Company Overview & ADG126 MSS CRC Clinical Results

March 2024

ADAGENE

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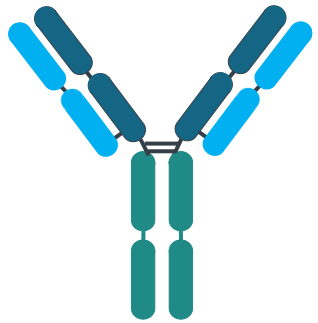
Company Highlights

Focus on masked, anti-CTLA-4 lead candidate	• SAFEbody® ADG126 (muzastotug) results from Ph2 dose expansion cohorts with pembrolizumab in MSS CRC show **best-in-class profile with higher, more frequent and repeat doses**
Validation of SAFEbody® technology by partners	• Sanofi and Exelixis technology licensing agreements for SAFEbody • Eligible to receive ≥$2.5B in potential milestones from existing partners
SAFEbody pipeline candidates showcase platform versatility	• Masked, Fc enhanced anti-CD137 (IgG1) in Ph1 dose escalation • IND-ready masked, anti-CD47 (IgG1) & double masked HER2xCD3 T-cell engager • Masked CD28 T-cell engagers in discovery
Strong cash balance with runway into 2026	• Unaudited consolidated cash balance: **~US$110M as of Dec. 31, 2023** • Potential to receive additional non-dilutive funding from collaborations • Cash runway with streamlined operations into 2026

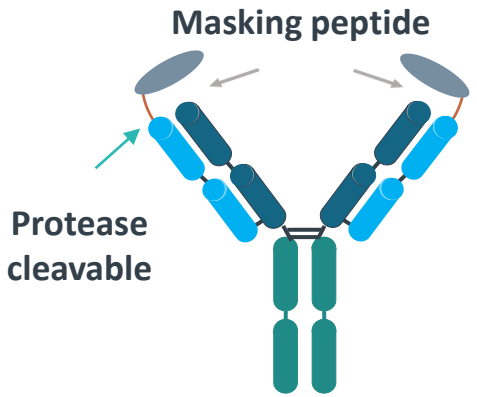
Dynamic Precision Library & Antibody Technologies Enable Wider Therapeutic Window for Anti-CTLA-4 & Other Immunotherapies

NEObody™



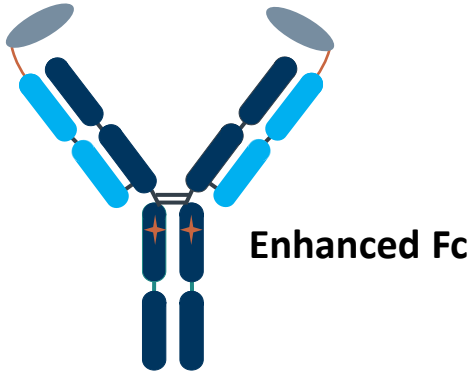
- Dynamic engagement with novel epitope of a given target
- Targets a unique epitope of CTLA-4 to widen therapeutic window

SAFEbody®



- Precision masking for antibody safety
- Further expands TI by preferential targeting of CTLA-4, which is highly expressed on Treg cells in TME

POWERbody™



- Empowered SAFEbody in different modalities with FC engineering for enhanced effector function

Why Focus on Next Generation Anti-CTLA-4 Therapies?

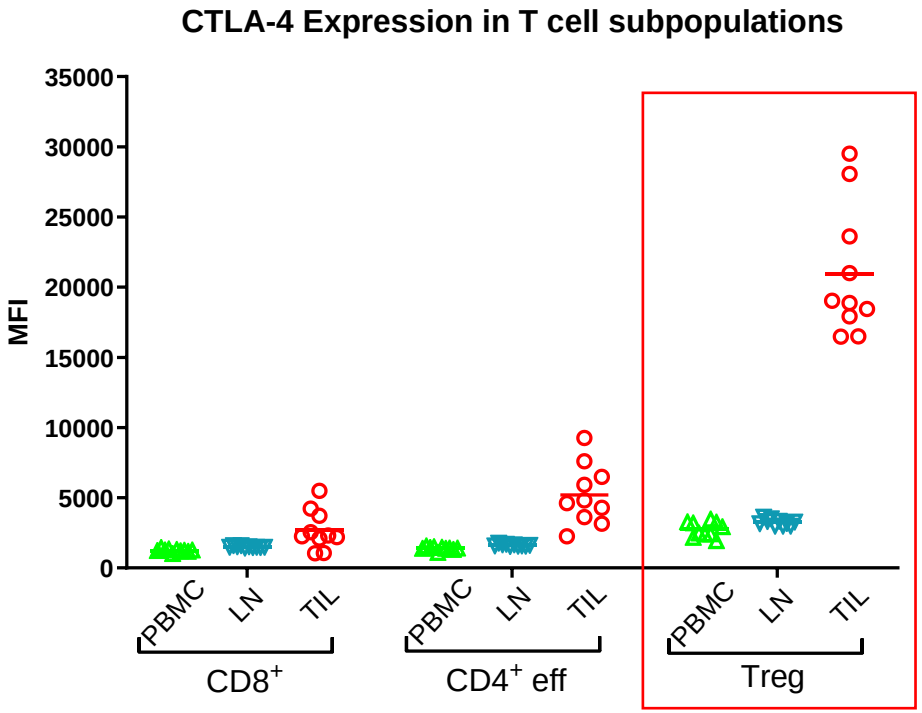
- CTLA-4 is a proven target where safety is limiting its therapeutic potential

- T regulatory cell depletion is crucial for overcoming immune suppression in the tumor microenvironment (TME) where CTLA-4 is overexpressed on Tregs

We are taking anti-CTLA-4 therapy to a new level by targeting a unique epitope combined with SAFEbody precision masking technology to reach tumor tissues with the best therapeutic index and unleash anti-CTLA-4 therapy

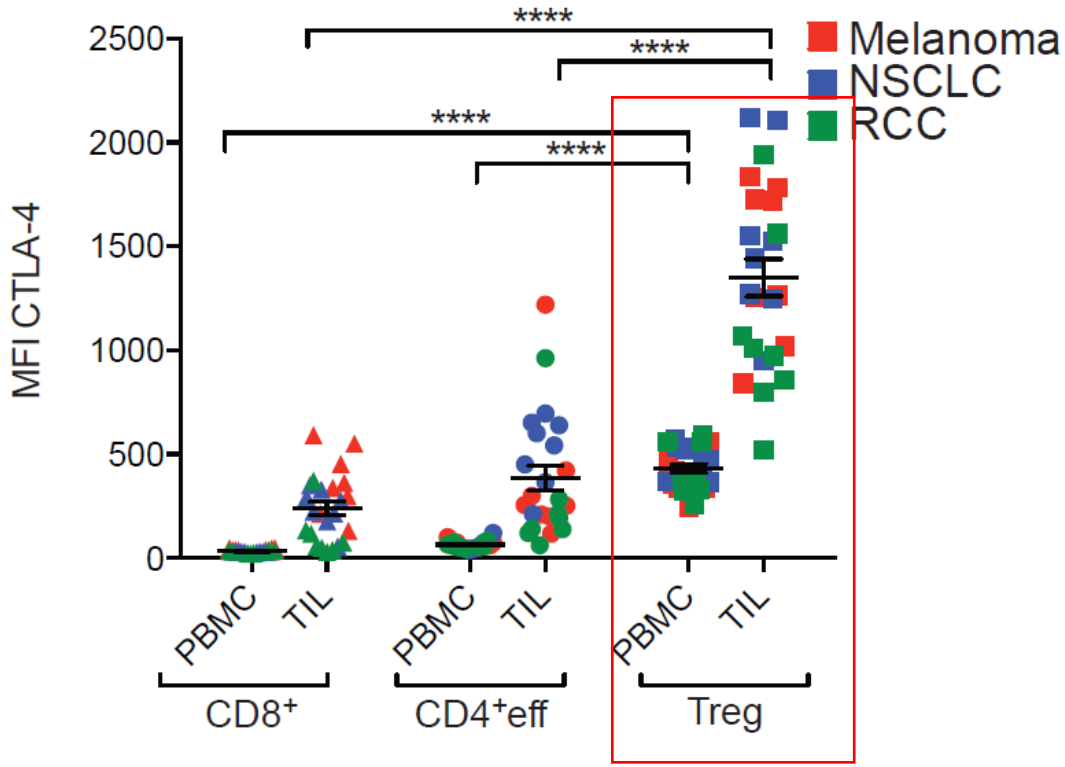
CTLA-4 is Constitutively and Highly Expressed in Tumor Tregs in Both Mouse and Human

Mouse Tumor CT26



(Adagene in-house data)

Human Cancers



(Arce Vargas et al., 2018, Cancer Cell 33, 649-663)

Tumor Tregs express much higher CTLA-4 than CD4+ T effector and CD8+ T cells

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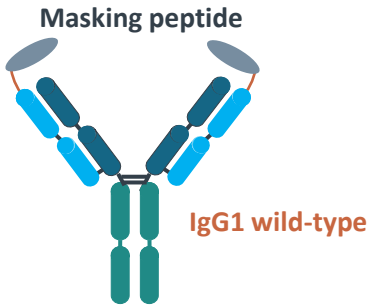
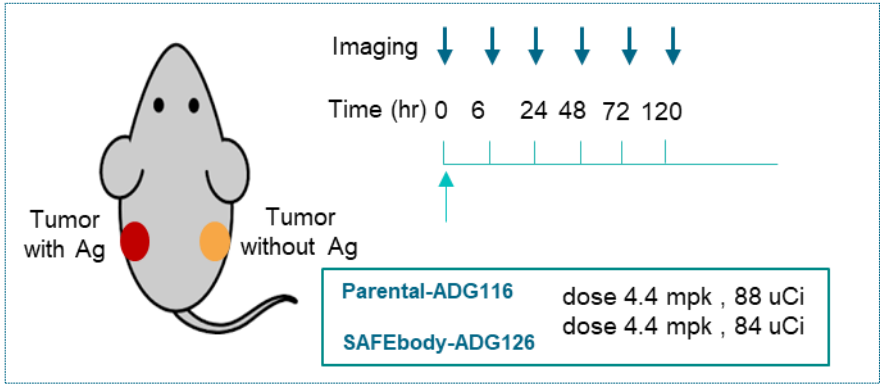
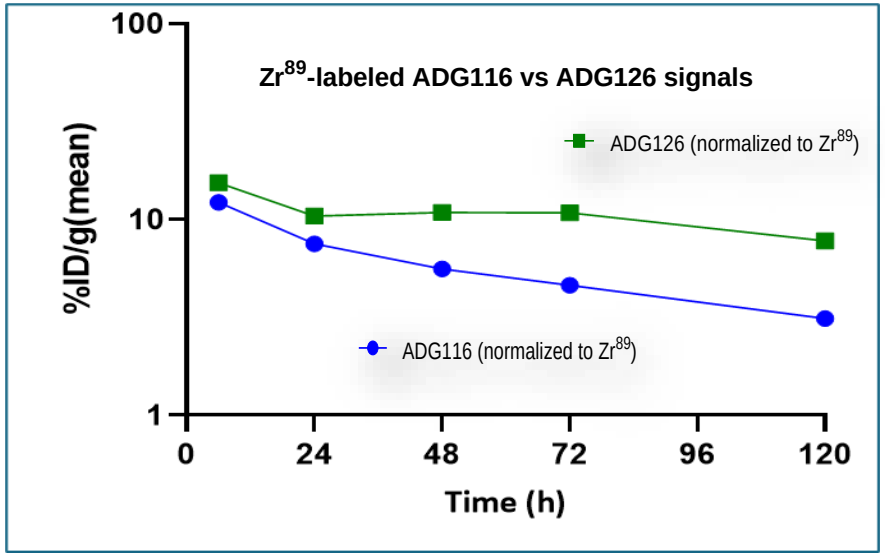
Preferential Accumulation and Prolonged Half-Life of SAFEbody® ADG126 vs Parental ADG116 in Tumor Sites by In Vivo Radioimaging Studies

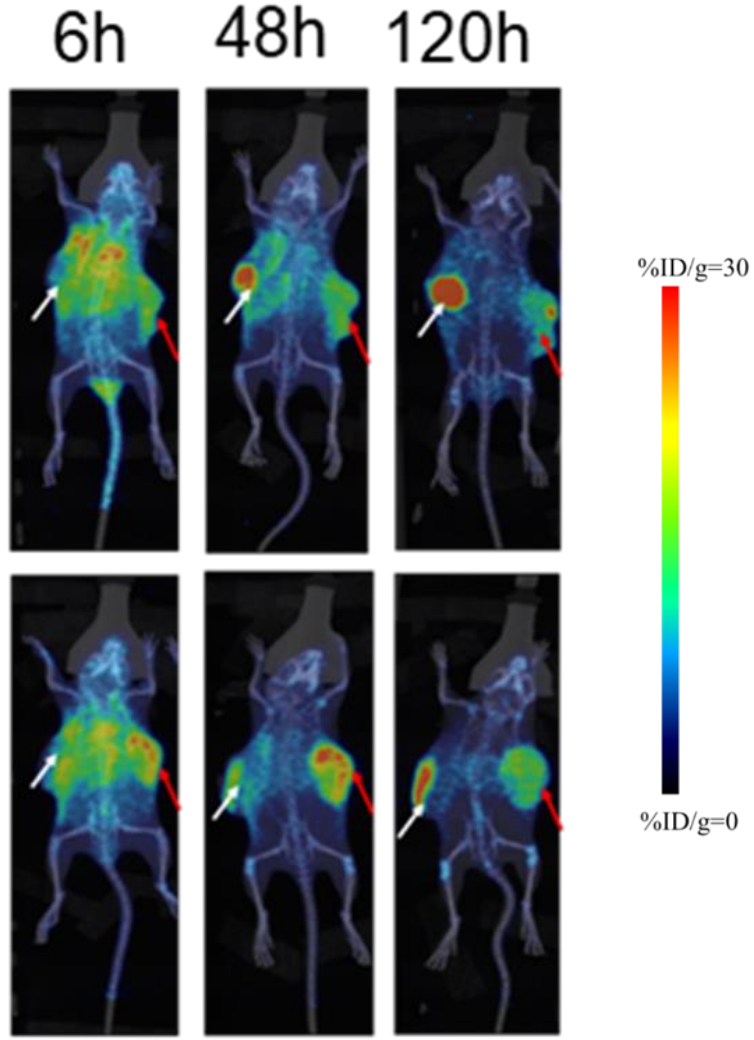
ADG126 SAFEbody®



ADG116 NEObody™
(Activated ADG126)







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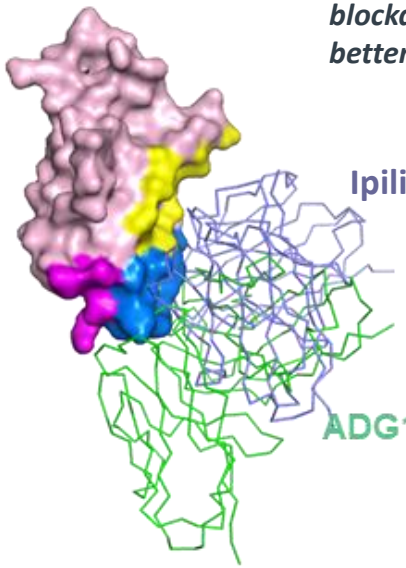
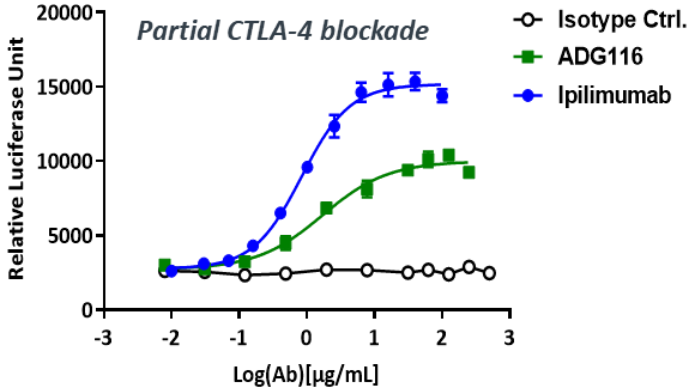
ADG116 & ADG126 Target a Distinct Epitope of CTLA-4 with Enhanced Safety and Efficacy Via Novel Mechanisms of Action



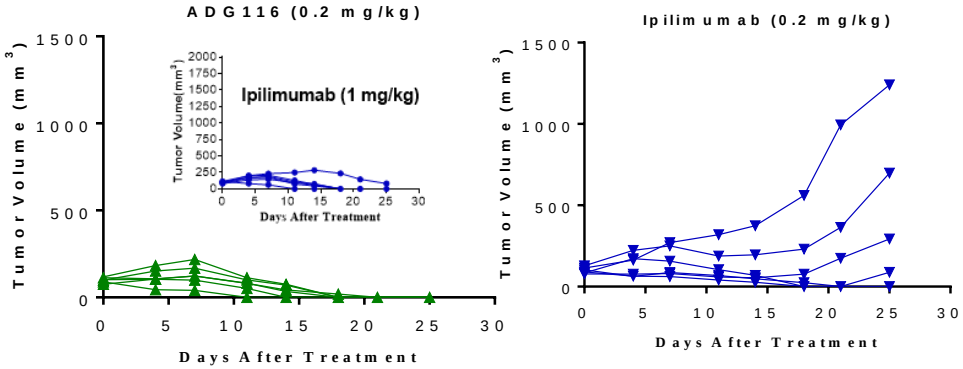
Partial CTLA-4 blockade for better safety

10X higher ADCC for intratumoral Treg depletion

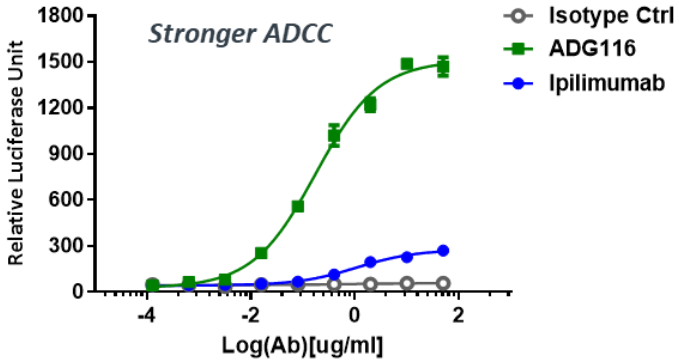
CD28 signaling reporter cell activity released by antibody mediated CTLA-4 functional blockade



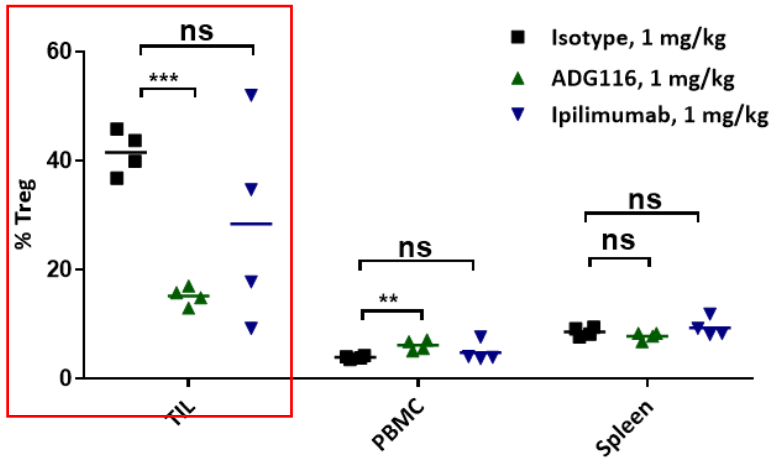
ADG116 shows superior potency to Ipilimumab



ADCC signaling reporter cell activity triggered by anti-CTLA-4 antibodies



% Treg in CD4+ T cells



Data on file.

Strong ADCC/ADCP for Intratumoral Treg Depletion in TME

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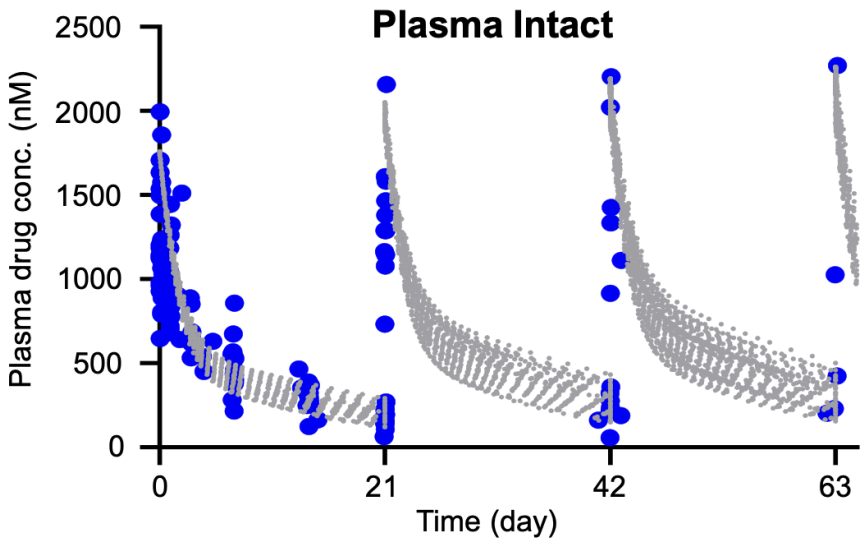
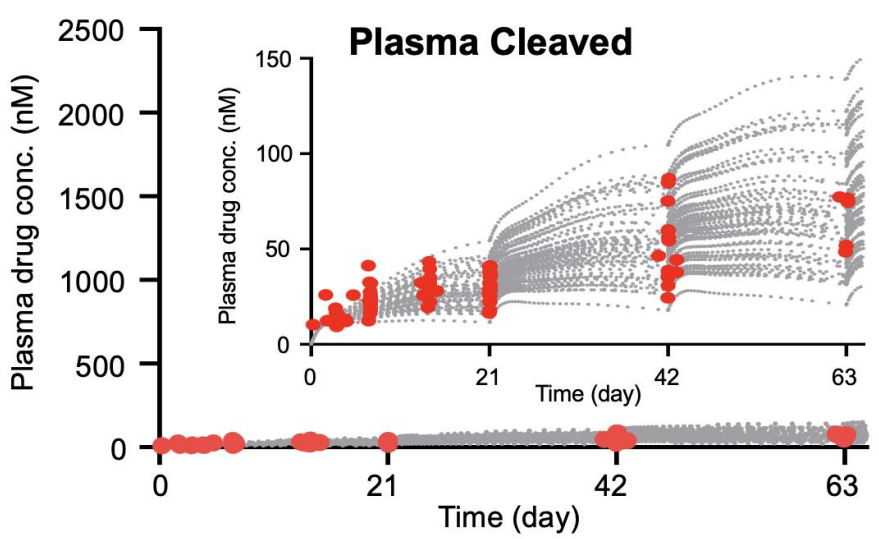
Cross-species reactivity of ADG126 in mice allows for integrating mPBPK model-estimated tumor cleavage parameter from tumor-bearing mice to human

Population mPBPK model fitting in patients (10 mpk Q3W)

- The mPBPK model succeeded in simultaneously fitting the measured plasma intact and cleaved drug concentrations across studied dose levels.



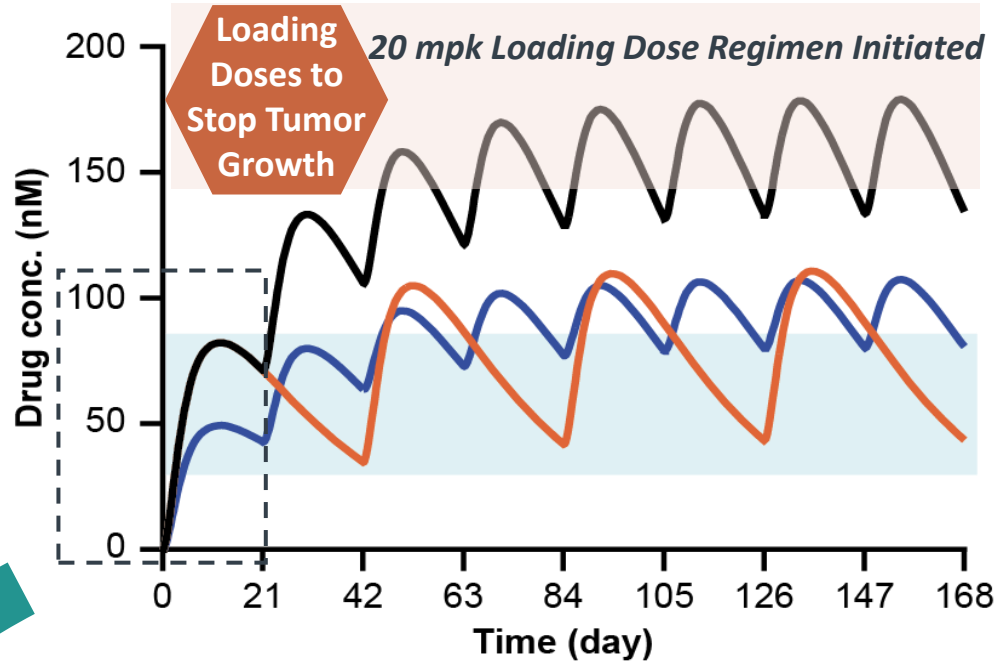


Symbols: Observed (PK data generated using ELISA)

Lines: mPBPK model-predicted

Cycle 3 mean plasma cleaved drug PK (e.g., model-predicted maximum) is <5% of mean Cmax of intact drug

Analysis of Cleaved ADG126 Supports Increased Clinical Efficacy in anti-PD1* Combination with Higher, More Frequent & Repeat Dosing



10 mpk Q3W
6 mpk Q3W
10 mpk Q6W

EC_{90} range of cleaved ADG126 for human T cell binding

ADG126 + Pembrolizumab (NCT05405595)	Dose escalation + Dose expansion				
	Safety (TRAEs)			Efficacy	
ADG126 Dosing Regimen	Patients Dosed[1] (N=46)	**≥ G3 TRAEs***	Discontinuation Rate due to TRAEs	Patients Evaluable[2] (N=37)	**DCR**
6 mg/kg Q3W	5	**20%**	0%	5	**20%**
10 mg/kg Q6W	17	**6%**	0%	16	**56%**
10 mg/kg Q3W	24	**13%**	0%	16	**75%**

* SITC 2023. Data cutoff: August 29, 2023.

[1] Dosed: Patient received at least one dose, used for safety evaluation

[2] Evaluable: Patient received at least one tumor assessment, used for efficacy evaluation

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2024 Milestones

- Data from ongoing Ph 1b/2 clinical trial of masked, anti-CTLA-4 SAFEbody ADG126 in combination dose with pembrolizumab, including dose expansion cohorts in MSS CRC:
  - Follow up of Part 1 evaluable patients at 10 mg/kg Q3W (n= 12) and 10 mg/kg Q6W (n=10)
  - Additional patients from Part 2 at 10 mg/kg Q3W (n=12)
- Evaluation of 20 mg/kg loading doses in combination with pembrolizumab for Project Optimus requirements, including safety data with repeat doses and dose expansion in MSS CRC (n~10)
- Data from additional patients in China for ADG126 in combination with pembrolizumab in MSS CRC (n≥10)
- Additional technology licensing agreement(s) and/or milestone(s)

Scientific Rationale

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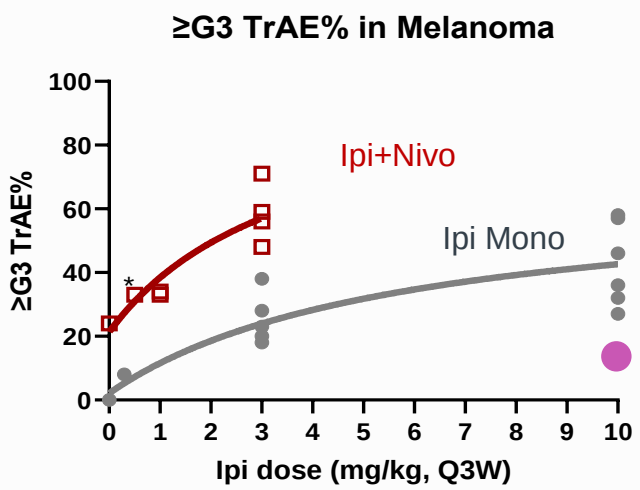
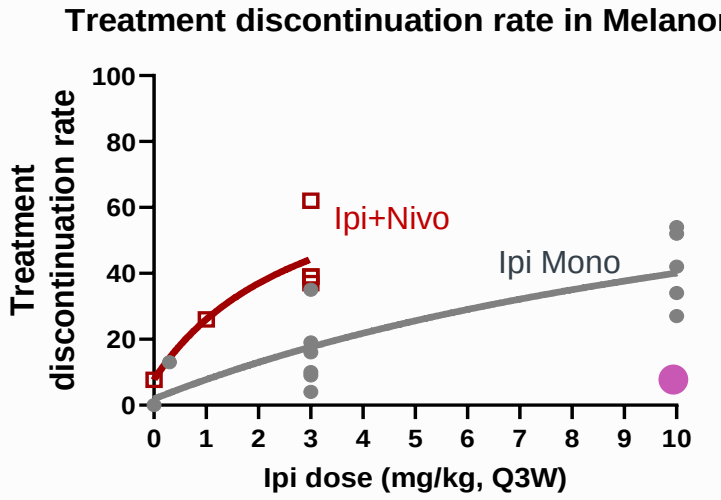
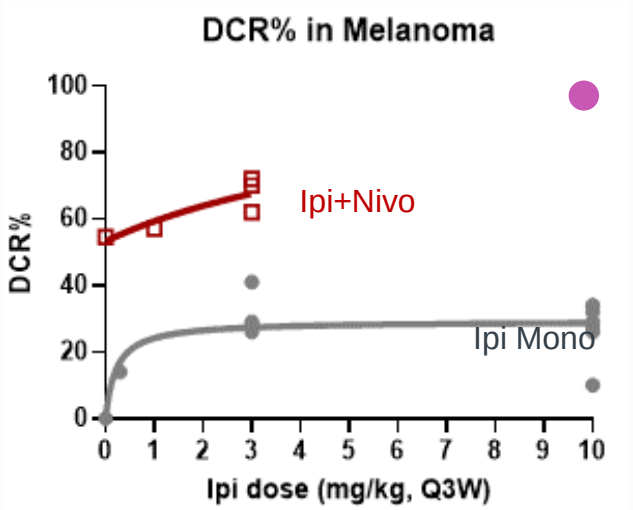
Published Ipilimumab (Ipi) Data Show High Dose-dependent Toxicity and Efficacy, Exaggerated in Combination with Nivo, but ADG126 Is Exceptional







* Ipi at 1mpk Q6W was graphed as 0.5mpk Q3W

Dose escalation and expansion data from 10 mg/kg ADG126 Q3W in combo with anti-PD-1 for patient w/o liver and peritoneal Mets

- Stronger dose-dependent increase in ≥G3 TRAEs relative to efficacy for Ipi monotherapy
- The dose-dependent efficacy and toxicity are much stronger in combo therapy, despite a 3-fold reduction in Ipi dose
- ADG126 successfully decouples safety from efficacy despite a 10-fold increase in dose of 126 vs Ipi, showing 100% DCR and <15% G3 TRAEs and <10% discontinuation rate in MSS CRC* at 10 mpk q3w (shown with purple dots)

Publications on file.

Adagene's View of Anti-CTLA-4 Therapy: Synergy to Combine CTLA-4-Mediated Treg Depletion with Teff via PD-1

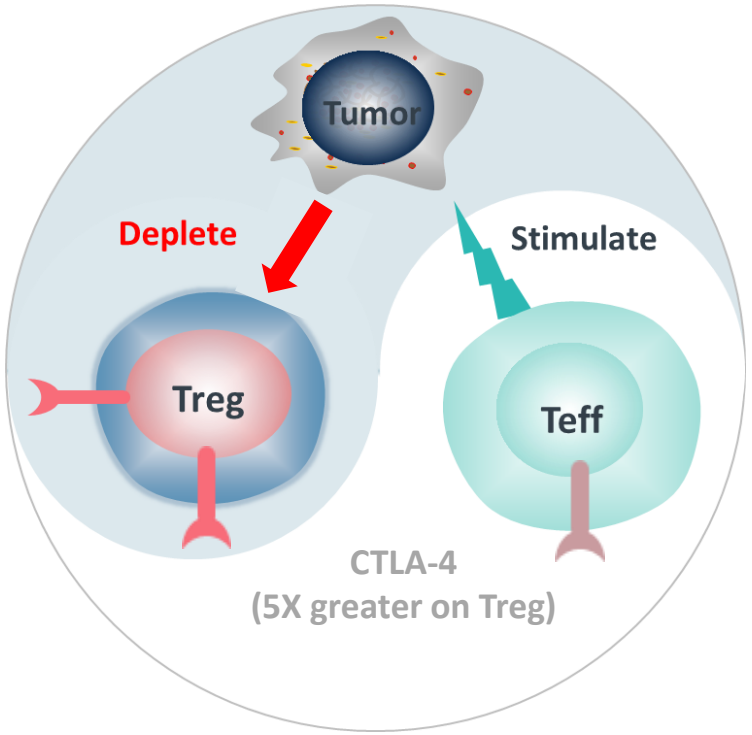
Adagene View

Deplete CTLA-4-mediated Intratumoral Treg Cells

Fundamental Biology

Constitutively expressed CTLA-4 on Tregs in TME

Stimulate PD-1 mediated $CD8^+$ T effector cell



Traditional View

Stimulate CTLA-4-mediated $CD4/8^+$ T effector Cells?

Fundamental Biology

Transiently expressed CTLA-4 on Teff For priming/activation

Tumor Specific

T effector ($CD8^+$ via PD-1) and ($CD4^+$ via CTLA-4) ↑

Tregs ($CD4^+$ via CTLA-4) ↓

Leach, DR, Krummel, MF, Allison, JP. et al. Enhancement of antitumor immunity by CTLA-4 blockade. Science. 1996;271:1734-6; Marabelle, A. et al. Depleting tumor-specific Tregs at a single site eradicates disseminated tumors. J. Clin.Invest. 2013; 123: 2447-2463; Selby, M.J. et al. Anti-CTLA-4 Antibodies of IgG2a Isotype Enhance Antitumor Activity through Reduction of Intratumoral Regulatory T Cells. Cancer Immunol. 2013;RES.1:32-42 ; Simpson, T.R. et al. Fc-dependent depletion of tumor-infiltrating regulatory T cells co-defines the efficacy of anti–CTLA-4 therapy against melanoma. J.Exp.Med. 2013;210:1695-710; Bulliard, Y. et al. Activating Fc receptors contribute to the antitumor activities of immunoregulatory receptor-targeting antibodies. J.Exp.Med. 2013;210:1685-93; Sharma, A. et al. Anti-CTLA-4 Immunotherapy Does Not Deplete FOXP3þ Regulatory T Cells (Tregs) in Human Cancers. Clin.Cancer.Res. 2019:25(4):1233-1238; Sanmamed, F and Chen, L. Leading edge perspective a paradigm shift in cancer immunotherapy: from enhancement to normalization. Cell. 2019;176(3):677; Marangoni F, Zhakyp A, Corsini M, et al. Expansion of tumor-associated Treg cells upon disruption of a CTLA-4-dependent feedback loop[J]. Cell. 2021;184(15):3998-4015.

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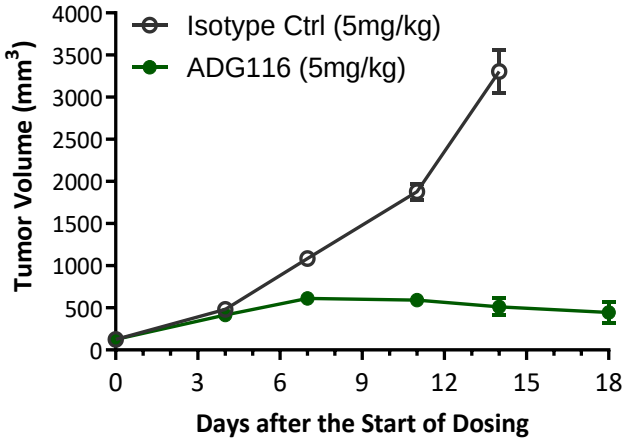
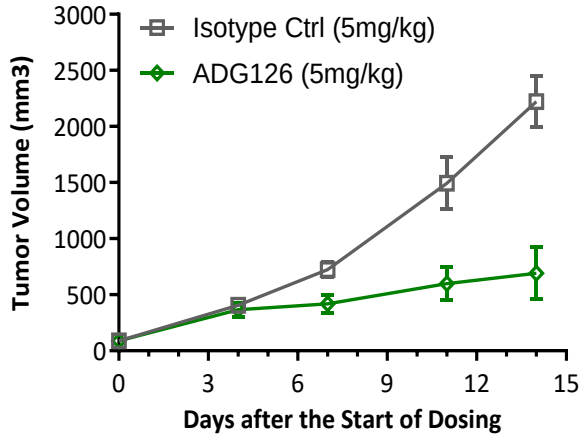
Species Cross-Reactive ADG126/116 Show Robust Anti-Tumor Efficacy and CTLA-4 Mediated Intratumoral Treg Depletion via Strong ADCC/ADCP Effect

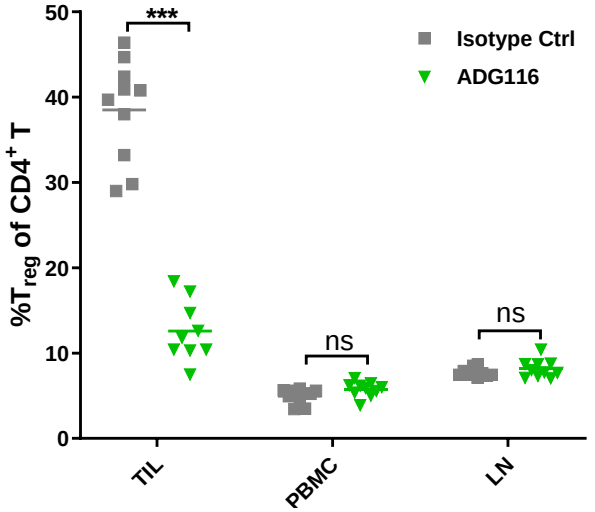
Antitumor efficacy of ADG116 in CT26 Cancer Model



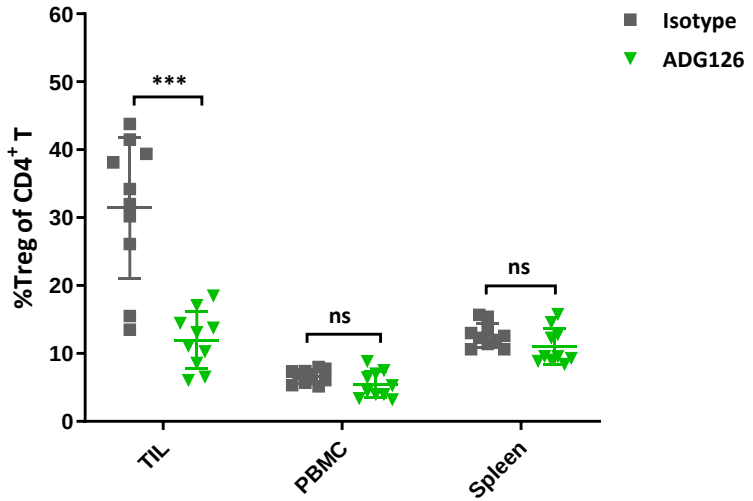
Antitumor efficacy of ADG126 in CT26 Cancer Model



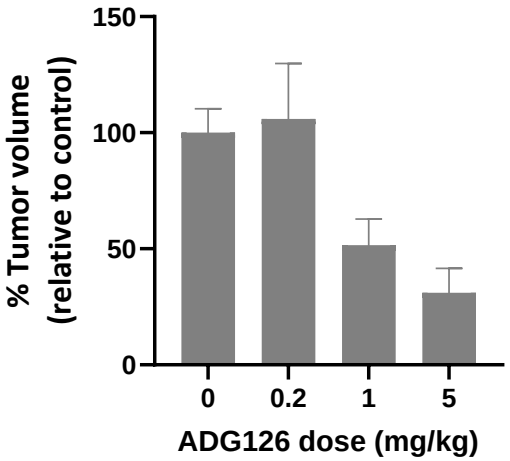
Changes of T_{reg} upon ADG116 treatment



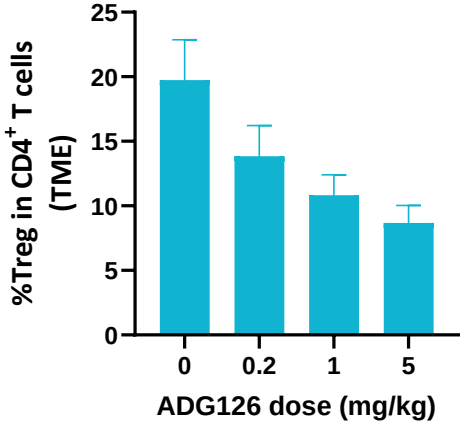
Changes of T_{reg} upon ADG126 treatment



Tumor dose response upon ADG126 treatment



Treg depletion dose response upon ADG126 treatment



Proceedings of the American Association for Cancer Research Annual Meeting 2021; Cancer Res. 2021;81(13_Suppl):1853
J Immunother Cancer. 2019;7(Suppl 1):P788

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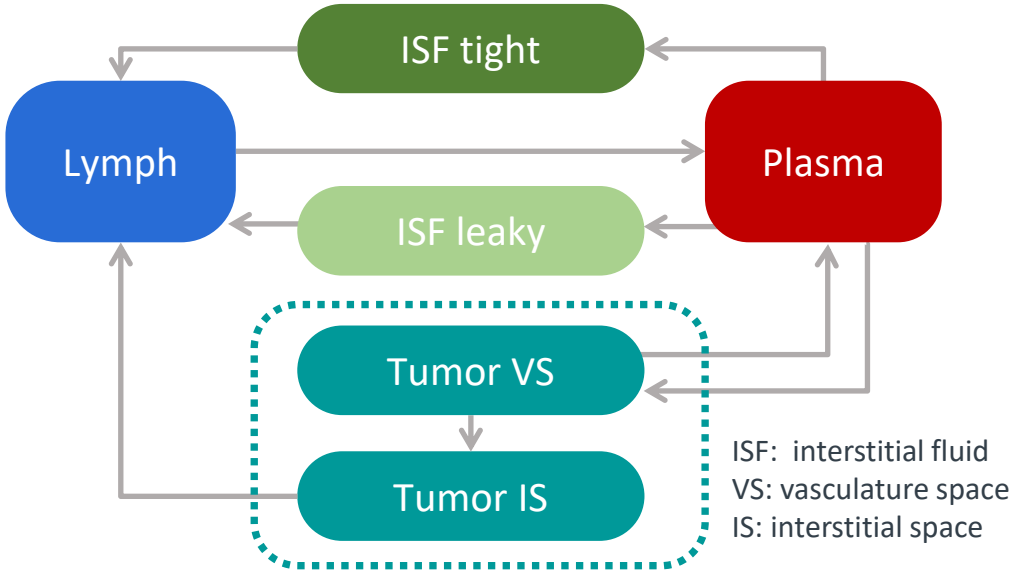
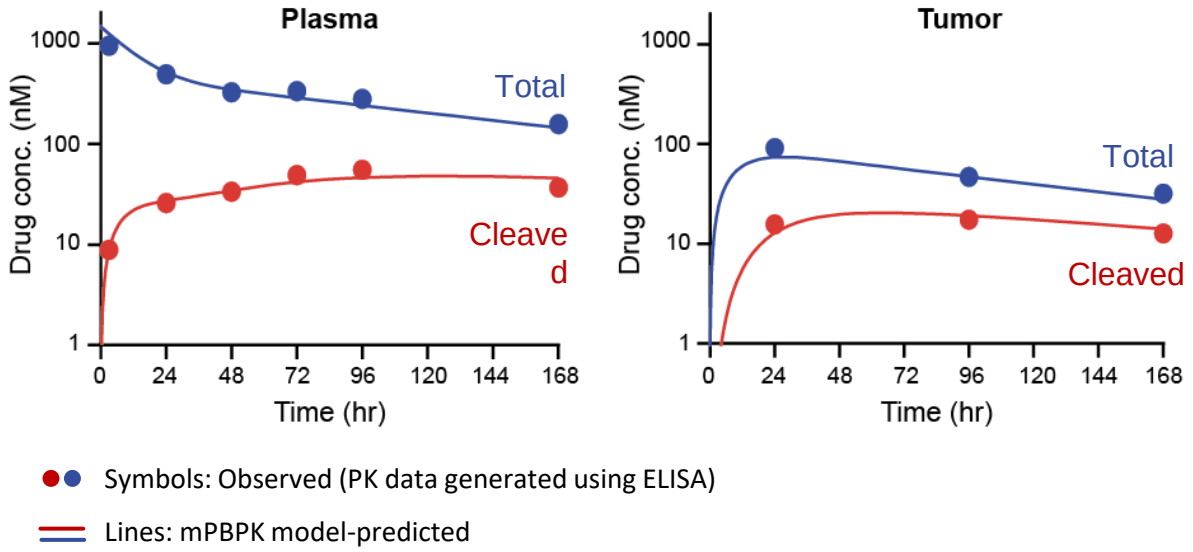
Minimal physiologically-based pharmacokinetic (mPBPK) modeling

- Known molecular transformation and mass balance for Total, Intact and Cleaved forms of ADG126 was integrated for all compartments.
- The same model structure was used for different species (e.g., mice, rat, monkey and human).



- For tumor related parameters, measured PK data (e.g., tumor PK and plasma PK) in tumor-bearing mice was modeled to estimate the tumor cleavage rate constant in mice and was kept the same for human PK modeling.

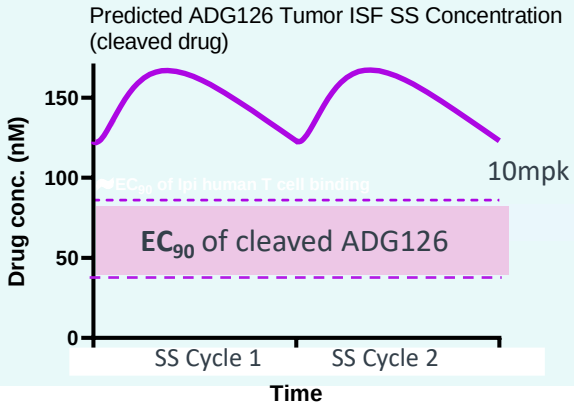


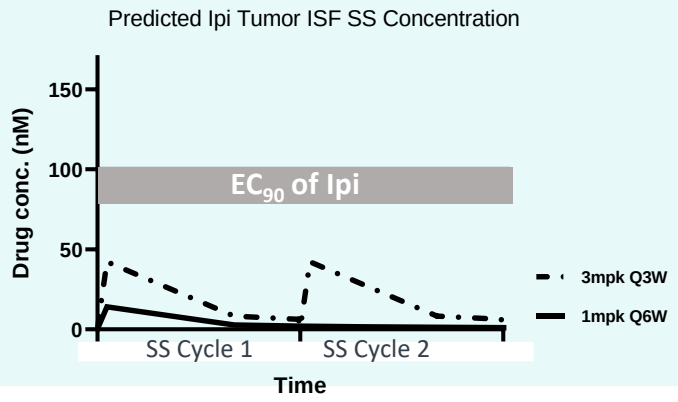
- mPBPK model can characterize plasma and tumor PK in tumor-bearing mice well after a 10 mpk single dose, allowing the estimation of tumor cleavage parameter of ADG126.

PK Modeling Quantifies the Enhanced Therapeutic Index (TI) of SAFEbody ADG126 Over Ipilimumab

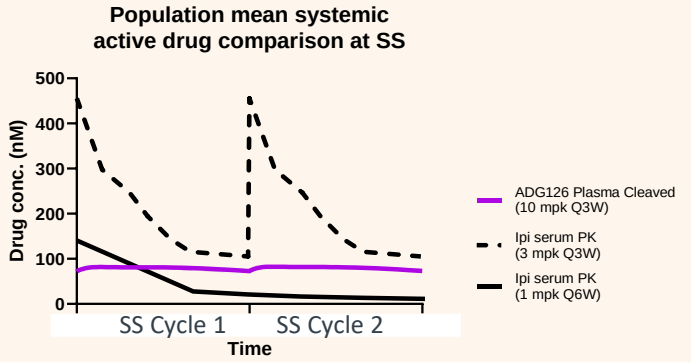
Dosage	Predicted $AUC_{ss,\ tumor\ ISF}$ fold difference	Predicted $C_{max,ss,tumor\ ISF}$ fold difference
ADG126 (10 mg/kg Q3W) vs. Ipilimumab (1 mg/kg Q6W) in combination with anti-PD-1	**~30X**	**~10X**

>90% RO (Receptor Occupancy) of activated ADG12610 mg/kg Q3W in tumor



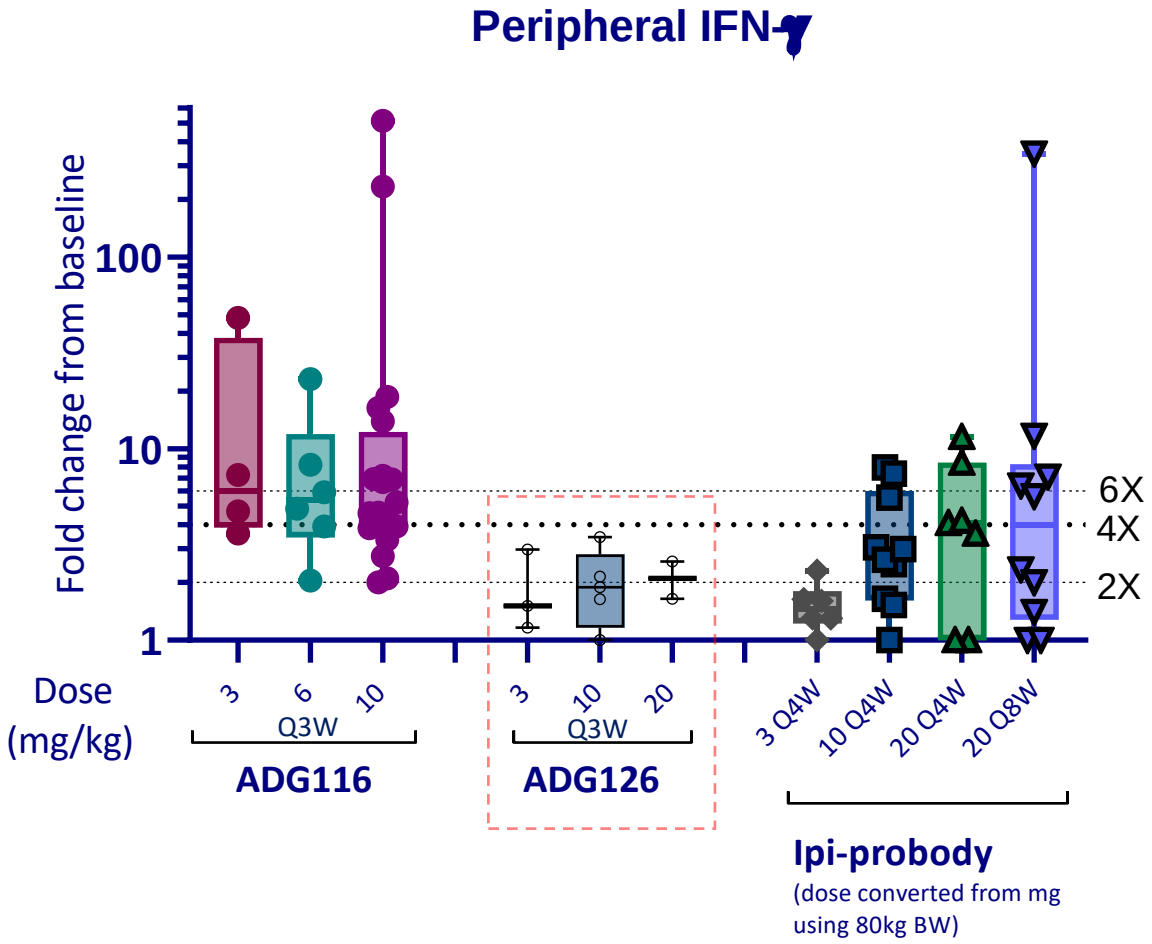


Reduced exposures of activated ADG126 in plasma



This slide contains information from various studies which are not head-to-head comparisons. Data on file. Ipi PK digitized from Sanghavi, K., et al. CPT Pharmacometrics Syst. Pharmacol. 2020;9:29-39.
Assuming ipi concentration ~10% tumor drug partition based on Ipi serum PK.

Peripheral IFN-γ Data of ADG126 Reinforce Superior Safety Profile



ADG126 is safe and well masked in circulation with reduced systemic cleavage compared to its parental ADG116 and masked 'Ipi-probody':

- ADG126 showed ~3X lower median peripheral IFN-γ levels relative to ADG116
- ADG126 showed ~2X lower median peripheral IFN-γ at 10 mpk for ADG126 @ Q3W vs. BMS-986249 (Ipi-probody) @Q4W

This slide contains information from various studies which are not head-to-head comparisons. Data on file.
BMS-986249 (Ipi-probody) data were digitized from poster 740P presented at European Society for Medical Oncology (ESMO) Congress 2022.
Ipi-Probody PK data were digitized from poster 3058 presented at 2020 ASCO Annual Meeting.

MSS CRC Opportunity

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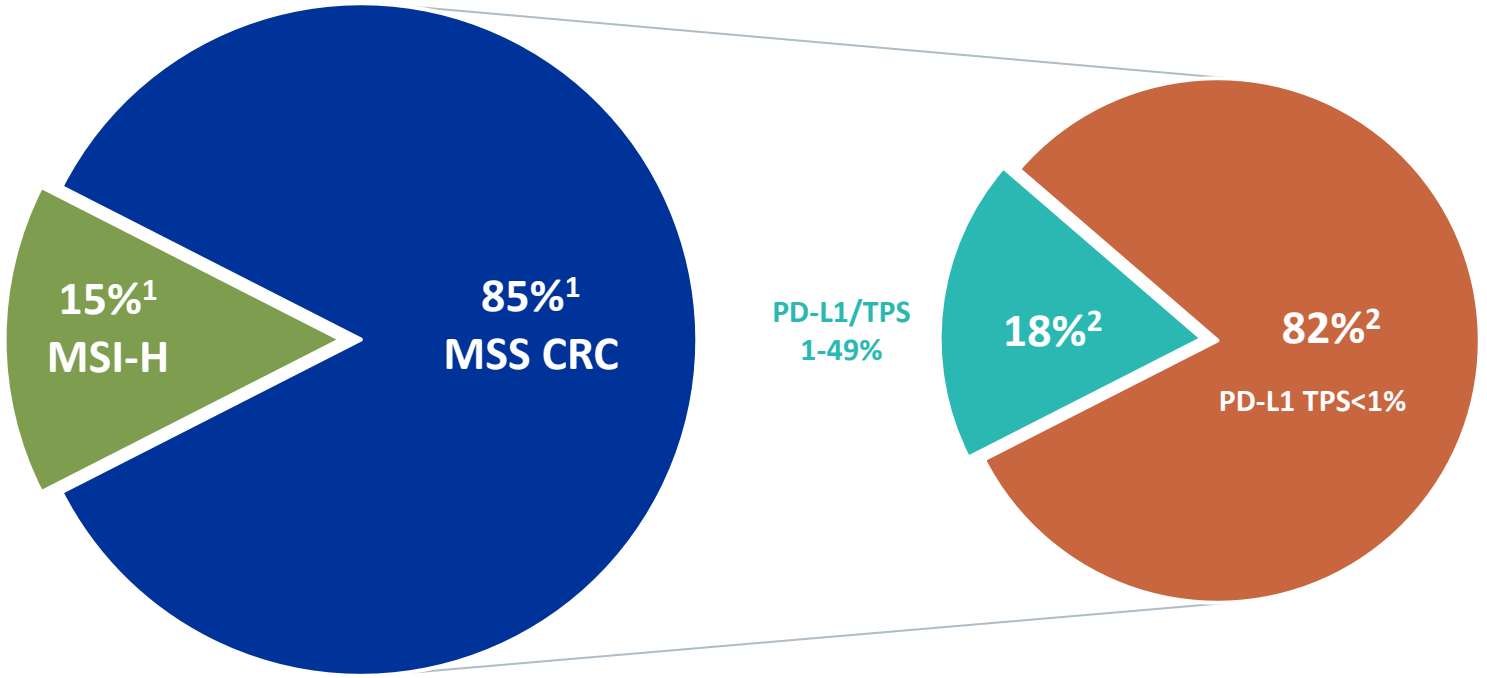
Reimagining the Anti-CTLA-4 Opportunity: MSS CRC is a High Unmet Medical Need Where CTLA-4 Mediated Treg Depletion Matters

MSS CRC	
W.W. Annual Incidence[1]	***~1.6 million (all stages)***



- **No PD-1 approved in MSS CRC; only approved in MSI-H CRC tumors**
- **PD-L1 expression is low in this cold tumor**

[1] Learn.colontown.org (MSS CRC accounts for ~85% of colorectal cancer cases across all stages and ~96% of stage 4 cases), Cancer.net
[2] Shun Xu et al. Distribution of PD-L1 expression level across major tumor types

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3L+ MSS CRC: A Promising Opportunity with High Unmet Need

	Standard of Care (FDA)				
Company	**Bayer**	**TAIHO**		**HutchMed/Takeda**	
Compounds	**Rego[1,2]**	**TAS-102[3,4]**	**Sunlight[5,6]** TAS102 plus Avastin	**Fruquintinib[7,8]**	
				w/o Liver mets	with Liver mets
ORR (%)	**1**	**2**	**6.3**	**4.3**	**4.9**
mPFS (month)	**1.9**	**2.0**	**5.6**	**3.9**	**3.7**
mOS (month)	6.4	7.1	10.8	10.8	8.6
≥G3 TRAEs	**54%**	**69%**	**72.4%**	**61.2%**	

[1]Grothey et al. Lancet. 2013;381: 303-312.; [2]FDA label, 12/10/2020; [3]Mayer et al. N Eng J Med. 2015;372:1909-1919; [4] Marcus et al. Clin Cancer Res; 23(12) June 15, 2017;2924-2927
[5]Josep Tabernero et al. 2023 ASCO Gastrointestinal; [6] Gerald W. Prager et al. N Engl J Med 2023 May 04;388(18); [7]Shukui Qin et al. 2019 CSCO; [8]Jin Li et al. JAMA. 2018;319(24):2486-2496;
[9]Andrea J. Bullock et al. 2023 ESMO-GI; [10]Anthony B et al. 2023 ASCO-GI; [11]Elena et al. 2021 ASCO; [12]E. Garralda et al. 2022 ESMO OPEN
*overall PFS ** N=87 + N=101

Failures of Immunotherapy and Their Combinations in MSS CRC

Regorafenib/Pembrolizumab Misses PFS End Point in MSS CRC, But Biomarker Analyses Are Ongoing

March 21, 2022
Ryan Scott

Article

In Partnership With: City of Hope

ESMO > Oncology News > Archive

ESMO World GI Congress 2018: IMblaze370 study Did Not Meet Its Primary Endpoint

Studying combination of atezolizumab with cobimetinib in patients with MSS/MSI-L metastatic CRC

MEDPAGE TODAY

Meeting Coverage > GICS

Immunotherapy Not Additive to Standard of Care for Untreated Metastatic CRC

— No difference in survival outcomes with add-on nivolumab to chemo, bevacizumab

by Charles Bankhead, Senior Editor, MedPage Today January 23, 2022

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SAN FRANCISCO -- Immunotherapy's limited activity against microsatellite stable (MSS) colorectal cancer (CRC) failed to improve when added to standard-of-care (SOC) therapy, a phase II randomized trial showed.

NEWS

BMS's RELATIVITY-123 Trial Fail: A Devastating End

By **Ferry Darma** - December 18, 2023

Bristol Myers Squibb announced the discontinuation of the Phase 3 RELATIVITY-123 trial, which was evaluating the fixed-dose combination of nivolumab and relatlimab as a treatment for microsatellite stable (MSS) metastatic colorectal cancer (mCRC) patients. This decision comes after an independent data monitoring committee determined that the trial was unlikely to meet its primary endpoints of overall survival.

Baseline Characteristics of Patients in DE and EXP

- Results of 46 Pts who participated in study ADG126-P001
- Three dose levels were evaluated in dose escalation phase (N = 11). The cancer types consisted of ovarian (N=1), colorectal (N=6), pancreatic (N=1), endometrial (n=1), cervical (N=1) and neuroendocrine tumor (N=1)
- Two dose schedules of ADG126 10 mg/kg were evaluated in dose expansion phase (N = 35)
- Tumor types were advanced MSS CRC (free of liver metastasis; N = 24) and other cancer types (I/O naïve and experienced; N=11)
- Majority of Pts (74.5%) have what are generally considered immunologically "cold" tumors
- Baseline characteristics of reported patients are summarized in table at right
- Median follow-ups (month) for DE and EXP patients included in this report are 10.9 (8.6-NR) and 6.7 (4.6-NR), respectively

Baseline Characteristics

Characteristics	N=46
Dose Escalation (# of pts)	11
Dose Expansion (# of Pts)	35
Age (Years), Median (Range)	60 (26-75)
Female, n (%)	21 (46%)
Race, n (%)	
Caucasian, n (%)	19 (41%)
Asian, n (%)	23 (50%)
Black or African American, n (%)	1 (2%)
Other, n (%)	3 (7%)
ECOG, n (%)	
0	20 (43%)
1	26 (56%)
Prior treatment regimens ≥3	17 (37%)
Prior immunotherapy, n (%)	6 (13%)

Data cutoff: Nov 30, 2023

Clinical Safety (TRAEs, N = 46)

- Highly manageable safety and tolerability profile; no dose-limiting toxicities
- Most TRAEs are G1 and G2, with no G4/5 TRAEs. A total of 5 Pts developed Grade 3 TRAEs (10.8%).
- Three Pts with TRAEs (G2 pneumonitis, G3 pancreatitis and G2 Diarrhea) led to study discontinuation (6.5%)
- Twelve Pts developed SAEs and 5 are treatment related, which are diarrhea (G2), secondary adrenocortical insufficiency, pancreatitis, asthenia and type 1 diabetes mellitus and hyperglycemia (G3)

TRAEs By Grade and Dose Level

ADG126 Dose Level	N	All Grades (%)	G1 (%)	G2 (%)	G3 (%)	G4-5 (%)	Discont. Rate
6 mg/kg Q3W	5	3 (60%)	1 (20%)	1 (20%)	1 (20%)	0	20%
10 mg/kg Q6W	17	12 (71%)	3 (18%)	8 (47%)	1 (6%)	0	0
10 mg/kg Q3W	24	16 (67%)	5 (21%)	8 (33%)	3 (13%)	0	8%

Data cutoff: Nov 30, 2023

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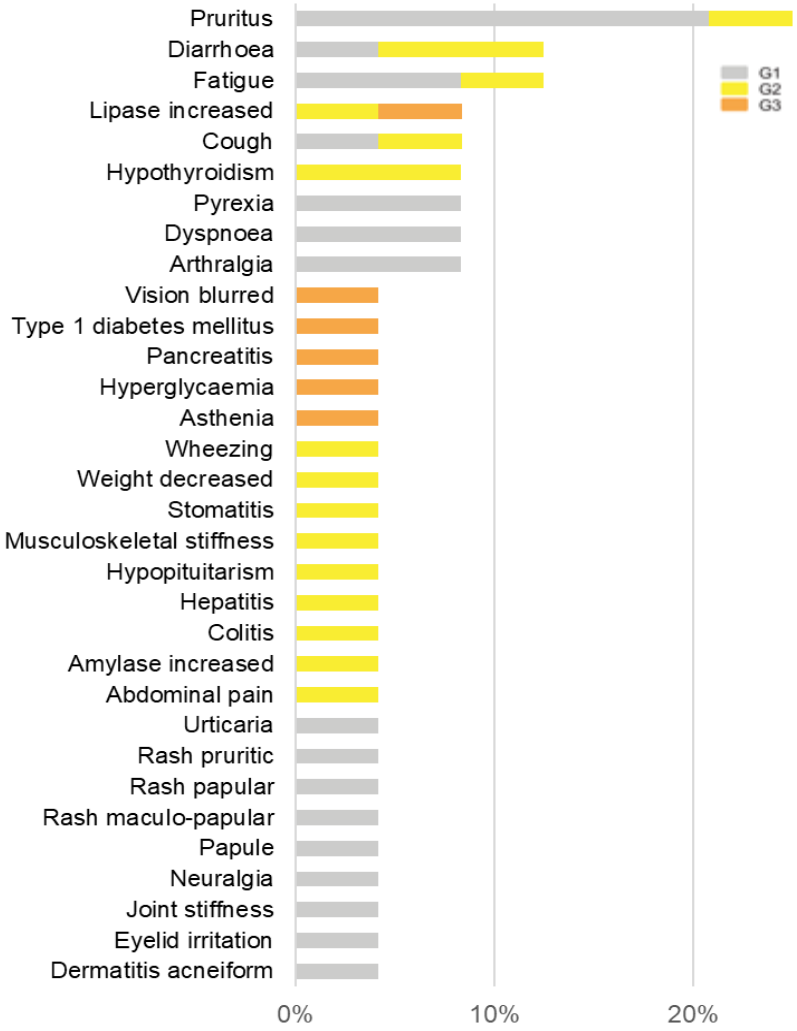
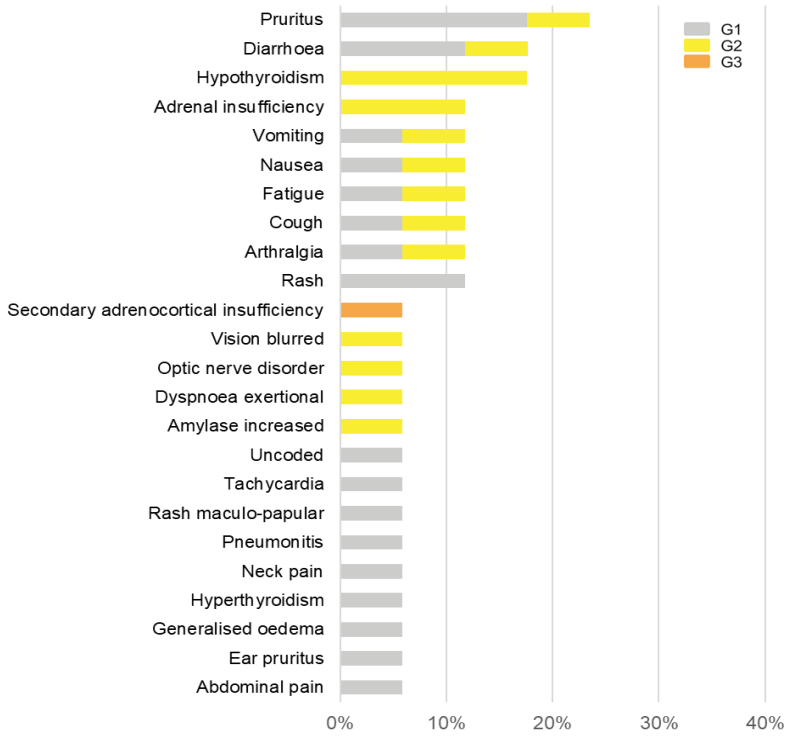
Safety ADG126 + Pembrolizumab Combo is Comparable to Pembrolizumab Alone

ADG126 10 mg/kg Q3W (N = 24)



ADG126 10 mg/kg Q6W (N = 17)



ADG126 6 mg/kg Q3W (N = 5)

TRAEs by Grade and Dose Level

ADG126 Dose Level	N	All Grades (%)	G1 (%)	G2 (%)	G3 (%)	G4-5 (%)	Discont. Rate
6 mg/kg Q3W	5	3 (60%)	1 (20%)	1 (20%)	1 (20%)	0	20%
10 mg/kg Q6W	17	12 (71%)	3 (18%)	8 (47%)	1 (6%)	0	0
10 mg/kg Q3W	24	16 (67%)	5 (21%)	8 (33%)	3 (13%)	0	8%

Data cutoff: Nov 30, 2023

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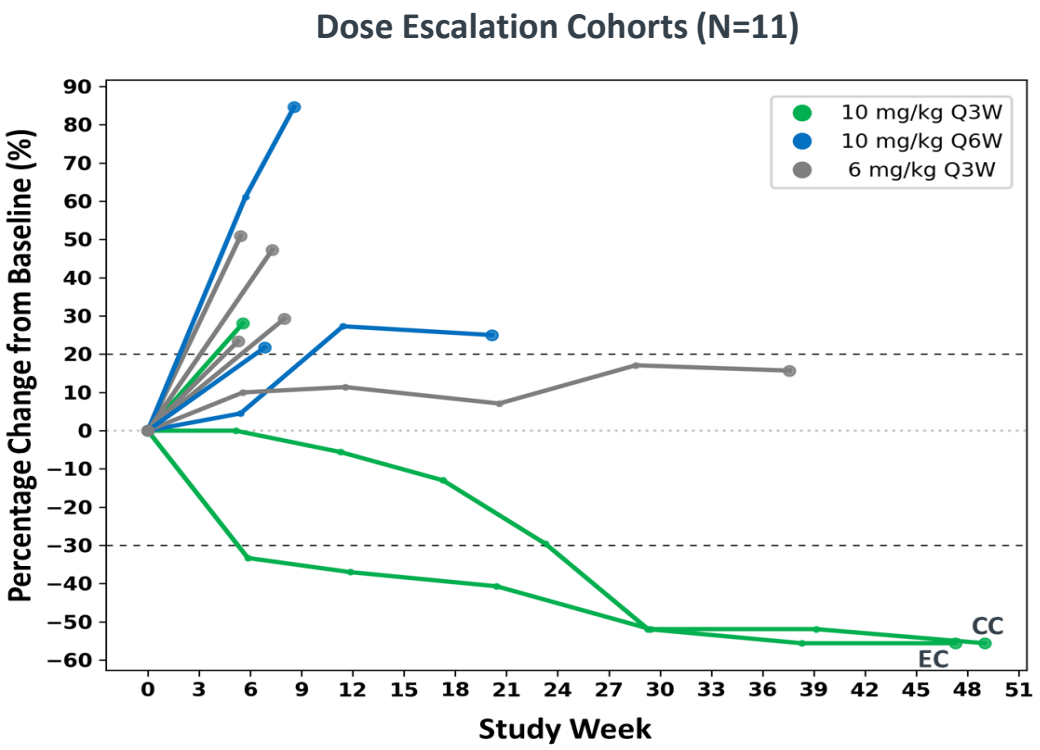
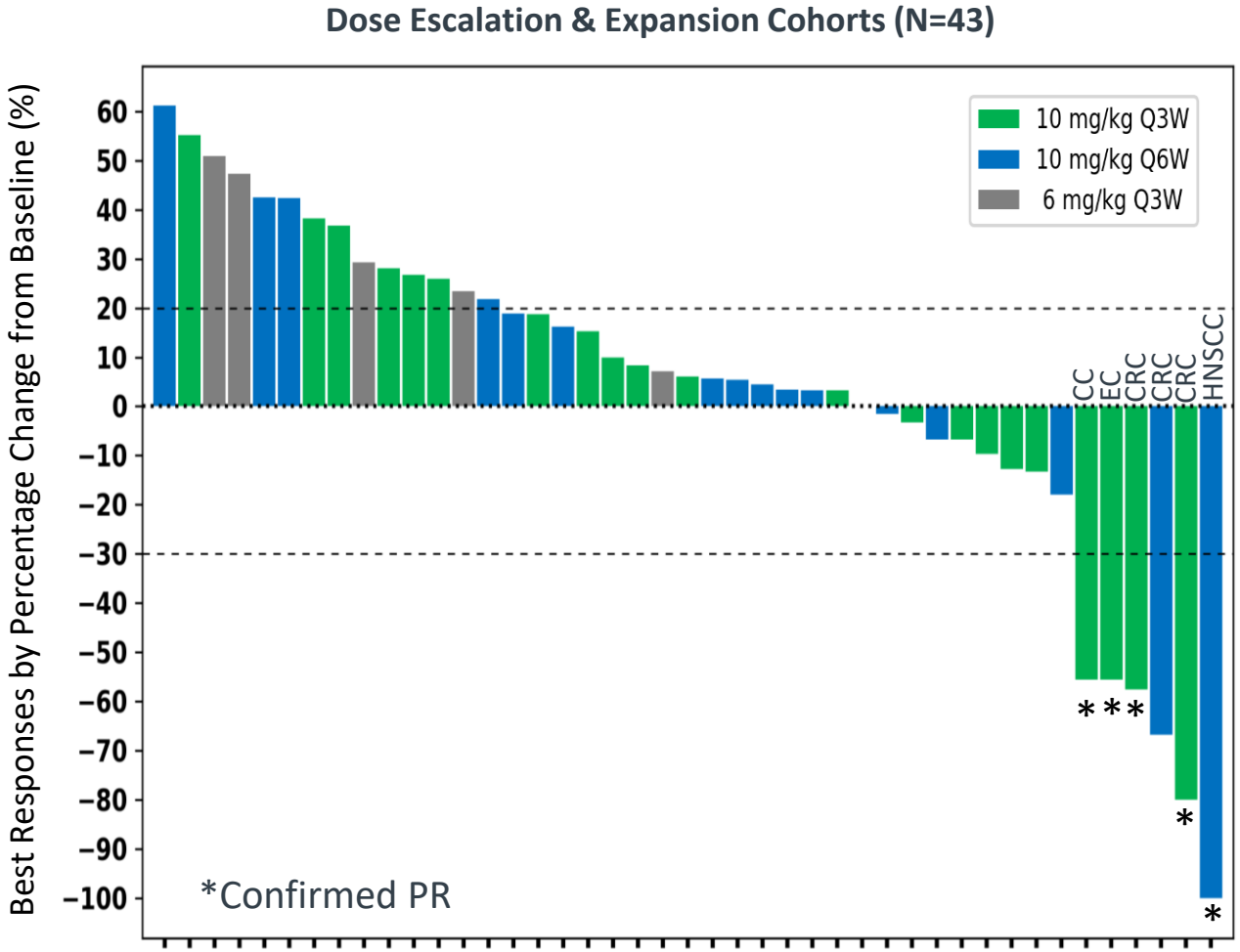
Efficacy Data of Evaluable Subjects from the Combo Dose Escalation & Expansion Cohorts





- Four of five confirmed PRs are from 10 mg/kg Q3W cohorts

Data cutoff: Nov 30, 2023

Clinical Efficacy of Patients with MSS CRC (Free of Liver Mets) in Dose Expansion

MSS CRC Patients Baseline Characteristics

CRC Patients Characteristics	N=24
Age (Years; median range)	60 (41-75)
Female, n (%)	12 (50%)
Race, n (%)	
Caucasian, n (%)	9 (38%)
Asian, n (%)	15 (62%)
Other	-
ECOG, n (%)	
0	9 (38%)
1	15 (62%)
With peritoneal metastasis, n (%)	8 (33%)
Prior Treatment ≥3	10 (42%)
Prior immunotherapy, n (%)	0

Summary of Response Rate in Evaluable MSS CRC Patients

Response Rate of MSS CRC		
ADG126 Dose and subset (N)	**10mpk Q3W** (12)	**10mpk Q3W w/o peritoneal metastasis** (9)
Confirmed ORR, % (95% CI)	**17** (2-48)	**22** (3-60)
BoR, N (%)		
PR	**2** (17)	**2** (22)
SD	**7** (58)	**7** (78)
DCR (CR+PR+SD), % (95% CI)	**75** (43-95)	**100** (66-100)

cPR: confirmed partial response. PFS: Progression-free survival. BoR: Best of Response. DCR: Disease control rate. NR: Not reached

Data cutoff: Nov 30, 2023

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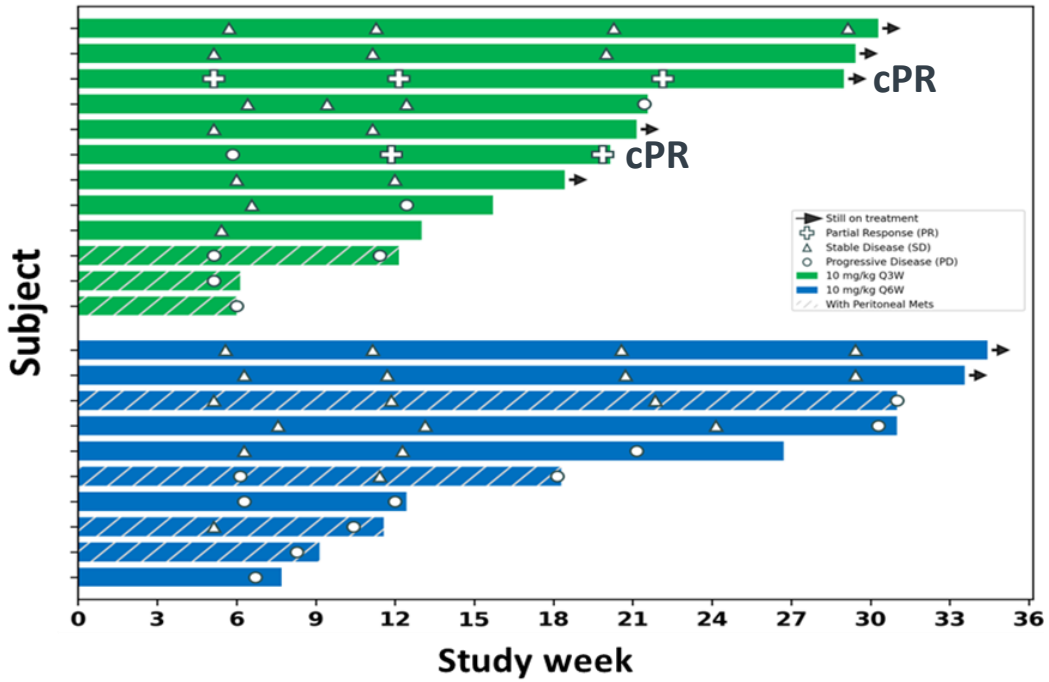
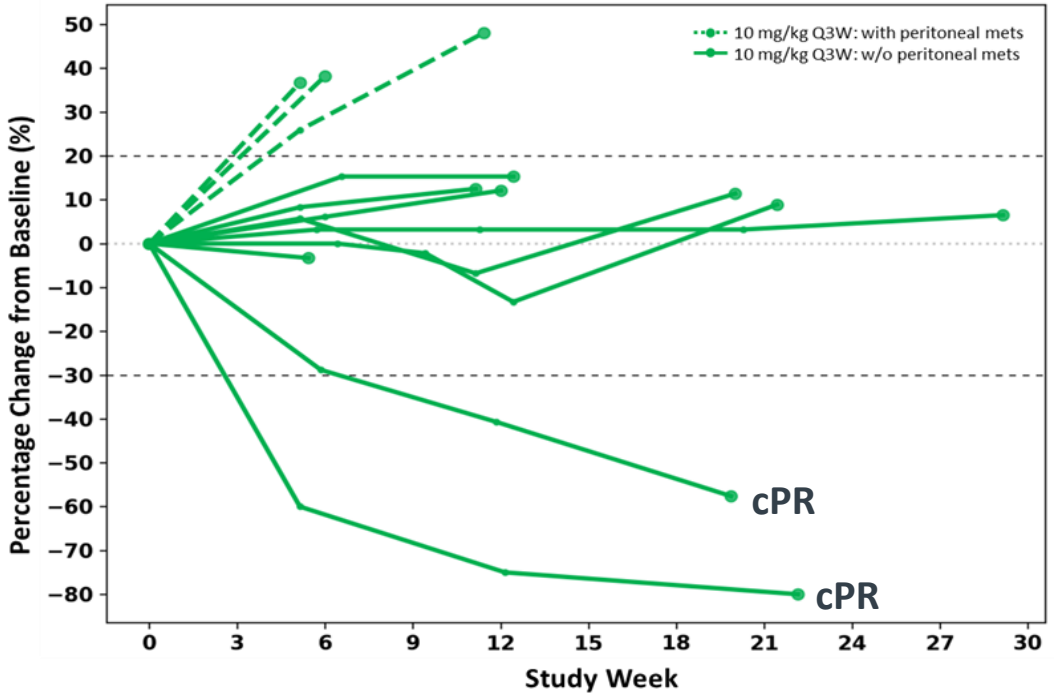
Clinical Efficacy of Patients with MSS CRC (Free of Liver Mets) in Dose Expansion

Duration of Treatment of MSS CRC Pts by 10mg/kg Q3W and Q6W of ADG126/pembrolizumab
(N=22 efficacy evaluable pts with at least one CT scan)

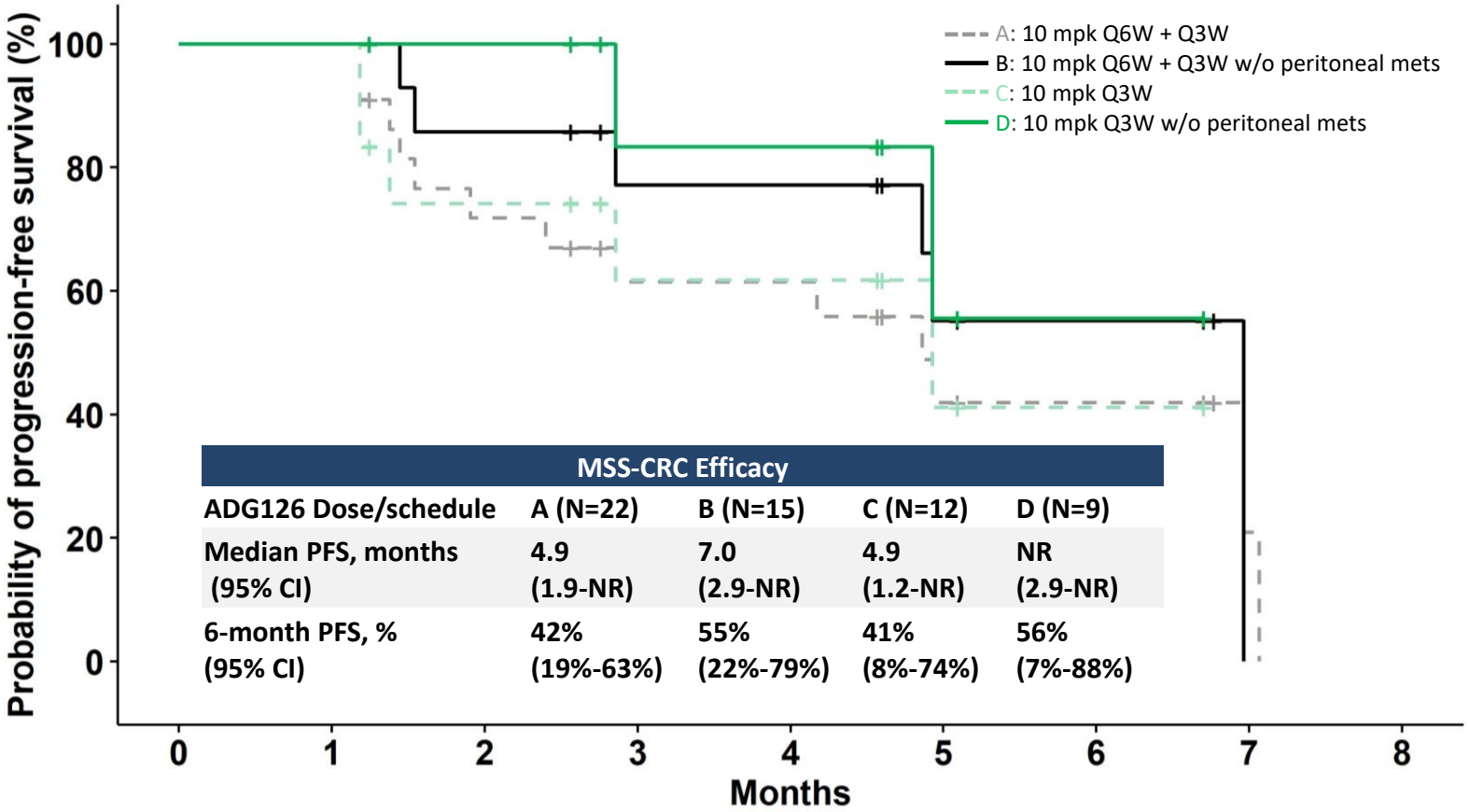


Spider plot of evaluable MSS CRC Pts treated by 10 mg/kg Q3W ADG126/Pembrolizumab (N = 12)



Data cutoff: Nov 30, 2023

PFS Summary of Efficacy in Evaluable MSS-CRC Pts (N=22)



MSS-CRC Efficacy				
ADG126 Dose/schedule	A (N=22)	B (N=15)	C (N=12)	D (N=9)
Median PFS, months (95% CI)	4.9 (1.9-NR)	7.0 (2.9-NR)	4.9 (1.2-NR)	NR (2.9-NR)
6-month PFS, % (95% CI)	42% (19%-63%)	55% (22%-79%)	41% (8%-74%)	56% (7%-88%)

Number at risk

A	22	22	15	11	11	6	5	1	0
B	15	15	12	9	9	5	4	0	0
C	12	12	8	5	5	2	1	0	0
D	9	9	8	5	5	2	1	0	0

Data cutoff: Nov 30, 2023

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Case Study : ADG126 10 mpk Q3W + Pembro 3L MSS CRC Patient: Confirmed PR and Reduced Liver Lesions

Tumor Type:

Female, 66 years old

Advanced rectal adenocarcinoma stage IV with lymph and lung metastasis

- KRAS WT, BRAF normal, MSS, TMB 11.07muts/mb

Prior Therapies:

Previously received 2 lines of therapies:

- FOLFIRI + Vectibix
- Clinical trial G1290 with Rivoceranib + SOC Lonsurf

Dose Regimen:

ADG126 **10 mg/kg Q3W** + Pembro 200 mg Q3W (5 cycles)

Data cutoff: Nov 30, 2023

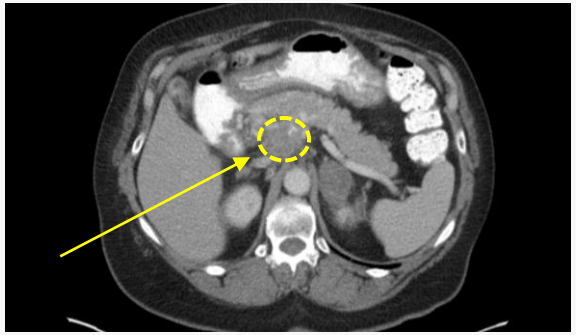
ADAGENE

Case Study Continued: ADG126 10 mpk Q3W + Pembro 3L MSS CRC Patient: Confirmed PR and Reduced Liver Lesions

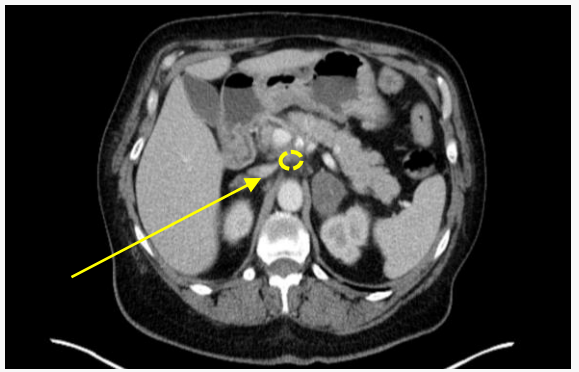
	Lesion #	Location	Baseline	Week 6	Week 12	Week 21
Target lesion (mm)	TL#1	Right lung	14 mm	10	8	8
	TL#2	Right lung	8 mm	8	6	0
	TL#3	Lymph node	22 mm	14	13	9
	TL#4	Lymph node	15 mm	10	8	8
	Total		59 mm	42 (-29%)	35 (-41%)	25 (-58%)
Non target lesions			Present	Present	Present	Present
New lesion (mm)	#1	Liver		16	8	0
	#2	Liver		12	7	6
	#3	Other		9	3	0
	Total			37	18 (-51%)	6 (-84%)
Overall response				**uPD**	**PR**	**PR**

*Based on iRECIST assessment

The treatment-induced change in the perihepatic lymph node



May 15, 2023 (Baseline)

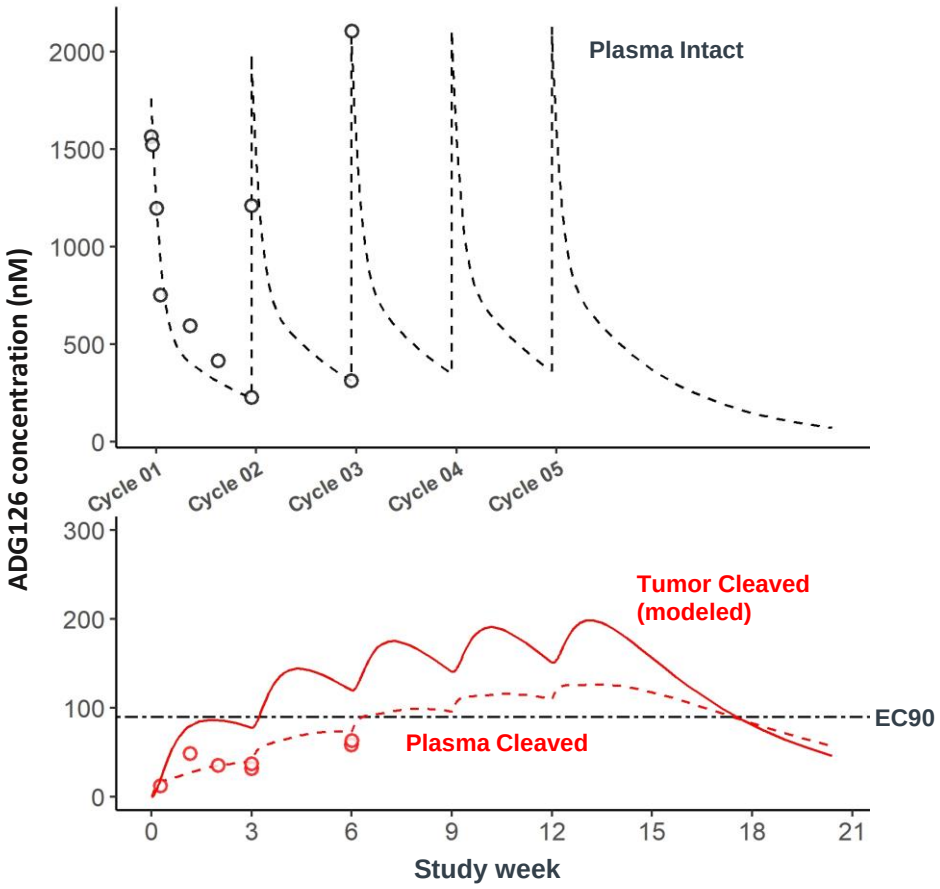


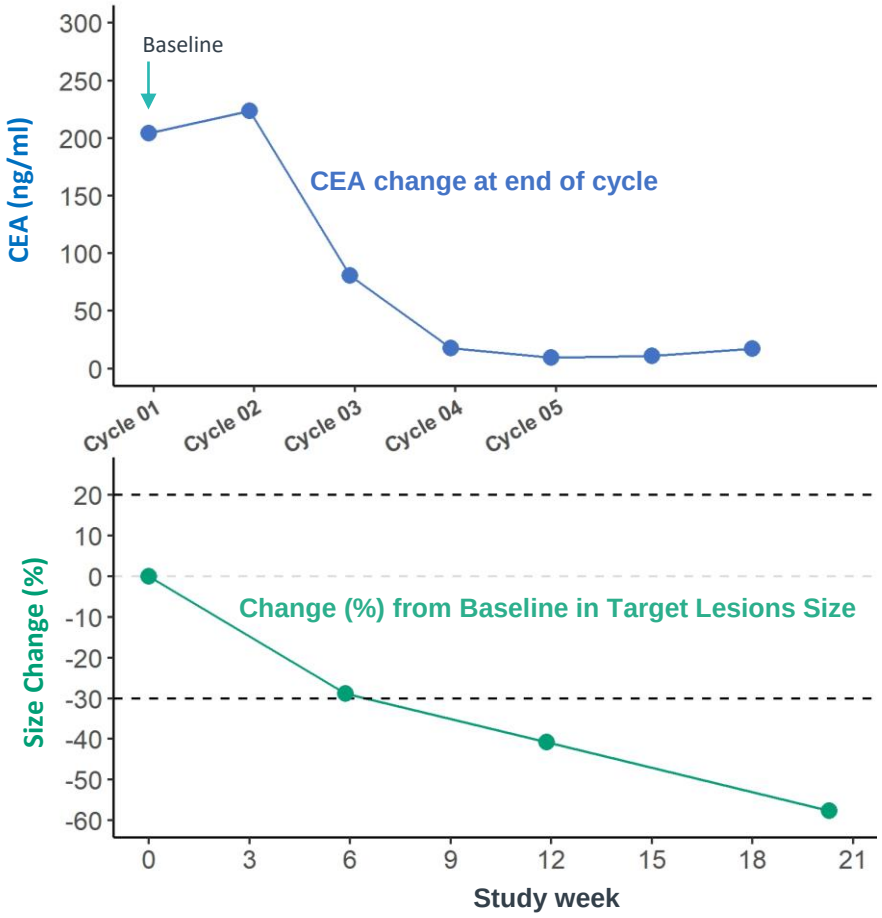
Oct 16, 2023 (week 21)

Courtesy of Dr Tammy Lamb, Florida Cancer Specialists

Case Study Continued- CEA Decrease and Tumor Accumulation Over Time

ADG126 10 mg/kg Q3W plus Pembro





Data cutoff: Nov 30, 2023

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ADG126/Pembrolizumab Demonstrates a Superior Safety Profile with Similar ORR but longer PFS to Bot/Bal in MSS CRC

	Safety (TRAEs)		
	Patients Dosed	≥ G3 TRAE	Discontinuation Rate
ADG126 10 mg/kg Q3W + Pembrolizumab 200 mg Q3W	24[#]	**13%[+]**	**8%**
Botensilimab 1 or 2 mg/kg Q6W + Balstilimab 3 mpk Q2W*	101	**39%**	**33%**

	Efficacy				
	Patient Group	Evaluable subjects	ORR	DCR	PFS month (95% CI)
ADG126 10 mg/kg Q3W + Pembrolizumab 200 mg Q3W	MSS CRC w/o liver & peritoneal Mets	9	22%	100%	**NR (2.9-NR)**
	MSS CRC w/o liver Mets	12	17%	75%	**4.9 (1.2-NR)**
Botensilimab 1 or 2 mg/kg Q6W + Balstilimab 3 mpk Q2W*	MSS CRC w/o liver Mets	69	23%	80%	**4.1^ (2.8-5.5)**

[+]No G4/5 TRAEs
Two patients used infliximab for the treatment-related diarrhea/colitis
Comparison based on publicly available information and represents a non-head-to-head summary comparison. Results of a -head-to-head comparison may different significantly.

[#]For the safety evaluation, the patients of other cancer types are included in addition to those with MSS CRC free of liver Mets
*Bullock AJ et al., Results from an expanded phase 1 trial of botensilimab, a multifunctional anti-CTLA4, plus balstilimab for metastatic heavily pretreated MSS CRC ESMO GI 2023
^Combined dataset for those with and without liver Mets, El-Khoueiry AB et al., Results from a phase 1a/ab study of botensilimab (BOT), a novel innate/adaptive immune activator, plus balstilimab (BAL; anti-PD-1 antibody) in metastatic heavily pretreated MSS CRC ASCO GI 2023

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Conclusions

- The masked anti-CTLA-4 SAFEbody ADG126 (muzastotug) is designed to widen the therapeutic index by targeting a unique epitope of CTLA-4, precision masking for enhanced intra-tumoral Treg depletion.
- ADG126 administered at up to 10 mg/kg Q3W with repeat dosing in combination with pembrolizumab is well tolerated with 13% G3 TRAEs, 8% discontinuation rate and no G4/5 TRAEs or DLT.
- In dose escalation, 2 confirmed PR were observed among 3 subjects treated with 10 mg/kg Q3W ADG126/Pembro, which triggered dose expansion at this dose level.
- In dose expansion, 10 mg/kg Q3W ADG126/Pembro treatment in 12 subjects with MSS CRC (9 w/out peritoneal metastasis) resulted in 2 confirmed PRs, and reduction of new liver lesions. This triggered further expansion into Stage 2 of the Simon's 2-stage design at this dose level.
- The favorable safety profile of ADG126/Pembro allows for continued treatment with repeated dosing, resulting in a long PFS ($\geq$ 7 mons), especially in MSS CRC patients without liver and peritoneal metastasis.
- These promising data support further evaluation of this potential best-in-class anti-CTLA-4 antibody ADG126 (muzastotug) in combination with pembrolizumab in MSS CRC.