ASCO 2022 Investor & Analyst Webcast

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Forward-Looking Statements

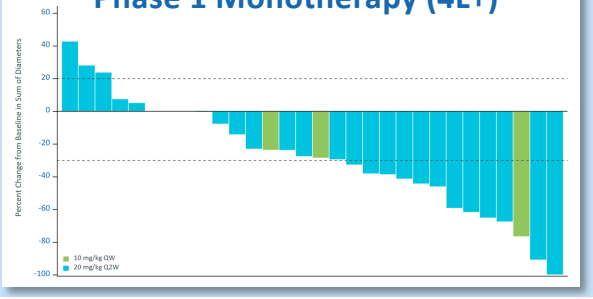
This presentation includes “forward-looking statements” within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and “forward-looking information” within the meaning of Canadian securities laws, or collectively, forward looking statements. Forward-looking statements include statements that may relate to our plans, objectives, goals, strategies, future events, future revenue or performance, capital expenditures, financing needs and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “subject to,” “believe,” “anticipate,” “plan,” “expect,” “intend,” “estimate,” “project,” “may,” “will,” “should,” “would,” “could,” “can,” the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements, including, without limitation, our examination of historical operating trends, are based upon our current expectations and various assumptions. We may not realize our expectations, and our beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of risks and uncertainties, including those described in the "Risk Factors" and other sections of our public filings with the Securities and Exchange Commission and Canadian securities regulators.

These forward-looking statements are made only as of the date hereof, and Zymeworks Inc. undertakes no obligation to update or revise the forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

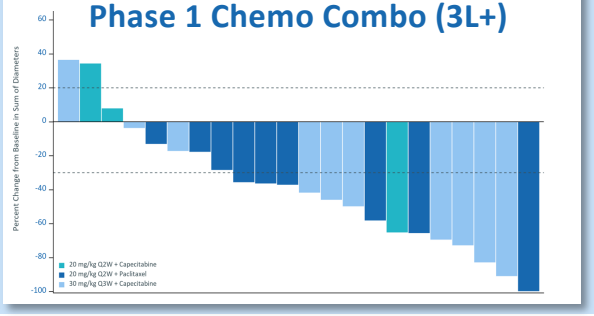
Breadth of Zanidatamab Clinical Data

Gastroesophageal

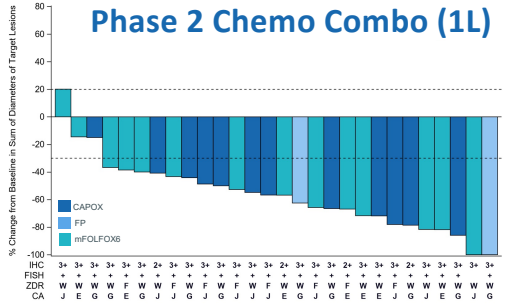
Phase 1 Monotherapy (4L+)



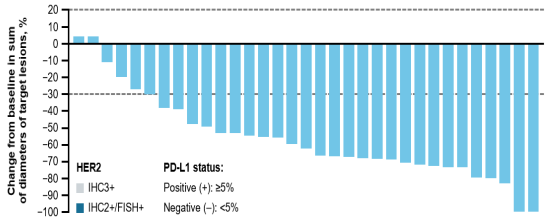
Phase 1 Chemo Combo (3L+)



Phase 2 Chemo Combo (1L)

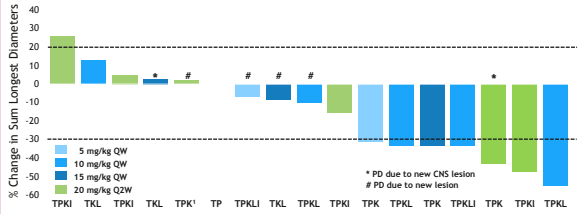


Phase 2 Tisle + Chemo Combo (1L)

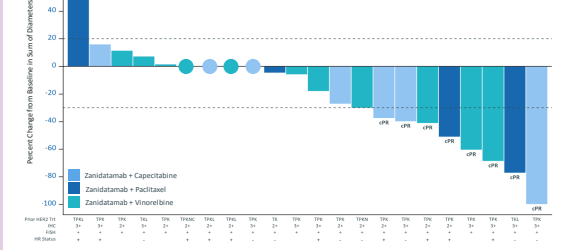


Breast Cancer

Phase 1 Monotherapy (Late-Line)



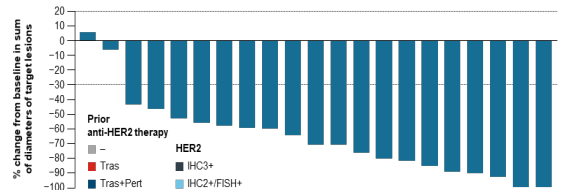
Phase 1 Chemo Combo (3L+)



Phase 2 CDK4/6 Combo (3L+)

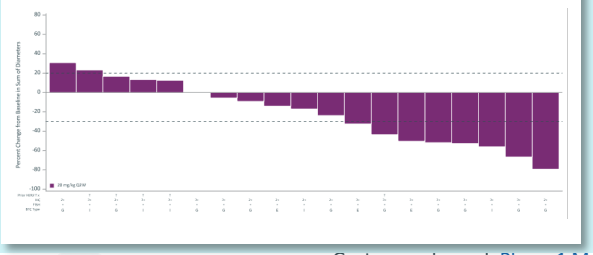
4Q 2022[1]

Phase 2 Chemo Combo (1L)

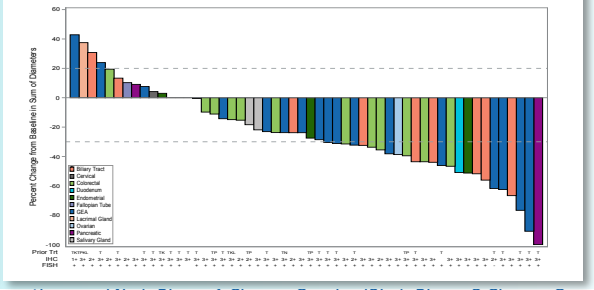


Other Solid Tumors

BTC: Phase 1 Monotherapy (2L+)



Others: Phase 1 Monotherapy (Late-Line)



Gastroesophageal: Phase 1 Monotherapy (4L+), Phase 1 Chemo Combo (3L+), Phase 2 Chemo Combo (1L), Phase 2 Tisle + Chemo Combo (1L)
Breast Cancer: Phase 1 Monotherapy (Late-Line), Phase 1 Chemo Combo (3L+), Phase 2 Chemo Combo (1L)
Other Solid Tumor: BTC Phase 1 Monotherapy (2L+), Others: Phase 1 Monotherapy (Late-Line)

[1] Data anticipated to be presented in the fourth quarter 2022

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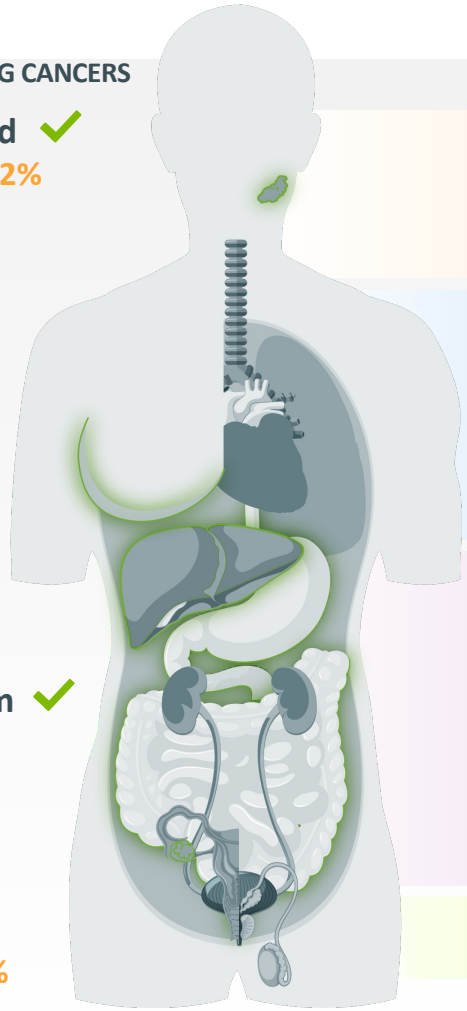
Broad Opportunity for Zanidatamab in HER2-Targeted Therapy

Advancing zanidatamab in two pivotal trials with broad opportunity for additional indications

HER2 EXPRESSING CANCERS

- **Salivary Gland** ✓ — 17-44% | 12-52%
- **Lung** ✓ — 2.5% | 2-3%
- **Pancreas** ✓ — 26% | 2%
- **Bladder** — 12.4% | 9%
- **Ovarian** ✓ — 27% | 7%
- **Endometrium** ✓ — 18-80% | 4%
- **Prostate** — 10% | 6%
- **Cervix** — 21% | 0.5-14%



HER2 EXPRESSION | AMPLIFICATION

✓ ZANIDATAMAB SINGLE AGENT ACTIVITY

	PHASE 1	PHASE 2	PIVOTAL
Biliary Tract ✓ 20% | 5-15%	2L Zanidatamab Monotherapy		HERIZON with BeiGene
	1L Zanidatamab + SOC (cisplatin + gemcitabine)		
Stomach ✓ 20% | 11-16%	1L Zanidatamab + SOC Chemo ± Tislelizumab *vs* Herceptin + SOC Chemo		HERIZON with BeiGene
	1L Zanidatamab + SOC Chemotherapy + Tislelizumab		with BeiGene
	1L Zanidatamab + SOC Chemotherapy		
Breast ✓ 15-20% | 20%	3L+ Zanidatamab + Ibrance (anti-CDK4/6) + Fulvestrant		with Pfizer
	1L Zanidatamab + Docetaxel		with BeiGene
	3L+ Zanidatamab + Evorpacept (CD47-blocker)		with ALX ONCOLOGY
	3L+ Zani + Chemo		
Colorectal ✓ 5% | 6%	1L Zanidatamab + SOC (mFOLFOX6 ± bevacizumab)		

SOC = Standard of Care

Modified from Oh D-Y & Bang Y-J 2019 Nat Rev Clin Onc

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Development Strategies for Lead Indications

Pivotal Studies in BTC and GEA Phase 2 studies in Breast Cancer

Zanidatamab in BTC and first-line GEA estimated to be significant commercial opportunity with additional expansion possible from other clinical indications

Biliary Tract Cancer (BTC)

- Strategy: First-to-Market HER2-targeted therapy for BTC
- Pivotal HERIZON-BTC-01 study has completed enrollment

Gastroesophageal Adenocarcinoma (GEA)

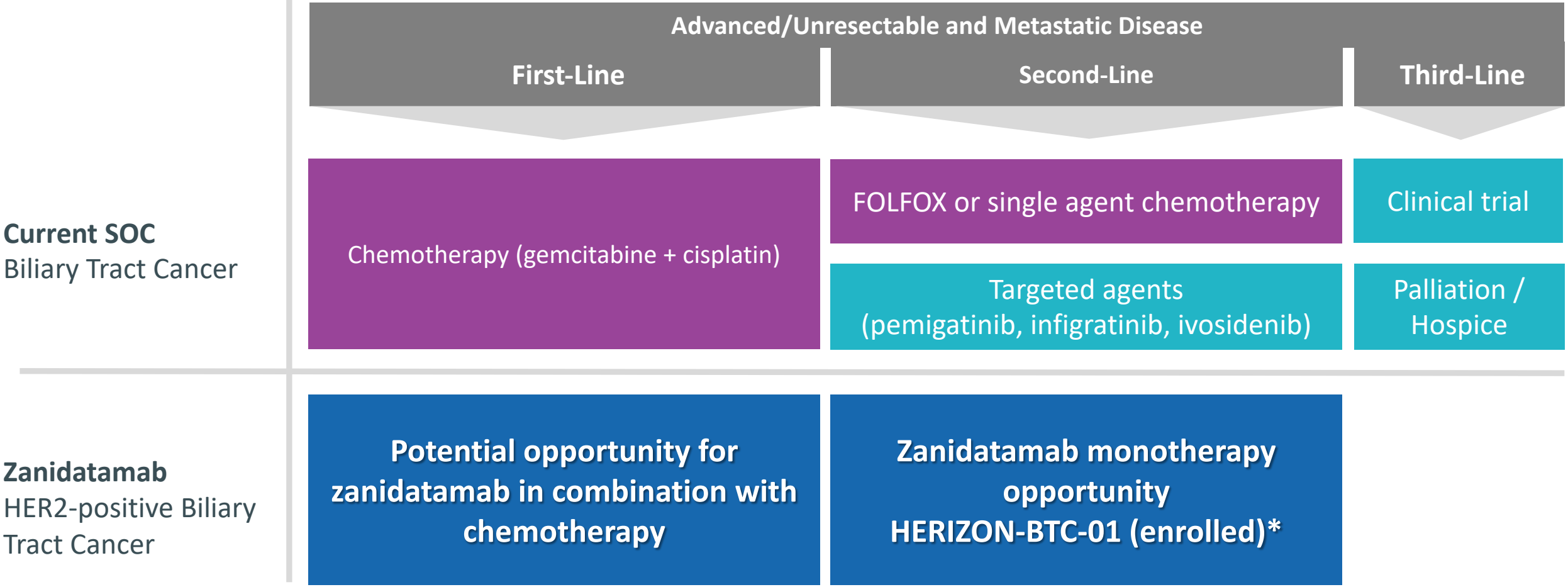
- Strategy: Position zanidatamab as best-in-class HER2-targeted therapy to displace trastuzumab in 1L HER2+ GEA
- Phase 3 registrational HERIZON-GEA-01 study open and enrolling globally

Breast Cancer

- Strategy: Develop for a growing population of HER2+ patients with progression after receiving ≥3 prior HER2-targeted agents for advanced disease; ongoing assessment of potential to move into earlier lines of treatment
- Ongoing evaluation of promising combinations in phase 1 and 2 trials

Biliary Tract Cancer

Zanidatamab Has Potential to Provide a Chemo-free Regimen for HER2 Therapy in Biliary Tract Cancer



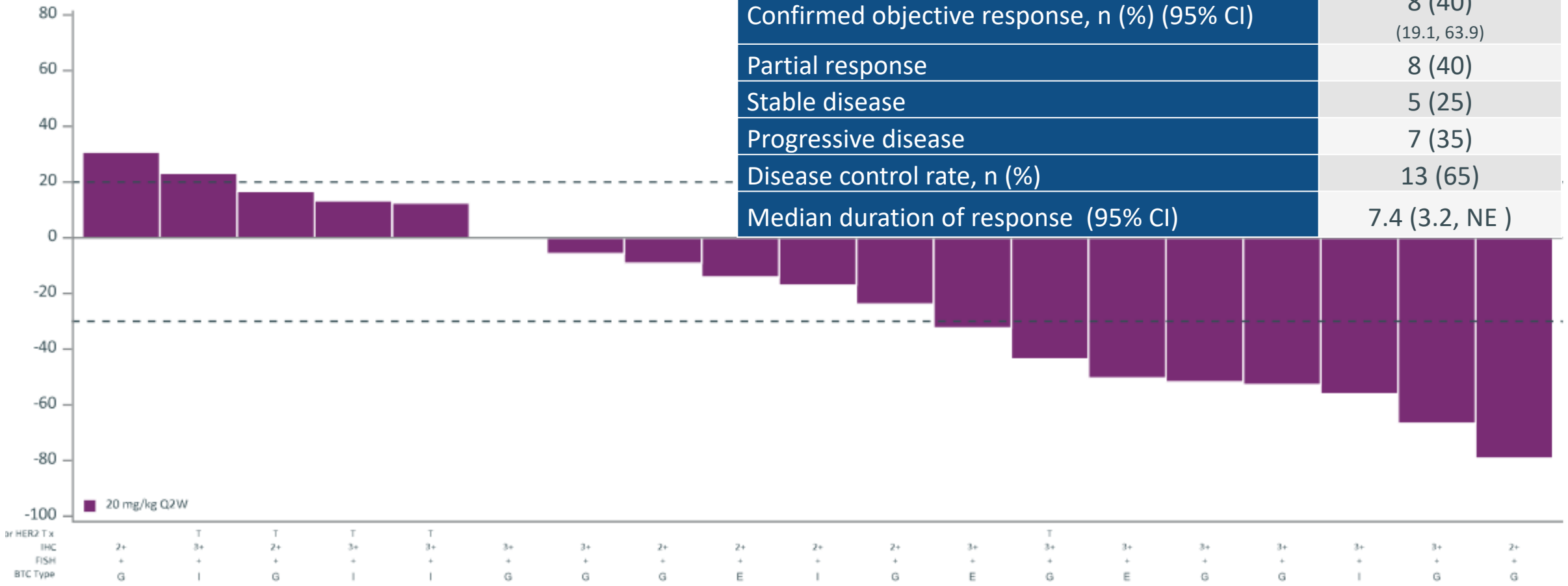
***Topline data anticipated by early Q1 2023**

SOC = standard of care

Zanidatamab Monotherapy in HER2-Expressing Late-Line BTC

Phase 1 data (NCT02892123) as reported at ASCO GI | Jan 2021

	(N = 20)
Confirmed objective response, n (%) (95% CI)	8 (40) (19.1, 63.9)
Partial response	8 (40)
Stable disease	5 (25)
Progressive disease	7 (35)
Disease control rate, n (%)	13 (65)
Median duration of response (95% CI)	7.4 (3.2, NE)



E: Extrahepatic Cholangiocarcinoma; FISH: fluorescence in situ hybridization; I: Intrahepatic Cholangiocarcinoma; IHC: immunohistochemistry; G: Gallbladder; T: trastuzumab; Trt: treatment.Response-evaluable: all treated patients with measurable disease who had at least one evaluable, post-baseline disease assessment (per RECIST 1.1) or discontinued study treatment due to death or clinical progression. Note: One patient was not response evaluable because they withdrew from the study. One patient in the response-evaluable set died prior to the post-baseline tumor measurement and is not included in the plot (counted as PD).

Source: Meric-Bernstam, et al. 2021, ASCO GI

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Zanidatamab Monotherapy in HER2-Expressing Late-Line BTC

Phase 1 data (NCT02892123) as reported at ASCO GI | Jan 2021

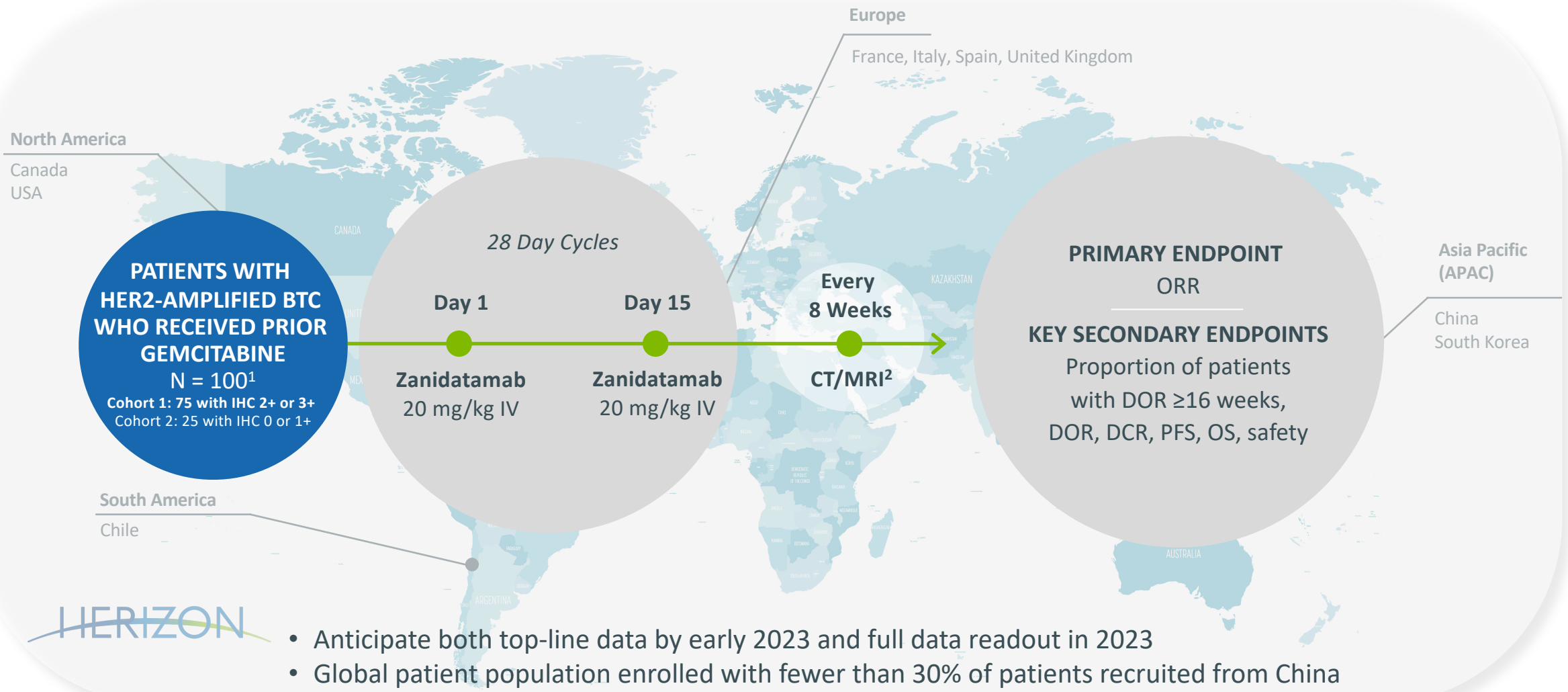
Well-tolerated with no patient experiencing a Grade 3 or higher zanidatamab-related AE

- A single zanidatamab-related serious adverse events (AE) (Grade 2 fatigue) was reported in one patient. The patient was hospitalized, treated with IV fluids, and recovered within a day
- Two deaths were reported during the study — one due to progressive disease and one due to an unrelated AE (cardiac arrest in the setting of bowel perforation)

Zanidatamab-related Adverse Events	(N = 21)
Patients with treatment-emergent AEs, n (%)	21 (100)
Patients with zanidatamab-related AEs (occurring in ≥ 15% of BTC patients)	
Any, n (%)	15 (71)
Diarrhea	9 (43)
Infusion-related reaction	7 (33)

Source: Meric-Bernstam, et al, 2021, ASCO GI

HERIZON-BTC-01: A Global Pivotal Study in Second-Line HER2-Amplified BTC



HERIZON

- Anticipate both top-line data by early 2023 and full data readout in 2023
- Global patient population enrolled with fewer than 30% of patients recruited from China

BTC: biliary tract cancer; DCR: disease control rate; DOR: duration of response; IHC: immunohistochemistry; IV: intravenous; MRI: magnetic resonance imaging; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; Q2W: every 2 weeks; RECIST: Response Evaluation Criteria in Solid Tumors.
[1]All patients on study are HER2-amplified as determined by in-situ hybridization (ISH) assay.
[2]For tumor assessment per RECIST v1.1.2.

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Benchmark Data in Relapsed BTC

No clear benefit with chemotherapy-based treatments

- ORR with single agent chemotherapy is <10% in multiple studies[1]
- ABC-06 study showed ORR with FOLFOX = 5% and <1 month prolongation of median OS vs supportive care[2]
- Marginal activity is offset by chemotherapy-related toxicities

Data in 75 subjects provides adequate power to compare against historical data

- An observed ORR of 20% excludes the lower 95% CI boundary of 11.7%
- An observed ORR of 30% excludes the lower 95% CI boundary of 20%
- Duration of response (DoR) is an important secondary endpoint

Accelerated approvals for FGFR2 inhibitors in relapsed BTC were based on:

- Pemigatinib: ORR = 36%, median DoR = 9.1 months
- Infigratinib: ORR = 23%, median DoR = 5 months

[1]Sasaki T et al, *J Clin Med*. 2021;10(14):3108
[2]Lamarca A et al, Lancet Oncol. 2021 May;22(5):690-701

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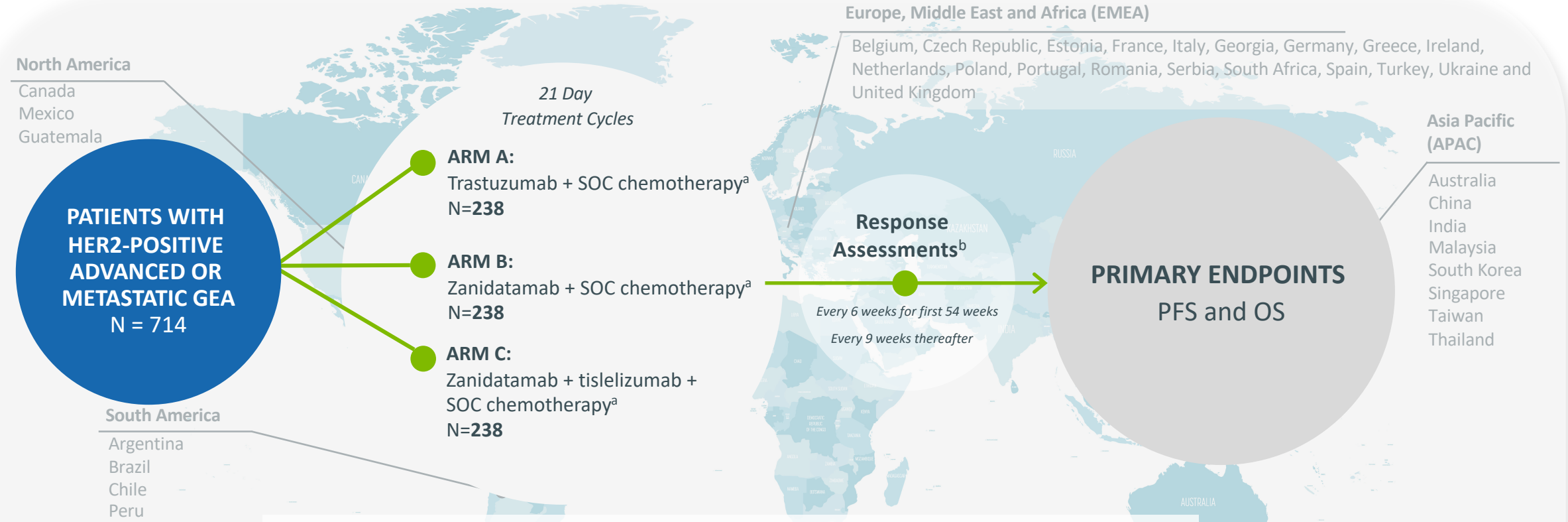
Gastroesophageal Adenocarcinoma

HERIZON-GEA-01: A Global Pivotal Study in First-Line HER2-Positive GEA

Study plans to enroll 714 patients at approximately 300 sites across 38 countries and is expected to complete enrollment by end of 2023



Dosing Regimens

- Zanidatamab: Subjects <70 kg: 1,800 mg IV of each 21-day cycle; Subjects ≥70 kg: 2,400 mg IV of each 21-day cycle
- Tislelizumab: 200 mg IV on Day 1 of each 21-day cycle
- Trastuzumab (Herceptin®; active comparator): 6 mg/kg IV of Day 1 of each 21-day cycle (8 mg/kg IV loading dose on Cycle 1, Day 1)
- CAPOX (combination chemotherapy): Capecitabine 1,000 mg/m² PO bid (total daily dose of 2,000 mg/m²) from the evening of Day 1 to the morning of Day 15 of each 21-day cycle plus oxaliplatin 130 mg/m² IV on Day 1 of each 21-day cycle.
- FP (combination chemotherapy): 5-FU 800 mg/m²/day continuous IV infusion on Days 1 to 5 of each 21-day cycle plus cisplatin 80 mg/m² (60 mg/m² for subjects with GFR 51-61 mL/min at baseline) IV on Day 1 of each 21-day cycle

[a] SOC (standard of care) chemotherapy: CAPOX or FP; [b] response assessments until progression per BICR or withdrawal of consent
BICR: Blind independent central review; GEA: gastroesophageal adenocarcinoma; PFS: Progression-free survival; OS: overall survival

HERIZON-GEA-01 Pivotal Study Features

- Patient population includes HER2-positive (IHC 3+ or IHC 2+/FISH-positive) gastric, gastroesophageal junction, and **esophageal** adenocarcinomas
- PD-L1 non-selected
- Dual Primary endpoints: PFS and OS
- Open-label with disease assessments per Blinded Independent Central Review (BICR)
- Three-arm design supports ability to demonstrate contribution of components
  - Confirm that zanidatamab is the **best-in-class HER2-targeted antibody** in 1L HER2+ GEA
  - Evaluate additional benefit of PD-1 inhibition to zanidatamab and SOC chemotherapy

Designed to support an indication for **zanidatamab and chemotherapy with or without tislelizumab as first-line treatment for HER2-positive gastric, esophageal, and gastroesophageal junction cancers**

(NCT04466891)

Zanidatamab Data in Late-Line GEA Supports First-Line Development

Phase 1 data (NCT02892123) as reported at ASCO GI | Jan 2021

	Zanidatamab Monotherapy (N = 35)	**Zanidatamab + Chemo** [Paclitaxel | Capecitabine] (N = 28) *(24 response evaluable)*
Line of therapy	4L+ (Median 3 prior)	3L+ (Median 2-3 prior)
Study Location	Enrolled in US, Canada, S Korea (37% Asian)	
ORR	**33% confirmed**	**54% confirmed ORR**
mDOR	**6.0m mDOR**	**8.9m mDOR**
mPFS	**3.6m mPFS**	**5.6m mPFS**
Treatment-related (TR) AEs Total (%) / Grade ≥3 (%)	**25 (71%) / 4 (11%)**	**26 (93%) / 9 (32%)**
Comment	**1 event of TR Gr 3 diarrhea**	**0 events of TR Gr ≥3 diarrhea** **1 event of TR pneumonitis (zanidatamab + paclitaxel)**

Source: Meric-Bernstam, et al, 2021, ASCO-GI

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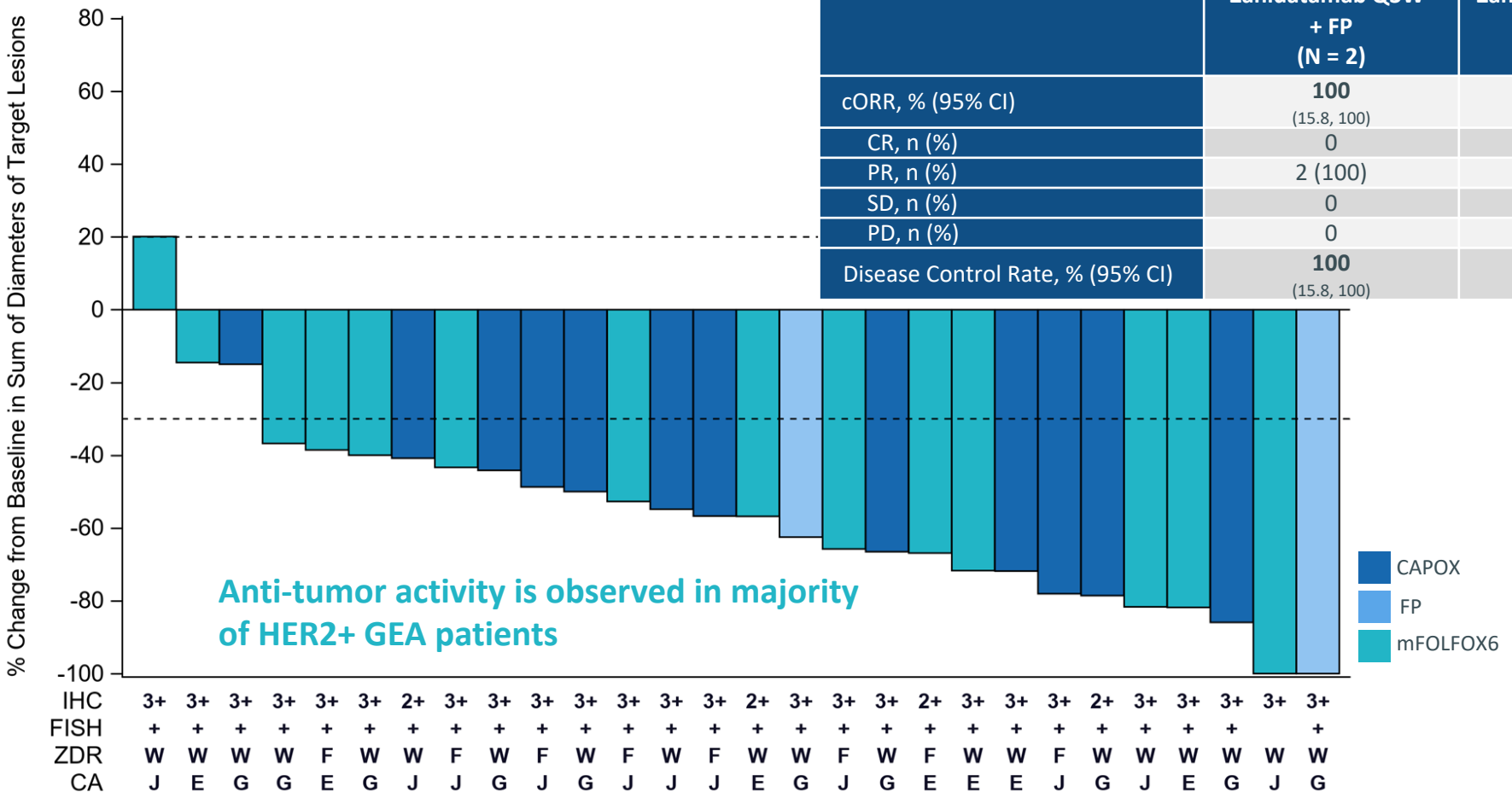
Zanidatamab Plus Chemotherapy in First-Line HER2-Positive GEA

Phase 2 data (NCT03929666) as reported at ESMO | Sep 2021

93% cORR for regimens (zanidatamab + CAPOX or FP) used in Phase 3 HERIZON-GEA-01

Disease Response Per Investigator Assessment (using RECIST 1.1) - HER2+ pts only				
	Zanidatamab Q3W[a] + FP (N = 2)	Zanidatamab Q2W[a] + mFOLFOX6 (N = 14)	Zanidatamab Q3W[a] + CAPOX (N = 12)	Total (N = 28)
cORR, % (95% CI)	**100** (15.8, 100)	**57** (28.9, 82.3)	**92** (61.5, 99.8)	**75** (55.1, 89.3)
CR, n (%)	0	1 (7)	0	1 (4)
PR, n (%)	2 (100)	7 (50)	11 (92)	20 (71)
SD, n (%)	0	3 (21)	1 (8)	4 (14)
PD, n (%)	0	3 (21)	0	3 (11)
Disease Control Rate, % (95% CI)	**100** (15.8, 100)	**79** (49.2, 95.3)	**100** (73.5, 100)	**89** (71.8, 97.7)



CA = cancer; G=gastric; J=gastroesophageal junction; E=esophageal; ZDR = zanidatamab dosing regimen; W = weight-based dose; F = flat dose; NE = not evaluable; ORR = objective response rate (CR+PR); CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; DOR = duration of response

Response-evaluable includes all patients with measurable disease who had at least one post-baseline disease assessment (per RECIST 1.1) or discontinued study treatment prior to reassessment due to death from any cause or clinical progression (response imputed as PD).

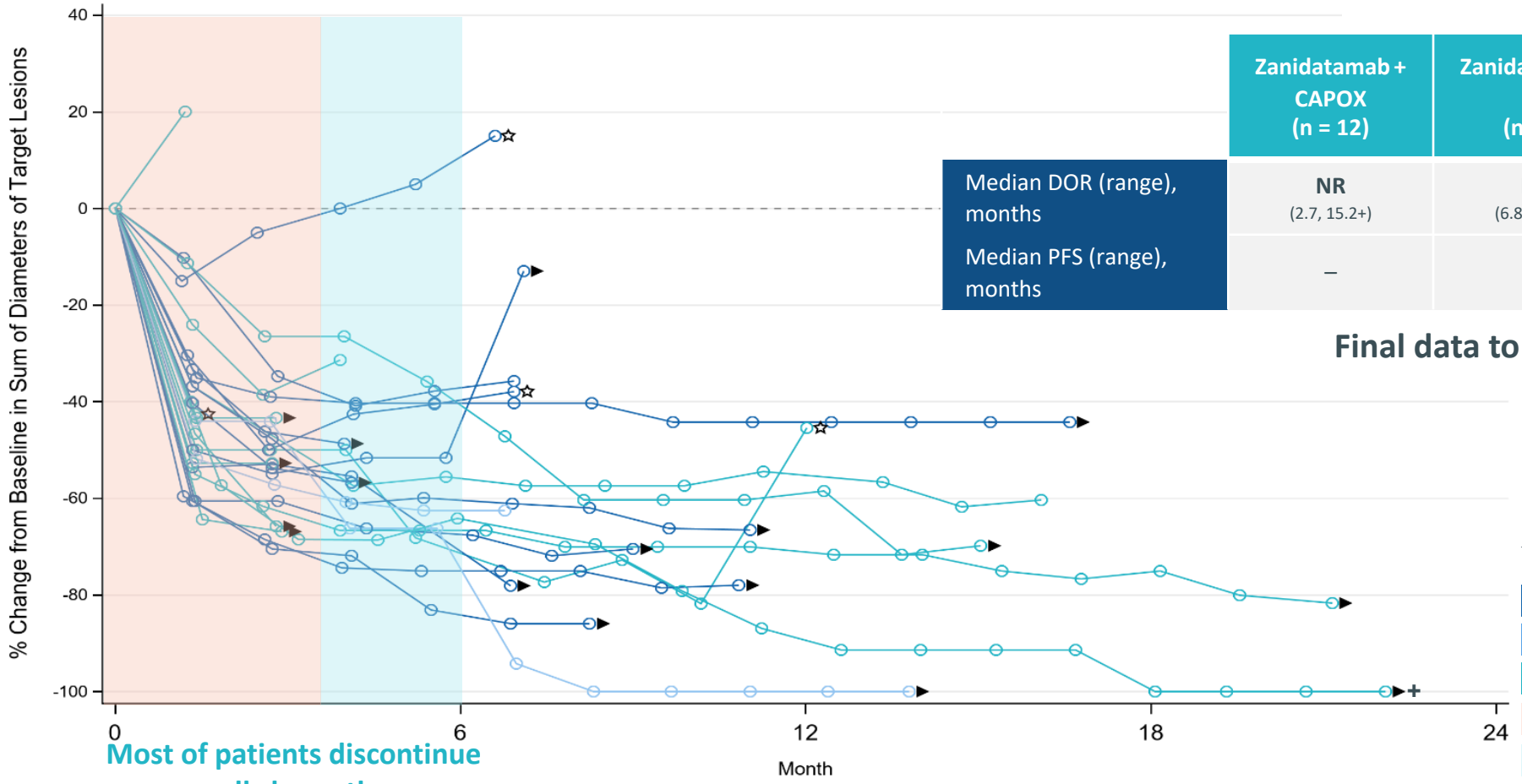
[a]ZW25 administration schedule: Q3W (21-day cycle) of 30 mg/kg or 1800/2400 mg IV, Day 1; Q2W (28-day cycle) of 20 mg/kg or 1200/1600 mg IV (Days 1, 15)

Source: Ku, et al, 2021 (e-poster 1380P; abstr 3678)

Zanidatamab Plus Chemotherapy in First-Line HER2-Positive GEA

Phase 2 data (NCT03929666) as reported at ESMO | Sep 2021

Zanidatamab in combination with chemotherapy produces deep and durable responses



	Zanidatamab + CAPOX (n = 12)	Zanidatamab + FP (n = 2)	Zanidatamab + mFOLFOX6 (n = 14)	Total (N = 28)
Median DOR (range), months	**NR** (2.7, 15.2+)	**NR** (6.8, 12.5+)	**16.4** (1.4, 19.8+)	**16.4** (1.4, 19.8+)
Median PFS (range), months	–	–	–	**12.0** (6.9, NE)

Final data to be presented in 1H 2023

▶ Treatment Ongoing

★ New Lesion

CAPOX

FP

mFOLFOX6

Time to complete CAPOX / FP regimen

Time to complete mFOLFOX6 regimen

Most of patients discontinue some or all chemotherapy after 4 to 6 months

NR – not reached; + An MRI performed for neurologic symptoms on Day 8 demonstrated brain metastases, which were treated with radiation therapy. Subject remained on mFOLFOX6-1 with zanidatamab and has had long term disease control since treatment of brain metastases. Source: Ku, et al. 2021 (e-poster 1380P; abstr 3678)

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Zanidatamab Plus Chemotherapy in First-Line HER2-Positive GEA

Phase 2 data (NCT03929666) as reported at ESMO | Sep 2021

Manageable safety profile; improved control of diarrhea with 1 week of prophylactic loperamide in cycle 1

	Zanidatamab + CAPOX (n = 14)		Zanidatamab + FP (n = 2)		Zanidatamab + mFOLFOX6 (n = 20)		Total (N = 36)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
TRAE,[a] n (%)	14 (100)	8 (57)	2 (100)	1 (50)	20 (100)	16 (80)	36 (100)	25 (69)
Treatment-related SAE[b]	2 (14)	2 (14)	1 (50)	1 (50)	4 (20)	4 (20)	7 (19)	7 (19)
TRAEs leading to treatment discontinuation	0	0	0	0	4 (20)	1 (6)	4 (11)	1 (3)
TRAEs occurring in ≥ 20% of subjects and/or Grade ≥ 3 TRAEs in > 1 subject[c]								
Diarrhea	13 (93)	5 (36)	2 (100)	1 (50)	19 (95)	9 (45)	34 (94)	15 (42)
Nausea	11 (79)	1 (7)	1 (50)	0	15 (75)	1 (5)	27 (75)	2 (6)
Peripheral neuropathy	10 (71)``	0	0	0	9 (45)	0	19 (53)	0
Fatigue	5 (36)	0	0	0	11 (55)	1 (5)	16 (44)	1 (3)
Decreased appetite	5 (36)	0	1 (50)	0	9 (45)	0	15 (42)	0
Hypokalemia	2 (14)	0	0	0	11 (55)	6 (30)	13 (36)	6 (17)
Vomiting	3 (21)	1 (7)	0	0	9 (45)	2 (10)	12 (33)	3 (8)
Hypomagnesemia	3 (21)	0	0	0	6 (30)	1 (5)	9 (25)	1 (3)
Dysgeusia	4 (29)	0	0	0	4 (20)	0	8 (22)	0
Stomatitis	2 (14)	0	0	0	6 (30)	0	8 (22)	0
Neutrophil count decreased	2 (14)	0	0	0	5 (25)	3 (15)	7 (19)	3 (8)
WBC decreased	0	0	0	0	6 (30)	2 (10)	6 (17)	2 (6)
Acute kidney injury	0	0	1 (50)	1 (50)	1 (5)	1 (5)	2 (6)	2 (6)
AESIs occurring in any subject								
Infusion-related reaction	4 (29)	0	1 (50)	0	0	0	5 (15)	0
Cardiac events[d]	0	0	0	0	3 (15)	0	3 (9)	0
Pneumonitis	0	0	0	0	1 (5)	0	1 (3)	0

- Majority of AEs Grade 1 or 2 and manageable in outpatient setting
- Grade 3 diarrhea (N=15) – introduction of prophylactic loperamide reduced incidence in Cycle 1 from 44% to 18%

[a]AEs were recorded using the Medical Dictionary for Regulatory Activities (MedDRA), with severity graded by investigators using NCI-CTCAE v5.0. [b] SAEs occurring in ≥ 2 subjects included 3 (9%) subjects with diarrhea, 2 (6%) with acute kidney injury, and 2 (6%) with hypokalemia. [c] Four (11%) subjects experienced grade 4 AEs: 1 (3%) lymphocyte count decreased, neutrophil count decreased, and white blood cell count decreased, and 3 (8%) hypokalemia; no treatment-related deaths were observed. [D] Includes 2 (6%) subjects with peripheral edema and 1 (3%) ejection fraction decreased.
5-FU = 5-fluorouracil; AE = adverse event; AESI = adverse event of special interest; CAPOX = capecitabine plus oxaliplatin; FP = 5-FU plus cisplatin; mFOLFOX6 = 5-FU plus oxaliplatin and leucovorin; SAE = serious adverse event; TRAE = treatment-related adverse event; WBC = white blood cell.
Source: Ku, et al. 2021 (e-poster 1380P; abstr 3678)

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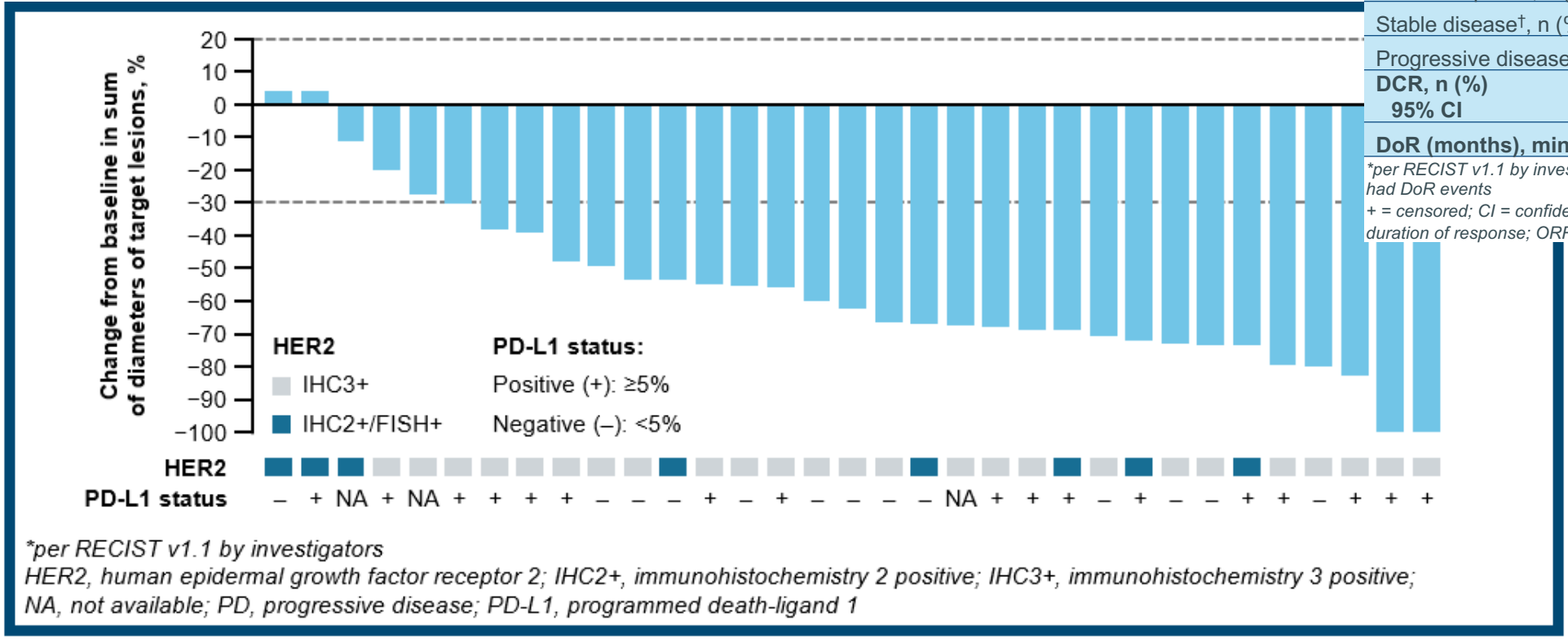
Zanidatamab Plus Tislelizumab and Chemotherapy in First-Line HER2-Positive GEA

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

Zanidatamab + tislelizumab + CAPOX induces deep responses in the majority of patients



*per RECIST v1.1 by investigators
HER2, human epidermal growth factor receptor 2; IHC2+, immunohistochemistry 2 positive; IHC3+, immunohistochemistry 3 positive; NA, not available; PD, progressive disease; PD-L1, programmed death-ligand 1

Table 3. Disease response*

	Total (N=33)
Confirmed ORR, n (%)	25 (75.8)
95% CI	57.7, 88.9
Complete response, n (%)	1 (3.0)
Partial response, n (%)	24 (72.7)
Stable disease†, n (%)	8 (24.2)
Progressive disease, n (%)	0 (0)
DCR, n (%)	33 (100.0)
95% CI	89.4, 100.0
DoR (months), min, max†	2.1+, 18.2+

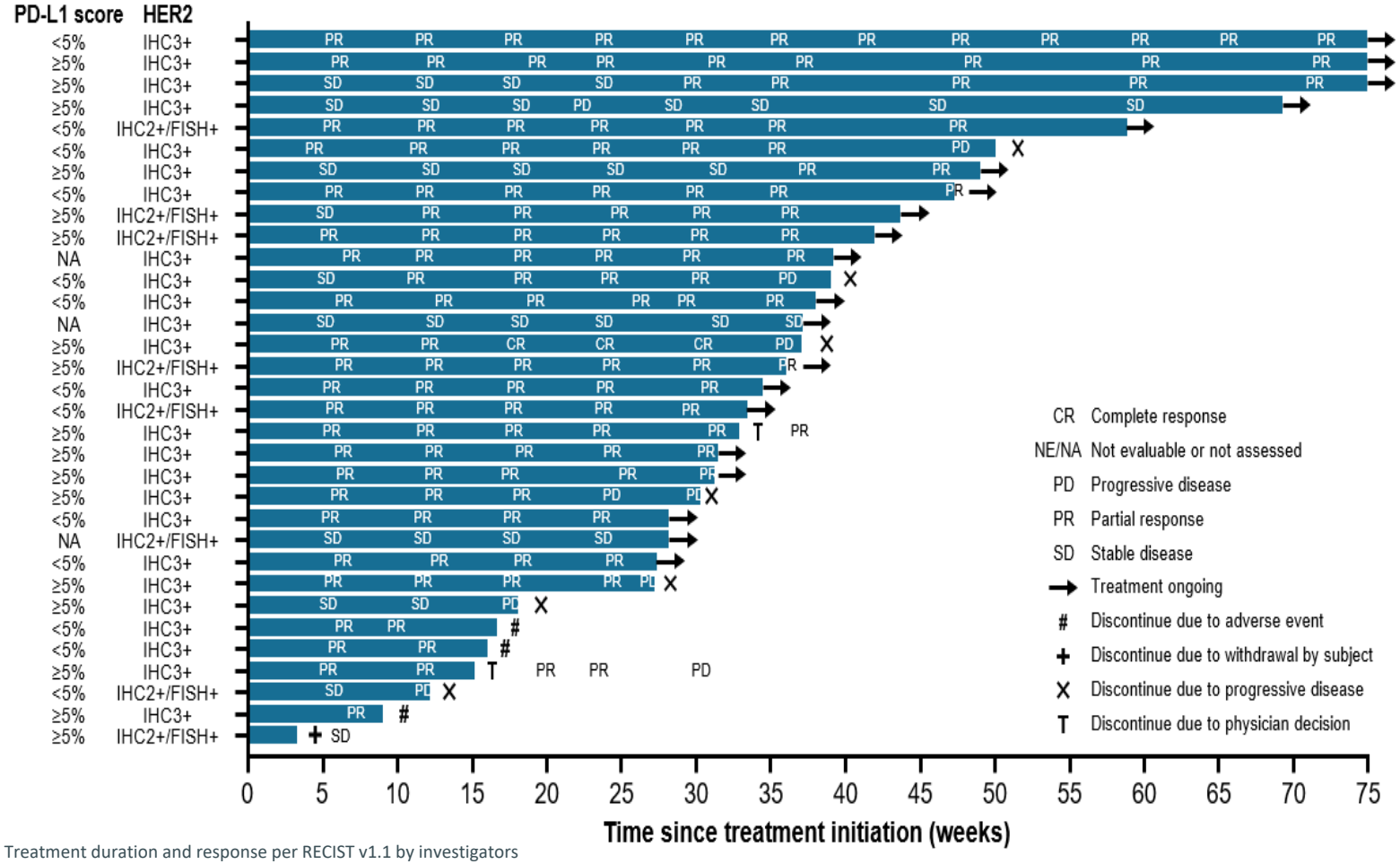
*per RECIST v1.1 by investigators; †28% of patients with a confirmed response had DoR events
+ = censored; CI = confidence interval; DCR = disease control rate; DoR = duration of response; ORR = objective response rate

Source: J Clin Oncol 40, 2022 (suppl 16; abstr 4032)

(NCT04276493) BeiGene zymeworks

Zanidatamab Plus Tislelizumab and Chemotherapy in First-Line HER2-Positive GEA

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022



Treatment duration and response per RECIST v1.1 by investigators

- Maturing data set shows durable responses
- 20 of 33 patients remain on study at time of the data cut

Source: J Clin Oncol 40, 2022 (suppl 16; abstr 4032)

Zanidatamab Plus Tislelizumab and Chemotherapy in First-Line HER2-Positive GEA

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

Table 2. TRAEs occurring in ≥ 20% of patients

	Cohort A (n=19)		Cohort B (n=14)		Total (N=33)	
Events, n (%)	Any grade	≥ Grade 3	Any grade	≥ Grade 3	Any grade	≥ Grade 3
Patients with at least one event	19 (100.0)	12 (63.2)	14 (100.0)	8 (57.1)	33 (100.0)	20 (60.6)
Diarrhea	18 (94.7)	7 (36.8)	14 (100.0)	1 (7.1)	32 (97.0)	8 (24.2)
Nausea	11 (57.9)	1 (5.3)	10 (71.4)	0 (0)	21 (63.6)	1 (3.0)
Decreased appetite	10 (52.6)	2 (10.5)	6 (42.9)	0 (0)	16 (48.5)	2 (6.1)
Vomiting	7 (36.8)	0 (0)	6 (42.9)	0 (0)	13 (39.4)	0 (0)
Peripheral sensory neuropathy	8 (42.1)	0 (0)	4 (28.6)	0 (0)	12 (36.4)	0 (0)
Pyrexia	8 (42.1)	0 (0)	4 (28.6)	0 (0)	12 (36.4)	0 (0)
Hypokalemia	6 (31.6)	2 (10.5)	3 (21.4)	0 (0)	9 (27.3)	2 (6.1)
Palmar-plantar erythrodysesthesia syndrome	6 (31.6)	1 (5.3)	2 (14.3)	0 (0)	8 (24.2)	1 (3.0)
Fatigue	4 (21.1)	1 (5.3)	3 (21.4)	1 (7.1)	7 (21.2)	2 (6.1)
Stomatitis	5 (26.3)	0 (0)	2 (14.3)	0 (0)	7 (21.2)	0 (0)
Weight decrease	4 (21.1)	0 (0)	3 (21.4)	0 (0)	7 (21.2)	0 (0)

Adverse events were recorded using the Medical Dictionary for Regulatory Activities (MedDRA), with severity graded by investigators using NCI CTCAE v5.0. Two subjects experienced Grade 5 TRAEs; one subject developed Grade 5 pneumonitis and pneumonia, and one subject experienced sudden death
NCI CTCAE, National Cancer Institute common terminology criteria for adverse events; TRAE, treatment-related adverse event

Safety

- Manageable safety profile
- Immune-mediated AEs (imAEs) occurred in nine patients (27.3%) of which seven (21.2%) were ≥ Grade 3
  - Otherwise, AE profile similar to that previously reported with zanidatamab + CAPOX
- Institution of mandatory prophylaxis with loperamide (4 mg twice daily × ≥ 7 days) decrease rate of Grade 3 diarrhea from 33.3% to 20.8%

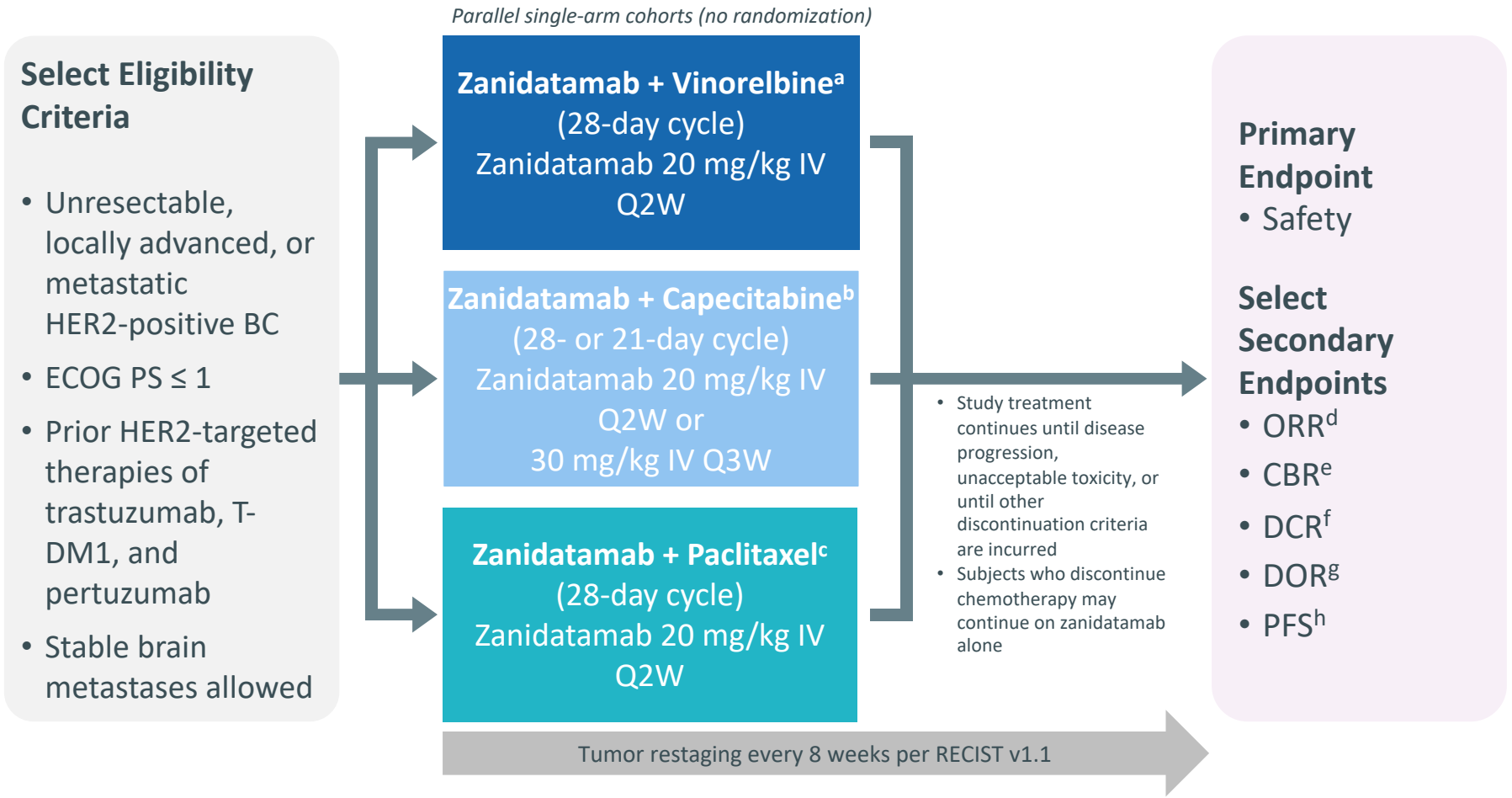
Source: J Clin Oncol 40, 2022 (suppl 16; abstr 4032)

(NCT04276493) BeiGene zymeworks

Breast Cancer

Zanidatamab Plus Chemotherapy in Third-Line+ HER2+ Breast Cancer

Phase 1 data (NCT02892123) as reported at SABCS | Dec 2021



CBR = clinical benefit rate; CR = complete response; DCR = disease control rate; DOR = duration of response; ECOG PS = Eastern Cooperative Oncology Group performance status; ORR = objective response rate; PD = progressive disease; PFS = progression-free survival; PR = partial response; SD = stable disease.

[a] Vinorelbine: vinorelbine 25 mg/m^2 QW on days 1, 8, 15, 22. [b] Capecitabine: with zanidatamab 20 mg/kg Q2W, 2000 mg twice daily for 7 days in weeks 1 and 3 *or* 1000 mg/m^2 twice daily on days 1-14 on a 21-day cycle; with zanidatamab 30 mg/kg Q3W, 1000 mg/m^2 twice daily on days 1-14 on a 21-day cycle. [c] Paclitaxel: paclitaxel 80 mg/m^2 QW for weeks 1-3. [d] ORR was defined as the percentage of subjects who have ≥ 1 overall tumor responses of CR/PR by RECIST v1.1. [e] CBR was defined as a best overall response of CR/PR, or SD or non-CR/non-PD ≥ 24 weeks. [f] DCR was defined as a best response of CR, PR, or SD. [g] DOR was defined as time from first confirmed objective response until PD or death in subjects who had a CR/PR followed by ≥ 1 additional response assessment. [h] PFS was defined as time from first dose of zanidatamab to the date of documented disease progression per RECIST v1.1, clinical progression, or death from any cause.

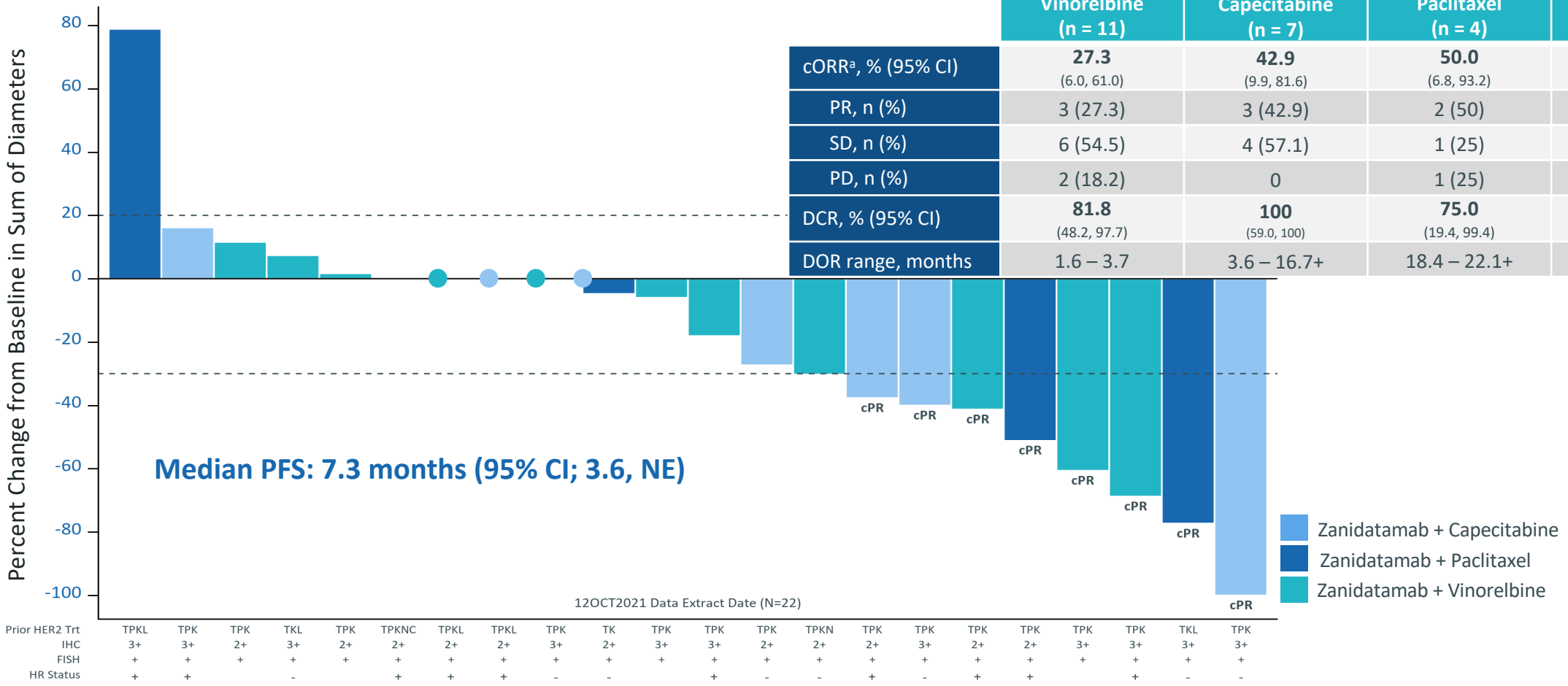
Source: Bedard, et al. (program P2-13-07; abstr 93); as reported at SABCS

Zanidatamab Plus Chemotherapy in Third-Line+ HER2+ Breast Cancer

Phase 1 data (NCT02892123) as reported at SABCS | Dec 2021

Promising antitumor activity Observed in Heavily Pretreated Breast Cancer Patients

	Zanidatamab + Vinorelbine (n = 11)	Zanidatamab + Capecitabine (n = 7)	Zanidatamab + Paclitaxel (n = 4)	Total (N = 22)
cORR[a], % (95% CI)	**27.3** (6.0, 61.0)	**42.9** (9.9, 81.6)	**50.0** (6.8, 93.2)	**36.4** (13.9, 54.9)
PR, n (%)	3 (27.3)	3 (42.9)	2 (50)	8 (36.4)
SD, n (%)	6 (54.5)	4 (57.1)	1 (25)	11 (50)
PD, n (%)	2 (18.2)	0	1 (25)	3 (13.6)
DCR, % (95% CI)	**81.8** (48.2, 97.7)	**100** (59.0, 100)	**75.0** (19.4, 99.4)	**86.4** (65.1, 97.1)
DOR range, months	1.6 – 3.7	3.6 – 16.7+	18.4 – 22.1+	1.6 – 22.1+



C: tucatinib; cORR: confirmed objective response rate; cPR: confirmed partial response; DOR: duration of response; DCR: disease control rate; FISH: fluorescence in situ hybridization; HR: hormone receptor; IHC: immunohistochemistry; K: T-DM1; L: lapatinib; N: neratinib; P: pertuzumab; T: trastuzumab; Trt: treatment

Source: Bedard, et al. (program P2-13-07; abstr 93); as reported at SABCS

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Zanidatamab Plus Chemotherapy in Third-Line+ HER2+ Breast Cancer

Phase 1 data (NCT02892123) as reported at SABCS | Dec 2021

Zanidatamab in combination with single agent chemotherapy is well tolerated

	Zanidatamab and/or Chemotherapy TRAEs							
	Zanidatamab + Vinorelbine (n = 12)		Zanidatamab + Capecitabine (n = 8)		Zanidatamab + Paclitaxel (n = 4)		Total (N = 24)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
TRAE,[a] n (%)	11 (92)	7 (58)	8 (100)	3 (38)	3 (75)	3 (75)	22 (92)	13 (54)
Treatment-related SAE	0	0	0	0	0	0	0	0
TRAEs leading to treatment discontinuation[b]	1 (8)	1 (8)	1 (13)	0	0	0	2 (8)	1 (4)
TRAEs occurring in ≥ 20% of subjects and/or Grade ≥ 3 TRAEs in > 1 subject								
Diarrhea	10 (83)	1 (8)	5 (63)	1 (13)	2 (50)	0	17 (71)	2 (8)
Nausea	3 (25)	0	5 (63)	0	0	0	8 (33)	0
Stomatitis	2 (17)	0	4 (50)	0	1 (25)	0	7 (29)	0
Fatigue	3 (25)	0	3 (38)	0	0	0	6 (25)	0
Peripheral neuropathy	1 (8)	0	2 (25)	0	3 (75)	1 (25)	6 (25)	1 (4)
PPE	0	0	6 (75)	0	0	0	6 (25)	0
Neutrophil count decreased	6 (50)	6 (50)	0	0	0	0	6 (25)	6 (25)
Neutropenia	2 (17)	1 (8)	0	0	2 (50)	2 (50)	4 (17)	3 (13)
AESI in any subject								
Infusion-related reaction	1 (8)	0	1 (13)	0	1 (25)	0	3 (13)	0
Cardiac events[c]	1 (8)	0	1 (13)	0	0	0	2 (8)	0
Pneumonitis	1 (8)	0	0	0	0	0	1 (4)	0

AESI = adverse event of special interest; PPE = palmar-plantar erythrodysesthesia; SAE = serious adverse event; TRAE = treatment-related adverse event. [a]AEs were recorded using the Medical Dictionary for Regulatory Activities (MedDRA), with severity graded by investigators using NCI-CTCAE v5.0. [b]One subject experience grade 1/2 nausea and abdominal pain, and 1 subject experienced grade 3 diarrhea. [c]Includes 2 subjects who experienced grade 2 ejection fraction decreased.

Source: Bedard, et al. (program P2-13-07; abstr 93); as reported at SABCS

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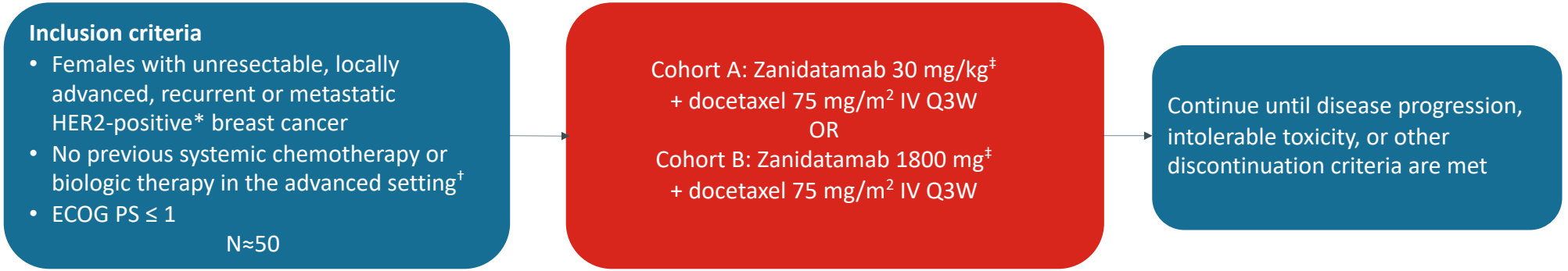
Zanidatamab in Combination with Docetaxel for First-Line Treatment

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

- Potential to replace SOC Trastuzumab + Pertuzumab
- Ongoing, open-label, multicenter, Phase 1b/2 study
- Enrollment in China and S Korea

Figure 1. Study design



*HER2 IHC3+, or IHC2+/ FISH+; †Except for one prior hormonal therapy for metastatic breast cancer, however, prior trastuzumab ± pertuzumab in the neoadjuvant or adjuvant setting is permitted if completed ≥ 12 months ago; ‡Patients enrolled under the original protocol received zanidatamab 30 mg/kg, and patients enrolled under the protocol amendment received zanidatamab 1800 mg. Flat dose of zanidatamab was implemented in the protocol amendment based on PK data which showed comparable exposure between weight-based vs flat dose; §RECIST v1.1 per INV
DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; INV, investigator; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Source: J Clin Oncol 40, 2022 (suppl 16; abstr 1031)

(NCT04276493)

Population Includes Patients with Prior Neoadjuvant/Adjuvant HER2-targeted Therapy

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

- As of November 26, 2021, 25 female patients were enrolled in the study. Patients included in this analysis received 30 mg/kg (n=10) or 1800 mg (n=14) zanidatamab, in combination with docetaxel (Table 1)
- At the data cutoff, 16 patients (66.7%) remained on treatment. Enrollment in this study is ongoing
- Median study follow-up was 7.0 months (range: 1.1–17.4) and the median number of treatment cycles was 10.0 (range: 2–20)
- Three patients without any post-baseline tumor assessments were excluded from the efficacy evaluable analysis set. One patient was excluded from both the safety and efficacy analysis sets

Table 1. Demographics and baseline characteristics

	Cohort A (n=10)	Cohort B (n=14)	Total (N=24*)
Median age, years (range)	59.5 (45–80)	56.0 (33–67)	57.0 (33–80)
Race, n (%)			
Chinese	3 (30.0)	11 (78.6)	14 (58.3)
Korean	7 (70.0)	3 (21.4)	10 (41.7)
ECOG PS, n (%)			
0	4 (40.0)	3 (21.4)	7 (29.2)
1	6 (60.0)	11 (78.6)	17 (70.8)
HER2 status†, n (%)			
IHC3+	8 (80.0)	11 (78.6)	19 (79.2)
IHC2+/FISH+	2 (20.0)	3 (21.4)	5 (20.8)
HR status, n (%)			
Positive	5 (50.0)	9 (64.3)	14 (58.3)
Negative	5 (50.0)	5 (35.7)	10 (41.7)
Brain metastases‡, n (%)	0 (0)	1 (7.1)	1 (4.2)
Prior systemic therapy§, n (%)	6 (60.0)	7 (50.0)	13 (54.2)
(Neo)adjuvant anti-HER2 therapy	4 (40.0)	3 (21.4)	7 (29.2)
Trastuzumab	4 (40.0)	3 (21.4)	7 (29.2)
Pertuzumab	1 (10.0)	0 (0)	1 (4.2)

**One patient was excluded because she received a biopsy after the end of treatment and the metastatic lesion in the lung was pathologically confirmed as 'pulmonary sarcomatoid carcinoma, spindle cell carcinoma'; †All subjects had HER2 status confirmed by local lab; ‡At study entry, must be asymptomatic and radiologically stable for inclusion; §Patients had neoadjuvant/adjuvant therapy and/or one prior hormone regimen (for metastatic breast cancer) ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry*

Source: J Clin Oncol 40, 2022 (suppl 16; abstr 1031)

(NCT04276493) BeiGene zymeworks

Zanidatamab with Docetaxel Has a Manageable Safety Profile

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

Safety

- In total, 22 patients (91.7%) experienced at least one TRAE (considered by the investigator to be related to any component of the study treatment), and 16 patients (66.7%) experienced at least one ≥ Grade 3 TRAE (Table 2)
- The most common TRAEs were neutrophil count decreased (13 patients; 54.2%), diarrhea (13 patients; 54.2%), and anemia (nine patients; 37.5%), and the most common ≥ Grade 3 TRAEs were neutrophil count decreased (12 patients; 50.0%), diarrhea (3 patients; 12.5%), and white blood cell count decreased (2 patients; 8.3%)
- Serious TRAEs occurred in two (8.3%) patients. One patient experienced febrile neutropenia, cholangitis, and diarrhea, and the other patient experienced decreased platelet count and an infusion-related reaction, in which the last one led to treatment discontinuation in one (4.0%) patient

Table 2. TRAEs occurring in ≥ 20% of patients

	Cohort A (n=10)		Cohort B (n=14)		Total (N=24)	
Events, n (%)	Any grade	≥ Grade 3	Any grade	≥ Grade 3	Any grade	≥ Grade 3
Patients with at least one event	9 (90.0)	9 (90.0)	13 (92.9)	7 (50.0)	22 (91.7)	16 (66.7)
Neutrophil count decreased	7 (70.0)	7 (70.0)	6 (42.9)	5 (35.7)	13 (54.2)	12 (50.0)
Diarrhea	7 (70.0)	3 (30.0)	6 (42.9)	0 (0)	13 (54.2)	3 (12.5)
Anemia	1 (10.0)	1 (10.0)	8 (57.1)	0 (0)	9 (37.5)	1 (4.2)
Chest discomfort	2 (20.0)	0 (0)	5 (35.7)	1 (7.1)	7 (29.2)	1 (4.2)
Nausea	4 (40.0)	0 (0)	3 (21.4)	0 (0)	7 (29.2)	0 (0)
Alopecia	1 (10.0)	0 (0)	5 (35.7)	0 (0)	6 (25.0)	0 (0)
Aspartate aminotransferase increased	1 (10.0)	0 (0)	5 (35.7)	0 (0)	6 (25.0)	0 (0)
Alanine aminotransferase increased	1 (10.0)	0 (0)	4 (28.6)	0 (0)	5 (20.8)	0 (0)
Decreased appetite	2 (20.0)	0 (0)	3 (21.4)	0 (0)	5 (20.8)	0 (0)
Platelet count decreased	0 (0)	0 (0)	5 (35.7)	0 (0)	5 (20.8)	0 (0)
White blood cell count decreased	0 (0)	0 (0)	5 (35.7)	2 (14.3)	5 (20.8)	2 (8.3)

AEs were recorded using the MedDRA, with severity graded by investigators using NCI CTCAE v5.0. No TRAEs led to death
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; NCI CTCAE, National Cancer Institute common terminology criteria for adverse events; TRAE, treatment-related adverse event

Source: J Clin Oncol 40, 2022 (suppl 16; abstr 1031)

(NCT04276493) BeiGene zymeworks

Highly Active Regimen with Deep Responses Observed

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

Efficacy

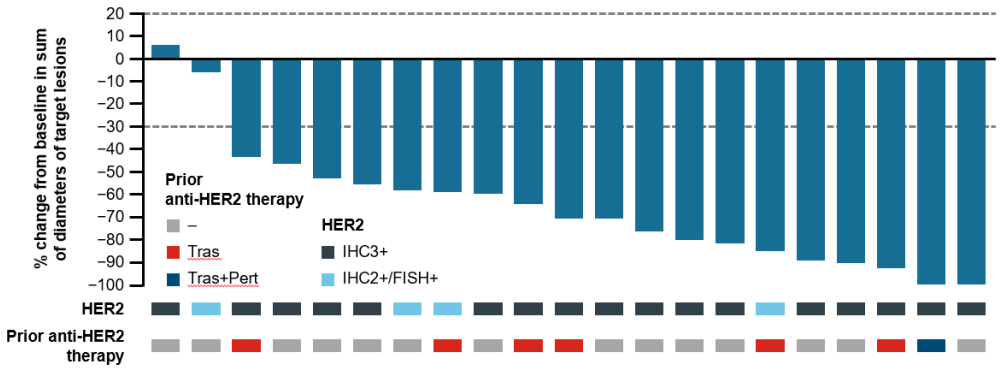
- Of the 21 efficacy evaluable patients, the confirmed objective response rate (ORR) was 90.5% (95% CI: 69.6, 98.8) (Table 3) with 15 patients (78.9%) who were ongoing responders. The treatment duration with overall response is shown in Figure 3
- The disease control rate was 95.2% (95% CI: 76.2, 99.9) (Table 3); 20 patients had controlled disease
- The 6-month progression-free survival rate was 95.2% (95% CI: 70.7, 99.3)

Table 3. Disease response*

	Total (N=21)
cORR†, %	90.5
95% CI	69.6, 98.8
Complete response, n (%)	1 (4.8)
Partial response, n (%)	18 (85.7)
Stable disease, n (%)	1 (4.8)
Progressive disease, n (%)	1 (4.8)
DCR†, %	95.2
95% CI	76.2, 99.9
DoR (months), min, max‡	1.4+, 12.4

*In the efficacy evaluable analysis set; †per RECIST v1.1 by investigators; ‡15.8% of patients had DoR events
+, censored; CI, confidence interval; cORR, confirmed objective response rate; DCR, disease control rate; DoR, duration of response

Figure 2. Best change in target lesion*



*per RECIST v1.1 by investigator in the efficacy evaluable analysis set which was defined as patients with at least one dose and at least one post-baseline tumor assessment
FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor 2; IHC2+, immunohistochemistry 2 positive; IHC3+, immunohistochemistry 3 positive; INV, investigator; Pert, pertuzumab; Tras, trastuzumab

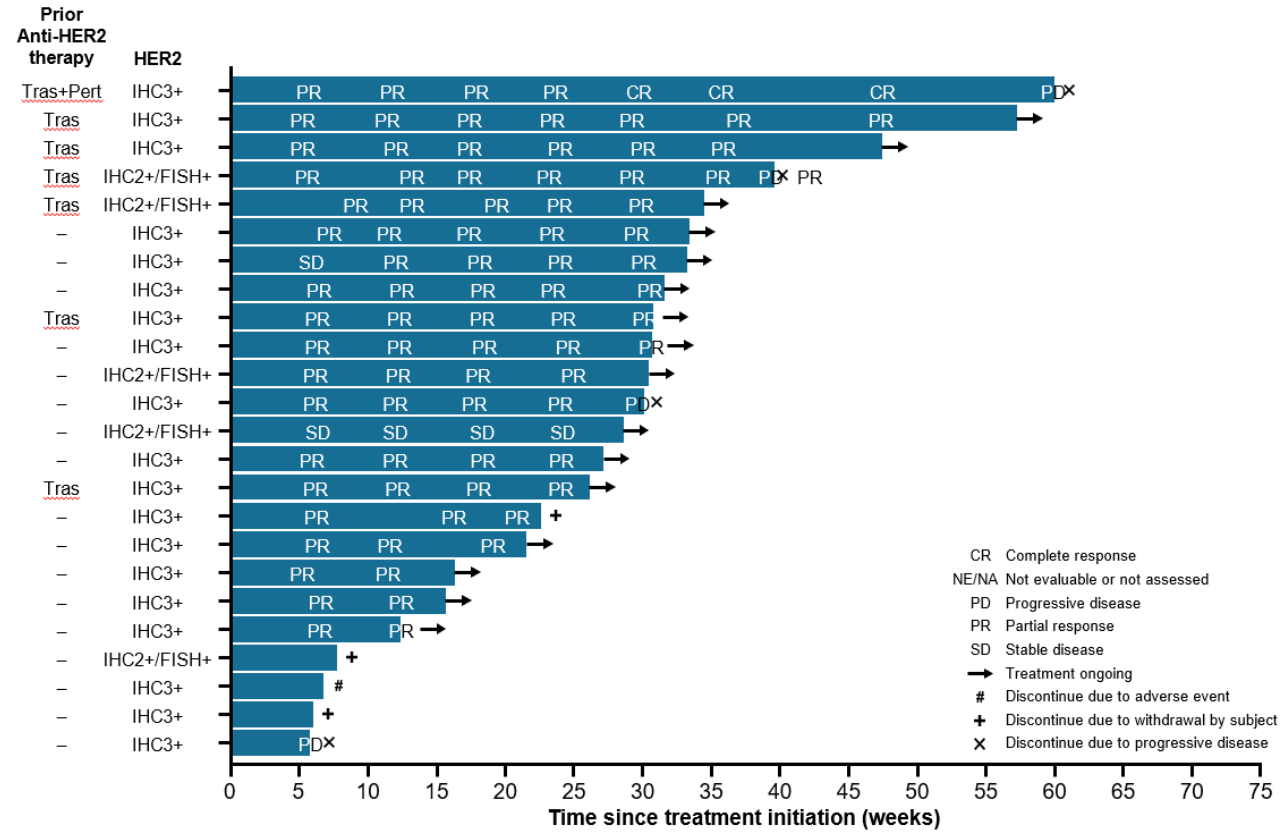
Source: J Clin Oncol 40, 2022 (suppl 16; abstr 1031)

(NCT04276493) BeiGene zymeworks

16/24 HER2-positive Patients Remain on Treatment

Phase 1b/2 data (NCT04276493) as reported at ASCO | Jun 2022

Figure 3. Treatment duration and response*



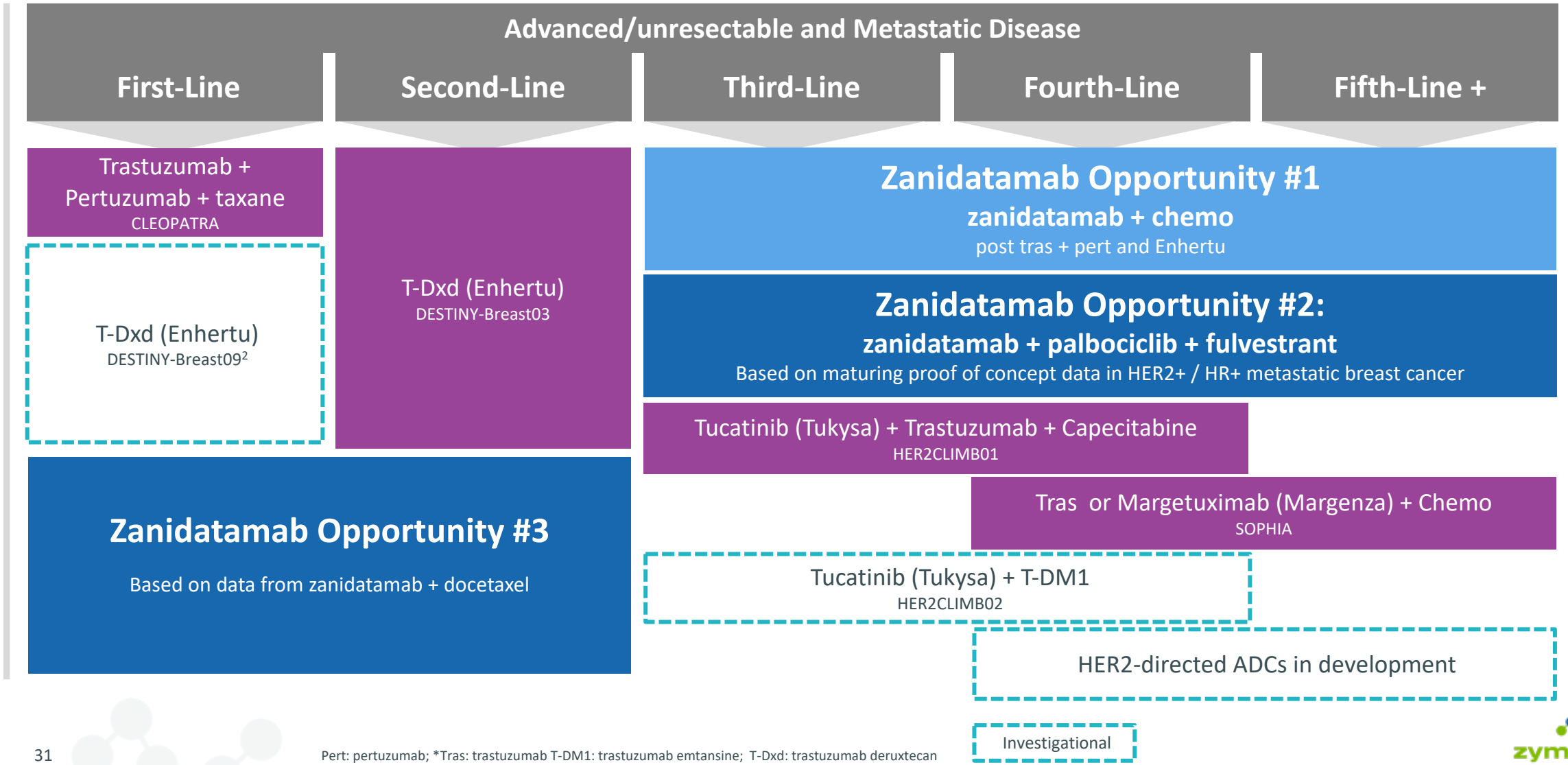
per RECIST v1.1 by investigators. CR, complete response; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; IHC2+, immunohistochemistry 2 positive; IHC3+, immunohistochemistry 3 positive; NA, not assessed; NE, not evaluable; PD, progressive disease; Pert, pertuzumab; PR, partial response; SD, stable disease; Tras, trastuzumab

Source: BeiGene (Study: BGB-A317-ZW25-101); Data snapshot from unlocked database 26 Nov 2021, and subject to change.

Source: J Clin Oncol 40, 2022 (suppl 16; abstr 1031)

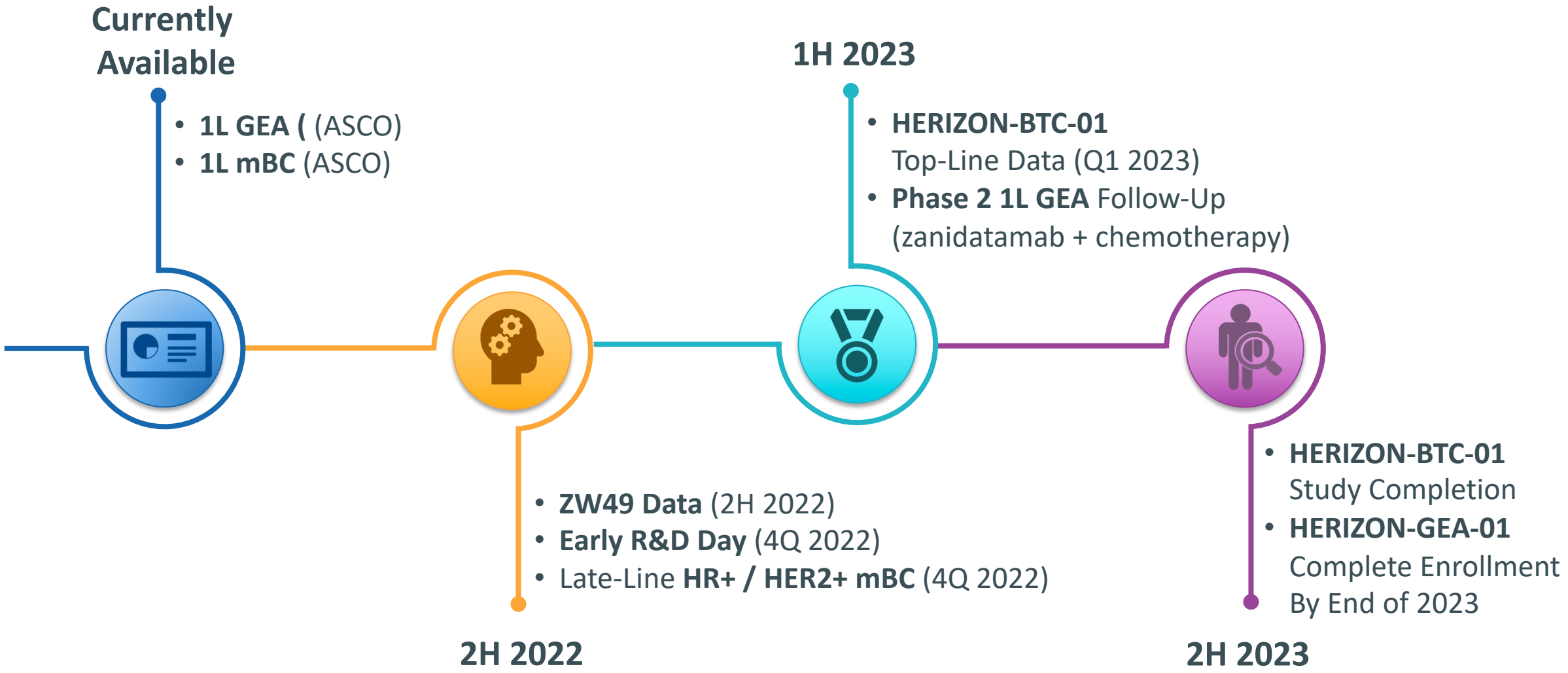
(NCT04276493)

Significant Opportunity for Zanidatamab in HER2+ mBC



Pert: pertuzumab; *Tras: trastuzumab T-DM1: trastuzumab emtansine; T-Dxd: trastuzumab deruxtecan

Anticipated Upcoming Data Catalysts



Q&A

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