MacroGenics®

Developing
Breakthrough Biologics,
Life-changing Medicines

ASCO 2019 Conference Call: Margetuximab

June 4, 2019

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Investigational Agents

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

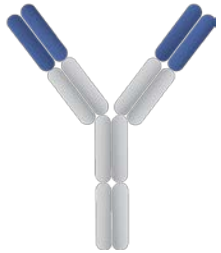
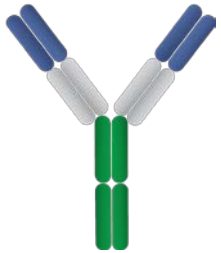
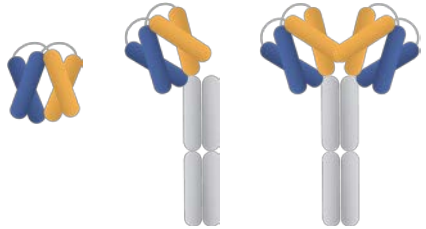
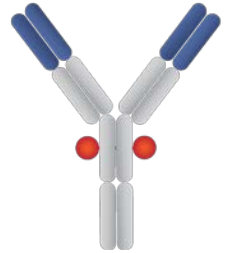
ASCO 2019 Conference Call Agenda

Introduction	Welcome & Margetuximab Overview	**Scott Koenig, M.D., Ph.D.** President & Chief Executive Officer
Breast Cancer	SOPHIA Phase 3 Study: Primary PFS Analysis	**Hope S. Rugo, M.D.** University of California San Francisco Helen Diller Family Comprehensive Cancer Center
Gastric Cancer	HER2-positive Advanced Gastric Cancer: Current Treatments & Unmet Need	**Daniel Catenacci, M.D.** The University of Chicago Medical Center
Margetuximab Program	Planned Development	**Jon Wigginton, M.D.** Senior Vice President, Clinical Development & Chief Medical Officer
Summary	Key Takeaways & Future Program Milestones	**Scott Koenig, M.D., Ph.D.** President & Chief Executive Officer
Q&A		

Committed to Developing Life-Changing Medicines

Engineering antibodies that leverage immune system to fight cancer

- MacroGenics today – engineering broad array of antibody formats
  - Nine immuno-oncology product candidates in clinical development
  - Advancing to becoming fully-integrated biopharma company

Antibody	Fc-Optimized Antibody	DART® Molecules	Antibody Drug Conjugate
			
• **MGA012 (anti-PD-1)***	• **margetuximab (anti-HER2)** • enoblituzumab (anti-B7-H3)	• flotetuzumab (CD123 x CD3) • **MGD013 (PD-1 x LAG-3)** • MGD019 (PD-1 x CTLA-4) • MGD009 (B7-H3 x CD3) • MGD007 (gpA33 x CD3)	• MGC018 (anti-B7-H3)

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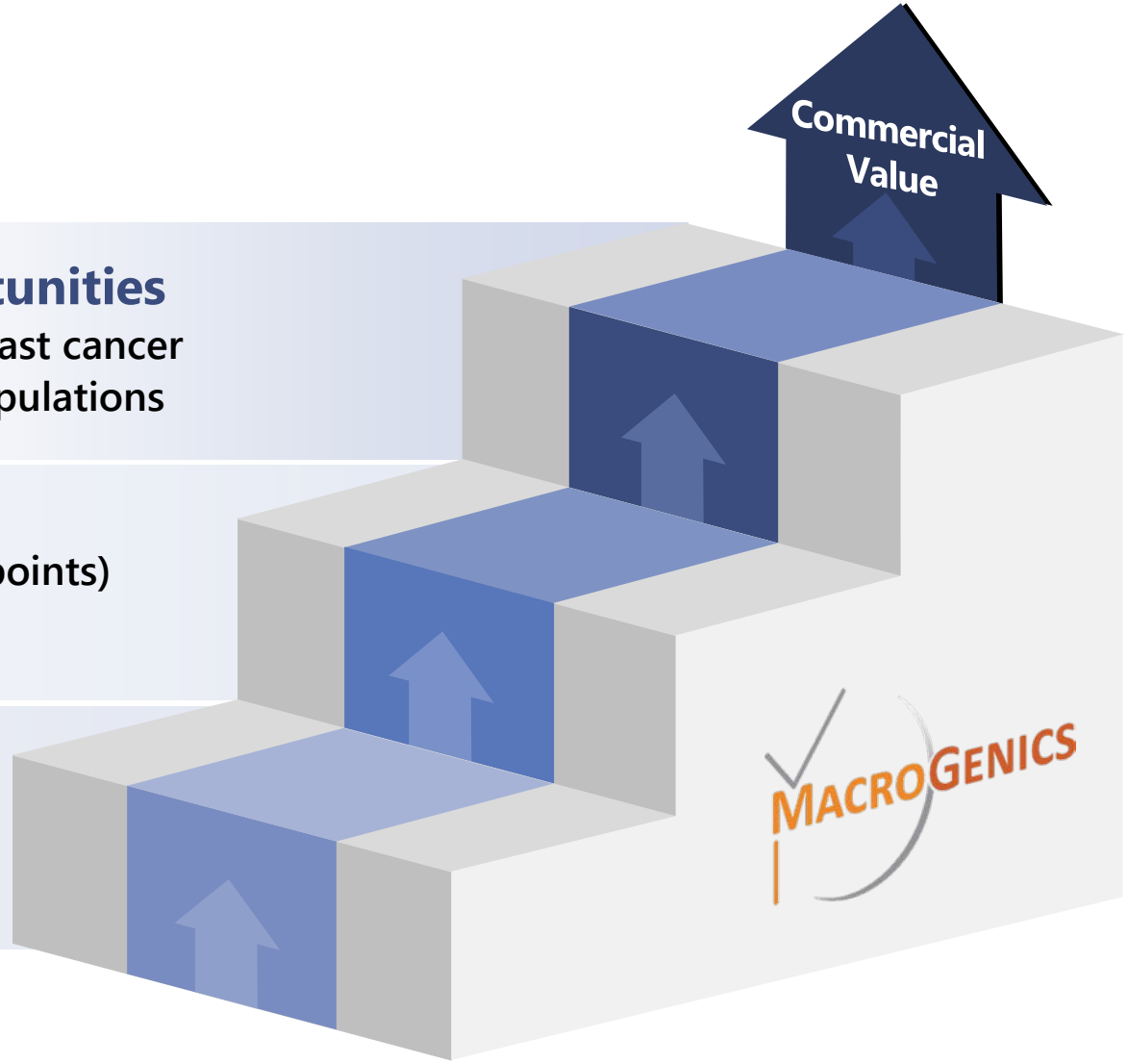
** MacroGenics retains rights to develop its pipeline assets in combination w/MGA012 (INCMGA0012) and to manufacture a portion of global clinical and commercial supply needs of MGA012.*

Fc Optimization Platform Designed to Enhance Innate and Adaptive Immunity

- Selected known target for platform validation (**HER2: margetuximab**)
  - Reported **positive Phase 3 SOPHIA study**
  - Expanding to other HER2-positive cancers
- Applying technology to novel target (B7-H3: enoblituzumab)
- Combining Fc-optimized antibodies with checkpoint inhibitors to boost anti-tumor immunity
  - MGA012 (anti-PD-1)
  - MGD013 (PD-1 x LAG-3)

Capturing Full Potential of Margetuximab

Planned development strategy



3 **Future Opportunities**

- Neoadjuvant breast cancer
- Other HER2+ populations

2 **Follow-on Indications**

- 1st Line Gastric Cancer (w/checkpoints)
  - IND active, CFDA engaged
  - Ph. 2/3 initiation in 2H2019

1 **Potential Approval**

- 3rd/4th Line mBC (w/chemo)

SOPHIA

SOPHIA Phase 3 Study: Primary PFS Analysis

Hope S. Rugo, M.D.

Clinical Professor of Medicine, UC San Francisco's Helen Diller Comprehensive Cancer Center

SOPHIA Primary PFS Analysis: A Phase 3 Study of Margetuximab + Chemotherapy vs Trastuzumab + Chemotherapy in Patients With HER2+ Metastatic Breast Cancer After Prior Anti-HER2 Therapies

Hope S. Rugo, MD,[1] Seock-Ah Im, MD, PhD,[2] Gail S. Wright, MD, FACP, FCCP,[3] Santiago Escrivá-de-Romaní, MD,[4] Michelino De Laurentiis, MD, PhD,[5] Javier Cortes, MD, PhD,[6] Shakeela W. Bahadur, MD,[7] Barbara B. Haley, MD,[8] Raul H. Oyola, MD,[9] David A. Riseberg, MD,[10] Antonino Musolino, MD, PhD, MSc,[11] Fatima Cardoso, MD,[12] Giuseppe Curigliano, MD, PhD,[13] Peter A. Kaufman, MD,[14] Mark D. Pegram, MD,[15] Sutton Edlich,[16] Shengyan Hong, PhD,[16] Edwin Rock, MD, PhD,[16] William J. Gradishar, MD,[17] on behalf of the SOPHIA Study Group

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Abstract #1000
PRESENTED AT: 2019 ASCO ANNUAL MEETING
#ASCO19

Persistent Unmet Need in HER2+ MBC After Anti-HER2 Therapy

- Current standard of care for HER2-positive MBC
  - First-line: trastuzumab and pertuzumab with chemotherapy[1-3]
  - Second-line: T-DM1[4,5]
- After the above therapies, there is no recognized standard of care
  - Subsequent therapies are poorly defined, including sequential chemotherapy with trastuzumab and/or lapatinib[6,7]
  - Continued anti-HER2 therapy after progression is generally preferred, in combination with chemotherapy[8-11]

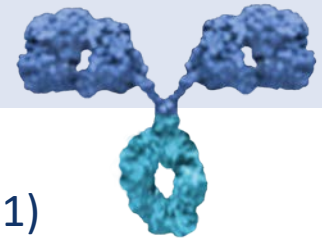
HER2=human epidermal growth factor receptor 2; MBC=metastatic breast cancer; T-DM1=ado-trastuzumab emtansine.

1. Baselga J, et al. *N Engl J Med.* 2012;366(2):109-119. 2. Swain SM, et al. *Lancet Oncol.* 2013;14(6):461-471. 3. Swain SM, et al. *N Engl J Med.* 2015;372(8):724-734. 4. Verma S, et al. *N Engl J Med.* 2012;367(19):1783-1791. 5. Diéras V, et al. *Lancet Oncol.* 2017;18(6):732-742. 6. Giordano SH, et al. *J Clin Oncol.* 2018;36(26):2736-2740. 7. Cardoso F, et al. *Ann Oncol.* 2018;29(8):1634-1657. 8. von Minckwitz G, et al. *J Clin Oncol.* 2009;27(12):1999-2006. 9. von Minckwitz G, et al. *Eur J Cancer.* 2011;47(15):2273-2281. 10. Geyer CE, et al. *N Engl J Med.* 2006;355(26):2733-2743. 11. Cameron D, et al. *Oncologist.* 2010;15(9):924-934.

Margetuximab: Fc-engineered to Activate Immune Responses

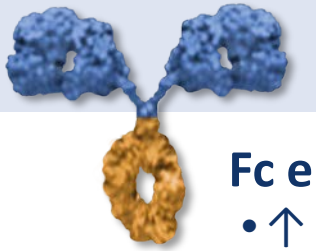
Trastuzumab

Fab:
- Binds HER2 with high specificity
- Disrupts signaling that drives cell proliferation and survival



Fc:
- Wild-type immunoglobulin G1 (IgG1) immune effector domains
- Binds and activates immune cells

Margetuximab[1,2]



Fab:
- Same specificity and affinity
- Similarly disrupts signaling

Fc engineering:
- ↑ Affinity for activating FcγRIIIA (**CD16A**)
- ↓ Affinity for inhibitory FcγRIIB (**CD32B**)

Margetuximab Binding to FcγR Variants:

Receptor Type	Receptor	Allelic Variant	Relative Fc Binding	Affinity Fold-Change
Activating	**CD16A**	158F	Lower	6.6x ↑
		158V	Higher	4.7x ↑
	CD32A	131R	Lower	6.1x ↓
		131H	Higher	↔
Inhibitory	**CD32B**	232I/T	Equivalent	8.4x ↓

1. Nordstrom JL, et al. *Breast Cancer Res*. 2011;13(6):R123. 2. Stavenhagen JB, et al. *Cancer Res*. 2007;67(18):8882-8890.

CD16A Genotype May Predict Anti-HER2 Antibody Benefit

- Two retrospective studies of HER2+ MBC[1] and early breast cancer[2] suggest patients with lower affinity CD16A-158F allele have lower PFS and ORR with trastuzumab than those homozygous for higher affinity CD16A-158VV
  - Two other retrospective studies showed no association between FcγR genotypes and outcome with adjuvant trastuzumab in early breast cancer[3,4]

- **Hypothesis**: Greater margetuximab benefit in lower binding CD16A-158F carriers
  - Increased affinity of margetuximab for CD16A-158F over trastuzumab (wild-type IgG1)

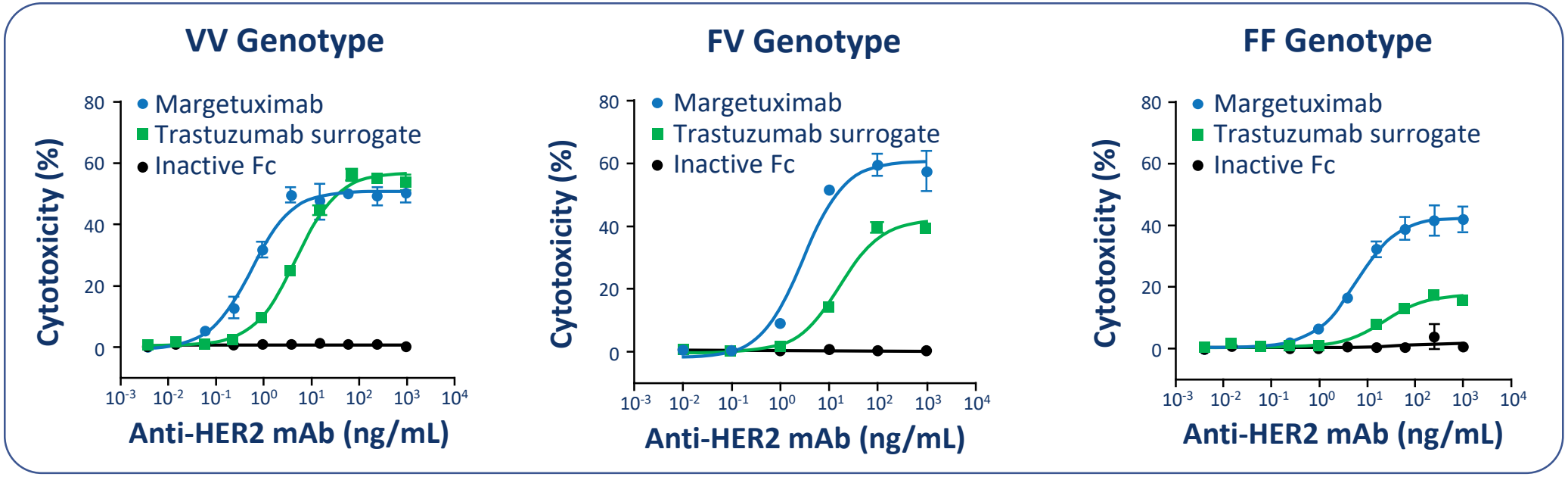
- **SOPHIA is first prospective* analysis of FcγR genotype impact on anti-HER2 antibody efficacy**

*Non-alpha allocating, exploratory analysis.
ORR=objective response rate; PFS=progression-free survival.

1. Musolino A, et al. *J Clin Oncol.* 2008;26(11):1789-1796. 2. Gavin PG, et al. *JAMA Oncol.* 2017;3(3):335-341.
3. Hurvitz SA, et al. *Clin Cancer Res.* 2012;18(12):3478-3486. 4. Norton N, et al. *Cancer Immunol Res.* 2014;2(10):962-969.

Margetuximab Enhances Innate Immunity *In Vitro*

Greater relative cytotoxicity of margetuximab with NK cells from CD16A-158F allele carriers



Preclinical Assay of Antibody-Dependent Cellular Cytotoxicity (ADCC)[1]

Effector Cells: Human NK cells from donors with CD16A genotypes 158VV, 158FV, and 158FF

Target Cells: JIMT-1 HER2+ breast cancer cell line resistant to trastuzumab antiproliferative activity

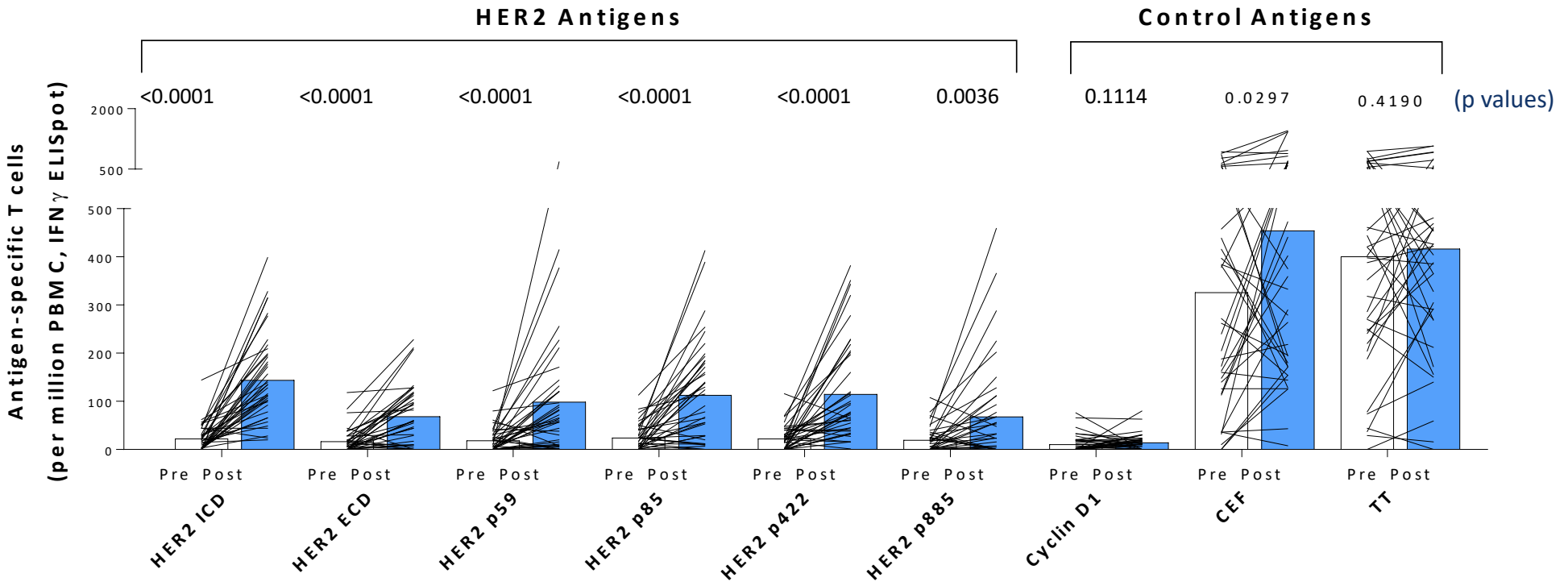
Cellular Assay: 3:1 Effector:Target ratio; 24-hour incubation time; endpoint: % lactate dehydrogenase release

mAb=monoclonal antibody; NK=natural killer.

Nordstrom JL, et al. *Breast Cancer Res*. 2011;13(6):R123.

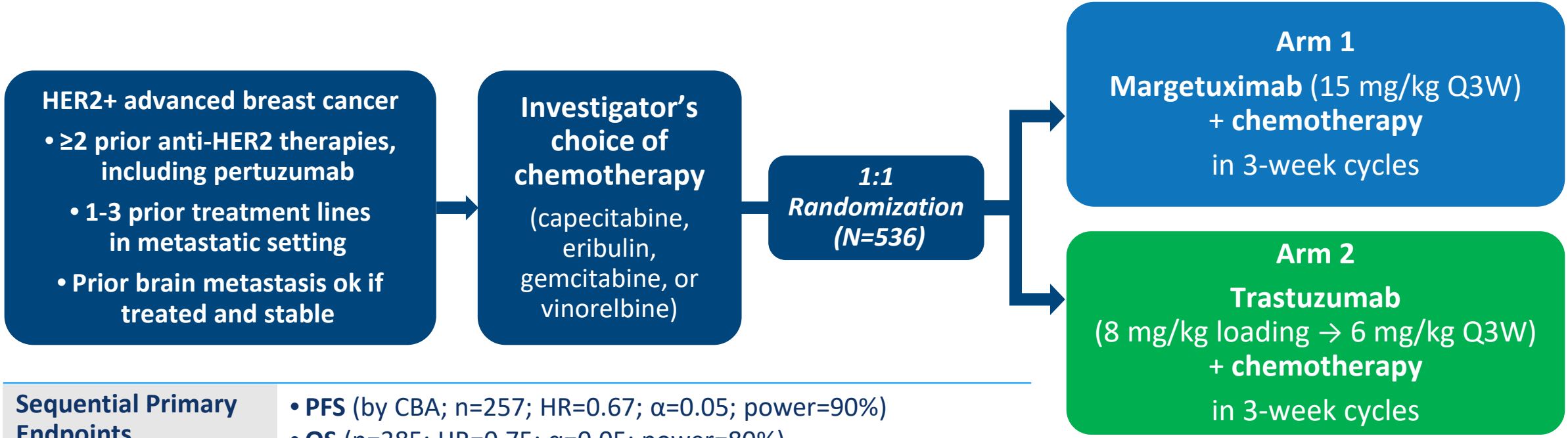
Margetuximab Enhances HER2-specific Adaptive Immunity[1,2]

- Phase 1 margetuximab monotherapy study in 66 pretreated patients with HER2+ carcinomas[3,4]:
  - Four (17%) confirmed responses in 24 evaluable patients with HER2+ MBC[3]
  - Three patients continue on margetuximab at least 4 to 6 years, as of 15-May-2019[4]
- Enhanced HER2-specific T- and B-cell responses after margetuximab monotherapy[5]



1. Nordstrom JL, et al. *Breast Cancer Res*. 2011;13(6):R123. 2. Stavenhagen JB, et al. *Cancer Res*. 2007;67(18):8882-8890. 3. Bang YJ, et al. *Ann Oncol.* 2017;28(4):855-861.
4. Im SA, et al. *Cancer Res.* 2019;79(suppl 4): Abstract P6-18-11. 5. Nordstrom JL, et al. ASCO 2019 Poster (Abstr. #1030).

Study CP-MGAH22-04 (SOPHIA) Design[1,2]



Sequential Primary Endpoints	• **PFS** (by CBA; n=257; HR=0.67; α=0.05; power=90%) • **OS** (n=385; HR=0.75; α=0.05; power=80%)
Secondary Endpoints	• PFS (Investigator assessed) • Objective response rate (by CBA)
Tertiary/Exploratory Endpoints	• Clinical benefit rate (CBR), duration of response (DoR) • Safety profile, antidrug antibody • Effect of CD16A, CD32A, and CD32B on margetuximab efficacy

Stratification:
- Chemotherapy choice
- Prior therapies (≤2 *vs* >2)
- Metastatic sites (≤2 *vs* >2)

HR=hazard ratio; CBA=central blinded analysis.

1. Rugo HS, et al. *J Clin Oncol*. 2016;34(suppl 15):TPS630. 2. Clinicaltrials.gov. NCT02492711. www.clinicaltrials.gov/ct2/show/NCT02492711. Accessed April 8, 2019.

ITT Population: Baseline Characteristics

		Margetuximab + Chemotherapy (n=266)	Trastuzumab + Chemotherapy (n=270)
Demographics	Median age	55	56
	Female sex	266 (100%)	267 (98.9%)
	Europe	152 (57%)	138 (51%)
	North America	85 (32%)	102 (38%)
	Other region	29 (11%)	30 (11%)
Disease Characteristics	ECOG PS 0	149 (56%)	161 (60%)
	ECOG PS 1	117 (44%)	109 (40%)
	Metastatic	260 (98%)	264 (98%)
	Locally advanced, unresectable	6 (2%)	6 (2%)
	Measurable disease by CBA	262 (99%)	262 (97%)
	≤2 metastatic sites	138 (52%)	144 (53%)
	>2 metastatic sites	128 (48%)	126 (47%)
	Hormone receptor positive	164 (62%)	170 (63%)
	Hormone receptor negative	102 (38%)	98 (36%)
Backbone chemotherapy	Capecitabine	71 (27%)	72 (27%)
	Eribulin	66 (25%)	70 (26%)
	Gemcitabine	33 (12%)	33 (12%)
	Vinorelbine	96 (36%)	95 (35%)

Treatment arms overall balanced

ITT population (all randomized patients): N=536.

ECOG=Eastern Cooperative Oncology Group; hormone receptor positive=ER+ and/or PgR+; hormone receptor negative=ER- and PgR-; ITT=intention to treat; PS=performance status.

ITT Population: Prior Cancer Therapy

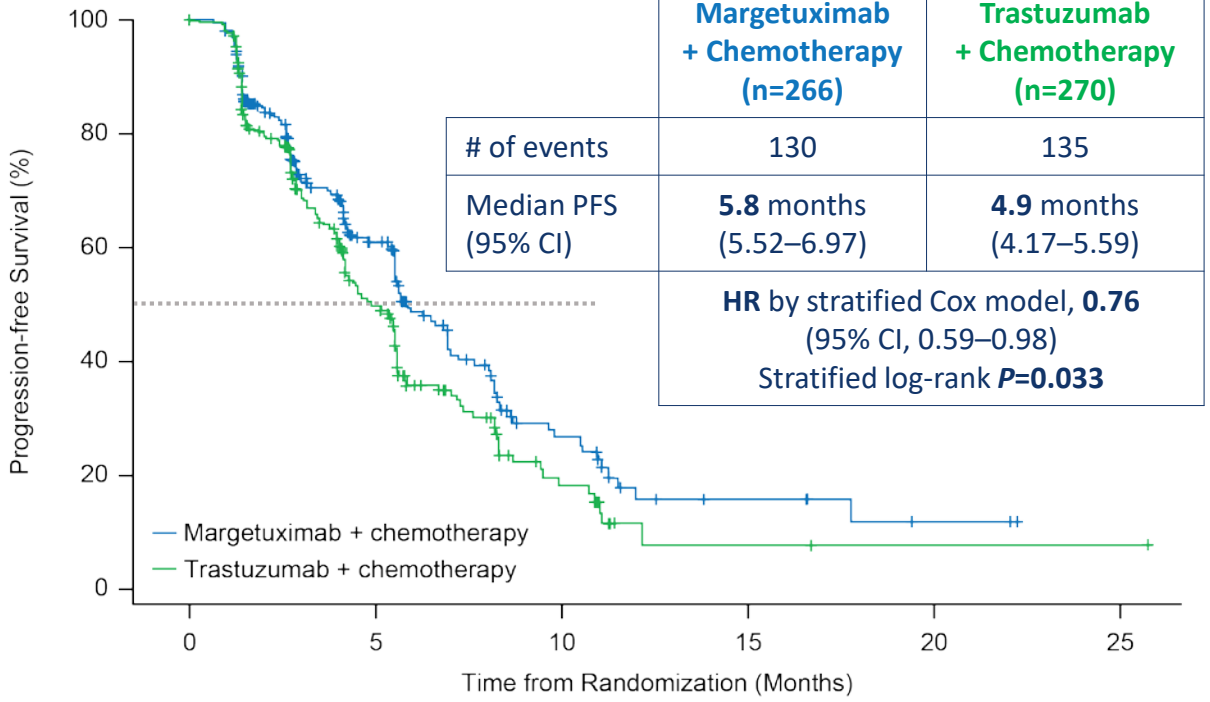
	Margetuximab + Chemotherapy (n=266)	Trastuzumab + Chemotherapy (n=270)
Settings of prior therapy		
Adjuvant and/or neoadjuvant	**158 (59%)**	**145 (54%)**
Metastatic only	108 (41%)	125 (46%)
Prior metastatic lines of therapy		
≤2	175 (66%)	180 (67%)
>2	91 (34%)	90 (33%)
Prior anti-HER2 therapy		
Trastuzumab	**266 (100%)**	**270 (100%)**
Pertuzumab	**266 (100%)**	**269 (100%)**
T-DM1	**242 (91%)**	**247 (92%)**
Lapatinib	41 (15%)	39 (14%)
Other HER2	6 (2%)	6 (2%)
Prior chemotherapy		
Taxane	252 (95%)	249 (92%)
Anthracycline	118 (44%)	110 (41%)
Platinum	34 (13%)	40 (15%)
Prior endocrine therapy	126 (47%)	133 (49%)

Treatment arms overall balanced

ITT population: N=536.

PFS Analysis in ITT Population

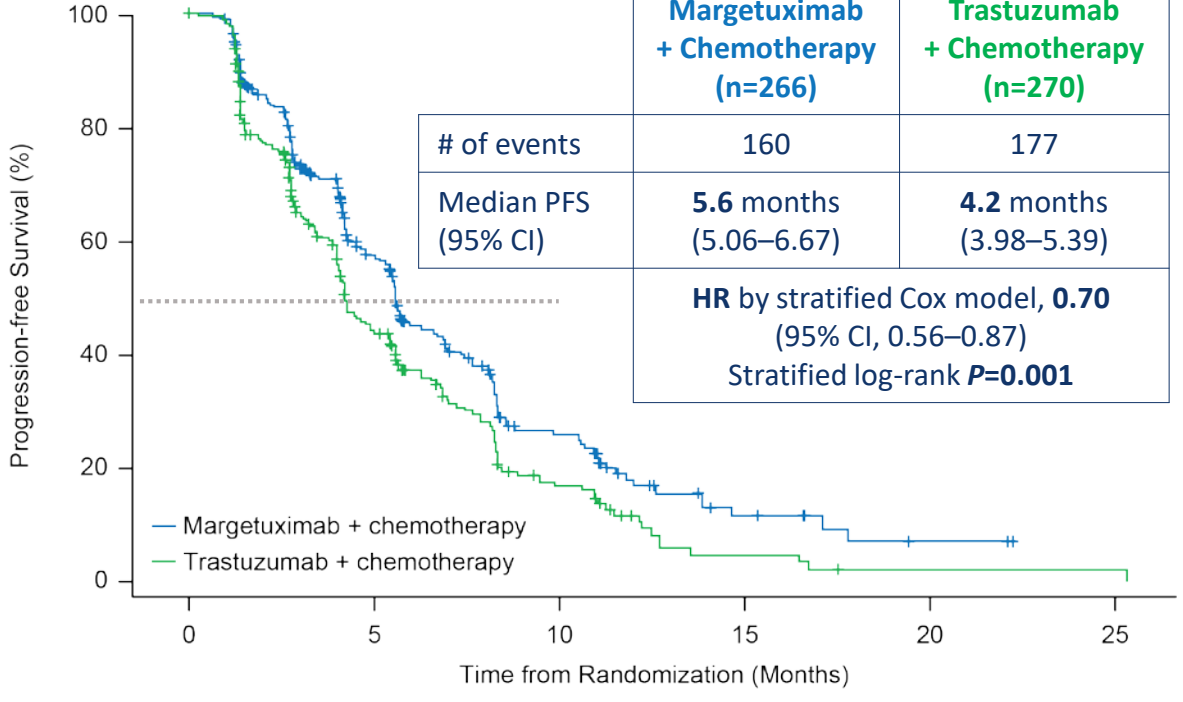
24% Risk Reduction of Disease Progression
Central Blinded Analysis (Primary Endpoint)



	Margetuximab + Chemotherapy (n=266)	Trastuzumab + Chemotherapy (n=270)
# of events	130	135
Median PFS (95% CI)	**5.8** months (5.52–6.97)	**4.9** months (4.17–5.59)
	HR by stratified Cox model, **0.76** (95% CI, 0.59–0.98) Stratified log-rank ***P*=0.033**	

Margetuximab	266	174	94	45	21	8	6	4	2	0	
Trastuzumab	270	158	74	33	13	2	2	1	1	1	1

30% Risk Reduction of Disease Progression
Investigator Assessed (Secondary Endpoint)



	Margetuximab + Chemotherapy (n=266)	Trastuzumab + Chemotherapy (n=270)
# of events	160	177
Median PFS (95% CI)	**5.6** months (5.06–6.67)	**4.2** months (3.98–5.39)
	HR by stratified Cox model, **0.70** (95% CI, 0.56–0.87) Stratified log-rank ***P*=0.001**	

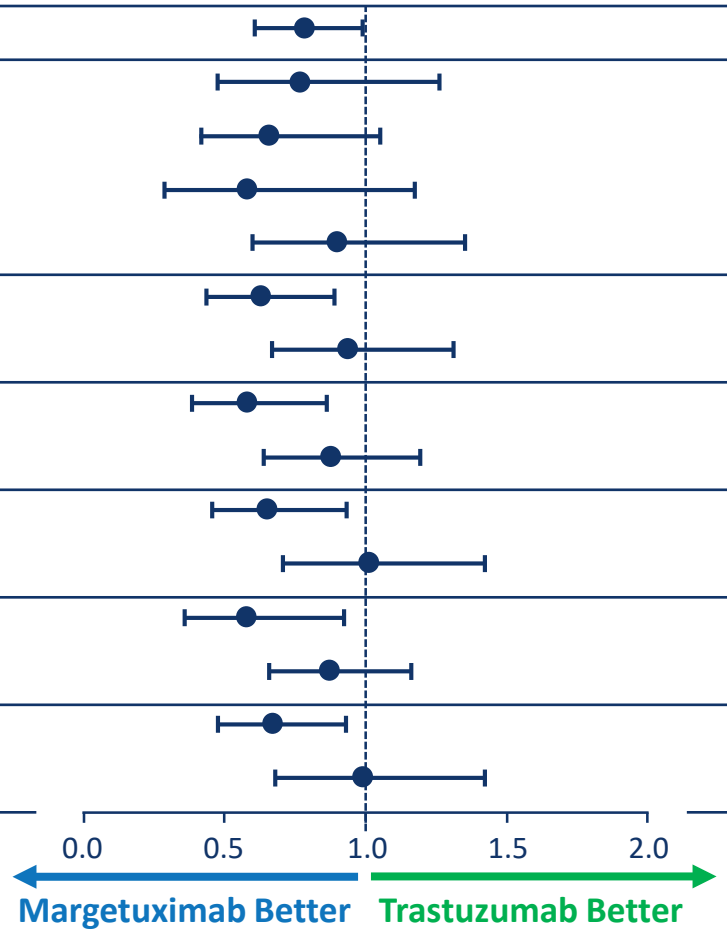
Margetuximab	266	206	155	112	72	61	33	32	16	13	8	7	3	2	2	0	
Trastuzumab	270	184	130	87	59	45	25	21	10	5	4	3	1	1	1	1	1	0

- PFS analysis was triggered by last randomization on October 10, 2018, after 265 PFS events occurred

ITT population: N=536. CI=confidence interval.

PFS Subgroup Analyses

	Median PFS (95% CI), Months		HR by Unstratified Cox Model	95% CI	Unstratified Log-Rank *P* Value
	Margetuximab + Chemotherapy	Trastuzumab + Chemotherapy			
All patients, n=536	**5.8** (5.52–6.97)	**4.9** (4.17–5.59)	0.78	(0.61–0.99)	0.044
Capecitabine, n=143	8.3 (5.55–11.50)	5.5 (4.17–8.28)	0.77	(0.47–1.26)	0.302
Eribulin, n=136	6.0 (3.81–8.05)	4.2 (3.38–5.55)	0.66	(0.42–1.05)	0.080
Gemcitabine, n=66	5.4 (4.07–11.01)	3.5 (1.45–7.16)	0.58	(0.29–1.18)	0.128
Vinorelbine, n=191	5.6 (4.24–6.97)	5.1 (3.42–6.67)	0.90	(0.60–1.35)	0.606
>2 metastatic sites, n=254	6.3 (5.42, 8.08)	4.2 (3.38, 5.55)	0.63	(0.44–0.89)	0.009
≤2 metastatic sites, n=282	5.7 (4.47, 6.97)	5.5 (4.24, 5.85)	0.94	(0.67–1.31)	0.702
Hormone Receptor-, n=200	5.8 (4.80, 7.23)	4.2 (2.83, 5.55)	0.58	(0.39–0.86)	0.007
Hormone Receptor+, n=334	5.7 (5.52, 8.18)	5.5 (4.24, 7.03)	0.88	(0.64–1.19)	0.393
HER2 IHC 3+, n=291	6.9 (5.55, 8.31)	5.6 (3.98, 5.85)	0.64	(0.46–0.90)	0.011
HER2 ISH amplified, n=245	5.5 (4.01, 6.60)	4.6 (4.07, 5.55)	1.01	(0.71–1.42)	0.972
Age >60 years, n=170	6.9 (5.52, 10.51)	5.6 (4.14, 5.85)	0.58	(0.36–0.92)	0.020
Age ≤60 years, n=366	5.6 (4.24, 6.97)	4.6 (4.01, 5.59)	0.87	(0.66–1.16)	0.337
Prior (neo)adjuvant Tx: yes, n=303	6.3 (5.55–8.05)	5.4 (4.01–5.59)	0.67	(0.48–0.93)	0.014
Prior (neo)adjuvant Tx: no, n=233	5.6 (3.71–6.97)	4.9 (4.07–7.16)	0.99	(0.68–1.42)	0.935

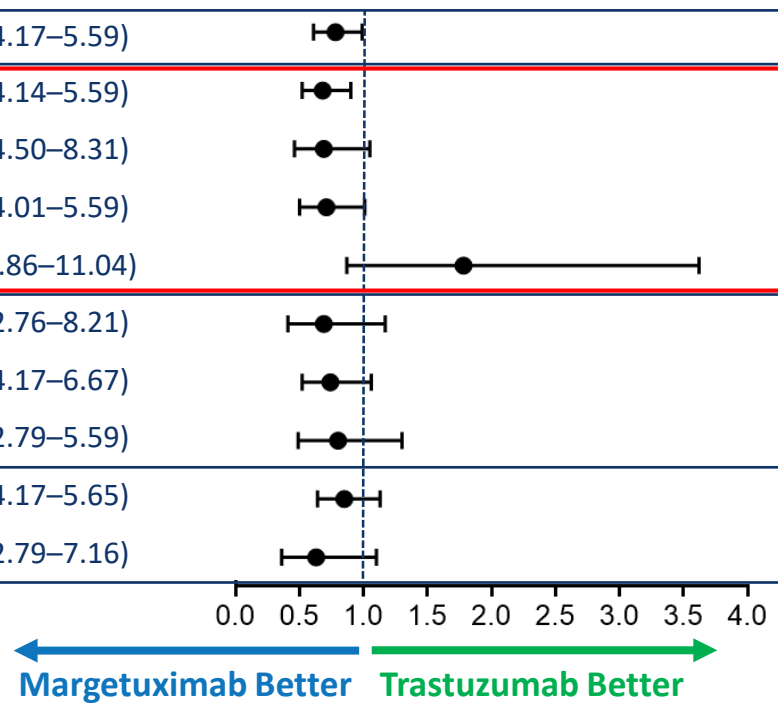


Hormone receptor positive=ER+ and/or PgR+; hormone receptor negative=ER- and PgR-; IHC=immunohistochemistry; ISH=in situ hybridization; Tx=treatment.

Planned* Exploratory PFS Analyses by FcγR Genotypes (CBA)

Margetuximab benefit appears to be increased in low-affinity CD16A-158F allele carriers

		Median PFS (95% CI), Months		HR by Unstratified Cox Model	95% CI	Unstratified Log-Rank *P* Value
		Margetuximab + Chemotherapy	Trastuzumab + Chemotherapy			
	All patients	5.8 (5.52–6.97)	4.9 (4.17–5.59)	0.78	(0.61–0.99)	0.044
Activating function	CD16A/F carrier (FV or FF), n=437	6.9 (5.55–8.15)	5.1 (4.14–5.59)	0.68	(0.52–0.90)	0.005
	CD16A/FF, n=192	8.2 (5.52–10.51)	5.6 (4.50–8.31)	0.69	(0.46–1.05)	0.080
	CD16A/FV, n=245	6.3 (5.52–7.23)	4.3 (4.01–5.59)	0.71	(0.50–1.01)	0.055
	CD16A/VV, n=69	4.8 (2.46–5.65)	5.6 (2.86–11.04)	1.78	(0.87–3.62)	0.110
	CD32A/RR, n=122	5.7 (4.80–10.55)	5.5 (2.76–8.21)	0.69	(0.41–1.17)	0.166
	CD32A/RH, n=247	6.9 (5.55–8.15)	5.6 (4.17–6.67)	0.74	(0.52–1.06)	0.102
	CD32A/HH, n=137	5.6 (3.29–8.28)	4.1 (2.79–5.59)	0.80	(0.49–1.30)	0.365
Inhibitory function	CD32B/II†, n=380	5.8 (5.55–7.66)	5.5 (4.17–5.65)	0.85	(0.64–1.13)	0.265
	CD32B/IT†, n=117	6.0 (4.14–NA)	5.5 (2.79–7.16)	0.63	(0.36–1.10)	0.098



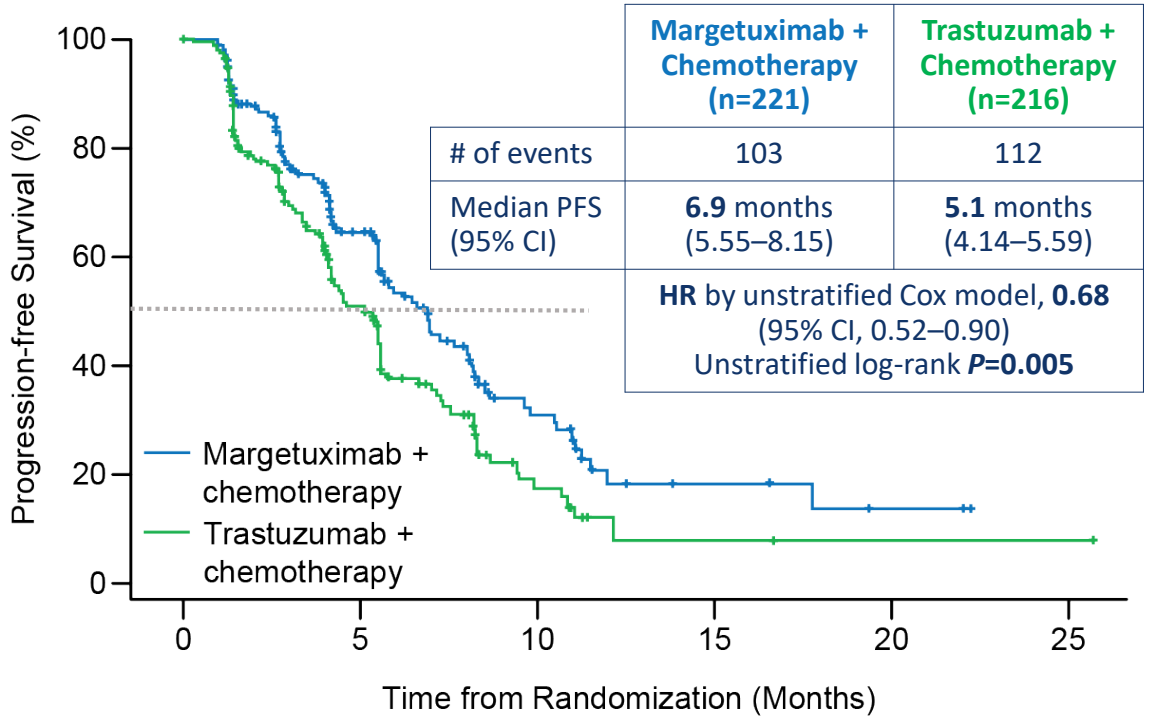
*Non-alpha allocating, exploratory analysis.

†CD32B/TT not included on forest plot because n=9 is too small (5 on margetuximab, 4 on trastuzumab) to make analysis meaningful.

Planned Exploratory PFS Analysis by CD16A Genotype, by CBA

506 patients genotyped (94%)

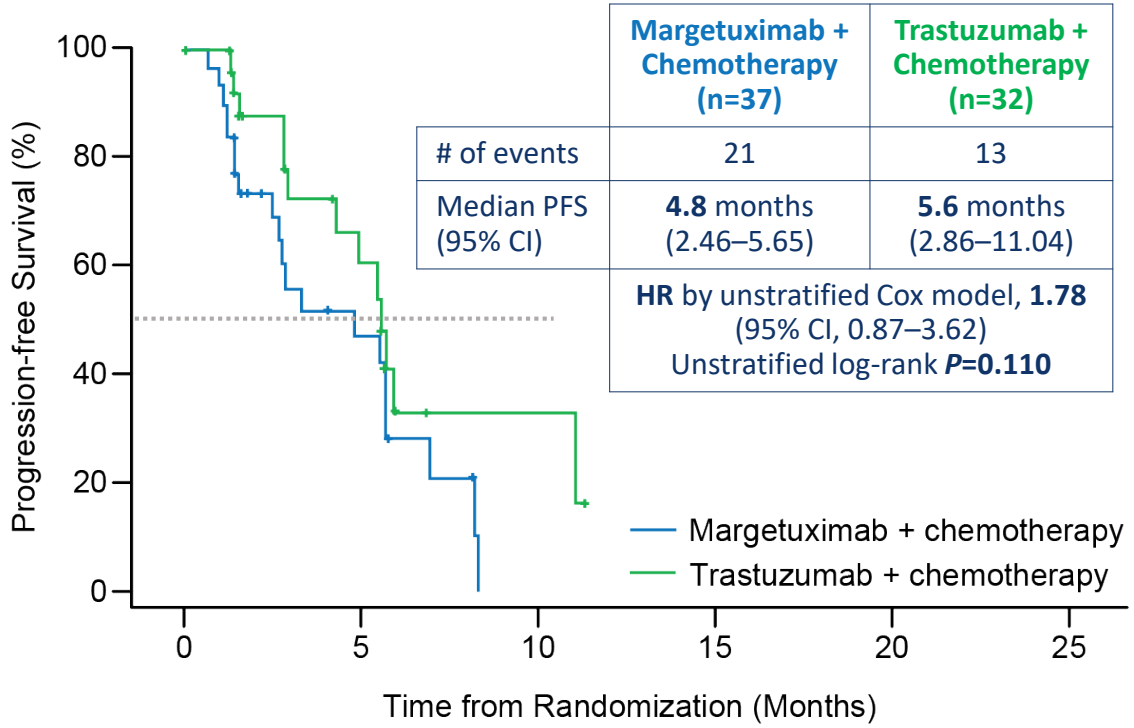
FF or FV, n=437 of 506 (86%)



	Margetuximab + Chemotherapy (n=221)	Trastuzumab + Chemotherapy (n=216)
# of events	103	112
Median PFS (95% CI)	**6.9** months (5.55–8.15)	**5.1** months (4.14–5.59)
HR by unstratified Cox model, **0.68** (95% CI, 0.52–0.90) Unstratified log-rank ***P*=0.005**		

Margetuximab	221	157	84	42	21	8	6	4	2	0	
Trastuzumab	216	129	62	30	11	2	2	1	1	1	1

VV, n=69 of 506 (14%)



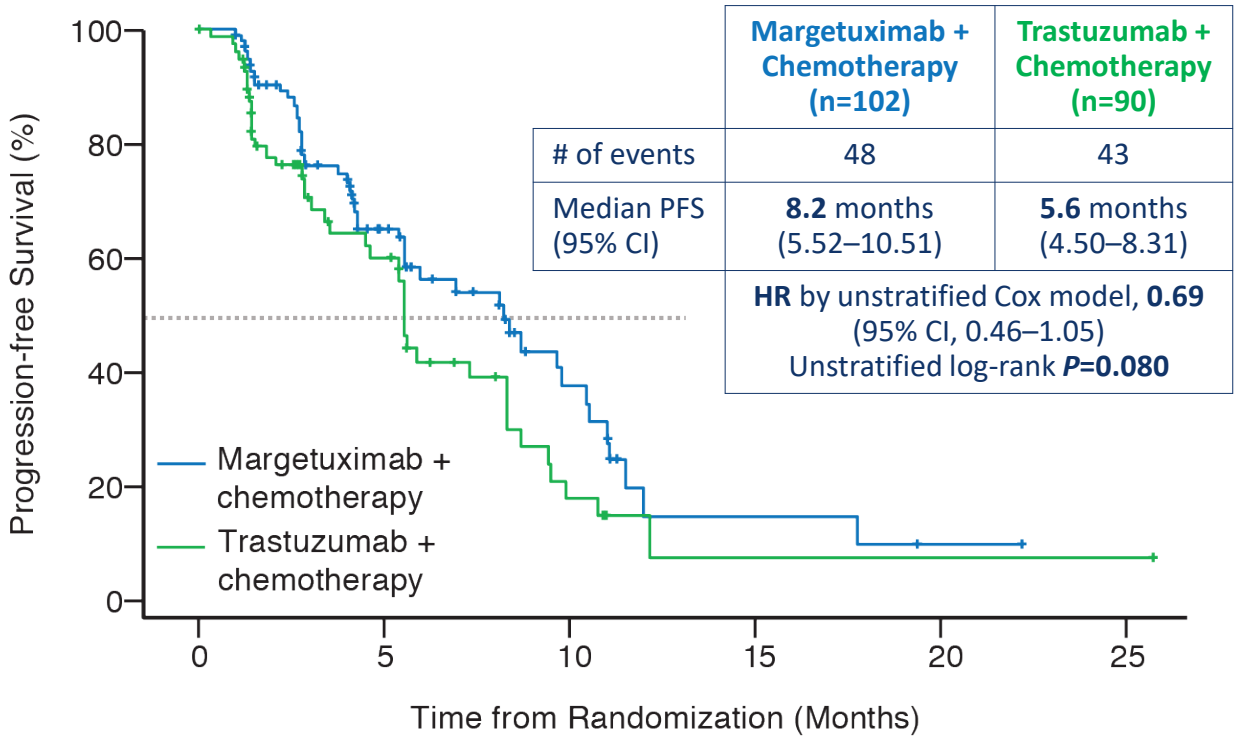
	Margetuximab + Chemotherapy (n=37)	Trastuzumab + Chemotherapy (n=32)
# of events	21	13
Median PFS (95% CI)	**4.8** months (2.46–5.65)	**5.6** months (2.86–11.04)
HR by unstratified Cox model, **1.78** (95% CI, 0.87–3.62) Unstratified log-rank ***P*=0.110**		

Margetuximab	37	16	10	3	0	
Trastuzumab	32	18	10	2	2	0

Planned Exploratory PFS Analysis by CD16A Genotype, by CBA

506 patients genotyped (94%)

FF, n=192 of 506 (38%)

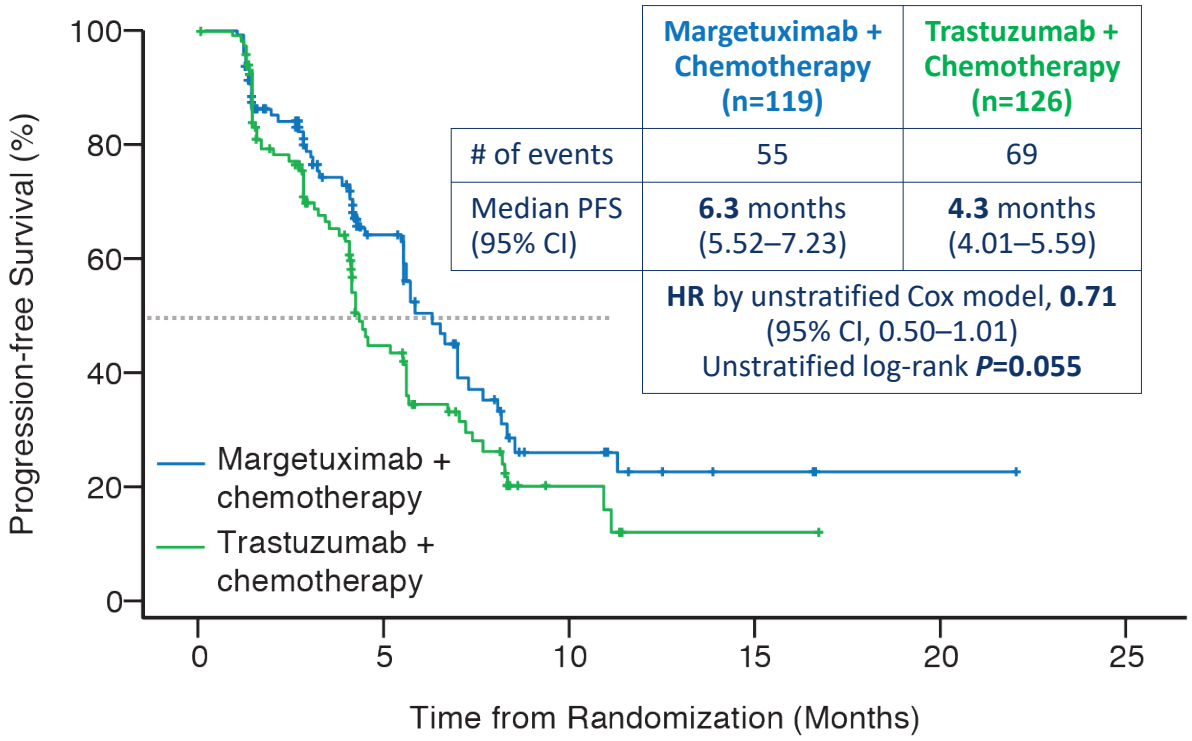


	Margetuximab + Chemotherapy (n=102)	Trastuzumab + Chemotherapy (n=90)
# of events	48	43
Median PFS (95% CI)	**8.2** months (5.52–10.51)	**5.6** months (4.50–8.31)

HR by unstratified Cox model, **0.69** (95% CI, 0.46–1.05)
Unstratified log-rank ***P*=0.080**

Margetuximab	102	75	41	23	12	3	3	3	1	0	
Trastuzumab	90	49	29	14	6	1	1	1	1	1	1

FV, n=245 of 506 (48%)



	Margetuximab + Chemotherapy (n=119)	Trastuzumab + Chemotherapy (n=126)
# of events	55	69
Median PFS (95% CI)	**6.3** months (5.52–7.23)	**4.3** months (4.01–5.59)

HR by unstratified Cox model, **0.71** (95% CI, 0.50–1.01)
Unstratified log-rank ***P*=0.055**

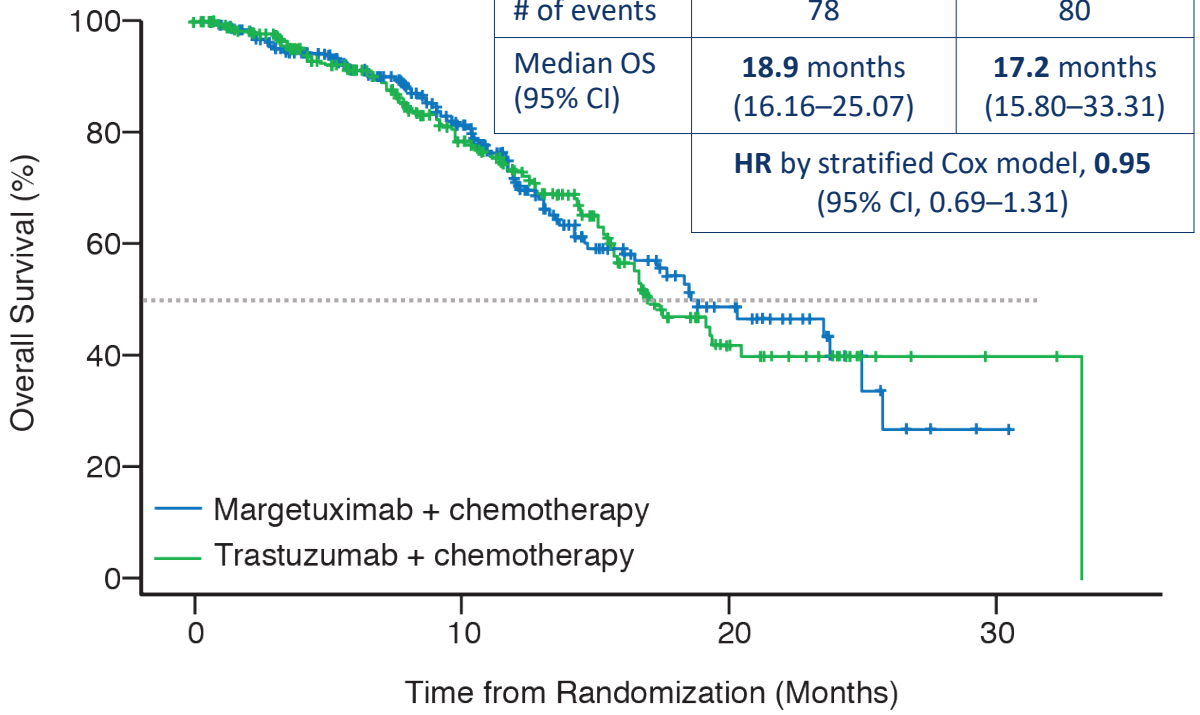
Margetuximab	119	82	42	19	9	5	3	1	1	0	
Trastuzumab	126	80	33	16	5	1	1	0			

October 2018 Interim OS* for ITT vs CD16A-158F Carriers

158 (41%) of 385 events needed for final OS analysis

ITT population, n=536

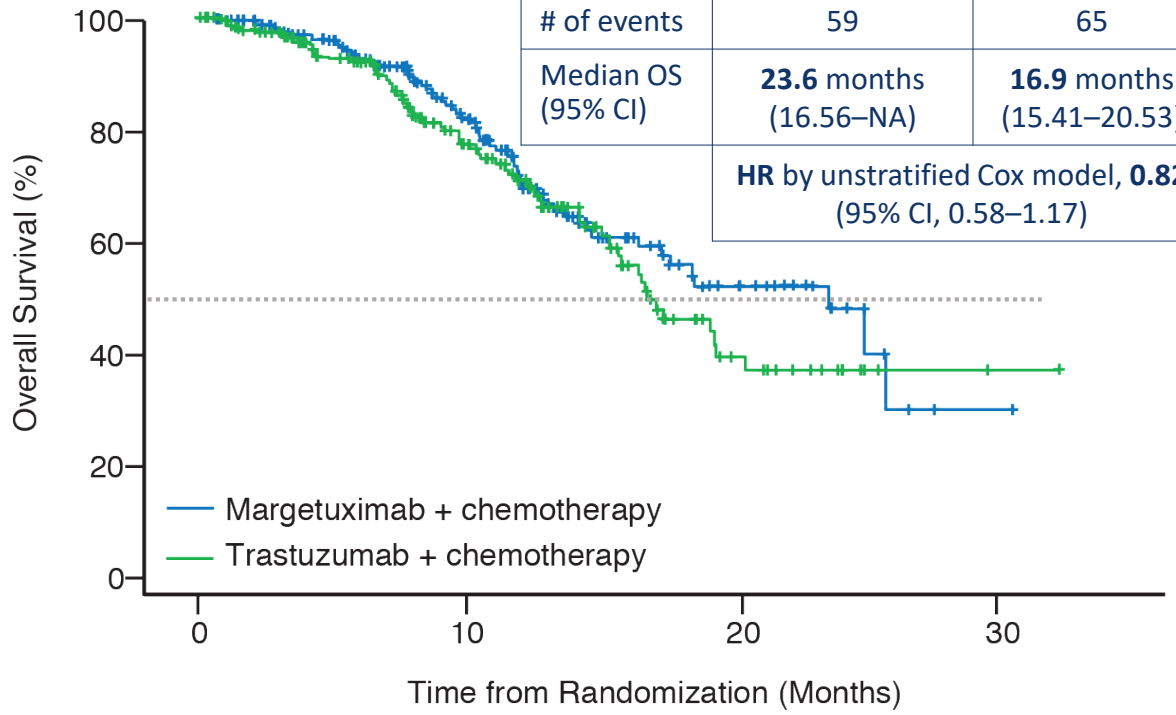
	Margetuximab + Chemotherapy (n=266)	Trastuzumab + Chemotherapy (n=270)
# of events	78	80
Median OS (95% CI)	**18.9** months (16.16–25.07)	**17.2** months (15.80–33.31)
	HR by stratified Cox model, **0.95** (95% CI, 0.69–1.31)	



Margetuximab	266	241	209	174	125	85	57	42	29	17	8	3	1	0	
Trastuzumab	270	237	194	163	122	92	63	37	24	14	6	3	2	1	0

CD16A/FF or FV, n=437 of 506 (86%)

	Margetuximab + Chemotherapy (n=221)	Trastuzumab + Chemotherapy (n=216)
# of events	59	65
Median OS (95% CI)	**23.6** months (16.56–NA)	**16.9** months (15.41–20.53)
	HR by unstratified Cox model, **0.82** (95% CI, 0.58–1.17)	



Margetuximab	221	207	179	147	104	69	46	34	24	15	7	2	1	0	
Trastuzumab	216	189	153	130	95	71	48	26	17	10	4	2	1	0	

*First interim overall OS analysis at time of PFS analysis (Oct 10, 2018) was immature with 41% of 385 deaths needed for final OS analysis; stopping boundary was not crossed. Second interim OS analysis will occur after 270 deaths. Final OS analysis will occur after 385 deaths. NA=not achieved.

Overall Response and Clinical Benefit Rates Complement PFS

	Margetuximab + Chemotherapy (n=262)	Trastuzumab + Chemotherapy (n=262)	*P* Value
Objective Response Rate (CR+PR), n (%) [95% CI]	58 (**22.1%**) [17.3–27.7]	42 (**16.0%**) [11.8–21.0]	0.060*
Clinical Benefit Rate (CR+PR+SD>6 months), n (%) [95% CI]	96 (**36.6%**) [30.8–42.8]	65 (**24.8%**) [19.7–30.5]	0.003*
Best Overall Response, n (%)			
Complete Response	7 (2.7%)	4 (1.5%)	
Partial Response	51 (19.5%)	38 (14.5%)	
Stable Disease	149 (56.9%)	147 (56.1%)	
Progressive Disease	35 (13.4%)	46 (17.6%)	
Not Evaluable/Not Available	20 (7.6%)	27 (10.3%)	
Duration of Response (CR, PR), median months (95% CI)	6.1 (4.11–9.13)	6.0 (4.01–6.93)	0.541†

Response evaluable population (randomized patients with baseline measurable disease): N=524.
*Stratified Mantel-Haenszel test *P* value (2-sided). †Unstratified log-rank *P* value (2-sided).

Summary of Adverse Events (AEs)

Similar overall safety profiles

	Margetuximab + Chemotherapy (n=264)	Trastuzumab + Chemotherapy (n=265)
Any grade AE, n (%)	258 (97.7)	255 (96.2)
Grade ≥3 AE, n (%)	138 (52.3)	128 (48.3)
SAE, n (%)	39 (14.8)	46 (17.4)
AE leading to treatment discontinuation, n (%)	8 (3.0)	7 (2.6)
AEs resulting in death,* n (%)	2 (0.8)†	2 (0.8)‡

Safety Population (randomized patients who received any study treatment): N=529.
*No AEs resulting in death were considered related to anti-HER2 study therapy.
†Pneumonia (n=1), pneumonia aspiration (n=1).
‡Pneumonia (n=1), acute kidney injury (n=1).
SAE=serious AE.

AEs Regardless of Causality

	Margetuximab + Chemotherapy (n=264)		Trastuzumab + Chemotherapy (n=265)	
Most common AEs, n (%)	**All Grade***	**Grade ≥3†**	**All Grade***	**Grade ≥3†**
Fatigue	103 (39.0)	12 (4.5)	92 (34.7)	7 (2.6)
Nausea	81 (30.7)	3 (1.1)	84 (31.7)	1 (0.4)
Neutropenia	73 (27.7)	51 (19.3)	51 (19.2)	30 (11.3)
Diarrhea	59 (22.3)	6 (2.3)	62 (23.4)	5 (1.9)
Anemia	48 (18.2)	12 (4.5)	55 (20.8)	17 (6.4)
Neutrophil count decreased	32 (12.1)	22 (8.3)	35 (13.2)	25 (9.4)
Febrile neutropenia	8 (3.0)	8 (3.0)	12 (4.5)	12 (4.5)
AEs of special interest, n (%)	**All Grade**	**Grade ≥3**	**All Grade**	**Grade ≥3**
Infusion-related reaction (IRR)‡	**34 (12.9)**	**4 (1.5)**	**10 (3.8)**	**0**
Left ventricular dysfunction	6 (2.3)	3 (1.1)	7 (2.6)	1 (0.4)
Discontinuation due to IRRs, n (%)	3 (1.1)	2 (0.8)	0	0

Safety Population: N=529.

*Incidence ≥20% in either treatment group.

†Incidence ≥5% in either treatment group.

‡All patients received prior trastuzumab. In pivotal trials of trastuzumab, IRRs occurred in 21% to 40% of patients (US package insert).

Conclusions

- Margetuximab is a novel Fc-engineered HER2 targeted antibody that stimulates mechanisms of both innate and adaptive immunity
- In patients with HER2+ MBC progressing after trastuzumab, pertuzumab, chemotherapy, and T-DM1:
  - Margetuximab plus chemotherapy improved PFS (CBA: HR=0.76, *P*=0.033; Inv: HR=0.70, *P*=0.001), ORR, and CBR, compared with trastuzumab plus chemotherapy
- This is the first prospective analysis of CD16A genotype as predictor of efficacy from anti-HER2 therapy
  - Enhanced PFS benefit with margetuximab in exploratory subpopulation of low-affinity CD16A-158F carriers (HR=0.68, *P*=0.005)
- Acceptable safety, similar to trastuzumab[1]
  - Increased IRRs (primarily low grade) on margetuximab (13% vs 4%), managed with premedications
- Next milestone: second interim OS analysis, expected late 2019

.

IRR=infusion-related reaction. 1. Thompson LM, et al. *Oncologist.* 2014;19(3):228-234.

Acknowledgments

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HER2-positive Advanced Gastric Cancer: Current Treatments & Unmet Needs

Daniel Catenacci, M.D.

Associate Professor of Medicine, The University of Chicago

Gastroesophageal Adenocarcinoma (GEA) Standard Therapy

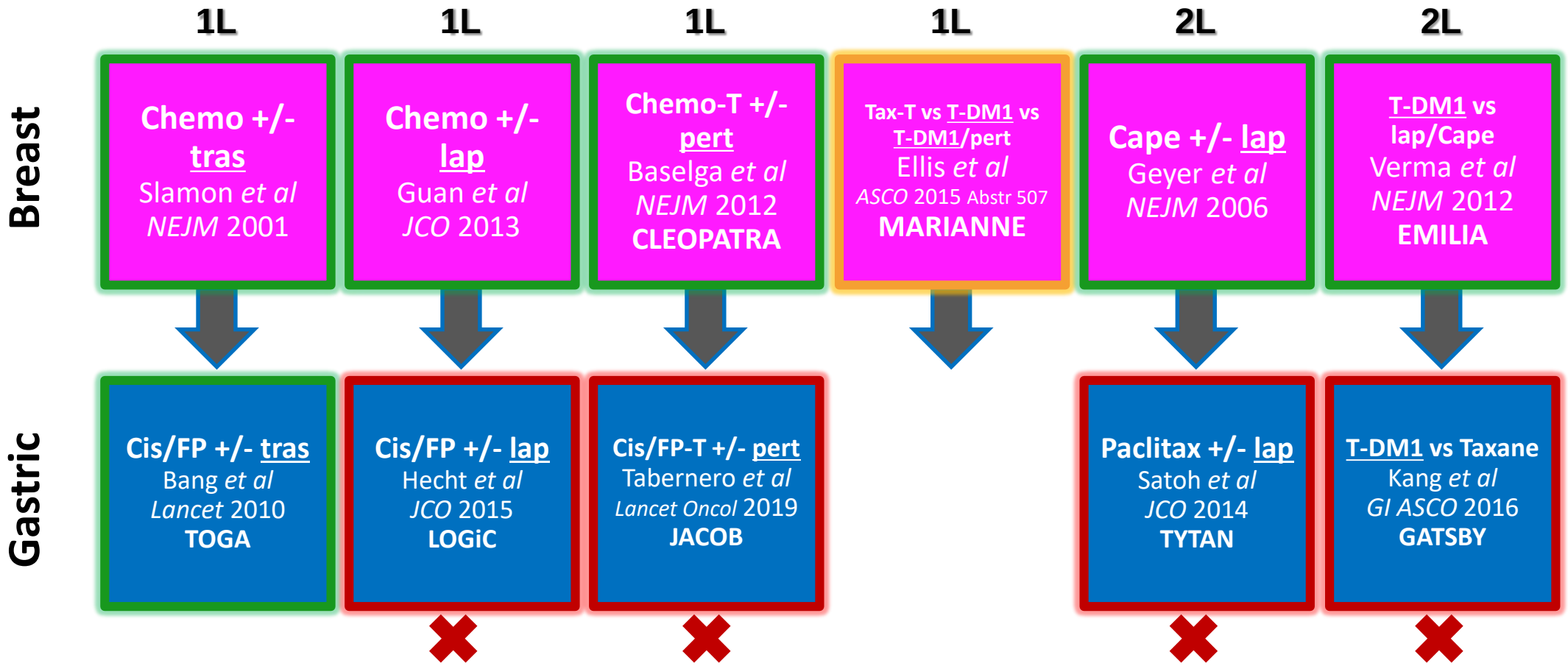
- **Cytotoxics: 5FU, platinum, irinotecan, taxane, TAS102**

  1L (FOLFOX) → 2L (FOLFIRI) → 3L (FOLTAX) → 4L (TAS102)

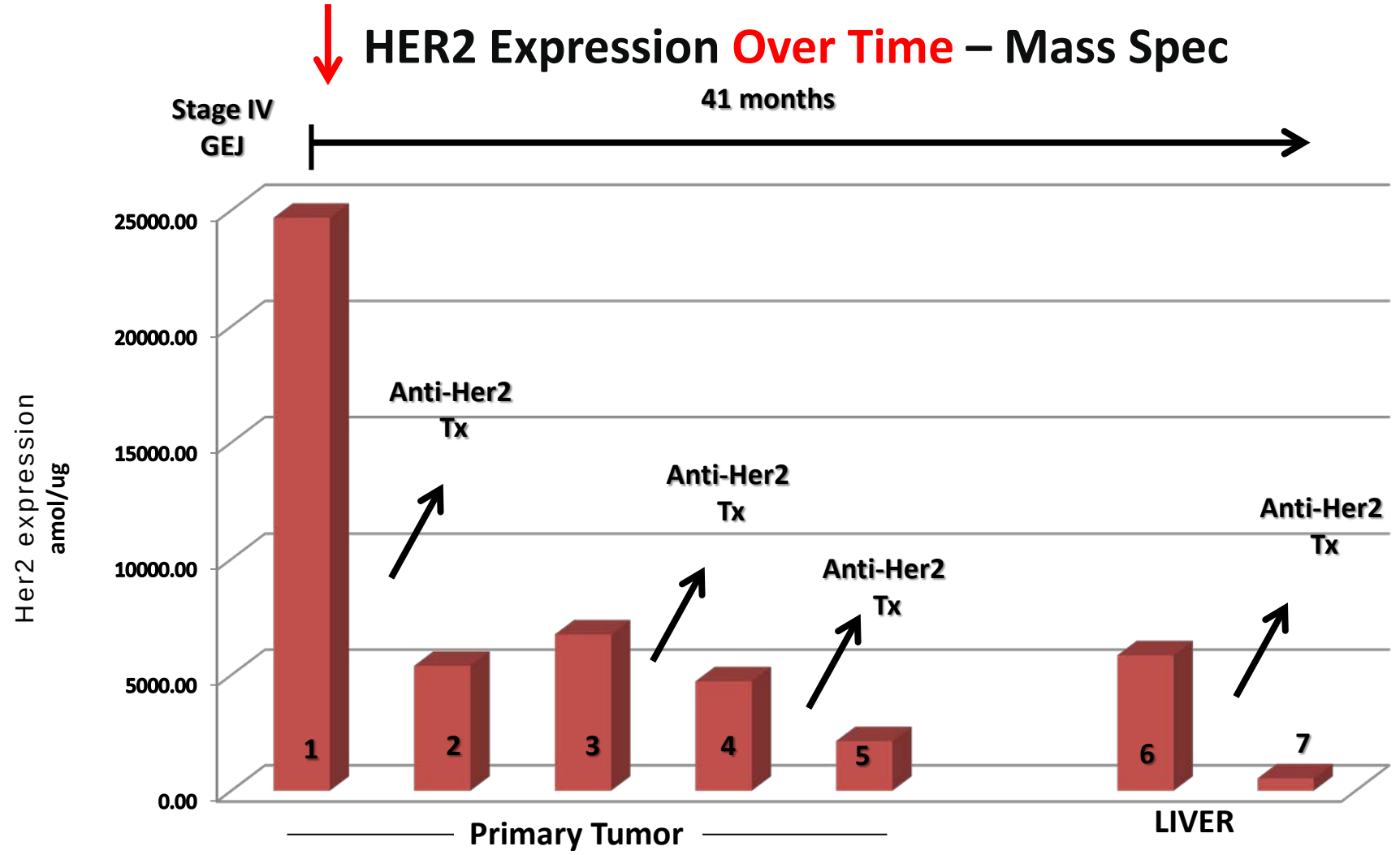
- **Few targeted therapies incorporated into routine care:**

Marker	Incidence	Treatment	Therapy Line	Approval	Benefit
HER2++	~15%	Chemo + Trastuzumab	1L	2010	HR 0.65
none	100%	Chemo + Ramucirumab	2L	2014/15	HR 0.8
MSI-High	~2-3%	Pembrolizumab	2L+	2017	HR? (great)
PD-L1+ ≥1%	~50-60%	Pembrolizumab	3L+	2017*	HR? (marginal)

GEA vs Breast Cancer
Anti-HER2 Therapy Phase III



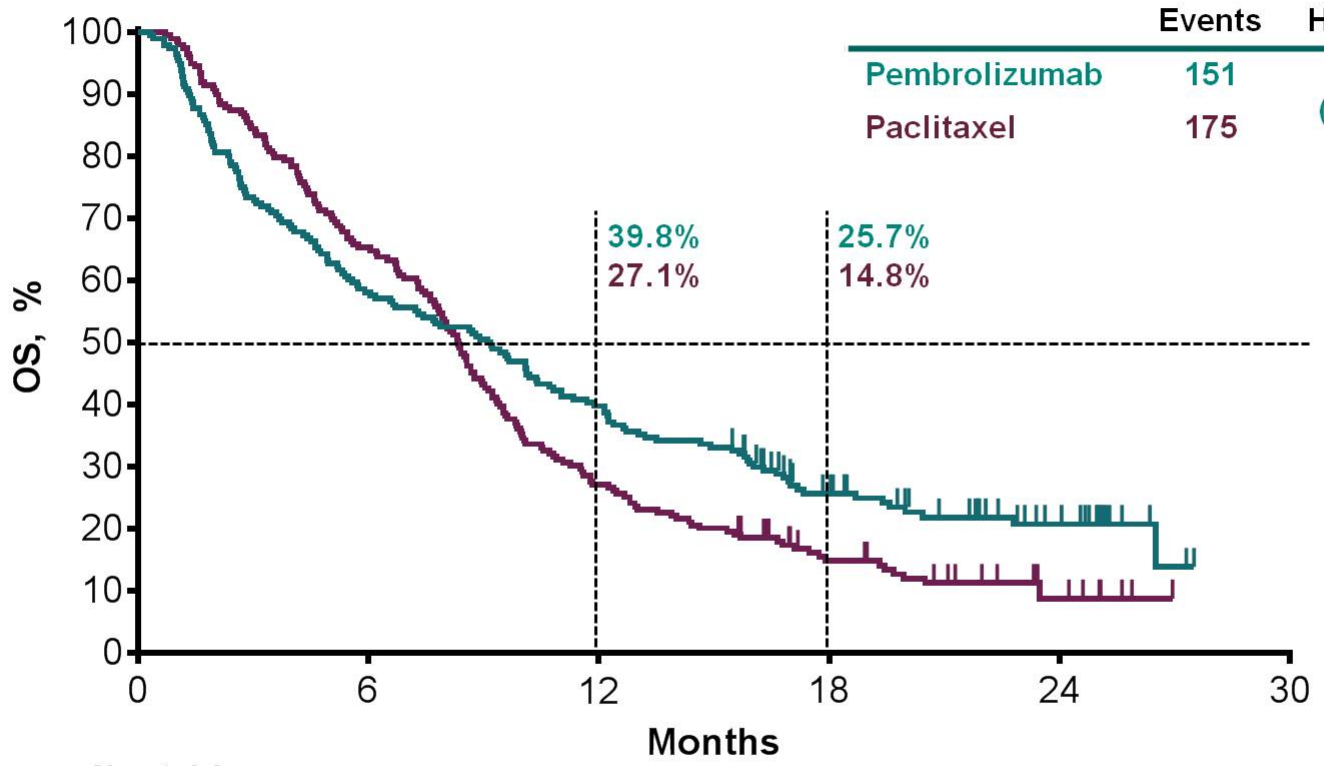
Intra-patient Heterogeneity Over Time: Mechanisms of Therapy Resistance



Seppallan et al. Therapeutically induced changes in Her2, Her3, and Egfr protein expression for treatment guidance. *JNCCN* 2016

KEYNOTE 061: pembrolizumab vs paclitaxel 2L

Overall Survival, CPS ≥1



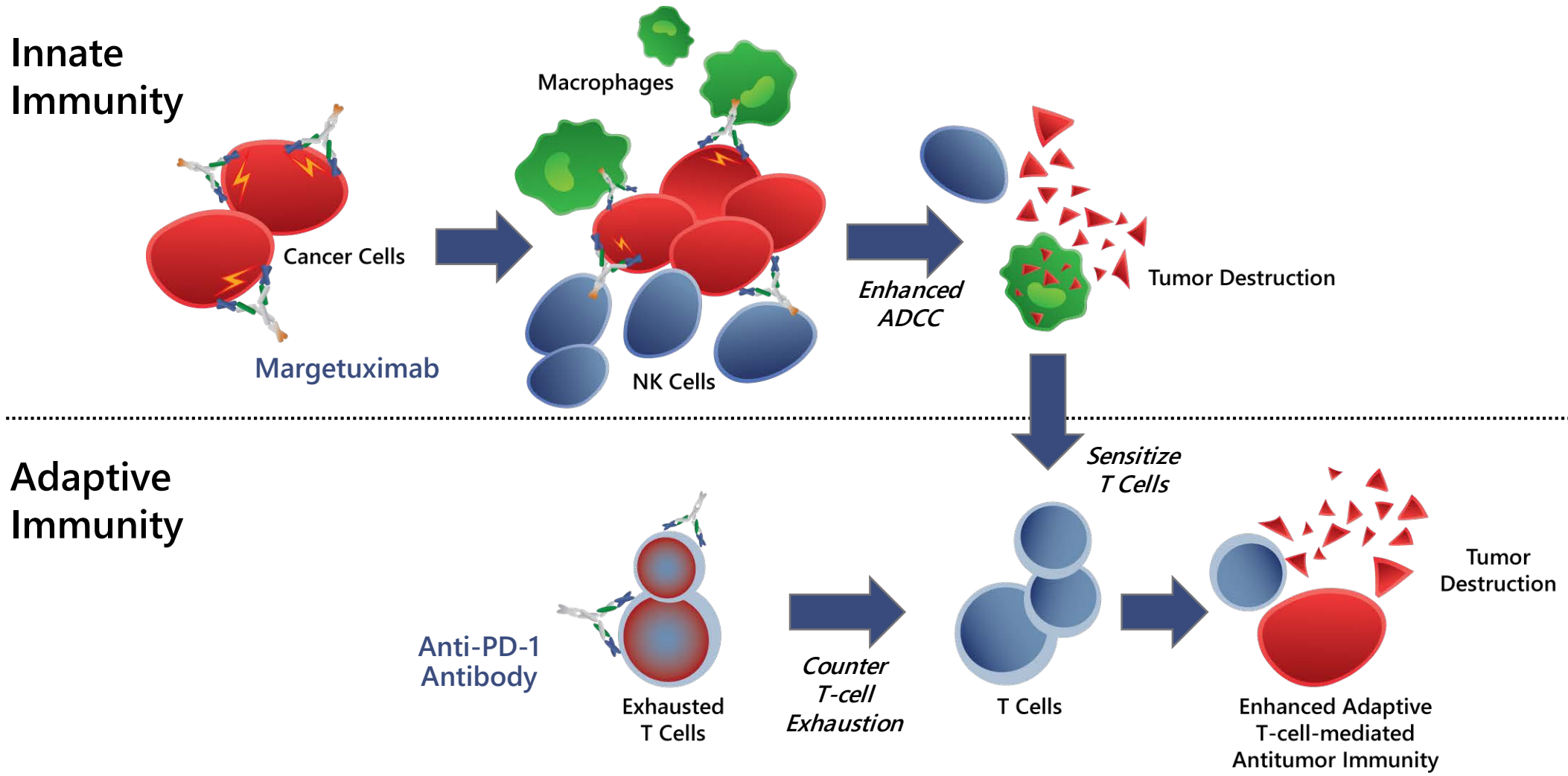
Data cutoff date: Oct 26, 2017.

RAINBOW
(Ramucirumab + Paclitaxel)
mPFS 4.4 m
mOS 9.6 m

Shitara et al. Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): a randomised, open-label, controlled, phase 3 trial. Lancet 2018

Rationale for Margetuximab + Anti-PD-1 Combination

Coordinate engagement of innate and adaptive immunity to mediate tumor regression



Fully Enrolled Phase 2 Study in Advanced HER2+ Gastric Carcinoma

Update provided at ASCO GI Symposium 2019

Dose Escalation

(n=3-6 per margetuximab dose)

Margetuximab 10 – 15 mg/kg q3w + pembrolizumab 200 mg q3w

MERCK

Clinical Supply Agreement

Dose Expansion #1

(margetuximab 15 mg/kg q3W + pembrolizumab 200 mg q3W)

Gastric and Gastroesophageal (n=60)

Dose Expansion #2

(margetuximab 15 mg/kg q3W + pembrolizumab 200 mg q3W)

Data presented at ASCO GI 2019

Gastric (HER2 3+) (n=25)

Treatment	• Potential for chemotherapy-free regimen • **Margetuximab and pembrolizumab** administered day 1 of every 3 week cycle
Inclusion/Exclusion Criteria	• Received ≥ 1 prior line of chemotherapy treatment • No prior immunotherapy
Endpoints	• Primary: safety, tolerability and efficacy (as evaluated by objective response rate (ORR)) of combo • Secondary: PFS, OS, immunogenicity

Summary of Patient Demographics

Ninety-two patients have been treated at recommended Phase 2 dose

Characteristic		Gastric Cancer (n=61)	GEJ Cancer (n=31)
Age	Mean ± SD	61.4 ± 13.6	57.9 ± 11.1
	Median (Range)	62.0 (19.0, 85.0)	60.0 (35.0, 79.0)
Gender [n(%0)]	Male	48 (78.7)	27 (87.1)
	Female	13 (21.3)	4 (12.9)
Race [n (%)]	Asian	48 (78.7)	3 (9.7)
	White	9 (14.8)	25 (80.6)
	Other	1 (1.6)	3 (9.7)
	Black or African American	3 (4.9)	0
ECOG Status [n (%)]	0	20 (32.8)	13 (41.9)
	1	41 (67.2)	18 (58.1)

** Data cut-off January 8, 2019*

Treatment with Combo of Margetuximab and Pembrolizumab is Well Tolerated

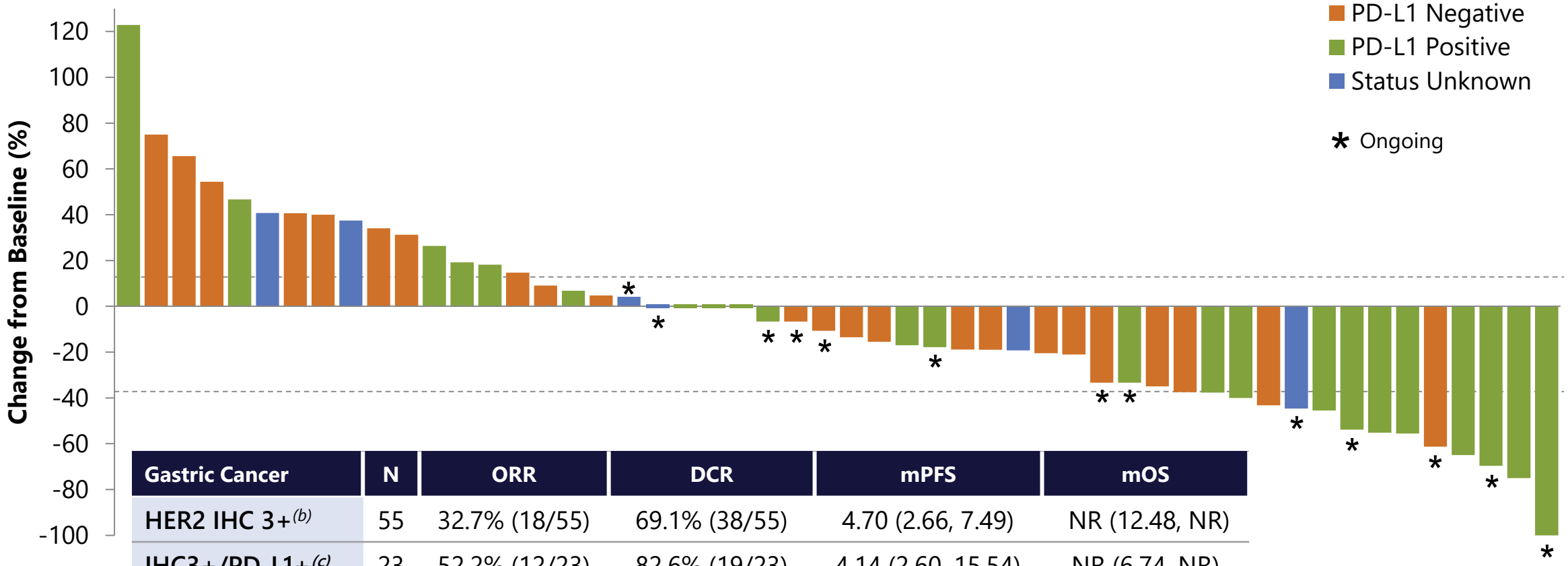
- 64% of patients experienced treatment related AE (TRAE) irrespective of grade
- 18% of patients with TRAE ≥ Grade 3
- Most common TRAE: pruritis (16.8%)
- 8 Treatment-related serious adverse events: autoimmune hepatitis [2], hyponatremia [1], diabetic ketoacidosis [1], and pneumonitis [1], hypotension [1], confusional state [1], dizziness [1]
- 17 Adverse events of special interest reported: infusion related reaction [11], autoimmune hepatitis [2], pneumonitis [1], endocrinopathy [1], others [1], LVEF dysfunction [1]

Adverse Events	TRAEs	
	All (N=95)*	≥Gr 3
TOTAL	**61 (64.2)**	**17 (17.9)**
Pruritus	16 (16.8)	
Diarrhea	14 (14.7)	
Infusion related reaction	13 (13.7)	3 (3.2)
Fatigue	12 (12.6)	
Rash	7 (7.4)	
Rash maculo-papular	5 (5.3)	
Anemia	5 (5.3)	2 (2.1)
Nausea	4 (4.2)	1 (1.1)
Decreased appetite	4 (4.2)	
Lipase increased	4 (4.2)	1 (1.1)
Aspartate aminotransferase increased	4 (4.2)	1 (1.1)
Chills	3 (3.2)	
Alanine aminotransferase increased	3 (3.2)	
Amylase increased	3 (3.2)	2 (2.1)
Hyperthyroidism	3 (3.2)	
Adrenal insufficiency	3 (3.2)	
Vomiting	2 (2.1)	1 (1.1)
Pyrexia	2 (2.1)	
Pain	2 (2.1)	
Ejection fraction decreased	2 (2.1)	
Blood alkaline phosphatase increased	2 (2.1)	1 (1.1)
Pneumonitis	2 (2.1)	1 (1.1)
Hypotension	2 (2.1)	1 (1.1)
Autoimmune hepatitis	2 (2.1)	2 (2.1)

** Data cut-off January 8, 2019; Events occurring > 2% pts; includes all pts treated on study*

Promising Activity in Gastric Cancer Population[(a)]

33% ORR in HER2 3+ gastric cancer



Gastric Cancer	N	ORR	DCR	mPFS	mOS
HER2 IHC 3+[(b)]	55	32.7% (18/55)	69.1% (38/55)	4.70 (2.66, 7.49)	NR (12.48, NR)
IHC3+/PD-L1+[(c)]	23	52.2% (12/23)	82.6% (19/23)	4.14 (2.60, 15.54)	NR (6.74, NR)

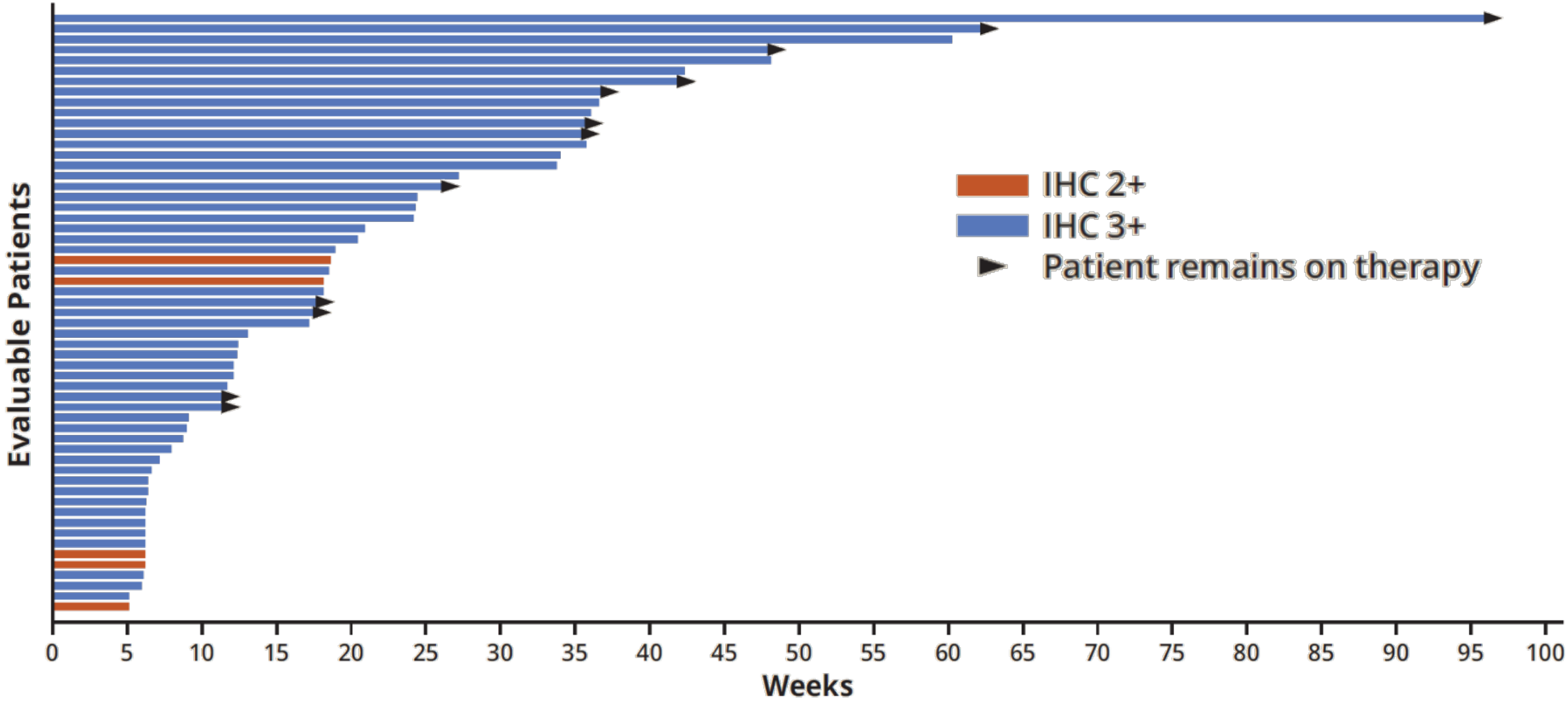
(a) Data cut-off January 8, 2019. Includes patients who received at least one margetuximab and pembro dose in expansion phase, and had baseline measurable disease and at least one post-baseline disease assessment.

(b) Immunohistochemistry (IHC) test gives score of 0 to 3+ that measures amount of HER2 receptor protein on surface of cells in cancer tissue sample. Score of 0 to 1+ is called "HER2 negative", score of 2+ is called "borderline", score of 3+ is called "HER2 positive."

(c) "PD-L1 Positive" reflects Combined Positive Score (per standard FDA approved assay) ≥1% (PD-L1 tested on archival tissue by IHC; clone 22C3 pharmDx).

Duration of Treatment in Overall Gastric Cancer Patients*

Presented at ASCO GI 2019



** Data cut-off January 8, 2019*

Margetuximab + Anti-PD-1 Data in 2L Presents Opportunity to Advance to 1L

HER2+ gastric cancer benchmarks

	1st Line	2nd Line			3rd Line
	SOC	SOC	Ongoing Study	Failed	Ongoing Study
Agent (Study)	Trastuzumab + Chemo[a] (TOGA)	Ramucirumab + Paclitaxel[b] (RAINBOW)	**Margetuximab+ Pembrolizumab[c]** (Ongoing Ph. 2)	Pembrolizumab[d] (KEYNOTE-61) ✖	DS-8201[e]
ORR	47%	28%	**33%** ***(52% in PD-L1+)***	15.8% *(PD-L1+)*	43%
Median PFS	6.7 mos.	4.4 mos.	**4.7 mos.**	1.5 mos.	5.6 mos.
Median OS	**13.1 mos.**	9.6 mos.	**16.8 mos. IHC 3+ GC; IHC3+/PD-L1+** (not reached)	9.1 mos.	NA
≥ Grade 3 TRAEs	**68%**	Overall: N/A 41% Neutropenia 15% Hypertension 12% Fatigue	**18%** **(All GC+GEJ)**	14.3%	50.2%[e]
Gastric/GEJ Patient Mix	80/20%	80/20%	**100%/0%** ***(All IHC 3+ Gastric)***	Not disclosed	NA

SOC = Standard of Care
(a) Data from Herceptin package insert; Bang, et al., Lancet, 2010;
(b) Data from Cyramza package insert; Wilkes, et al., Lancet Oncology, 2014;
(c) Data presented at ASCO GI 2019; Median OS for HER2 IHC 3+ gastric cancer as of April 2019.
(d) Data presented at ASCO 2018, Abstract 4062.
(e) Powell, et al., SABCS 2018, Poster P6-17-06, at 5.4 mg/kg dose in breast cancer patients (n=269), 5 cases of ILD reported, 2 x Gr1, 2 x Gr2, and 1 x Gr5; ILD is a well-characterized risk.

Margetuximab Program: Planned Development

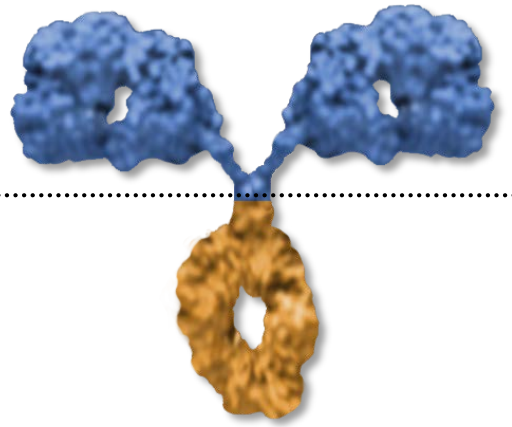
Jon Wigginton, M.D.,

Chief Medical Officer, MacroGenics

Margetuximab: Hypothesized Mechanisms of Action

Fab

Fc



Margetuximab

Inhibit tumor cell signaling and proliferation

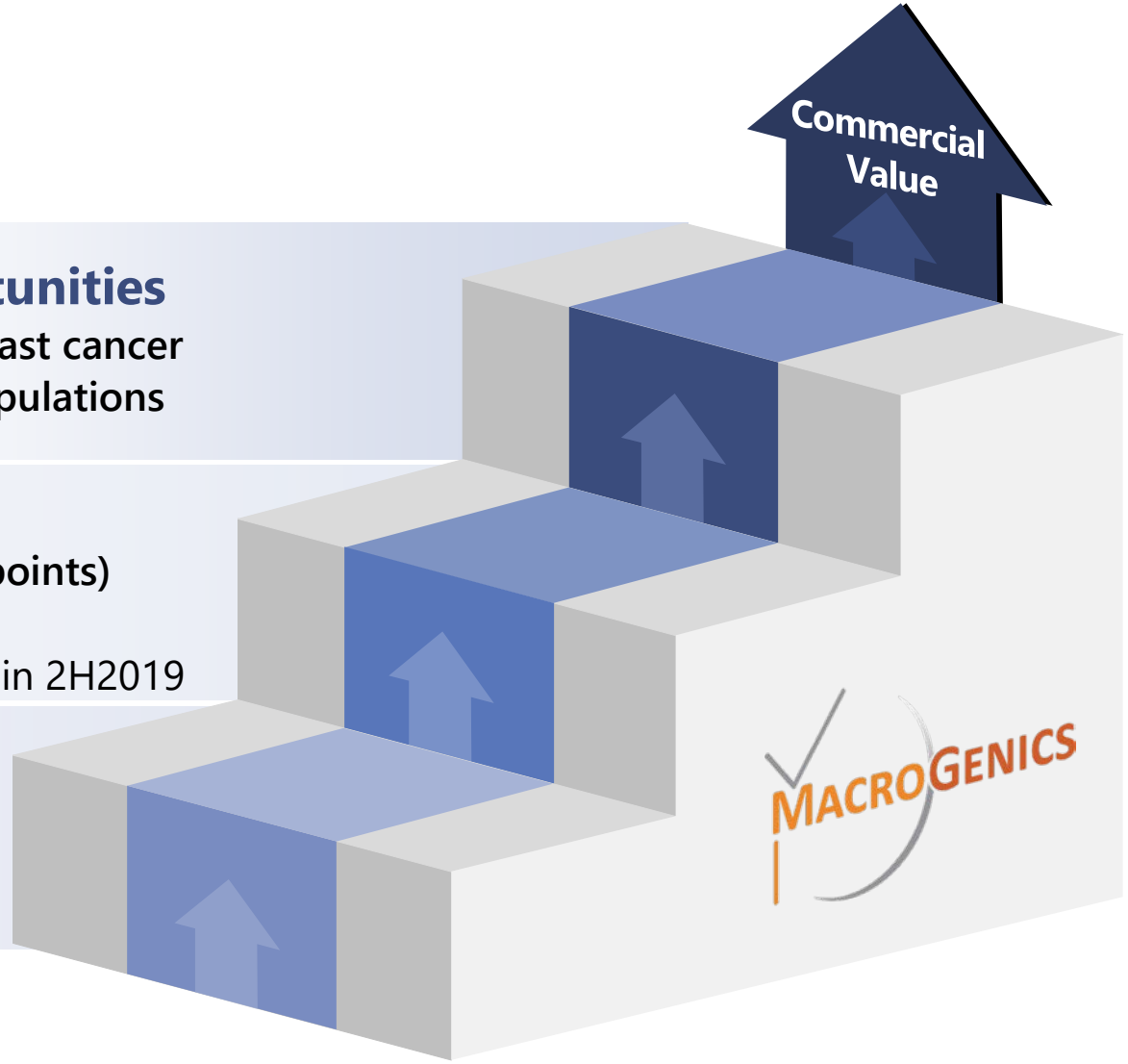
Enhance *innate* immunity
- NK cell activation and proliferation
- NK cell expression of perforin and granzyme B
- Enhance ADCC

Enhance *adaptive* immunity
- HER2-specific T-cell reactivity
- Anti-HER2 antibody response

Tumor Regression

Capturing Full Potential of Margetuximab

Planned development strategy



3 Future Opportunities

- Neoadjuvant breast cancer
- Other HER2+ populations

2 Follow-on Indications

- 1st Line Gastric Cancer (w/checkpoints)
  - IND active, CFDA engaged
  - Ph. 2/3 MAHOGANY initiation in 2H2019

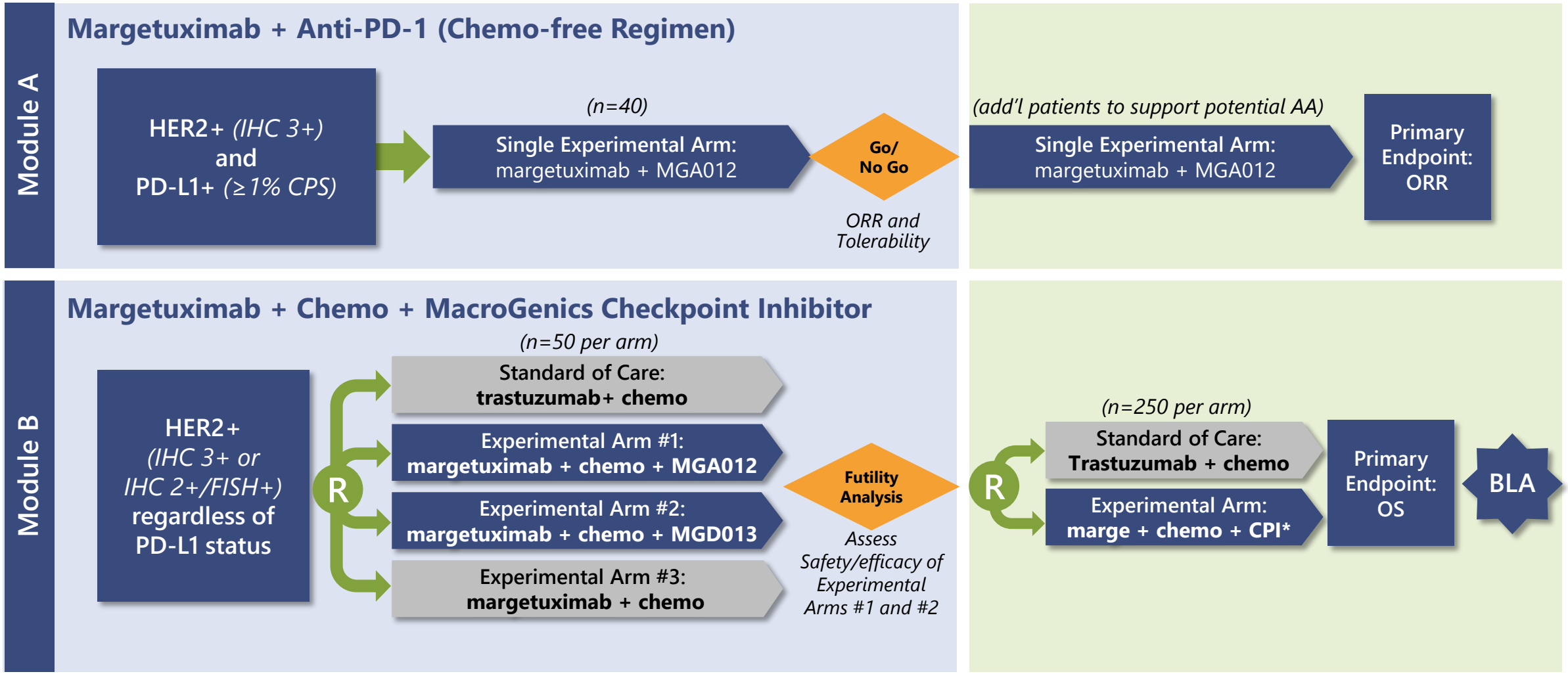
1 Potential Approval

- 3rd/4th Line mBC (w/chemo)

SOPHIA

MACROGENICS

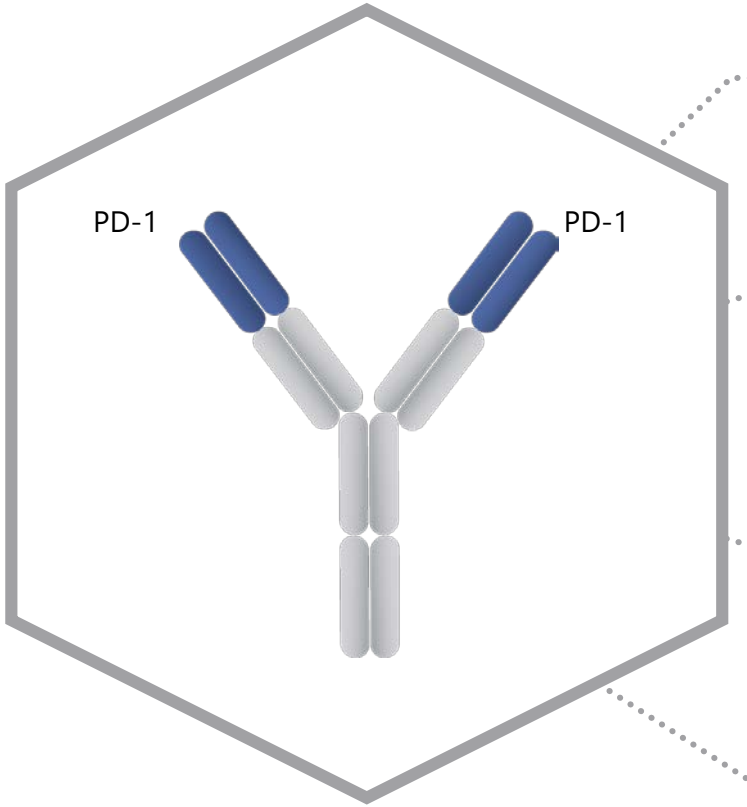
MAHOGANY Phase 2/3 Study: Registration Path in 1L Gastric & GEJ Cancer



** Pending chronic tox study (if regimen with MGD013 is selected).*

MGA012: Initial Activity Profile Similar to Approved Anti-PD-1 mAbs

Global collaboration with Incyte; significant development effort across multiple studies

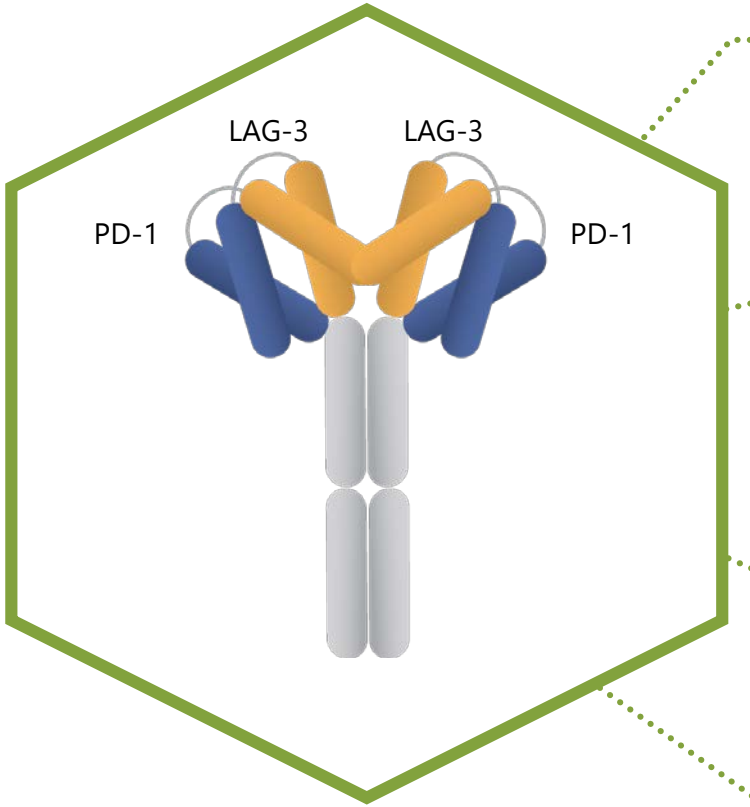


Function/ MoA	• Humanized, hinge-stabilized IgG4 mAb • Inhibits PD-1
Status	• Eleven monotherapy/combo studies ongoing • Initial monotherapy data projected in 2020* • Planned combination with margetuximab +/- chemo in Phase 2/3 MAHOGANY study in gastric cancer
Global Incyte Transaction	• $150M Upfront cash payment • Up to $750M in milestones ($15M received in 2018) • Tiered royalties of 15-24% on future MGA012 sales
MacroGenics' Retained Rights	• Develop pipeline assets in combination with MGA012 • Manufacture portion of global MGA012 supply

Incyte

** Ongoing studies in MSI-high endometrial cancer, Merkel cell carcinoma and anal cancer are potentially registration-directed.*

MGD013: First Bispecific Checkpoint Molecule in Clinic

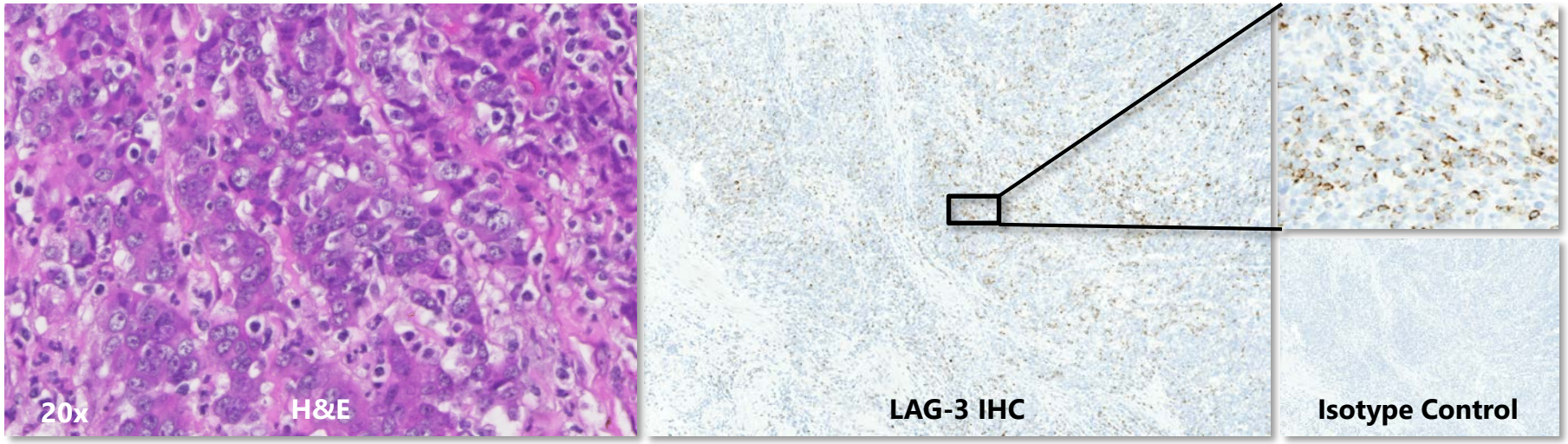


Function/ MoA	• Simultaneous and/or independent blockade of two checkpoint molecules • Reactivation of exhausted T cells
Targeted Indications	• Patients with solid and liquid tumors: – Progressed on prior checkpoint inhibitor – Checkpoint-naïve
Status	• Ongoing Phase 1 dose expansion in nine tumor types • Exploring correlative biomarkers (with Nanostring) • Initiating Phase 2/3 MAHOGANY study with margetuximab and chemotherapy in gastric cancer
MacroGenics' Retained Rights	• Global rights (excl. Greater China)

Rationale for MGD013: High LAG-3 Expression in Gastric Cancer

- LAG-3 positivity: 88% (30/34) observed across gastric cancer samples*

H&E and LAG-3 IHC profile for gastric cancer patient sample

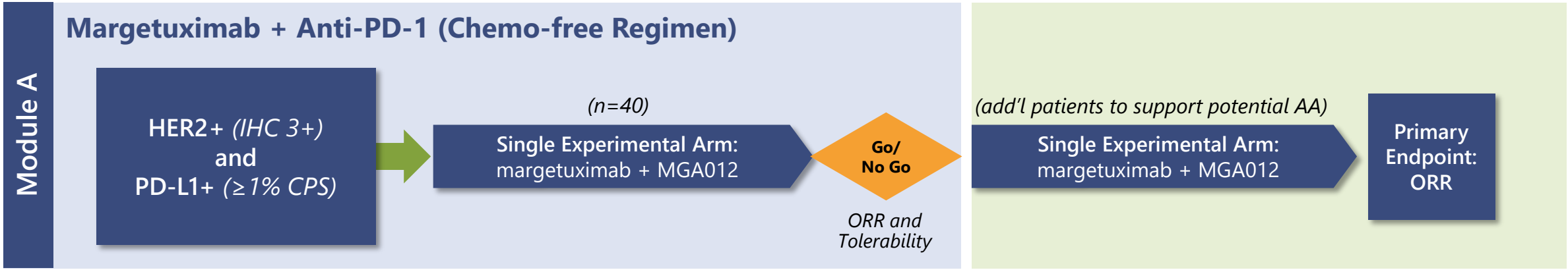


** IHC performed using anti-LAG-3 mAb EPR43292(2); Positivity defined as detection of at least one LAG-3 positive Tumor Infiltrating Lymphocyte (TIL)*

- **cPR in 67 y.o. patient in MGD013 monotherapy Phase 1 study**
  - Refractory to nivolumab
  - Complete resolution of target lesions
  - Treatment ongoing as of May 2019 for ~31 weeks

MAHOGANY Phase 2/3 Study: Registration Path in 1L Gastric & GEJ Cancer

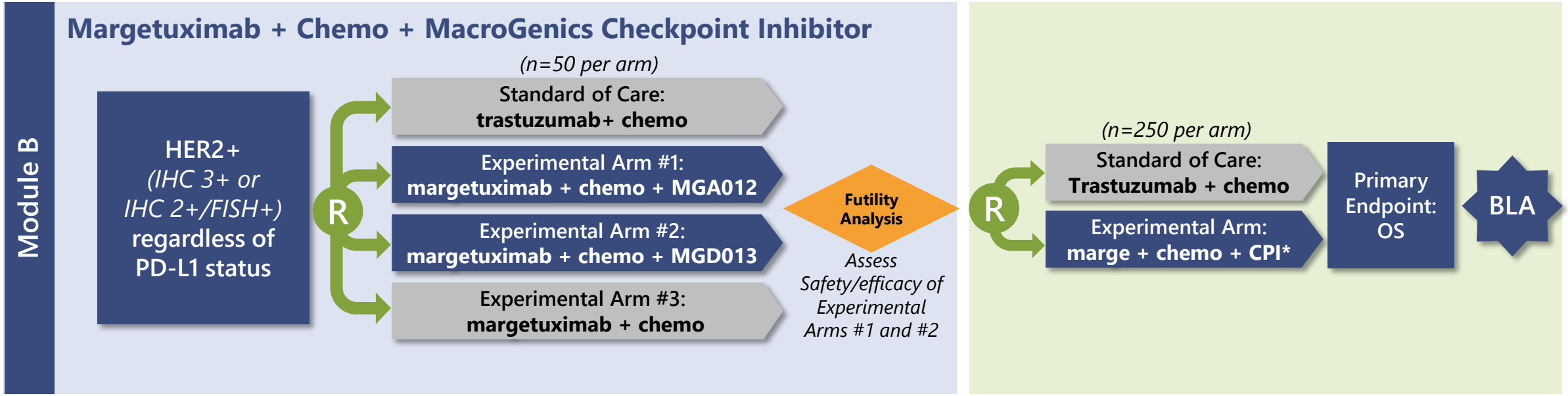
Seeks to establish chemotherapy-free regimen for treatment of HER2+/PD-L1+ patients in 1L setting



- Designed to establish meaningful clinical activity with favorable safety profile using single arm trial
- ≥Grade 3 AEs in 18% of patients treated with margetuximab/pembrolizumab
- Historical experience in patients treated with TOGA regimen: 68% ≥Grade 3 AEs
- Potential opportunity for accelerated approval in U.S. based on primary endpoint of ORR
- Planned initiation in 2H2019

MAHOGANY Phase 2/3 Study: Registration Path in 1L Gastric & GEJ Cancer

Integrates margetuximab and checkpoint inhibition in combination with standard chemotherapy



- Assess both **MGA012** (anti-PD-1) and **MGD013** (anti-PD-1 x LAG-3) based regimens
- Margetuximab+chemotherapy arm to help define contribution of components
- Primary endpoint: overall survival (OS); interim futility: ORR

** Pending chronic tox study (if regimen with MGD013 is selected).*

Key Takeaways & Future Program Milestones

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

President and Chief Executive Officer, MacroGenics

Margetuximab – Key Takeaways

- **Margetuximab has shown ability to engage both innate and adaptive immunity**
- **SOPHIA Phase 3 demonstrates superiority to trastuzumab**
  - Prolonged PFS in first sequential primary analysis
  - Consistent with putative mechanism of action, OS data is trending favorably at first interim analysis
  - Enhanced activity observed in CD16A F-carrier exploratory subpopulation
  - Comparable safety/tolerability profile with trastuzumab
- **Seeking first approval in 3rd/4th line HER2-positive mBC**
- **Significant opportunity to expand commercial potential with additional indications**
  - Phase 2/3 MAHOGANY trial in 1L gastric cancer
  - Neoadjuvant mBC study via investigator-sponsored trial *(in discussion)*
  - mBC bridging studies being planned in China (Zai Lab)
  - Checkpoint combinations align well with margetuximab's mechanism of action

Margetuximab – Future Program Milestones

2H2019

- Initiate Phase 2/3 MAHOGANY first-line gastric study
- Conduct SOPHIA second interim OS analysis at 270 events
- Submit BLA in HER2-positive mBC

2020

- Potential U.S. approval in 3rd/4th line HER2-positive mBC
- Conduct SOPHIA final OS analysis at 385 events
- Submit application to EMA

Q&A Session

Scott Koenig, M.D., Ph.D.	President & Chief Executive Officer, MacroGenics
Jon Wigginton, M.D.	Chief Medical Officer, MacroGenics
Hope S. Rugo, M.D.	Clinical Professor of Medicine, UCSF Helen Diller Family Comprehensive Cancer Center
Daniel Catenacci, M.D.	Associate Professor of Medicine, The University of Chicago Medical Center

Thank You!

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