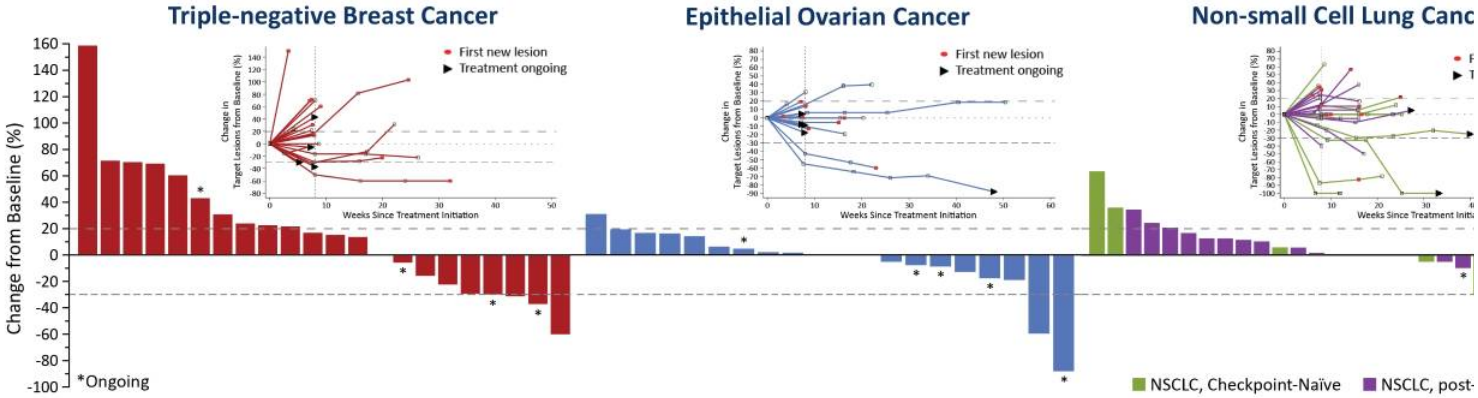
Overall AE Totals	No. (%) of Patients	
	All Grades (N=205)	≥ Grade 3 (N=205)
AE (irrespective of causality)	178 (86.8)	86 (42.0)
Treatment-related AE	118 (57.6)	37 (18.0)[a]
SAE (irrespective of causality)	63 (30.7)	47 (22.9)
Treatment-related SAE	18 (8.8)	11 (5.4)
AE leading to discontinuation	18 (8.8)	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 *Generalize*
[a]Grade 4 drug-related AEs include: lipase increased (n=3), neutrophil count decreased, and IRR (n=1, each). No Grade 5 TRAEs have bee
AESI = adverse events of special interest. Data cutoff: April, 25, 2020.

MGD013 Monotherapy Cohort Expansion: Activity

Anti-tumor activity observed in multiple tumor types



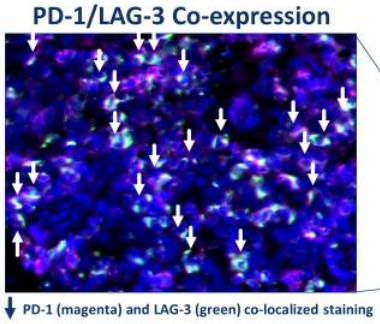
	TNBC	EOC	NSCLC, CPI-Naïve	NSCLC, post-PD-1
Evaluable Patients	23	23	14	15
ORR (Confirmed)	4.3% (1/23)	8.7% (2/23)	14.3% (2/14)	0% (0/15)
ORR (Confirmed + Unconfirmed)	17.4% (4/23)	8.7% (2/23)	21.4% (3/14)	13.3% (2/15)
SD	34.8% (8/23)	43.5% (10/23)	50.0% (7/14)	53.3% (8/15)
DCR	39.1% (9/23)	52.2% (12/23)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

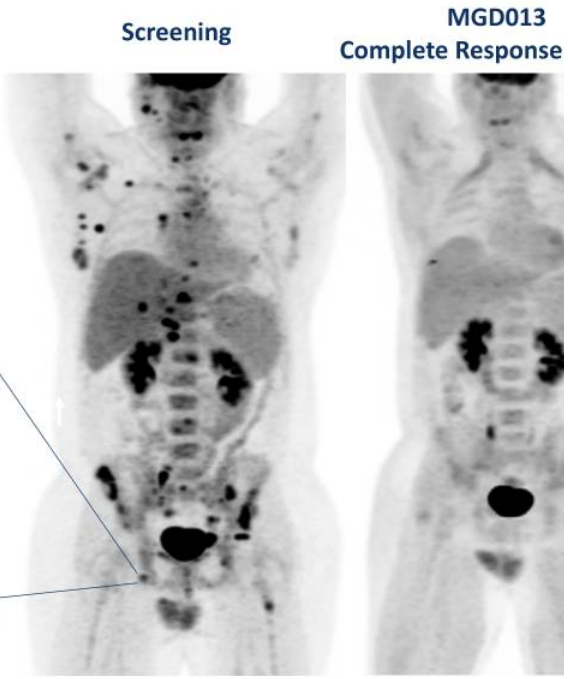
Data cutoff: April, 25, 2020

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

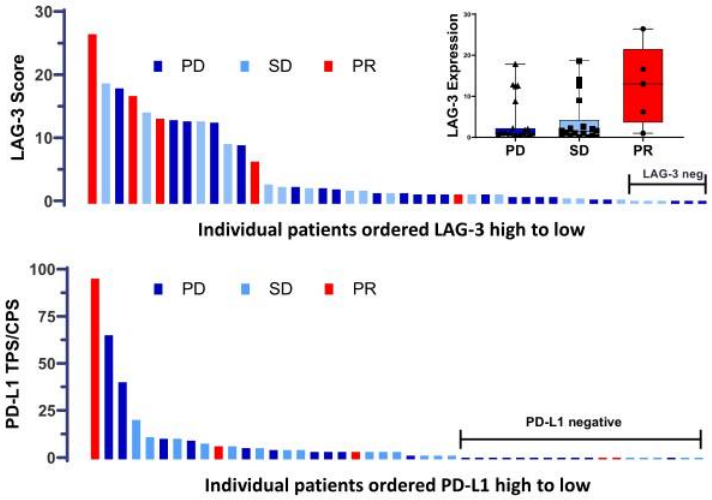




Objective Responses Associated with LAG-3 Expression

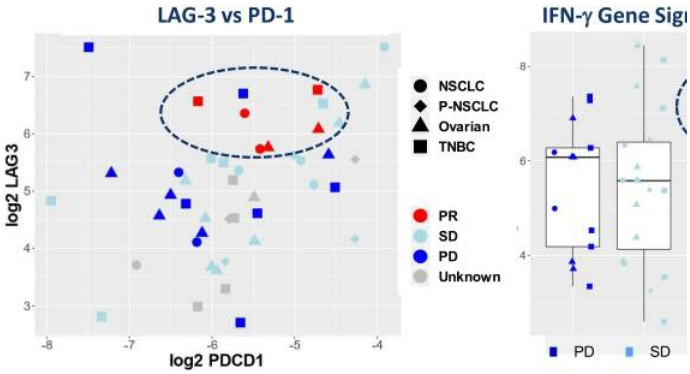
Inflammatory interferon-γ signature elevated in patients with clinical response

Retrospective IHC Analyses



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.

Transcript Profiling (Baseline Tumor Biopsy)



Objective responses associated with high baseline LAG-3/P expression and IFN-γ gene signature (CXCL9, CXCL10, CXC1

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

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

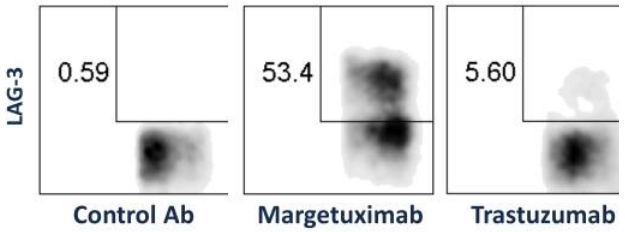
Enhancing effector-cell activation via Fc-engineered mAb

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 Ce

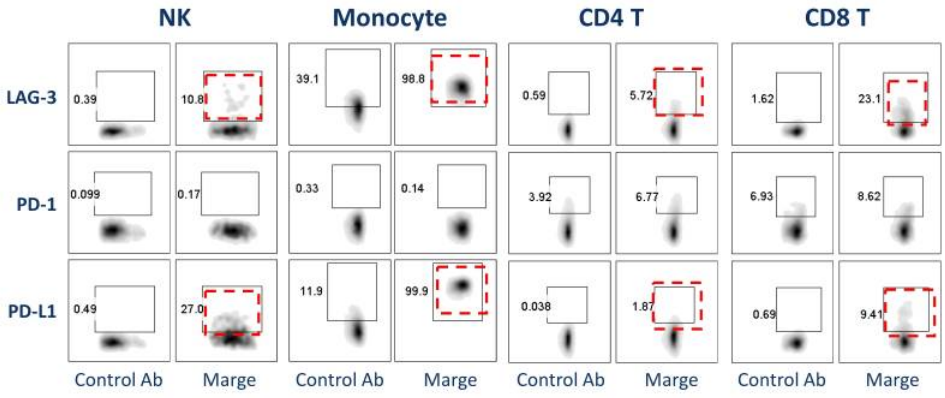


[a] Nordstrom, et al., 2011 *Breast Cancer Research*, 13: R123
[b] Rugo, et al., *ASCO 2019*, Chicago, IL
[c] Catenacci, et al., ASCO GI 2019, San Francisco, CA | Catenacci et al. 2020 *Lancet Oncology*, in press

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-CD5

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

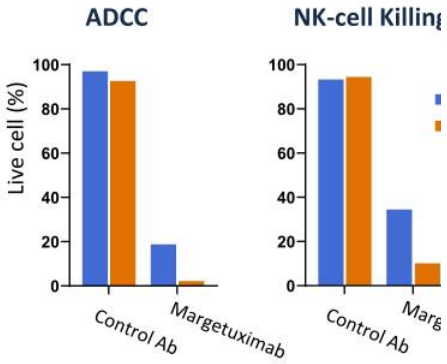
Fc-engineered Margetuximab Up-regulates LAG-3/PD-L1 Expression



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)

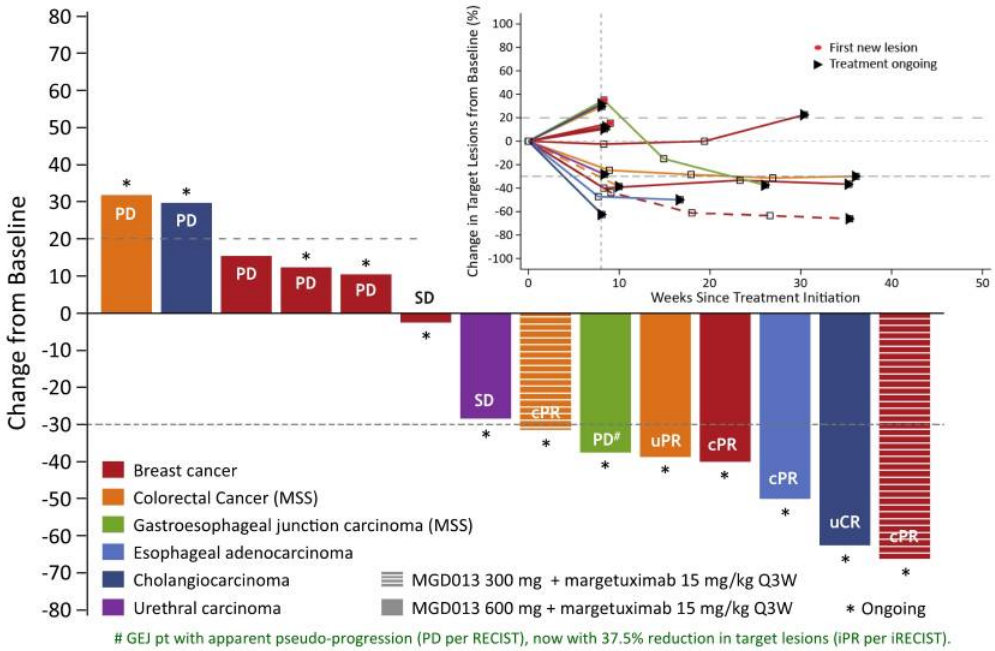
PD-1 x LAG-3 (MGD013) Enhances Activity of Immune Cells Primed Fc-engineered mAb (Margetuxim



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

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

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 pt
  - Includes unconfirmed objective r
- Well-tolerated
  - Responding patients remain on tl

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

PD-L1 CPS:	< 1	1	
N	4	1	

LAG-3 Score:	< 5	5-15	T
N	3	1	

Durable Response in Patient Receiving MGD013 *plus* Margetuxi

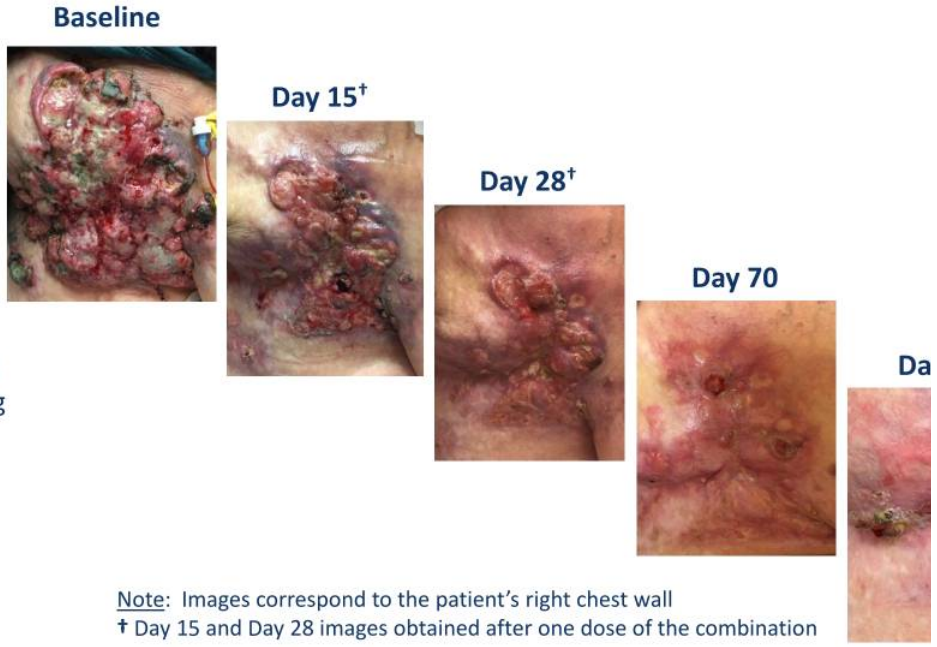
Resolution of chest wall disease with confirmed PR of overall tumor burden

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 m

- >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 mAb (incl. margetuximab) is ongoing

Investigators

Australia
Philip Clingan
Anthony Joshua
Girish Mallesara
Andrew Weickhardt

Spain
Analia Azaro Pedrazzoli
Javier Cortes Castan
Maria Jose De Miguel Luken

United States of Americ
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

Bulgaria
Nadezhda Miteva
Krasimir Nikolov
Krasimir Oreshkov

Thailand
Chaiyut Charoentum
Arunee Dechapunkul
Virote Sriuranpong

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

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Yevhen Hotko
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Abstract #308859

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

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NCT03729596

Background

High B7-H3 Expression Levels in Solid Tumors

Potential Indications	B7-H3 Positive*		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%

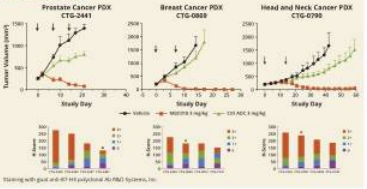
*IF1+/2 passing reflects any grade staining (1-3+) via FFPE tumor microarray (cytoplasmic, membrane, and vasculature staining); B7-H3 is expressed on tumor as well as tumor vasculature.

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 AF; R&D Systems, Inc.

Rationale

- B7-H3 is highly expressed in multiple solid tumors, with limited expression in normal tissue
- MGC018 is a novel ADC that delivers a potent duocarmycin payload to dividing and non-dividing B7-H3-expressing cells

Study Design and Objectives

- Phase 1 study evaluates safety, dose-limiting toxicities (DLT), and maximum tolerated dose (MTD) of MGC018 in a dose escalation 3+3+3 design
- MGC018 dosed intravenously every 21 days (q3w)
- 6 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 and every 12 weeks thereafter
- Cohort expansion will enroll at the RP2D to assess safety and tumor response

Primary Objective

- Safety and MTD (or maximum administered dose)

Secondary Objectives

- PK and immunogenicity
- Antitumor activity

Key Eligibility Criteria

Inclusion

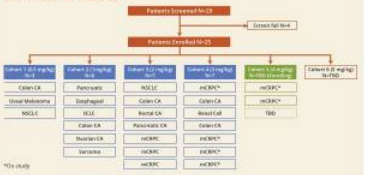
- Patients with histologically proven, relapsed or refractory, unresectable locally advanced or metastatic solid tumors of any histology
- Patients for whom no therapy with demonstrated clinical benefit is available
- Tumor tissue available to evaluate B7-H3 IHC (B7-H3 expression not required for eligibility)

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

Results

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

Safety Summary

Related Adverse Events ≥ 10%, All Grades

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)	3 (71.4)	11 (47.8)
Fatigue	1 (33.3)	1 (16.7)	2 (28.6)	1 (57.1)	5 (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)
Pruritus/generalized pruritus	0	2 (33.3)	4 (57.1)	4 (57.1)	10 (43.5)
Palmar-plantar erythrodysaesthesia syndrome	0	0	3 (42.9)	2 (28.6)	5 (21.7)
Rash maculo-papular	0	1 (16.7)	1 (14.3)	2 (28.6)	4 (17.4)
Rash macular	0	0	2 (28.6)	1 (14.3)	3 (13.0)

*Includes events with causality ratings of 'Possible', 'Probable' or 'Definite'. Subjects are counted once for each Preferred Term reported. Note: 1 pt at 1.0 mg/kg and 2.0 mg/kg experienced angioedema; both AEs were Grade 2 and resolved to baseline.)

Grade ≥ 3 Related Adverse Events

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)	6 (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)	1	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)

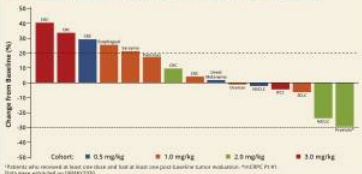
Overall Summary of Treatment-Emergent Adverse Events

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*	3 (100)	4 (66.7)	7 (100)	7 (100)	21 (91.3)
Adverse Event ≥ Grade 3*	3 (100)	4 (66.7)	7 (100)	6 (85.7)	18 (78.3)
Treatment-Related Adverse Event ≥ Grade 3*	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)

*Includes events with causality assessments of 'Possible', 'Probable' or 'Definite'. Based on CTCAE criteria version 4.0.3.
†Determination applied to all two-dose modification.

- 3 treatment-related serious adverse events occurred in 3 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

Best Percent Change of Target Lesions by MGC018 Dose Level and Tumor Type in the Evaluable Population[1]



[1]Patients who received at least one dose and had at least one post-baseline tumor evaluation. †mCRPC, PI-91. Data were extracted on 06MAY2020.

Percent Change of Target Lesions by Tumor Type

Tumor Responses with MG

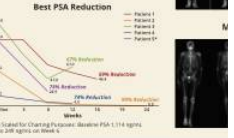
- Reduction of pleural-based tumor in NSCLC patient fol after 5L of prior therapy

Line of Tx	Treatment	Cycles	Duration of Tx (Months)
1	Carboplatin+Paclitaxel+Bevacizumab	4	2
2	Nivolumab	40	16
3	MK-7162 (EDO1 inhibitor)	3	2
4	APG-1252 (Bcl-2 inhibitor)	2	1
5	Pembrolizumab (MK-3475)	2	1
6	MGC018	2	2

- 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	1	Docetaxel	4	
3 mg/kg	2	Enzalutamide	24	
One target lesion (lymph node); non-target lesions & bone lesions	3	Prostvac	5	SD (~29%); 69% PSA Decline
	4	Abiraterone	6	
	5	Nivolumab	6	
	6	MGC018	4	
Patient #2	1	Docetaxel	6	
1 mg/kg	2	Abiraterone	4	SD (Ongoing); 89% PSA Decline
Bone only disease	3	Enzalutamide	12	
	4	Radium 223	6	
	5	MGC018	3	
Patient #3	1	Docetaxel	8	
3 mg/kg	2	Provenge	2	SD (Ongoing); 67% PSA Decline
Bone only disease	3	Enzalutamide	6	
	4	Abiraterone	9	
	5	MGC018	1.5	
Patient #4	1	Abiraterone	Unknown	SD (Ongoing); 74% PSA Decline
3 mg/kg	2	Nivolumab + Ipilimumab	Unknown	
Bone only disease	3	MGC018	1.5	
Patient #5	1	Docetaxel	4	
3 mg/kg	2	Provenge	12	SD (Ongoing); 70% PSA Decline
Bone only disease	3	Enzalutamide	7	
	4	Abiraterone	7	
	5	Docetaxel	4	
	6	MGC018	1.5	

Patient 1 had 59% PSA reduction with near partial response, and several patients with ongoing stable disease.



*Patient 5 Scaled for Charting Purposes: Baseline PSA 1,114 ng/mL dropped to 349 ng/mL on Week 6

- Patient 2: 9 with substa in metastat thoracic/lu sternum, a

B7-H3 IHC Data

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

Conclusions

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

Presented at the ASCO20 Virtual Scientific Program, May 29–31, 2020

Abstract #1040

SOPHIA Analysis by Chemotherapy (Ctx) Choice: A Phase 3 (P3) Study of Margetuximab (M) + Ctx vs Trastuzumab (T) + Ctx in Patients (pts) with Pretreated HER2+ Metastatic (met) Breast Cancer (MBC)

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Background/Methods

- Despite advances, pretreated HER2+ MBC remains incurable with ongoing need for new therapies. Investigational M has similar HER2 binding and antiproliferative effects as T. Relative to T, M Fc engineering increases binding affinity for both variants of activating Fc receptor (FcR) CD16A and decreases affinity for inhibitory FcR CD32B, coordinately activating innate and adaptive immunity
- SOPHIA (NCT02492711), an open-label P3 trial, enrolled pts with HER2+ MBC after pertuzumab and 1–3 lines of prior treatment (Tx) for MBC. Randomization was 1:1 to M (15 mg/kg IV q3w + Ctx) or T (6 [8 for loading dose] mg/kg IV q3w + Ctx), stratified by met sites (≤2, >2), Tx lines for met disease (≤2, >2), and Ctx choice, including capecitabine (Cap), eribulin (Eri), gemcitabine (Gem), or vinorelbine (Vin). Primary endpoints were central blinded PFS and OS, assessed sequentially using the stratified log-rank test
- M + Ctx prolonged PFS over T + Ctx (Table 1). Second interim OS results from Sept 2019 favor M without significance (hazard ratio [HR], 0.89; 95% CI 0.69–1.13; nominal P=0.326)

Results

- Investigator chemotherapy choices, PFS hazard ratios (HRs), and safety results by chemotherapy are shown in **Table 1** and **Figure 1**
- Patients receiving Eri and Gem had the lowest PFS HRs, favoring M over T, although no statistical significance of individual Ctx subgroups was seen
- **Table 1:** There was variable toxicity among Ctx subgroups. Fewer subjects receiving Cap had Ctx related ≥Grade 3 Adverse Events (AEs)
- In this unblinded study, more pts on M than T in all subgroups discontinued Ctx alone due to AE; 8 on M and 7 on T also discontinued antibody
- **Table 2:** AEs leading to chemotherapy discontinuation were diverse; 3 such AEs were considered probably or definitely related to antibody therapy, including 2 on M (seroma, IRR) and 1 on T (pneumonia)

Table 1. PFS and Safety Results by Chemotherapy

Population[1]	PFS, 265 events HR (95% CI)[1]	≥ Grade 3 Ctx Related AEs[2]	AEs Leading to Ctx Discontinuation[2]
Intent-To-Treat (N=536)	0.76 (0.59-0.98)	41.7% M vs 40.6% T	11% M vs 6.4% T
Capecitabine (n=143)	0.77 (0.47-1.26)	25% M vs 28% T	11.8% M vs 8.5% T
Eribulin (n=136)	0.66 (0.42-1.05)	45.5% M vs 48.5% T	13.6% M vs 5.9% T
Gemcitabine (n=66)	0.58 (0.29-1.18)	40% M vs 53.1% T	17.1% M vs 15.6% T
Vinorelbine (n=191)	0.90 (0.60-1.35)	51.6% M vs 40% T	6.3% M vs 2.1% T

[1]Primary PFS data cutoff 10-Oct-2018: 536 Intent-To-Treat subjects.
[2]Safety data cutoff 10-Apr-2019: 530 subjects who received any study therapy.

Figure 1. Progression-Free Survival Results by Chemotherapy

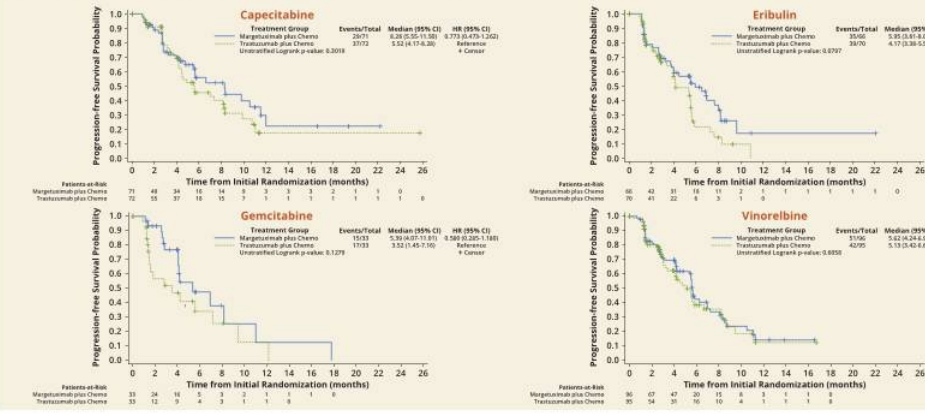

Table 2. Adverse Events Leading to Chemotherapy Discontinuation

Population[1]	Total	Grade (G)					≥ Grade 3 Adverse Events
		G5	G4	G3	G2	G1	
M + Ctx (n=264)	**29**	**1**	**1**	**13**	**11**	**3**	
Cap (n=68)	8	1	1	2	4	–	Aspiration pneumonia (G5), septic shock (G4), hydronephrosis (G3), co
Eri (n=66)	9	–	–	5	3	1	Left ventricular (LV) dysfunction, neuropathy, neutropenia, **seroma[3]**, s
Gem (n=35)[2]	6	–	–	4	1	1	Asthenia, edema, stress, vasculitis
Vin (n=95)	6	–	–	2	3	1	Abdominal pain, **infusion related reaction (IRR)[3]**
T + Ctx (n=266)	**17**	**–**	**–**	**7**	**1**	**1**	
Cap (n=71)	6	–	–	5	1	-	Fatigue, GI toxicity, leukemia, neuropathy, palmar-plantar erythrodyse
Eri (n=68)	4	–	–	3	1	-	Intracranial hemorrhage, neuralgia, transaminase elevations
Gem (n=32)	5	–	–	3	1	1	Clostridium difficile infection, osteonecrosis of jaw, bilirubin elevation
Vin (n=95)	2	–	–	2	-	-	Intestinal obstruction, **pneumonia[3]**

[1]Safety data cutoff 10-Apr-2019: 530 subjects who received any study therapy. [2]2 subjects had capecitabine selected but received gemcitabine. [3]Considered probably or definitely related to antibody study therapy.

Conclusions

- Margetuximab improved PFS over trastuzumab across all chemotherapy subgroups
- Hazard ratio differences among chemotherapy subgroups may be driven by selection bias and/or tumor sensitivity to individual chemothera
- Safety was acceptable and manageable in all chemotherapy subgroups

We thank the patients who consented to this research and study teams at all pa

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