



Puma Biotechnology

H.C. Wainwright Global Life Sciences Conference

March 2021



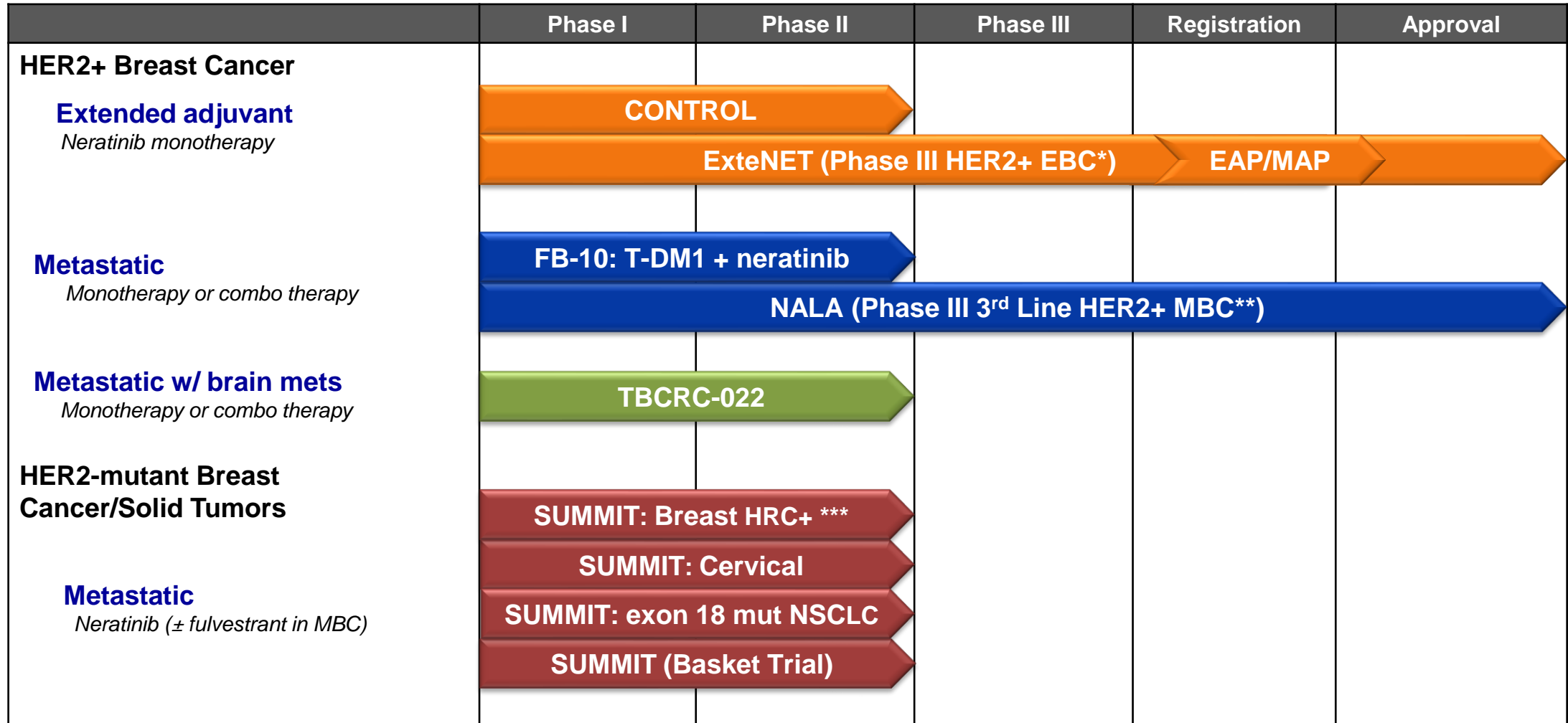
Forward-Looking Safe-Harbor Statement

This presentation contains forward-looking statements, including statements regarding commercialization of NERLYNX® and the potential indications and development of our drug candidates. All forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are based on our current expectations, forecasts and assumptions, and actual outcomes and results could differ materially from these statements due to a number of factors, which include, but are not limited to, any adverse impact on our business or the global economy and financial markets, generally, from the global COVID-19 pandemic, and the risk factors disclosed in our periodic and current reports filed with the Securities and Exchange Commission from time to time, including our Annual Report on Form 10-K for the year ended December 31, 2020. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. We assume no obligation to update these forward-looking statements except as required by law.



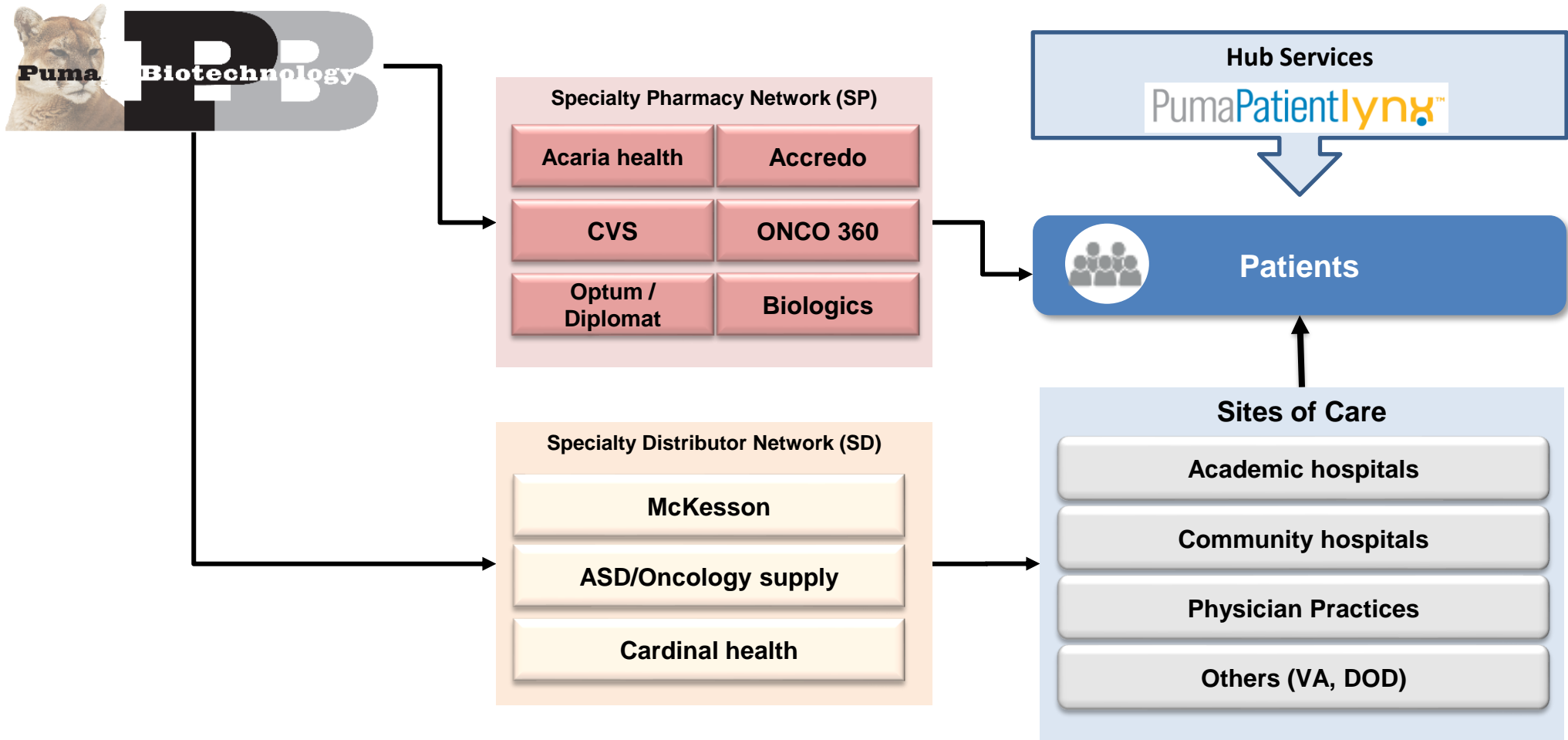
Product Pipeline

Neratinib across the breast cancer therapy spectrum



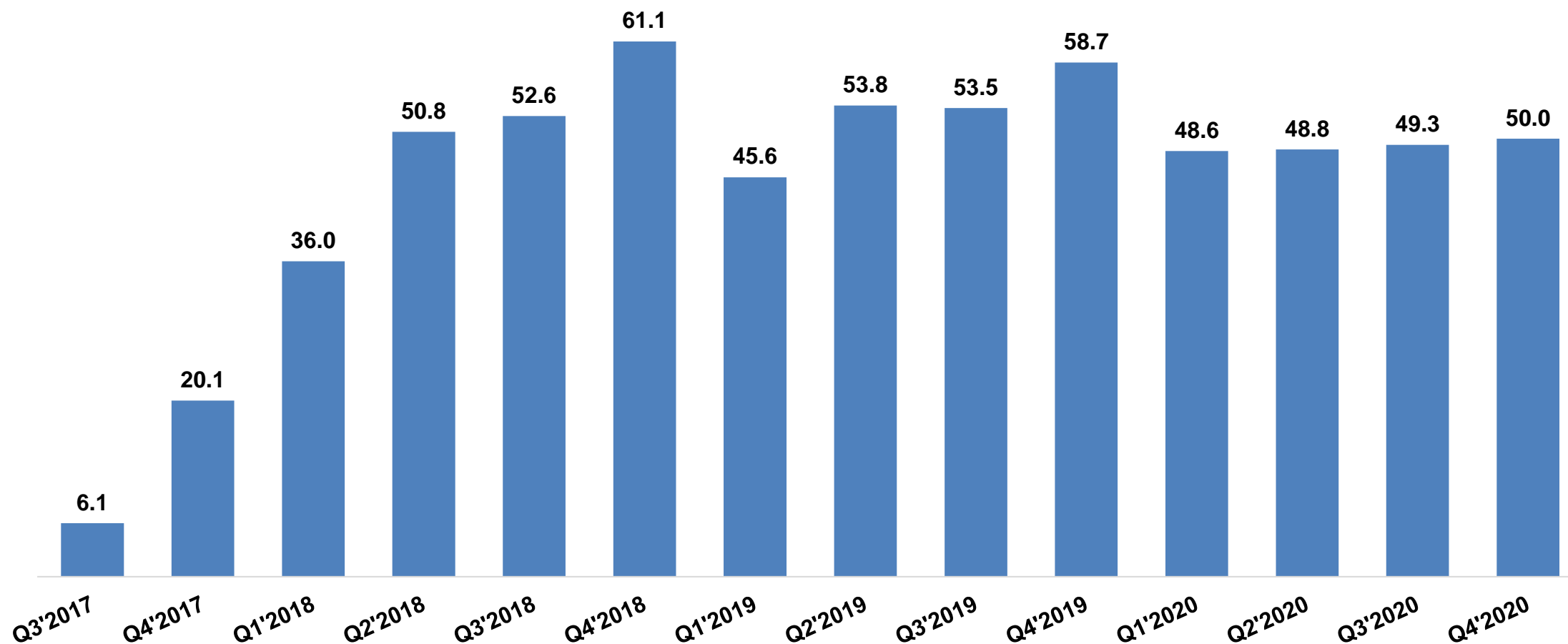
* EBC: Early breast cancer ** MBC: Metastatic breast cancer *** HRC+: Hormone receptor positive

PUMA's Pharmacy and Distributor Network



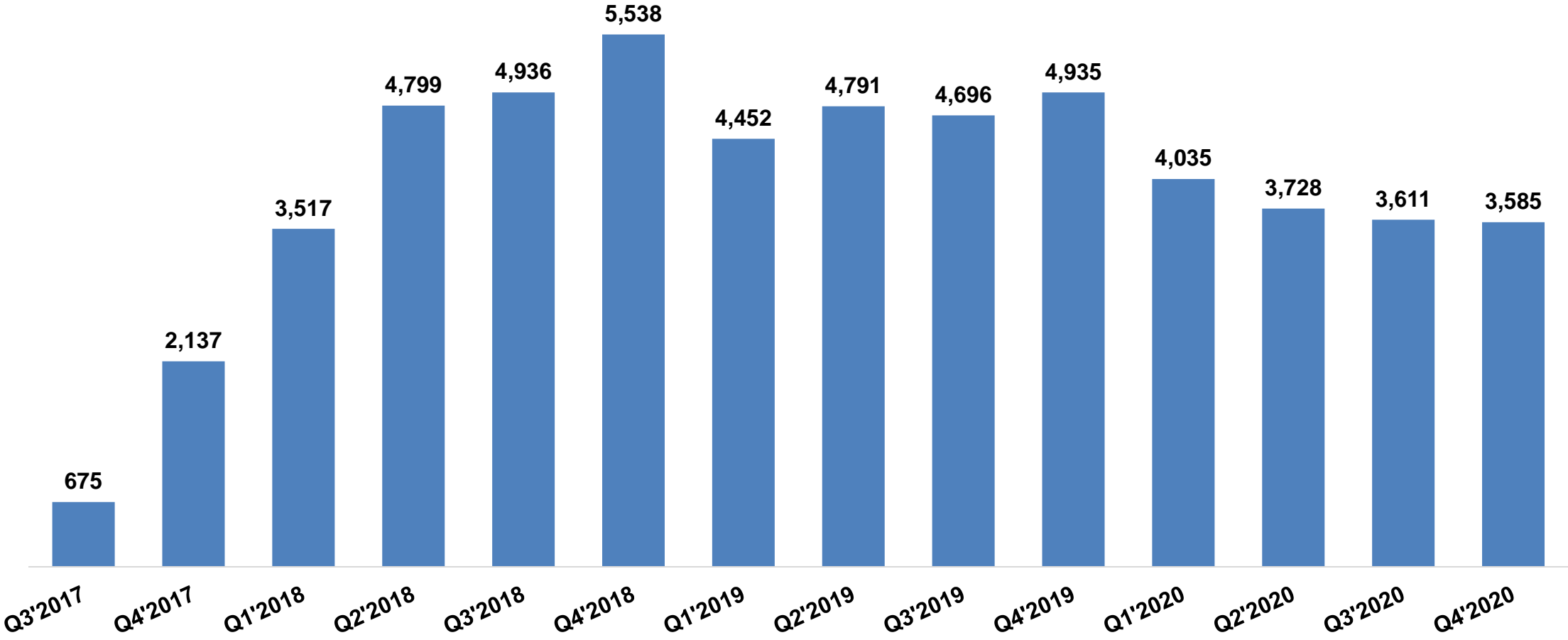
~\$50 Million Net NERLYNX Revenue in Q4'20

Quarterly Net Revenue (in \$MM)



~3,600 Ex-factory Bottles were Sold in Q4'20

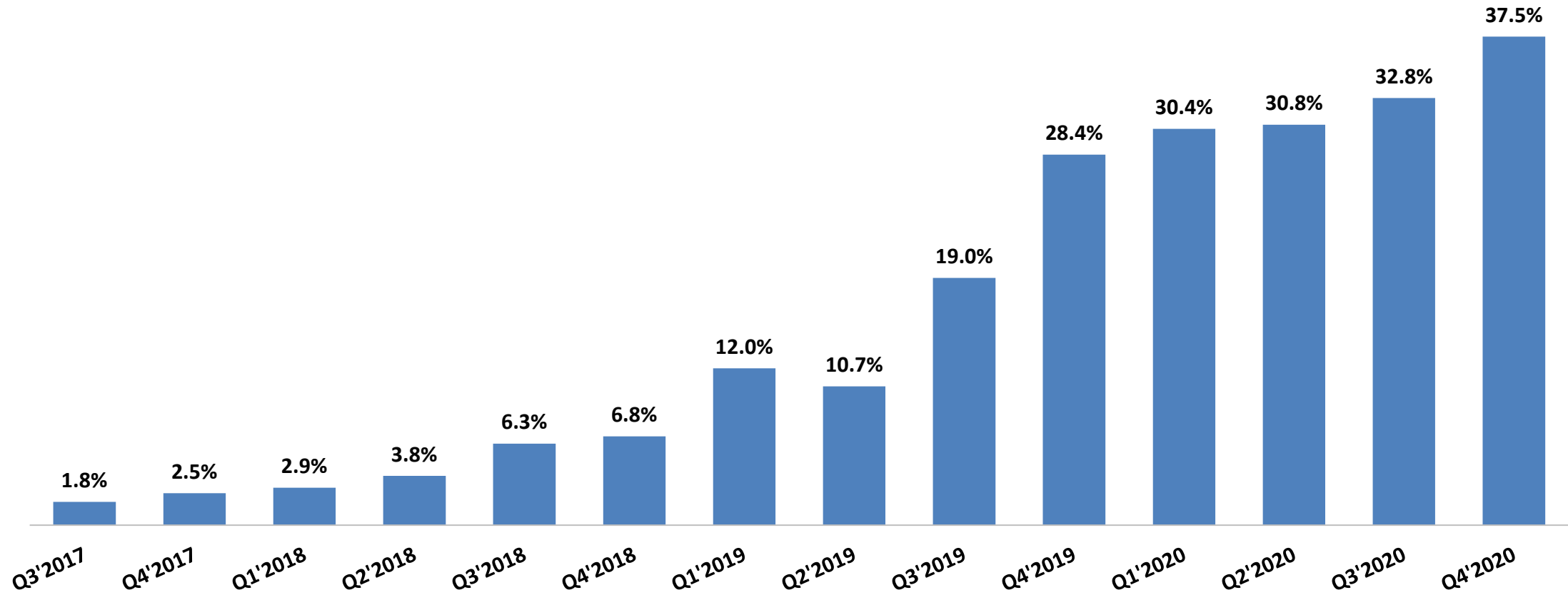
Bottles Sold (SP + SD) by Quarter



Includes Commercial SP and SD







~38% of Patients in Q4'20 Started at a Reduced Dose

% of patients starting at reduced dose



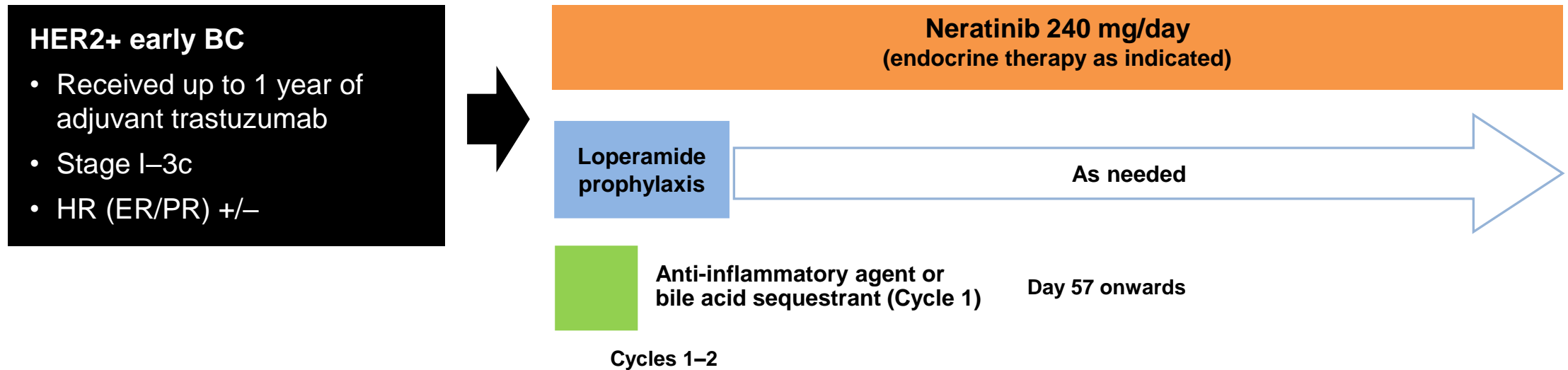
Reduced dose defined as fewer than 6 pills per day

Rest of World Partnerships – Timelines

Region	Partner	Regulatory / Launch Milestones
Australia / SE Asia	 Specialised Therapeutics	<ul style="list-style-type: none"> • March 2019 – Approved in Australia • December 2019 – Approved in Singapore • Q2/Q3 2020 – Approved in Brunei, Malaysia, New Zealand
Israel	 MEDISON Driving Innovative Healthcare	<ul style="list-style-type: none"> • Q1 2020 – Launched • Q3 2020 – Approved in metastatic breast cancer
Canada	 Knight	<ul style="list-style-type: none"> • July 2019 – Approved • September 2020 – metastatic sNDS accepted by HC
Latin America	 PINT PHARMA	<ul style="list-style-type: none"> • Q1 2020 – Argentina Launched; mBC approved January 2021 • Q2 2020 – Approved in Chile • Q3 2020 – Approved in Ecuador • 2021 – Expected approvals in Brazil, Colombia, Mexico, Peru
Europe Greater China Middle East North and West Africa South Africa Turkey	 Pierre Fabre	<ul style="list-style-type: none"> • Q4 2019 – Germany, UK, Austria Launched • Q1 2020 – Sweden Launched • Q2 2020 – Hong Kong Launched • Q2 2020 – Approved in China • Q3 2020 – Approved in Taiwan • Q4 2020 – Finland / Switzerland Launched
South Korea	 BIINK THERAPEUTICS	<ul style="list-style-type: none"> • October 2020 – NDA Filed

CONTROL Study Design

Phase 2 trial to characterize the incidence and severity of diarrhea in patients with HER2+ early breast cancer treated with neratinib and loperamide prophylaxis \pm an investigational agent



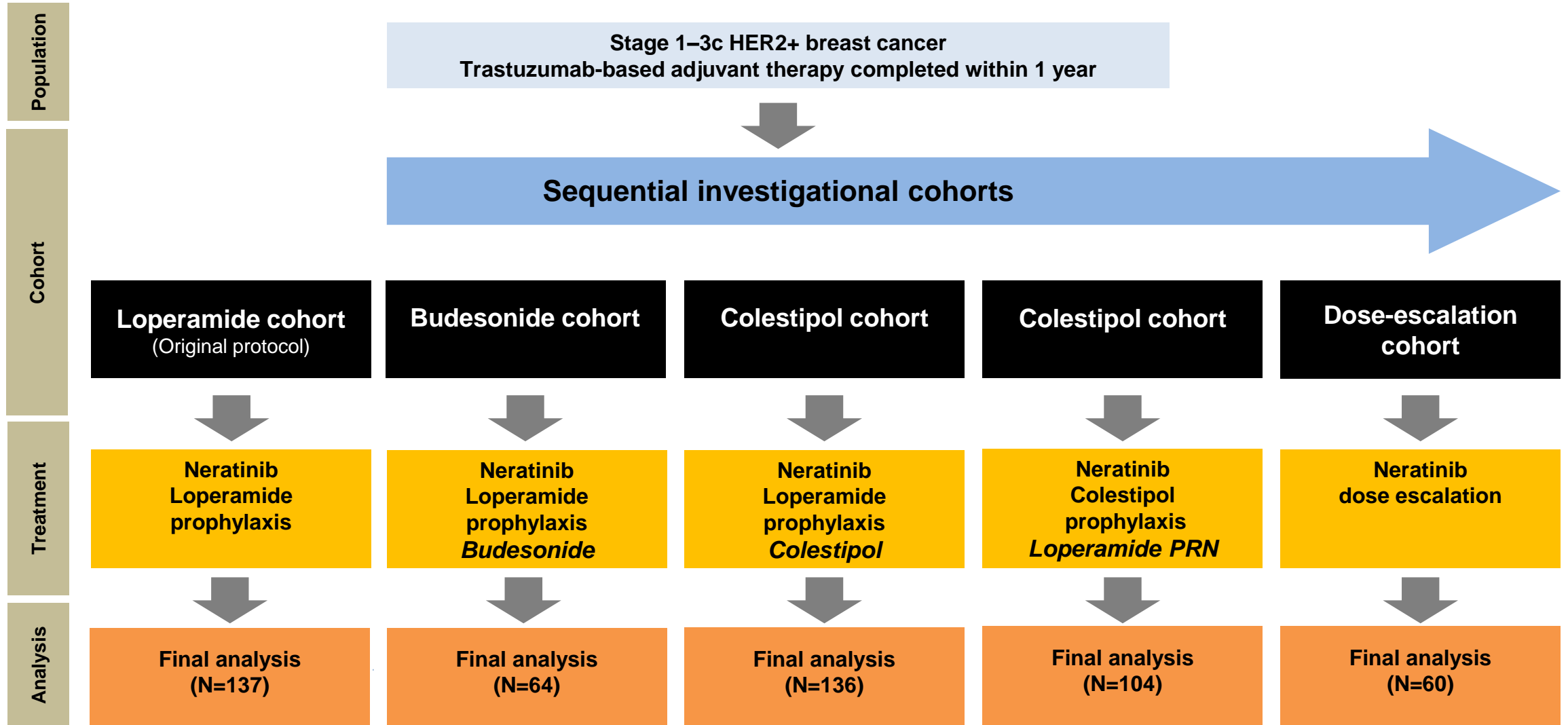
STUDY ENDPOINTS

Primary endpoint: incidence of grade ≥ 3 diarrhea

Secondary endpoints: frequency distribution of maximum-grade diarrhea; incidence and severity of diarrhea by loperamide exposure

CONTROL

Study Flowchart



CONTROL vs ExteNET: Neratinib Treatment-Emergent Diarrhea

Loperamide prophylaxis reduces incidence and severity of diarrhea

	CONTROL ¹					ExteNET ³
	Loperamide (n=137)	Budesonide + loperamide (n=64)	Colestipol + loperamide (n=136)	Colestipol + loperamide prn (n=104)	Neratinib dose escalation + loperamide prn (n=60) ²	Loperamide prn (n=1408)
Treatment-emergent diarrhea incidence, n (%)						
No diarrhea	28 (20)	9 (14)	23 (17)	5 (5)	1 (2)	65 (5)
Grade 1	33 (24)	16 (25)	38 (28)	34 (33)	24 (40)	323 (23)
Grade 2	34 (25)	21 (33)	47 (35)	32 (31)	27 (45)	458 (33)
Grade 3	42 (31)	18 (28)	28 (21)	33 (32)	8 (13)	561 (40)
Grade 4	0	0	0	0	0	1 (<1)
Diarrhea leading to discontinuation	28 (20)	5 (8)	5 (4)	8 (8)	2 (3)	237 (17)
Hospitalization (due to diarrhea)	2 (1)	0	0	0	0	20 (1)
Diarrhea leading to dose reduction	10 (7)	3 (5)	10 (7)	12 (12)	2 (3)	372 (26)

1. Barcenas et al. *Annals of Oncology*, 2020

2. Ruiz-Borrego et al. SABCS 2020 3. Chan et al. *Lancet Oncology* 2016

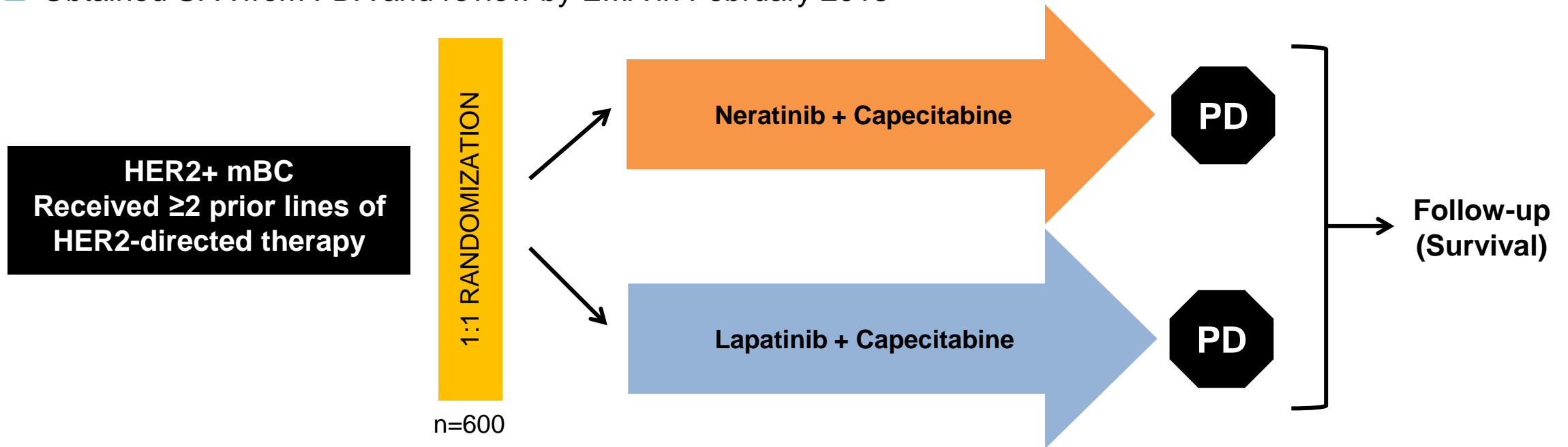
NERLYNX[®] Extended Adjuvant HER2+ Breast Cancer Market Size

- Approximately 28,300 patients (US) with early stage HER2+ breast cancer treated with adjuvant treatment¹
- Approximately 37,000 patients (EU) with early stage HER2+ breast cancer treated with adjuvant treatment¹
 - Approximately 65–70% of patients have HR+ disease

¹Roche epidemiology slides 09/18

Phase III Trial – Third-Line HER2+ MBC (NALA) Study Design

- 3rd- or later-line therapy for patients with HER2+ mBC
- Patients with asymptomatic CNS metastatic disease are eligible
- Obtained SPA from FDA and review by EMA in February 2013



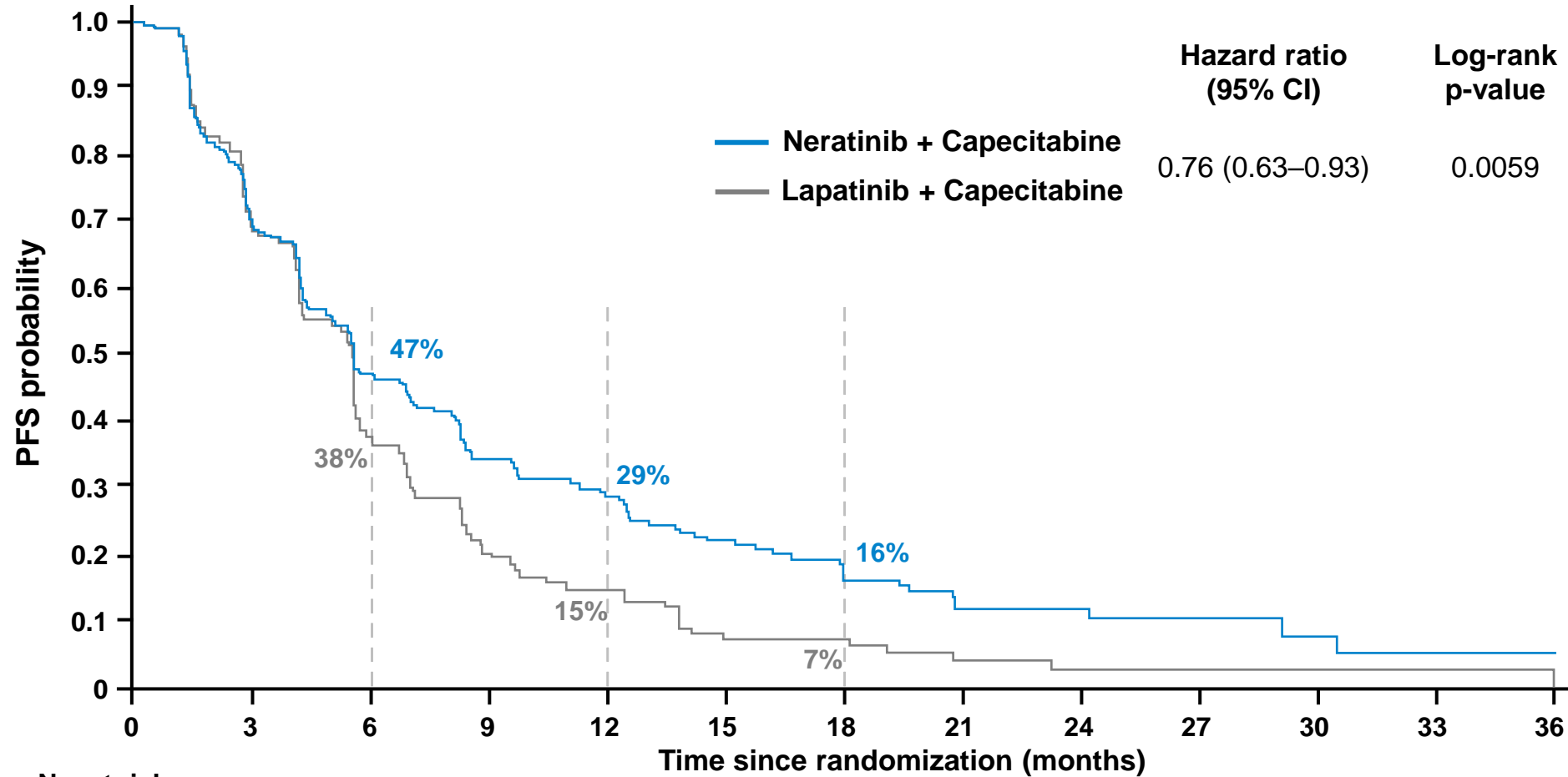
STUDY OBJECTIVES

Co-Primary: PFS (central) and OS

Secondary: PFS (local), ORR, DoR, CBR, time to intervention for CNS metastases, safety, health outcomes

Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

Centrally Confirmed PFS (co-primary endpoint)



No. at risk:

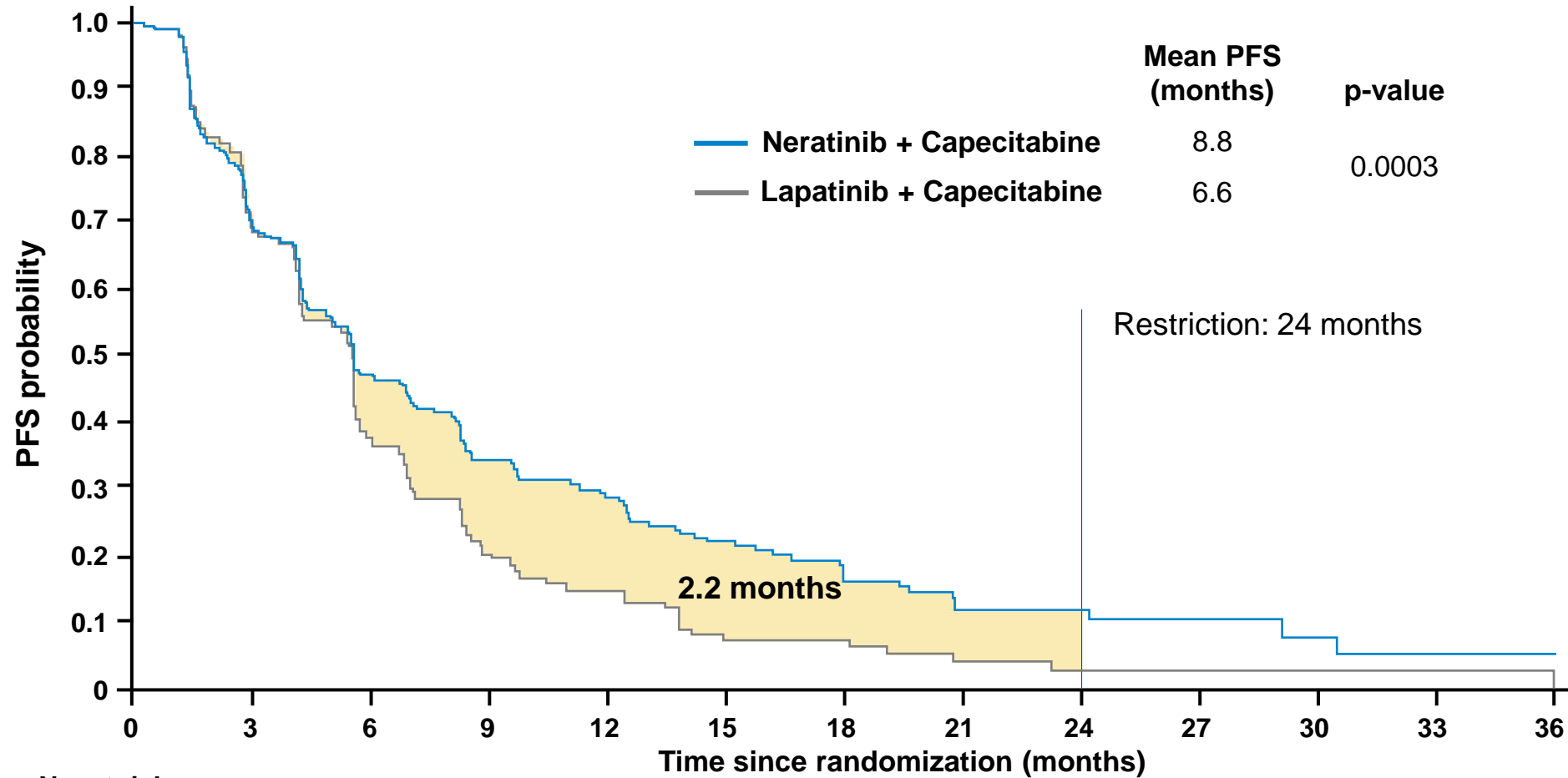
	0	3	6	9	12	15	18	21	24	27	30	33	36
N+C	307	183	113	69	54	35	20	13	9	7	3	2	2
L+C	314	183	82	39	24	9	8	3	2	2	2	2	1

Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019



Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

Prespecified restricted means analysis – PFS



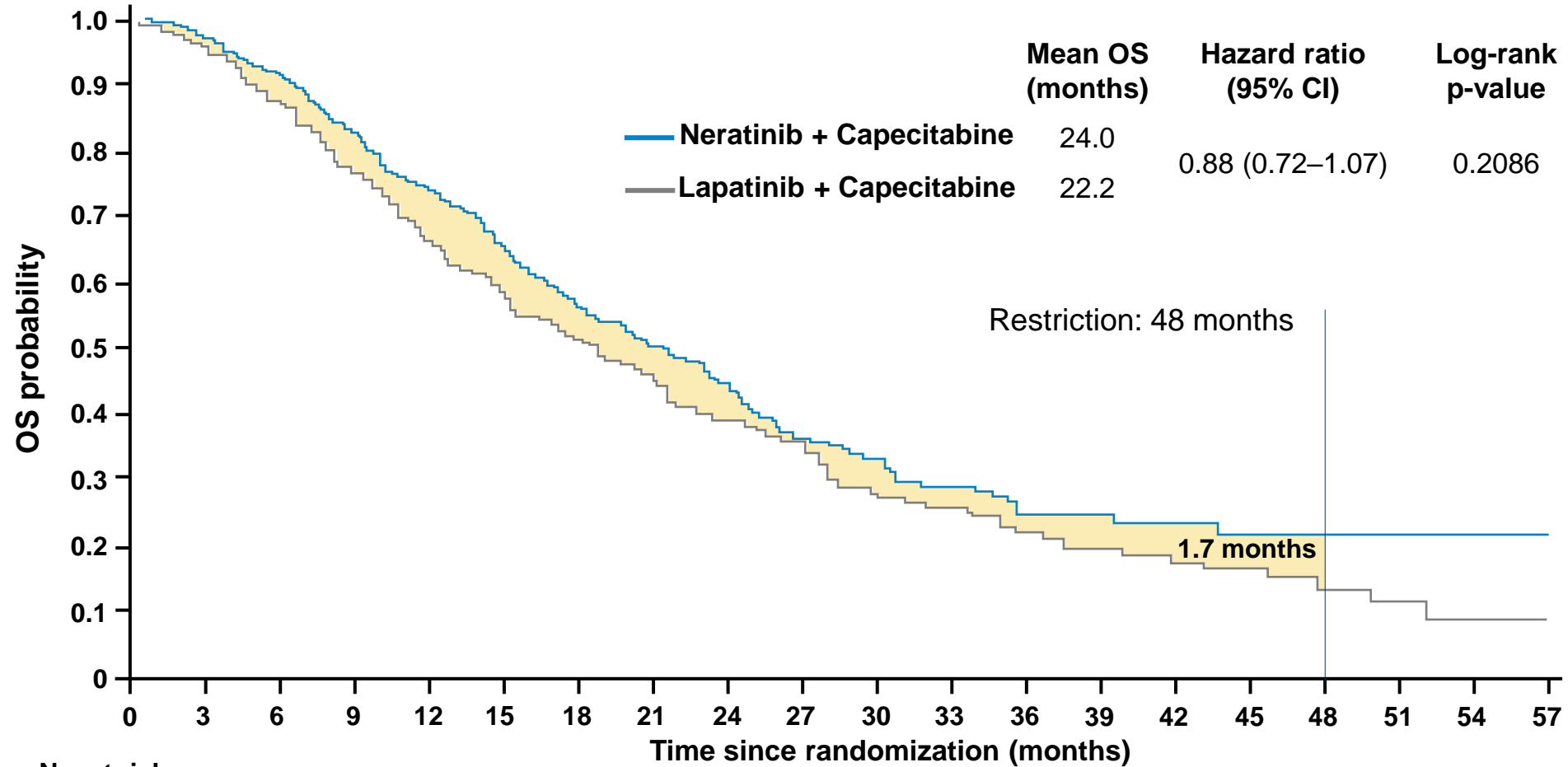
No. at risk:

N+C	307	183	113	69	54	35	20	13	9	7	3	2	2
L+C	314	183	82	39	24	9	8	3	2	2	2	2	1

Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

OS (co-primary endpoint)



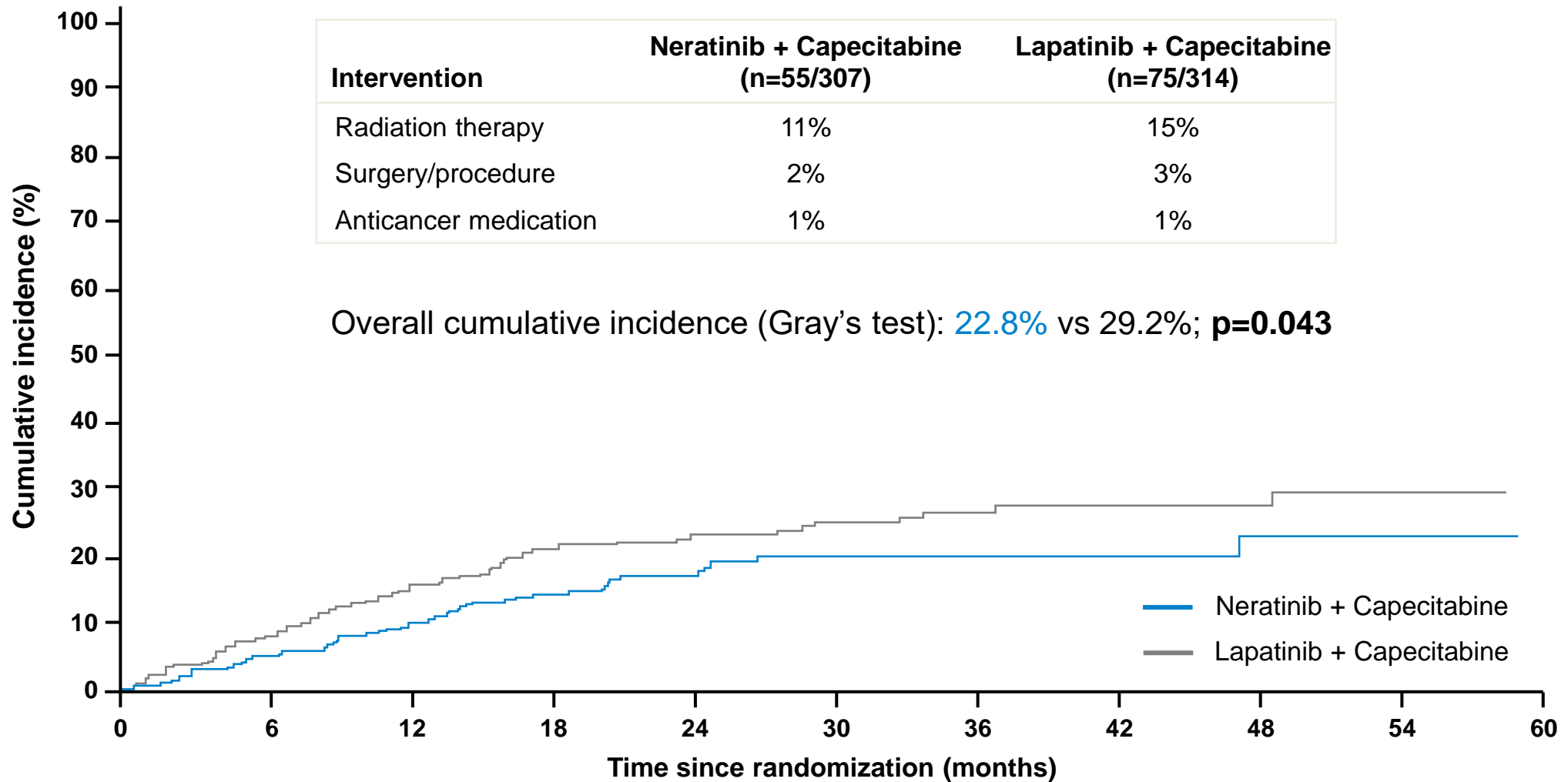
No. at risk:

N+C	307	294	275	244	220	182	142	112	82	64	47	34	28	18	15	13	6	4	2	1
L+C	314	303	273	240	208	170	132	107	84	67	47	36	27	22	17	12	8	4	3	1

Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

Time to intervention for CNS metastases



Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

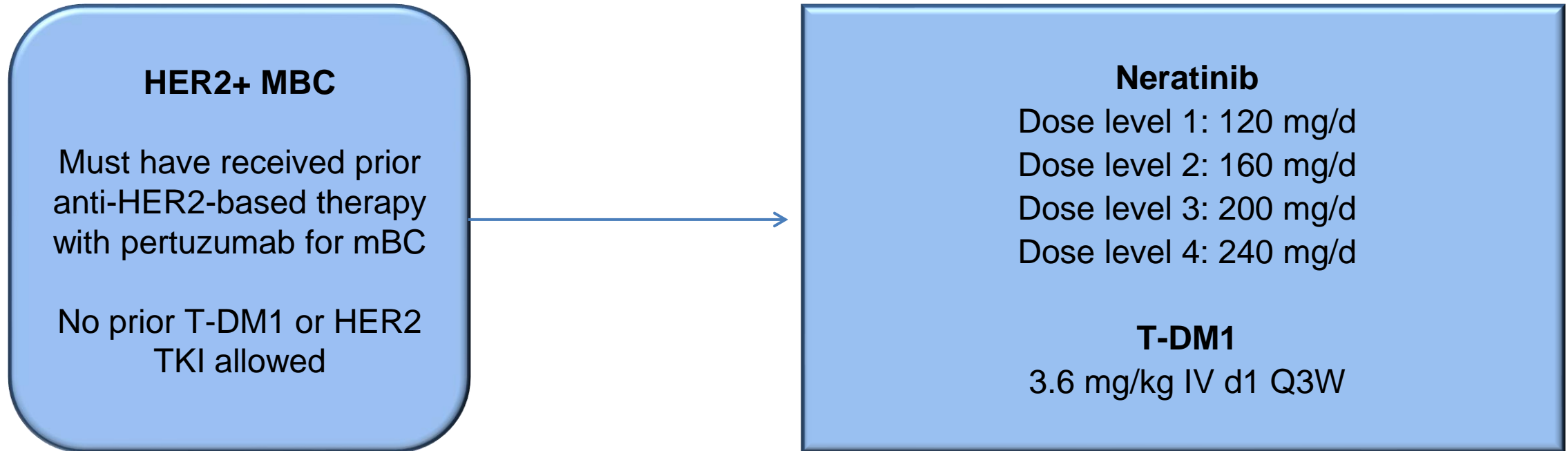


Third-Line HER2+ MBC Market Size

- Approximately 6,400 patients (US) with third-line HER2+ metastatic breast cancer and 4,700 patients (US) with fourth-line HER2+ metastatic breast cancer¹

¹Roche epidemiology slides 09/18

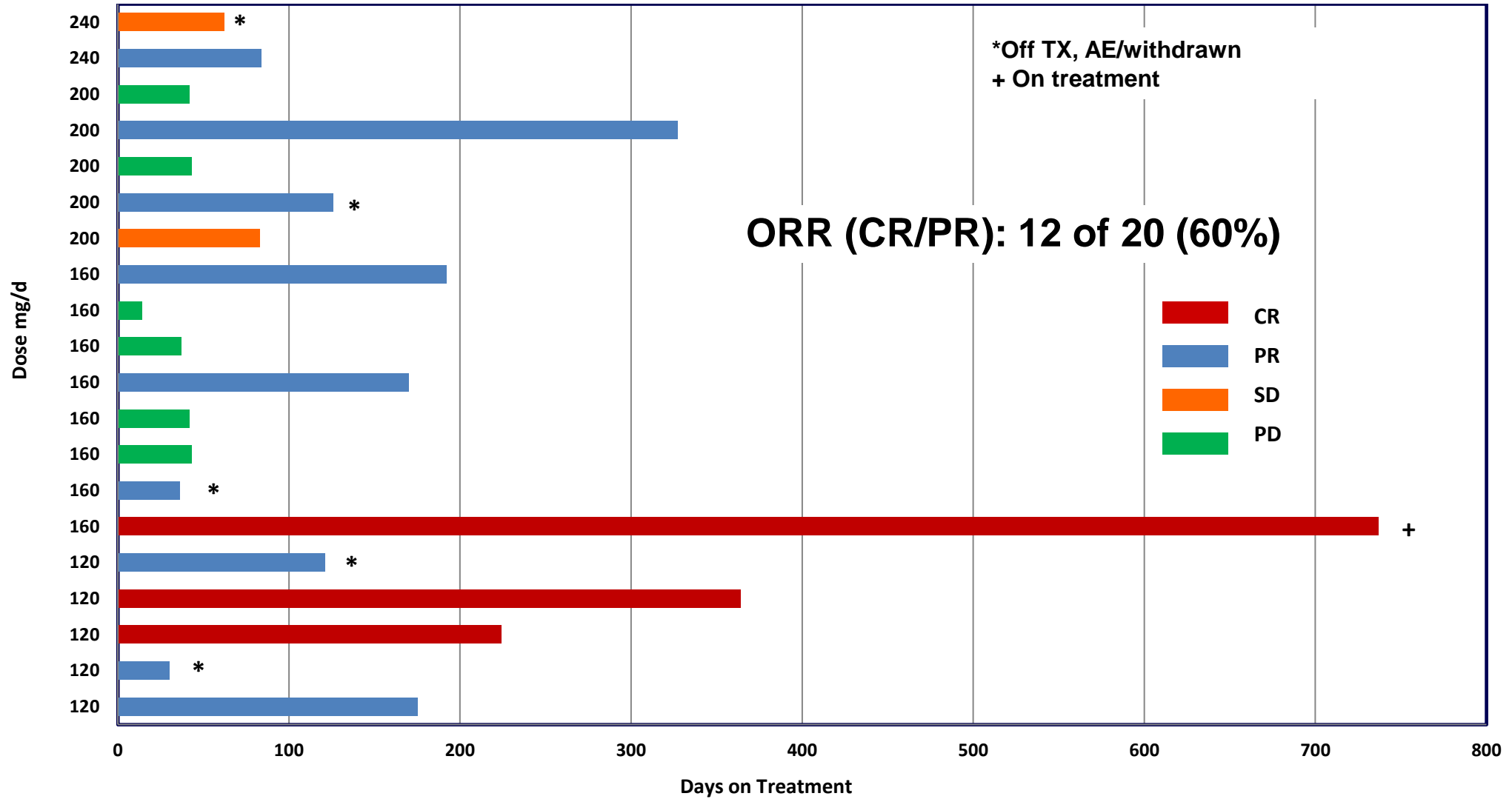
FB-10 – Phase I/II Trial of Kadcylya (T-DM1) + Neratinib



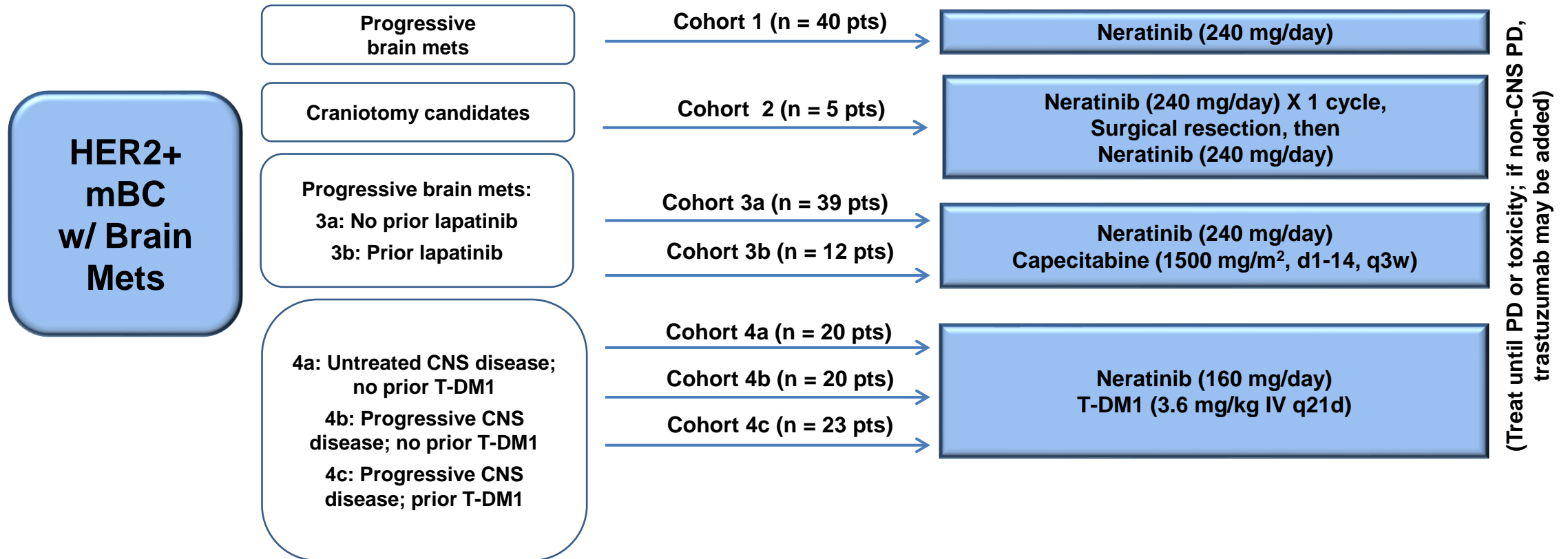
Primary endpoint: Phase I: Recommended dose of neratinib when given with T-DM1; Phase 2: Objective response rate (CR/PR)

Secondary endpoint: Clinical benefit rate (CR/PR/SD), PFS, PK, tumor biopsy for PDX model (optional)

FB-10 – Phase I/II Trial of Kadcylya (T-DM1) + Neratinib



TBCRC 022: Phase II Trial of HKI-272 (Neratinib) + Capecitabine for Patients with HER2+ Breast Cancer and Brain Metastases



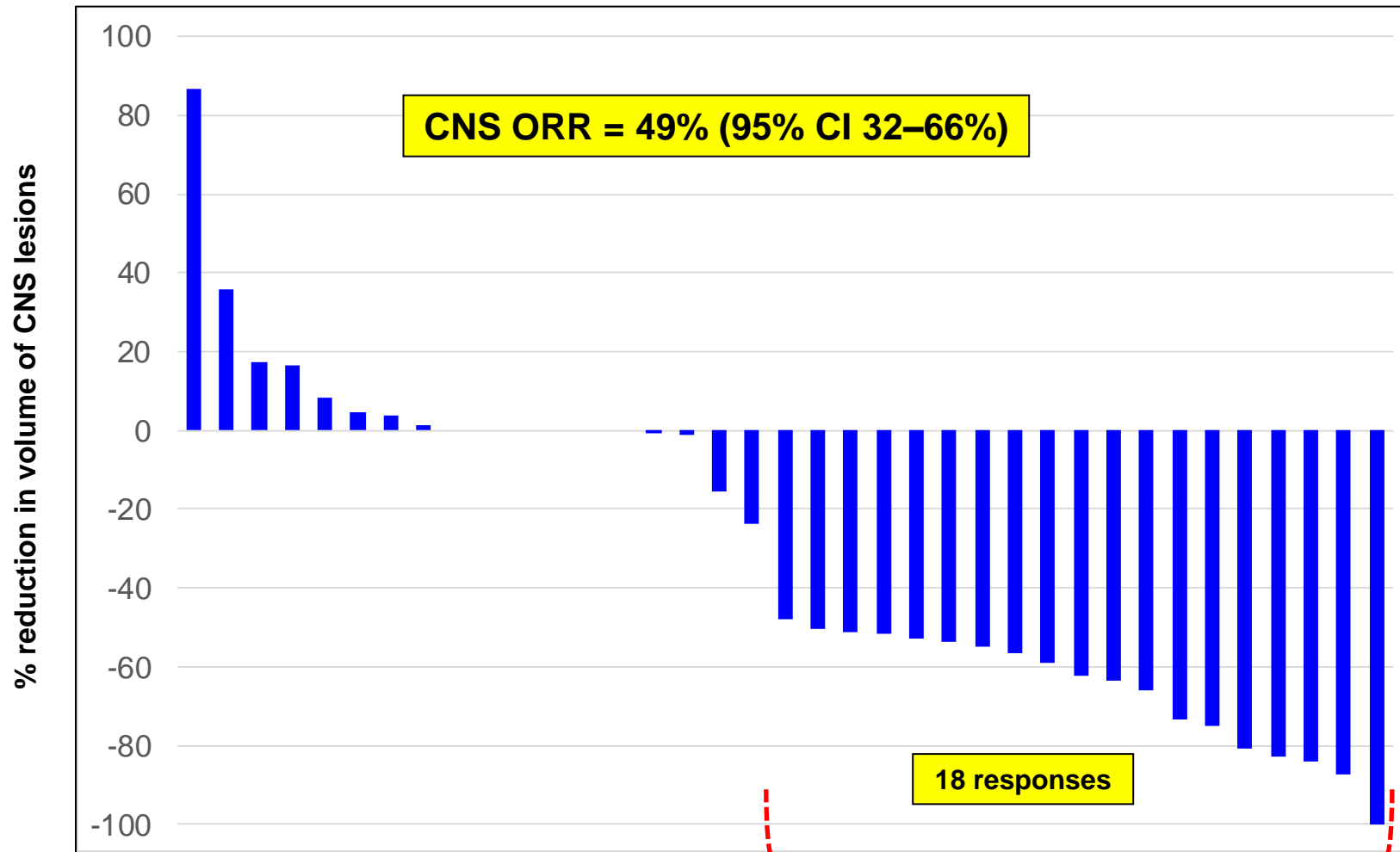
Primary endpoint: ORR in CNS: Cohort 1 ≥ 5 pts (12.5%); Cohort 3a ≥ 9 pts (25.7%); Cohort 3b ≥ 2 pts (8%); Cohort 2 PFS

Secondary endpoints: ORR in non-CNS, PFS, OS

TBCRC-022 Cohort 3a

CNS Response

Best Volumetric Response (n=31)*



Neratinib Recently Included as a Treatment Option for Recurrent Breast Cancer CNS Metastases By NCCN[®] Guidelines¹

Guidelines updated March 2020

Category 2A: Neratinib + Capecitabine

TBCRC 022²

A Phase II Trial of Neratinib and Capecitabine for Patients with HER2+ Breast Cancer Brain Metastases (NCT01494662)

Category 2B: Neratinib + Paclitaxel

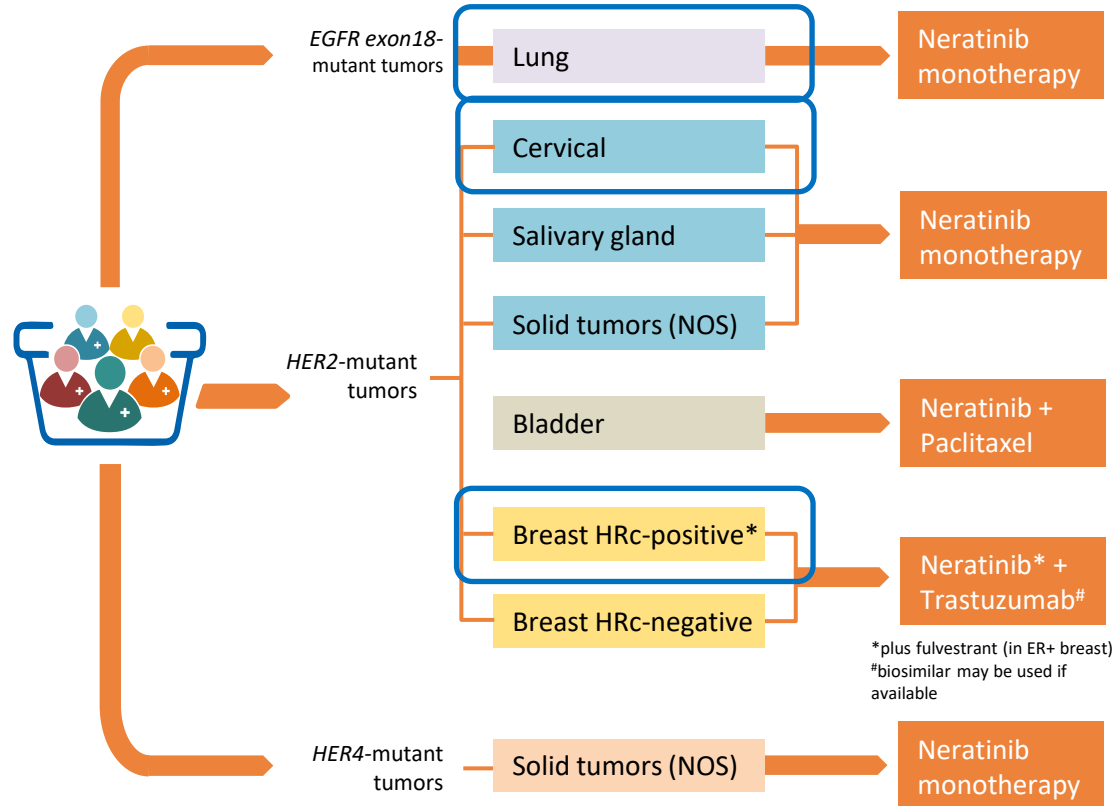
NEfERT-T^{3,4}

Randomized, Multi-Center, International Study of HER2-Directed Therapy in 1st-line mBC (NCT00915018)

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Central Nervous System Cancers V.1.2018. © National Comprehensive Cancer Network, Inc. 2018. All rights reserved. Accessed [March 20, 2018]. To view the most recent and complete version of the guideline, go online to NCCN.org

1. NCCN Guidelines v 1.2018. Central Nervous System Cancers.
2. Freedman RA, et al. Presented at ASCO Annual Meeting, 2017. Abstract 1005
3. Awada A, et al. *Poster Presentation at ASCO Annual Meeting, 2015. #610.*
4. Awada A, et al. *JAMA Oncol.* 2016;2:1557-1564.

Current SUMMIT 'Basket' Trial: Study Design



EGFR, HER2 or HER4 mutations
(documented by local testing)

Primary endpoint

- Objective response rate at first post-baseline tumor assessment (ORR_{first})

Secondary endpoints

- ORR (confirmed)
- Clinical benefit rate (CBR)
- Progression-free survival (PFS)
- Safety
- Biomarkers

Simon 2-stage design

- If ≥1 response in first evaluable 7 patients, expand cohort to Stage 2 (N=18)
- If ≥4 responses in Stage 2, expand or breakout

Tumor assessments

- RECIST v1.1 (primary criteria)
- PET response criteria (RECIST non-evaluable)

Statistical methods

- ORR_{first}, ORR, CBR: associated 95% CI
- Median PFS: Kaplan-Meier estimate with 95% CI

Key Inclusion Criteria

- Histologically confirmed cancers for which no curative therapy exists
- Documented EGFR exon 18, HER2 or HER4 mutation
- ECOG status of 0 to 2
- RECIST 1.1 evaluable disease (measurable or non-measurable disease): if RECIST non-measurable, evaluable by other accepted criteria

Key Exclusion Criteria

- Prior treatment with any pan-HER TKI (eg, lapatinib, afatinib, dacomitinib, neratinib)
- Patients who are receiving any other anticancer agents
- Symptomatic or unstable brain metastases
- Women who are pregnant or breast-feeding

SUMMIT

Hormone Receptor-Positive Breast Cancer Cohort



Somatic Mutations in *HER2* (*ERBB2*) in HR+ Breast Cancer

■ Incidence:

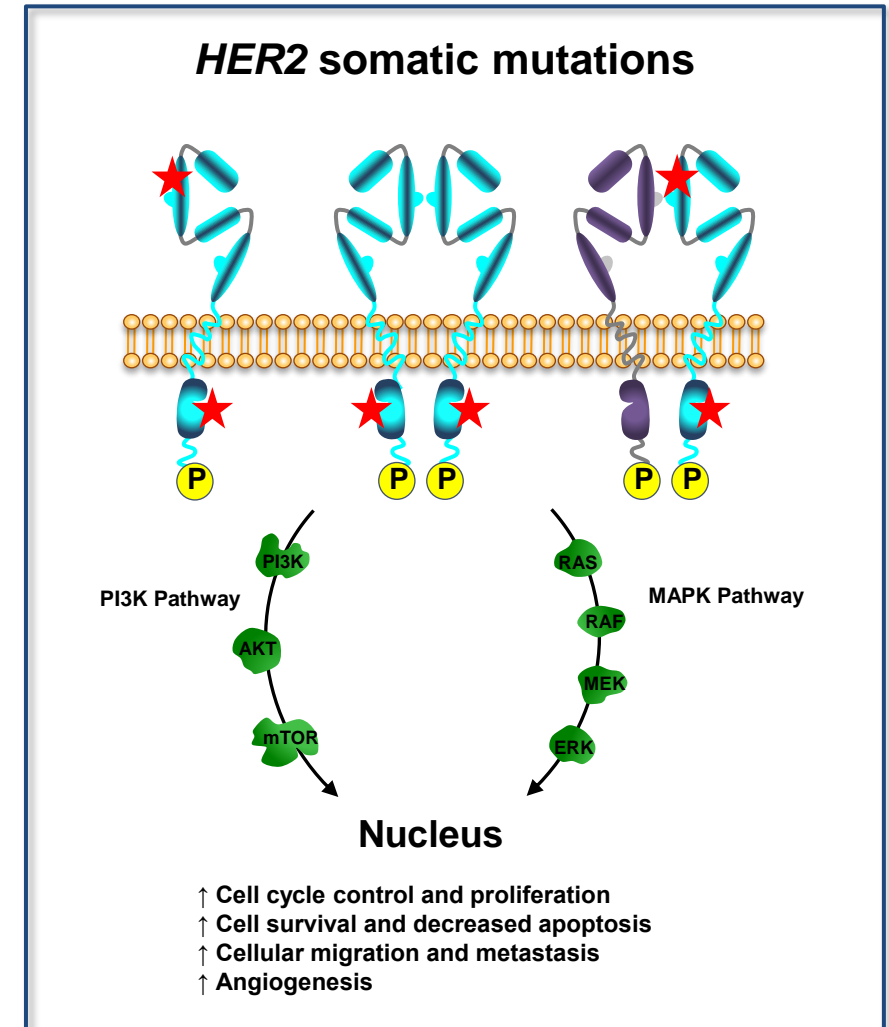
- 7–9%, pre-treated ER+ MBC¹

■ Tumor characteristics:

- Usually mutually exclusive to *HER2* amplifications

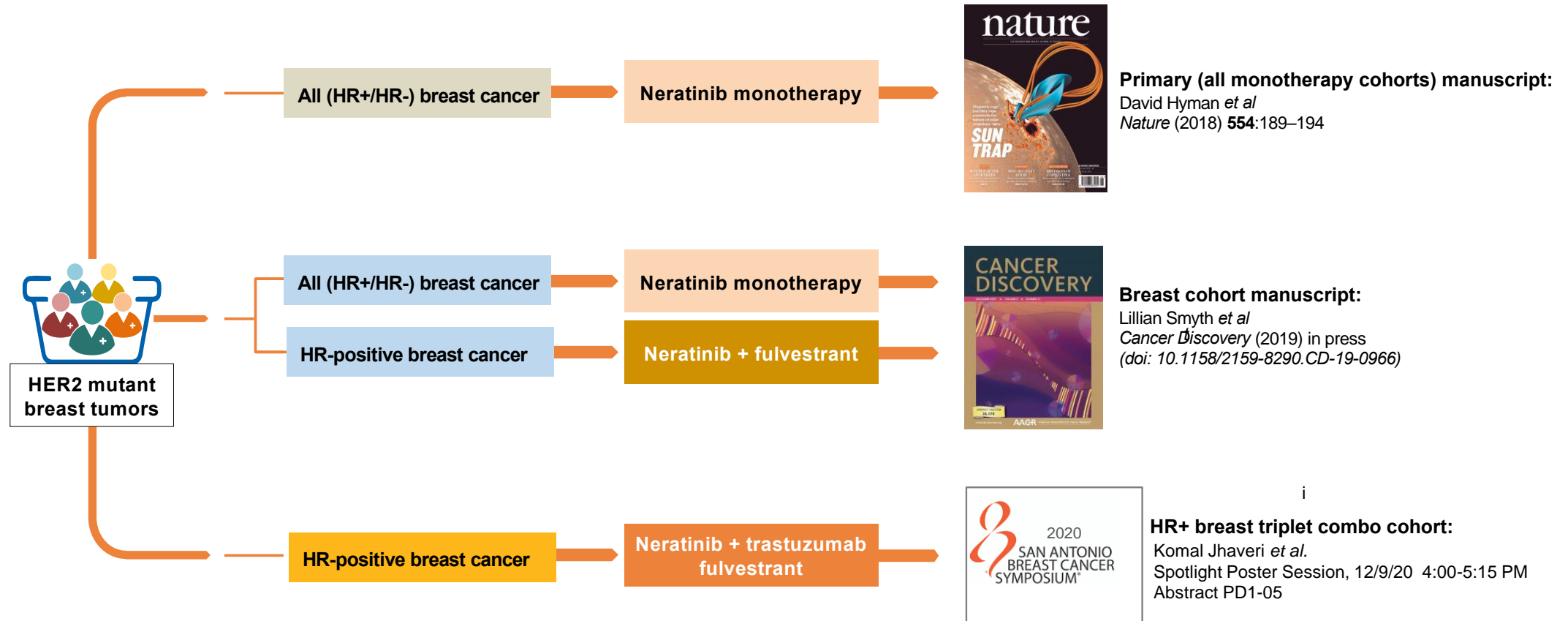
■ Preclinical evidence of oncogenic activity:

- Constitutive activation of intracellular kinase and downstream signaling pathways²
- Increased cell proliferation and tumor growth²
- Cross-talk occurs between ER and *HER2* mutation (modified SUMMIT trial to add fulvestrant to ER-positive patients)
- *HER2* amplification seen as potential mechanism of resistance to neratinib + fulvestrant (modified SUMMIT trial to add trastuzumab to neratinib + fulvestrant in ER-positive patients)



HR+ *HER2*-Mutated Breast

Publications from SUMMIT trial *HER2*-mutant breast cohorts

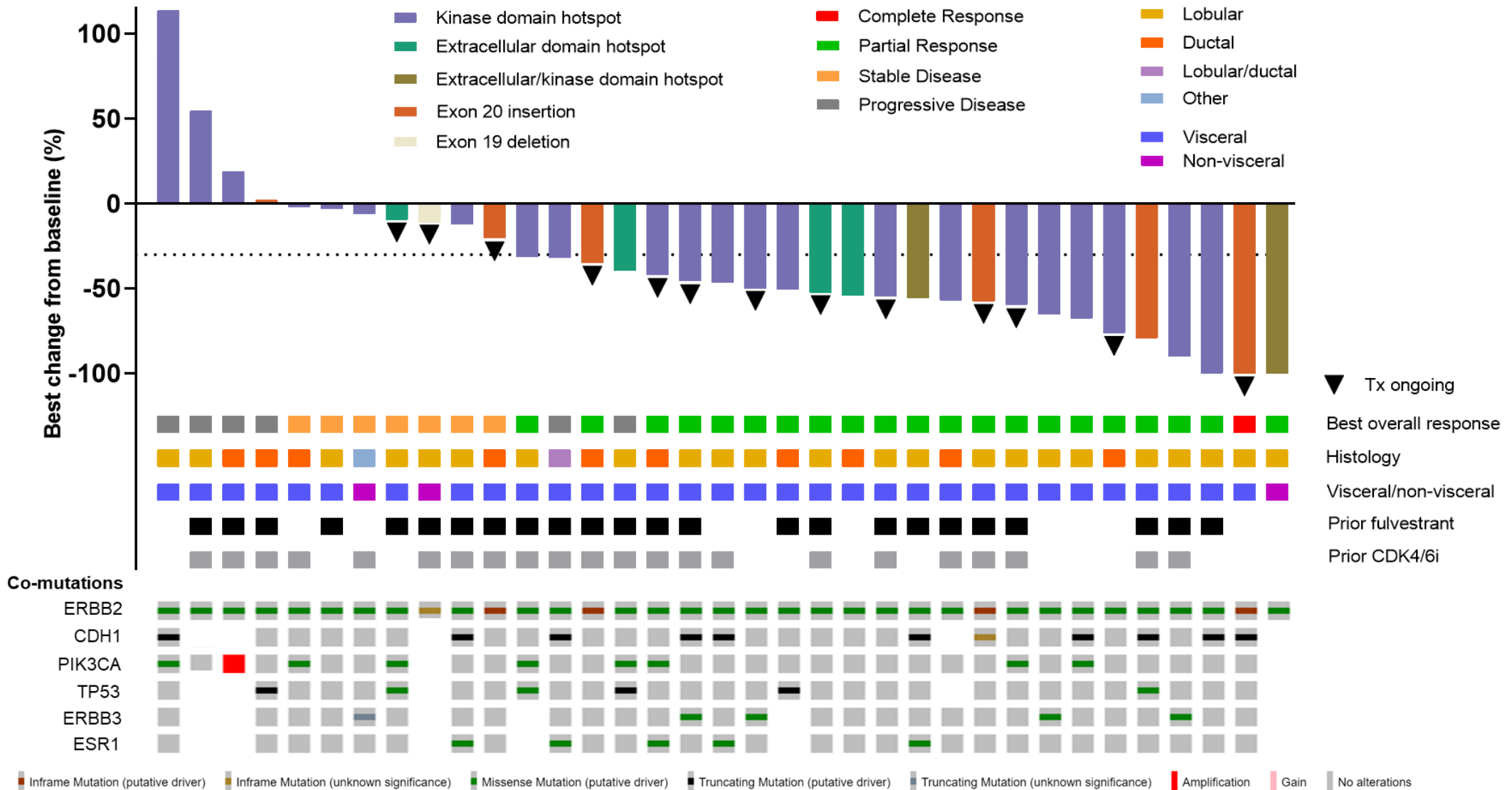


Other case reports or secondary publications:

1. A. Hanker *et al.* *Cancer Discovery* (2017) 7:575-585 (L869R sensitizing mutation and T798I *HER2* gatekeeper mutation – case study)
2. G. Ulaner *et al.* (2019) *Clin Cancer Res.* in press (doi: 10.1158/1078-0432.CCR-19-1658) (Exploring use of FDG-PET imaging for response assessments)
3. A. Medford *et al.* *NPJ Precision Oncology* (2019) Jul 16;3:18 (Blood based monitoring identifies actionable *HER2* mutations – case study)

HR+ *HER2*-Mutated Breast

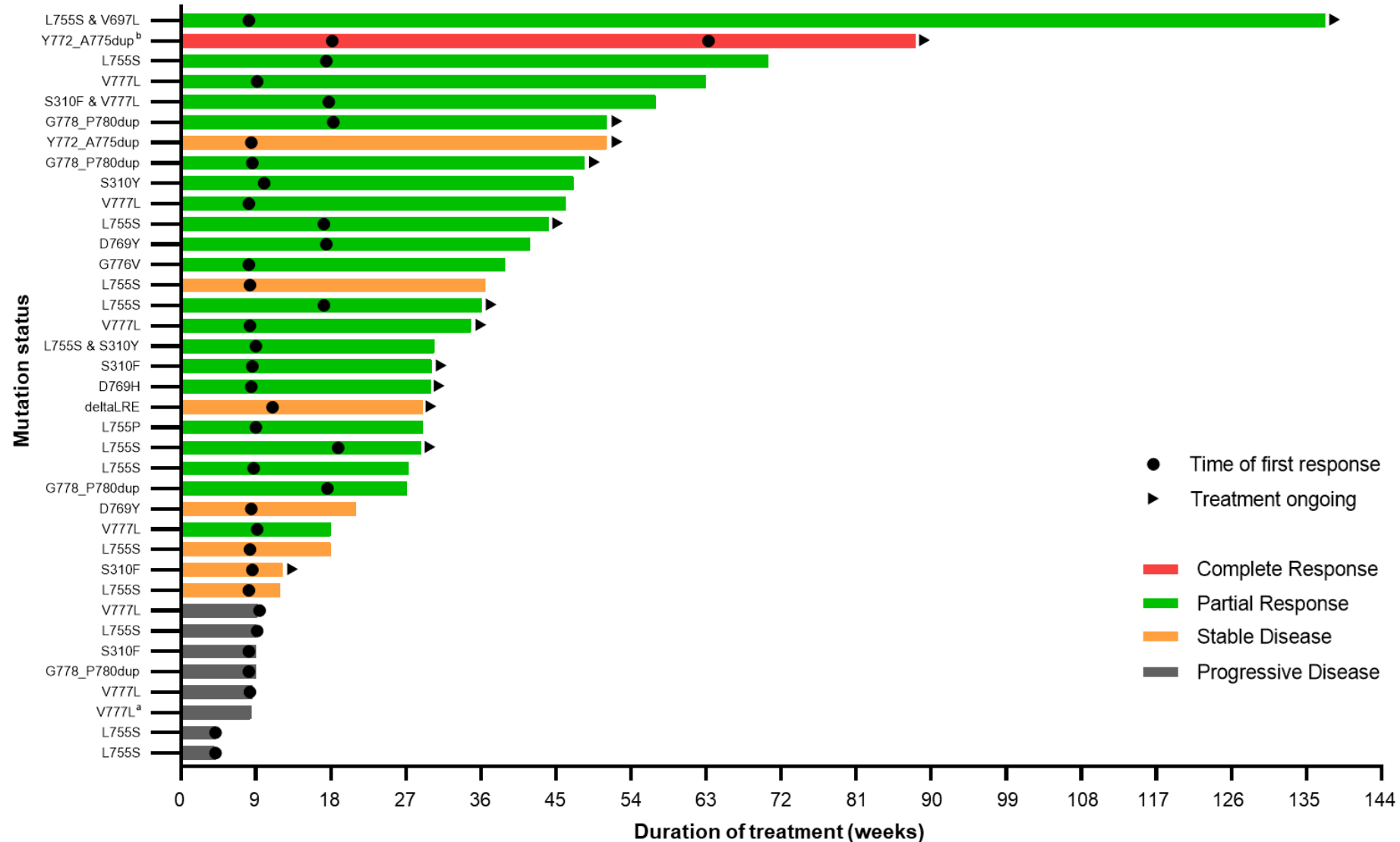
Change in tumor size and characteristics with neratinib + trastuzumab + fulvestrant (n=35)^a



SABCS 2020

HR+ *HER2*-Mutated Breast

Duration of treatment and best response with neratinib + trastuzumab + fulvestrant (n=37)



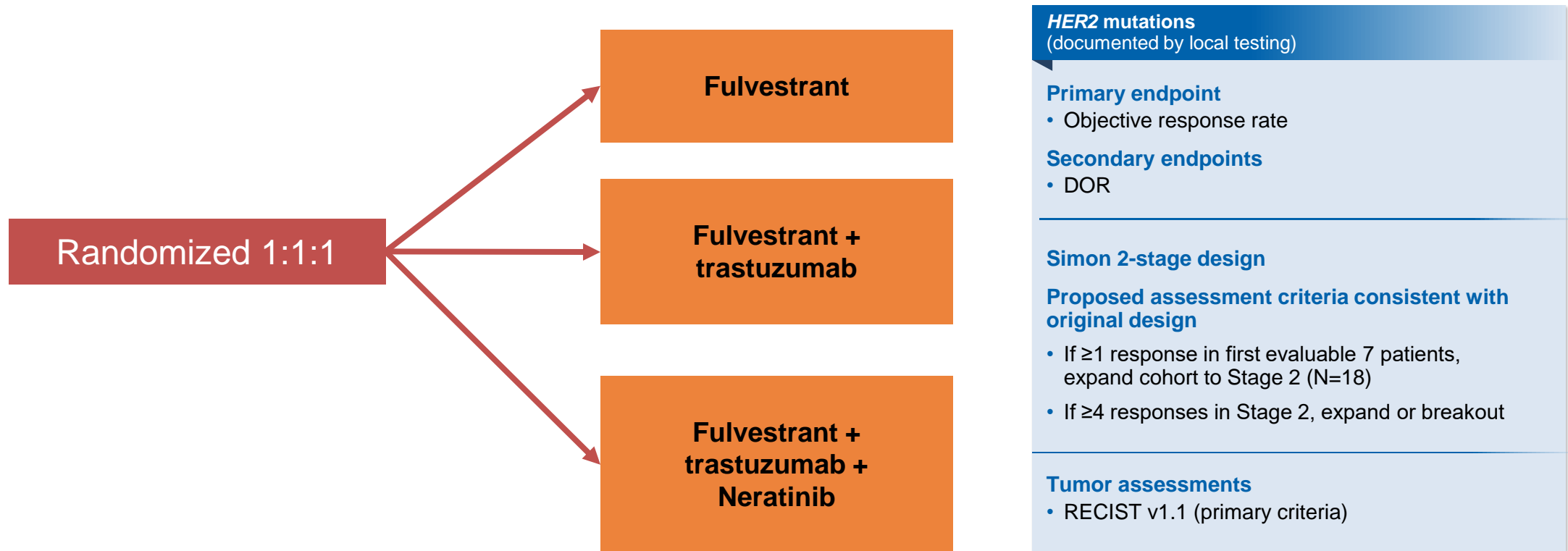
SABCS 2020



^aThis patient died in hospice due to clinical progression and did not have a tumor assessment before she died

^bThis patient had a first partial response at week 18 and a first complete response at week 63

Amendment to Breast Cancer Cohort in SUMMIT for HR+/HER2-HER2mut MBC Cohort to Support Accelerated Approval



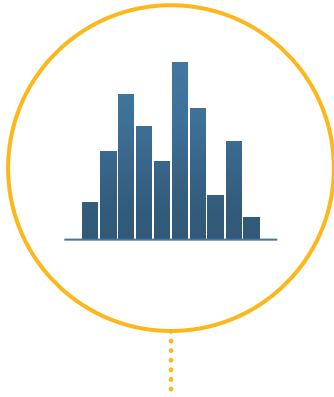
Puma to schedule pre-NDA meeting with FDA after initial Simon 2 stage results to discuss potential for accelerated approval (anticipated Q1 2021 – Q2 2021)

SUMMIT

Cervical Cancer Cohort

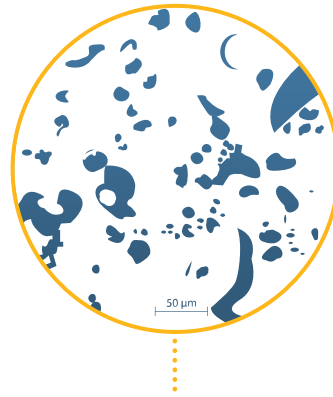


Characteristics of *HER2*-Mutant Cervical Cancer



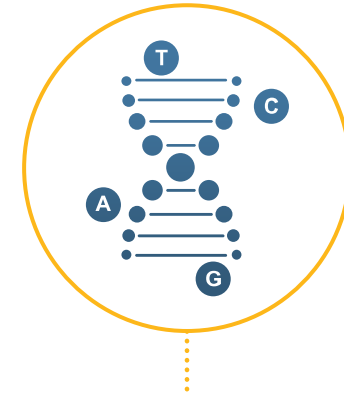
Incidence

- 5% metastatic cervical cancers
- May be negatively prognostic for survival



Histology

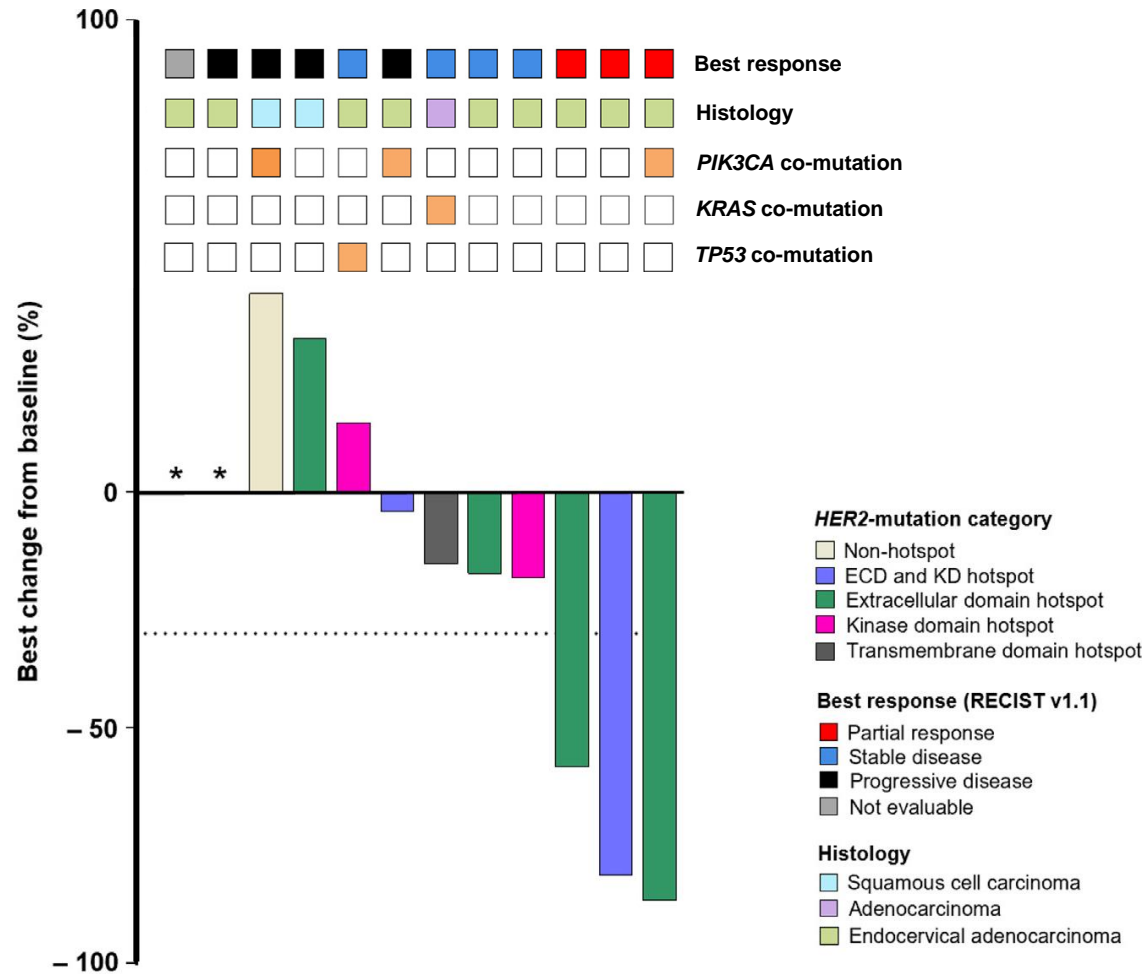
- Enriched in adenocarcinomas
- High occurrence in HPV+ tumors



Genomics

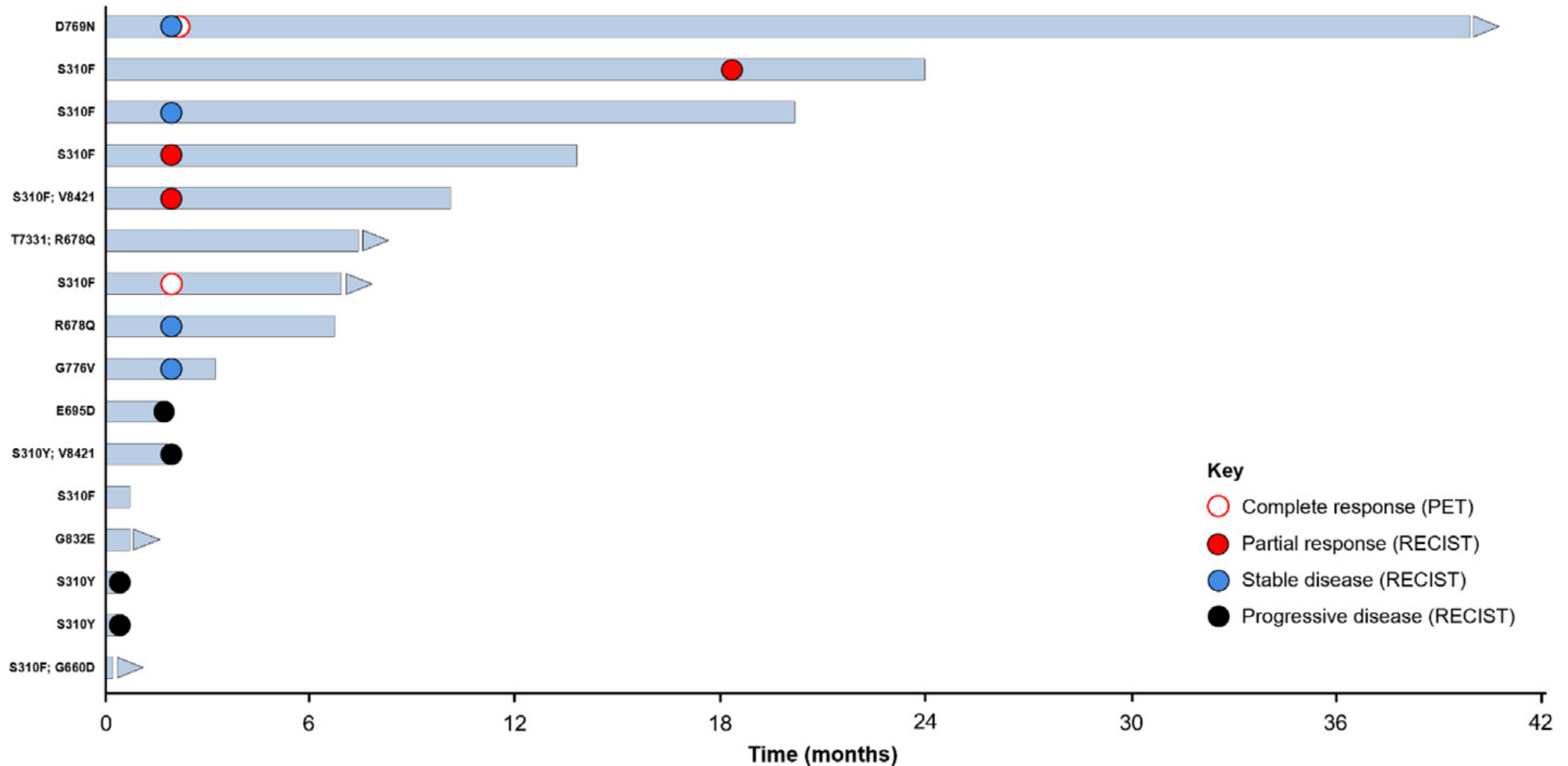
- Most common *HER2*^{mut} is S310 extracellular domain hotspot mutation
- Usually exclusive to *HER2* amplifications
- Most common co-mutations include *TP53*, *PIK3CA*

Neratinib Monotherapy Results Published in Gynecologic Oncology



Gynecologic Oncology, 2020

Neratinib Monotherapy Results Published in Gynecologic Oncology



Gynecologic Oncology, 2020

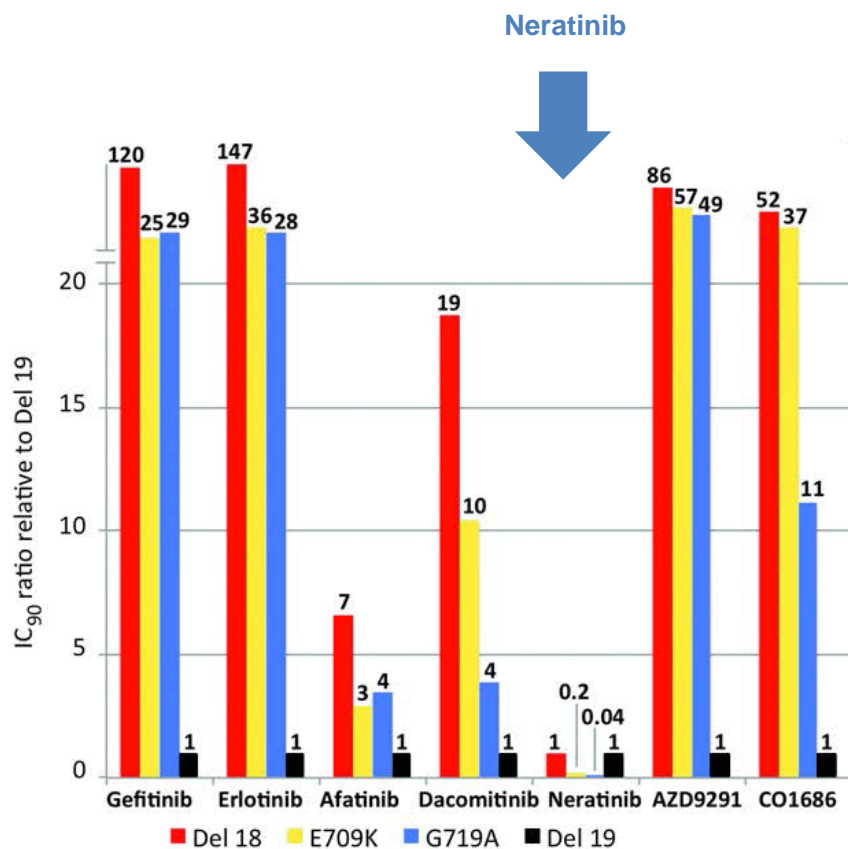
SUMMIT (PUMA-NER-5201) Basket Trial

EGFR exon 18 lung cancer cohort update

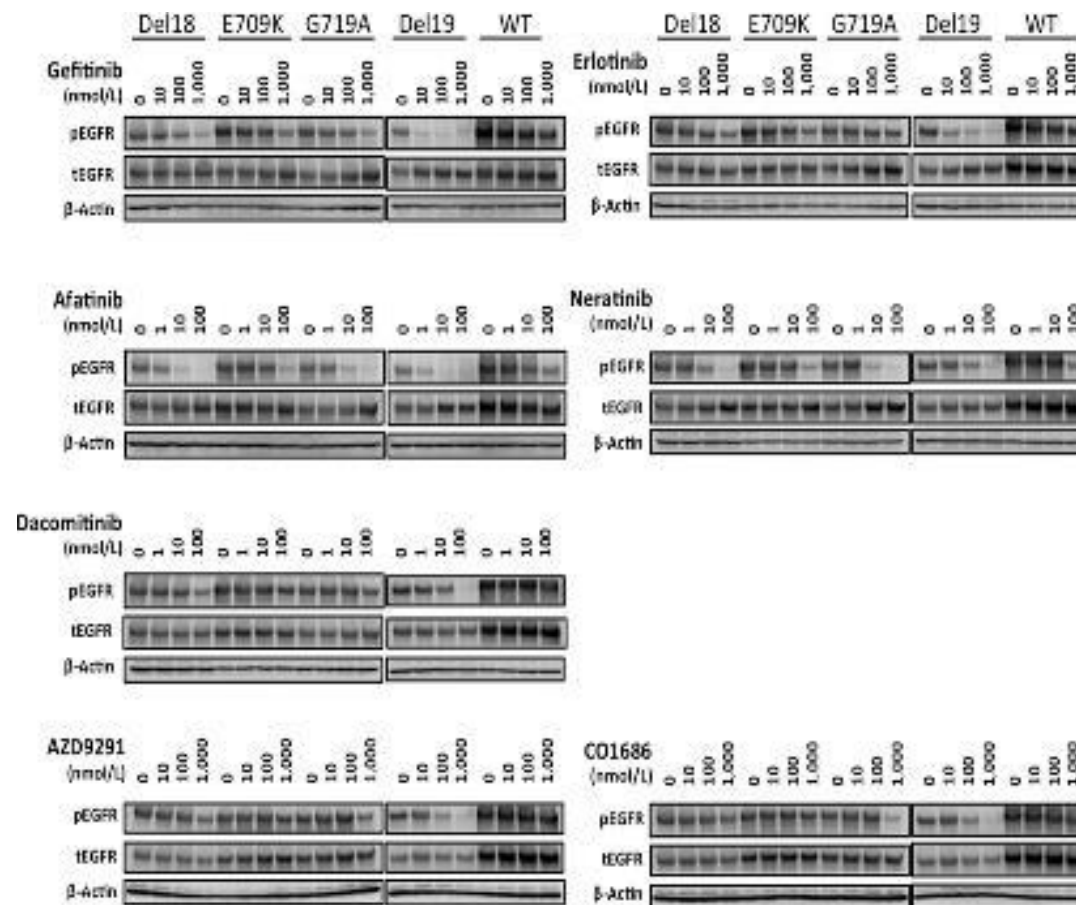


EGFR Exon 18 Mutations are Highly Sensitive to Neratinib (Irreversible Pan-HER TKIs) *In Vitro* Studies

Comparative TKI affects in EGFR exon 18+ cells

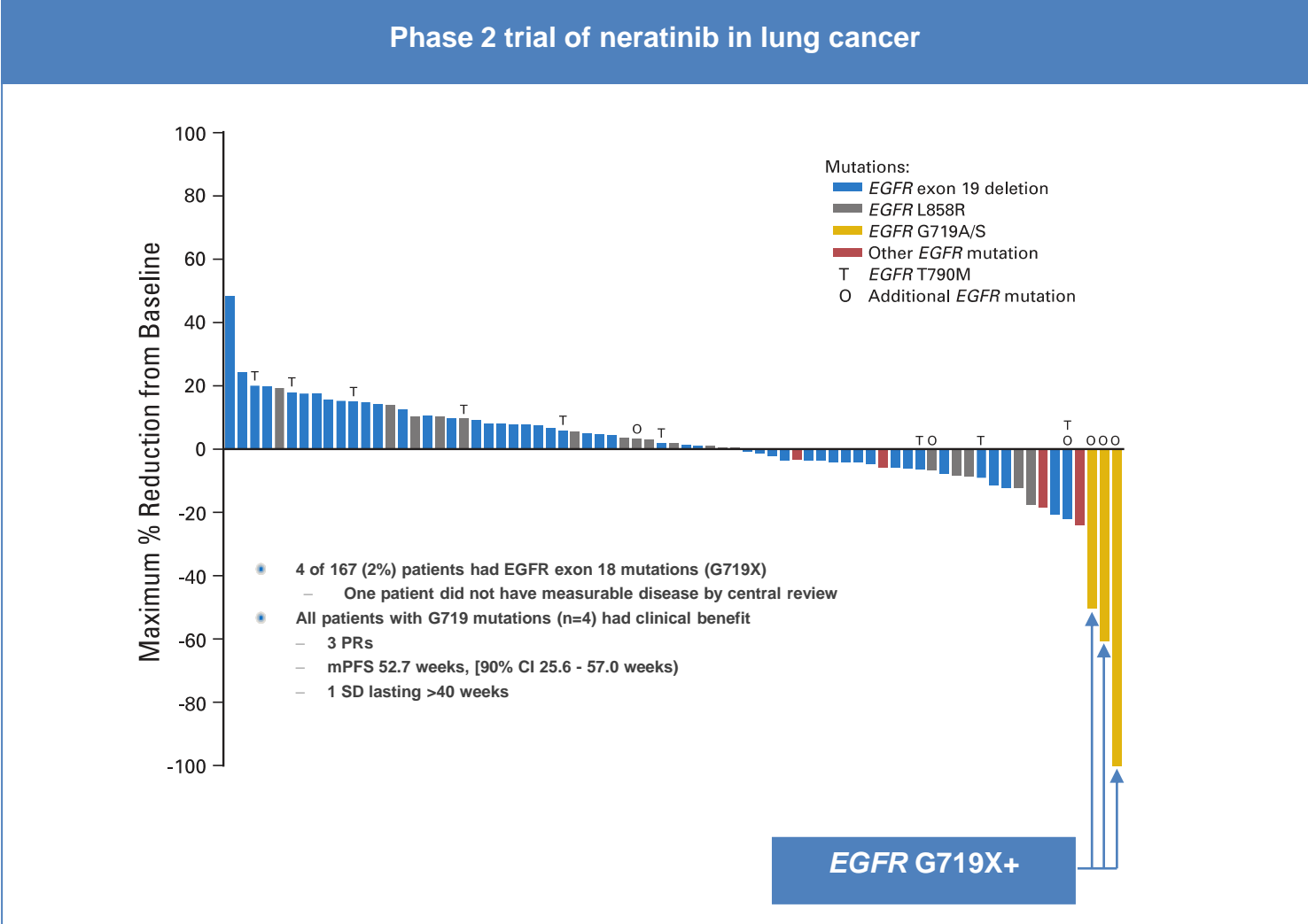


Western blot analyses of transfected HEK293 cells



Source: Kobayashi et al. Clin Cancer Res 2015;21:5305-5313.

EGFR Exon 18 Mutations are Highly Sensitive to Neratinib in NSCLC Patients from POC Trial



Source: L. Sequist et al (2010) J. Clin. Oncol. 28:3076-3083..

EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Baseline Demographics and Patient Characteristics

Patient characteristics	Safety/Efficacy evaluable patients (n=11)
Median (range), years	67 (56-83)
<65 years, n (%)	4 (36)
≥65 years, n (%)	7 (64)
Gender, n (%)	
Female	5 (45)
Male	6 (55)
ECOG performance status, n (%)	
0	5 (45)
1	6 (55)
Race, n (%)	
Black or African American	1 (9)
White	10 (91)
Median number of prior therapies in metastatic/locally advanced setting (range)	2 (1 – 3)
Prior checkpoint inhibitor, n (%)	3 (27)
Prior chemotherapy, n (%)	6 (55)
Prior tyrosine kinase inhibitor, n (%)	10 (91)
gefitinib/erlotinib (reversible 1 st gen EGFR TKI)	7 (58)
osimertinib (irreversible EGFR T790M TKI)	3 (25)
afatinib (irreversible pan-HER TKI)	2 (17)

Data cut-off: 21-Aug-2020

EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Efficacy Summary

Parameter	Efficacy evaluable patients (n=11)	TKI Pre-Treated (n=10)
Objective response (confirmed), ^a n	4	4
CR	0	0
PR	4	4
Objective response rate, % (95% CI)	36 (11–69)	40 (12–74)
Best overall response, n	6	6
CR	0	0
PR	6	6
Best overall response rate, % (95% CI)	54 (23–83)	60 (26–88)
Median DOR, ^b months (95% CI)	7.5 (4.0–NE) (1.9*, 4.0, 7.5, 9.2*)	7.5 (4.0–NE) (1.9*, 4.0, 7.5, 9.2*)
Clinical benefit, ^c n	8	8
CR or PR	4	4
SD ≥16 weeks	4	4
Clinical benefit rate, % (95% CI)	73 (39–94)	80 (44–97)
Median PFS time to event, months (95% CI)	6.9^b (2.1–NA)	9.1 (3.7–NA)

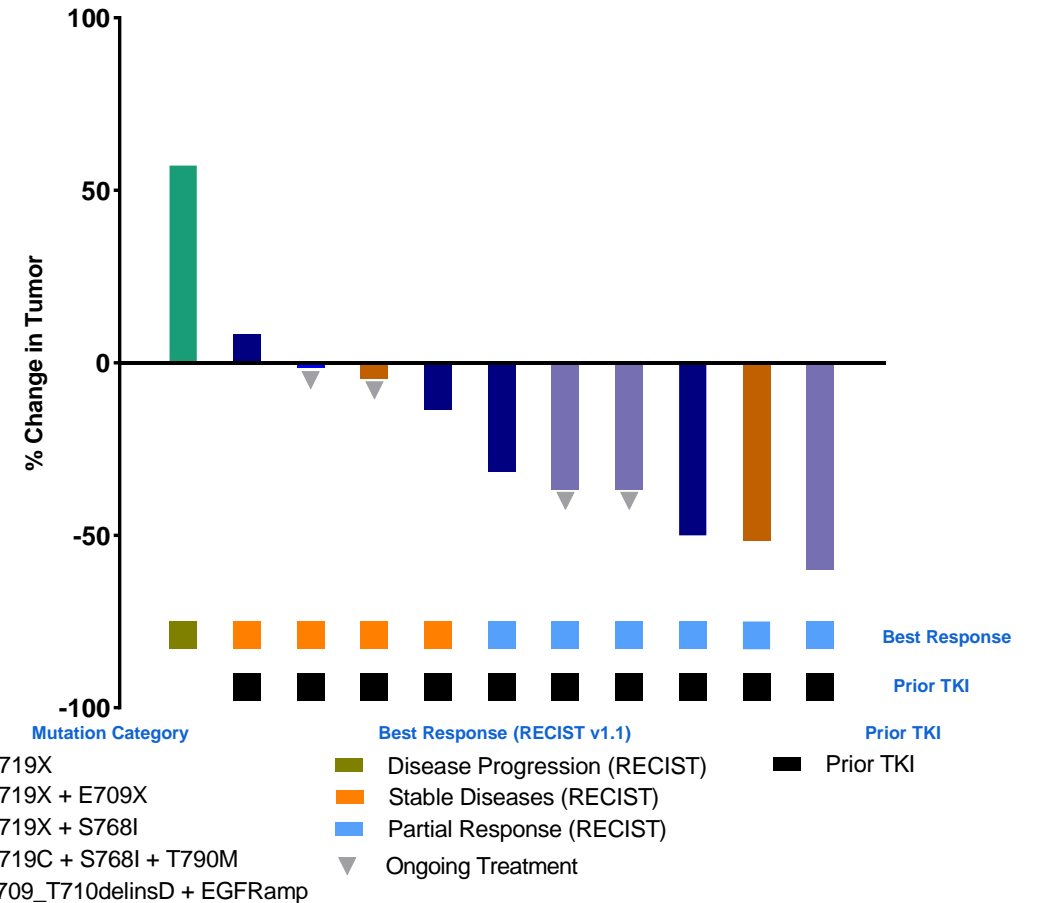
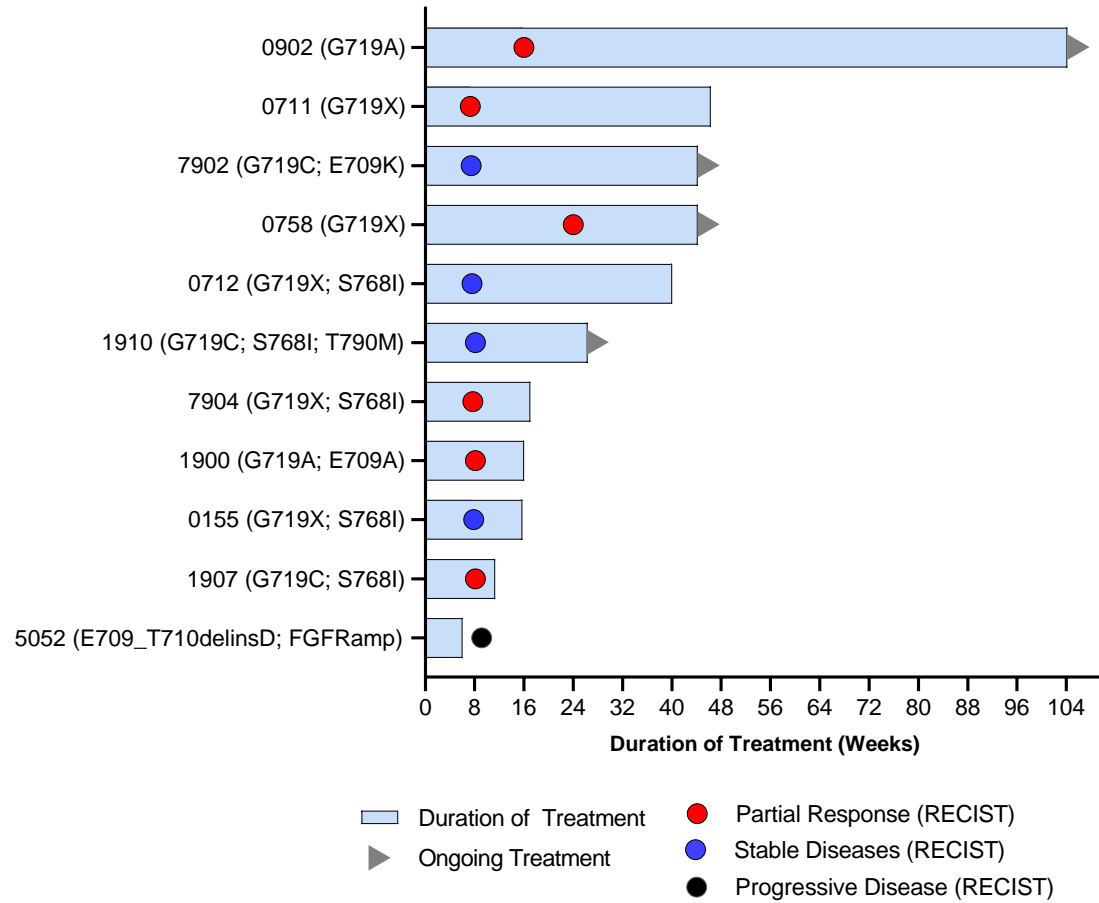
^a Objective response rate (ORR) is defined as either a complete or partial response that is confirmed no less than 4-weeks after the criteria for response are initially met

^b Kaplan-Meier analysis in safety population. ^c Clinical benefit rate (CBR) is defined as confirmed CR or PR or stable disease (SD) for ≥16 weeks (within +/- 7-day visit window)

DOR, duration of response; PFS, progression-free survival, * response ongoing

Data cut-off: 21-Aug-2020

EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Treatment Duration, Best Response and Best Change in Tumor



Data cut-off: 21-Aug-2020



EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Most Common Treatment-Emergent Adverse Events >10%

TEAE	Safety evaluable patients (n=11)	
	Any grade	Grade ≥ 3
Diarrhea	5 (45.5)	0
Vomiting	4 (36.4)	0
Constipation	3 (27.3)	0
Nausea	3 (27.3)	0
Decreased appetite	3 (27.3)	1 (9.1)
Dizziness	2 (18.2)	0
Hypertension	2 (18.2)	0
Dry mouth	2 (18.2)	0
Fatigue	2 (18.2)	0

Data cut-off: 21-Aug-2020

EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Characteristics of Treatment-Emergent Diarrhea

	Lung EGFR (N=11)
Incidence of diarrhea, n (%)^a	
Any grade	5 (45.5)
Grade 1	4 (36.4)
Grade 2	1 (9.1)
Grade 3	0
Action taken with neratinib, n (%)	
Leading to temporary hold	0
Leading to dose reduction	0
Leading to permanent discontinuation	0
Diarrhea leading to hospitalization, n (%)	0
Time to first diarrhea, median (range) in days	15 (3 – 253)
Time to first grade 2 diarrhea, median (range) in days	8 (8 – 8)
Duration of grade 2 diarrhea per episode, median (range) in days	2 (1 – 2)

Data cut-off: 21-Aug-2020

Historical Response Rates of Afatinib in NSCLC Patients With *EGFR* Exon 18 Mutations (G719X)

Table 3. Response Rates With Afatinib in Patients With NSCLC Harboring Uncommon Mutations

Mutation Type	CR, n (%)	PR, n (%)	SD, n (%)	PD, n (%)	DCR, n (%)	ORR, n (%)	DoR, Mo (95% CI)
EGFR TKI-naïve patients							
Major uncommon mutation (n = 110)	5 (4.5)	61 (55.5)	35 (31.8)	9 (8.2)	101 (91.8)	66 (60.0)	17.1 (11.0-20.8)
G719X (n = 55)	4 (7.3)	31 (56.4)	16 (29.1)	4 (7.3)	51 (92.7)	35 (63.4)	17.1 (10.3-22.0)
L861Q (n = 47)	0 (0.0)	28 (59.6)	14 (29.8)	5 (10.6)	42 (89.4)	28 (59.6)	13.8 (7.4-20.6)
S768I (n = 8)	1 (12.5)	4 (50.0)	3 (37.5)	0 (0.0)	8 (100.0)	5 (62.5)	NR (15.9-NR)
Compound (n = 35)	0 (0.0)	27 (77.1)	5 (14.3)	3 (8.6)	32 (91.4)	27 (77.1)	16.6 (13.8-18.7)
With major uncommon mutation (n = 23)	0 (0.0)	18 (78.3)	4 (17.4)	1 (4.3)	22 (95.7)	18 (78.3)	17.1 (14.7-NR)
Exon 20 insertion (n = 70)	2 (2.9)	15 (21.4)	41 (58.6)	12 (17.1)	58 (82.9)	17 (24.3)	11.9 (5.4-26.7)
T790M (n = 25)	0 (0.0)	6 (24.0)	13 (52.0)	6 (24.0)	19 (76.0)	6 (24.0)	4.7 (3.8-11.0)
Others (n = 23)	0 (0.0)	15 (65.2)	5 (21.7)	3 (13.0)	20 (87.0)	15 (65.2)	9.0 (3.5-11.9)
EGFR TKI-pretreated patients							
Major uncommon mutation (n = 32)	0 (0.0)	8 (25.0)	14 (43.8)	10 (31.3)	22 (68.8)	8 (25.0)	4.9 (2.0-18.0)
G719X (n = 19)	0 (0.0)	2 (10.5)	10 (52.6)	7 (36.8)	12 (63.2)	2 (10.5)	10.0 (2.0-18.0)
L861Q (n = 11)	0 (0.0)	5 (45.5)	3 (27.3)	3 (27.3)	8 (72.7)	5 (45.5)	4.4 (4.3-8.4)
S768I (n = 2)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)	2 (100.0)	1 (50.0)	NR
Compound (n = 21)	0 (0.0)	6 (28.6)	10 (47.6)	5 (23.9)	16 (76.2)	6 (28.6)	16.7 (9.9-21.8)
With major uncommon mutation (n = 8)	0 (0.0)	3 (37.5)	3 (37.5)	2 (25.0)	6 (75.0)	3 (37.5)	16.7 (9.9-16.7)
Exon 20 insertion (n = 21)	0 (0.0)	3 (14.3)	9 (42.9)	9 (42.9)	12 (57.1)	3 (14.3)	3.7 (2.7-10.1)
T790M (n = 64)	0 (0.0)	12 (18.8)	31 (48.4)	21 (32.8)	43 (67.2)	12 (18.8)	6.1 (2.6-7.9)
Others (n = 25)	0 (0.0)	9 (36.0)	8 (32.0)	8 (32.0)	17 (68.0)	9 (36.0)	6.3 (0.8-11.3)

CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; PD, progressive disease; ORR, overall response rate; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor; NR, not reported.

Milestones for Neratinib in *EGFR* Exon 18-Mutant Lung Cancer Cohort in SUMMIT Study

- The success criteria for the 1st stage and 2nd stage of the Simon's 2-stage design has been met
 - Enrollment in the 2nd stage is continuing up to a total of 30 patients
- Anticipate presentation of additional data from SUMMIT in patients with *EGFR* exon 18-mutant lung cancer in second half of 2021
- Anticipate scheduling meeting with FDA to discuss potential accelerated approval strategy for patients with *EGFR* exon 18-mutant lung cancer who have been treated with a prior *EGFR* TKIs in 2021

IST Landscape – Other Cancers

ISTs	FC-7 (NSABP) Quad Wild-Type mCRC w/ prior cetuximab or panitumumab, dose finding for N + Cetuximab		NEREA (SOLTI) HR+/HER2-/HER2-enriched mBC, N + Ex/Ful/Tam	MCC-17-13821 (VCU) P1 dose finding N + sodium valproate in advanced solid tumors, expansion in HER2+ BC and K-/N-RAS mutant cancers
	FC-11 (NSABP) Quad Wild-Type mCRC, HER2+ w/ prior EGFR ther or HER2-mutated: N+T, HER2+ w/o prior EGFR therapy: N+Cetuximab		201209135/MutHER (WU) HER2-mutated mBC, ER-: N, ER+: N+Ful	POE 16-01 (MSKCC) Pediatric solid tumors and acute leukemias, N dose finding followed by N at RP2D
	ACOMPLI (INSERM) HER2+ or HER2-mutated mCRC, N vs. SOC	INSIGHt (DFCI) Tumors w/ unmethylated MGMT promoters, w/o IDH1 R132H mutation, SOC (temozolomide) vs. N vs. CC-115 vs. Abemaciclib	PlasmaMATCH (ICR) HER2-mut mBC, line 2+, ER-: N, ER+: N+Ful	2016-0430 (MDACC) Advanced/metastatic cancer with HER2/3/4 mutation or HER2/3+, N+Everolimus vs. N+Palbo vs. N+Trametinib
Puma	None	None	SUMMIT (HER2-mutated breast cancer)	SUMMIT (HER2-mutated tumors)
	Colorectal Cancer	Glioblastoma	Breast Cancer	Multiple Tumor Types

Puma – Expected Milestones

- Complete enrollment in randomized Phase II cohort in SUMMIT basket trial in HR+ breast cancer with HER2 mutation Q2 2020)
- Report top line data from cohort of patients in SUMMIT basket trial with HR+ breast cancer with *HER2* mutation (2021)
- Report Phase II data from cohort of patients in SUMMIT basket trial of neratinib in non-small cell lung cancer patients with *EGFR* exon 18 mutations (H2 2021)
- Conduct pre-NDA meeting with the FDA to discuss accelerated approval of neratinib in *HER2*-mutated HR+ breast cancer and *HER2*-mutated cervical cancer (2021)
- Report Phase II TBCRC-022 trial of the combination of Kadcylla + neratinib in patients with *HER2*+ breast cancer with brain metastases who have previously been treated with Kadcylla (H2 2021)
- Conduct meeting with the FDA to discuss the potential for an accelerated approval pathway for neratinib in non-small cell lung cancer patients with *EGFR* exon 18 mutations who have been previously treated with an *EGFR* tyrosine kinase inhibitor (2021)

Intellectual Property

- Composition of matter patent issued (expires 2025)
 - Can be extended w/ Hatch/Waxman
- Use in the treatment of cancer issued (expires 2025)
- Two polymorph patents issued (both expire 2028)
- Combination with capecitabine (expires 2031)
- Use in extended adjuvant breast cancer (expires 2030)
- Composition of specific salt of neratinib (recently issued)

Intellectual Property on *EGFR* T790M Mutations

- Issued claims in Europe, Asia, Australia (expires 2026)
 - Possibility to extend up to 5 years
- Issued claims in United States (expires 2026)
- Patent claims upheld after European Opposition Hearing (February 2014)
 - Patent claims upheld after Appeal to European Opposition (December 2020)
- Claims for the pharmaceutical composition comprising an irreversible EGFR inhibitor for use in treating cancer having a T790M mutation
- Claims for the pharmaceutical composition for use in the treatment of cancer including lung cancer and non-small cell lung cancer

Experienced Management Team

Alan H. Auerbach

Chairman, Chief Executive Officer, President, Founder

– *Chief Executive Officer, President, Founder, Cougar Biotechnology*

Richard Bryce, MD

Chief Medical and Scientific Officer

– *Onyx, Roche, ICON Clinical Research*

Jeff Ludwig

Chief Commercial Officer

– *Astellas, Amgen*

Maximo F. Nougues

Chief Financial Officer

– *Getinge AB, Boston Scientific, The Clorox Company*

Douglas Hunt

Senior Vice President, Regulatory Affairs

– *ArmaGen, Baxter Healthcare, Amgen*

Board of Directors

Alan H. Auerbach

Chairman, Chief Executive Officer, President, Founder, Puma Biotechnology, Inc.

Ann Miller, M.D.

Former VP, Marketing, Global Marketing, Sanofi S.A.; Eisai; Amgen; Merck

Michael Miller

Former EVP U.S. Commercial, Jazz Pharmaceuticals; VP, Sales & Marketing, Genentech

Jay Moyes

Former CFO, Myriad Genetics

Hugh O'Dowd

President & CEO, Neon Therapeutics; Former Chief Commercial Officer, Novartis Oncology

Adrian Senderowicz, M.D.

SVP & Chief Medical Officer, Constellation Pharmaceuticals; Ignyta; Sanofi; AstraZeneca; FDA (Division of Oncology Drug Products)

Brian Stiglich, R.Ph.

CEO, Verastem; Founder, Proventus Health Solutions; Former VP and Chief Marketing Officer, Eli Lilly Oncology

Troy Wilson, PhD, JD

CEO, Kura Oncology; CEO, Wellspring Biosciences; CEO Avidity Nanomedicines; Former CEO, President, Intellikine

Puma Biotechnology – Financial

- Currently trading on NASDAQ: PBYY
- Cash, cash equivalents and marketable securities at December 31, 2020: ~\$93 million
- Cash burn in Q4 2020: ~\$15.6 million
- Amended term loan agreement (June 2019)
 - New term loan of \$100 million replaces loan of \$155 million
 - \$100 million drawn down
 - Oxford Finance
- Shares issued and outstanding: 40.2 million

Company Highlights

- NERLYNX[®] – first HER2-directed drug approved by FDA for extended adjuvant treatment of early-stage HER2+ breast cancer in patients who have received prior trastuzumab
- NERLYNX[®] – first HER2-directed tyrosine kinase inhibitor approved in both early-stage and metastatic HER2+ breast cancer
- Additional potential indications:
 - HER2+ metastatic breast cancer with brain metastases
 - *HER2*-mutated breast cancer
 - HER2-mutated cervical cancer
 - *EGFR* exon 18-mutated non-small cell lung cancer
 - *HER2*-mutated solid tumors
- Retain full U.S. commercial rights to NERLYNX[®]
- Large initial market opportunity with additional label expansion potential

Puma Biotechnology

H. C. Wainwright Global Life Sciences Conference

March 2021



Puma Biotechnology

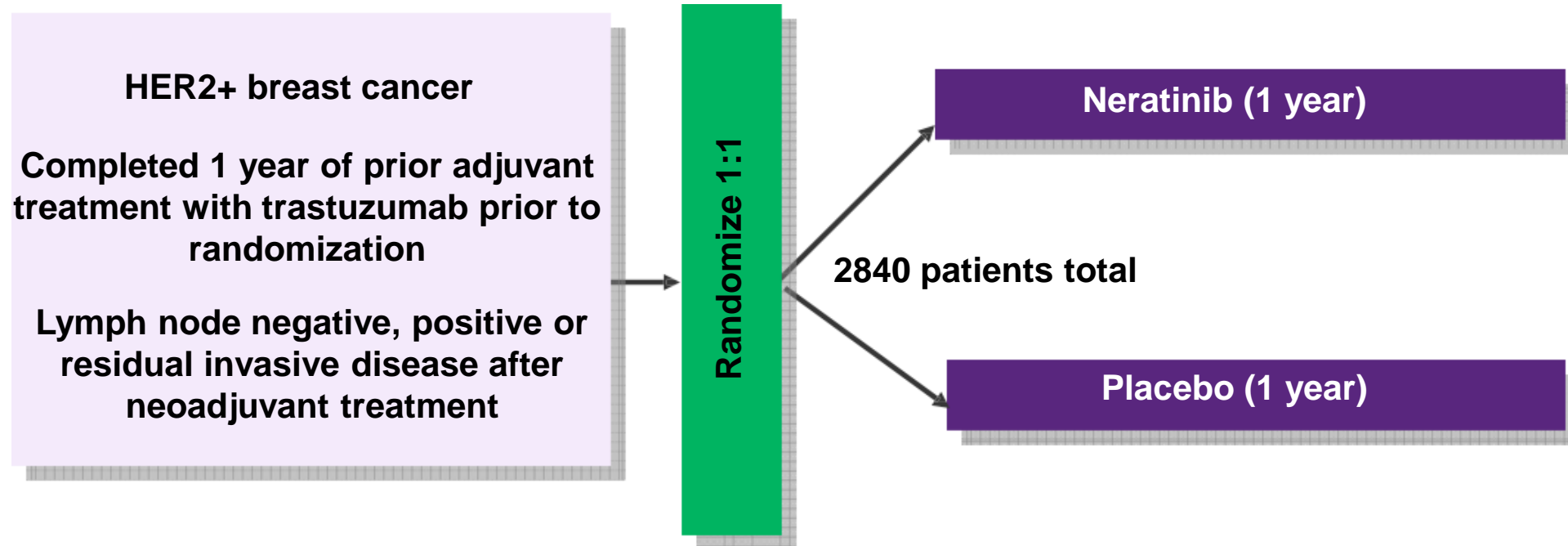
H. C. Wainwright Global Life Sciences Conference

APPENDIX

March 2021



ExteNET Trial – HER2+ Extended Adjuvant Breast Cancer

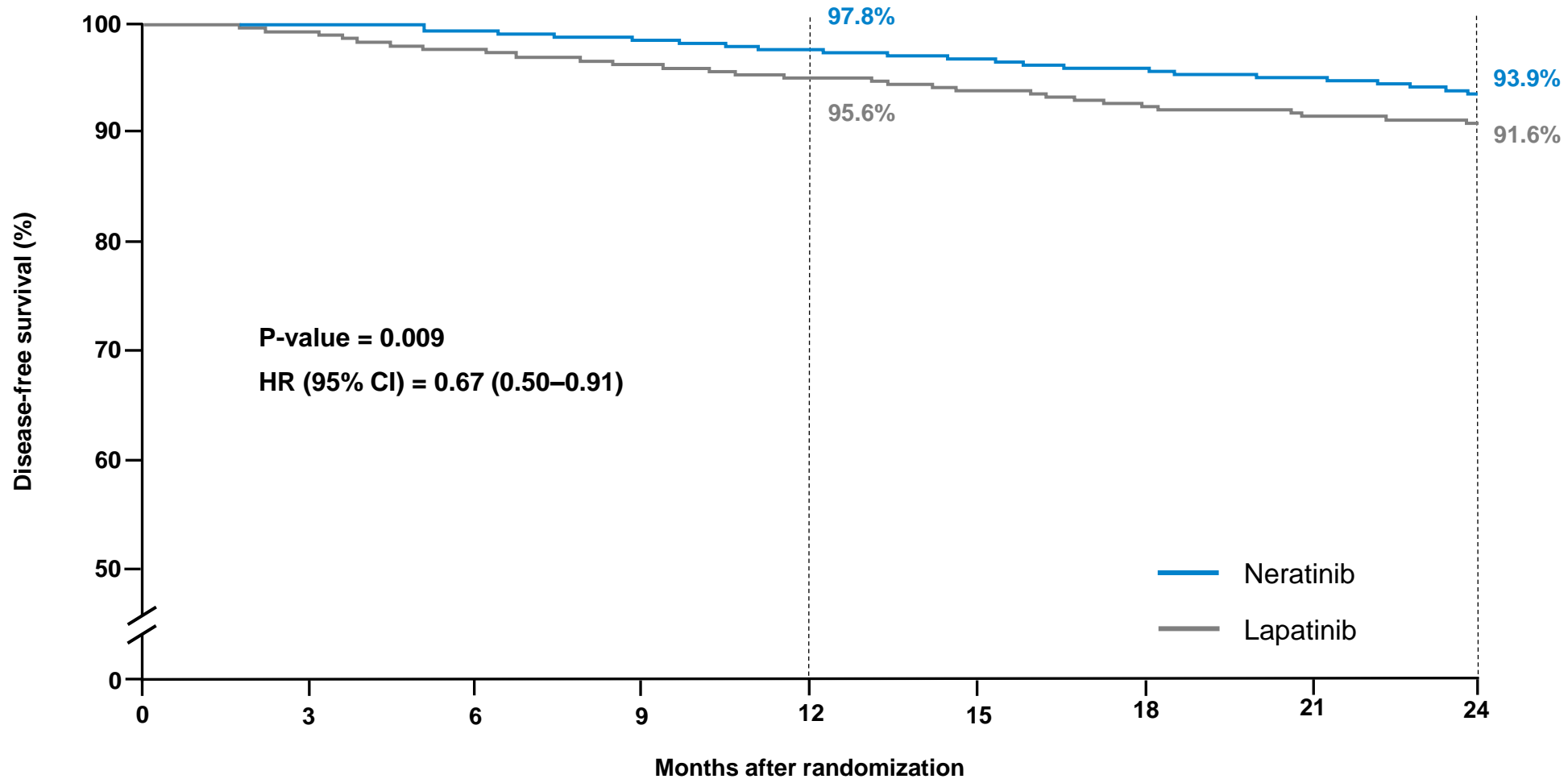


Primary endpoint: invasive disease-free survival (IDFS)

Secondary endpoints: disease-free survival including ductal carcinoma in-situ (DFS-DCIS), time to distant recurrence, incidence of CNS recurrence, overall survival

No loperamide prophylaxis used to prevent neratinib-related diarrhea

Kaplan-Meier Estimates of Disease-Free Survival ITT Population

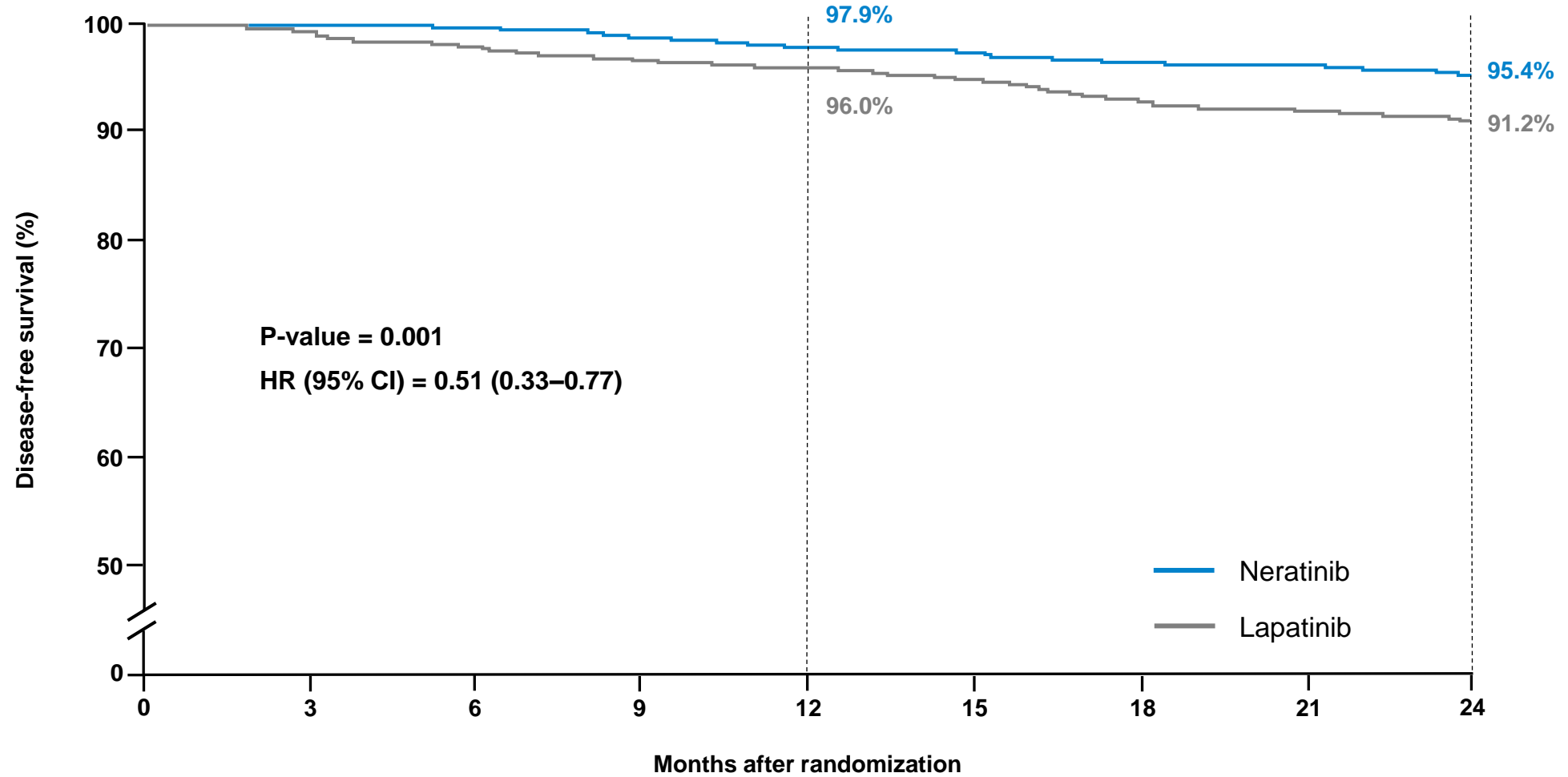


No. at risk

Neratinib	1420	1291	1260	1229	1189	1150	1108	1033	662
Placebo	1420	1367	1324	1292	1243	1209	1163	1090	704

Kaplan-Meier Estimates of DFS

HR+ Patients ITT Population

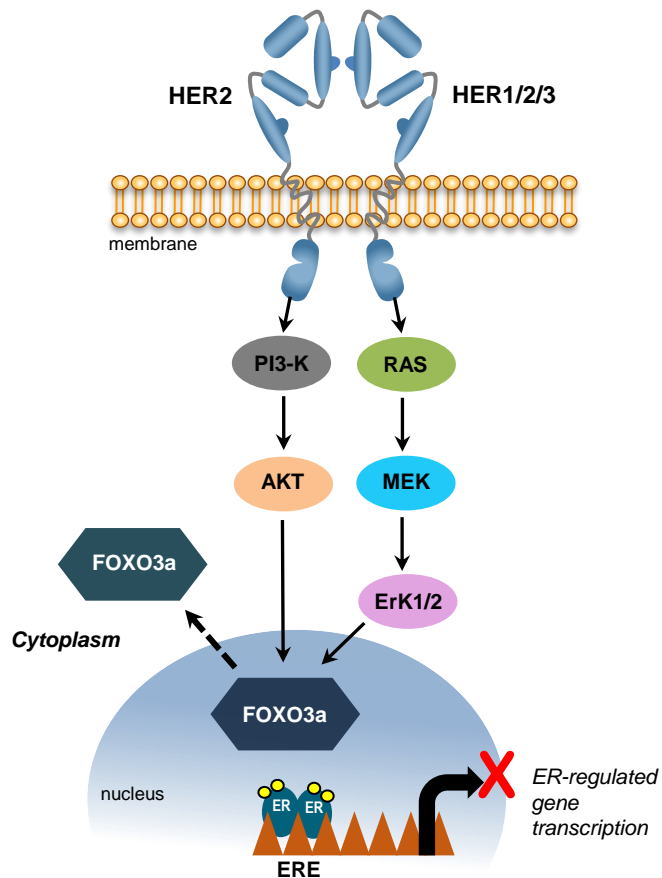


No. at risk

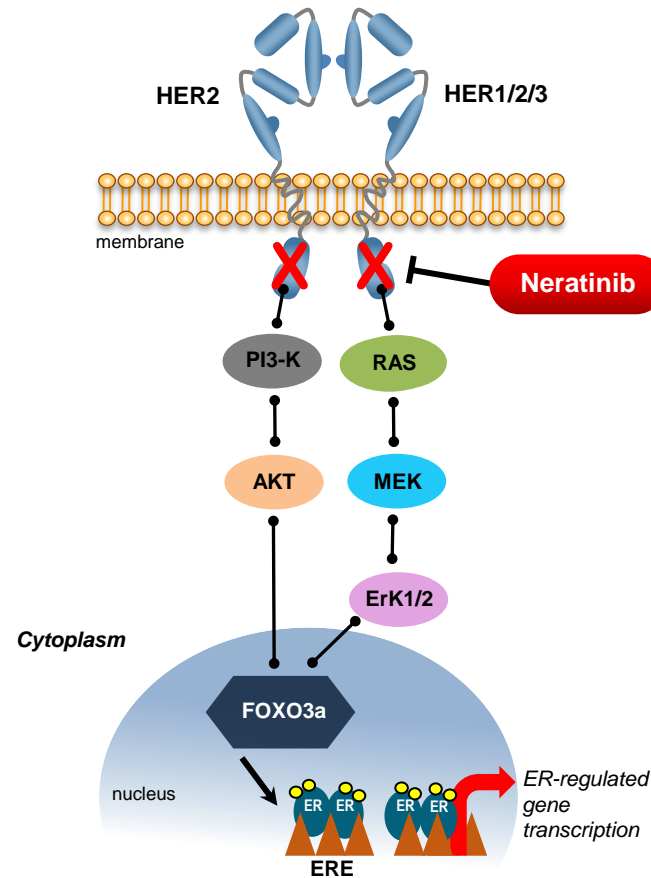
Neratinib	816	737	721	698	677	653	629	591	380
Placebo	815	784	761	741	716	699	669	622	401

Rationale for Efficacy of Neratinib in HR+ Subgroup

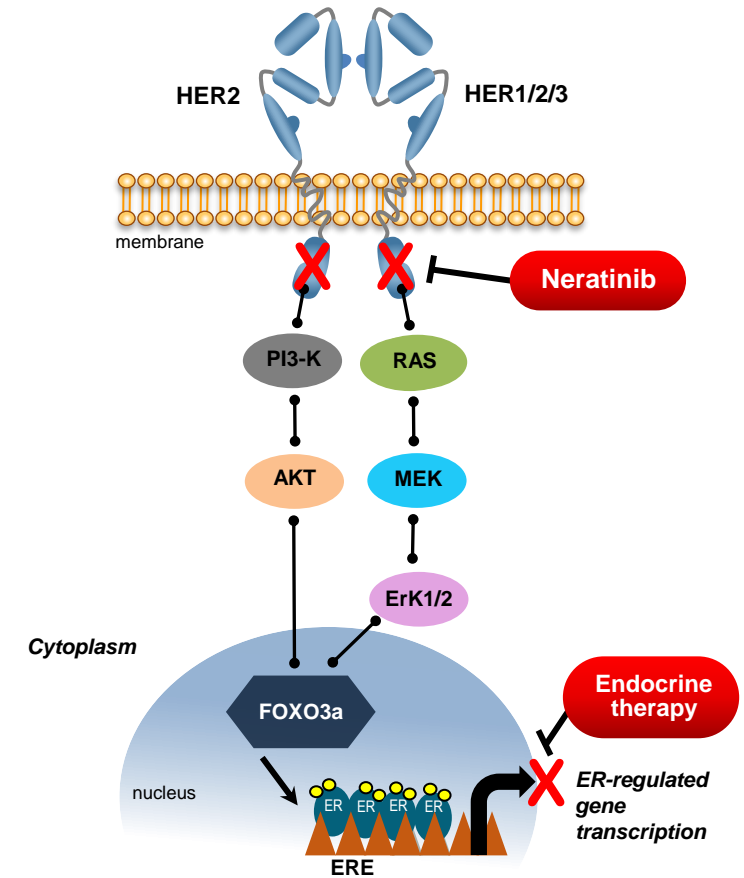
HER2 signalling decreases ER-regulated gene transcription



HER2 inhibition upregulates ER-regulated gene transcription

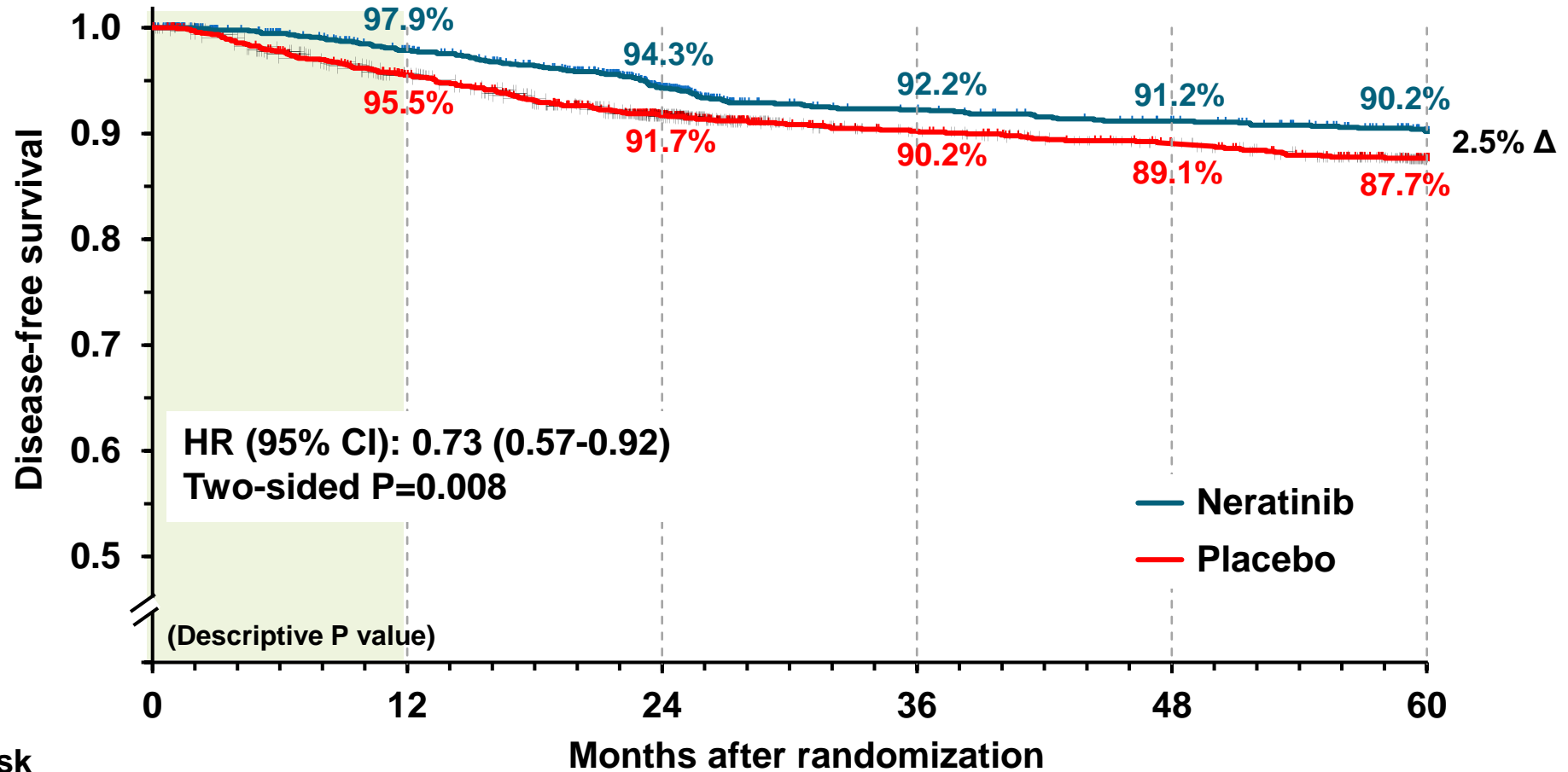


Inhibition of HER2 and ER is required for effective blockage in HER2+/HR+ tumors



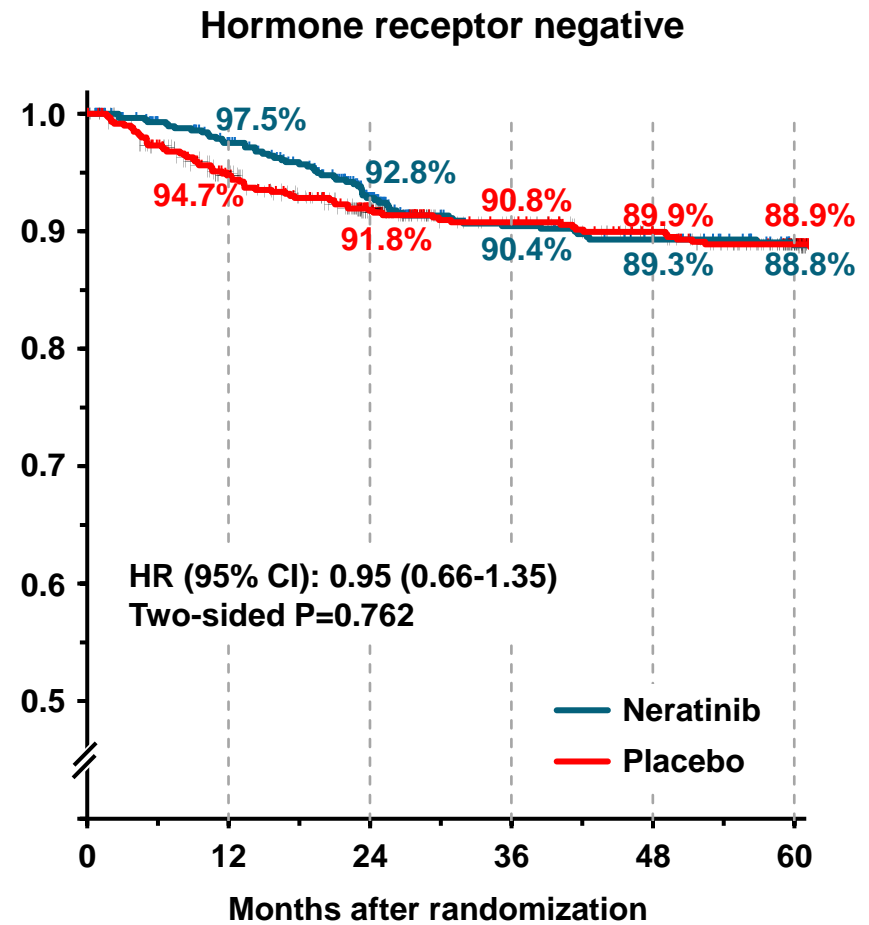
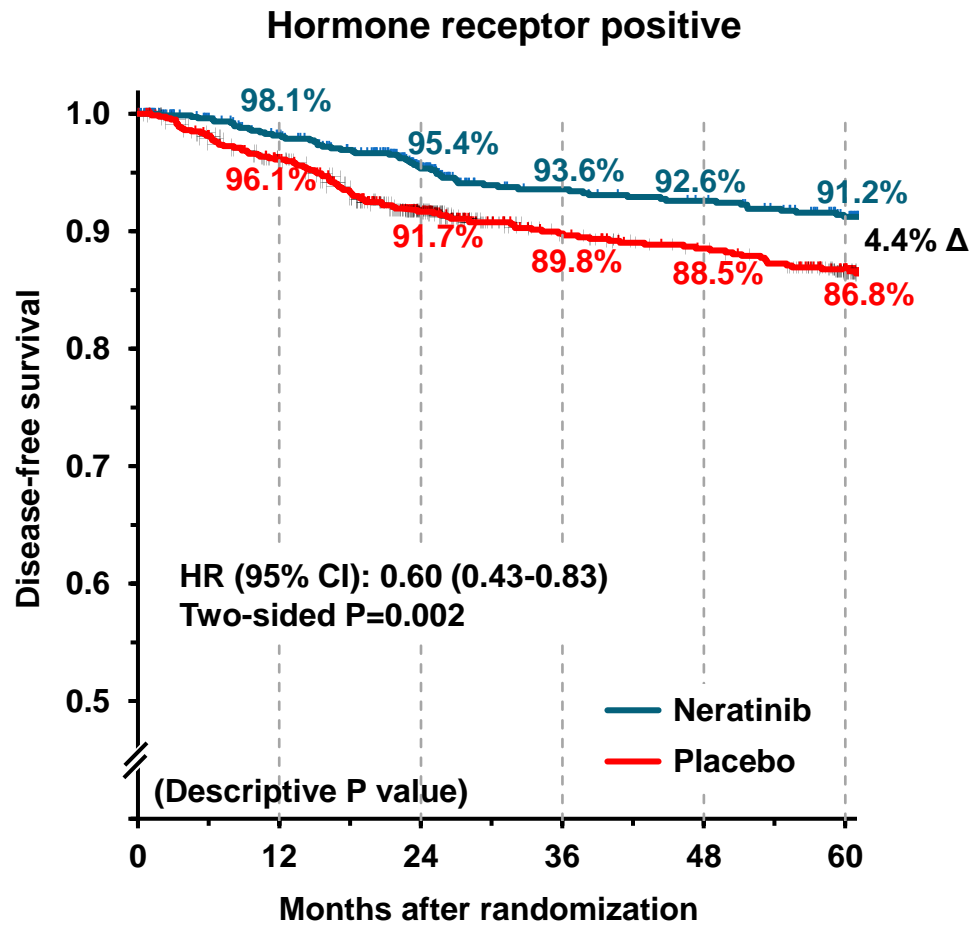
Adapted from: Paplomata et al. Cancer 2015

5-year Analysis Shows Durable iDFS Benefit ITT Population



At risk	0	12	24	36	48	60
— Neratinib	1420	1316	1272	1225	1106	978
— Placebo	1420	1354	1298	1248	1142	1029

iDFS by Hormone Receptor Status 5-Year Analysis



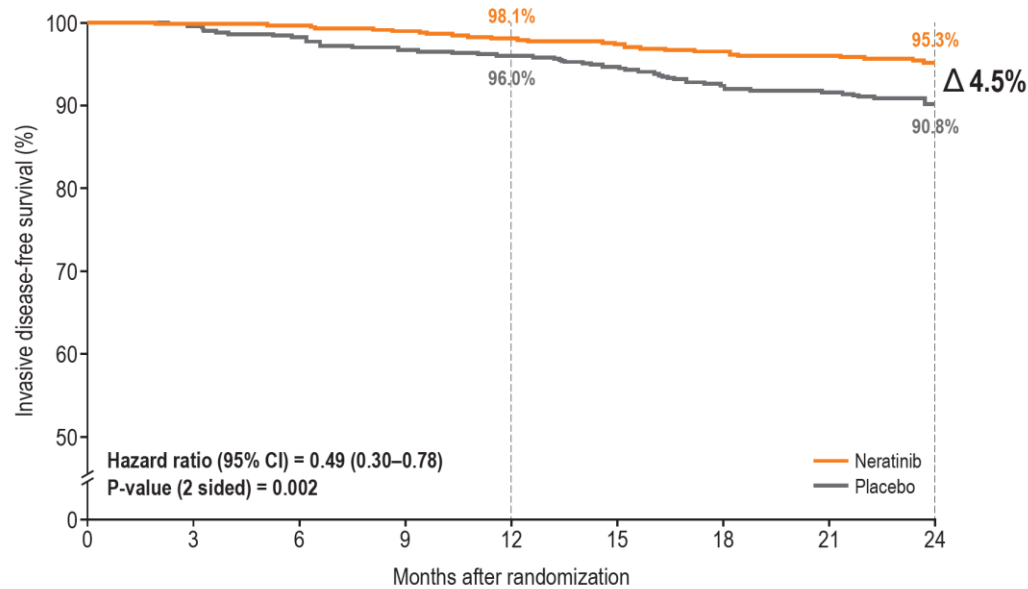
At risk

	0	12	24	36	48	60
Neratinib	816	757	731	705	642	571
Placebo	815	779	750	719	647	581

	0	12	24	36	48	60
Neratinib	604	559	541	520	464	407
Placebo	605	575	548	529	495	448

iDFS for HR+ Patients Completing Prior Trastuzumab ≤ 1 Year From Randomization (2-Year and 5-Year Analyses) EC Approved Indication

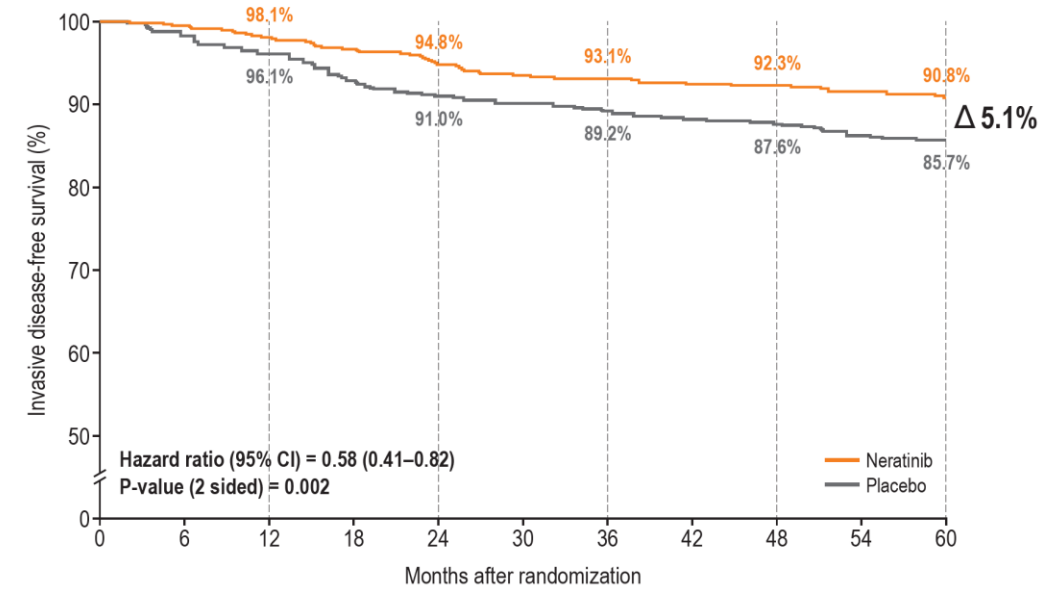
2-year (primary) analysis



No. at risk		HR+/ ≤ 1 year from trastuzumab							
Neratinib	670	605	593	577	559	538	516	485	307
Placebo	664	638	619	602	580	563	541	501	326

51% relative reduction in risk of recurrence

5-year analysis

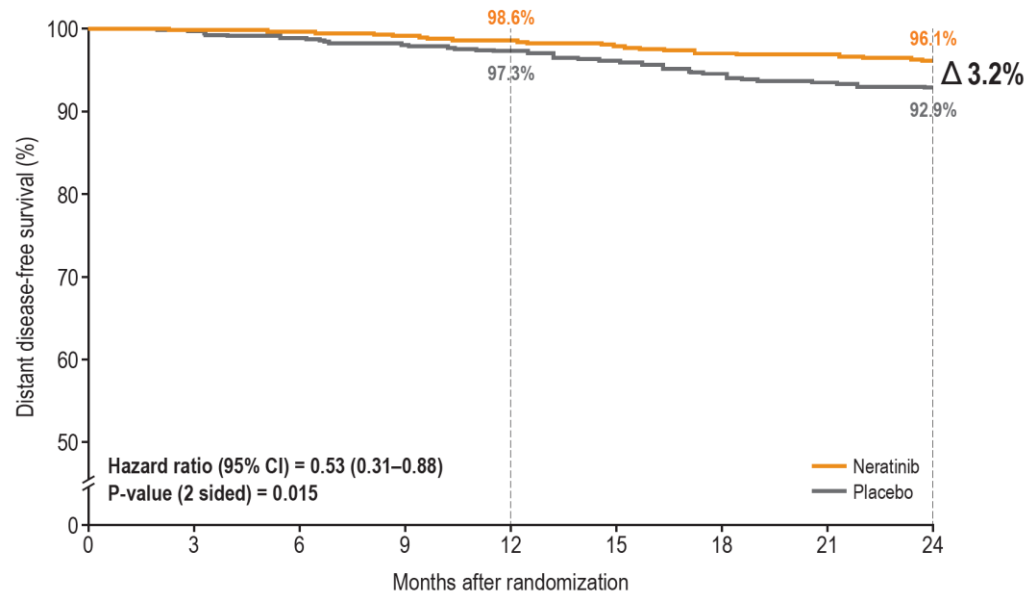


No. at risk		HR+/ ≤ 1 year from trastuzumab									
Neratinib	670	620	599	577	523	469	465	460	457	448	428
Placebo	664	634	609	583	535	481	471	462	458	450	433

42% relative reduction in risk of recurrence

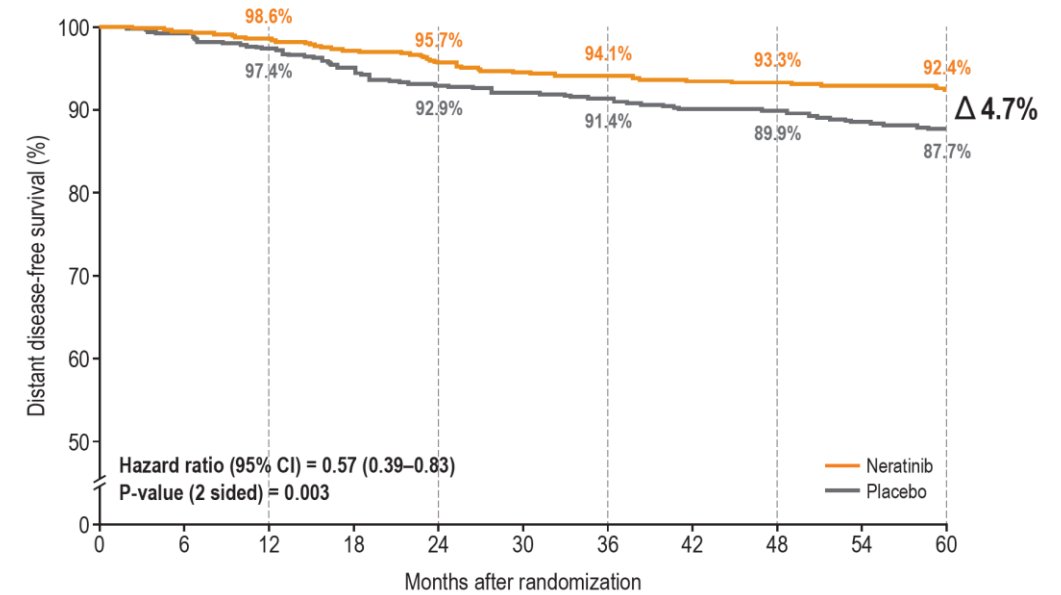
DDFS for HR+ Patients Completing Prior Trastuzumab ≤ 1 Year From Randomization (2-Year and 5-Year Analyses) EC Approved Indication

2-year (primary) analysis



No. at risk	HR+ ≤ 1 year from trastuzumab								
Neratinib	670	605	593	578	561	540	518	488	309
Placebo	664	638	624	609	587	572	551	511	336

5-year analysis



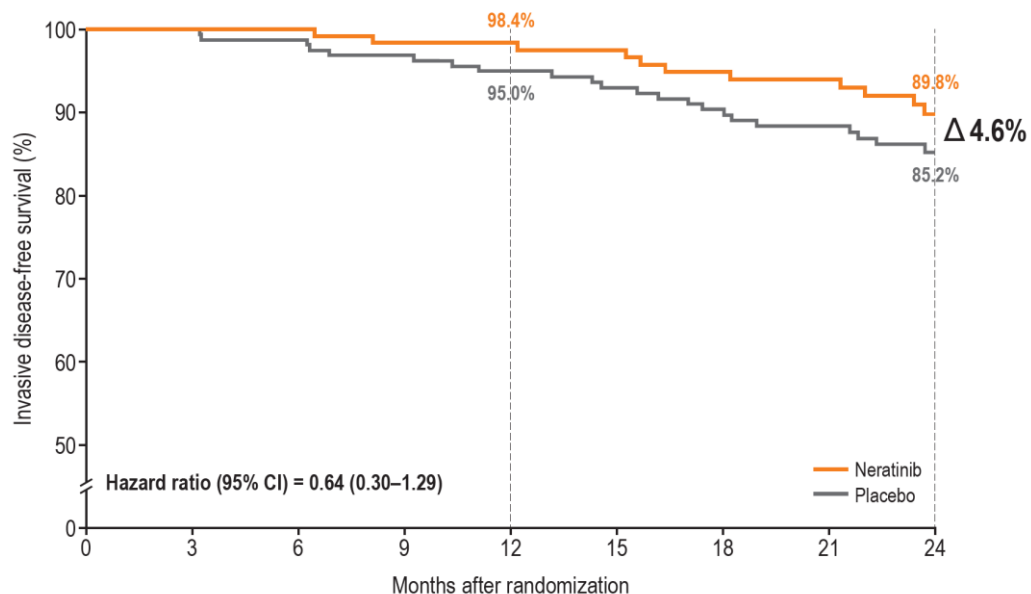
No. at risk	HR+ ≤ 1 year from trastuzumab										
Neratinib	670	620	602	580	526	473	469	464	461	454	434
Placebo	664	639	616	594	546	489	480	469	467	457	438

47% relative reduction in risk of recurrence

43% relative reduction in risk of recurrence

iDFS for HR+ Patients Completing Prior Trastuzumab ≤ 1 Year From Randomization (2-Year and 5-Year Analyses) Who Had Prior Neoadjuvant Therapy With No pCR

2-year (primary) analysis



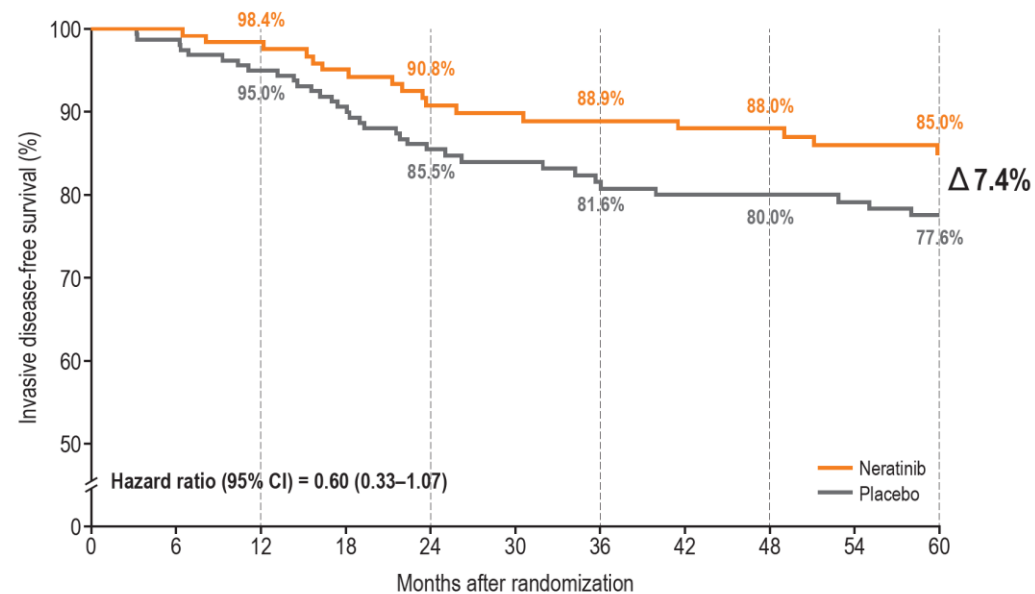
No. at risk

HR+/ ≤ 1 year from trastuzumab without pCR

	0	3	6	9	12	15	18	21	24
Neratinib	131	124	123	119	116	111	103	99	66
Placebo	164	161	157	153	145	142	135	124	71

36% relative reduction in risk of recurrence

5-year analysis



No. at risk

HR+/ ≤ 1 year from trastuzumab without pCR

	0	6	12	18	24	30	36	42	48	54	60
Neratinib	131	126	121	113	100	94	93	91	91	88	84
Placebo	164	159	151	143	125	107	103	99	99	98	94

40% relative reduction in risk of recurrence