Puma Biotechnology

39th Annual J.P. Morgan Healthcare Conference

January 2021

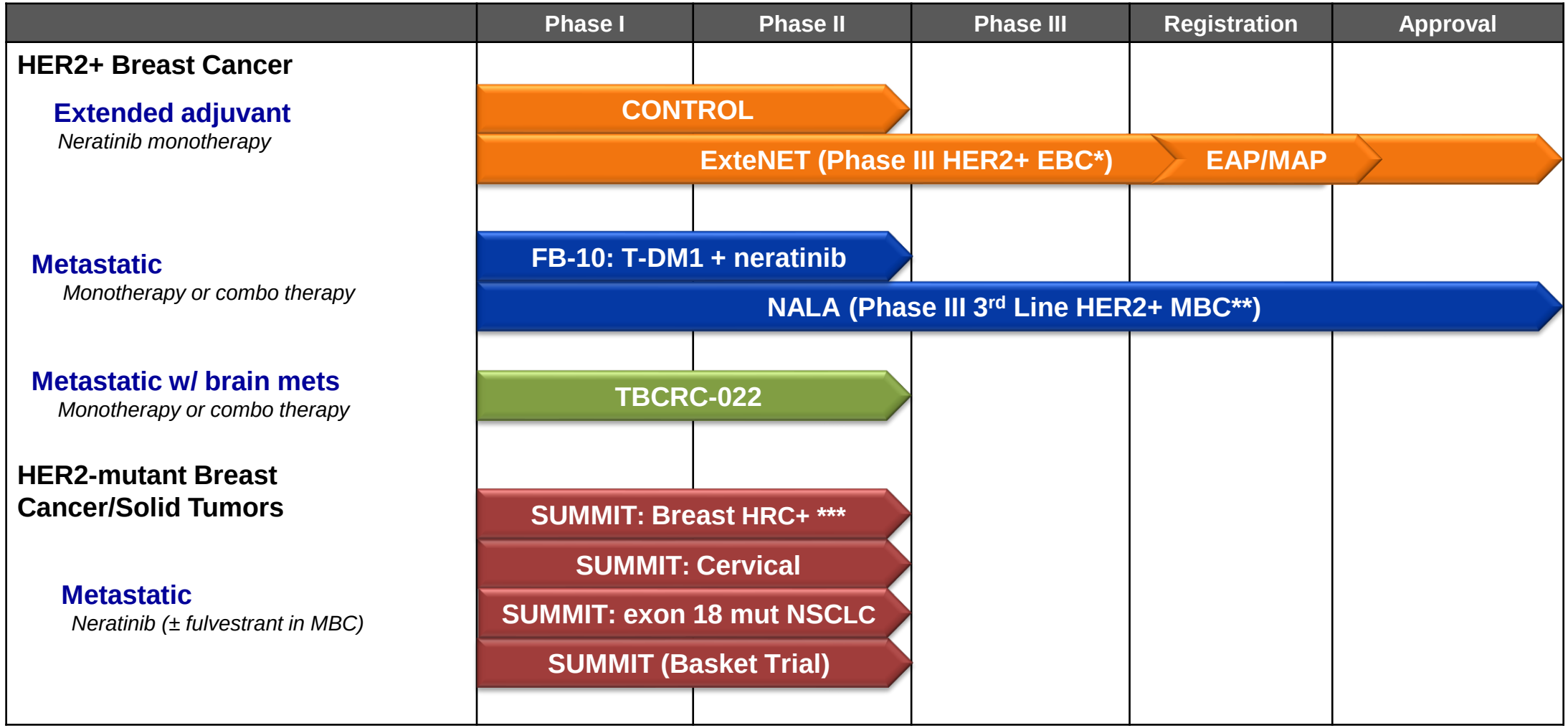
Forward-Looking Safe-Harbor Statement

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, 2019, Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, and subsequent reports. 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.

Puma Biotechnology

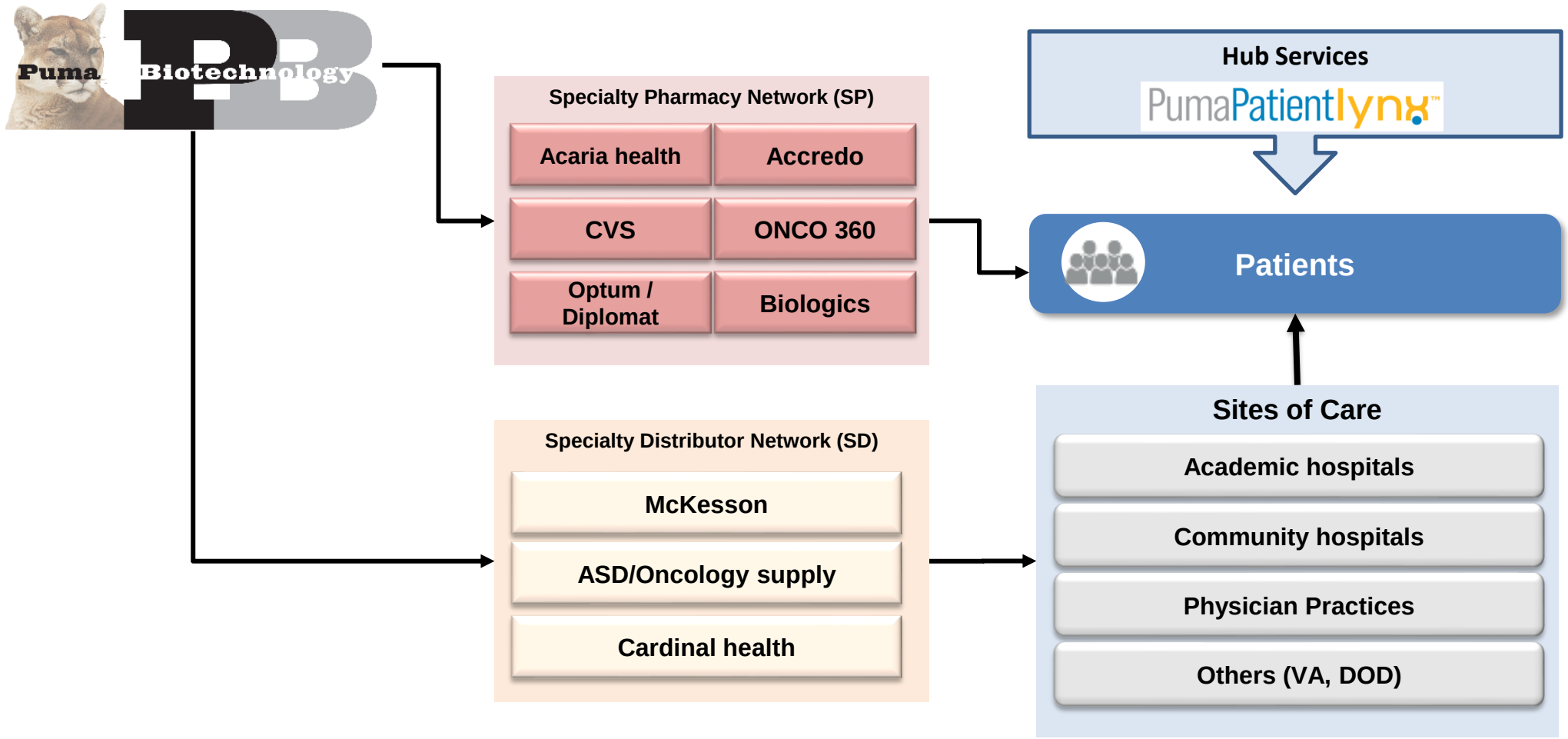
Product Pipeline

Neratinib across the breast cancer therapy spectrum

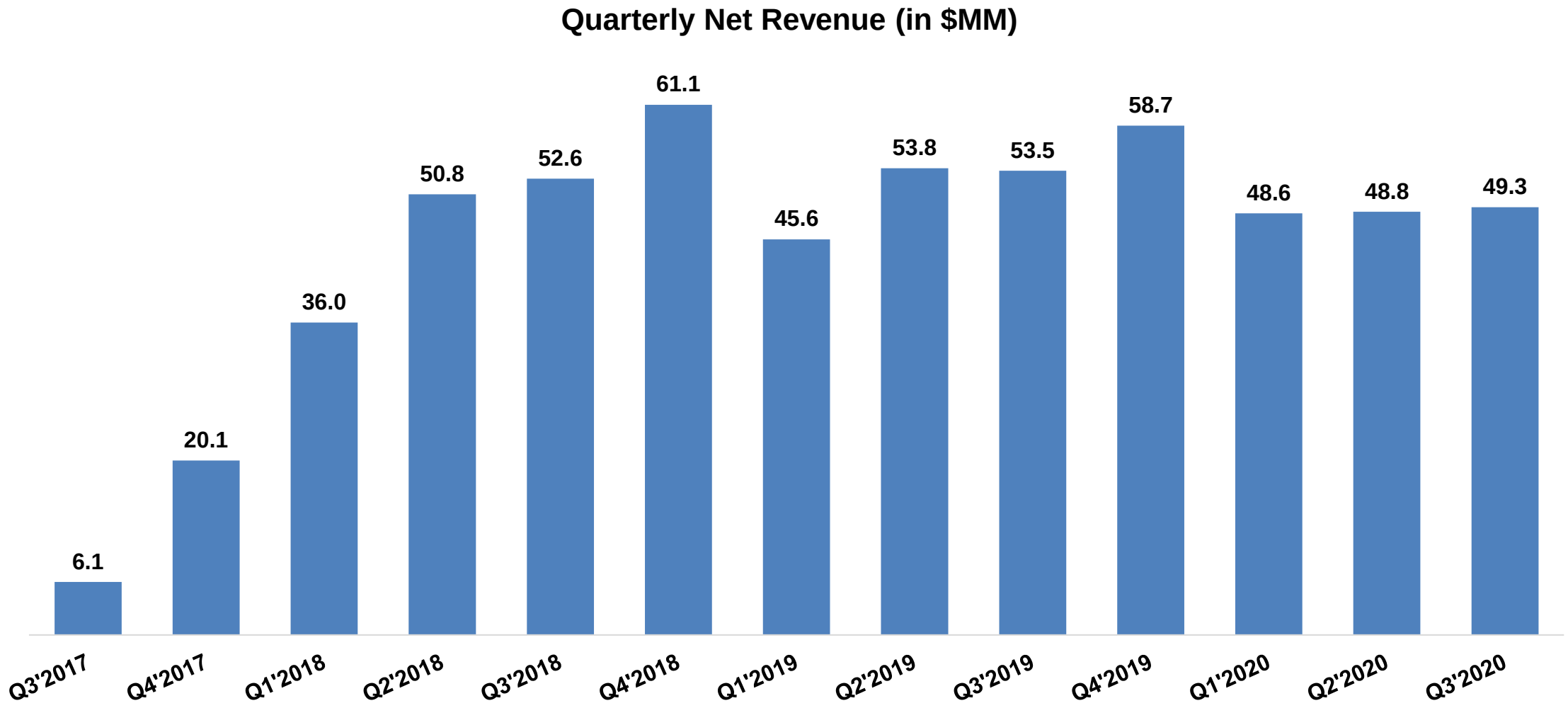


* EBC: Early breast cancer ** MBC: Metastatic breast cancer *** HRC+: Hormone receptor positive

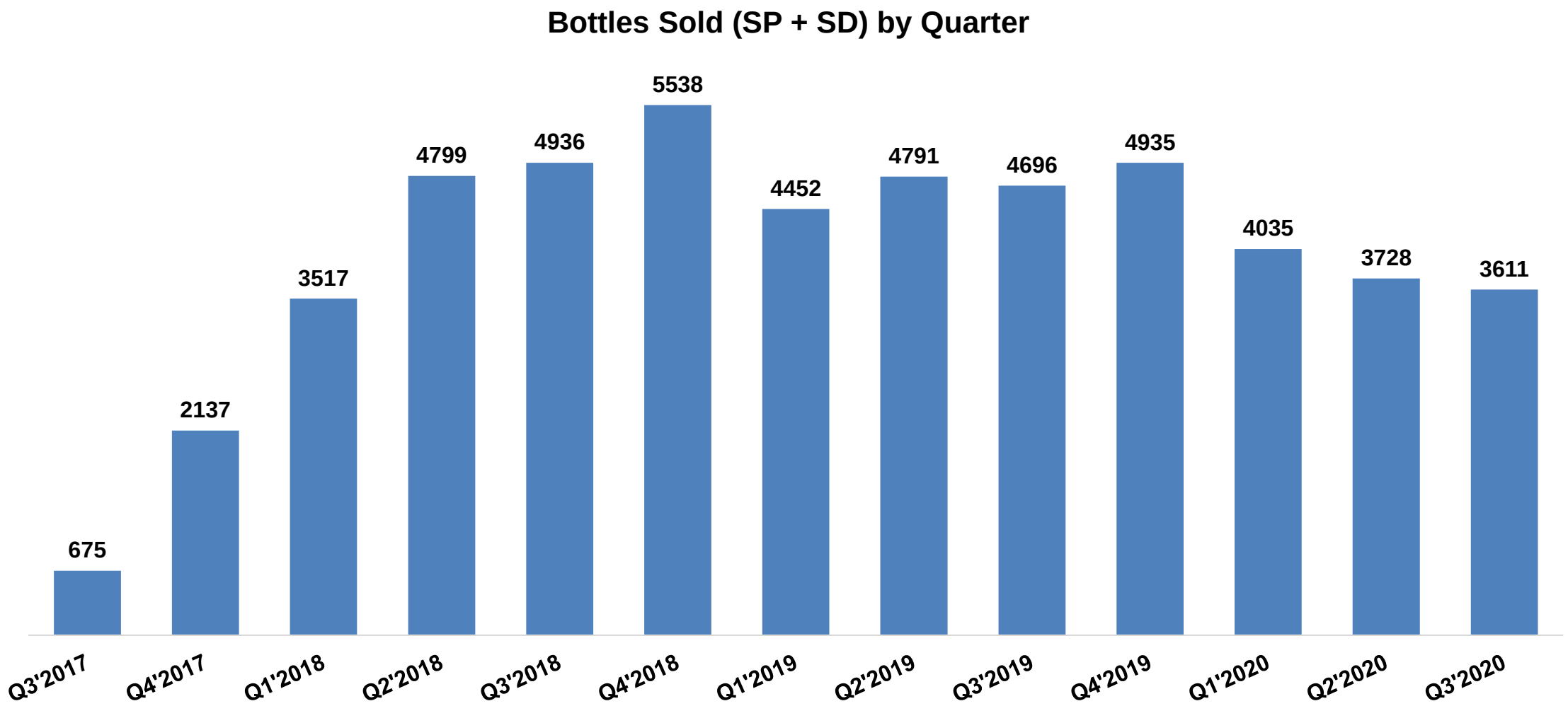
PUMA's Pharmacy and Distributor Network



~$49.3 Million Net NERLYNX Revenue in Q3’2020

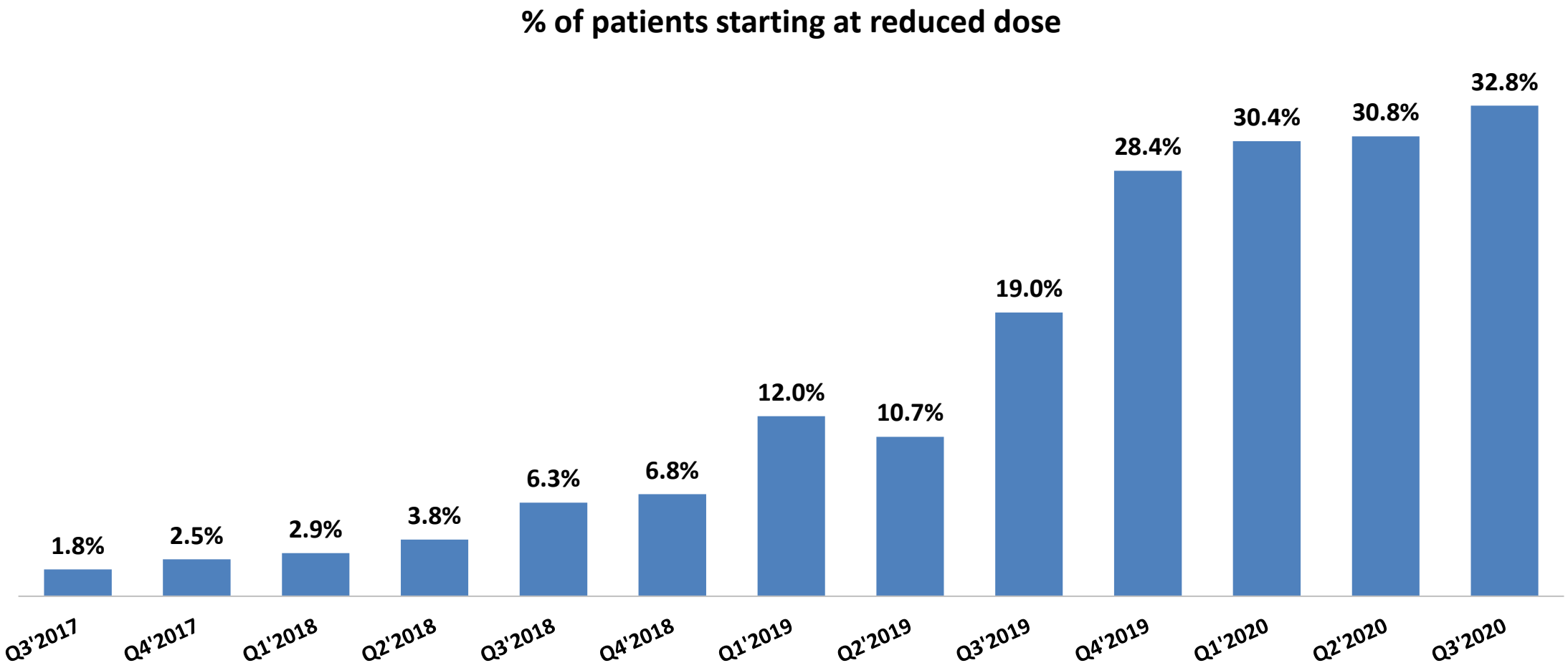


~3,600 Ex-factory Bottles were Sold in Q3’20



Includes Commercial SP and SD

~33% of Patients in Q3’20 Started at a Reduced Dose



Reduced dose defined as fewer than 6 pills per day

Rest of World Partnerships – Timelines

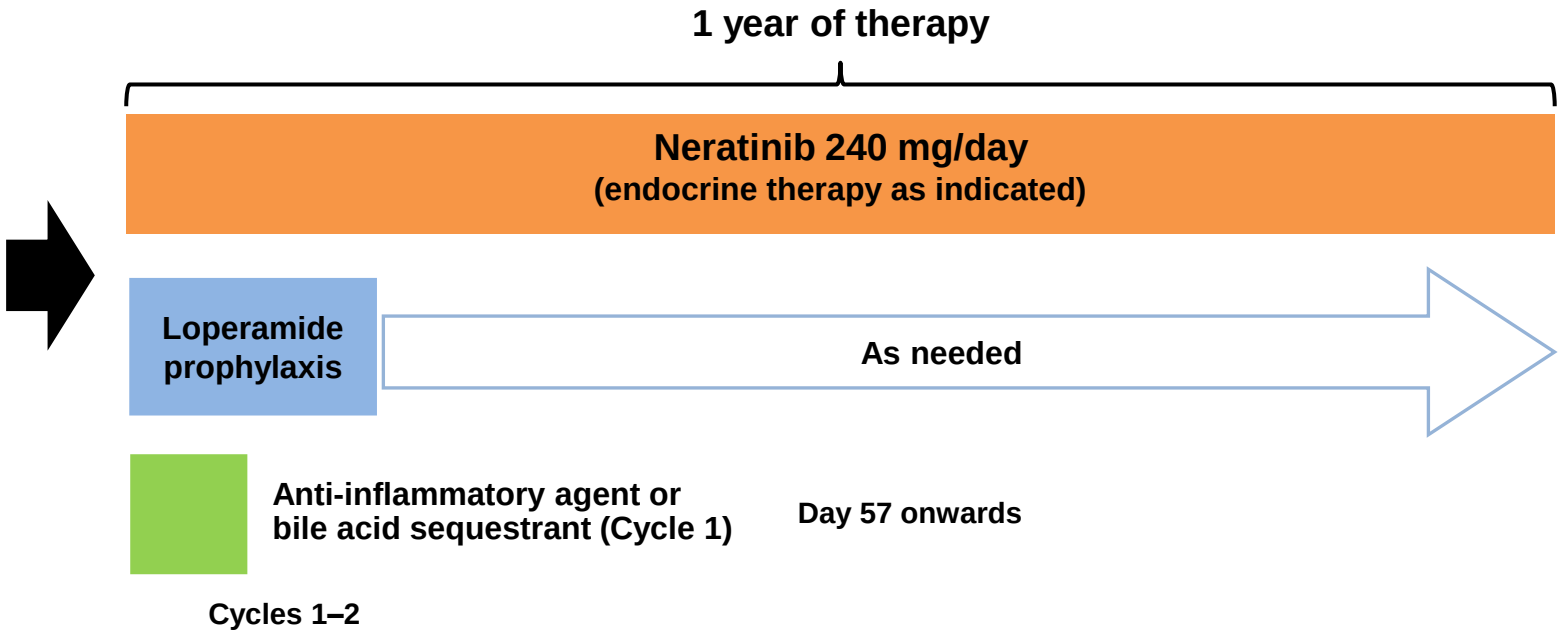
Region	Partner	Regulatory / Launch Milestones
Australia / SE Asia	Specialised Therapeutics	• March 2019 – Approved in Australia • December 2019 – Approved in Singapore • Q2/Q3 2020 – Approved in Brunei, Malaysia, New Zealand
Israel	MEDISON	• Q1 2020 – Launched • Q3 2020 – Approved in metastatic breast cancer
Canada	Knight	• July 2019 – Approved • September 2020 – metastatic sNDS accepted by HC
Greater China	CANbridge 北海康成	• November 2019 – Approved in Hong Kong • April 2020 – Approved in China • August 2020 – Approved in Taiwan
Latin America	PINT PHARMA	• Q1 2020 – Argentina Launched • Q2 2020 – Approved in Chile • Q3 2020 – Approved in Ecuador • 2021 – Expected approvals in Brazil, Colombia, Mexico, Peru
Europe Middle East North and West Africa South Africa Turkey	Pierre Fabre	**Launch Timelines** • Q4 2019 – Germany Launched • Q4 2019 – United Kingdom Launched • Q4 2019 – Austria Launched • Q1 2020 – Sweden Launched • Q1 2020 – Approved in Switzerland • Q4 2020 – Planned launch in Finland
South Korea	BIXINK	• 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 ± an investigational agent

HER2+ early BC

- Received up to 1 year of adjuvant trastuzumab
- Stage I–3c
- HR (ER/PR) +/–

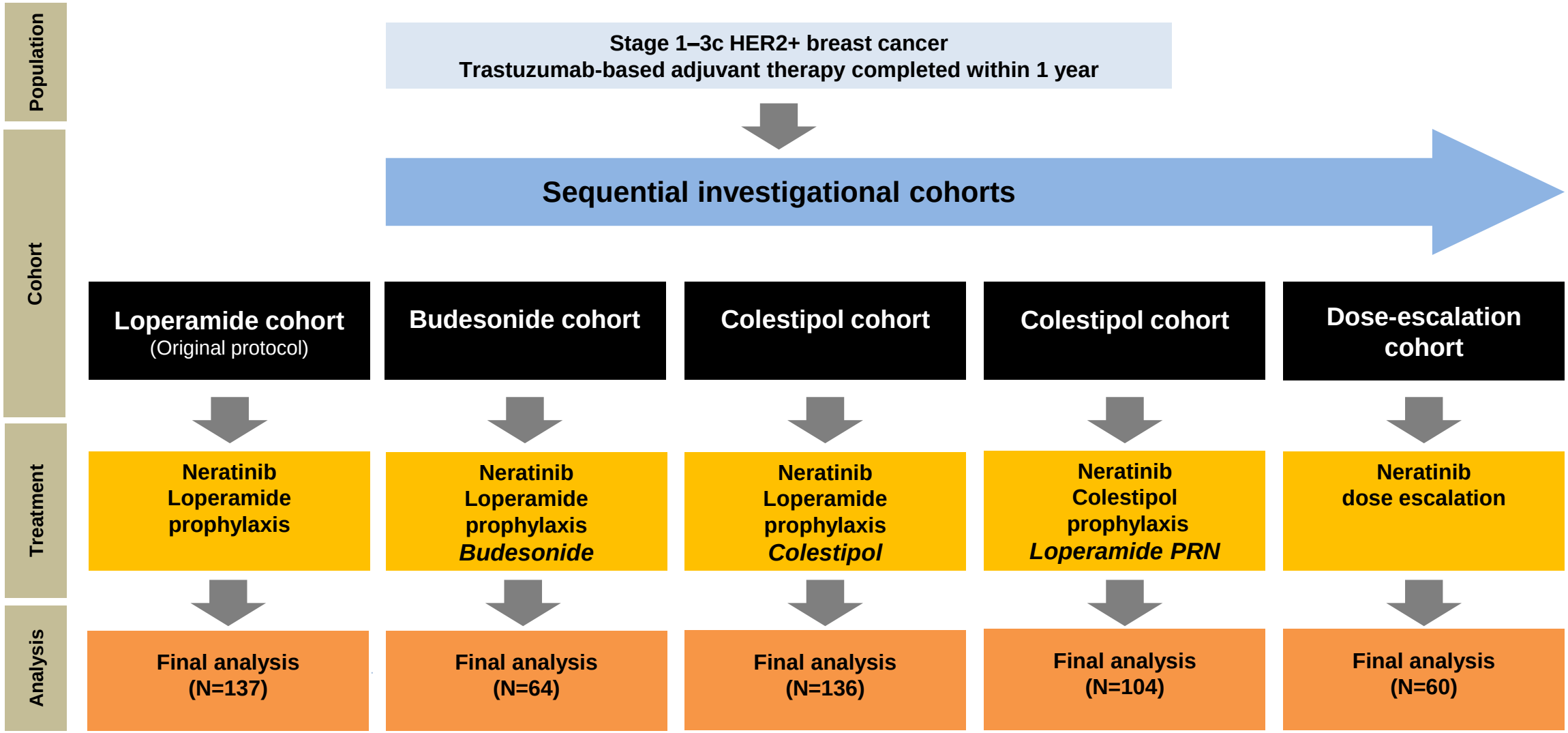


STUDY ENDPOINTS

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

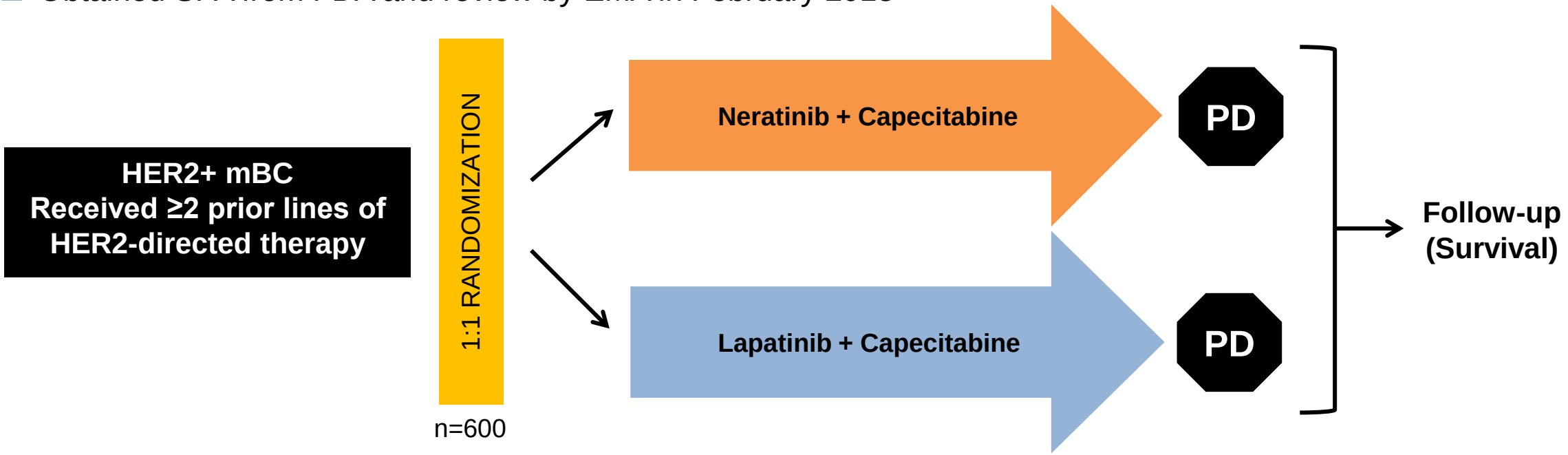
NERLYNX® Extended Adjuvant HER2+ Breast Cancer Market Size

- Approximately 28,300 patients (US) with early stage HER2+ breast cancer treated with adjuvant treatment[1]
- Approximately 37,000 patients (EU) with early stage HER2+ breast cancer treated with adjuvant treatment[1]
  - Approximately 65–70% of patients have HR+ disease

[1]Roche 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



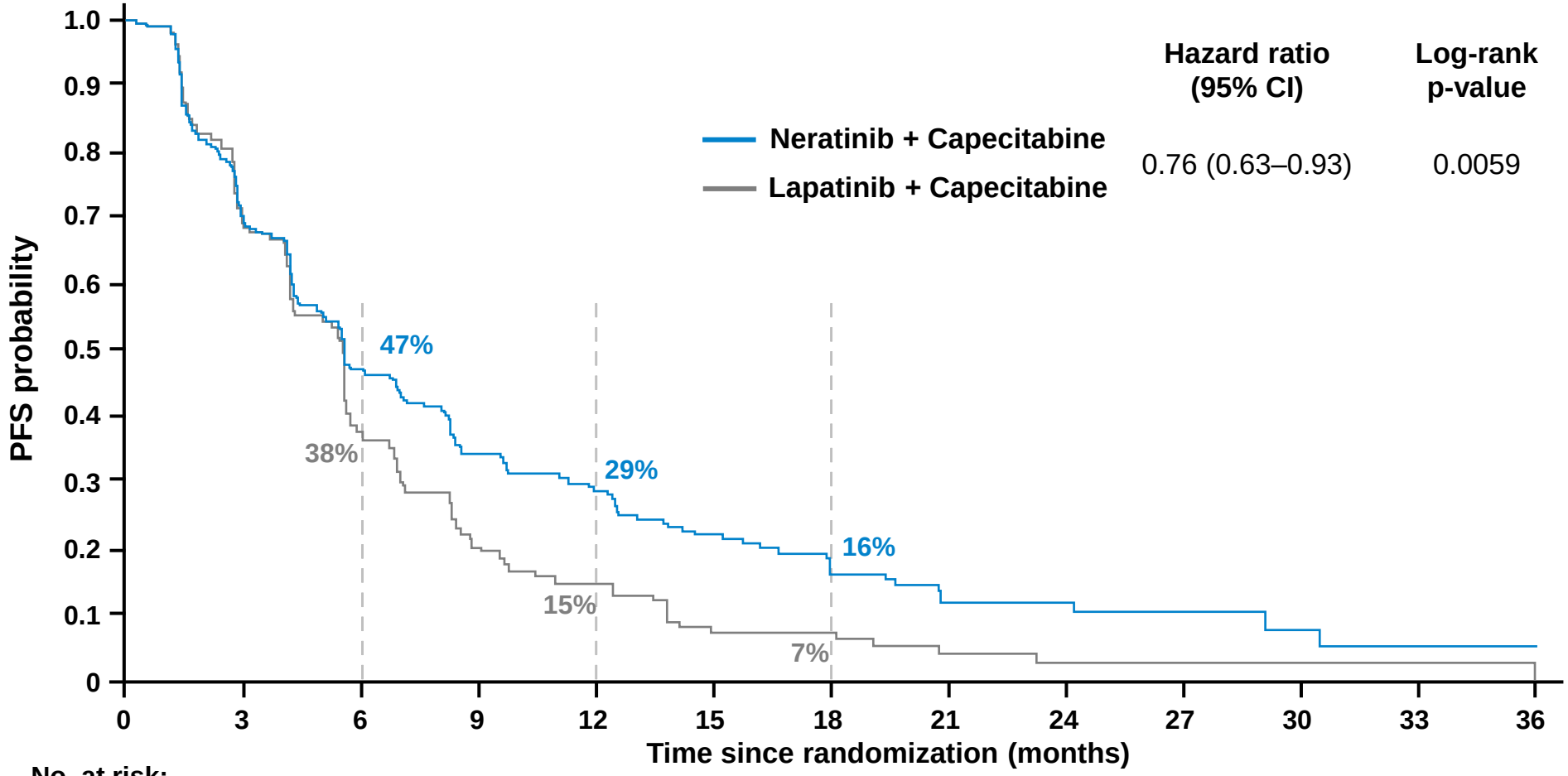
STUDY OBJECTIVES

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

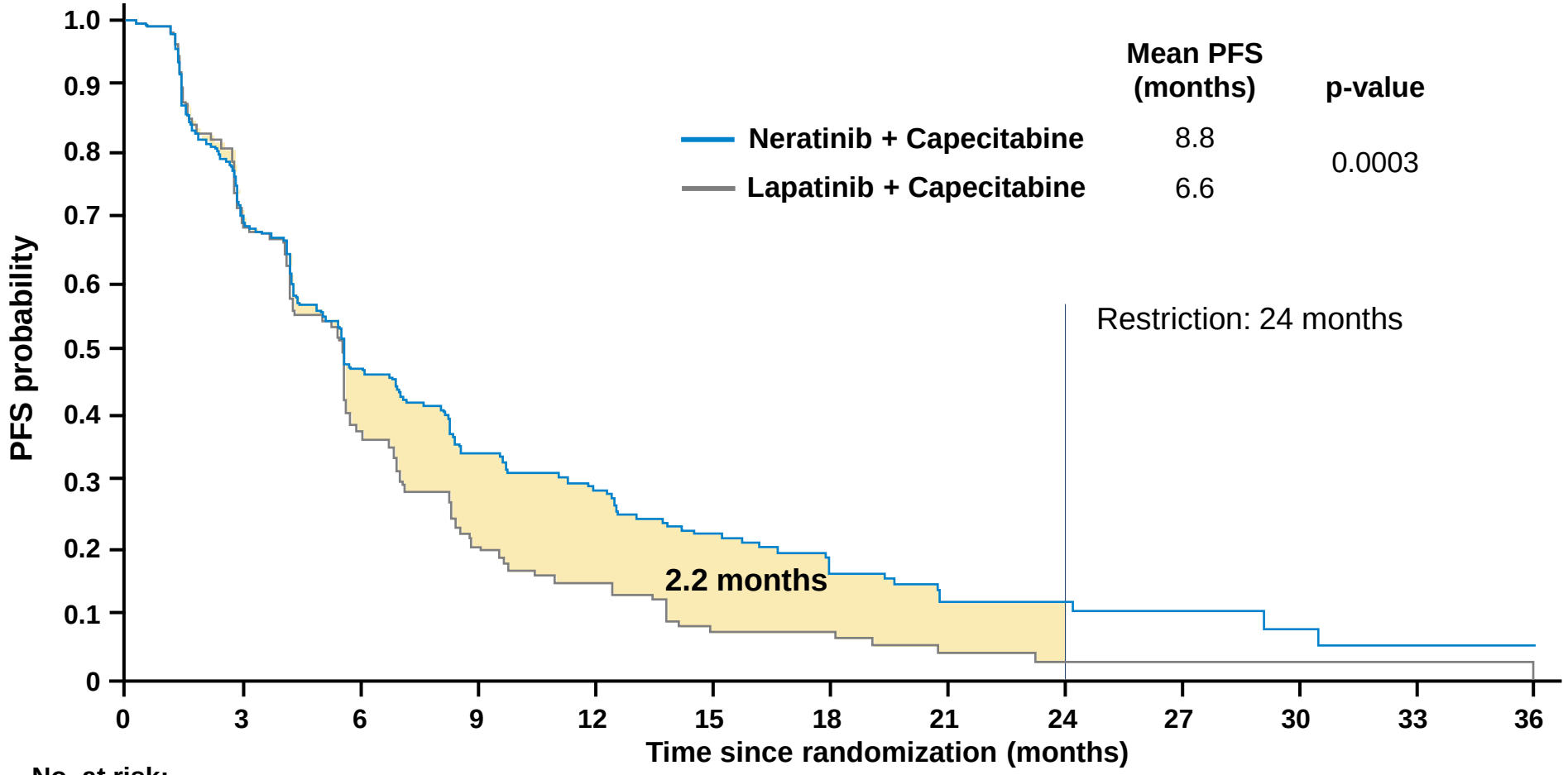
Centrally Confirmed PFS (co-primary endpoint)



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

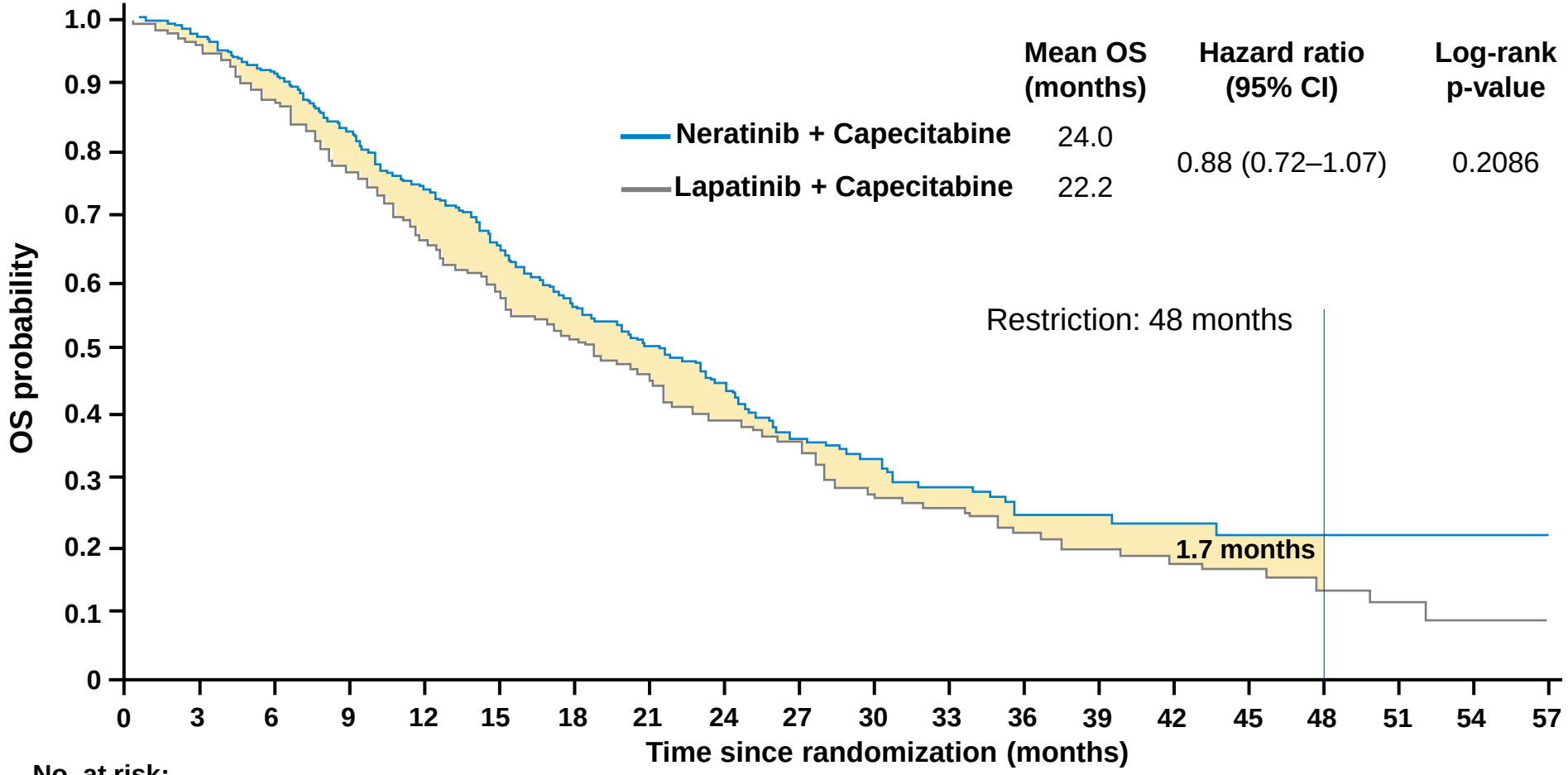
Prespecified restricted means analysis – PFS



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

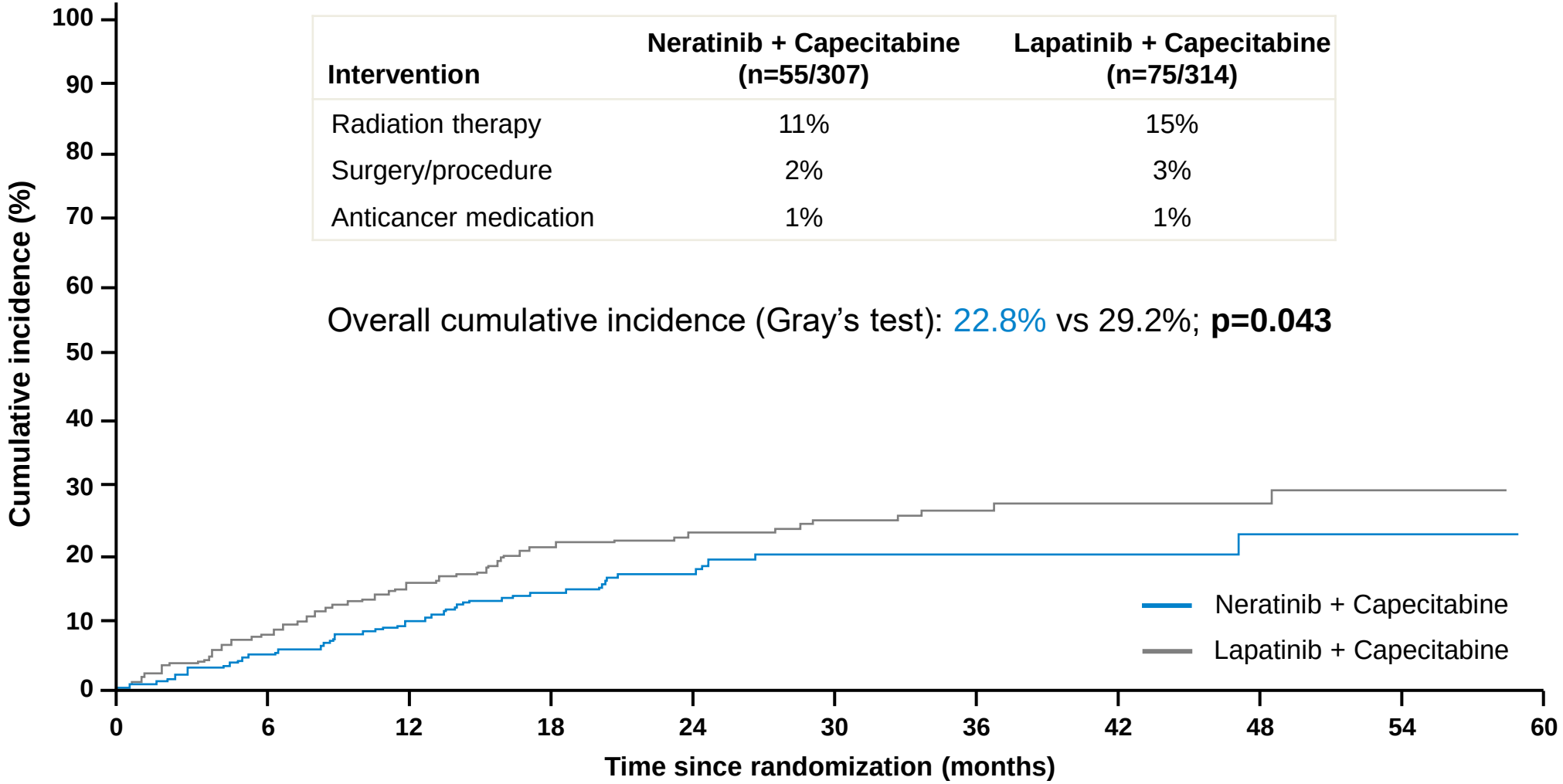
Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

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

Time to intervention for CNS metastases

Intervention	Neratinib + Capecitabine (n=55/307)	Lapatinib + Capecitabine (n=75/314)
Radiation therapy	11%	15%
Surgery/procedure	2%	3%
Anticancer medication	1%	1%

Overall cumulative incidence (Gray's test): 22.8% vs 29.2%; **p=0.043**



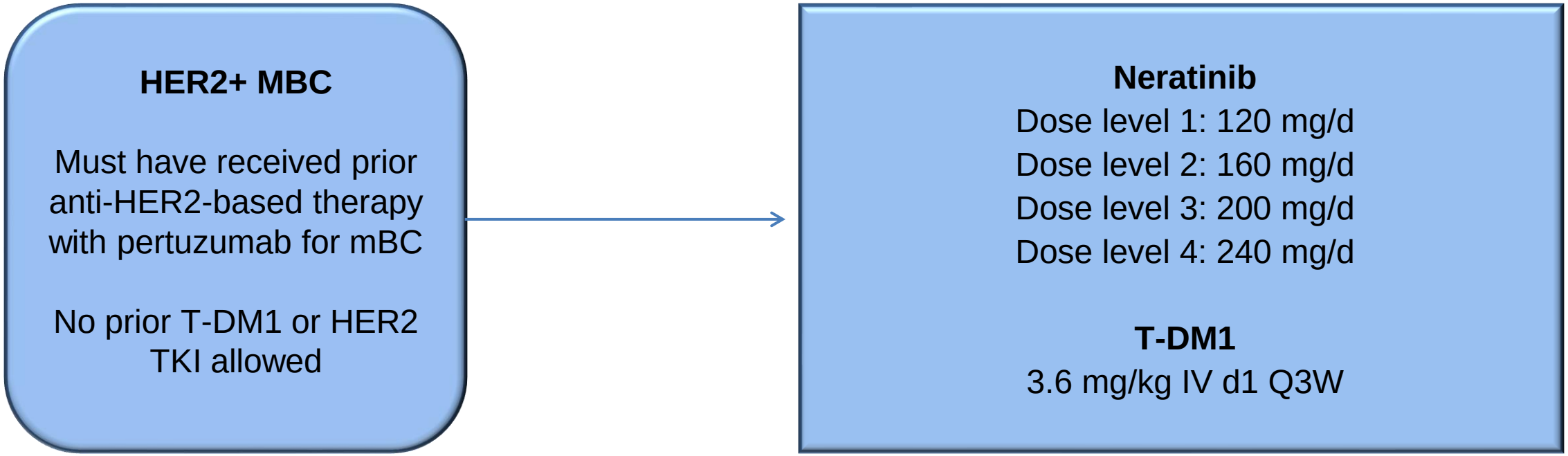
Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

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 cancer[1]

[1]Roche epidemiology slides 09/18

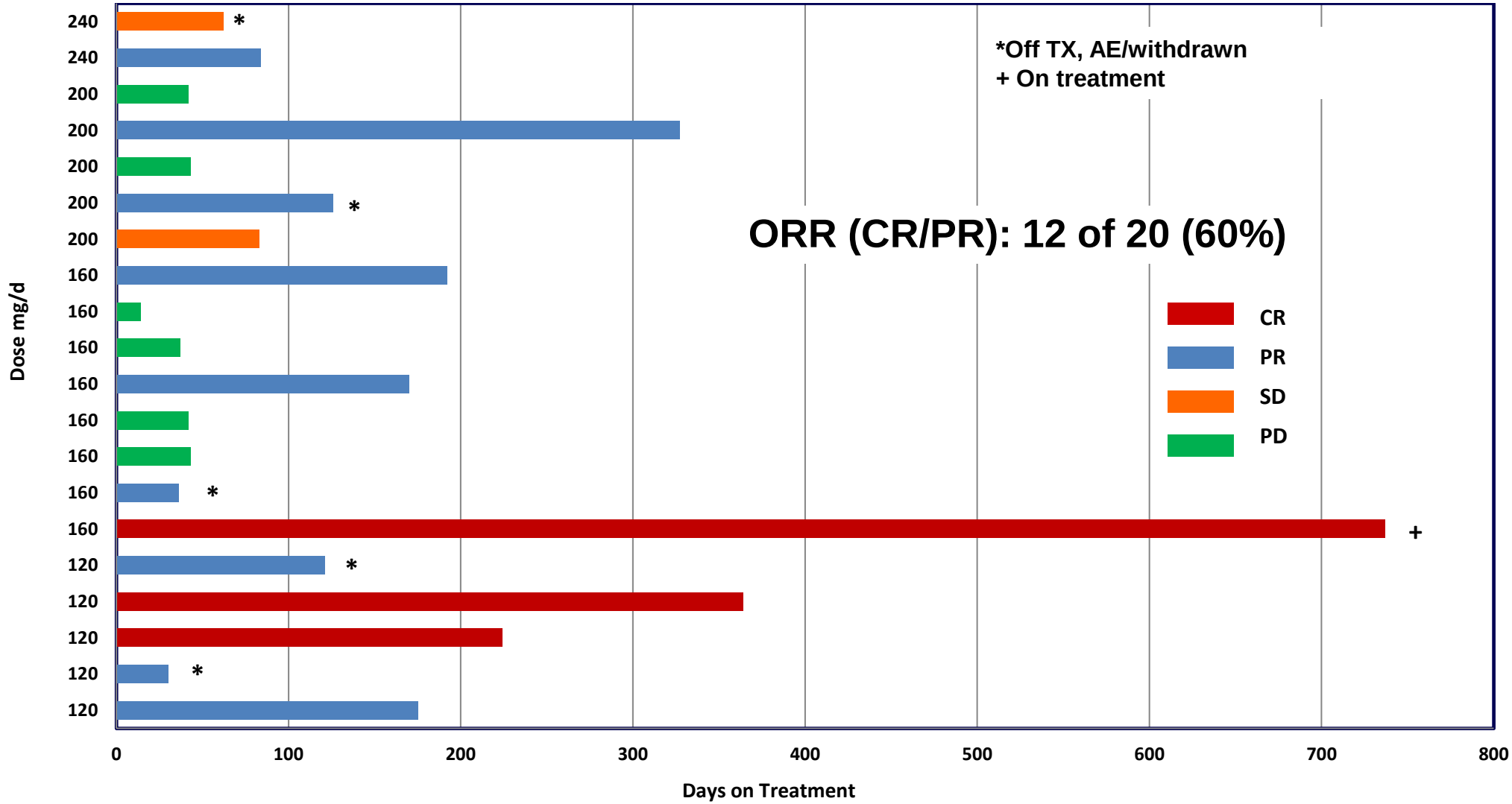
FB-10 – Phase I/II Trial of Kadcyla (T-DM1) + Neratinib



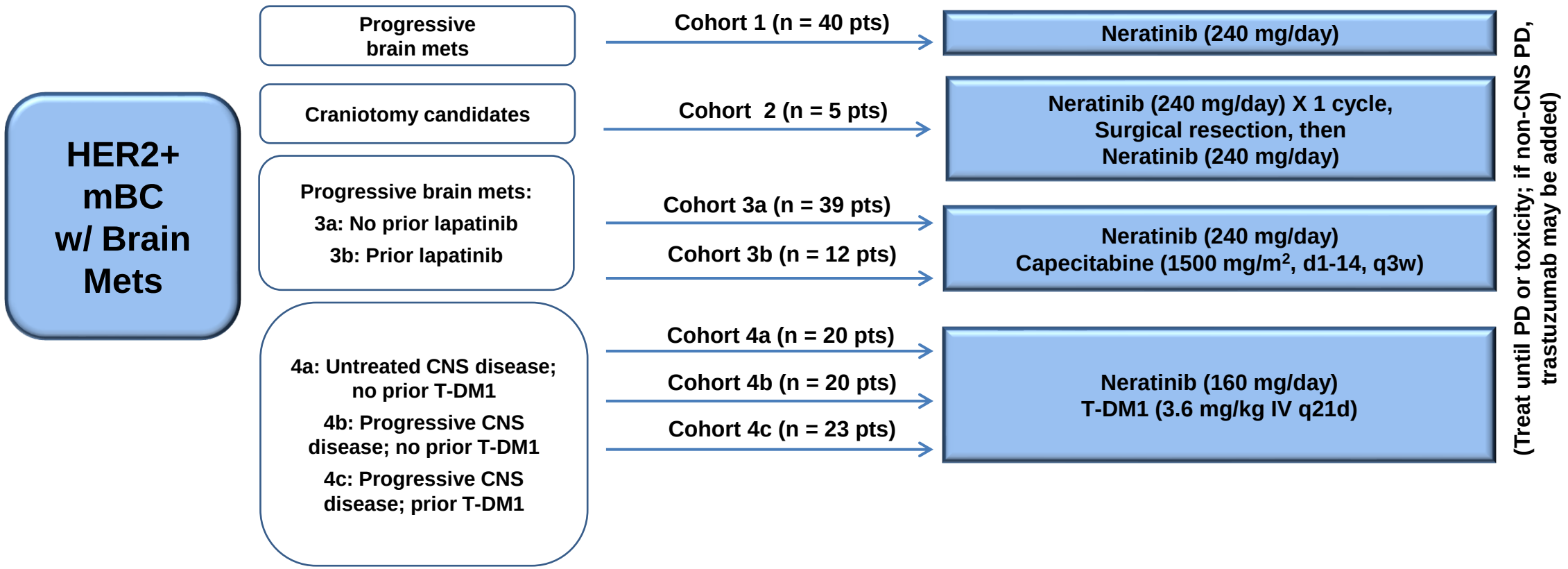
Primary endpoint: Phase I: Recommended dose of neratinib when given with T-DM1; Phase 2: Objective response rate (CR/PR)

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

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



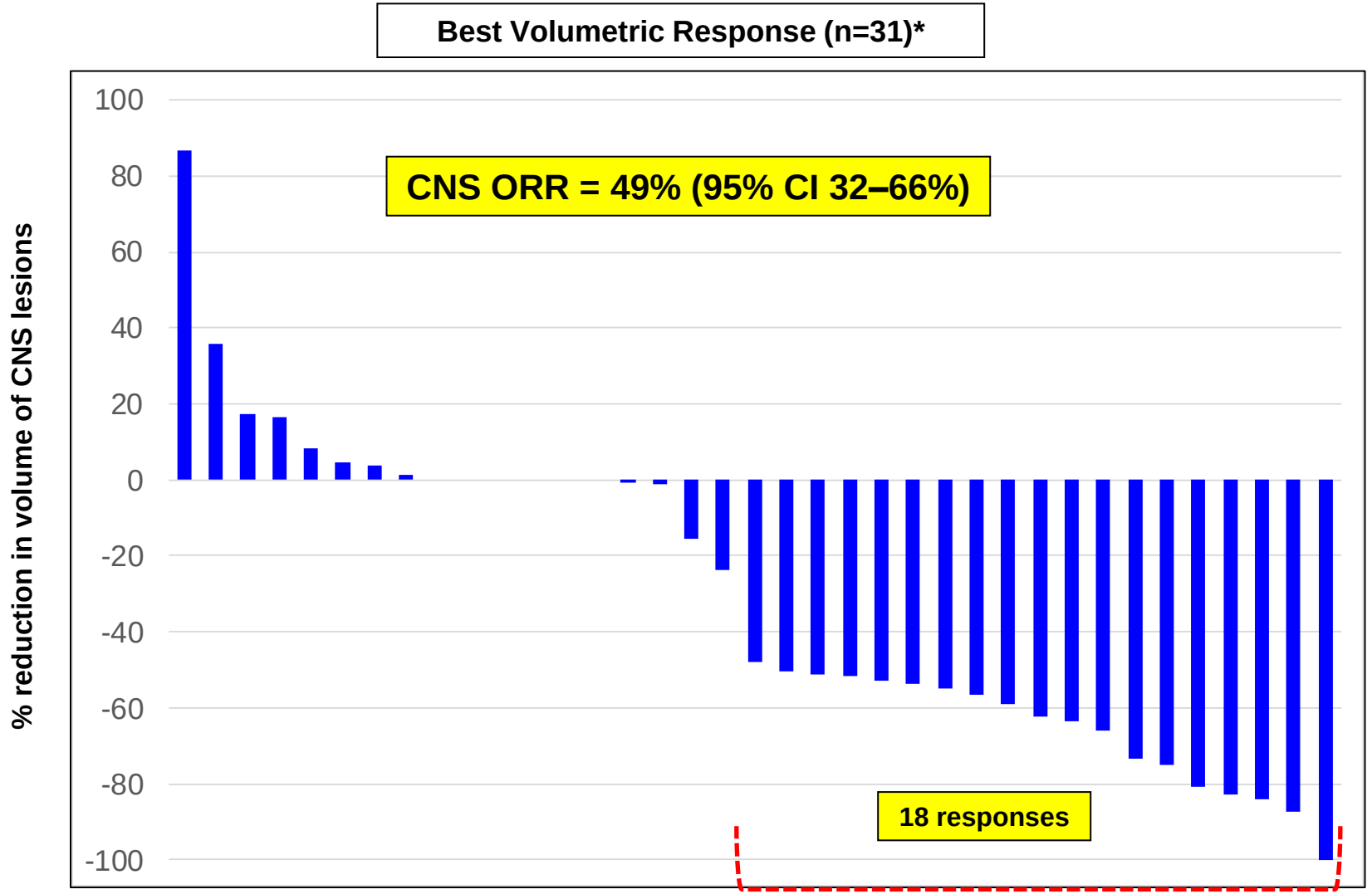
TBCRC 022: Phase II Trial of HKI-272 (Neratinib) + Capecitabine for Patients with HER2+ Breast Cancer and Brain Metastases



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



Neratinib Recently Included as a Treatment Option for Recurrent Breast Cancer CNS Metastases By NCCN® Guidelines[1]

Guidelines updated March 2020

Category 2A: Neratinib + Capecitabine

TBCRC 022[2]

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

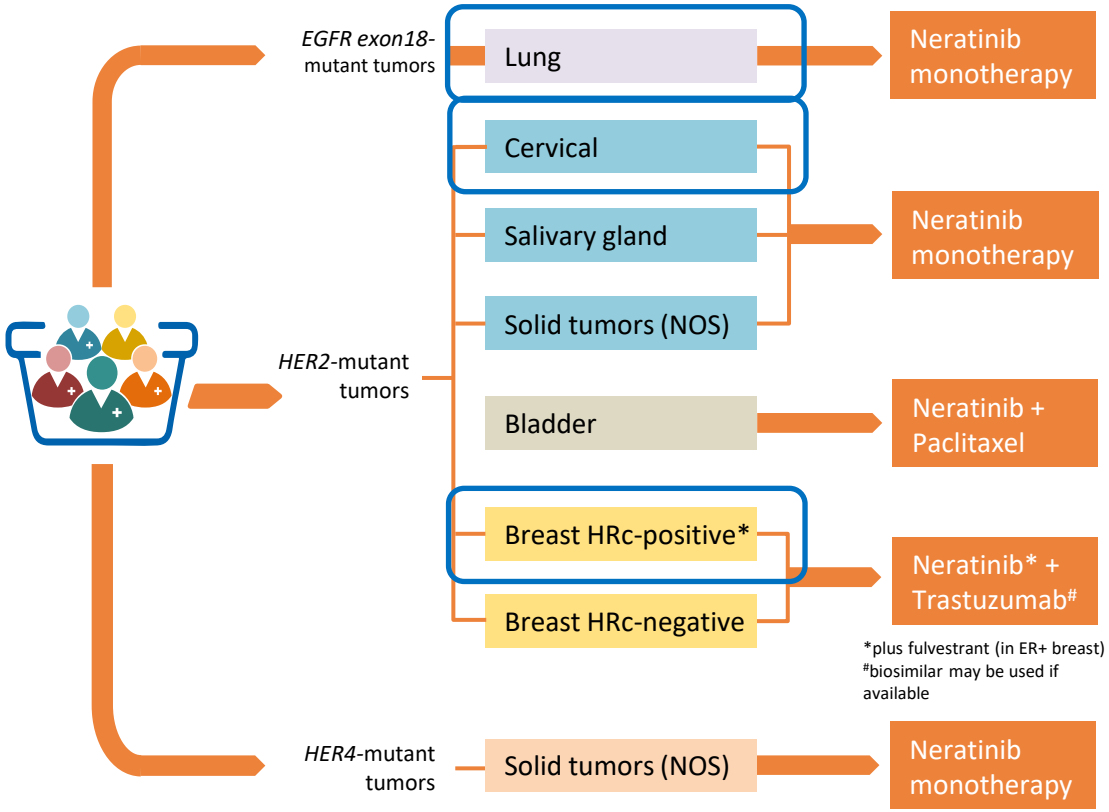
Category 2B: Neratinib + Paclitaxel

NEfERT-T[3,4]

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

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

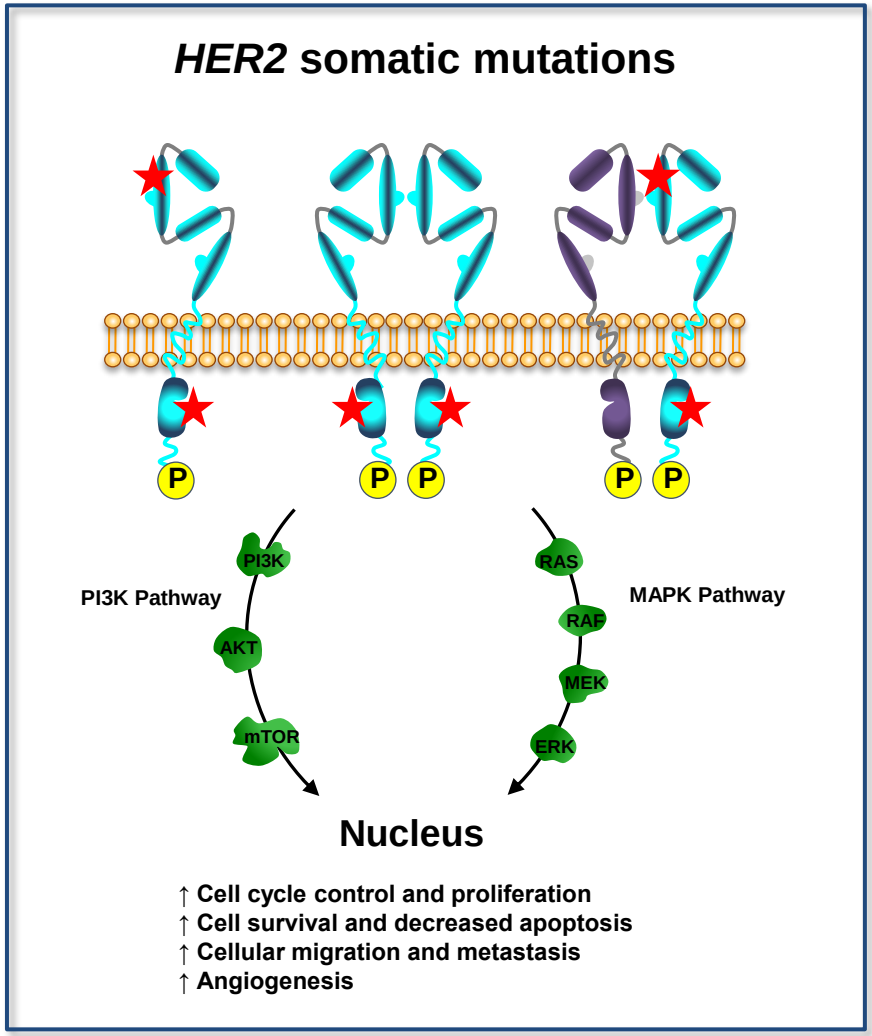
Key Exclusion Criteria
- Prior treatment with any pan-HER TKI (eg, lapatinib, afatinib, dacomitinib, neratinib)
- Patients who are receiving any other anticancer agents
- Symptomatic or unstable brain metastases
- Women who are pregnant or breast-feeding

SUMMIT

Hormone Receptor-Positive Breast Cancer Cohort

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

- **Incidence:**
  - 7–9%, pre-treated ER+ MBC[1]
- **Tumor characteristics:**
  - Usually mutually exclusive to *HER2* amplifications
- **Preclinical evidence of oncogenic activity:**
  - Constitutive activation of intracellular kinase and downstream signaling pathways[2]
  - Increased cell proliferation and tumor growth[2]
  - 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)



1. Wagle et al. ASCO 2016; 2. Bose et al. Cancer Discov 2013

HR+ *HER2*-Mutated Breast

Publications from SUMMIT trial *HER2*-mutant breast cohorts

HER2 mutant breast tumors

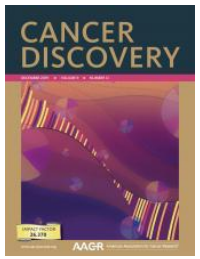
All (HR+/HR-) breast cancer → Neratinib monotherapy

All (HR+/HR-) breast cancer → Neratinib monotherapy

HR-positive breast cancer → Neratinib + fulvestrant

HR-positive breast cancer → Neratinib + trastuzumab fulvestrant

Primary (all monotherapy cohorts) manuscript:
David Hyman *et al*
Nature (2018) **554**:189–194



Breast cohort manuscript:
Lillian Smyth *et al*
Cancer Discovery (2019) in press
(doi: 10.1158/2159-8290.CD-19-0966)

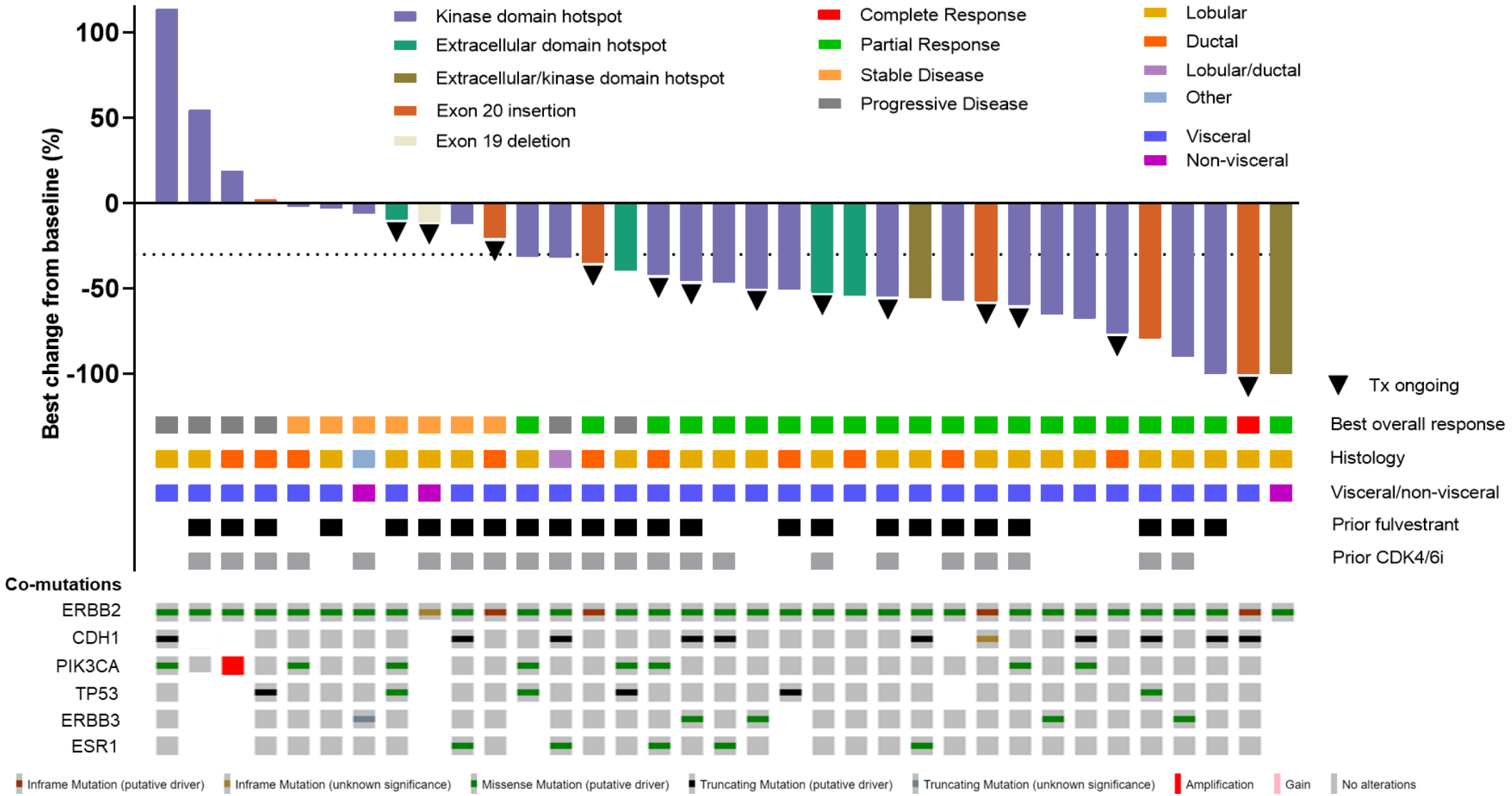
HR+ breast triplet combo cohort:
Komal Jhaveri *et al.*
Spotlight Poster Session, 12/9/20 4:00-5:15 PM
Abstract PD1-05

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]

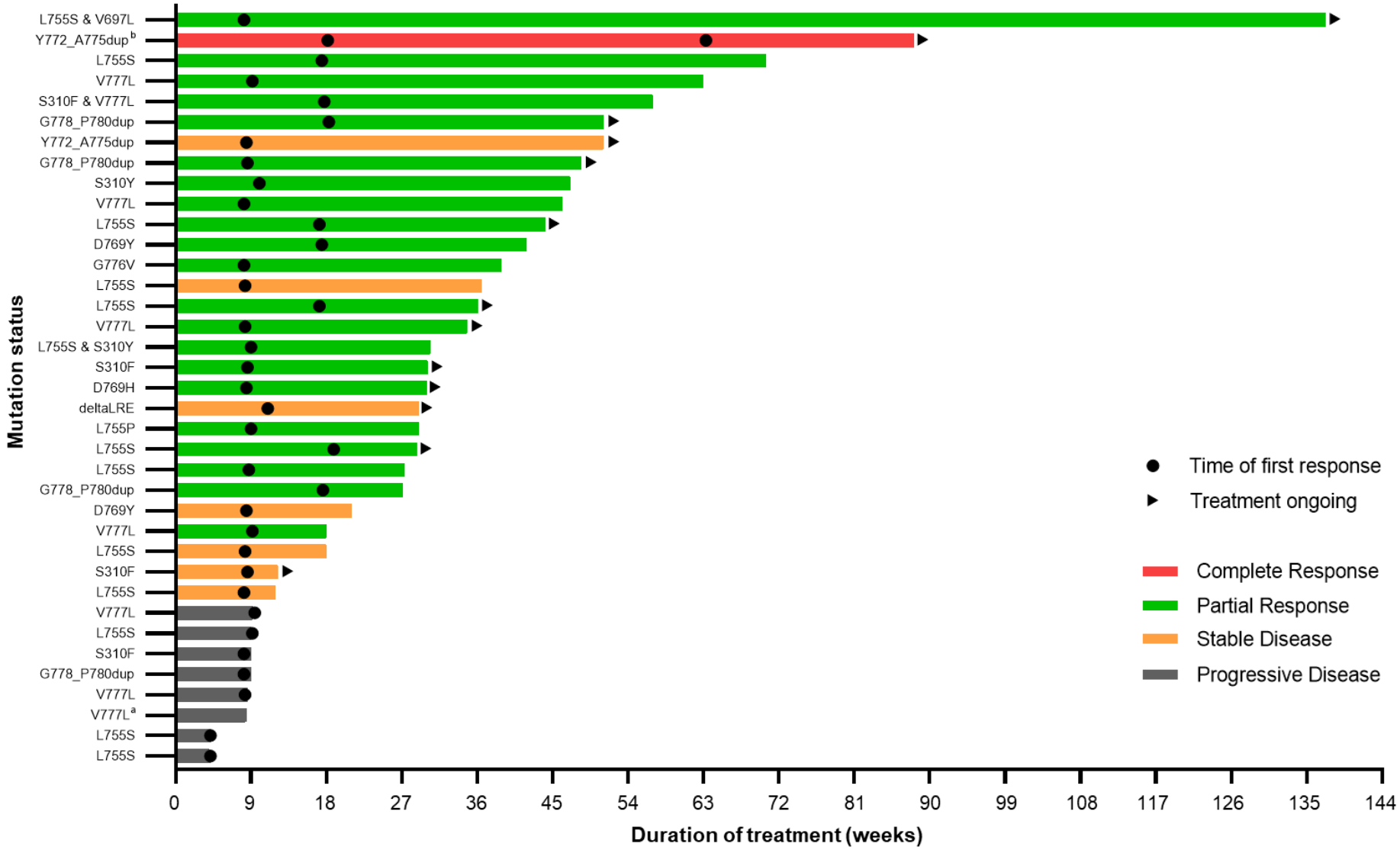


SABCS 2020

[a]Two of the 37 RECIST evaluable patients are not included in this figure because they did not have a tumor assessment before they died

HR+ *HER2*-Mutated Breast

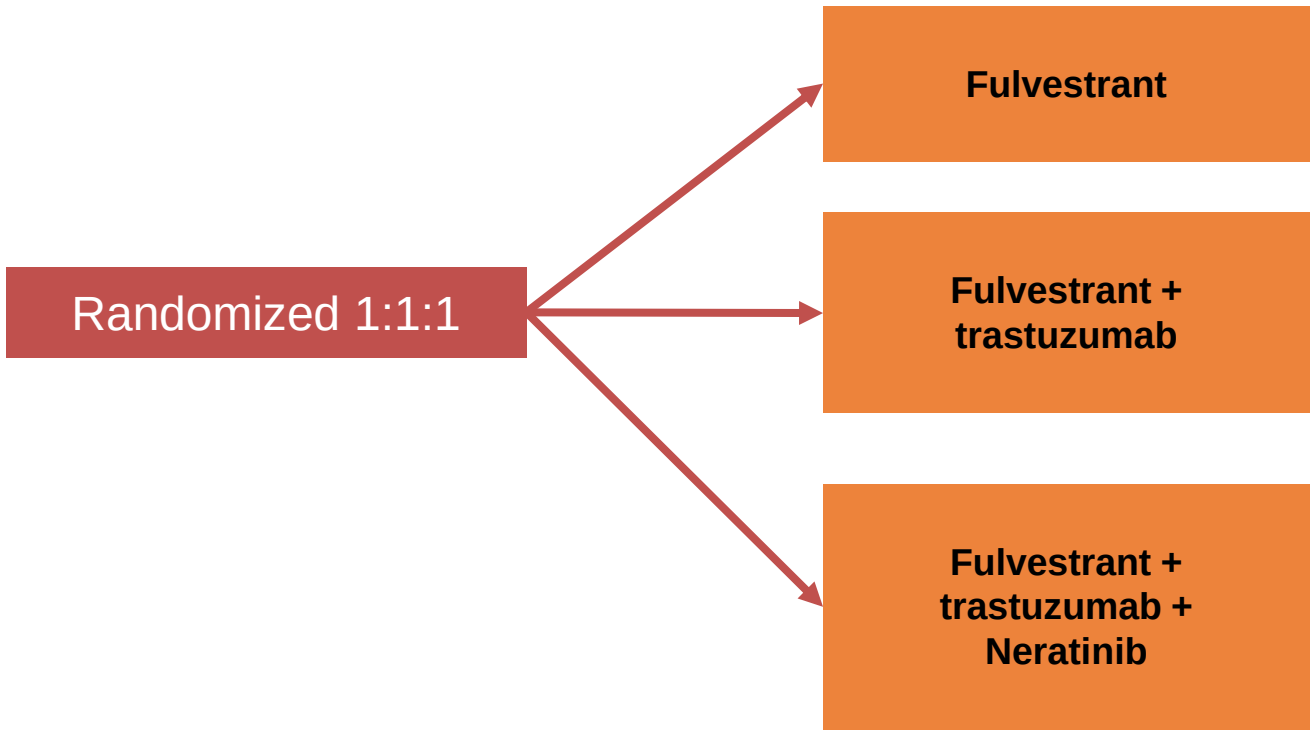
Duration of treatment and best response with neratinib + trastuzumab + fulvestrant (n=37)



SABCS 2020

[a]This patient died in hospice due to clinical progression and did not have a tumor assessment before she died
[b]This 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



***HER2* mutations**
(documented by local testing)

Primary endpoint
- Objective response rate

Secondary endpoints
- DOR

Simon 2-stage design

Proposed assessment criteria consistent with original 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)

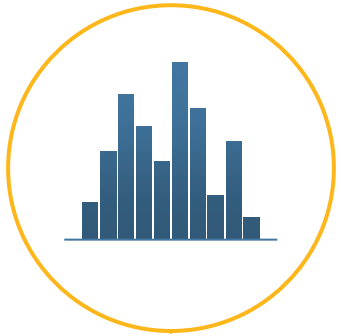
Puma to schedule pre-NDA meeting with FDA after initial Simon 2 stage results to discuss potential for accelerated approval (anticipated Q1 2021 – Q2 2021)

SUMMIT

Cervical Cancer Cohort

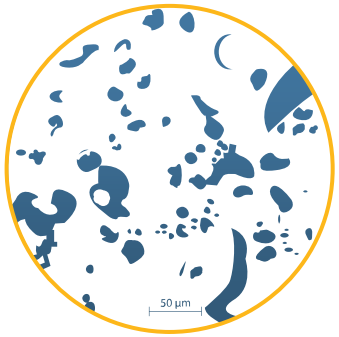
Puma Biotechnology

Characteristics of *HER2*-Mutant Cervical Cancer



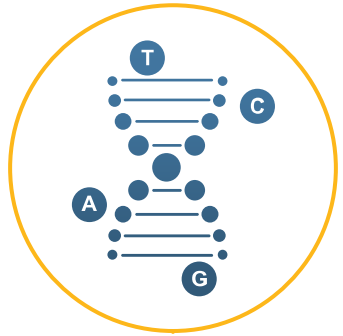
Incidence

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



Histology

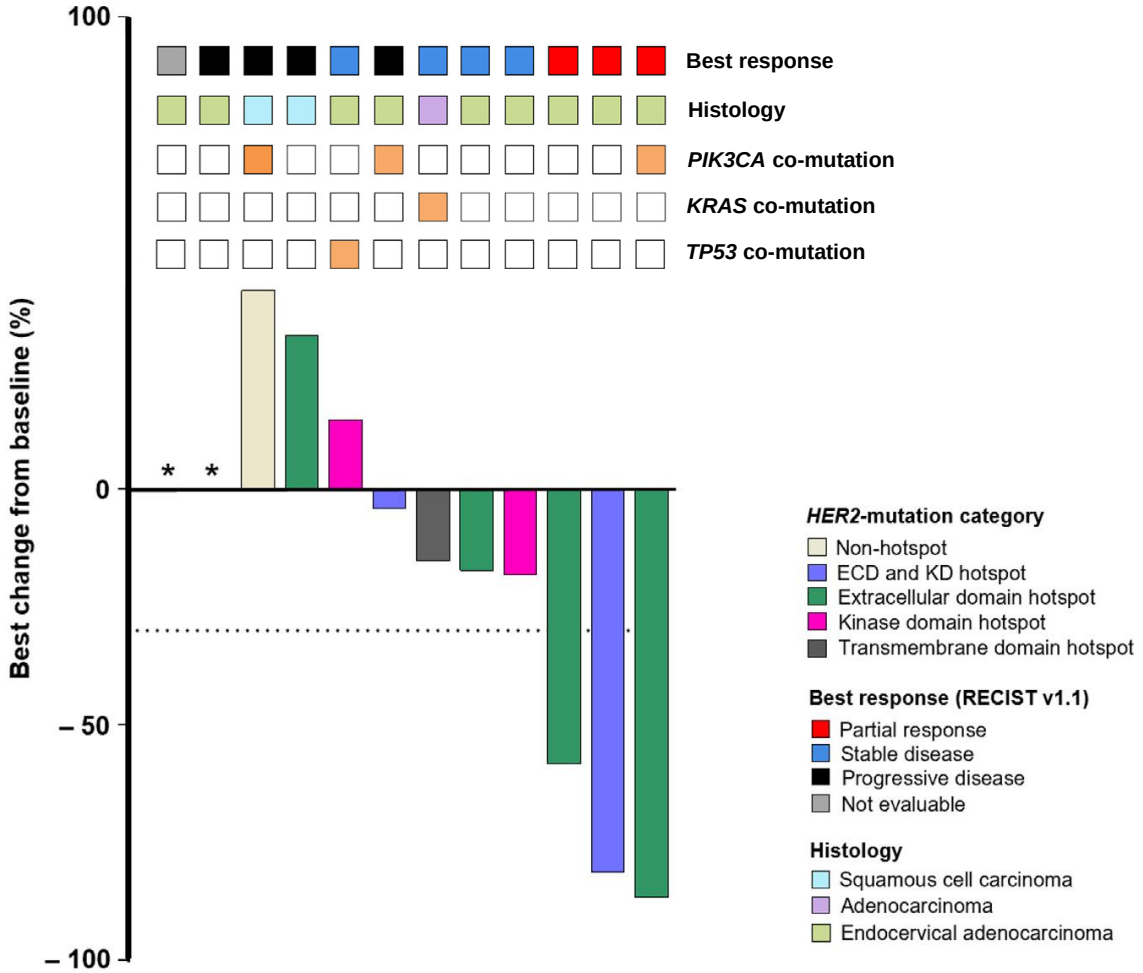
- Enriched in adenocarcinomas
- High occurrence in HPV+ tumors



Genomics

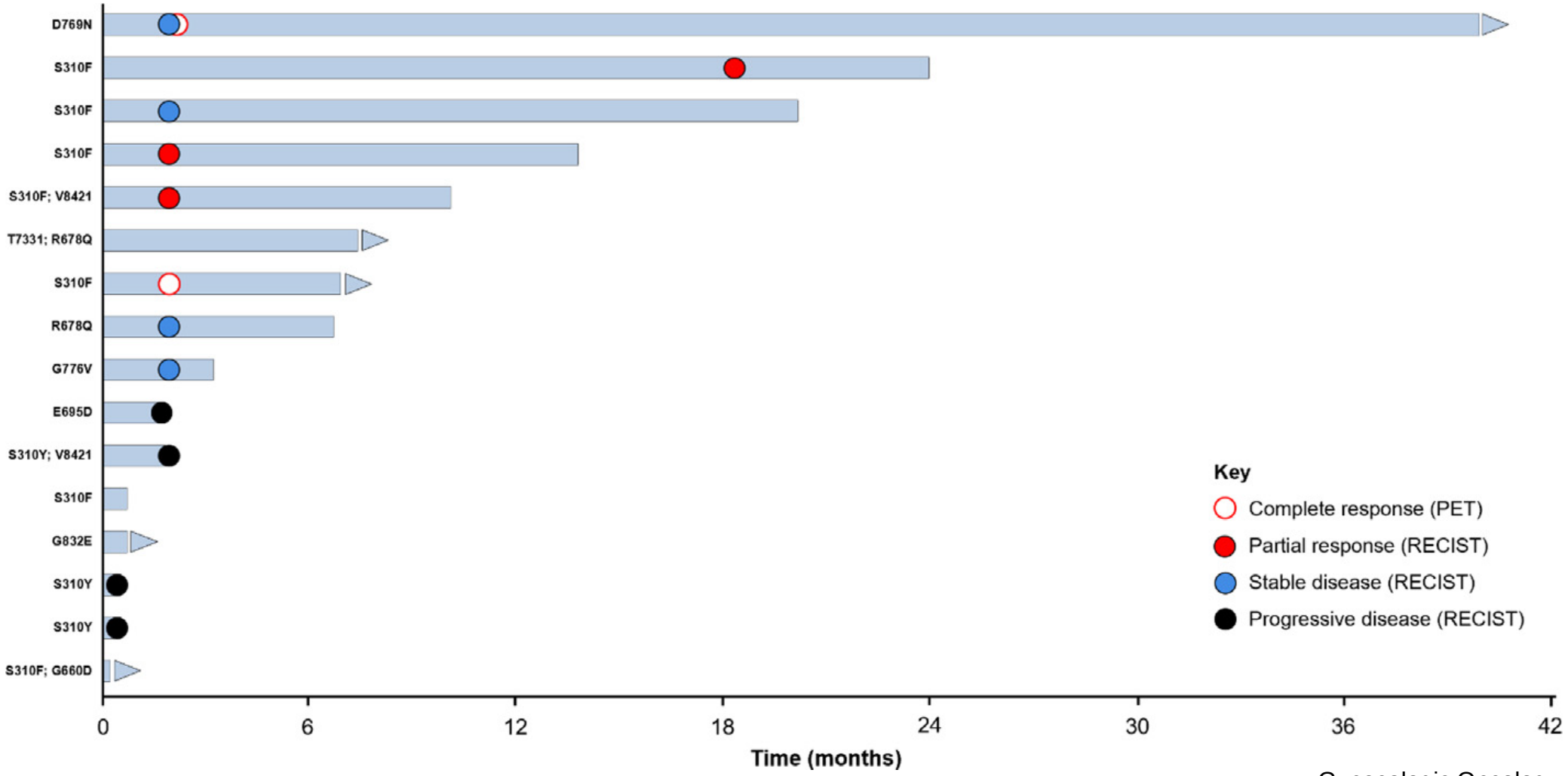
- Most common *HER2*^{mut} is S310 extracellular domain hotspot mutation
- Usually exclusive to *HER2* amplifications
- Most common co-mutations include *TP53*, *PIK3CA*

Neratinib Monotherapy Results Published in Gynecologic Oncology



Gynecologic Oncology, 2020

Neratinib Monotherapy Results Published in Gynecologic Oncology



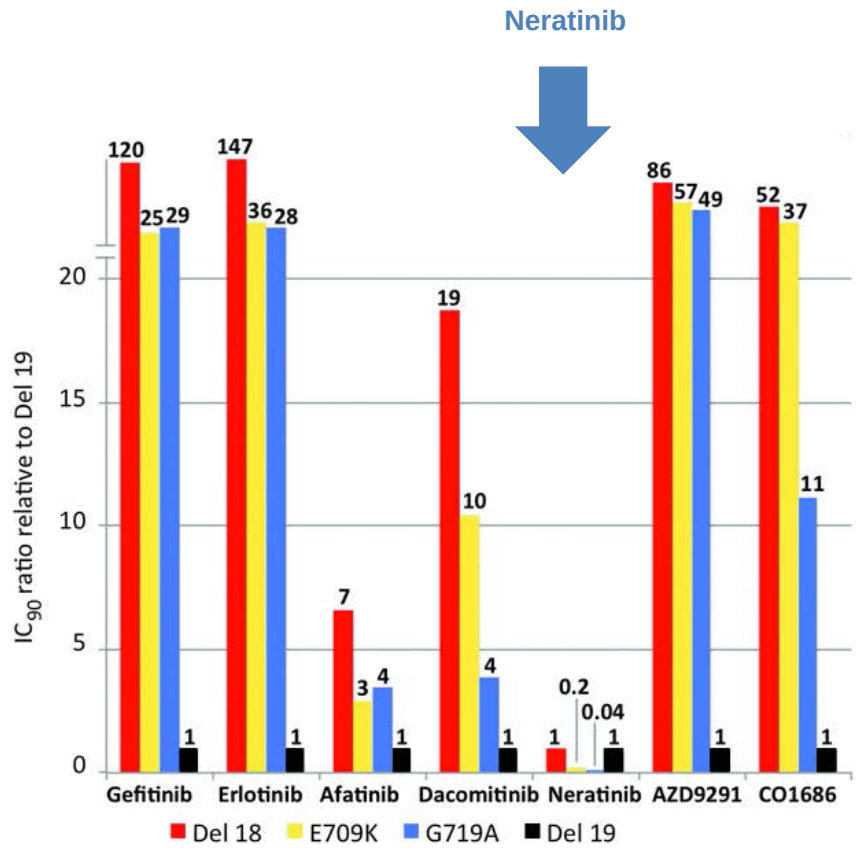
Gynecologic Oncology, 2020

SUMMIT (PUMA-NER-5201) Basket Trial

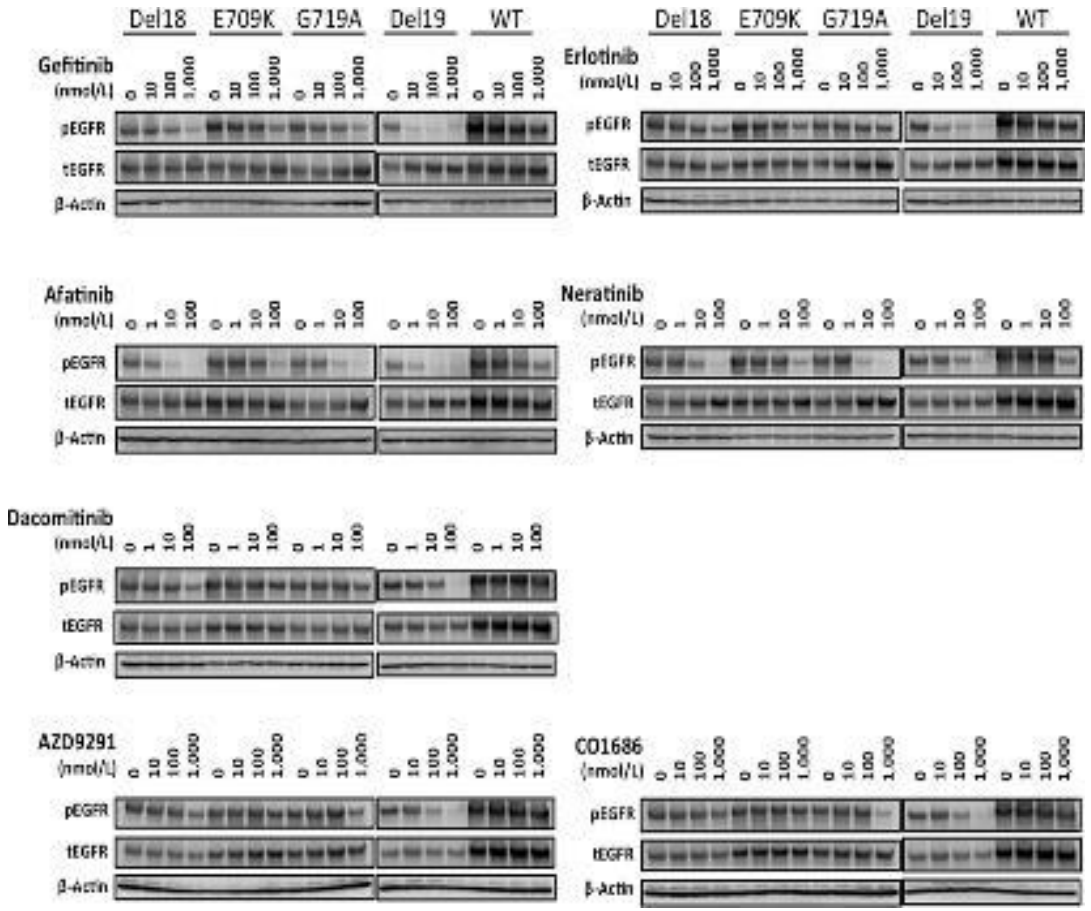
EGFR exon 18 lung cancer cohort update

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

Comparative TKI affects in *EGFR* exon 18+ cells

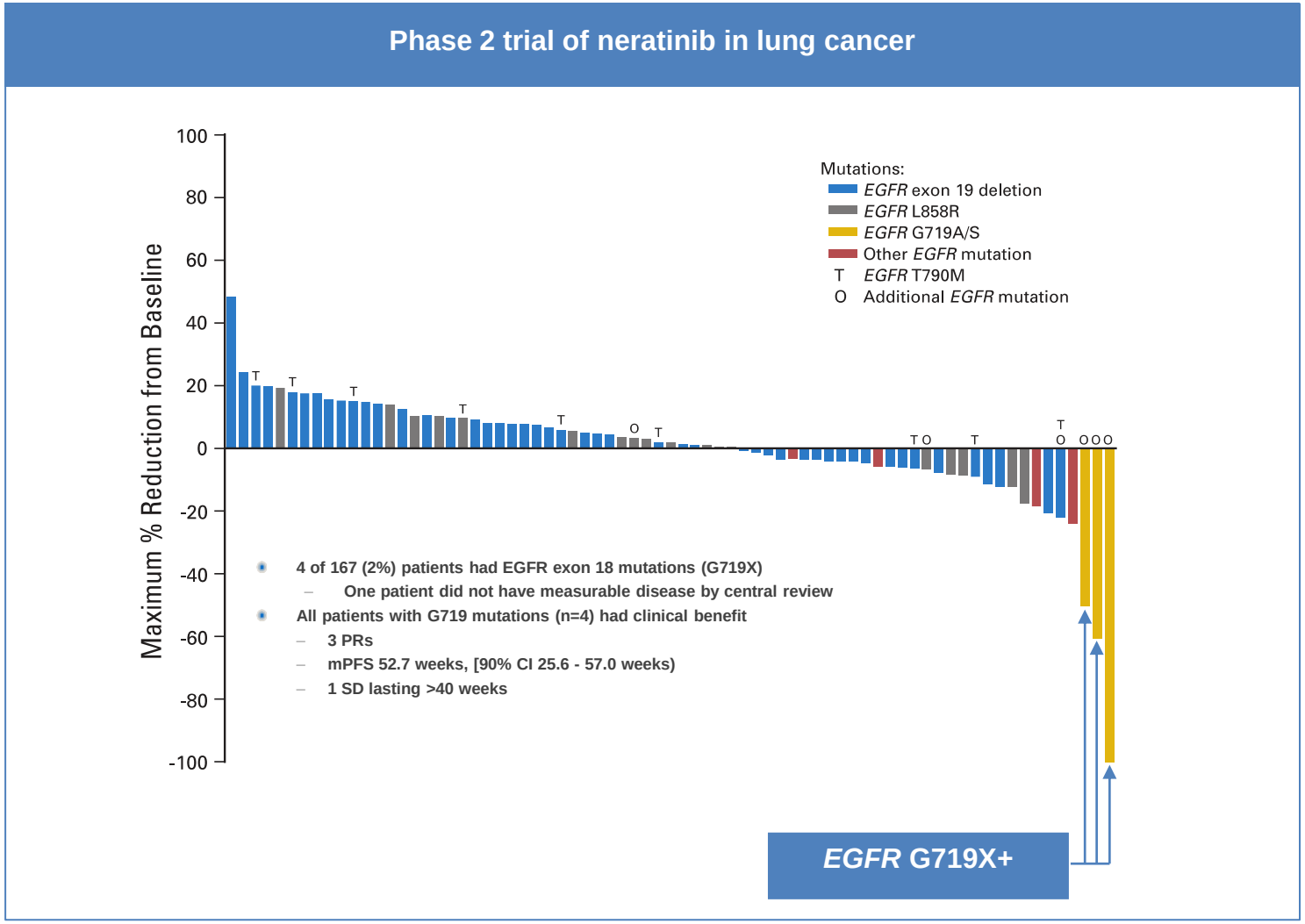


Western blot analyses of transfected HEK293 cells



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 1st 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

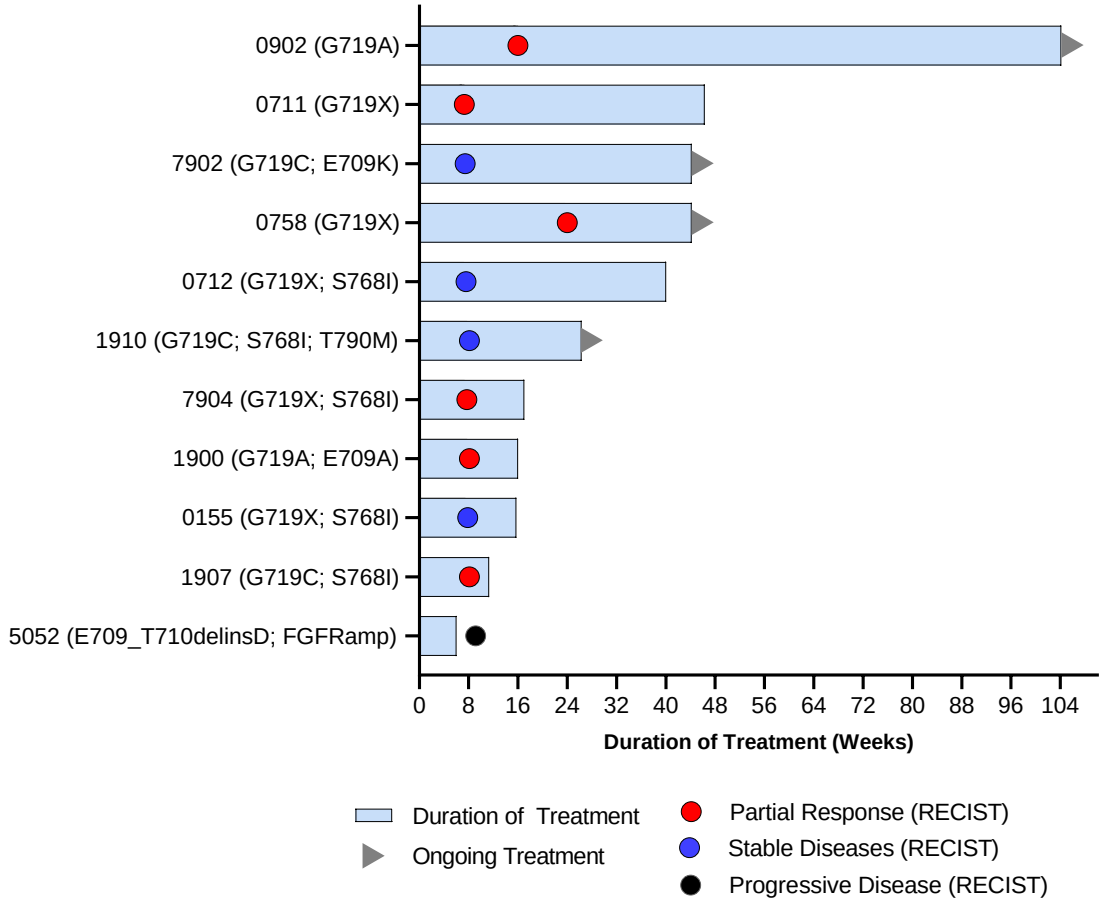
EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib **Monotherapy:** Efficacy Summary

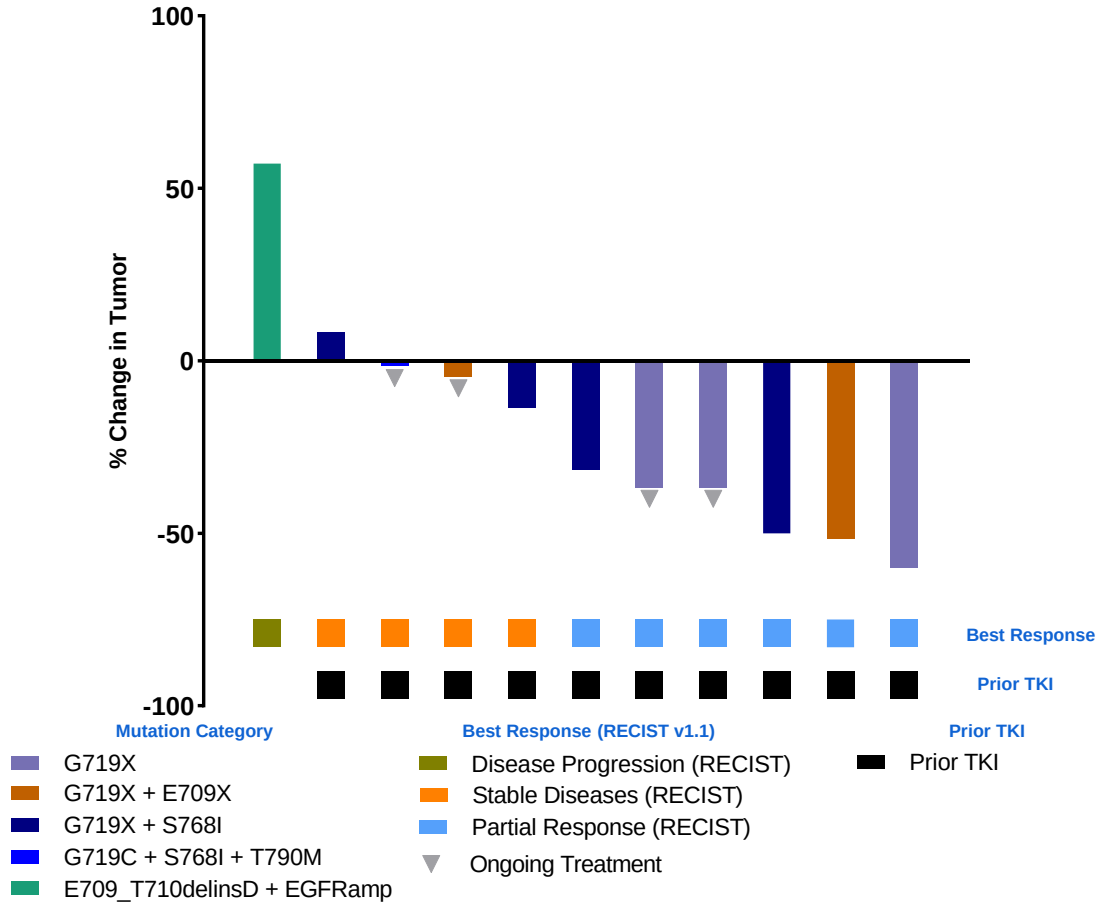
Parameter	Efficacy evaluable patients (n=11)	TKI Pre-Treated (n=10)
Objective response (confirmed),[a] n CR PR Objective response rate, % (95% CI)	**4** 0 4 **36** (11–69)	**4** 0 4 **40** (12–74)
Best overall response, n CR PR Best overall response rate, % (95% CI)	**6** 0 6 **54** (23–83)	**6** 0 6 **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 CR or PR SD ≥16 weeks Clinical benefit rate, % (95% CI)	**8** 4 4 **73** (39–94)	**8** 4 4 **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)

TKI-naïve patients

TKI-pre-treated patients

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-naive 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.

Yang *et al*. Journal of Thoracic Oncology (2020) 15(5): 803-815

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 first 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

HER-Seq (PUMA-NER-9501)

HER2-mutation screening protocol

Puma Biotechnology

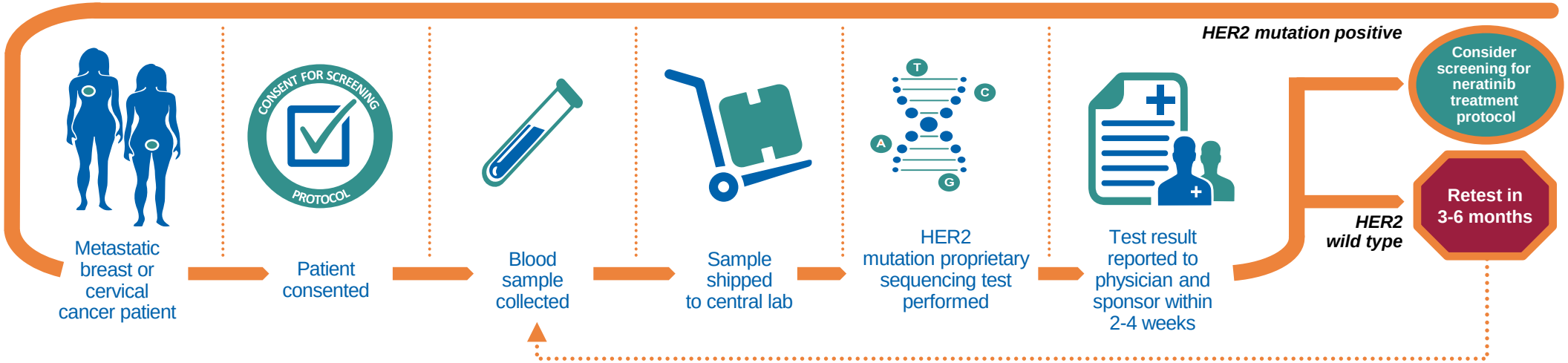
HER-Seq: A Convenient, Minimally-Invasive Blood-Based Screening Protocol to Identify HER2-Mutant Patients for Neratinib Clinical Trials

Clinical trials.gov NCT: NCT03786107.

- Simple, non-invasive blood-based screening protocol for identifying *HER2* mutations from plasma cfDNA
- HER-Seq NGS assay is analytically-validated, CE-marked, and ISO-certified
- Convenient for sites/institutions that lack access to routine/reimbursable molecular sequencing
- Allows for routine serial testing to identify acquired *HER2* mutations through advancement of disease or therapy
- Patients identified with *HER2* mutations can be readily tracked for protocol screening and seamless registration into SUMMIT or other neratinib clinical trials

HER-Seq (PUMA-NER-9501) Study Protocol

- HER-Seq: A Blood-based Screening Study to Identify Patients with *HER2* Mutations for Enrollment into SUMMIT (initiated December 2018)



PRIMARY OBJECTIVE:

To identify patients with *HER2* mutations who may be eligible for screening into the SUMMIT 'basket' trial or other disease-specific neratinib treatment protocol.

Key Inclusion Criteria

- Women and men who are ≥18 years old at signing of informed consent.
- Histologically-confirmed metastatic breast or cervical cancer
- ECOG status of 0 to 2
- Provide written, informed consent to participate in the study and for circulating tumor DNA screening
- Must provide blood sample(s) for *HER2* mutation testing

Key Exclusion Criteria

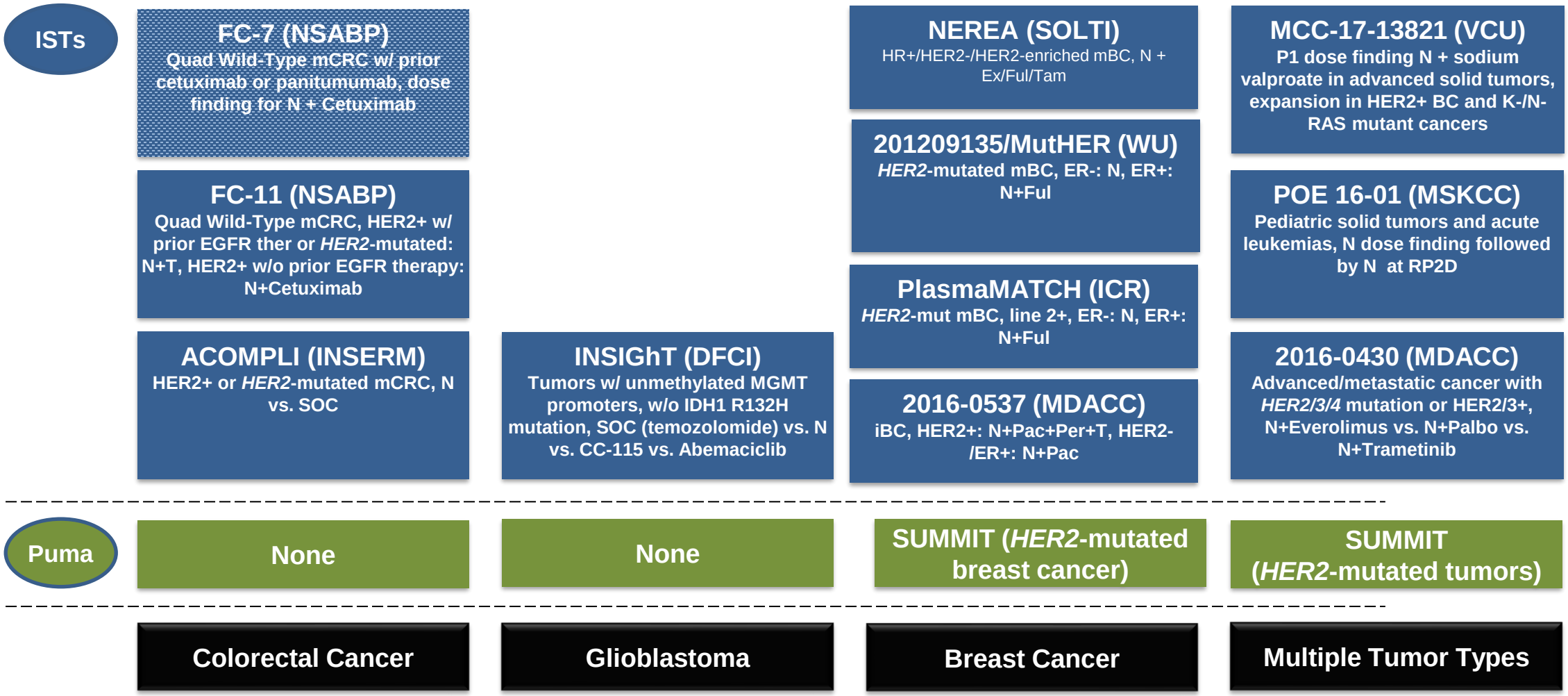
- Patients with known HER2+ or *HER2*-amplified tumors
- Patients who have received neratinib or any other prior EGFR/HER2 tyrosine kinase inhibitor

Clinical trials.gov NCT: NCT03786107

HER-Seq Trial

- Currently open at ~21 sites
  - Being expanded to other SUMMIT sites
- Utilizes proprietary next generation sequencing assay for *HER2* mutations
- Screening goals:
  - Breast cancer: screen 2500 patients
  - Cervical cancer: screen 1200 patients
- Patients with *HER2* mutations identified through HER-Seq will be considered for enrollment in SUMMIT

IST Landscape – Other Cancers



Puma – Expected Milestones

- Report Phase II data from cohort of patients in SUMMIT basket trial with bile duct cancer with *HER2* mutations treated with neratinib monotherapy (Q1 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 (H1 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 (H1 2021)
- Report Phase II TBCRC-022 trial of the combination of Kadcyla + neratinib in patients with HER2+ breast cancer with brain metastases who have previously been treated with Kadcyla (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 Stuglich, 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: PBYI
- Cash, cash equivalents and marketable securities at September 30, 2020: ~$109 million
- Cash earned in Q3 2020: ~$1.8 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: 39.8 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

39th Annual J.P. Morgan Healthcare Conference

January 2021

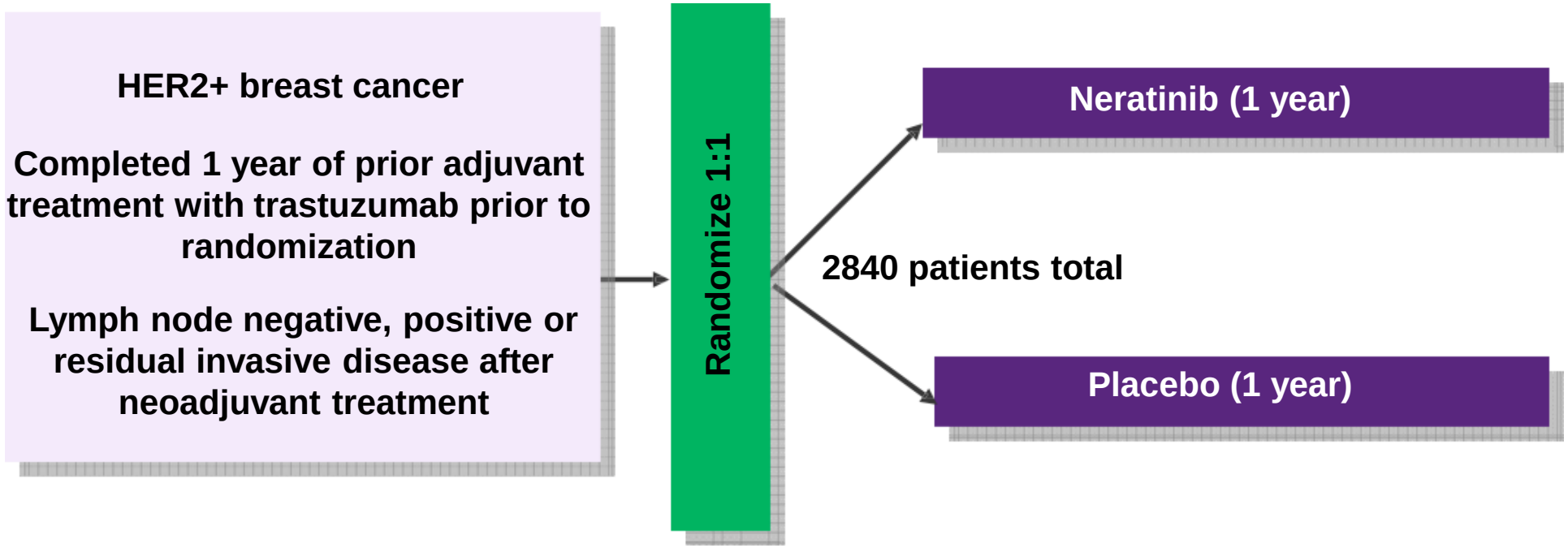
Puma Biotechnology

39th Annual J.P. Morgan Healthcare Conference

APPENDIX

January 2021

ExteNET Trial – HER2+ Extended Adjuvant Breast Cancer

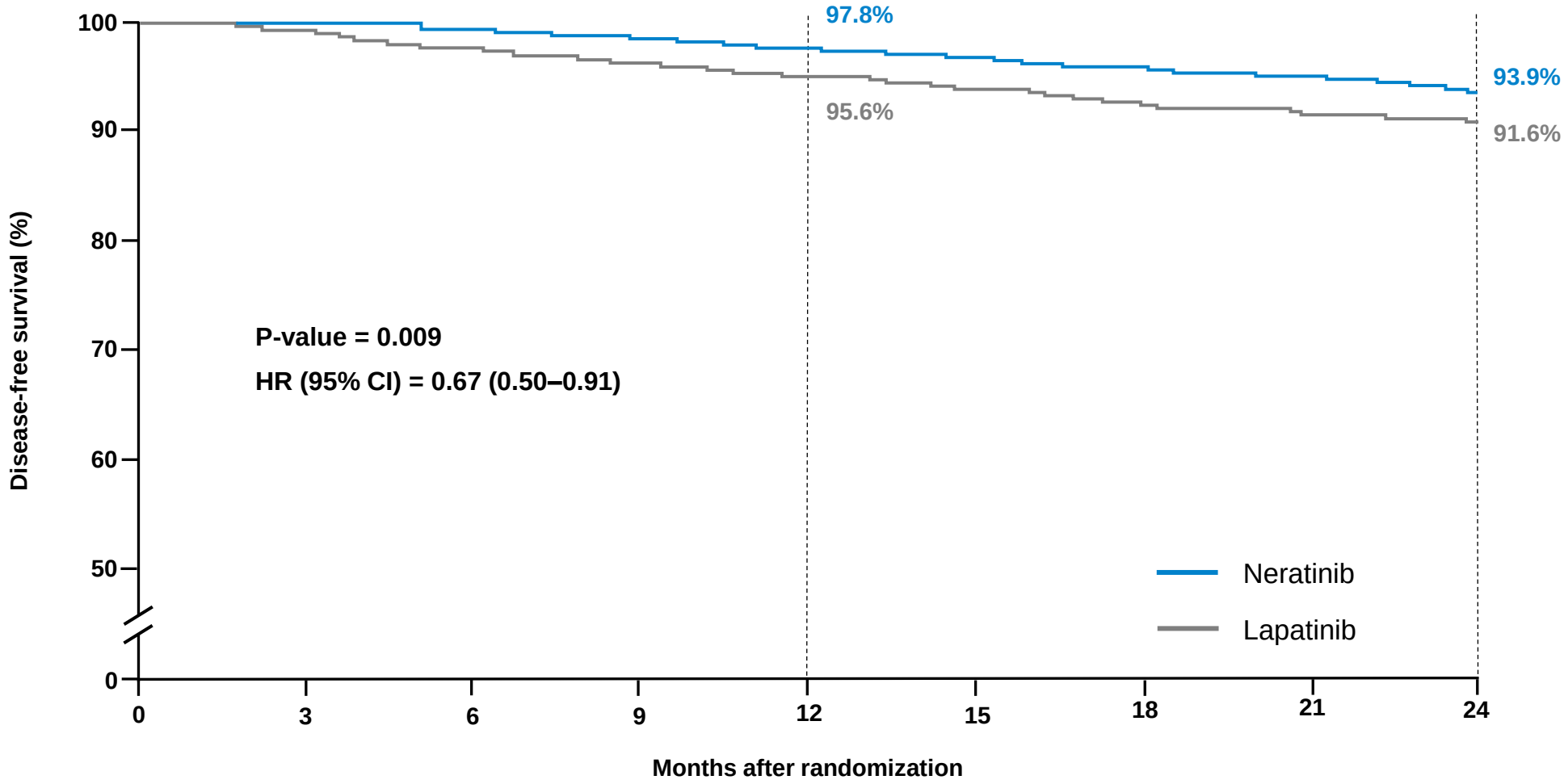


Primary endpoint: invasive disease-free survival (IDFS)

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

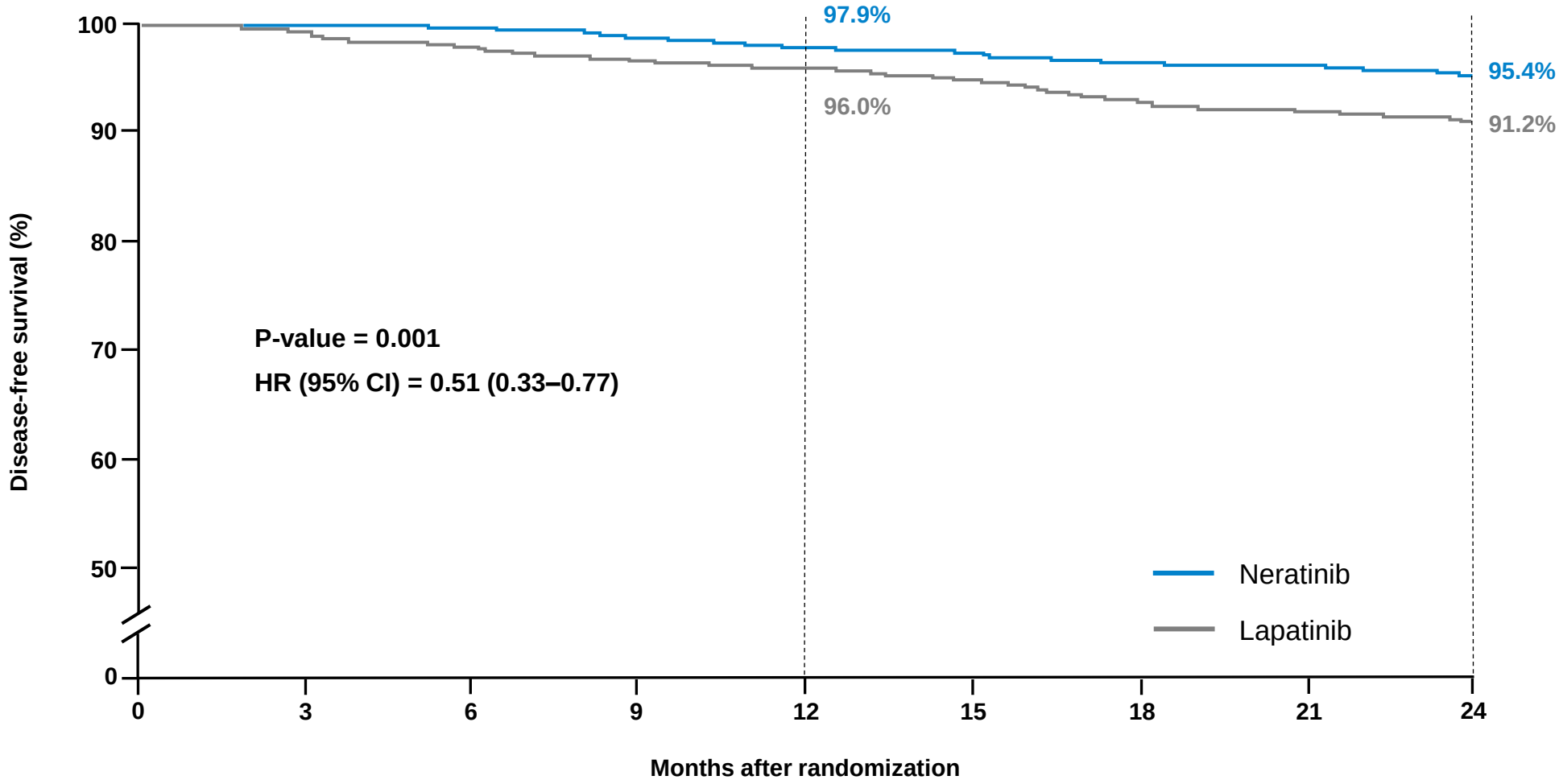
No loperamide prophylaxis used to prevent neratinib-related diarrhea

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

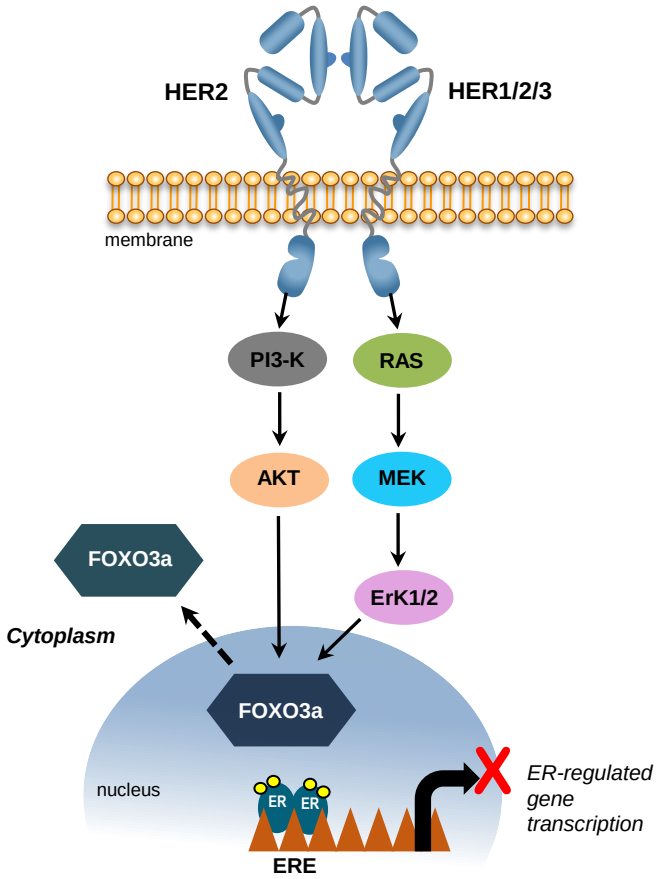
Kaplan-Meier Estimates of DFS
HR+ Patients ITT Population



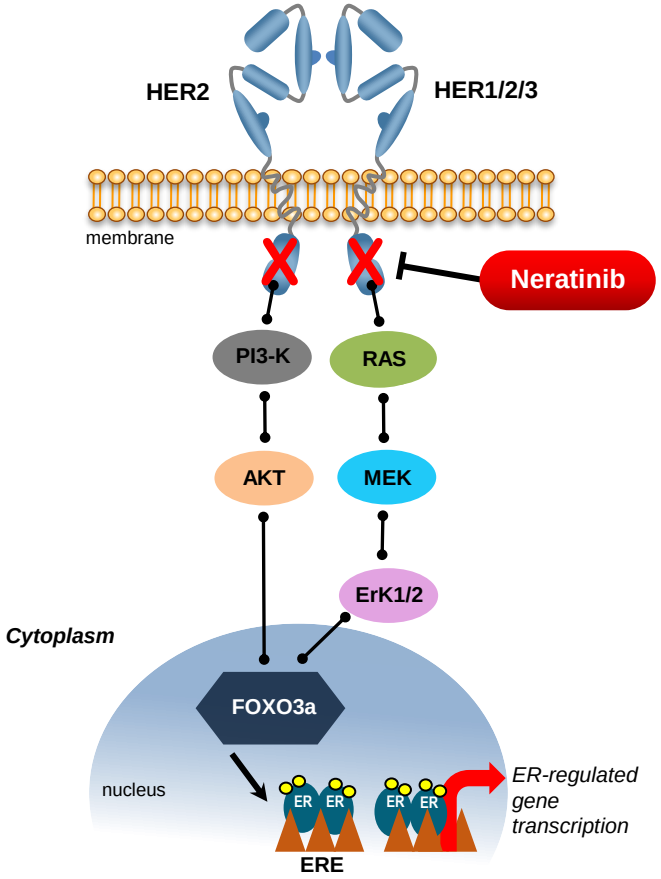
No. at risk									
Neratinib	816	737	721	698	677	653	629	591	380
Placebo	815	784	761	741	716	699	669	622	401

Rationale for Efficacy of Neratinib in HR+ Subgroup

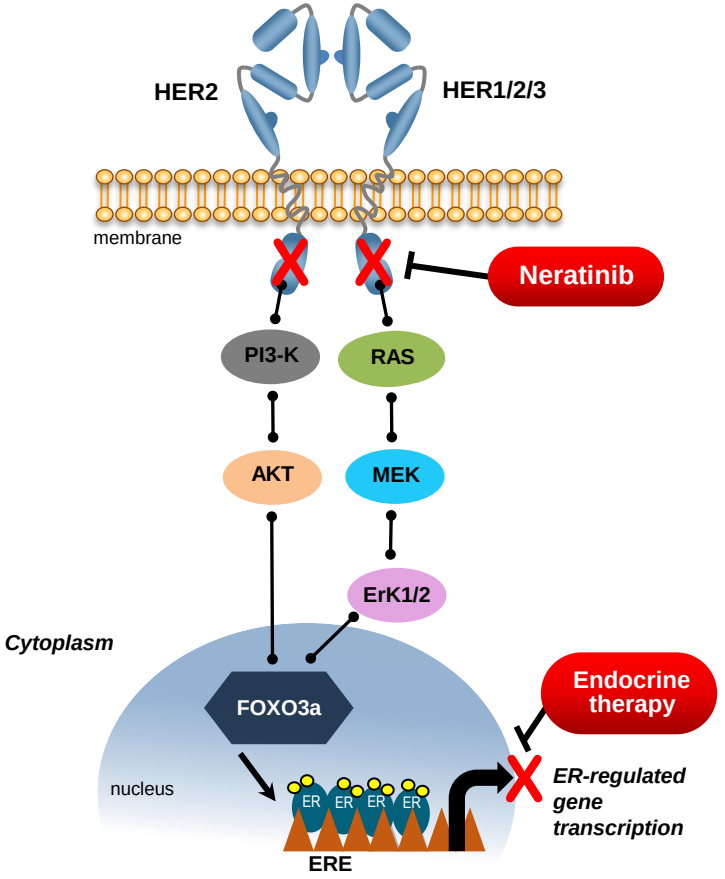
HER2 signalling decreases ER-regulated gene transcription



HER2 inhibition upregulates ER-regulated gene transcription



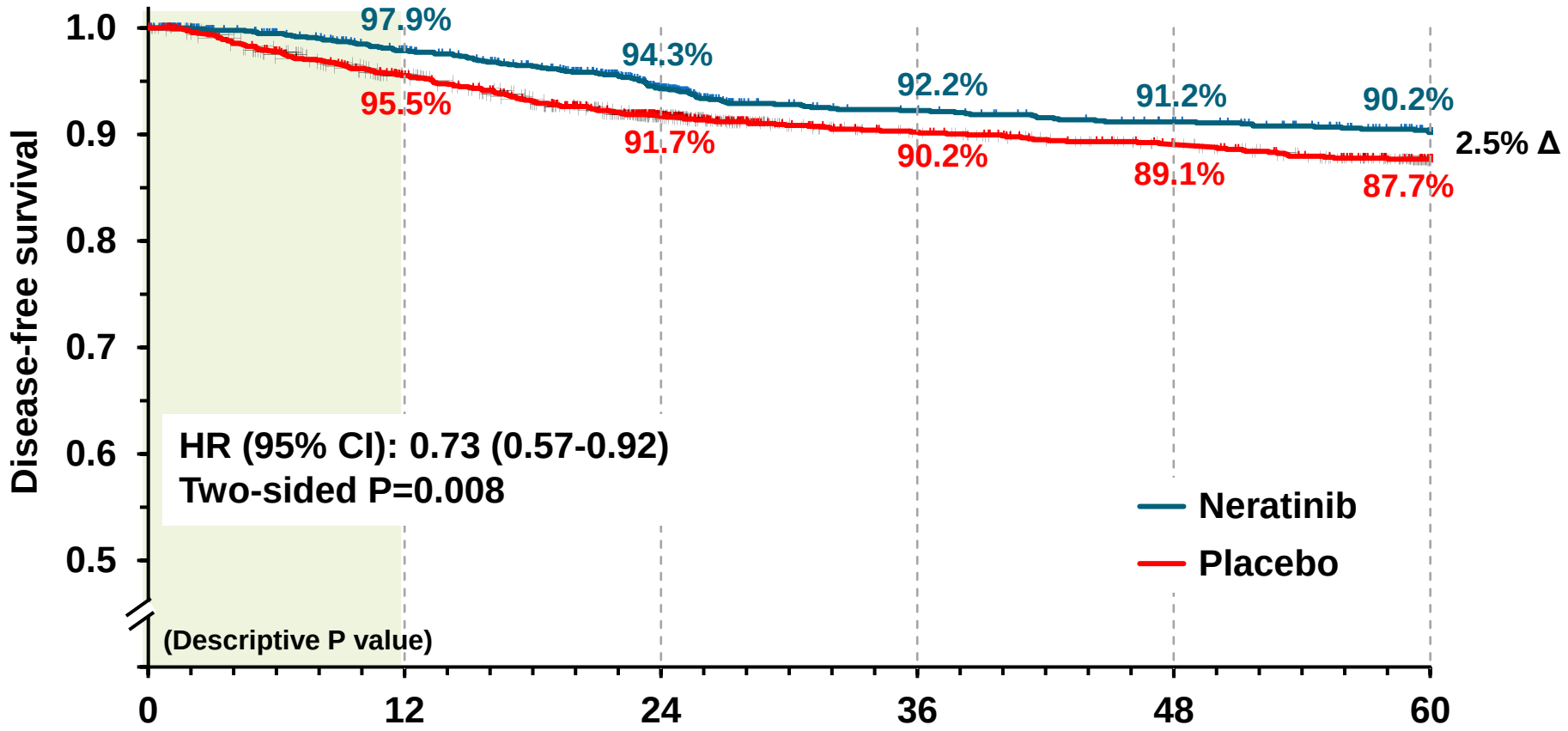
Inhibition of HER2 and ER is required for effective blockage in HER2+/HR+ tumors



Adapted from: Paplomata et al. Cancer 2015

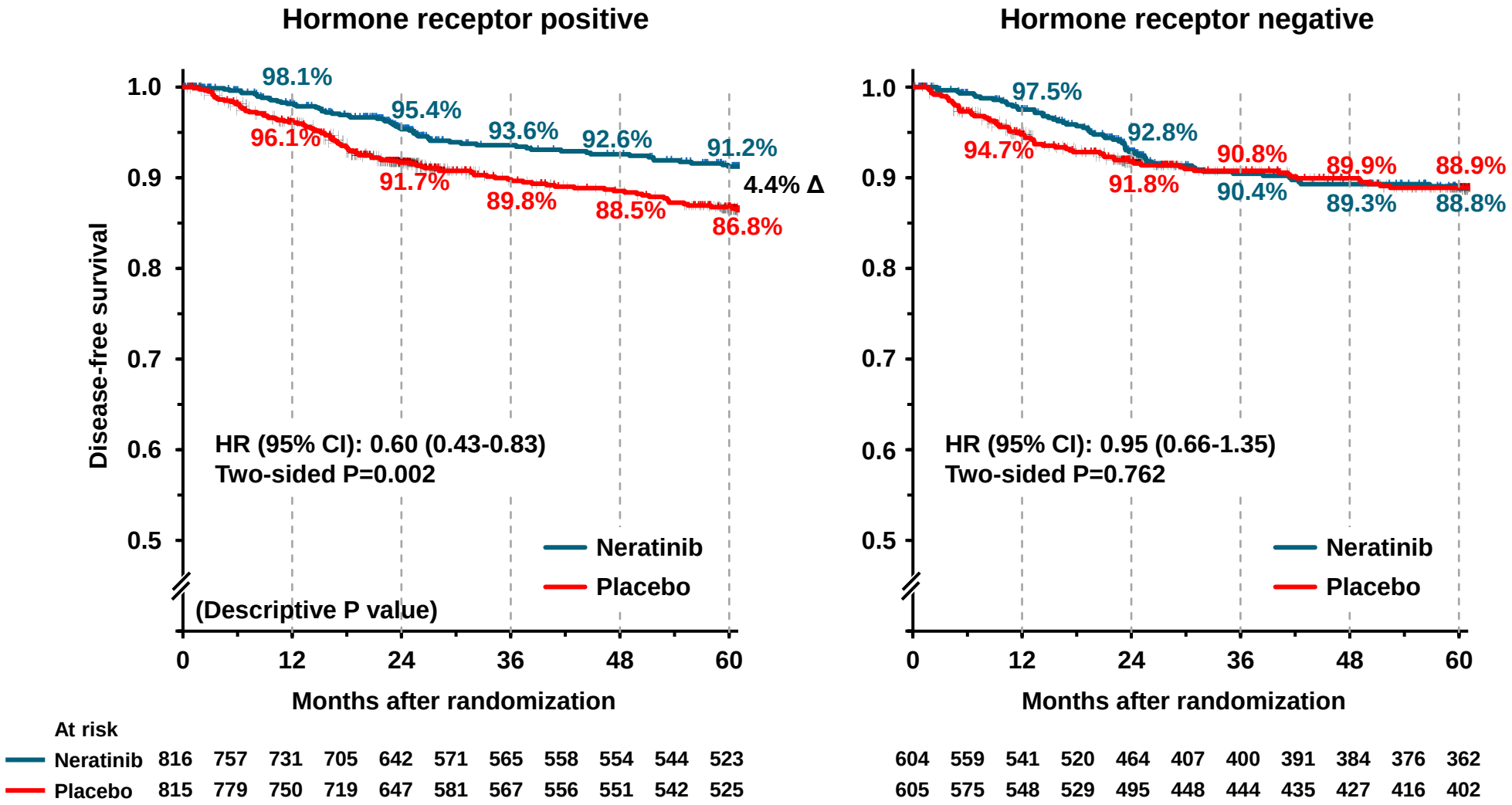
5-year Analysis Shows Durable iDFS Benefit

ITT Population



At risk											
Neratinib	1420	1316	1272	1225	1106	978	965	949	938	920	885
Placebo	1420	1354	1298	1248	1142	1029	1011	991	978	958	927

iDFS by Hormone Receptor Status
5-Year Analysis

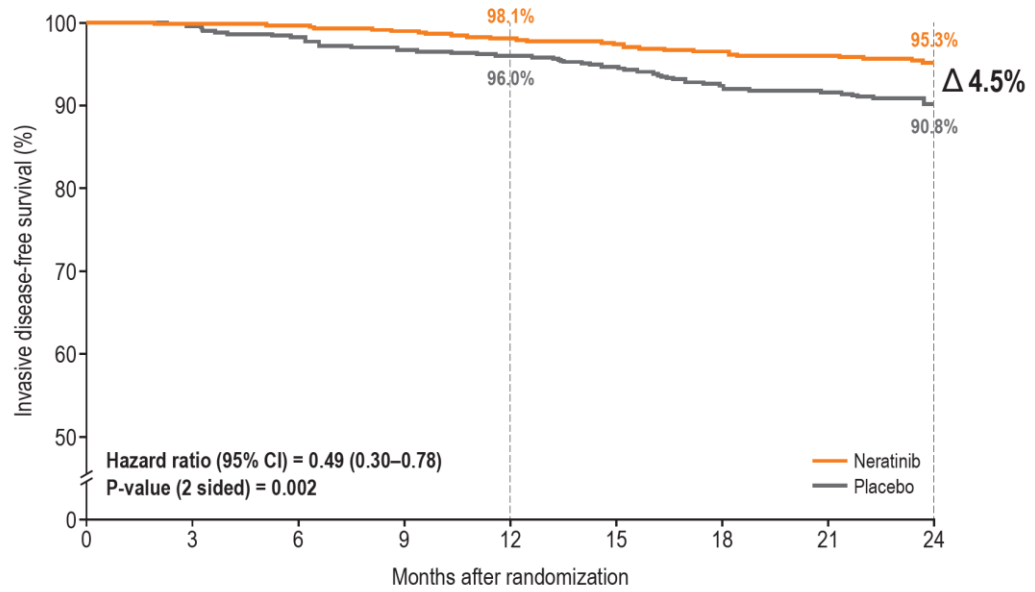


At risk											
Neratinib	816	757	731	705	642	571	565	558	554	544	523
Placebo	815	779	750	719	647	581	567	556	551	542	525

Neratinib	604	559	541	520	464	407	400	391	384	376	362
Placebo	605	575	548	529	495	448	444	435	427	416	402

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

2-year (primary) analysis

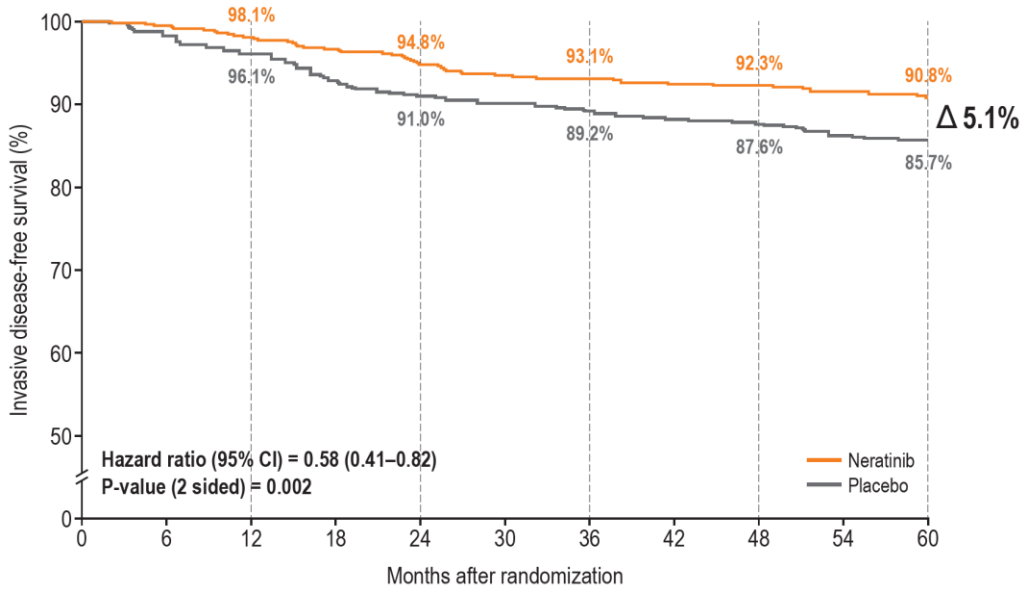


No. at risk
HR+/≤1 year from trastuzumab

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

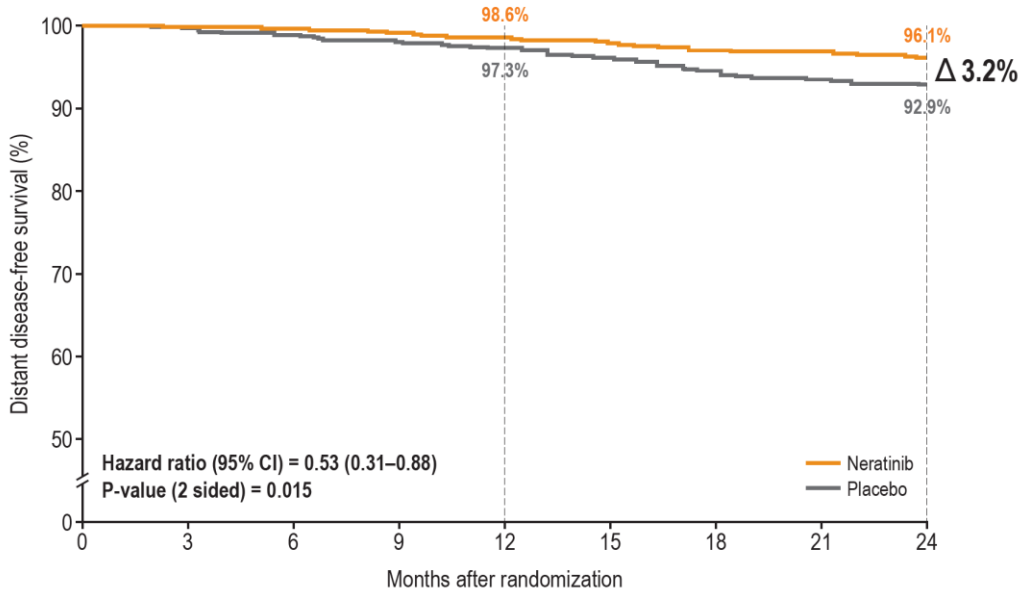
Neratinib	670	620	599	577	523	469	465	460	457	448	428
Placebo	664	634	609	583	535	481	471	462	458	450	433

42% relative reduction in risk of recurrence

Gnant M, et al. SABCS 2018, poster #P2-13-01

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

2-year (primary) analysis

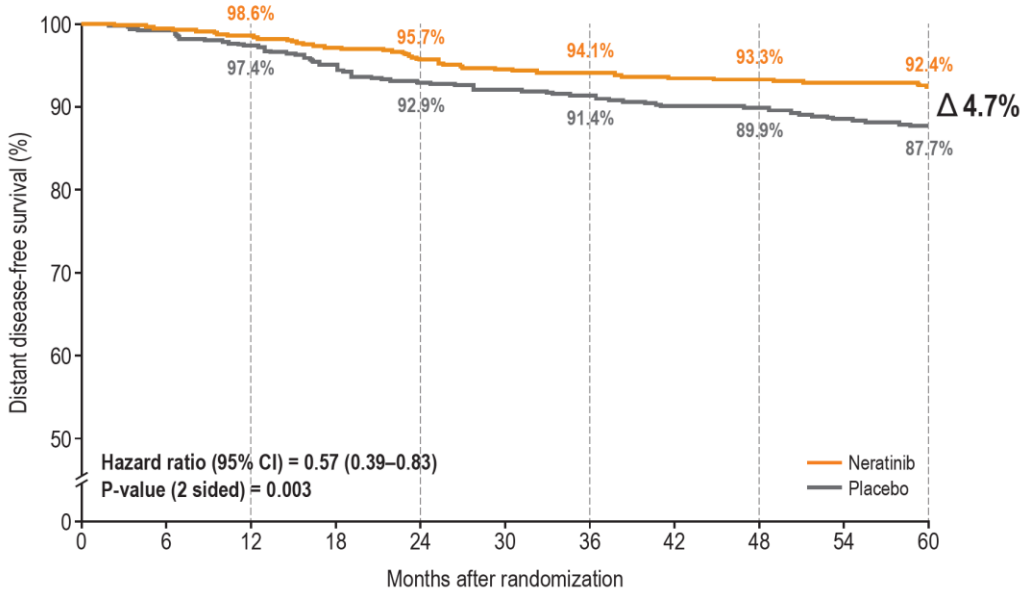


No. at risk
HR+/≤1 year from trastuzumab

Neratinib	670	605	593	578	561	540	518	488	309
Placebo	664	638	624	609	587	572	551	511	336

47% relative reduction in risk of recurrence

5-year analysis



No. at risk
HR+/≤1 year from trastuzumab

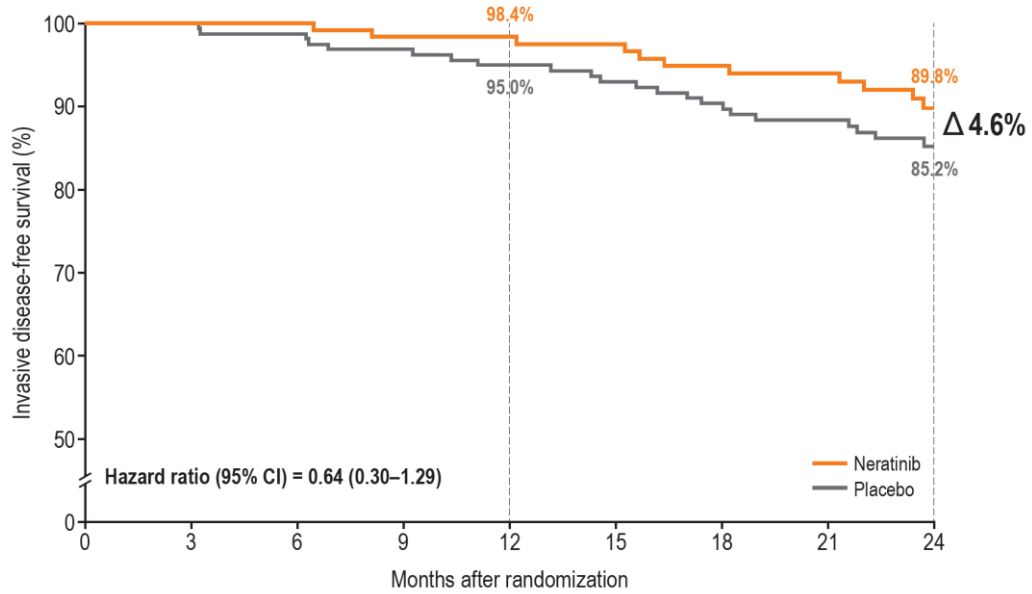
Neratinib	670	620	602	580	526	473	469	464	461	454	434
Placebo	664	639	616	594	546	489	480	469	467	457	438

43% relative reduction in risk of recurrence

Gnant M, et al. SABCS 2018, poster #P2-13-01

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



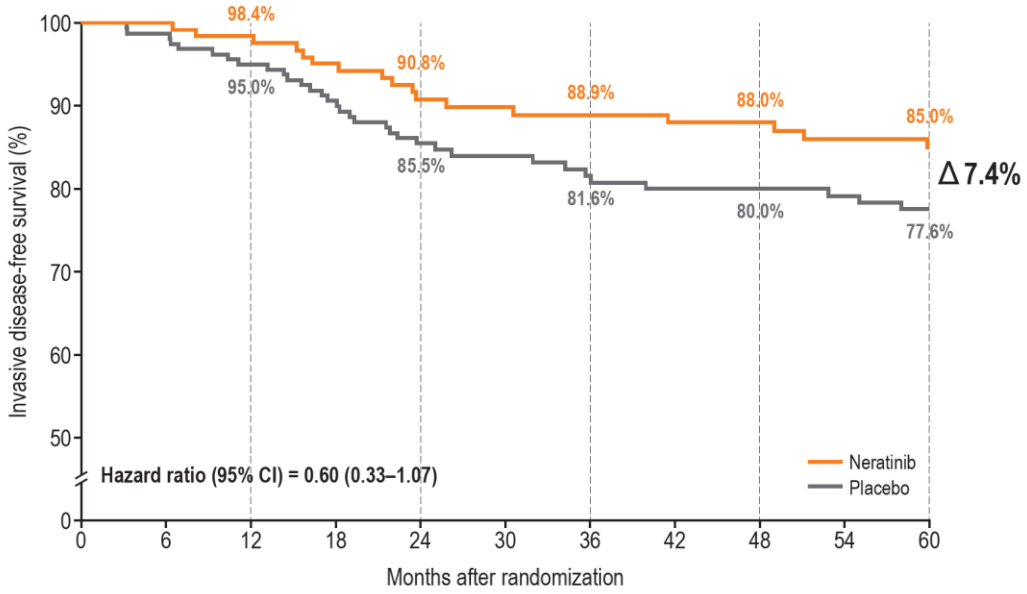
No. at risk

HR+/≤1 year from trastuzumab without pCR

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

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

Gnant M, et al. SABCS 2018, poster #P2-13-01