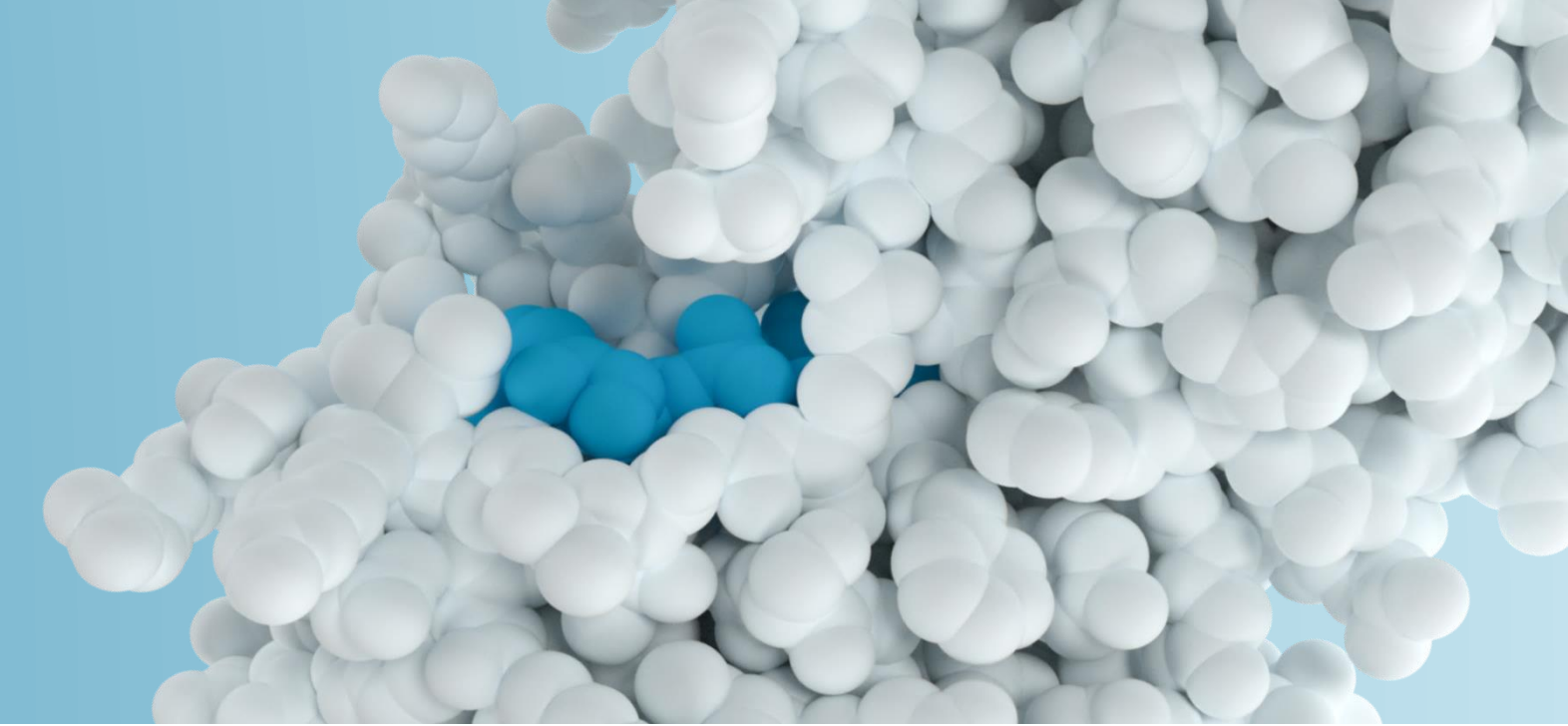


Safety and Activity of IAM1363, a CNS-penetrant HER2 TKI in Participants with HER2 Altered Advanced Cancers



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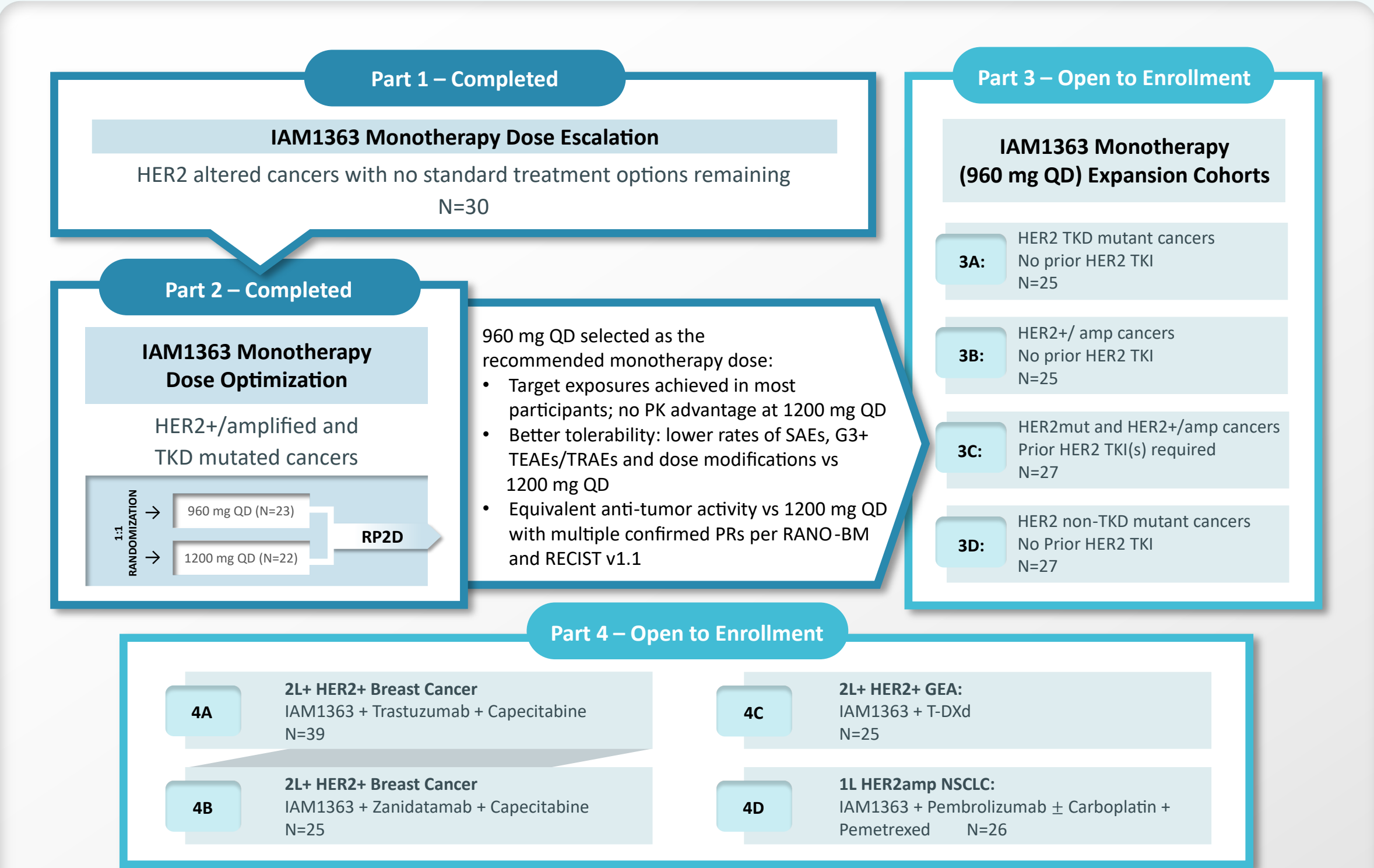
Background

IAM1363: Selective & Brain Penetrant HER2-directed TKI

- IAM1363 potently and irreversibly inhibits wild type and TKD mutant HER2
- Active in the CNS, with 10X greater penetrance over tucatinib
- High selectivity (>5000-fold selectivity for HER2 over EGFR) and preferential tumor enrichment with high tumor/plasma ratio and longer half life in the tumor to maximize target engagement and mitigate toxicity
- Intracranial and systemic activity demonstrated across tumor types and HER2 alterations

Methods

IAM1363-01 Study Design (Four Parts)



Key Eligibility Criteria (All Parts)

- HER2-altered advanced cancers*
- Radiographically measurable disease by either/both of the following:
 - CNS disease*: modified RANO-BM, target lesions ≥ 5 mm
 - Non-CNS disease: RECIST v1.1
- Leptomeningeal and other non-measurable disease allowed

*Definition of HER2 alteration varies by study part
†Provided local therapy not indicated

Results

Disposition and Demographics

- As of the 31Aug26 DCO, 122 participants received IAM1363 across study Parts 1-4; 103 pts received monotherapy at doses ≥ 960 mg and 68 pts received the recommended dose of 960 mg
- Median age was 62 years (range, 29-79)
- Most pts were female (71%) and white (71%); 70% had ECOG performance status of 1
- At DCO, 40 pts (33%) remain on study treatment, with the most common reason for treatment discontinuation being disease progression (74%)

Disease Characteristics and Prior Therapies

- Most common tumor type was BC, majority were HER2+
- One-third of participants had HER2 TKD mutated disease across a variety of tumor types
- Over 40% of participants had CNS metastases
- Heavily pre-treated in the metastatic setting
 - 61% prior T-DXd; 36% prior tucatinib

Baseline Disease Characteristics (IAM1363 Monotherapy ≥ 960 mg)	N=103 N (%)
Tumor Type	
Breast Cancer	39 (37.9)
Non-Small Cell Lung Cancer	20 (19.4)
Gynecologic†	11 (10.7)
Gastroesophageal Adenocarcinoma*	9 (8.7)
Colorectal Cancer	8 (7.8)
Other	16 (15.5)
CNS Metastases Present	45 (43.7)
Local HER2 Subtype	
Overexpressing/amplified	55 (53.4)
Mutated	32 (31.1)
Amplified by NGS	9 (8.7)
Other#	7 (6.8)
Prior Therapies (metastatic setting), Median (range)	
Total Regimens	3.0 (1-11)
HER2 Targeted Regimens	3.0 (1-8)

*Gastric, esophageal, and gastroesophageal junction cancers
†Cervical, ovarian, and endometrial cancers
IHC 1+ and 2+ regardless of ISH status allowed in Part 1

Key Monotherapy Safety Findings

TEAEs in Pts Dosed ≥ 960 mg	Any Grade N=103 N (%)	G3+* N=103 N (%)	Comparison: 960 mg vs. 1200 mg	
TEAEs in $\leq 10\%$ of pts			960 mg N=68 N (%)	1200 mg N=29 N (%)
Diarrhea	61 (59.2)	6 (5.8)		
Nausea	55 (53.4)	1 (1.0)		
Vomiting	50 (48.5)	0 (0.0)		
Fatigue	18 (17.5)	0 (0.0)		
Anemia	17 (16.5)	5 (4.9)		
Constipation	15 (14.6)	0 (0.0)		
Cough	13 (12.6)	0 (0.0)		
Decreased appetite	11 (10.7)	1 (1.0)		
Headache	11 (10.7)	2 (1.9)		

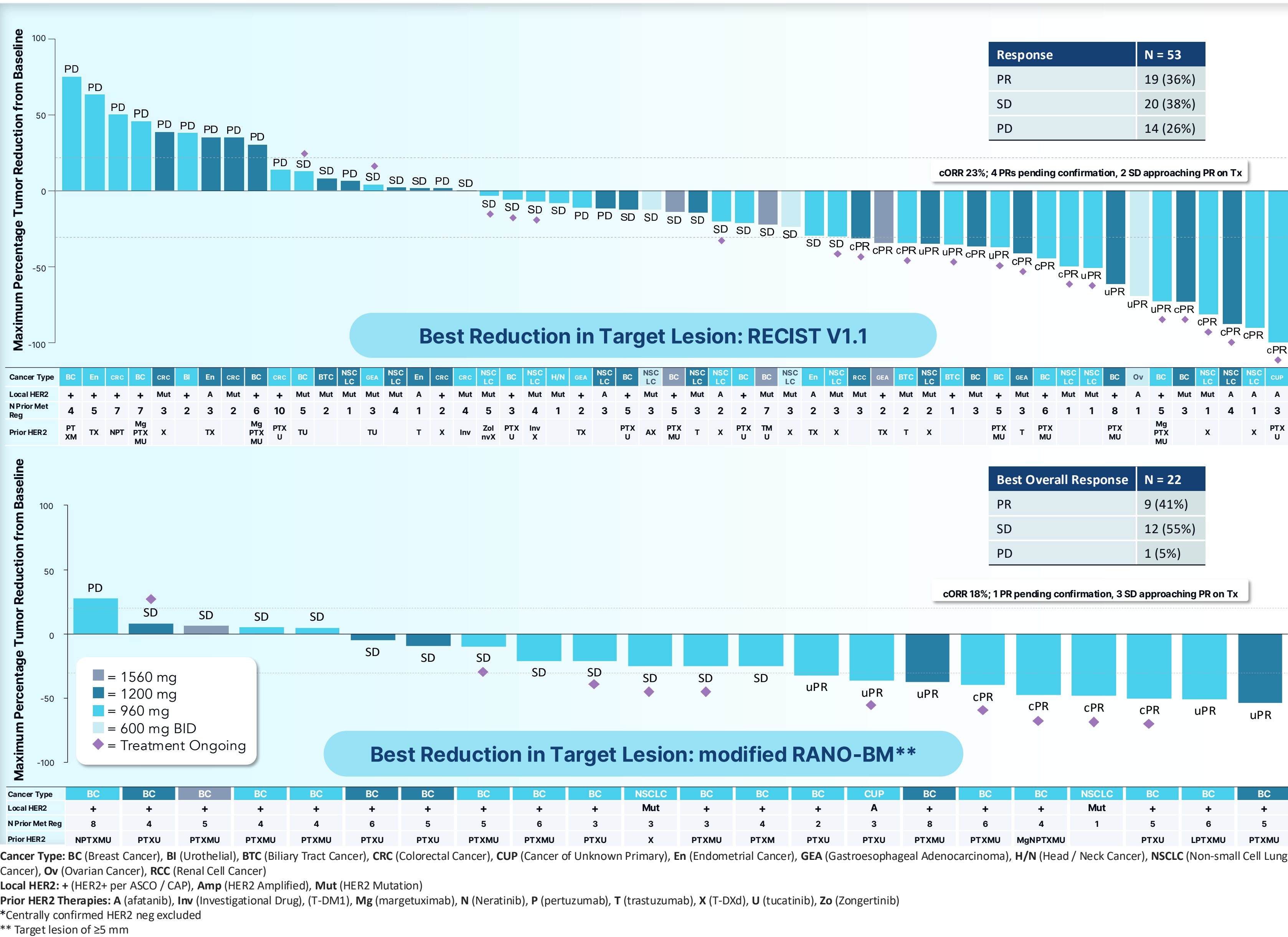
*No Grade 4 TEAEs; one Grade 5 TEAE (death of unknown cause) assessed as unrelated to IAM1363. No Grade 5 TRAEs

- Most TEAEs and TRAEs were low grade
- The most common TRAEs were similar to the profile for TEAEs
- At the RD of 960 mg compared with 1200 mg:
 - Fewer G3 TRAEs
 - Lower rate of dose reductions and no treatment discontinuations due to TRAEs
 - Fewer TRSAEs

Results

Efficacy: Anti-Tumor Activity

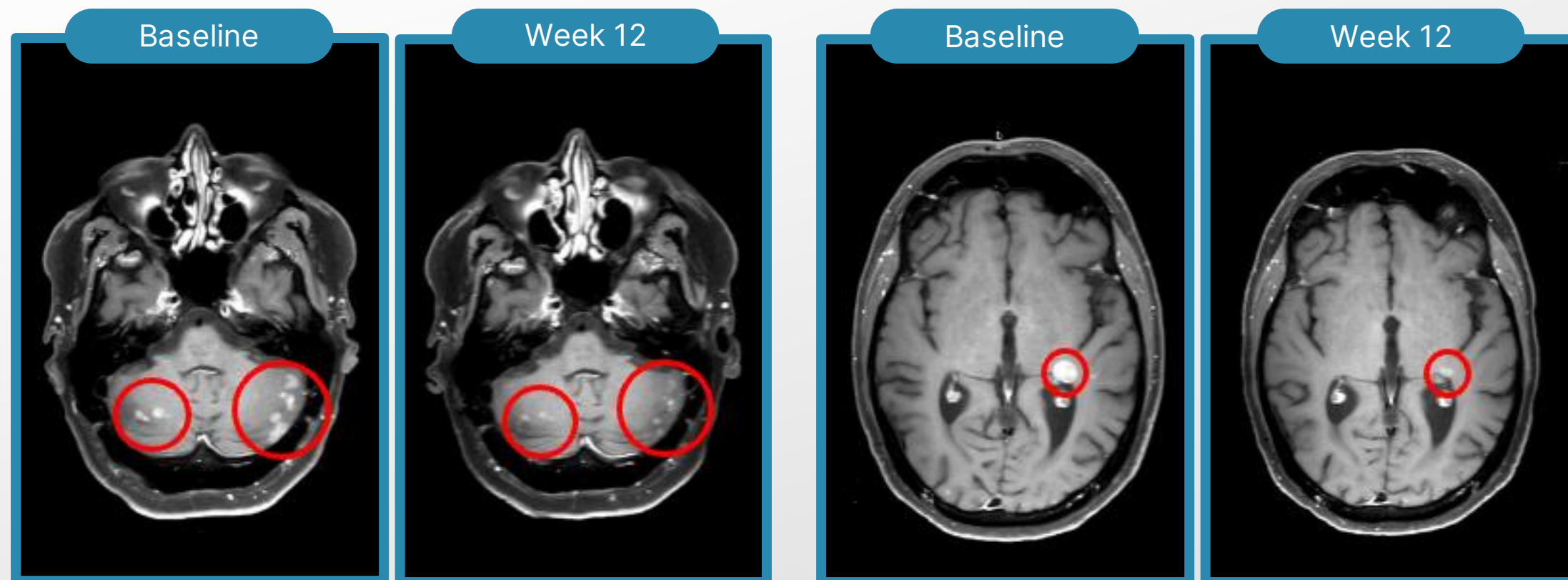
Participants with Targetable HER2 alterations treated ≥ 960 mg*



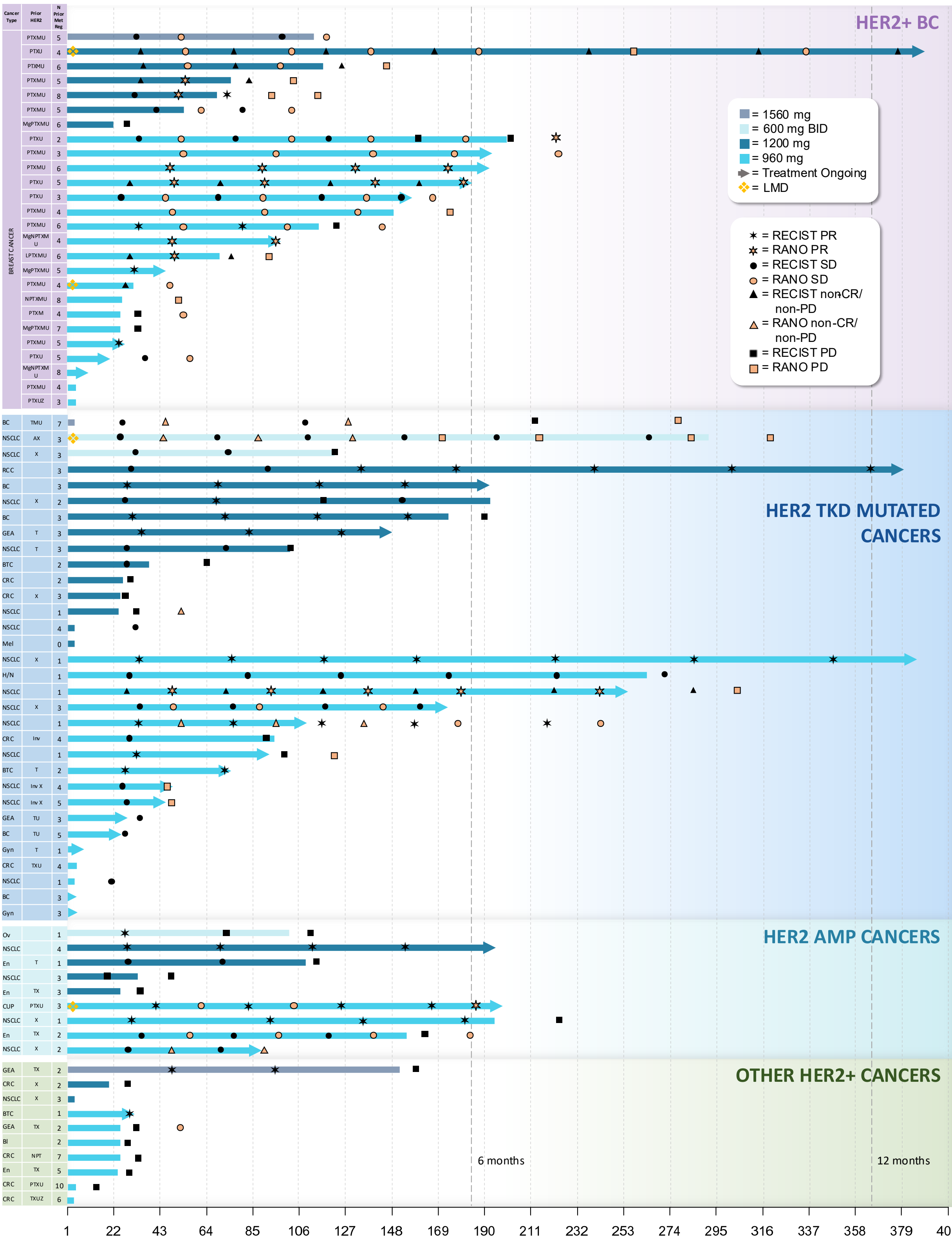
- Evolving data set, as more than half of participants dosed at 960 mg remain on study treatment. Early anti-tumor activity includes:
- Intracranial and systemic responses observed in participants with HER2+ BC, majority post T-DXd and tucatinib, including 3 cPRs per RANO-BM (all post T-DXd and tucatinib); all remaining on treatment, 2 for >6 mos
- Intracranial and systemic responses seen in participants with HER2 mutated NSCLC, including a cPR per RECIST in a participant post T-DXd, ongoing at >12 mos, and a cPR per RANO-BM with disease control for >10 mos, and across a variety of other HER2 mutated cancers including BC, BTC, GEA and RCC, including 5 cPRs per RECIST, 4 still on treatment, 1 for >12 mos
- 3 participants with HER2 amplified cancers detected on NGS had durable responses including 2 cPRs per RECIST with NSCLC, 1 still ongoing and 1 cPR with CUP still ongoing
- 4 participants with leptomeningeal disease, with 2 on treatment >6 mos

Case Study: Intracranial Response

- 40-year-old male with HR+ HER2+ breast cancer
- >50 intracranial metastases at time of enrollment
- Prior treatment with trastuzumab, pertuzumab, margetuximab, T-DXd, T-DM1, neratinib and tucatinib
- All TEAEs were low grade
- Intracranial cPR is ongoing



Treatment Duration



Conclusions

- IAM1363 is well-tolerated at efficacious doses. At the recommended dose of 960 mg QD, it exhibits a favorable PK profile, maximal anti-tumor activity, and a low rate of treatment-related G3+ AEs, SAEs, and dose modifications.
- IAM1363 demonstrates promising monotherapy activity and durable disease control in heavily pretreated participants, including against progressive CNS disease in participants with HER2+ BC post T-DXd and tucatinib
- Responses were seen across a range of tumors harboring HER2 gene amplification and TKD mutations as detected by NGS

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