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Investigational Agents

The safety and efficacy of investigational agents and/or investigational uses of approved products have not been established.

MGC018 Conference Call Agenda

Topic	Presenter	Organization
Welcome	Scott Koenig, M.D., Ph.D.	MacroGenics
B7-H3 Background / MGC018 Overview	Chet Bohac, M.D.	MacroGenics
Dose Escalation Data Presented at ASCO 2021	Chet Bohac, M.D.	MacroGenics
Review of Melanoma Patients in Dose Escalation	Sekwon Jang, M.D.	Inova Schar Cancer Institute
Initial Dose Expansion mCRPC Data (ASCO 2021)	Chet Bohac, M.D.	MacroGenics
mCRPC Commentary	Emmanuel Antonarakis, M.B.B.Ch. Eugene Shenderov, M.D., Ph.D.	Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
Wrap-up	Scott Koenig, M.D., Ph.D.	MacroGenics
Q&A	All	

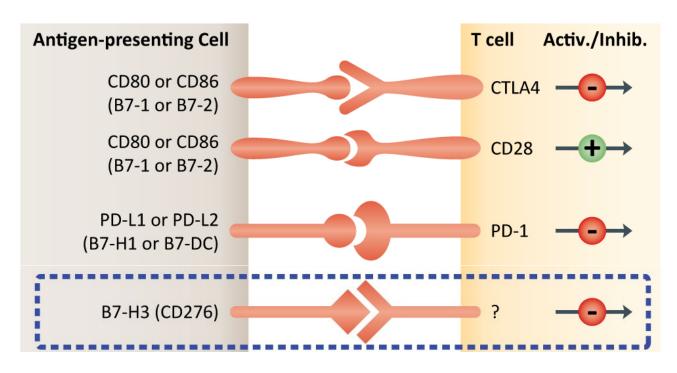
B7-H3 Background

Chet Bohac, M.D. Executive Director, Clinical Research, MacroGenics



B7-H3: Member of B7 Family of Immune Regulators

Expression contributes to tumor immune evasion and cancer cell metabolism



Adapted from Pardoll, et al., Nature, April 2012.

B7-H3 over-expression in multiple solid tumors correlates with poor patient prognosis (reviewed in *Liu 2021*)

Immunosuppressive Role

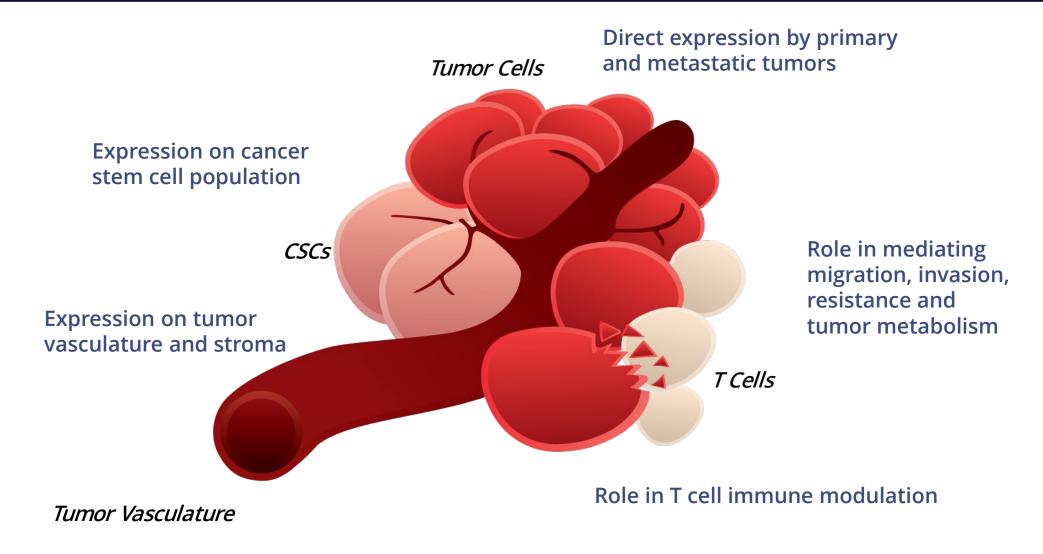
- Crystal structure resolved: T-cell inhibitory domain mapped (*Vigdorovich 2013*)
- Tumor-expressed B7-H3 suppresses T-cell mediated antitumor immune responses
 - High B7-H3 correlates with non-responsiveness to anti PD-1 in NSCLC (Yonesaka 2018)
 - Associated with reduced CD8 infiltrate and CD8 T-cell exhaustion in ovarian cancer (*Cai 2020*)
 - Enables cancer stem cells (HNSCC) to evade immune surveillance (Wang 2021)

Tumor Metabolism & Metastatic Role

- Mediates chemotherapy resistance in pancreatic and CRC (Zhao 2013, Ma 2020)
- Promotes tumor cell progression, migration and metastases in prostate, CRC and melanoma (*Yuan 2011, Tekle 2012, Liu 2015*)
- Regulates glucose metabolism in breast cancer and CRC (Lim 2016, Shi 2019)



Rationale for Targeting B7-H3



Indications Being Evaluated with MGC018, Enoblituzumab

Majority express high levels of B7-H3, with limited expression in normal tissue

	IHC Summary of >1,530 Tumor Tissue Samples Screened						
Potential Indications:		B7-H3 Positive ^(a)	2+ or Above				
Head and Neck	19/19	100%	19/19	100%			
Kidney Cancer	77/78	99%	75/78	96%			
Glioblastoma	65/66	98%	63/66	95%			
Bladder	86/88	98%	78/88	89%			
Thyroid Cancer	34/35	97%	33/35	94%			
Mesothelioma	45/47	96%	34/47	72%			
Anal Cancer	34/37	92%	33/37	89%			
Triple Negative Breast Cancer	120/131	92%	114/131	87%			
Melanoma	132/146	90%	94/146	64%			
Prostate Cancer	88/99	89%	51/99	52%			
Pancreatic Cancer	69/78	88%	45/78	58%			
Non Small Cell Lung Cancer	323/371	87%	297/371	80%			
Breast Cancer	189/249	76%	156/249	63%			
Ovarian Cancer	59/79	75%	36/79	46%			

MGC018 Expansion Cohorts

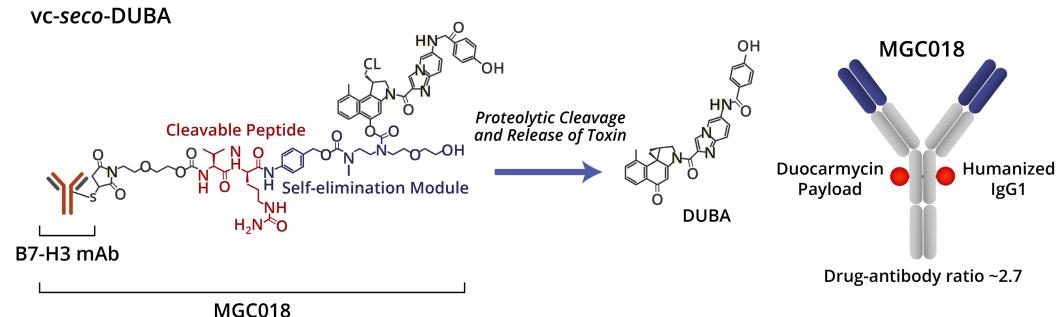
⁽a) B7-H3 positivity reflects any grade staining via fixed tumor microarray; B7-H3 is expressed on tumor as well as tumor vasculature.

MGC018 Overview



MGC018: B7-H3 Directed ADC with Duocarmycin-based Linker Payload

Leveraging high B7-H3 expression in solid tumors



- vc-seco-DUocarmycin-hydroxyBenzamide Azaindole (DUBA) is a DNA alkylating agent
- DUBA cytotoxic activity is cell-cycle independent
- DUBA retains potency in multidrug-resistant cell lines
- B7-H3 epitope chosen on basis of internalization and tumor selectivity
- Cleavable peptide linker facilitates bystander effect
- Induces immunogenic cell death in preclinical models

Duocarmycin payload and cleavable peptide linker technology was licensed from Byondis.

MGC018 is investigational and has not yet been approved for marketing by any regulatory authority

MGC018 Phase 1 Study Design

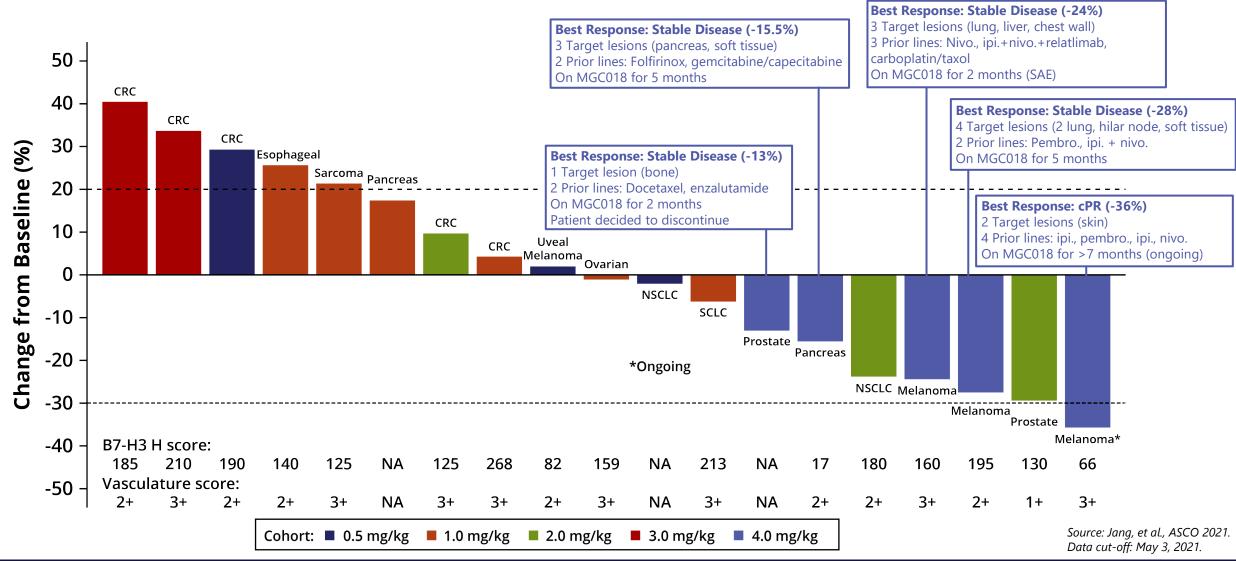
Dosing is every three weeks (q3W) **Tumor Response** by Investigator **PSA** per RECIST v1.1 **Evaluation** 3+3+3 Dose Escalation **MGC018 MGC018 MGC018 MGC018 MGC018** Every 6 Every 6 Weeks Weeks 0.5 mg/kg 2.0 mg/kg 3.0 mg/kg 4.0 mg/kg 1.0 mg/kg Every 3 **Metastatic Castration-Resistant Prostate Cancer** Weeks (n=40)**Non-small Cell Lung Cancer** Cohort Expansion (3 mg/kg q3W) (n=20)**Triple Negative Breast Cancer** Every 9 Weeks (n=20)Melanoma (n=20)**Squamous Cell Carcinoma of the Head and Neck** (n=20)

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Dose Escalation Data Presented at ASCO 2021

Dose Escalation: Best Percent Change of Target Lesions



Dose Escalation: Percent Change of Target Lesions

MGC018 provided target lesion reductions and disease stabilization for several months **NSCLC Uveal Melanoma** 90 Change in Target Lesions from Baseline (%) **Prostate** 80 **SCLC** Sarcoma 70 CRC 60 Ovarian **Pancreas** 50 Esophageal 40 Melanoma First new lesion 30 **Treatment ongoing** 20 10 -10 -20 -30 -40 -50 · 10 20 25 30 35

Source: Jang, et al., ASCO 2021. Data cut-off: May 3, 2021.

Weeks Since Treatment Initiation

Dose Escalation: Related Adverse Events ≥ 20%, All Grades

Fatigue, nausea, infusion related reaction, skin disorders, and neutropenia were most common

System Organ Class Preferred Term	0.5 mg/kg	1.0 mg/kg	2.0 mg/kg	3.0 mg/kg	4.0 mg/kg	All
	(N=3)	(N=6)	(N=7)	(N=7)	(N=6)	(N=29)
AT LEAST ONE EVENT	3 (100%)	5 (83.3%)	6 (85.7%)	7 (100%)	6 (100%)	27 (93.1%)
Blood and lymphatic system disorders	0	1 (16.7)	2 (28.6)	3 (42.9)	2 (33.3)	8 (27.6)
Neutropenia	0	1 (16.7)	2 (28.6)	3 (42.9)	2 (33.3)	8 (27.6)
Gastrointestinal disorders	0	5 (83.3)	2 (28.6)	2 (28.6)	3 (50.0)	12 (41.4)
Nausea	0	2 (33.3)	2 (28.6)	1 (14.3)	3 (50.0)	8 (27.6)
General disorders and administration site conditions Fatigue Chills Pyrexia	2 (66.7)	2 (33.3)	2 (28.6)	4 (57.1)	5 (83.3)	15 (51.7)
	1 (33.3)	1 (16.7)	2 (28.6)	4 (57.1)	3 (50.0)	11 (37.9)
	1 (33.3)	0	2 (28.6)	0	4 (66.7)	7 (24.1)
	1 (33.3)	1 (16.7)	2 (28.6)	0	2 (33.3)	6 (20.7)
Injury, poisoning and procedural complications Infusion-related reaction	0	0	2 (28.6)	5 (71.4)	2 (33.3)	9 (31.0)
	0	0	2 (28.6)	5 (71.4)	2 (33.3)	9 (31.0)
Skin and subcutaneous tissue disorders Skin hyperpigmentation Palmar-plantar erythrodysaesthesia syndrome	0	3 (50.0)	5 (71.4)	5 (71.4)	4 (66.7)	17 (58.6)
	0	3 (50.0)	1 (14.3)	3 (42.9)	2 (33.3)	9 (31.0)
	0	0	3 (42.9)	3 (42.9)	2 (33.3)	8 (27.6)

Includes events with causality ratings of 'Possible', 'Probable' or 'Definite'. Subjects are counted once for each Preferred Term reported.



Dose Escalation: Grade ≥ 3 Related Adverse Events

Cytopenias were most common

System Organ Class Preferred Term	0.5 mg/kg	1.0 mg/kg	2.0 mg/kg	3.0 mg/kg	4.0 mg/kg	All
	(N=3)	(N=6)	(N=7)	(N=7)	(N=6)	(N=29)
AT LEAST ONE EVENT	2 (66.7%)	2 (33.3%)	6 (85.7%)	4 (57.1%)	5 (83.3%)	19 (65.5%)
Blood and lymphatic system disorders Neutropenia Lymphopenia	0	0	2 (28.6)	2 (28.6)	2 (33.3)	6 (20.7)
	0	0	2 (28.6)	2 (28.6)	2 (33.3)	6 (20.7)
	0	0	1 (14.3)	1 (14.3)	1 (16.7)	3 (10.3)
General disorders and administration site conditions Fatigue	0	0	0	0	2 (33.3)	2 (6.9)
	0	0	0	0	2 (33.3)	2 (6.9)
Investigations Lymphocyte count decreased Neutrophil count decreased Platelet count decreased Lipase increased White blood cell count decreased	1 (33.3) 0 0 0 1 (33.3) 0	2 (33.3) 1 (16.7) 1 (16.7) 0 0 1 (16.7)	3 (57.1) 2 (28.6) 1 (14.3) 1 (14.3) 0	2 (28.6) 1 (14.3) 0 1 (14.3) 0	2 (33.3) 0 0 0 1 (16.7) 1 (16.7)	10 (34.5) 4 (13.8) 2 (6.9) 2 (6.9) 2 (6.9) 2 (6.9)
Metabolism and nutrition disorders Hypophosphataemia	0	0	2 (28.6)	0	0	2 (6.9)
	0	0	2 (28.6)	0	0	2 (6.9)
Skin and subcutaneous tissue disorders Palmar-plantar erythrodysaesthesia syndrome Rash maculo-papular	0	0	3 (42.9)	1 (14.3)	0	4 (13.8)
	0	0	1 (14.3)	1 (14.3)	0	2 (6.9)
	0	0	2 (28.6)	0	0	2 (6.9)

Dose Escalation: Treatment-Emergent Adverse Events

Manageable safety profile

Patients Experiencing 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)	4.0 mg/kg (N=6)	AII (N=29)
Adverse Event	3 (100%)	6 (100%)	7 (100%)	7 (100%)	6 (100%)	29 (100%)
Treatment-Related Adverse Event ¹	3 (100)	5 (83.3)	6 (85.7)	7 (100)	6 (100)	27 (93.1)
Adverse Event ≥ Grade 3 ²	3 (100)	4 (66.7)	7 (100)	5 (71.4)	5 (83.3)	24 (82.8)
Treatment-Related Adverse Event ≥ Grade 3 ²	2 (66.7)	2 (33.3)	6 (85.7)	4 (57.1)	5 (83.8)	19 (65.5)
Serious Adverse Event	1 (33.3)	1 (16.7)	3 (42.9)	2 (28.6)	2 (33.3)	9 (31.0)
Dose-limiting Toxicity	0	0	1 (14.3) ³	0	1 (16.7) ⁴	2 (6.9)
Event that Resulted in Study Discontinuation	1 (33.3)	2 (33.3)	3 (42.9)	4 (57.1)	2 (33.3)	10 (34.5)
Event that Resulted in MGC018 Withdrawal	1 (33.3)	1 (16.7)	3 (42.9)	4 (57.1)	2 (33.3)	11 (37.9)
Event that Resulted in MGC018 Dose Reduction	0	0	1 (14.3)	2 (28.6)	2 (33.3)	5 (17.2)
Event that Resulted in MGC018 Interruption	1 (33.3)	0	1 (14.3)	5 (71.4)	5 (83.3)	12 (41.4)
Fatal Adverse Event (pneumonitis/pneumonia)	1 (33.3)	0	0	0	0	1 (3.4)
Adverse Event of Special Interest (AESI) – Infusion Reaction	0	0	2 (28.6)	5 (71.4)	2 (33.3)	9 (31.0)

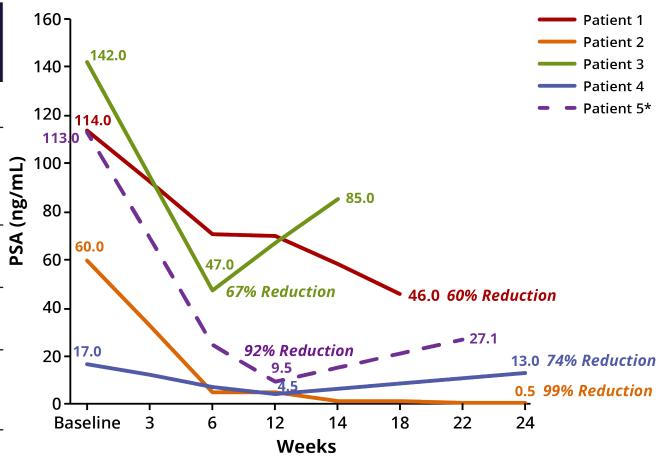


⁽¹⁾ Includes events with causality assessments of 'Possible', 'Probable' or 'Definite'. (2) Based on CTCAE criteria version 4.0.3. (3) Grade 4 neutropenia resolved to baseline. (4) G3 fatigue > 72 hours. *Amendment during 3.0 mg/kg dose level applied to allow dose modification.

Dose Escalation: Update on PSA Responders from ASCO 2020

Participants without progression for ≥6 months

Patient (Dose)	Duration of Therapy	MGC018 Best Response	MGC018 PSA Reduc- tion	MGC018 Time to Progression	Reason for MGC018 Discontinuation
Patient #1 2 mg/kg	4 mos.	SD (-29%)	-60%	Unknown (>4 mos.)	Patient decision due to numerous clinic visits
Patient #2 3 mg/kg Bone only	6 mos.	SD	–99 %	6 mos.	New skull lesions on CT scan obtained for head injury; skull lesions not seen on baseline bone scan (no head CT)
Patient #3 3 mg/kg Bone only	3 mos.	SD	-67%	Not yet progressed (7 mos.)	Palmar plantar erythrodysesthesia
Patient #4 3 mg/kg Bone only	5 mos.	SD	-74 %	Not yet progressed (7 mos.)	Pericardial effusion
Patient #5 3 mg/kg Bone only	3 mos.	SD	-92%	Initiated subsequent therapy (6 mos.)	Increasing PSA



^{*} Patient 5 data scaled (1/10) for charting purposes.

Dose Escalation: Update on PSA Responders from ASCO 2020

Patient (Dose)	B7-H3 H Score (Vasculature Score)	Line of Therapy	Treatment	Duration of Therapy (# months)	MGC018 Best Response	MGC018 PSA Reduction	MGC018 Time to Progression (# months)	Reason for MGC018 Discontinuation
Patient #1 2 mg/kg One target lesion (lymph node); non-target abdominal adenopathy and bone lesions	130 (1+)	1 2 3 4 5 6	Docetaxel Enzalutamide Prostvac Abiraterone Nivolumab MGC018	4 24 5 6 6	SD (-29%)	-60%	Unknown (>4)	Patient decision due to numerous clinic visits
Patient #2 3 mg/kg Bone only disease	N/A (insufficient invasive tumor)	1 2 3 4 5	Docetaxel Abiraterone Enzalutamide Radium 223 MGC018	6 4 12 6 6	SD	-99%	6	New skull lesions on CT scan obtained for head injury; skull lesions not seen on baseline bone scan: no baseline head CT
Patient #3 3 mg/kg Bone only disease	250 (2+)	1 2 3 4 5	Docetaxel Provenge Enzalutamide Abiraterone MGC018	8 2 6 9 3	SD	-67%	Not yet progressed (7)	Palmar plantar erythrodysesthesia
Patient #4 3 mg/kg Bone only disease	279 (2+)	1 2 3	Abiraterone Nivo + Rucaparib MGC018	Unknown Unknown 5	SD	-74%	Not yet progressed (7)	Pericardial effusion
Patient #5 3 mg/kg Bone only disease	215 (1+)	1 2 3 4 5 6	Docetaxel Provenge Enzalutamide Abiraterone Docetaxel MGC018	4 12 7 7 4 3	SD	-92%	Initiated subsequent therapy (6)	Increasing PSA

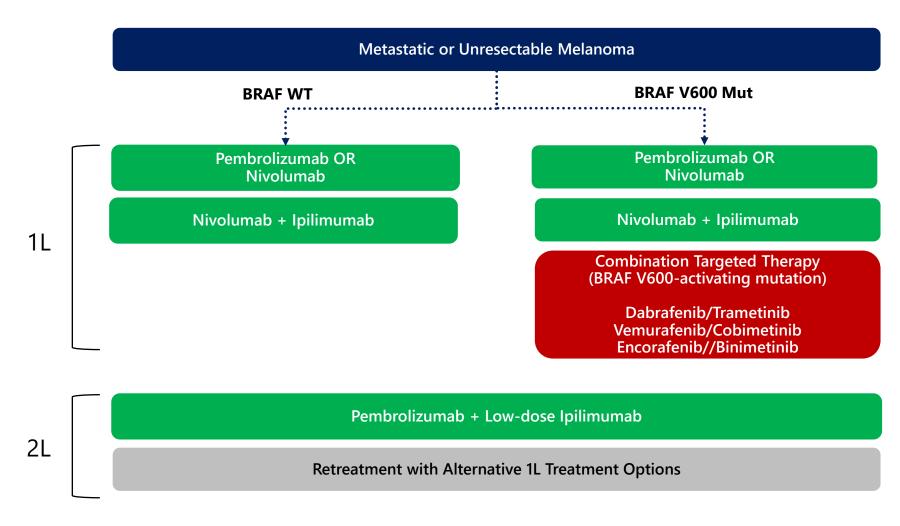
Review of Melanoma Patients in Dose Escalation



Sekwon Jang, M.D.Director of Melanoma and Cutaneous Oncology Therapeutics and Research, Inova Schar Cancer Institute

Limited Options for Melanoma Patients Progressing after 1L Systemic Therapy¹

Potential to position $MGC018 \ge 2^{nd}$ line



¹ NCCN Guidelines, Melanoma: Cutaneous, Version 2. 2021 – February 19, 2021; Preferred regimens are displayed.



Activity in Metastatic Melanoma Patients

Enrolled in MGC018 dose escalation cohort at 4.0 mg/kg

Patient	Prior Radiation/ Surgery	B7-H3 H Score (Vasculature Score)	Line of Therapy	Treatment	Duration of Therapy	Reason for MGC018 Discontinuation	Best Response in Target Lesions
Patient #1 3 target lesions (lung, liver, chest wall) Non-target pelvic nodes and perirectal/lung lesions	Radiation and Surgery	160 (3+)	1 2 2 2 3 4	Nivolumab Ipilimumab Nivolumab Relatlimab Carboplatin/Taxol MGC018	10/18 - 07/19 08/19 - 09/19 08/19 - 02/20 11/19 - 02/20 04/20 (1 dose) 05/20 - 07/20	SAE hematuria/ thrombocytopenia (Hx of radiation cystitis)	-24%
Patient #2 4 target lesions (2 lung, hilar node, soft tissue) Non-target bilateral lung lesion	Surgery	195 (2+)	1 2 3	Pembrolizumab Ipilim. + Nivo. MGC018	03/20 - 07/20 07/20 - 08/20 10/20 - 03/21	PD	-28%
Patient #3 2 target lesions (skin) Non-target multiple lower extremity lesions	Radiation and Surgery	66 (3+)	1 2 3 4 5	Ipilimumab Pembrolizumab Ipilimumab Nivolumab MGC018	02/15 - 05/15 08/15 - 10/17 06/18 - 08/18 10/18 - 09/20 10/20 - Ongoing	N/A, ongoing	cPR (-36%)

PD = progressive disease; cPR = confirmed partial response; N/A = not applicable.



Activity in Post anti-PD-1 Metastatic Melanoma

Investigational programs

	ILLUMINATE-301 ⁽¹⁾ Tilsotolumod + Ipilimumab	Phase IB ⁽²⁾ Vidutolimod + Pembrolizumab	LEAP-004 ⁽³⁾ Lenvatinib + Pembrolizumab	Phase I/II ⁽⁴⁾ RP1 + Nivolumab	C-144-01 Phase II ^(5,6) Lifileucel (LN-144)
Drug Class	TLR9 Agonist	TLR9 Agonist/VLP	Anti-VEGF/TKI	Modified Oncolytic HSV Vector	TILs
Previous Treatment	Post anti-PD-1	Post anti-PD-1	Post anti-PD-(L)1	Post anti-PD-1	Post anti-PD-1
Data cut-off or Median Follow-up	NA	September 30, 2020	June 10, 2020 12.0 months	October 15, 2020	Dec 14, 2020 / 28 months
N	481 Total	98	103	16	66
Median PFS	NA	NA	4.2 months	Not Stated	4.1 months
Median Overall Survival	NA	NA	13.9 months	Not Stated	17.4 months
ORR	8.8%	23% (23/98)	21.4% (22/103)	31.3%	36.4%
Duration of Response	NA	19.9 months	6.3 months	>6.98 months	Not Reached
Treatment-Related Adverse Events Grade 3+	61.1%	36.5% (58/159)	44.7% (46/103)	Fatigue, 8.8%	97% Grade 3 or 4 TEAE 3% Grade 5 TEAE

⁽¹⁾ Idera Pharmaceuticals Press Release, 2021-03-18 – Trial did not meet primary endpoint; (2) Checkmate Pharmaceuticals Investor Deck, May 2021; (3) Arance, et al., ESMO, 2020; (4) Middleton, et al., SITC 2020, RP1 is an oncolytic HSV-1 expressing GALV-GP R- and GM-CSF; (5) J Clin Oncol 39, 2021 (suppl 15; abstr 9505), Lifileucel is an autologous TIL-based therapy; (6) Sarnaik, et al., JCO DOI https://doi.org/10. 1200/JCO.21.00612, 2021

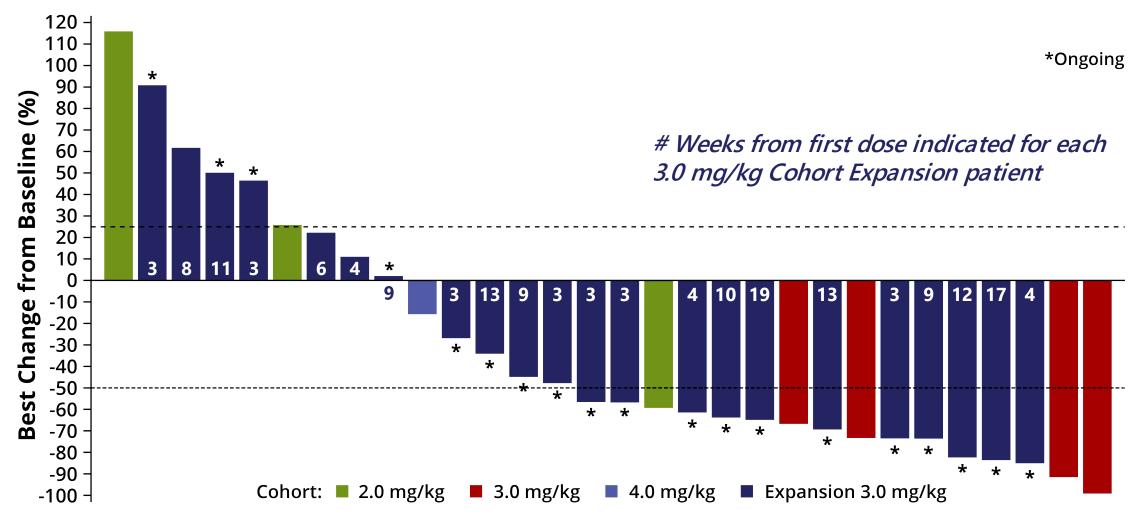
Initial Dose Expansion mCRPC Data (ASCO 2021)

Chet Bohac, M.D. Executive Director, Clinical Research, MacroGenics



Best Percent Change in PSA: Dose Escalation and Cohort Expansion

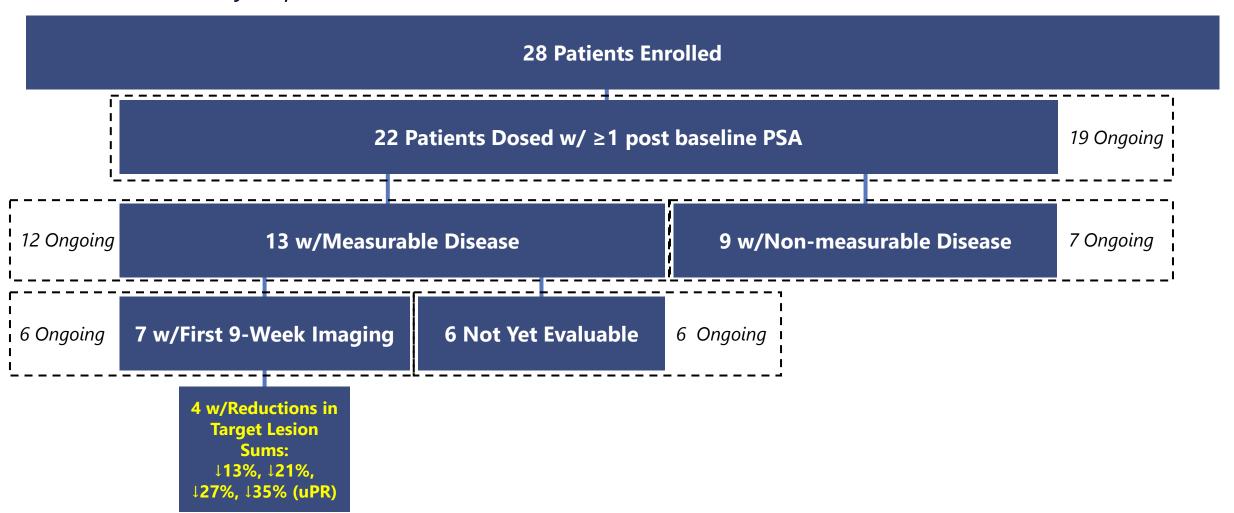
>50% PSA Reduction in 11/22 (50%) mCRPC expansion patients; 16/31 (52%) in escalation + expansion



Patients who received at least one dose and had at least one post-baseline PSA evaluation.

MGC018 mCRPC Dose Expansion Patient Status (as of Data Cut-off)

Anti-tumor activity in patients with measurable disease



mCRPC Commentary

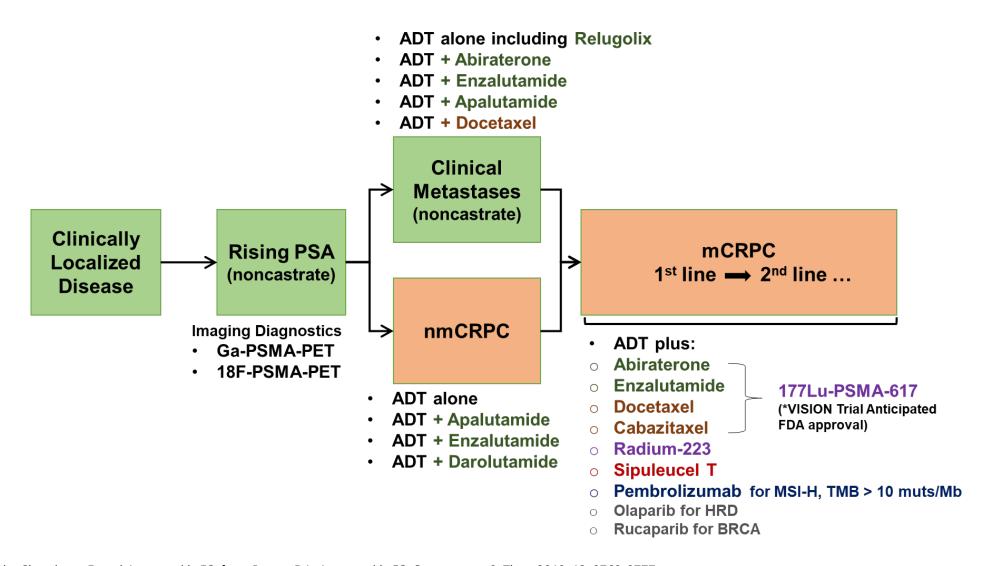


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Prostate Cancer Treatment Landscape



Modified by Shenderov E. and Antonarakis ES. from Bastos DA, Antonarakis ES. Oncotargets & Ther 2019; 12: 8769-8777.



Activity in mCRPC Patients Progressing After Taxane and NHT

	MGC018 Cohort Expansion	CARD ⁽¹⁾ Cabazitaxel (FDA Approved)	VISION ⁽²⁾ ¹⁷⁷ Lu-PSMA-617 Phase 3 + SOC	KEYNOTE-19 Pembro		
Previous Treatment	Median 4 prior lines of therapy	Post-docetaxel and post-NHT	PSMA+ Post-docetaxel Post-doceta and post-NHT and post-N			_
Data cut-off or Median Follow-up	May 3, 2021	9.2 months	NA	<u>Cohort 1</u> 9.5 mo.	<u>Cohort 2</u> 7.9 mo.	<i><u>Cohort 3</u></i> 14.1 mo.
N	28 Enrolled	129	551	133	66	59
Median rPFS	NA	8.0 months	8.7 months HR=0.40, p<0.001	2.1 mo.	2.1 mo.	3.7 mo.
Median PFS	NA	4.4 months	NA	NA	NA	NA
Median Overall Survival	NA	13.6 months	15.3 months HR=0.62, p<0.001	9.5 mo.	7.9 mo.	14.1 mo
PSA response (≥50% PSA reduction)	50% (11/22) 52% (16/31), including dose escalation (5/9)	35.7%	NA	6%	8%	2%
ORR	NA	36.5% (23/63)	29.8%	5%	3%	NA
Adverse Events, Grade 3+	NA	56.3%	28.4%	15% (5%	6 discontir	nuation)

NHT, next generation hormone therapy (abiraterone or enzalutamide)

⁽¹⁾ De Wit, et al., NEJM, 2019; (2) Morris, et al., J Clin Oncol 39, 2021 (suppl 15; LBA4); (3) Antonarakis, et al., J Clin Oncol 38, 2020:395-405 (Cohort 1: RECIST-measurable PD-L1-positive, Cohort 2: RECIST-measurable PD-L1-positive, Cohort 3: Bone-predominant disease regardless of PD-L1 expression).

Broad Overview of Patient Treatment Flow

Line of Therapy Metastatic CRPC Enzalutamide Docetaxel + Abiraterone + Relugolix First Line **Prednisone** (Xtandi) Prednisone Abiraterone + Prednisone **Enzalutamide** Cabazitaxel + **Docetaxel Prednisone Second Line** Pembrolizumab (MSI-H/dMMR, TMB > 10 muts/Mb) Olaparib (HRD) Docetaxel + Prednisone, Rucaparib (BRCAd) Chemotherapy Third Line Cabazitaxel + Prednisone 177Lu-PSMA-617 (*Vision Trial Anticipated FDA Approval)



Wrap-up | Q&A

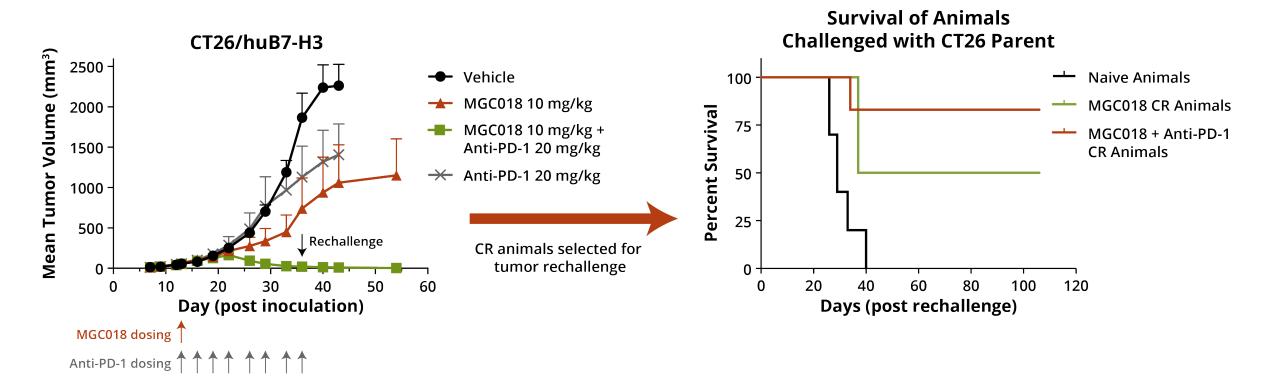
Scott Koenig, M.D., Ph.D.

President & CEO, MacroGenics



Antitumor Activity of MGC018 in Combination with Anti-PD-1: Preclinical Data

Induction of immunological memory in CT26 (colorectal) model

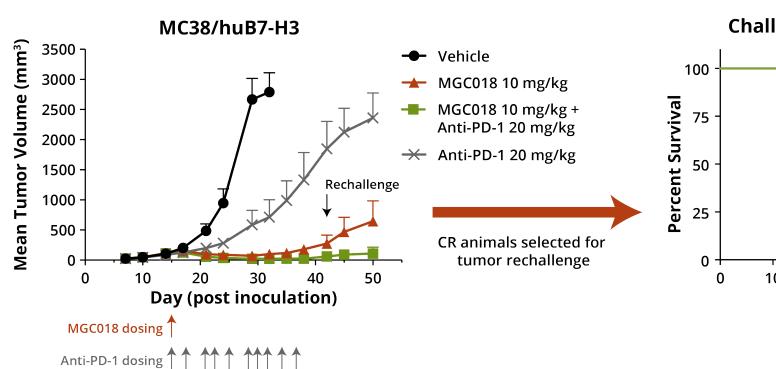


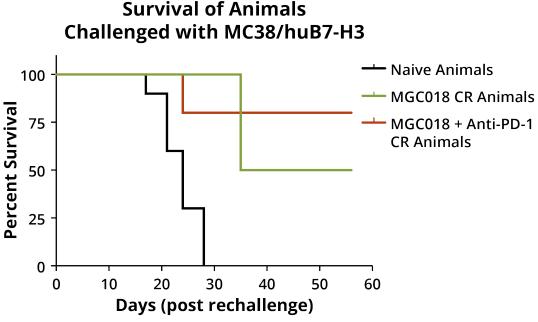
- Antitumor activity of MGC018 is enhanced by anti-PD-1
- MGC018 and MGC018 + anti-PD-1 induces immunological memory

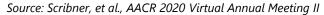


Antitumor Activity of MGC018 in Combination with Anti-PD-1: Preclinical Data

Induction of immunological memory in MC38 (colorectal) model

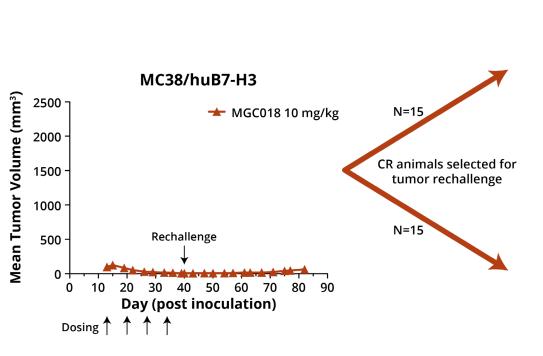


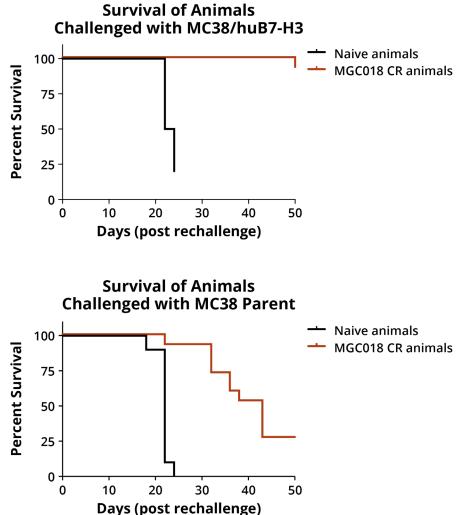




Antitumor Activity of MGC018 in Combination with Anti-PD-1: Preclinical Data (cont'd)

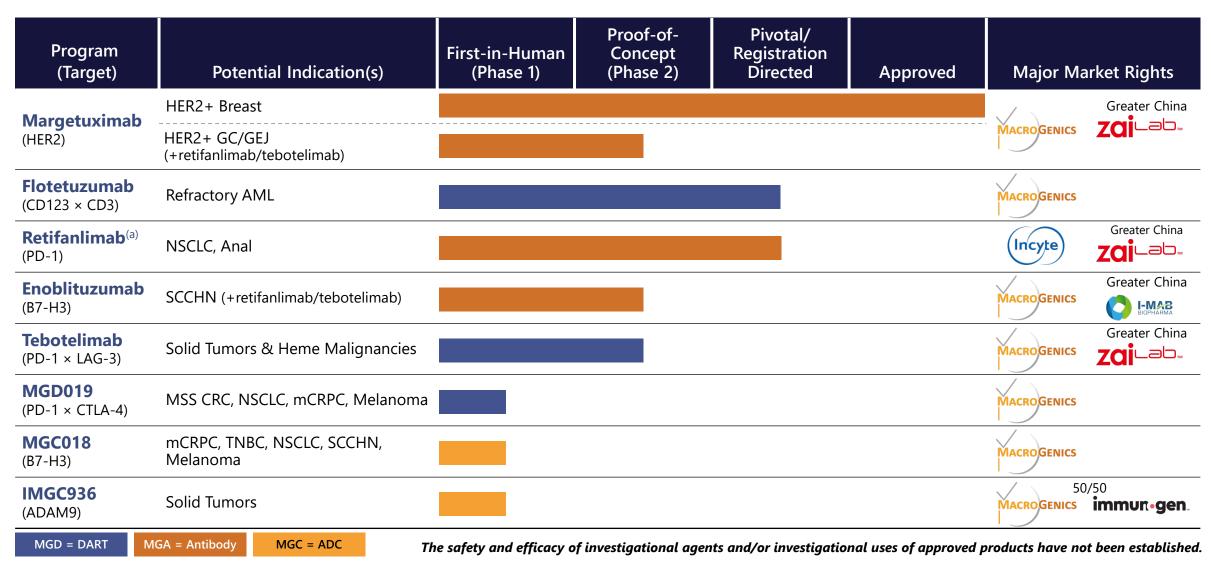
Induction of immunological memory in MC38 (colorectal) model





Source: Scribner, et al., AACR 2020 Virtual Annual Meeting II

Deep and Differentiated Immuno-Oncology Pipeline



⁽a) MacroGenics retains rights to develop its pipeline assets in combination w/retifanlimab (formerly MGA012) and to manufacture a portion of global clinical and commercial supply needs of retifanlimab.



Thank You!



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