Puma Biotechnology

B. Riley Securities' 3rd Annual Oncology Conference

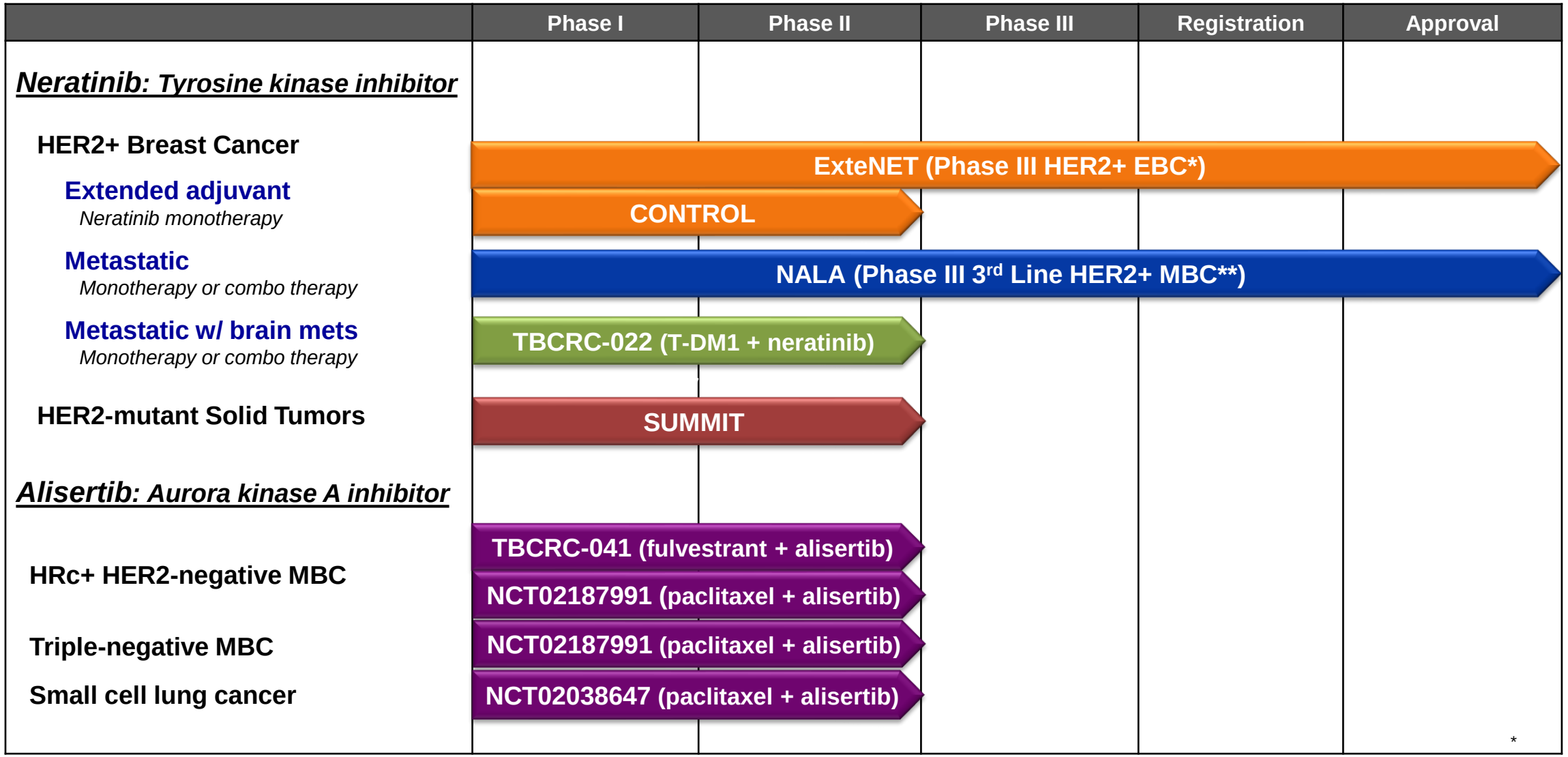
January 2023

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, 2021, and subsequent filings. 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.

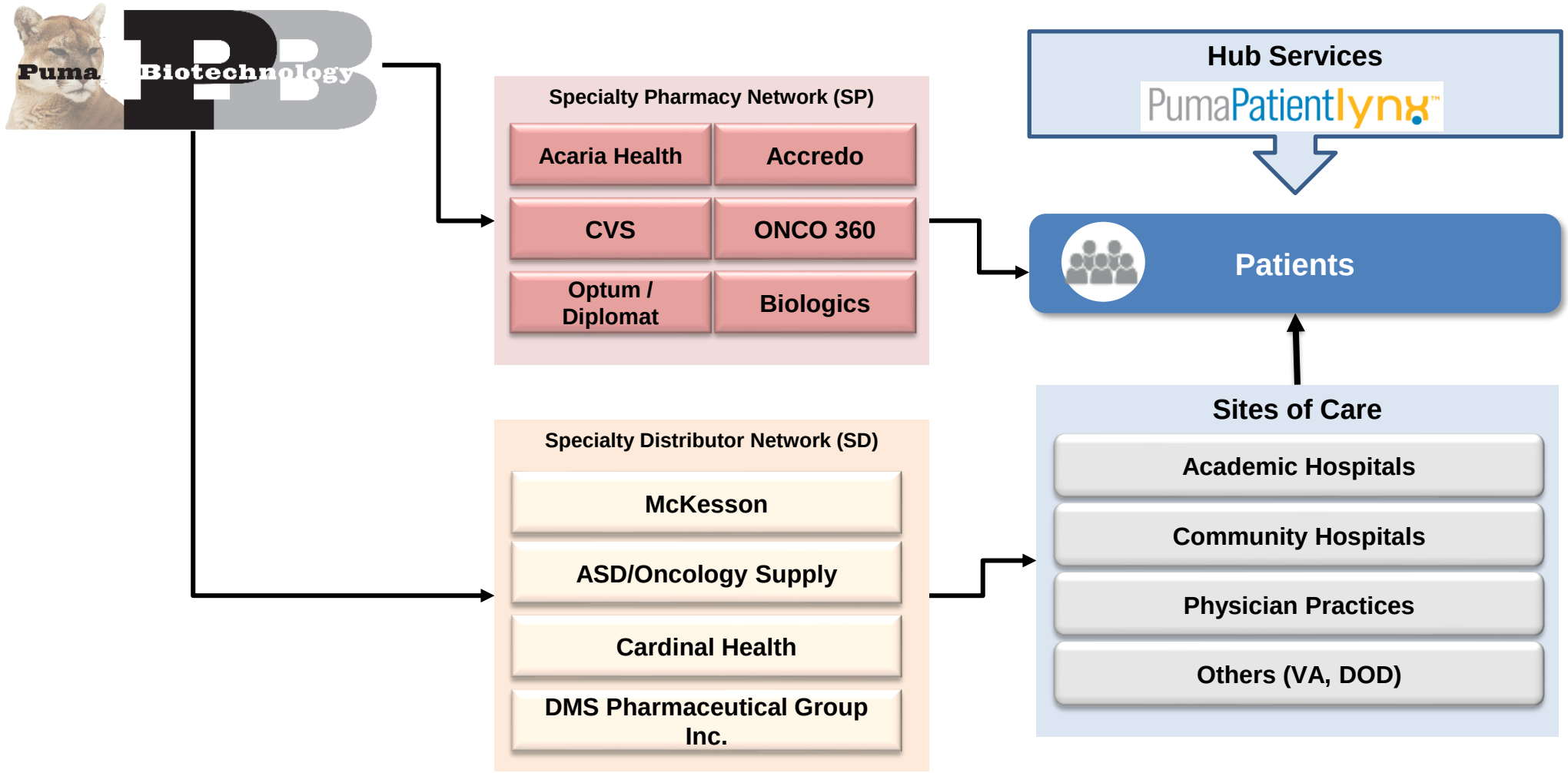
Puma Biotechnology

Product Pipeline

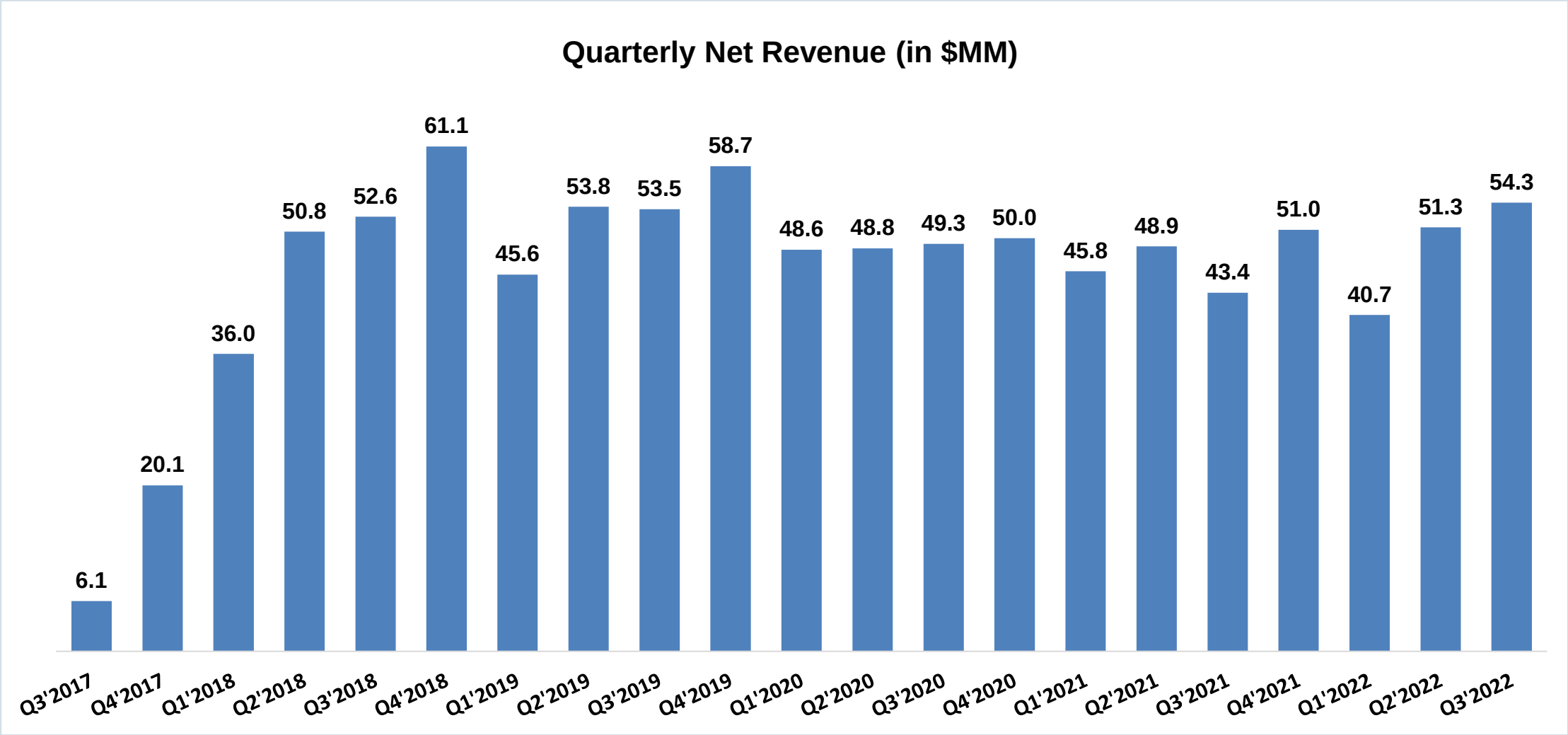


* ECB: Early breast cancer ** MBC: Metastatic breast cancer *** HRc+: Hormone receptor positive

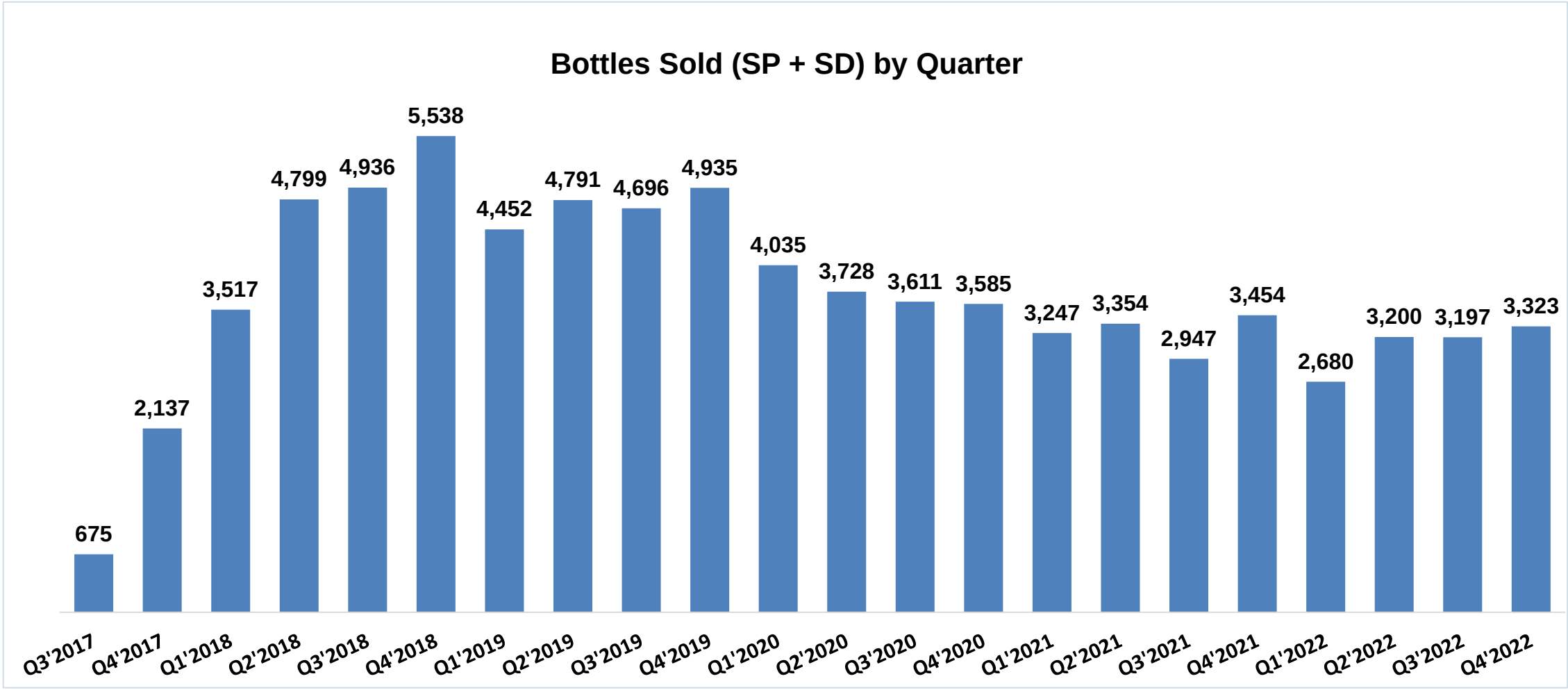
PUMA's Pharmacy and Distributor Network



~$54 Million net NERLYNX revenue in Q3’22



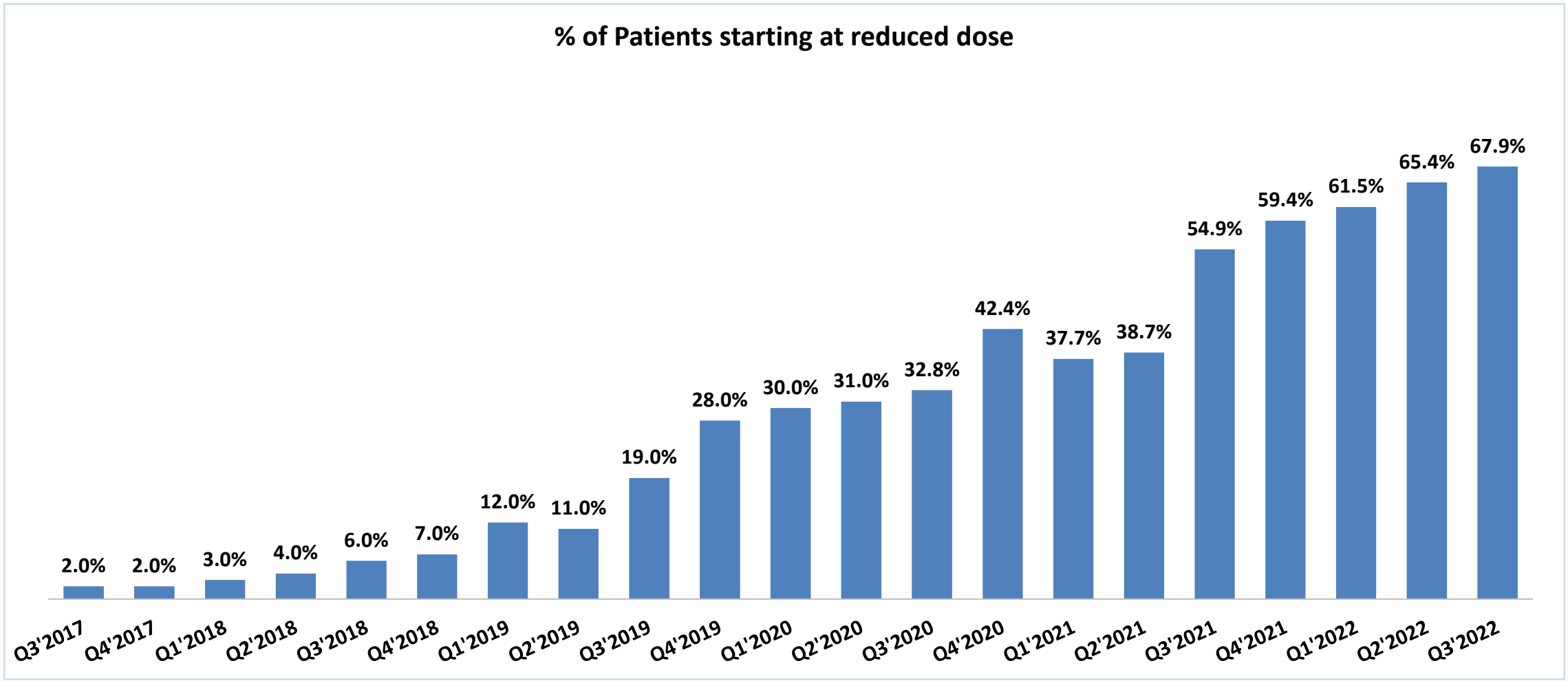
3,323 Ex-factory bottles were sold in Q4’22*



Includes Commercial SP and SD

***Q4’22 Ex-factory is preliminary estimate and not yet final. Q4’22 bottle count includes ~200 additional bottles due to increase in inventory**

~68% of patients in Q3’22 started at a reduced dose* **



*Reduced dose defined as fewer than 6 pills per day

** FDA approved dose-escalation label supplement in June 2021

Rest of World Partnerships – Timelines

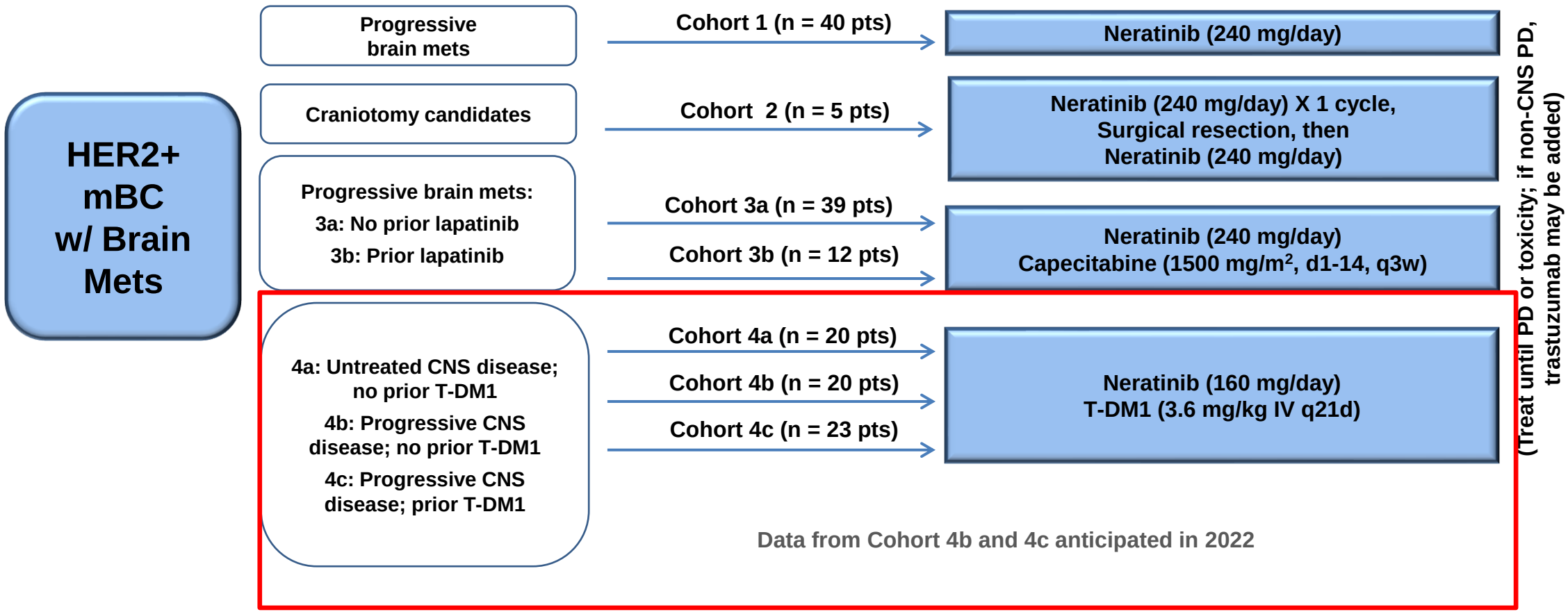
Region	Partner	Regulatory Approvals	Commercial Launches
Australia / SE Asia	Specialised Therapeutics	• 2019 – Ext. Adj. in Australia, Singapore • 2020 – Ext. Adj. in Brunei, Malaysia, New Zealand • Q2 2022 – Ext. Adj. in the Philippines • Q3 2022 – mBC in Singapore	• 2020 – Singapore • Q2 2021 – Malaysia • Q3 / Q4 2021 – Brunei, New Zealand
Israel	MEDISON	• 2020 – Approved in Ext. Adj. and mBC	• 2020 – Launched
Canada	Knight	• 2019 – Ext. Adj. approved • Q2 2021 – mBC approved	• 2020 – Launched
Latin America	PINT PHARMA	• 2019 – Ext Adj in Argentina • 2020 – Ext. Adj in Chile, Ecuador • 2020 – mBC in Argentina • 2021 – Ext Adj and mBC in Peru; mBC in Chile • Q4 2021 – Ext. Adj. in Brazil • Q1 2022 – Ext. Adj. in Mexico • Q3 2022 – mBC in Ecuador	• 2020 – Argentina • Q2 2021 – Chile • Q4 2021 – Peru • Q3 2022 – Brazil
Europe Greater China Middle East North and West Africa South Africa Turkey	Pierre Fabre	• 2019 – EMA approval • 2019 – Ext. Adj. in Hong Kong • 2020 – Ext. Adj. in China, Taiwan • Q4 2021 – mBC in Taiwan	• 2019 – Germany, UK, Austria • 2020 – Sweden, Finland, Scotland, Switzerland, Denmark • 2020 – Hong Kong • Q1 2021 – China (added to 2021 NRDL), Taiwan • Q1 2021 – Greece, Czech Republic • Q1 2022 – Ireland • Q3 2022 – Spain
South Korea	BIXINK THERAPEUTICS	• Q4 2021 – Ext. Adj. in S. Korea	• Q1 2022 – Launched

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 6,000 patients (US) with HR positive early stage HER2+ breast cancer and no pathological complete response to neoadjuvant treatment (high risk disease)
- Approximately 37,000 patients (EU) with early stage HER2+ breast cancer treated with adjuvant treatment[1]
  - Approximately 65–70% of patients have HR positive disease

[1]Roche epidemiology slides 09/18

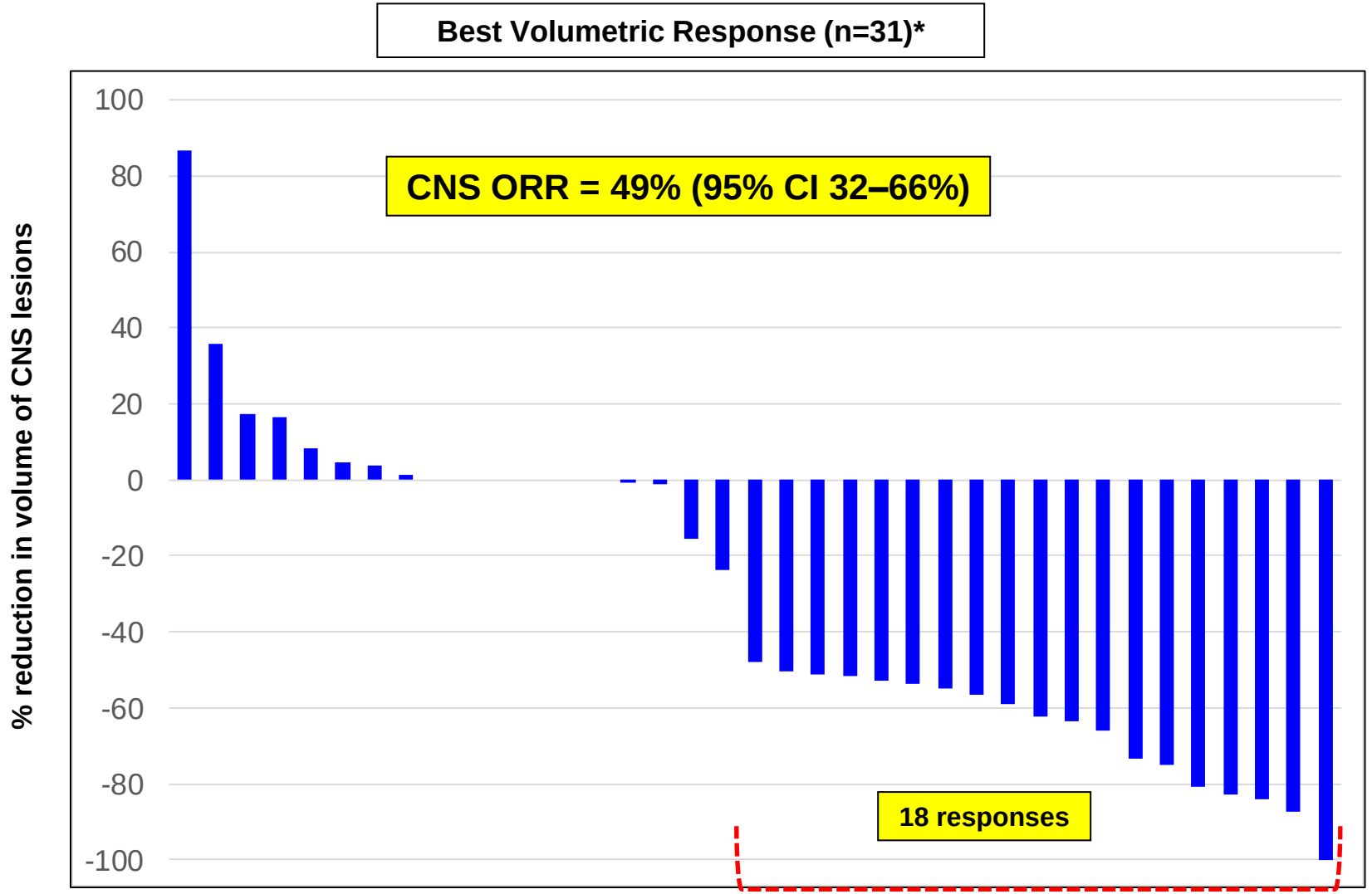
TBCRC 022: Phase II Trial of HKI-272 (Neratinib) for Patients with HER2+ Breast Cancer and Brain Metastases



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

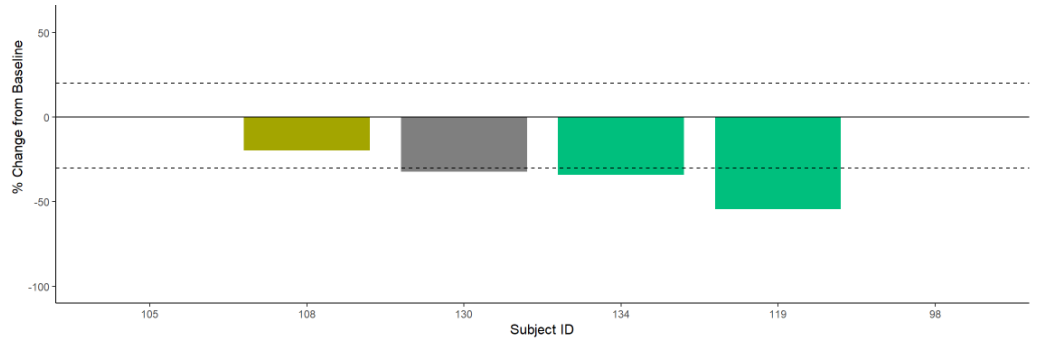
TBCRC-022 Cohort 3a
CNS Response



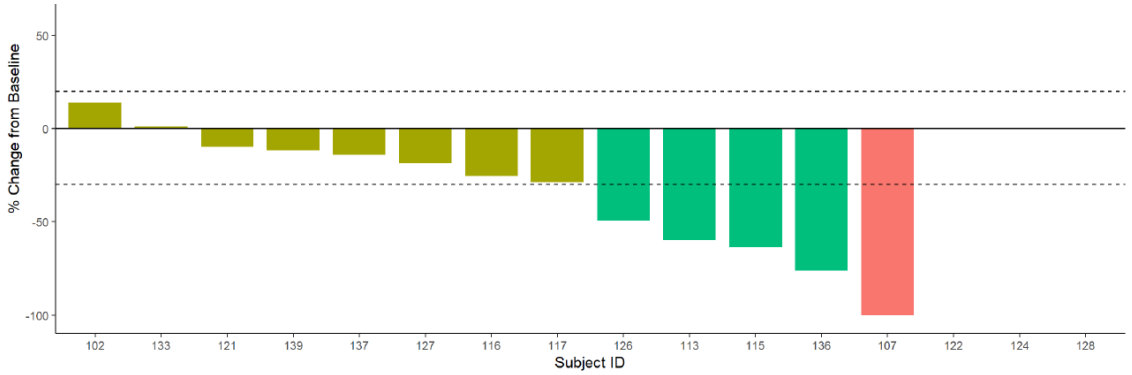
* ASCO 2017

TBCRC-022 Cohort 4
CNS Response*

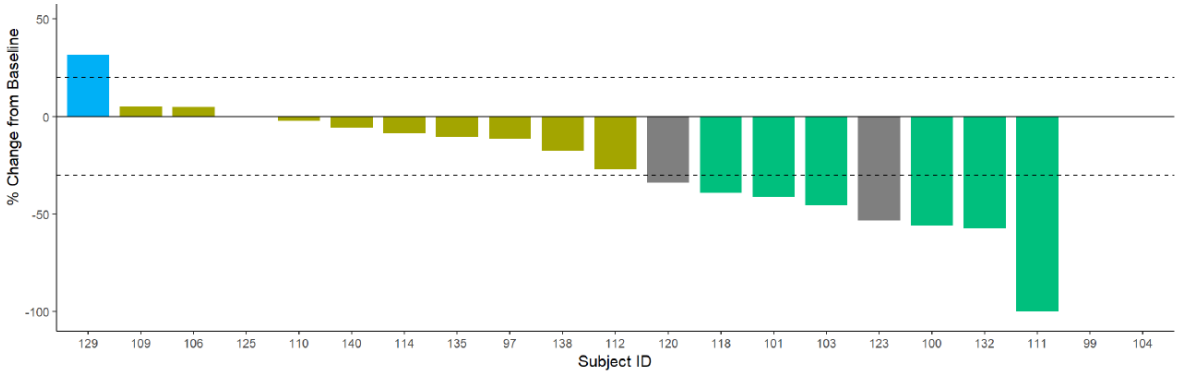
Cohort 4A

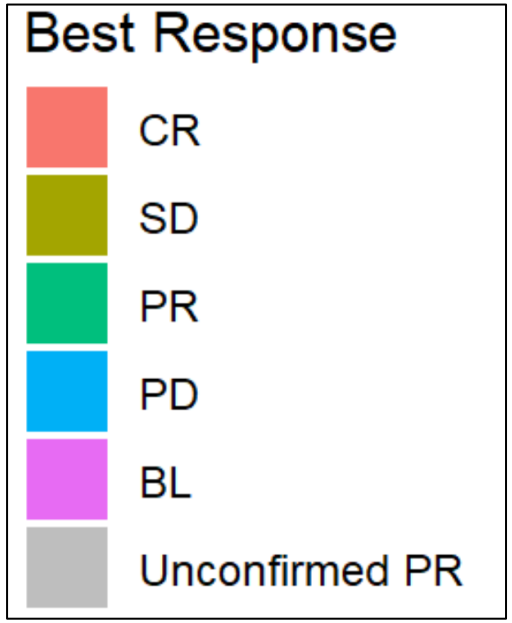


Cohort 4B



Cohort 4C





Neratinib 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)

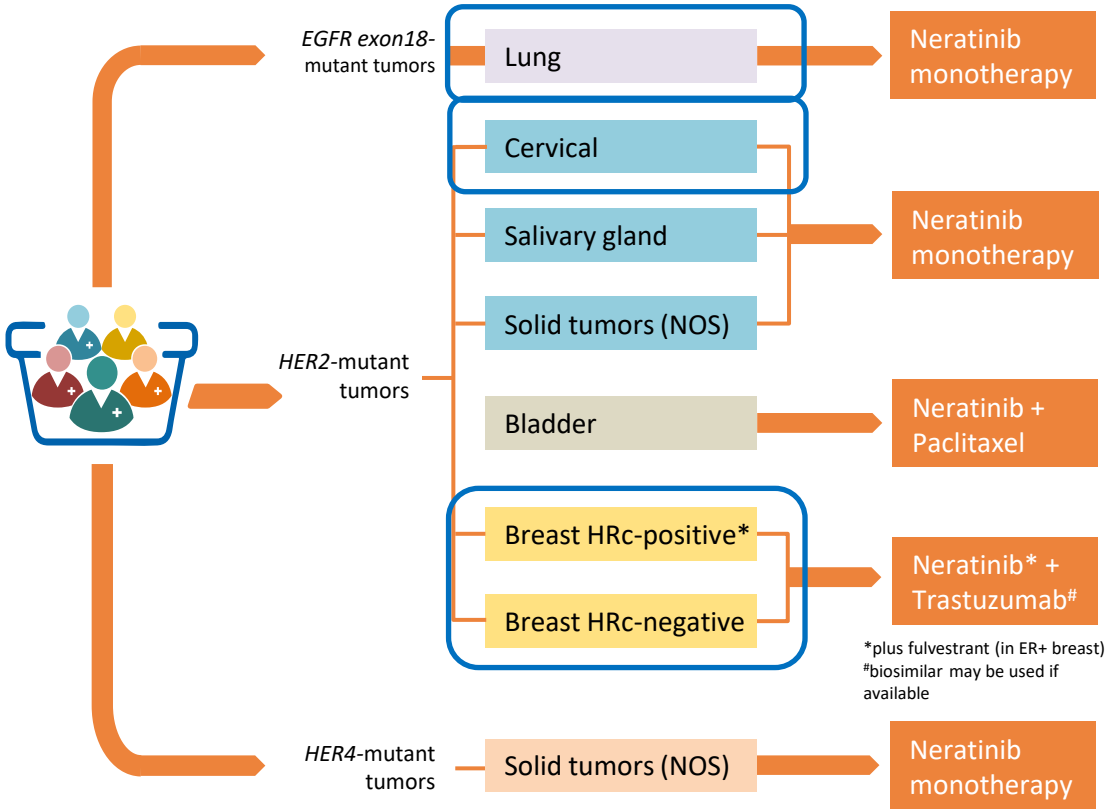
Category 2B: Neratinib + Paclitaxel

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

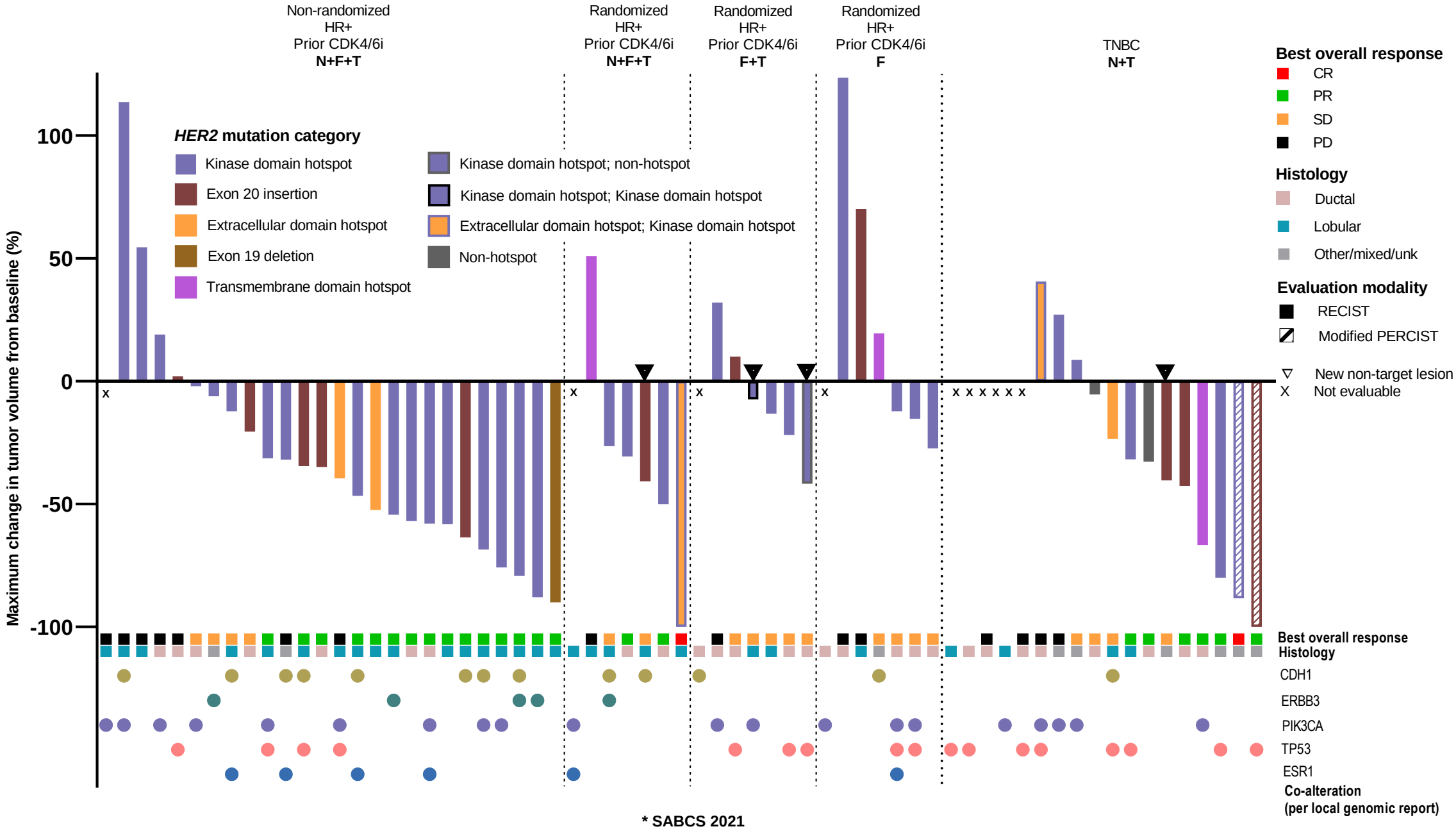
Key Exclusion Criteria
- Prior treatment with any pan-HER TKI (eg, lapatinib, afatinib, dacomitinib, neratinib)
- Patients who are receiving any other anticancer agents
- Symptomatic or unstable brain metastases
- Women who are pregnant or breast-feeding

SUMMIT

Breast Cancer Cohort

Puma Biotechnology

Change in tumor size (target lesion) and characteristics*



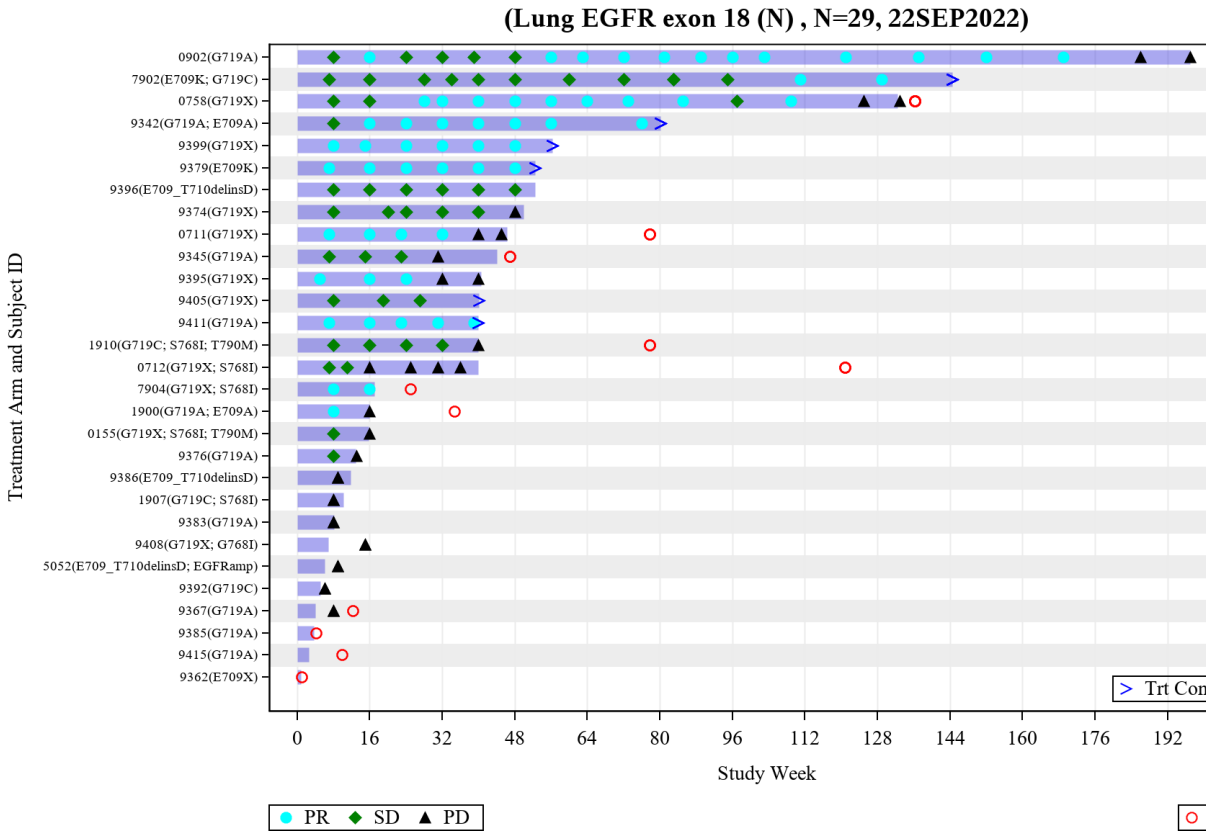
* SABCS 2021

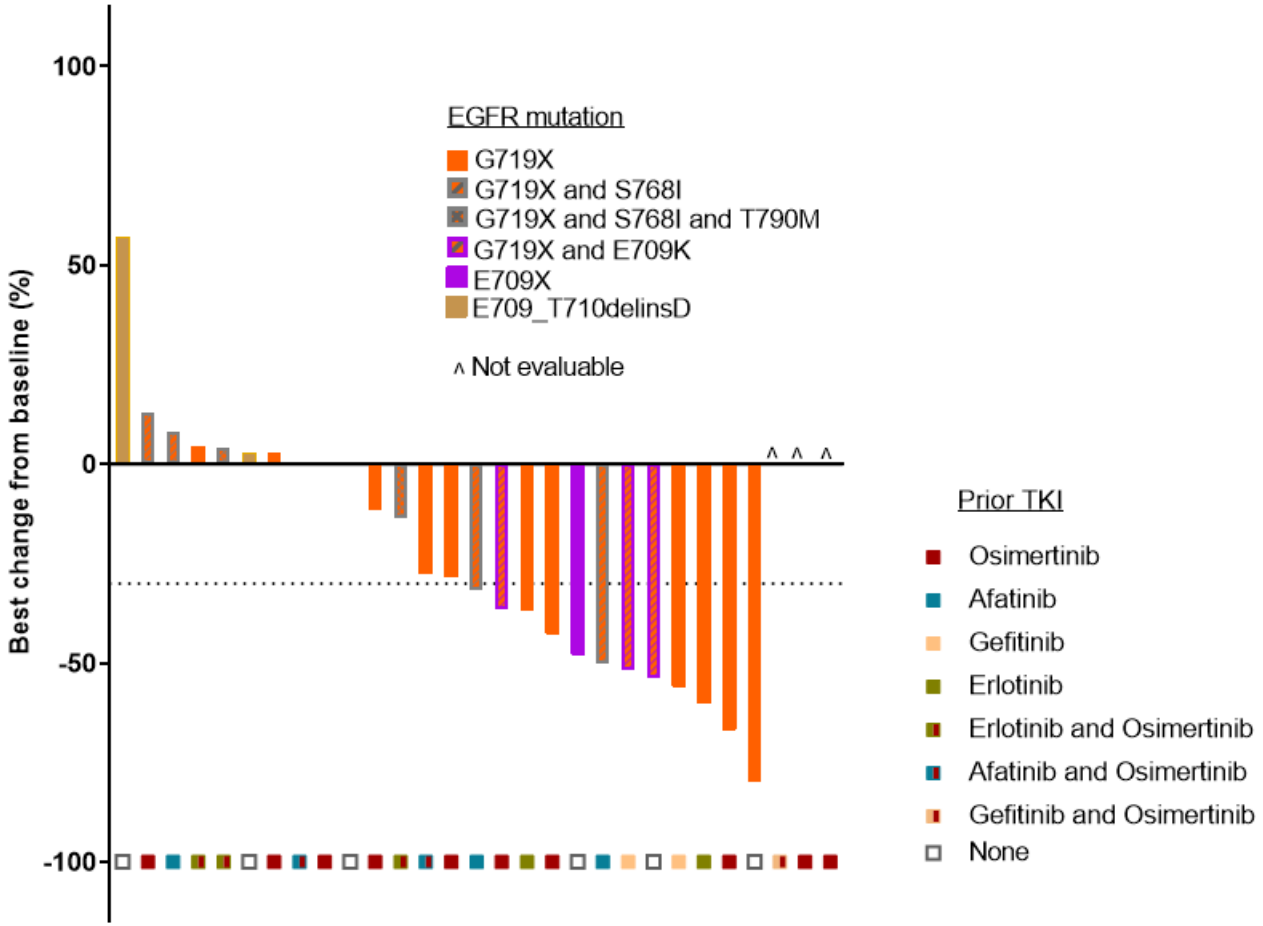
SUMMIT (PUMA-NER-5201) Basket Trial

EGFR exon 18 lung cancer cohort update

Puma Biotechnology

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





Data cutoff date: Sep 2022

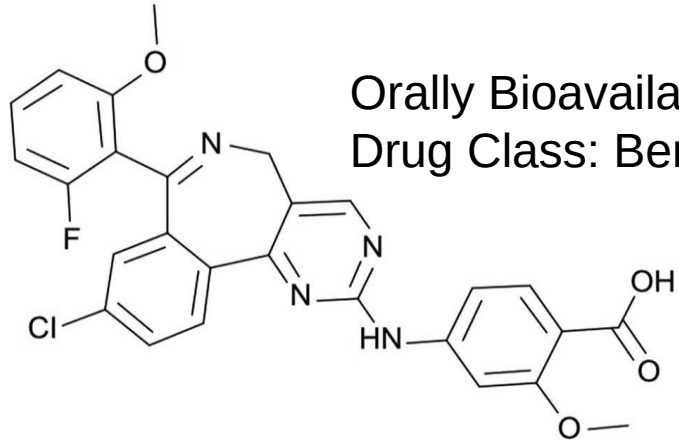
ALISERTIB

Breast Cancer and Small-Cell Lung Cancer

Puma Biotechnology

Alisertib (MLN 8237)

Aurora Kinase A (AURKA) inhibitor

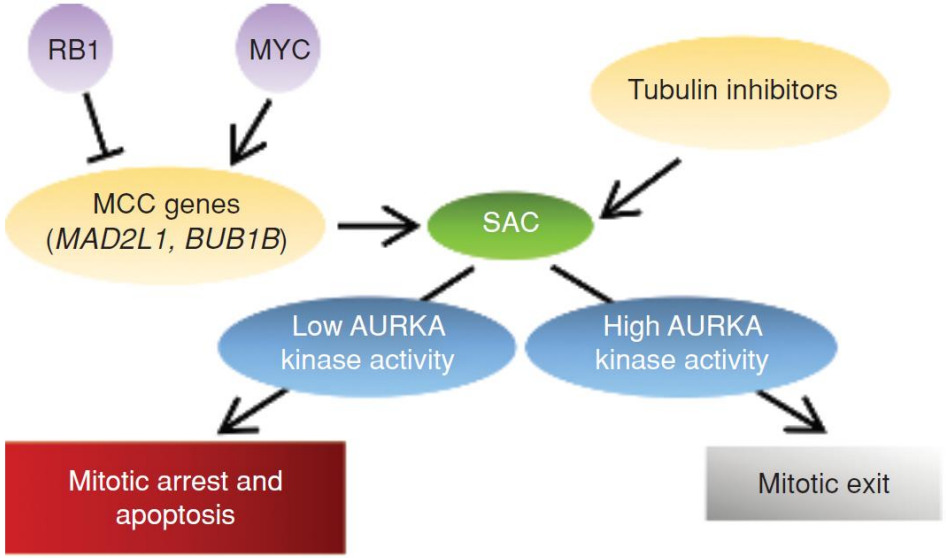


Orally Bioavailable
Drug Class: Benzazepine

- Single-agent and combinational clinical activity in solid tumors including hormone receptor-positive breast cancer (HR+ MBC), triple negative breast cancer (TNBC), small cell lung cancer (SCLC), and head and neck cancer
- Single-agent clinical activity in hematologic malignancies including peripheral T-cell lymphoma (PTCL) and aggressive non-Hodgkin's lympohoma (NHL)
- Well-characterized safety profile: ~1,300 patients treated across 22 company-sponsored trials

Synthetic Lethality of AURKA and Rb1

Cancers with a hypersensitive spindle assembly checkpoint (SAC) depend on AURKA for mitotic exit and survival[1]

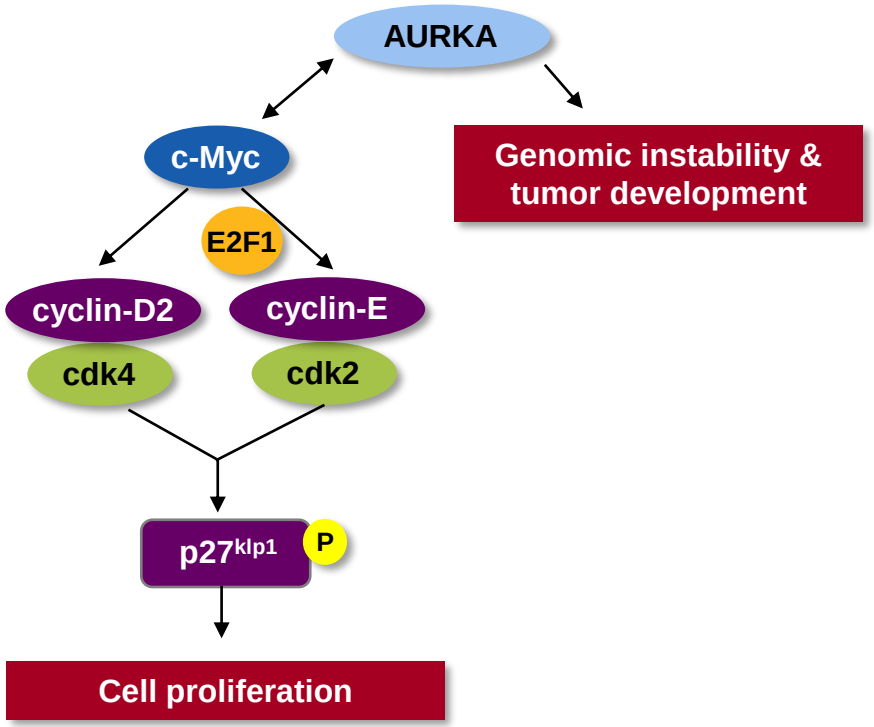


- Loss of function of Rb1 is a common event in cancer and can emerge as a mechanism of resistance to EGFR, CDK4, and ER-targeted therapies in breast and lung cancers
- Rb1 controls entry into S phase of mitosis, and loss of Rb1 function leads to a hyperactivated, primed, SAC
- Cancers with a hyperactivated SAC depend on AURKA in order to overcome SAC priming, which leads to stalled mitosis

[1]Dick F Cancer Discovery Feb 2019, Gong X Cancer Discov 2019

AURKA and c-Myc Co-regulate Each Other

Nuclear AURKA exerts kinase-independent functions by acting as a transcription factor



- AURKA and c-Myc transcriptionally upregulate each other, suggesting the existence of a positive feedback loop
- c-Myc upregulates Cyclin D2, CDK4, and cyclin-E, contributing to complex formation and subsequent phosphorylation of p27Kip1, which leads to cell proliferation

Naso FD Oncogene 2021, Tang A Oncotarget 2017

Clinical Experience in Small-Cell Lung Cancer

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- SCLC Cohorts

Study design:

- Pts had to have undergone ≤ 2 previous cytotoxic regimens, not including adjuvant or neoadjuvant treatments
- Alisertib administration: orally in 21-day cycles at 50 mg twice daily for 7 days followed by a break of 14 days
- 1° Endpoint: Objective Response Rate (RECIST 1.1)

	All (n=48)	Chemotherapy-sensitive relapse (n=36)	Refractory or chemotherapy-resistant relapse (n=12)
Median (range) number of cycles	2·0* (1–17)	3·5 (1–17)	2·0 (2–6)
Best response			
Objective response†	10 (21%) (10–35)	7 (19%)	3 (25%)
Stable disease	16 (33%) (20–48)	13 (36%)	3 (25%)
Stable disease for ≥6 months	2 (4%)	2 (6%)	0
Progressive disease	22 (46%) (31–61)	16 (44%)	6 (50%)
Duration of response (months)	4·1 (3·1–NE)	3·1	4·3
Progression-free survival (months)	2·1 (1·4–3·4)	2·6 (1·4–3·7)	1·7 (1·2–3·9)
Time to progression (months)	2·6 (1·4–3·8)	2·8 (1·4–3·9)	1·4 (1·2–4·4)

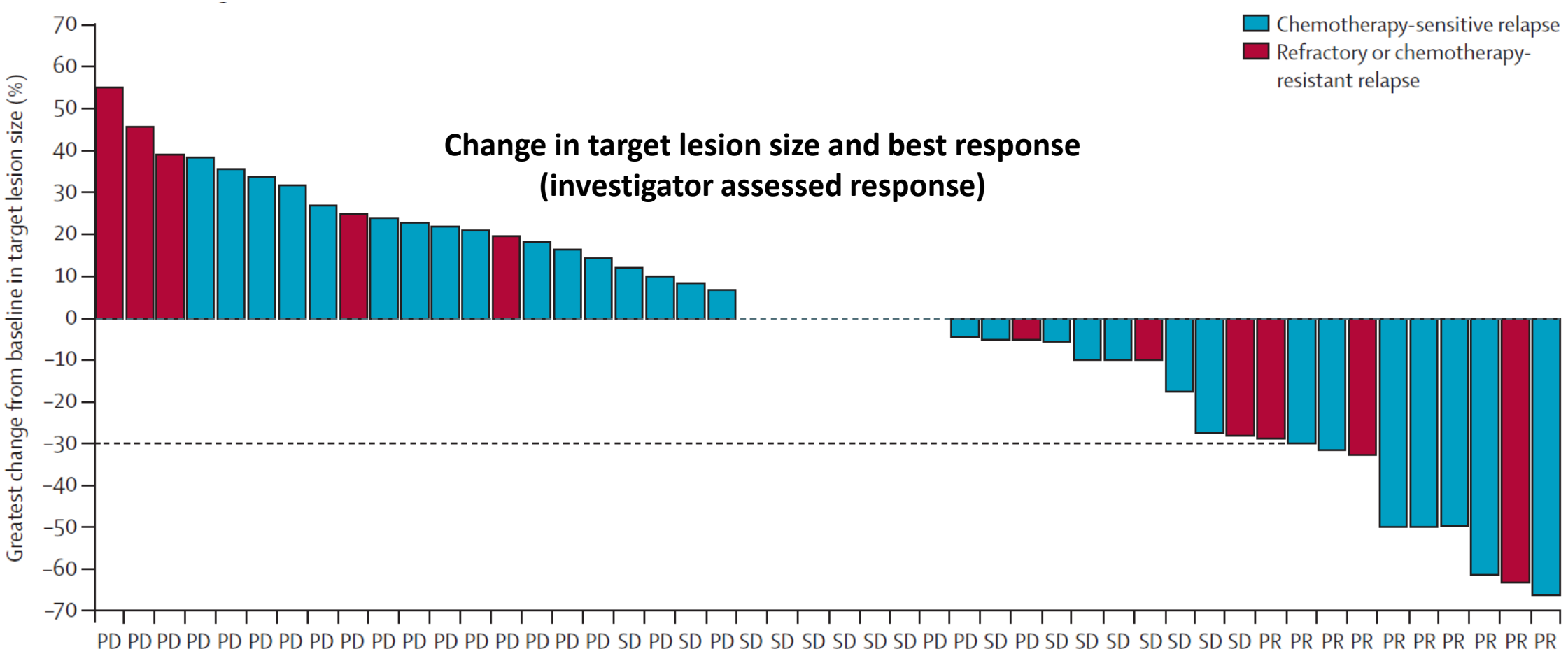
Table adapted from Melichar B Lancet Oncol 2015. Data are either number of patients (%) (95% CI), or median (95% CI), unless otherwise stated. NE=not estimable. *Safety population. †All were partial responses. All responses were based on investigator tumor assessments (RECIST v1.1).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- SCLC Cohorts

10 (21%; 95% CI 10–35) of 48 patients had an objective response; all responders achieved a partial response



PD=progressive disease. SD=stable disease. PR=partial response. Dotted line at –30% represents a partial response, according to RECIST 1.1 (investigator tumor assessments).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- SCLC Cohorts

All-cause adverse events in safety evaluable SCLC cohort (n=60)

	Grade 1–2	Grade 3–4
Any adverse event	14 (23%)	43 (72%)
Neutropenia	5 (8%)	22 (37%)
Fatigue	23 (38%)	5 (8%)
Anaemia	9 (15%)	10 (17%)
Alopecia	16 (27%)	NA
Diarrhoea	16 (27%)	2 (3%)
Nausea	18 (30%)	0
Leukopenia	4 (7%)	8 (13%)
Stomatitis	9 (15%)	4 (7%)
Decreased appetite	18 (30%)	0
Vomiting	10 (17%)	1 (2%)
Thrombocytopenia	5 (8%)	6 (10%)
Somnolence	8 (13%)	1 (2%)
Dyspnoea	10 (17%)	0
Constipation	5 (8%)	0
Pyrexia	4 (7%)	0
Peripheral oedema	4 (7%)	0
Headache	8 (13%)	1 (2%)
Insomnia	7 (12%)	0
Cough	5 (8%)	0
Asthenia	6 (10%)	1 (2%)
Dehydration	3 (5%)	3 (5%)

Table adapted from Melichar B Lancet Oncol 2015. Data are number of patients with AE (%) for AEs of any grade in at least 10% of patients overall. NA = not applicable

Melichar B Lancet Oncol 2015

Grade 3-4 AEs Present in ≥ 10% of SCLC Patients - alisertib monotherapy compared to lurbinectedin monotherapy

	Alisertib (n=60)[1]		Lurbinectedin (n=105)[2]	
AE	**All grade, n (%)**	**Grade 3-4, n (%)**	**All grade, n (%)**	**Grade 3-4, n (%)**
Neutropenia	27 (45%)	22 (37%)	75 (71%)	48 (46%)
Anemia	19 (32%)	10 (17%)	100 (95%)	9 (9%)
Leukopenia	12 (20%)	8 (13%)	83 (79%)	30 (29%)
Thrombocytopenia	11 (18%)	6 (10%)	46 (44%)	7 (7%)

1. alisertib: 50 mg BID; 21-day cycle, 7 days followed by 14-day break

[1]Melichar B Lancet Oncol 2015, [2]Trigo Lancet Oncol 2020

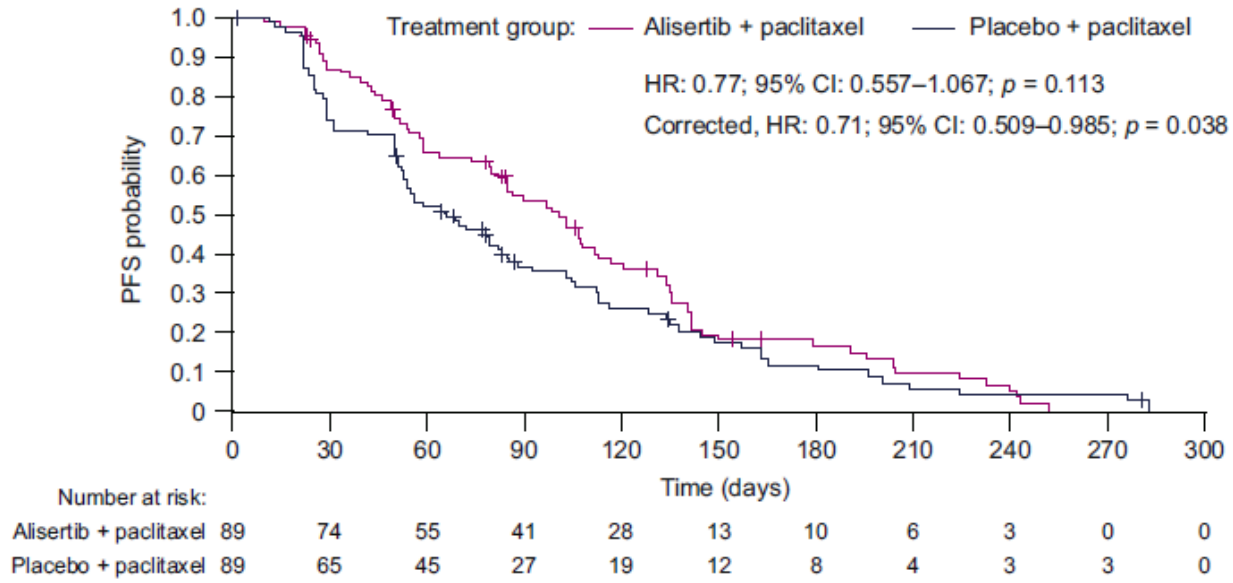
Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Primary Analysis

Study design:

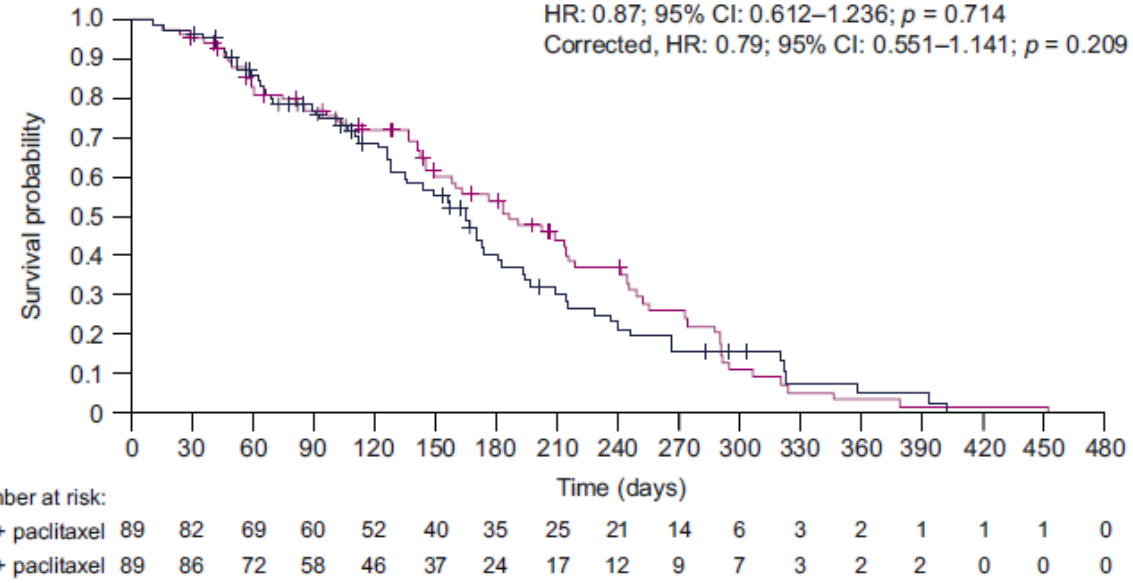
- Patients with relapsed or refractory SCLC stratified by relapse type (sensitive vs resistant or refractory)
- Randomized 1:1 to alisertib + paclitaxel or placebo + paclitaxel in 28-day cycles
- Alisertib (40 mg BID for 3 weeks on days 1–3, 8–10, and 15–17) plus paclitaxel (60 mg/m2 intravenously on days 1, 8, and 15) or placebo plus paclitaxel (80 mg/m2 intravenously on days 1, 8, and 15) in 28-day cycles
- 1° endpoint PFS

Biomarkers: associations between c-Myc expression in tumor tissue (prespecified) and genetic alterations in ctDNA (retrospective) with clinical outcome

PFS in ITT



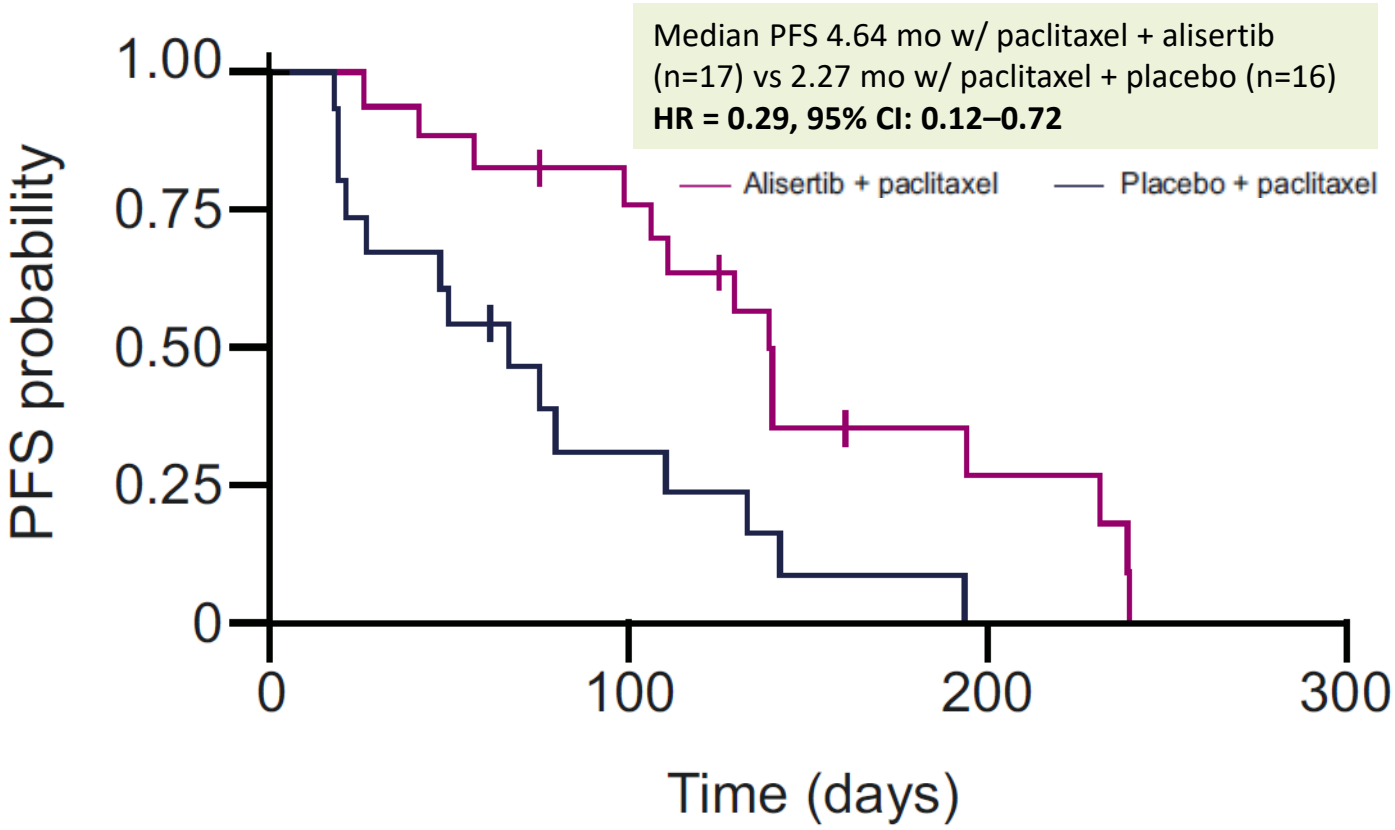
OS in ITT



Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Correlative Biomarker Analysis

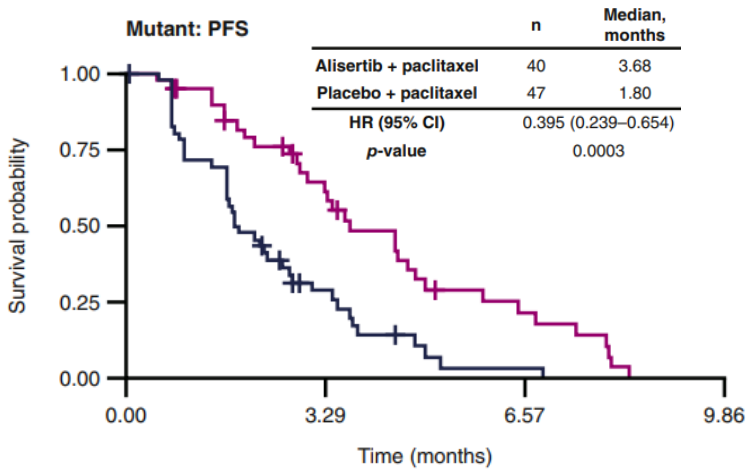
Improved PFS observed among patients positive versus negative for *c-Myc* expression

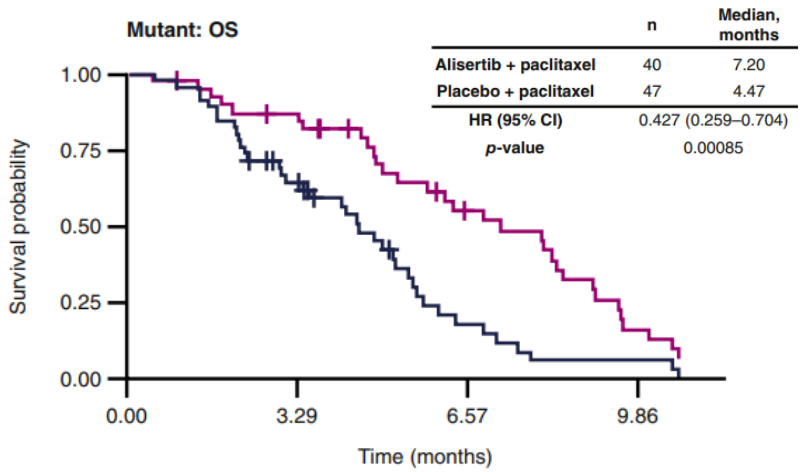
PFS in patients positive for *c-Myc* expression

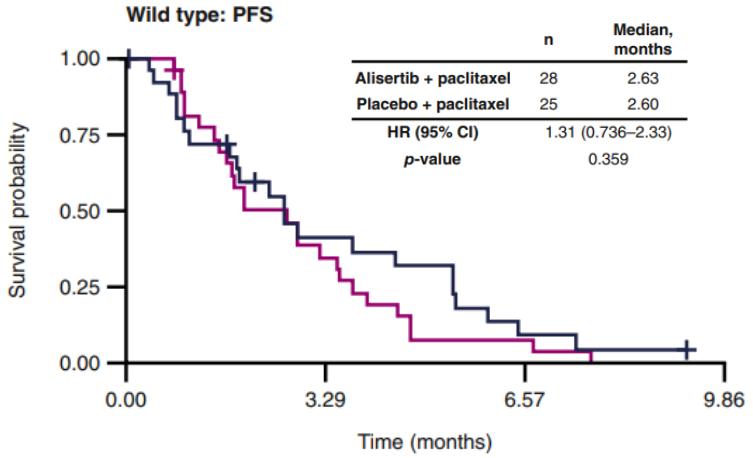


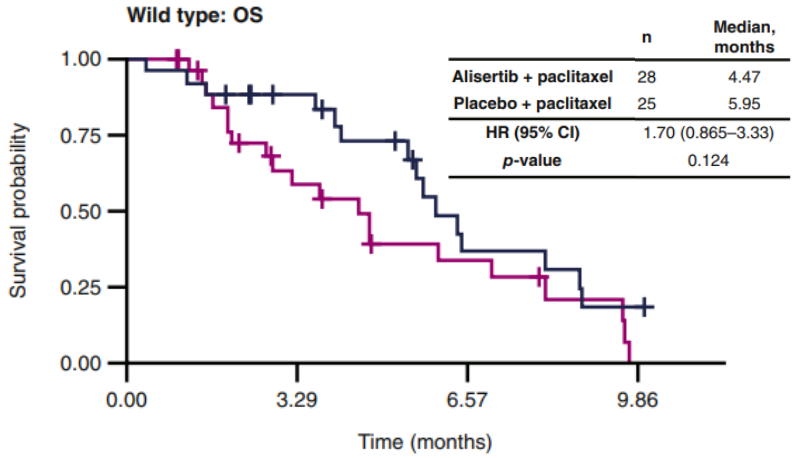
Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Correlative Biomarker Analysis

Improved outcomes among pts with genetic alternations in cell cycle genes *CDK6*, *RBL1*, *RBL2*, and *RB1* (collectively referred to as "mutant")









Owonikoko J Thorac Oncol 2020

Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Safety

Table 3. Most Frequently Reported All-Cause and Drug-Related Treatment-Emergent AEs, Occurring in at Least 15% (All-Cause) or at Least 10% (Drug-Related) of Patients Overall (Any Grade) in Either Arm, Respectively, with the Corresponding Grade 3 or higher AEs (Safety Population), and All Drug-Related Fatal AEs

	Alisertib/Paclitaxel (n = 87)		Placebo/Paclitaxel (n = 89)	
AE	Any Grade	Grade ≥3	Any Grade	Grade ≥3
All-cause AE, n (%)	86 (99)	66 (76)	85 (96)	45 (51)
Diarrhea	51 (59)	14 (16)	18 (20)	1 (1)
Fatigue	38 (44)	9 (10)	29 (33)	5 (6)
Nausea	29 (33)	2 (2)	30 (34)	4 (4)
Anemia	38 (44)	12 (14)	18 (20)	3 (3)
Neutropenia	43 (49)	35 (40)	7 (8)	5 (6)
Vomiting	28 (32)	2 (2)	21 (24)	3 (3)
Decreased appetite	29 (33)	3 (3)	19 (21)	3 (3)
Dyspnea	21 (24)	4 (5)	19 (21)	2 (2)
Stomatitis	29 (33)	12 (14)	6 (7)	2 (2)
Cough	17 (20)	0	17 (19)	0
Constipation	8 (9)	1 (1)	21 (24)	0
Asthenia	14 (16)	3 (3)	11 (12)	0
Dizziness	14 (16)	0	8 (9)	0
Alopecia	14 (16)	0	5 (6)	0
Leukopenia	13 (15)	7 (8)	5 (6)	2 (2)
Decreased neutrophil count	14 (16)	11 (13)	4 (4)	1 (1)
Weight decreased	13 (15)	0	5 (6)	0
Drug-related fatal AE, n (%)				
Neutropenic sepsis	–	1 (1)	–	0
Sepsis	–	1 (1)	–	0
Febrile neutropenia	–	1 (1)	–	0
Septic shock	–	1 (1)	–	0

AE, adverse event

Owonikoko J Thorac Oncol 2020

Clinical Studies of Alisertib in Breast Cancer

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- Breast Cancer Cohorts

Study design:

- Pts had to have undergone ≤ 2 previous cytotoxic regimens, not including adjuvant or neoadjuvant treatments
- Alisertib administered orally in 21-day cycles at 50 mg twice daily for 7 days followed by a break of 14 days
- 1° Endpoint: Objective Response Rate (RECIST 1.1)

	All (n=49)	Hormone receptor-positive and HER2-negative (n=26)	HER2-positive (n=9)	Triple negative (n=14)
Median (range) number of cycles	4·0* (1–23)	8·0 (1–23)	6·0 (1–19)	2·0 (1–14)
Best response				
Objective response†	9 (18%) (9–32)	6 (23%)	2‡ (22%)	1 (7%)
Stable disease	25 (51%) (36–66)	17 (65%)	3 (33%)	5 (36%)
Stable disease for ≥6 months	10 (20%)	8 (31%)	1 (11%)	1 (7%)
Progressive disease	15 (31%) (18–45)	3 (12%)	4 (44%)	8 (57%)
Duration of response (months)	5·6 (2·8–12·0)	4·2	11·2	4·2
Progression-free survival (months)	5·4 (2·6–7·9)	7·9 (4·2–12·2)	4·1 (0·95–15·0)	1·5 (1·2–3·2)
Time to progression (months)	5·4 (2·6–7·9)	7·9 (4·2–12·2)	4·1 (0·95–15·0)	1·5 (1·2–3·2)

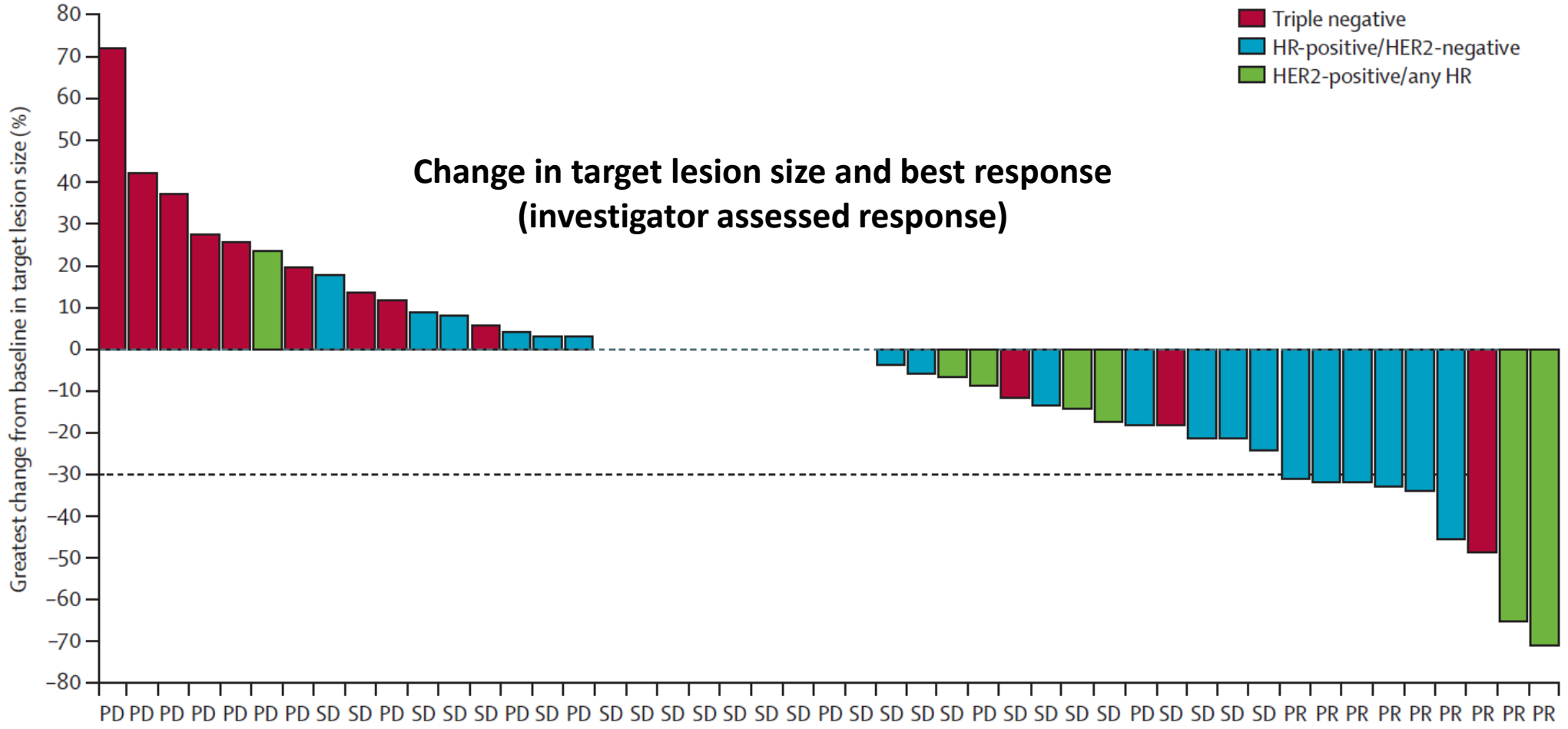
Data are either number of patients (%) (95% CI), or median (95% CI), unless otherwise stated. For the breast cancer subgroup, numbers of patients were too small to calculate 95% CIs. *Safety population. †All were partial responses. . ‡ These two patients had the only hormone receptor-negative tumors in the cohort. All responses were based on investigator tumor assessments (RECIST v1.1).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- Breast Cancer Cohorts

9 / 49 patients (18%; 95% CI 9–32) had an objective response; all responders achieved a partial response



PD=progressive disease. SD=stable disease. PR=partial response. Dotted line at –30% represents a partial response, according to RECIST 1.1 (investigator tumor assessments).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- Breast Cancer Cohorts

All-cause adverse events in safety evaluable breast cancer cohort (n=53)

	Grade 1-2	Grade 3-4
Any adverse event	8 (15%)	44 (83%)
Neutropenia	3 (6%)	30 (57%)
Fatigue	23 (43%)	6 (11%)
Anaemia	17 (32%)	4 (8%)
Alopecia	26 (49%)	NA
Diarrhoea	25 (47%)	2 (4%)
Nausea	15 (28%)	2 (4%)
Leukopenia	5 (9%)	19 (36%)
Stomatitis	16 (30%)	8 (15%)
Decreased appetite	13 (25%)	0
Vomiting	11 (21%)	1 (2%)
Thrombocytopenia	8 (15%)	4 (8%)
Somnolence	14 (26%)	1 (2%)
Dyspnoea	9 (17%)	3 (6%)
Constipation	9 (17%)	0
Pyrexia	4 (8%)	1 (2%)
Peripheral oedema	9 (17%)	0
Headache	11 (21%)	0
Insomnia	6 (11%)	0
Cough	8 (15%)	1 (2%)
Asthenia	2 (4%)	3 (6%)
Dehydration	5 (9%)	3 (6%)

Table adapted from Melichar B Lancet Oncol 2015. Data are number of patients with AE (%) for AEs of any grade in at least 10% of patients overall. NA = not applicable

Melichar B Lancet Oncol 2015

Phase 2 Randomized Trial of Alisertib + Fulvestrant vs Alisertib in Advanced HR+ Breast Cancer

Patients (n=96)

Inclusion Criteria

- Post-menopausal women
- Histologically-proven ER+ (>10% expression) and HER2 negative
- No more than two prior chemotherapy regimens
- Prior treatment with fulvestrant in the metastatic setting required
- Disease that is measurable as defined by the RECIST criteria

Regimen & Schedule

- **Alisertib + Fulvestrant**: Alisertib 50 mg PO BID on days 1-3, 8-10, 15-17 q 28-day cycle with fulvestrant 500 mg IM on days 1 and 15 of cycle 1 then day 1 of all subsequent cycles
- **Alisertib Alone**: Alisertib 50 mg PO BID on days 1-3, 8-10, 15-17 q 28-day cycle

Patient Characteristics

	Alisertib (n=45)	Alisertib + Fulvestrant (n=45)
Prior Chemotherapy		
(Neo)Adjuvant Setting	27 (60.0%)	27 (60.0%)
Metastatic Setting	21 (46.7%)	31 (69.9%)
Prior Adjuvant Endocrine Therapy		
Aromatase Inhibitor	24 (53.3%)	20 (44.4%)
Tamoxifen	14 (31.1%)	22 (48.8%)
Fulvestrant	7 (15.5%)	2 (4.4%)
Prior Endocrine Therapy for MBC		
Anastrozole/Letrozole	26 (57.8%)	35 (77.8%)
Exemestane	15 (33.3%)	26 (57.8%)
Fulvestrant	44 (97.8%)	45 (100.0%)
Prior Targeted Therapy for MBC		
CDK 4/6 inhibitor	45 (100%)	45 (100%)
Everolimus	16 (35.6%)	26 (57.8%)

Clinical Outcomes

	Alisertib (n=45)	Alisertib + Fulvestrant (n=45)
Confirmed Responses	8 PR	1 CR; 8 PR
Objective Response Rate	17.8% (90% CI: 9.2-29.8%)	20.0% (90% CI: 10.9-32.3%)
Clinical Benefit Rate (24-week)	42.2% (90% CI: 29.7-55.6%)	28.9% (90% CI: 18.0-42.0%)
Median PFS (months)	5.6 (95%CI: 3.9 – 9.3)	5.1 (95%CI: 3.8 – 7.6)
Deaths 6-month OS rate	n=10 90. 6% (95% CI: 82.2-99.8%)	n=14 75.6% (95% CI: 63.9-90.2%)

Phase 2 Randomized Trial of Alisertib + Fulvestrant vs Alisertib in Advanced HR+ Breast Cancer

Safety				
	Alisertib (n=45)		Alisertib + Fulvestrant (n=45)	
	G3	G4	G3	G4
Hematologic Adverse Events				
Anemia	13%	2%	9%	0%
Lymphocyte Count Decreased	2%	0%	13%	0%
Neutropenia Count Decreased	24%	18%	20%	22%
White Blood Cell Count Decreased	13%	4%	22%	9%
Non-Hematologic Adverse Events				
Fatigue	0%	0%	11%	0%

Reason for Treatment Discontinuation	Alisertib* (n=45)	Alisertib + Fulvestrant (n=45)
Disease progression	28	28
Intolerability	2	6
Patient Refusal	0	4
Physician Decision	1	0
Second Primary	0	1
Death	2	1

*Discontinuation of monotherapy

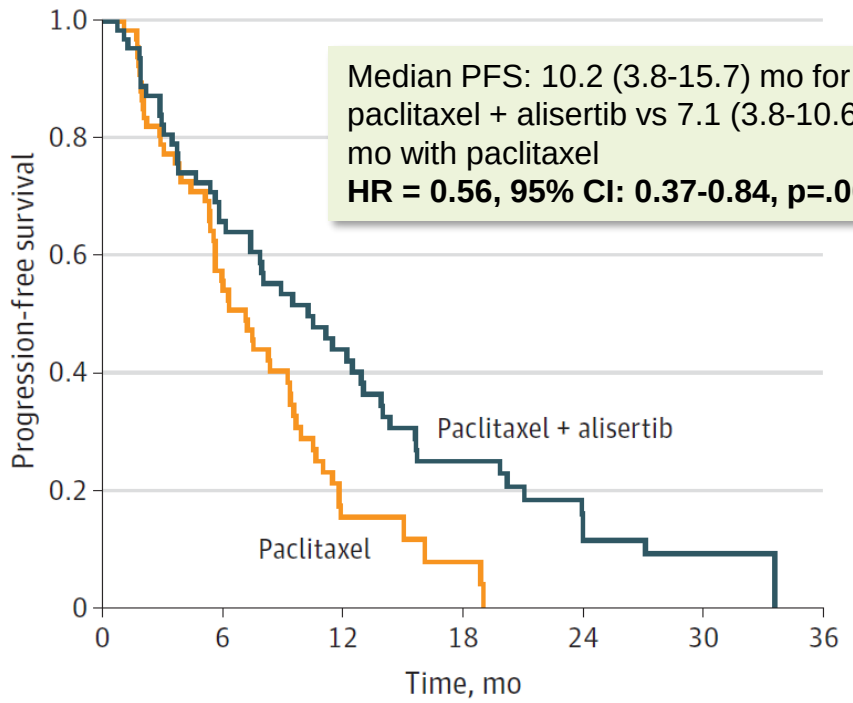
Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

- Efficacy in ER+/HER2- MBC Cohort

Study design:

- Patients with ER+/HER2- or triple negative metastatic breast cancer stratified by prior neo or adjuvant taxane and by line of metastatic therapy
- Randomized 1:1 to paclitaxel + alisertib or paclitaxel alone in 28-day cycles
- Paclitaxel 60mg/m2 intravenously (IV) on days 1, 8, and 15 plus alisertib 40 mg twice daily on days 1 to 3, 8 to 10, and 15 to 17 of a 28-day cycle or to single agent paclitaxel 90mg/m2 IV on days 1, 8, and 15 of a 28-day cycle
- 1° endpoint PFS

PFS in ER+/HER2- ITT



No. at risk							
Paclitaxel + alisertib	69	39	23	12	5	2	0
Paclitaxel	70	32	8	2	0		

Median OS: 26.3 (12.4-37.2) mo for paclitaxel + alisertib vs 25.1 (11.0-31.4) mo for paclitaxel (HR, 0.89; 95%CI, 0.58-1.38; *P* = .61)

O'Shaughnessy J JAMA Netw Open 2021

Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

- Efficacy in ER+/HER2- MBC Cohort Pretreated with Palbociclib

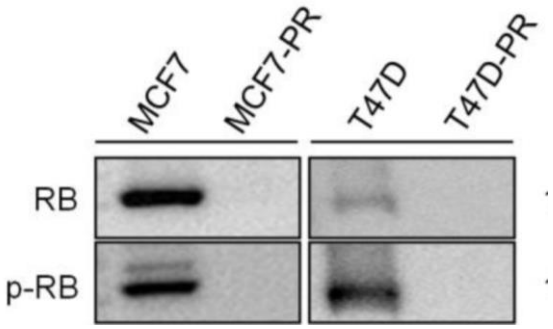
Efficacy in patients pretreated with palbociclib (n=30)

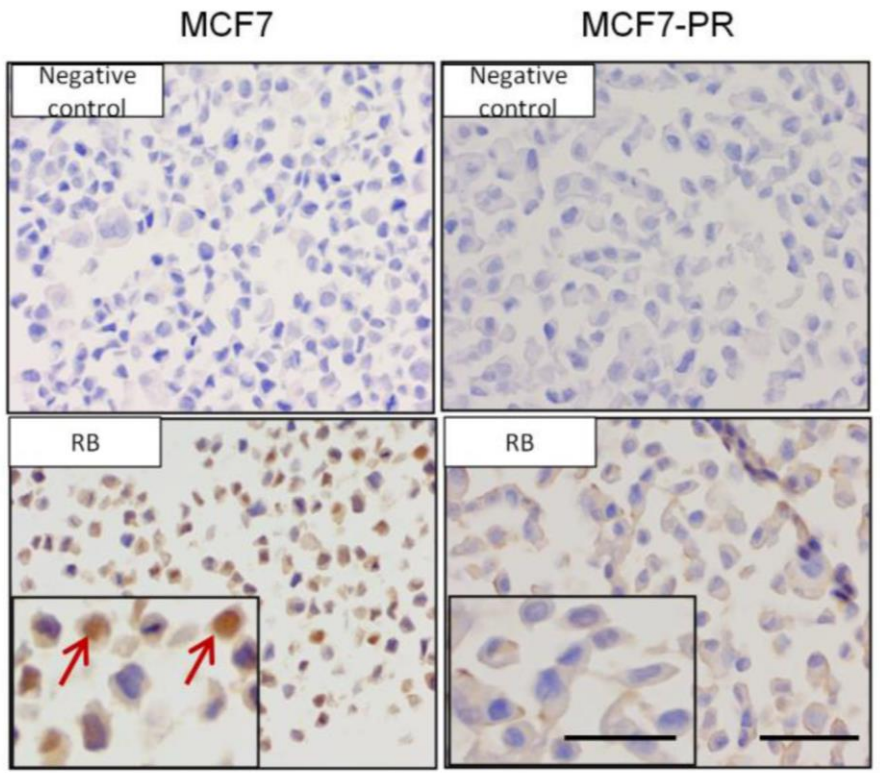
- Median PFS: 13.9 (5.6-15.6) mo (14 pts) w/ paclitaxel + alisertib vs 5.6 (3.0-10.6) mo (16 pts) w/ paclitaxel alone (HR, 0.58; 95%CI, 0.26-1.32; *P* = .19)
- CBR: 61.5% w/ paclitaxel + alisertib (95%CI,31.6%-86.1%) vs 37.5% (95%CI, 15.2%-64.6%) w/ paclitaxel alone

Rb1 Loss and *c-Myc* Upregulation Correlate with Palbociclib Resistance

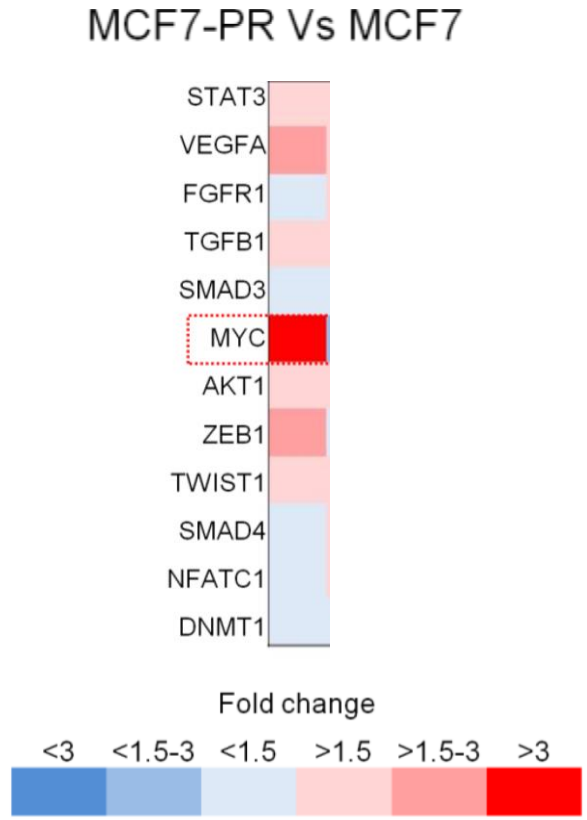
Both RB1 loss and MYC upregulation were observed in palbociclib-resistant HR+ breast cancer cell lines, supporting a role for alisertib in this setting

RB1 Loss





C-Myc Upregulation



Summary of Alisertib Efficacy in Metastatic Breast Cancer

Tumor Type	Active Regimen			Comparator			Reference
	Regimen (N)	N	Median PFS (mo, 95% CI)	Regimen (N)	N	Median PFS (mo, 95% CI)	
HR+/HER2-	alisertib 50 mg BID[1]	26	7.9 (4.2-12.2)	NA		NA	Melichar B Lancet Oncol 2015
ER+/HER2-	alisertib 50 mg BID[2]	45	5.6 (3.9-9.3)	alisertib 50 mg BID[2] + fulvestrant	45	5.1 (3.8-7.6)	Haddad SABCS 2020 PD2-05
ER+/HER2-	paclitaxel 60mg/m2[3] IV + alisertib 40 mg BID[2]	69	10.2 (3.8-15.7)	paclitaxel 90mg/m2 IV[3]	70	7.1 (3.8-10.6)	O'Shaughnessy JAMA Netw Open 2021
ER+/HER2-, Palbociclib pretreated	paclitaxel 60mg/m2[3] IV + alisertib 40 mg BID[2]	14	13.9 (5.6-15.6)	paclitaxel 90mg/m2 IV[3]	16	5.6 (3.0-10.6)	O'Shaughnessy JAMA Netw Open 2021
TNBC	paclitaxel 60mg/m2[3] IV + alisertib 40 mg BID[2]	19	9.6 (6.1-22.6)	paclitaxel 90mg/m2 IV[3]	16	5.7 (2.9-8.2)	O'Shaughnessy JAMA Netw Open 2021

1. alisertib: 21-day cycle, 7 days followed by 14-day break, 2. alisertib: 28-day cycle, on days 1-3, 8-10, 15-17, 3. paclitaxel: 28-day cycle on days 1, 8, and 15

Study-related Neutropenia in Metastatic Breast Cancer - Alisertib compared to other agents

Regimen	All-grade Neutropenia (%)	Grade 3/4 Neutropenia (%)	Febrile Neutropenia (%)
Alisertib monotherapy 50 mg BID[1]	63%[1]	57%[1]	4%[1]
Alisertib monotherapy 50 mg BID[2]	Not reported[2]	42%[2]	Not reported[2]
Alisertib 50 mg BID + fulvestrant[2]	Not reported	42%	Not reported
Alisertib 40 mg BID + paclitaxel[3]	67.9%	59.5%	1.2%
Eribulin mesylate (HALAVEN)[4]	82%	57%	5%
Physician's Choice of Chemotherapy[5]	51.2%	40.7%	Not reported
Palbociclib (IBRANCE)[6] + fulvestrant (PALOMA-3) or letrazole (PALOMA-2)	P+F: 83% P+L: 80%	P+F: 66% P+L: 66%	P+F: 0.9% P+L: 2.5%
Sacituzumab govitecan (TRODELVY)[7] for ER+	70%	51% (G ≥3 neutropenia)	5%
Sacituzumab govitecan (TRODELVY)[8] for TNBC	64%	52%	6%

1. alisertib: 21-day cycle, 7 days followed by 14-day break, 2. alisertib: 28-day cycle, on days 1-3, 8-10, 15-17, 3. paclitaxel: 28-day cycle on days 1, 8, and 15

Alisertib-associated neutropenia is thought to be cumulative and possibly can be managed/reduced with G-CSFs for prophylaxis of neutropenia per NCCN Guidelines[9]

[1]Melichar B Lancet Oncol 2015, [2]Haddad SABCS 2020 PD2-05, [3]O'Shaughnessy J JAMA Netw Open 2021, [4]HALAVEN USPI, [5]Modi S N Engl J Med 2022, [6]IBRANCE USPI, [7]Rugo HS ASCO 2022, [8]TRODELVY USPI, [9]NCCN Guideline Hematopoietic Growth Factors Version 1.2022

Overview of Alisertib Clinical Development Plan

Target Patient Population(s)	Rationale for Selected Indication	Potential Biomarker-defined Subgroups
HR+/HER2- metastatic breast cancer (MBC)	• Prior Clinical Data • Puma experience in breast cancer	• *c-Myc* amplification • Rb1 deficiency
Small Cell Lung Cancer (SCLC)	• Prior Clinical Data	

Puma plans to meet with FDA to discuss alisertib clinical development plan and Project Optimus in H1 2023

Puma – Expected Milestones

- Publication of the biomarker studies from the randomized trial of alisertib plus fulvestrant versus alisertib alone in hormone receptor-positive, HER2-negative breast cancer (H1 2023)
- Biomarker data from the randomized trial of alisertib plus paclitaxel versus paclitaxel alone in hormone receptor-positive, HER2-negative breast cancer (H1 2023)
- Report data from an ongoing investigator sponsored Phase I/II trial of alisertib plus pembrolizumab for the treatment of patients with Rb-deficient head and neck squamous cell cancer (2023)
- Conduct a meeting with the FDA to discuss the registration pathway of neratinib in HER2-mutated HR-positive breast cancer (H1 2023)
- Conduct a 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 (H1 2023)
- Conduct a meeting with the FDA to discuss the registration pathway for alisertib in hormone receptor positive, HER2-negative breast cancer and small cell lung cancer (H1 2023)

Experienced Management Team

Alan H. Auerbach
Chairman, Chief Executive Officer, President, Founder
- *Chief Executive Officer, President, Founder, Cougar Biotechnology*

Jeff Ludwig
Chief Commercial Officer
- *Eli Lilly, Astellas, Amgen*

Maximo F. Nougues
Chief Financial Officer
- *Getinge AB, Boston Scientific, The Clorox Company*

Alvin Wong, Pharma.D.
Chief Scientific Officer
- *Proteolix, Novacea, Genentech*

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.

Alessandra Cesano, MD, PhD
Chief Medical Officer, ESSA Pharmaceuticals; NanoString; Cleave Biosciences; Nodality; Amgen; Biogen; SmithKline

Allison Dorval
CFO, Verve Therapeutics; Former CFO Voyager Therapeutics, Inc.; VP and Controller, Juniper Pharmaceuticals, Inc.

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

Jay Moyes
CFO, Sera Prognostics, Inc.; Former CFO, Myriad Genetics

Adrian Senderowicz, MD
Senior Advisor and former SVP and 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, 2022: $78 million
- Net loss in Q3 2022: $0.4 million
- Cash earned in Q3 2022: $17.4 million
- Private placements:
  - March 2022: 3,584,228 shares issued to Alan Auerbach and Athyrium Capital Management
  - December 2022: 568,181 shares issued to Alan Auerbach
- Shares issued and outstanding: 46.3 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
- Retain full U.S. commercial rights to NERLYNX®
- Clinical activity demonstrated for alisertib in Phase 2 clinical trials in HR-positive, HER2-negative breast cancer, Triple Negative Breast Cancer (TNBC), Small Cell Lung Cancer (SCLC)
- Potential for novel biomarker directed commercial opportunities with alisertib compared to other marketed drugs and drugs in development

Puma Biotechnology

B. Riley Securities 3rd Annual Oncology Conference

January 2023