Puma Biotechnology
Alisertib Exclusive License Agreement

September 20, 2022

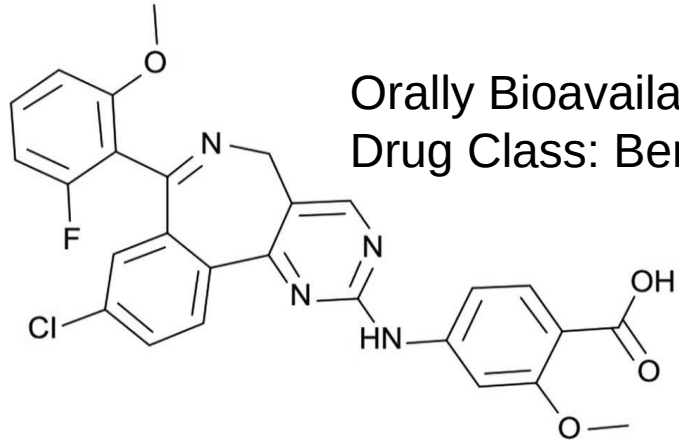
Forward-Looking Safe-Harbor Statement

This presentation contains forward-looking statements, including statements regarding 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

Alisertib (MLN 8237)

Aurora Kinase A (AURKA) inhibitor

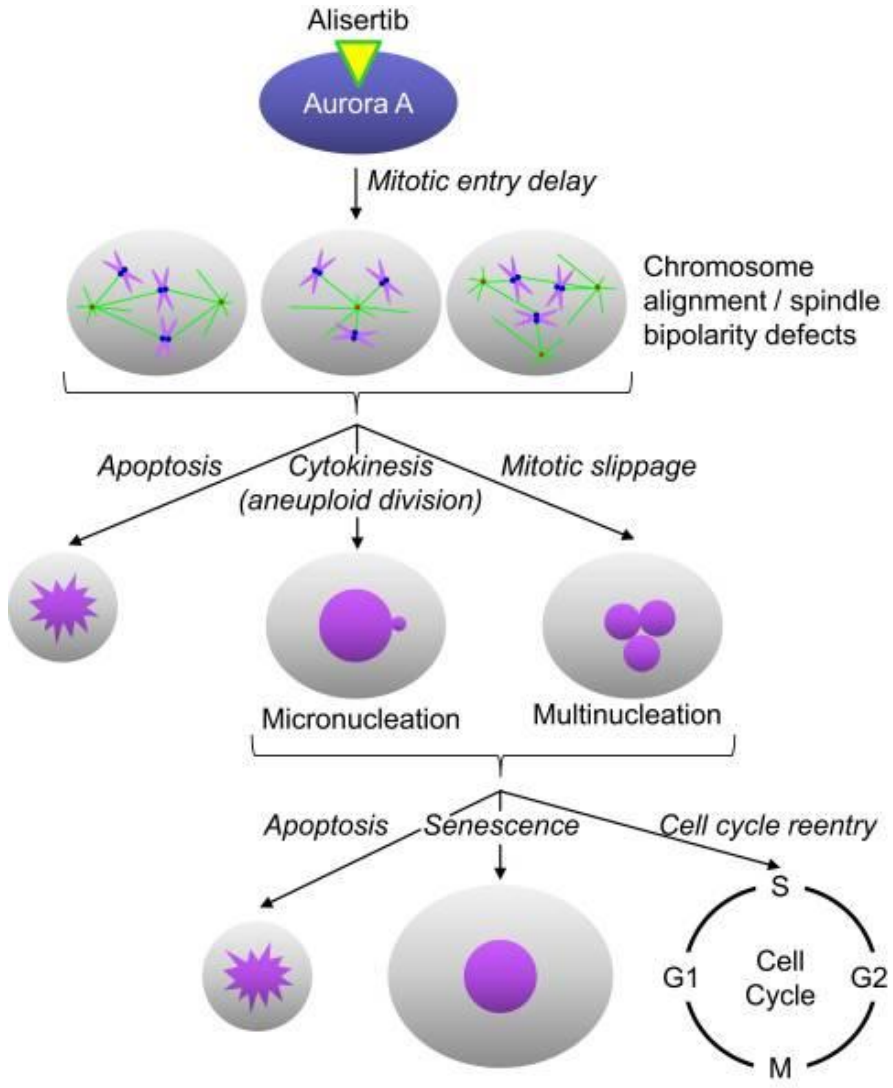


Orally Bioavailable
Drug Class: Benzazepine

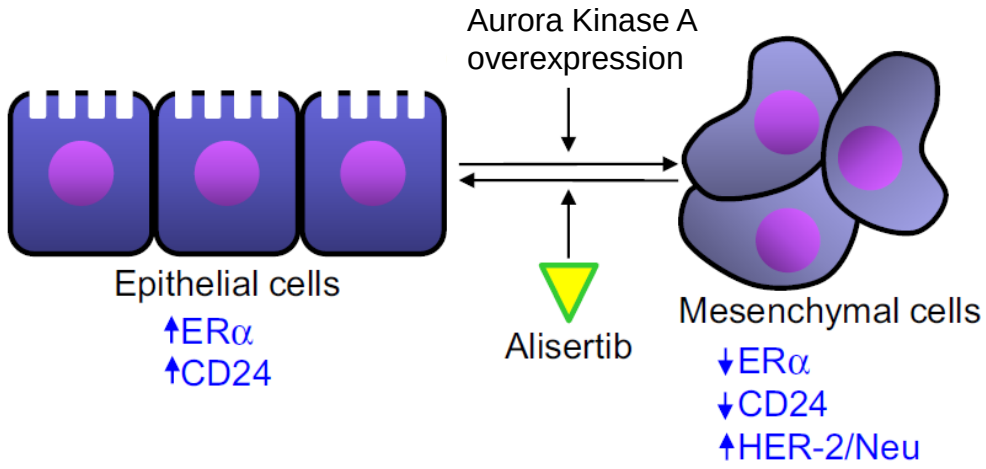
- Single-agent and combinational clinical activity in solid tumors including hormone receptor-positive breast cancer (HR+ MBC), triple negative breast cancer (TNBC), small cell lung cancer (SCLC), and head and neck cancer
- Single-agent clinical activity in hematologic malignancies including peripheral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

Alisertib Mechanism of Action

- Inhibits Aurora Kinase A (AURKA), a serine/threonine protein kinase and transcription factor
- Leads to:
  - Disruption of mitotic spindle apparatus assembly
  - Disruption of chromosome segregation
  - Inhibition of cell proliferation
- Highly selective, reversible ATP competitive inhibitor
  - IC50 <10 nM for AURKA



Aurora Kinase A and Epithelial to Mesenchymal Transition



- AURKA promotes epithelial to mesenchymal transition in breast cancer cells
- *AURKA* overexpression leads to the transition from an epithelial phenotype to a mesenchymal phenotype, leading to decreased ERα and CD24 expression and HER2/Neu overexpression
- Alisertib counteracts the effects of *AURKA* overexpression and abrogates the epithelial to mesenchymal transition

Prognostic Implications of High Aurora Kinase A Expression

High *AURKA* expression is correlated with worse overall survival in multiple solid tumor types

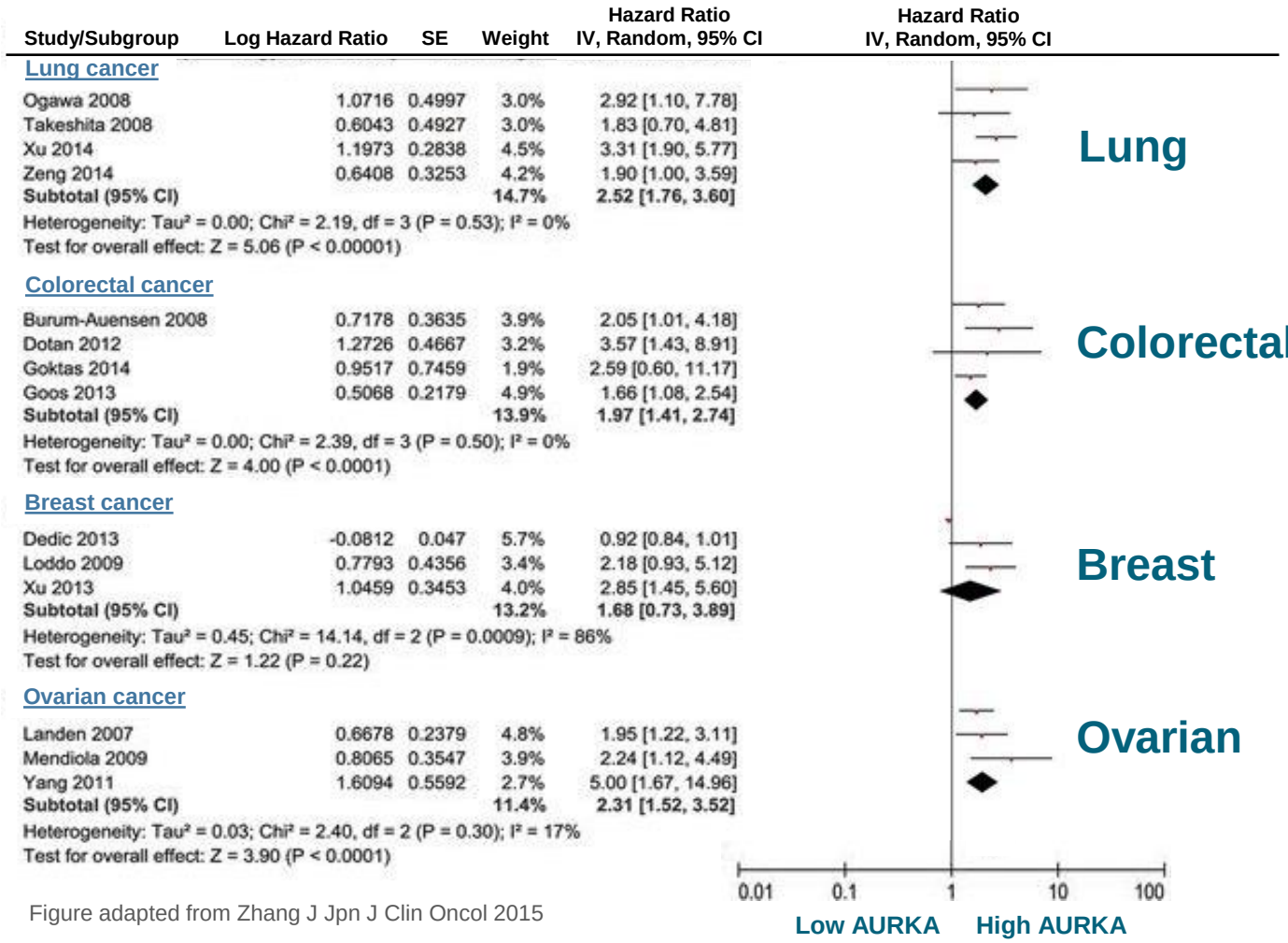


Figure adapted from Zhang J Jpn J Clin Oncol 2015

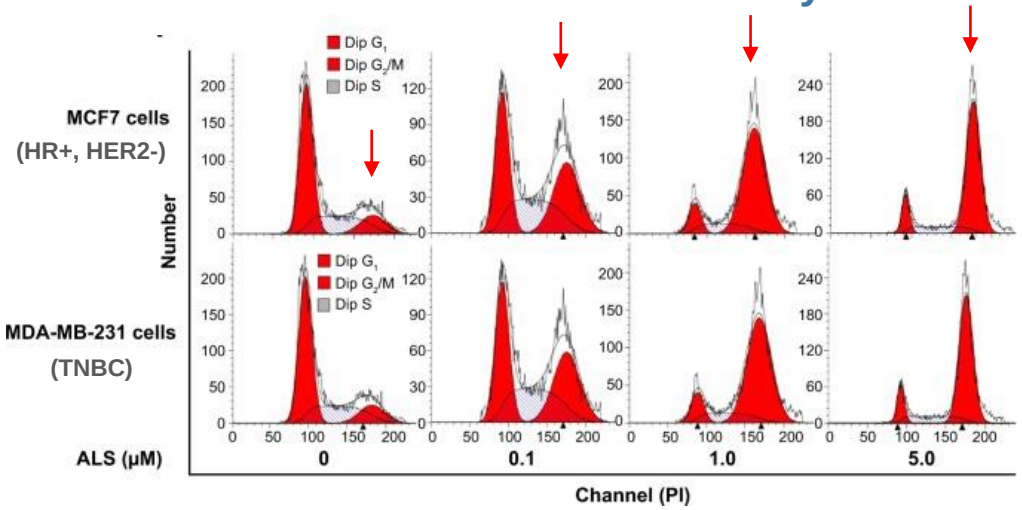
Meta-analysis of *AURKA* expression and overall survival

Zhang J Jpn J Clin Oncol 2015

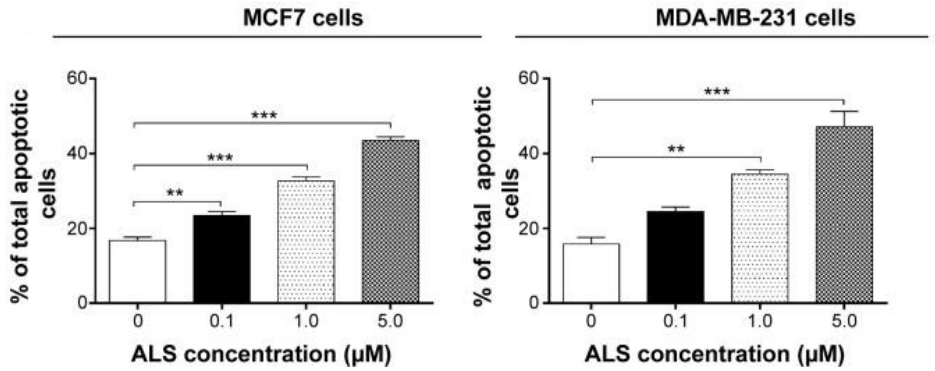
Alisertib in Breast Cancer Cell Lines

Alisertib inhibits proliferation and induces G2/M cell cycle arrest, apoptosis, and autophagy

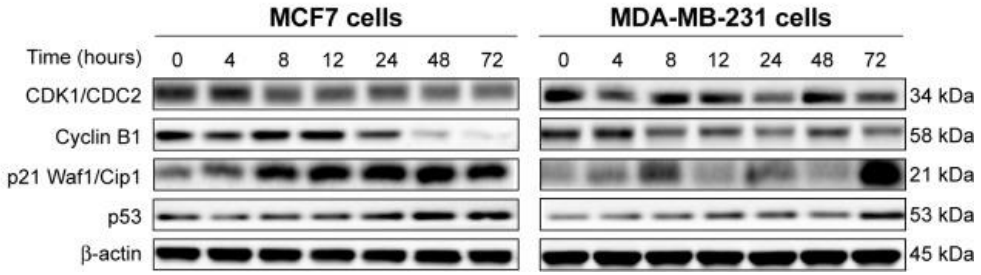
Alisertib induces G2/M cell cycle arrest



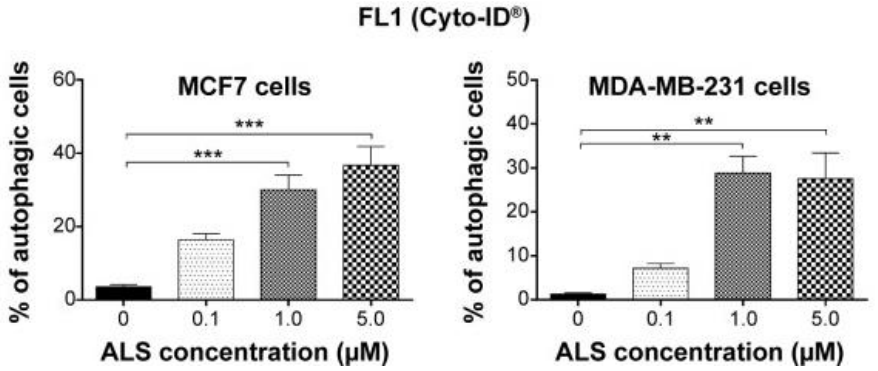
Alisertib induces apoptosis



Alisertib inhibits CDK1 and Cyclin B1 and induces p21 and p53



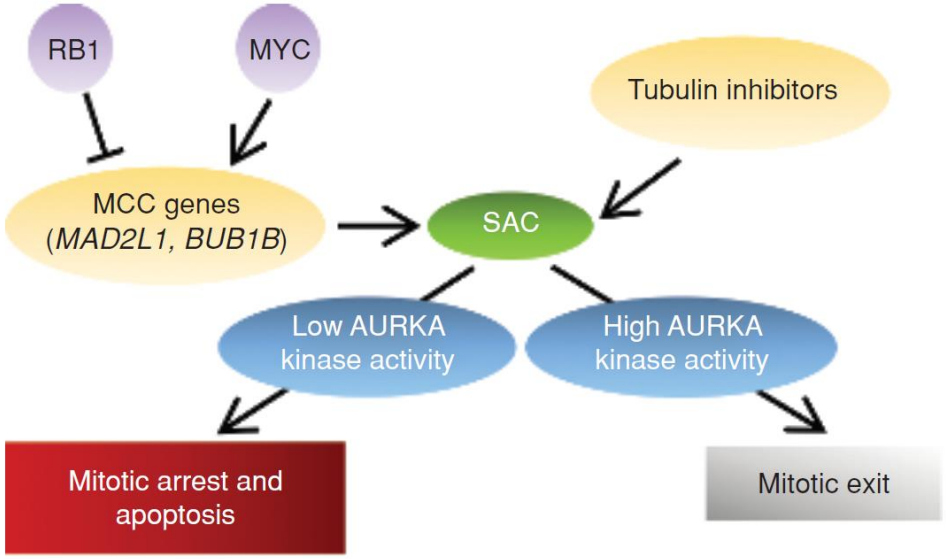
Alisertib induces autophagy



Li J Drugs Des Devel Ther 2015

Synthetic Lethality of AURKA and Rb1

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

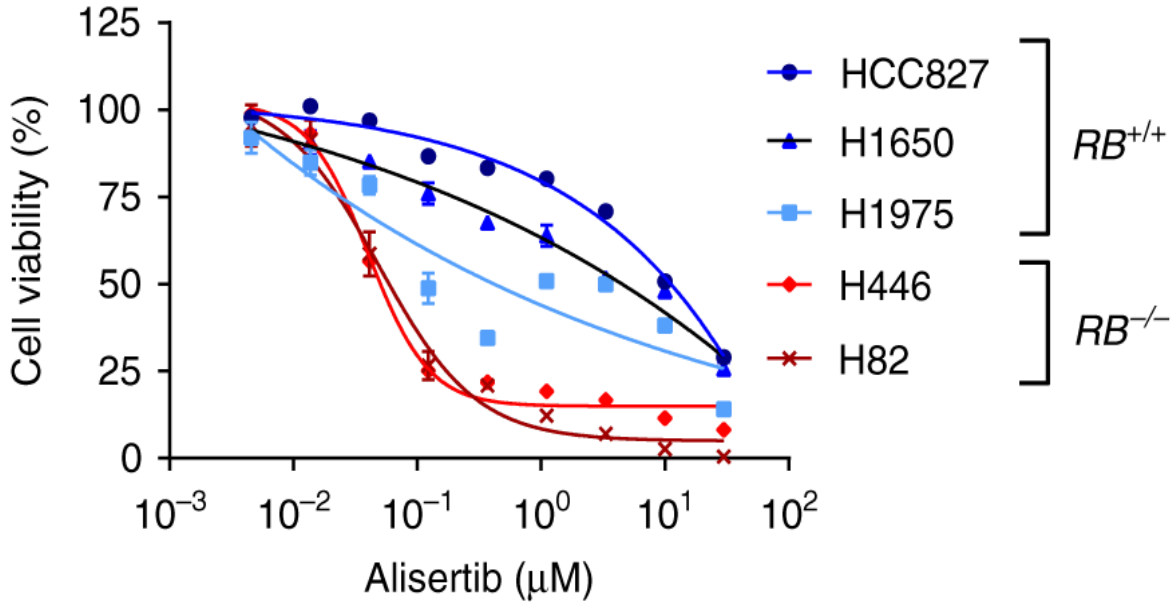


- Loss of function of Rb1 is a common event in cancer and can emerge as a mechanism of resistance to EGFR, CDK4, and ER-targeted therapies in breast and lung cancers
- Rb1 controls entry into S phase of mitosis, and loss of Rb1 function leads to a hyperactivated, primed, SAC
- Cancers with a hyperactivated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

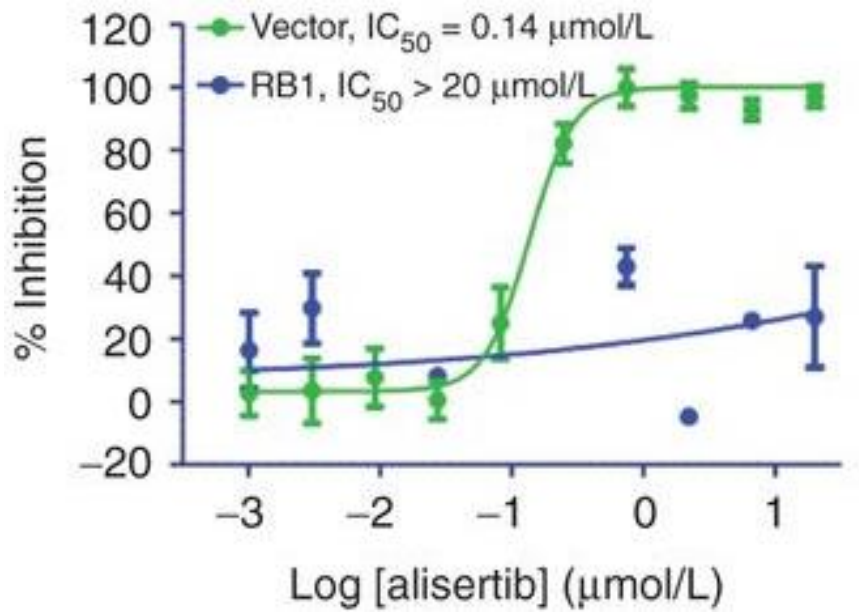
[1]Dick F Cancer Discovery Feb 2019, Gong X Cancer Discov 2019

RB1-mutant Cell Lines are Sensitive to Alisertib

Alisertib inhibits Rb1 deficient small-cell lung cancer cell line models to a much greater degree than wild-type



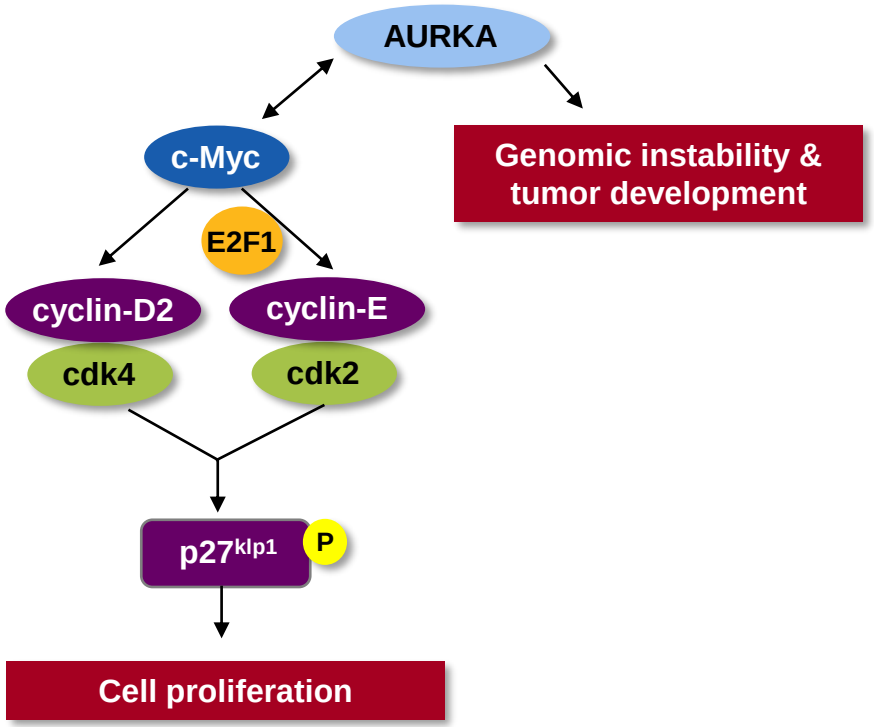
Alisertib inhibits *RB1*-mutant TNBC cell line (green) but not when transfected with wild-type RB1 (blue)



Gong X Cancer Discov 2019, Lyu J Nat Commun 2020

AURKA and c-Myc Co-regulate Each Other

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

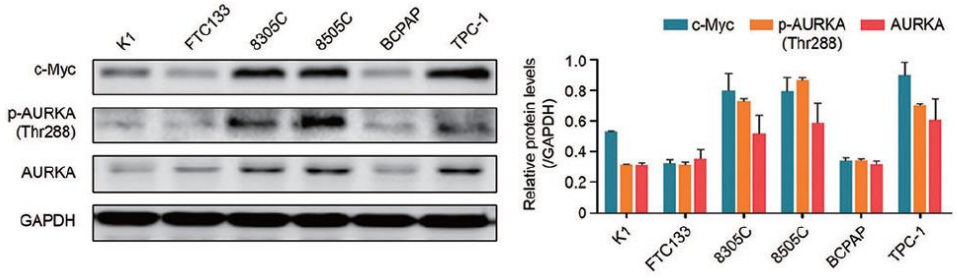


- AURKA and c-Myc transcriptionally upregulate each other, suggesting the existence of a positive feedback loop
- c-Myc upregulates Cyclin D2, CDK4, and cyclin-E, contributing to complex formation and subsequent phosphorylation of p27Kip1, which leads to cell proliferation

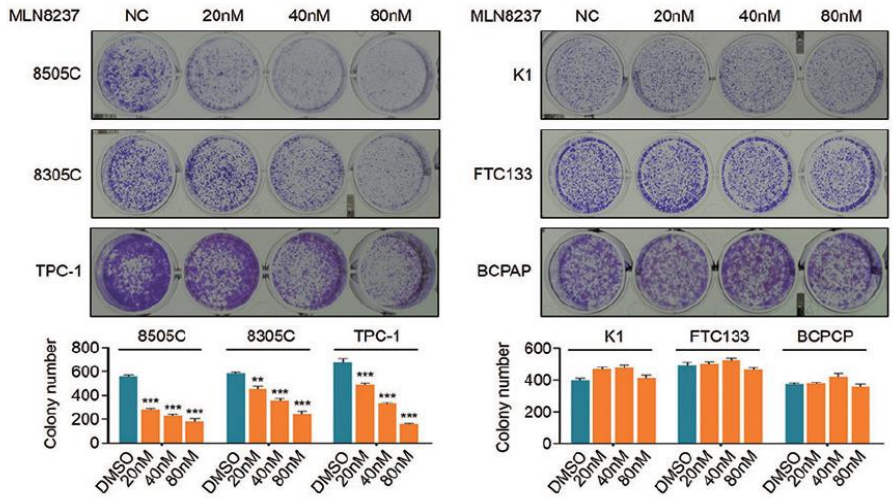
Naso FD Oncogene 2021, Tang A Oncotarget 2017

Alisertib in *c-MYC*-amplified Cancer Models

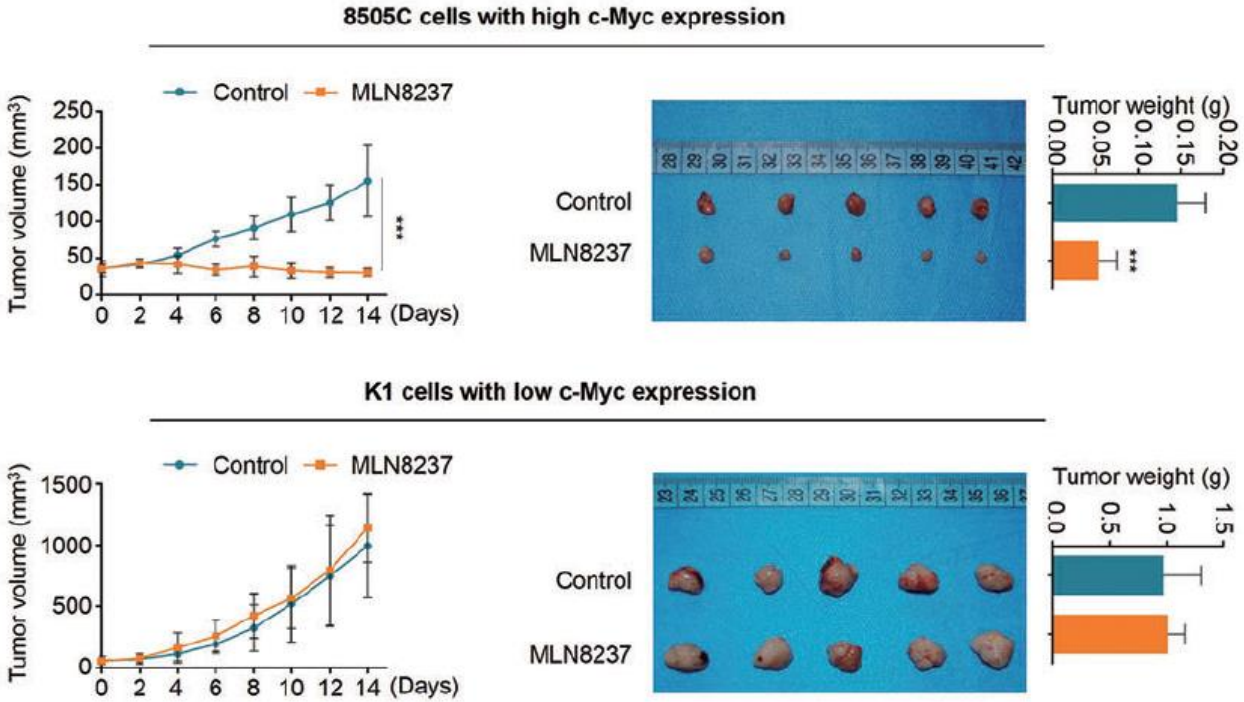
c-Myc, AURKA, and p-AURKA protein levels trend together in a panel of thyroid cancer cell lines



Alisertib inhibits growth of cells with high but not low levels of *c-Myc* expression



Alisertib inhibits tumor growth in xenograft models of thyroid cancer with high *c-Myc* expression, but not low *c-Myc* expression



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)

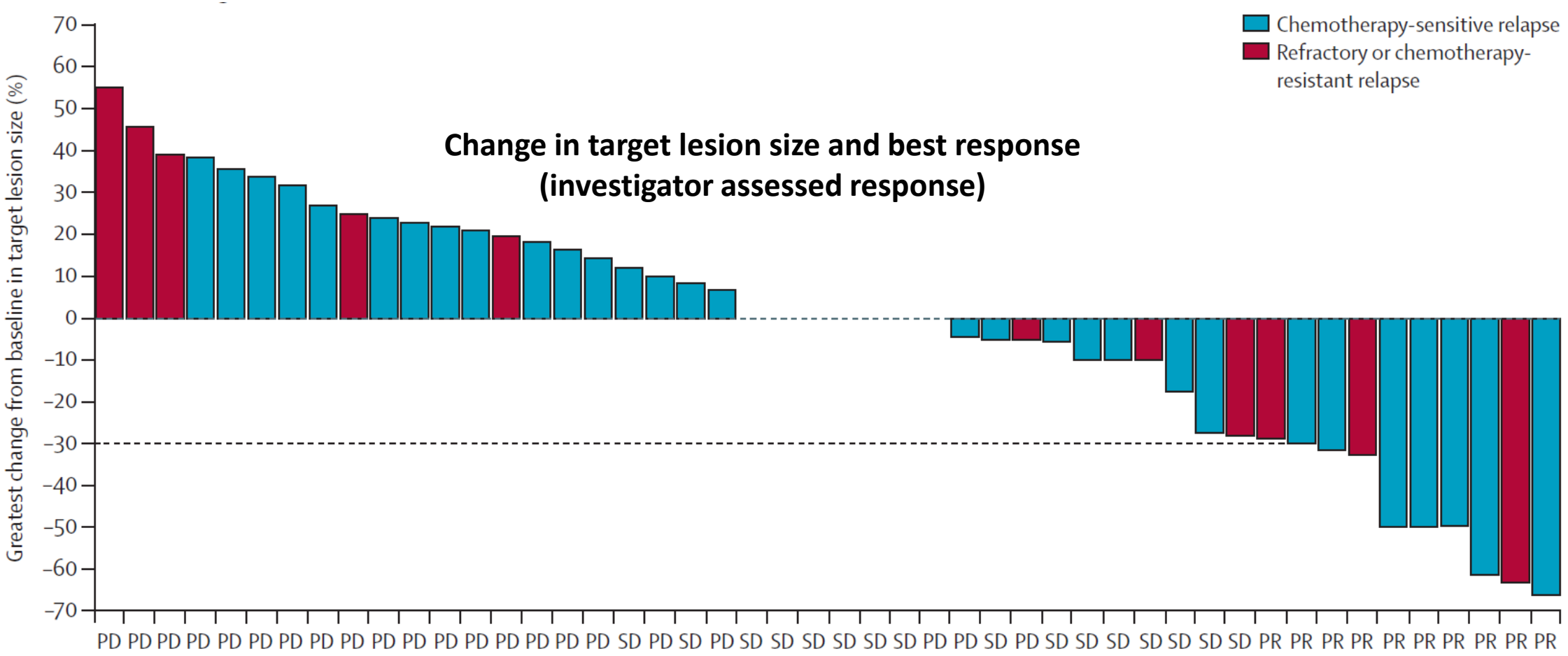
Table adapted from Melichar B Lancet Oncol 2015. Data are either number of patients (%) (95% CI), or median (95% CI), unless otherwise stated. NE=not estimable. *Safety population. †All were partial responses. All responses were based on investigator tumor assessments (RECIST v1.1).

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

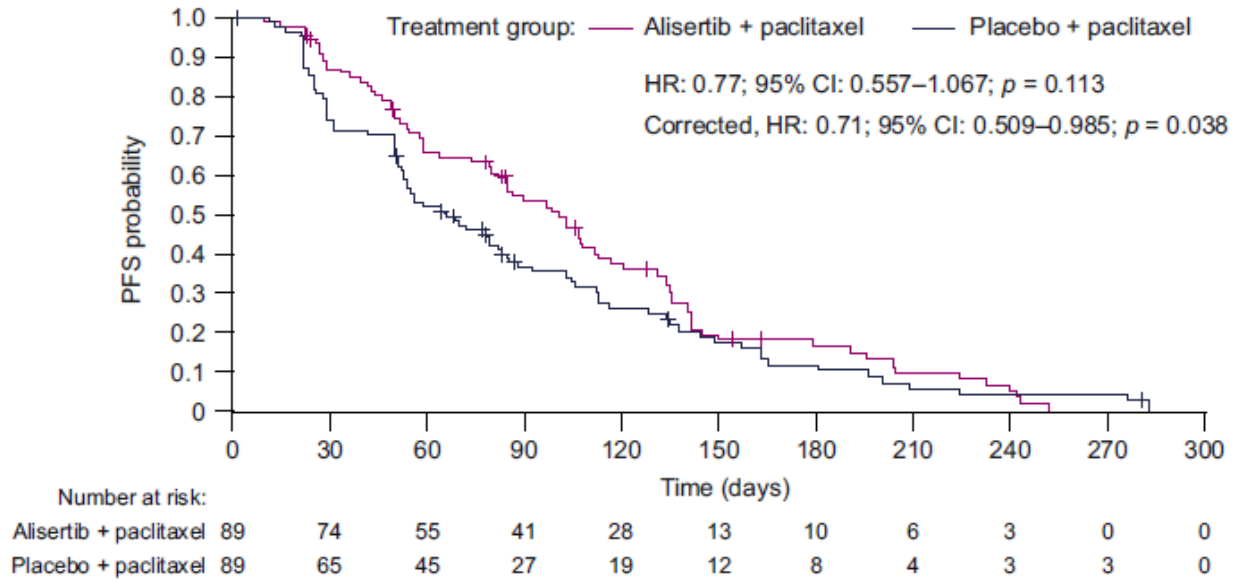
Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Primary Analysis

Study design:

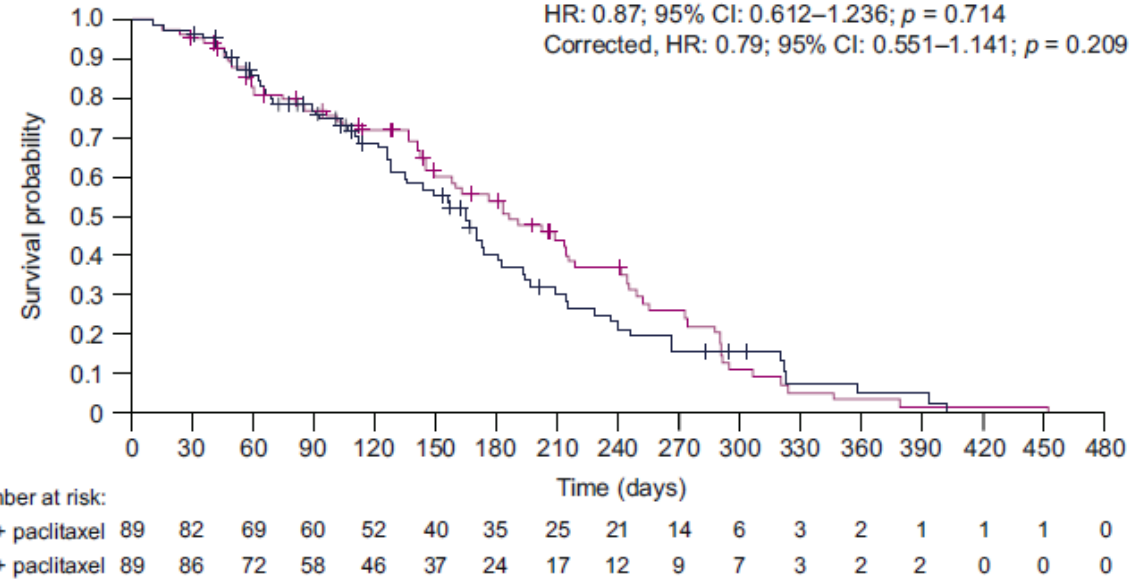
- Patients with relapsed or refractory SCLC stratified by relapse type (sensitive vs resistant or refractory)
- Randomized 1:1 to alisertib + paclitaxel or placebo + paclitaxel in 28-day cycles
- Alisertib (40 mg BID for 3 weeks on days 1–3, 8–10, and 15–17) plus paclitaxel (60 mg/m2 intravenously on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



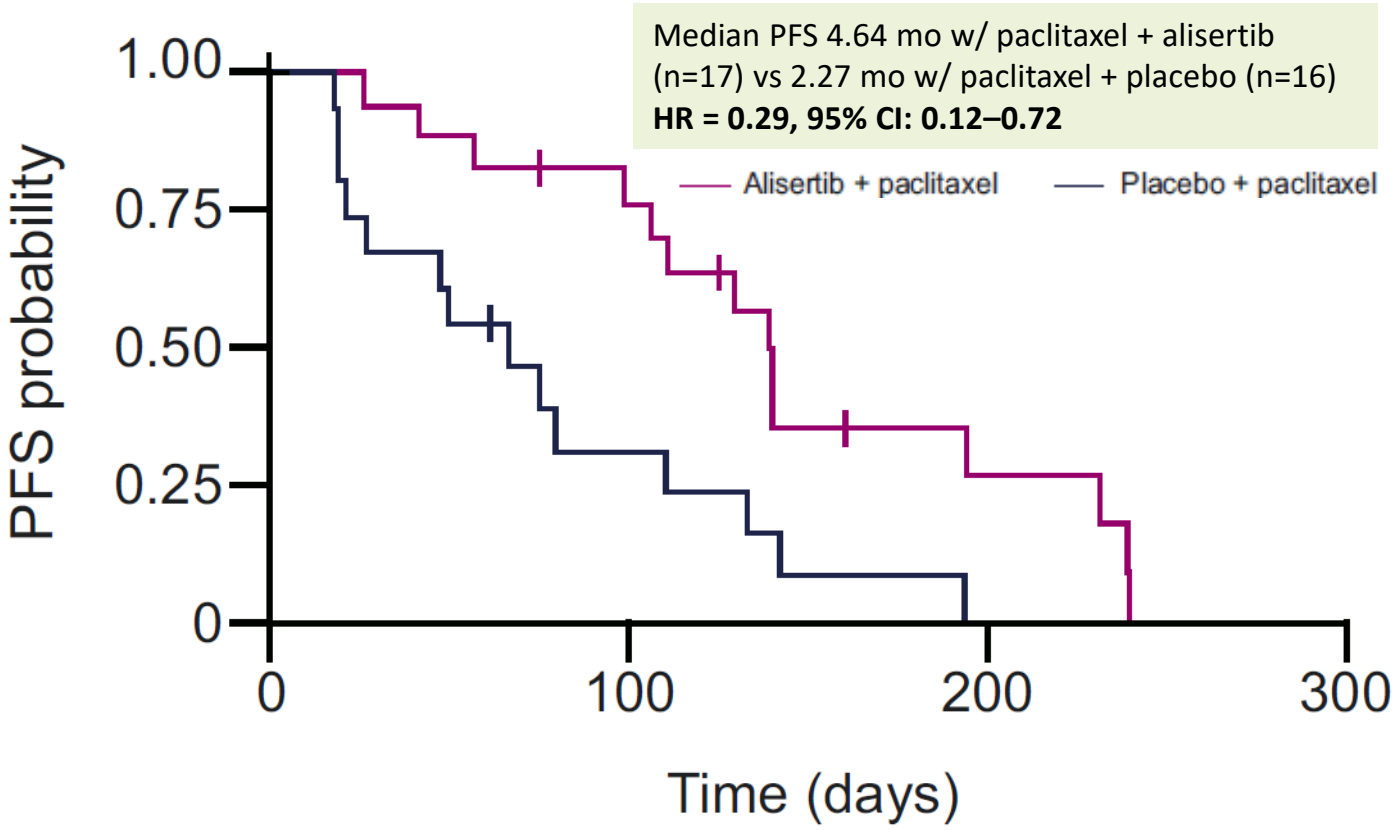
OS in ITT



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

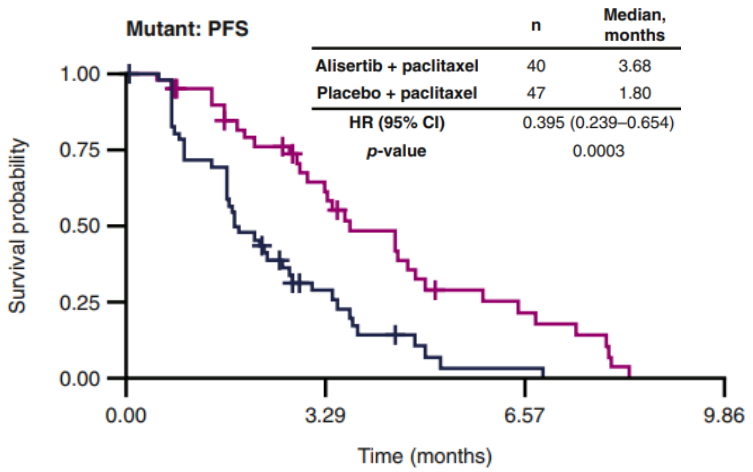
Improved PFS observed among patients positive versus negative for *c-Myc* expression

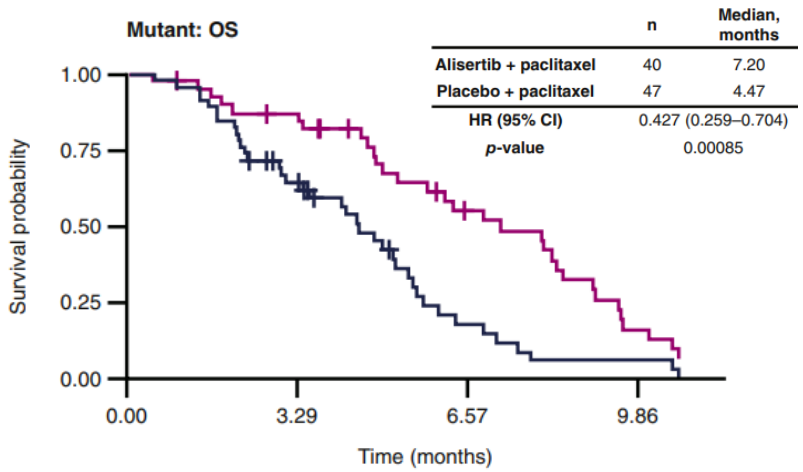
PFS in patients positive for *c-Myc* expression

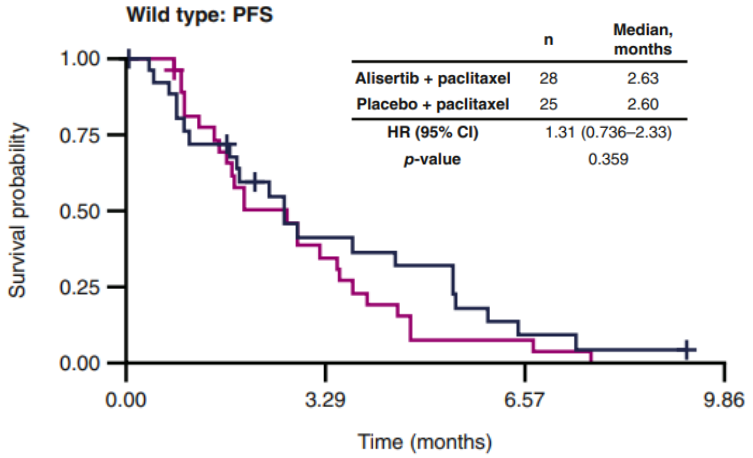


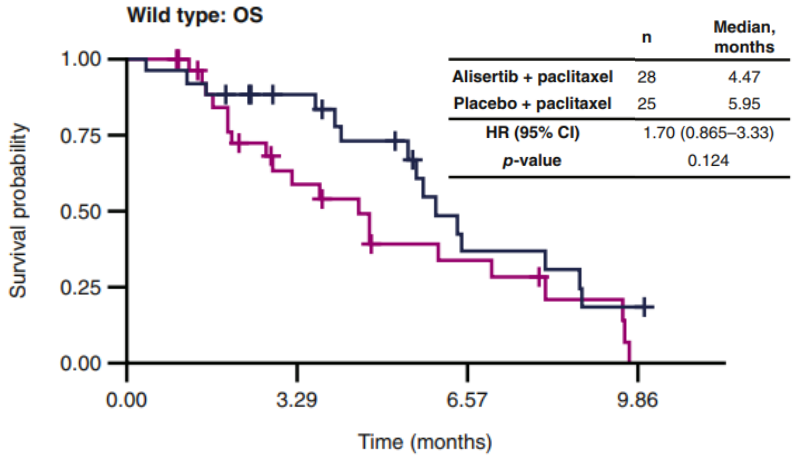
Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Correlative Biomarker Analysis

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)

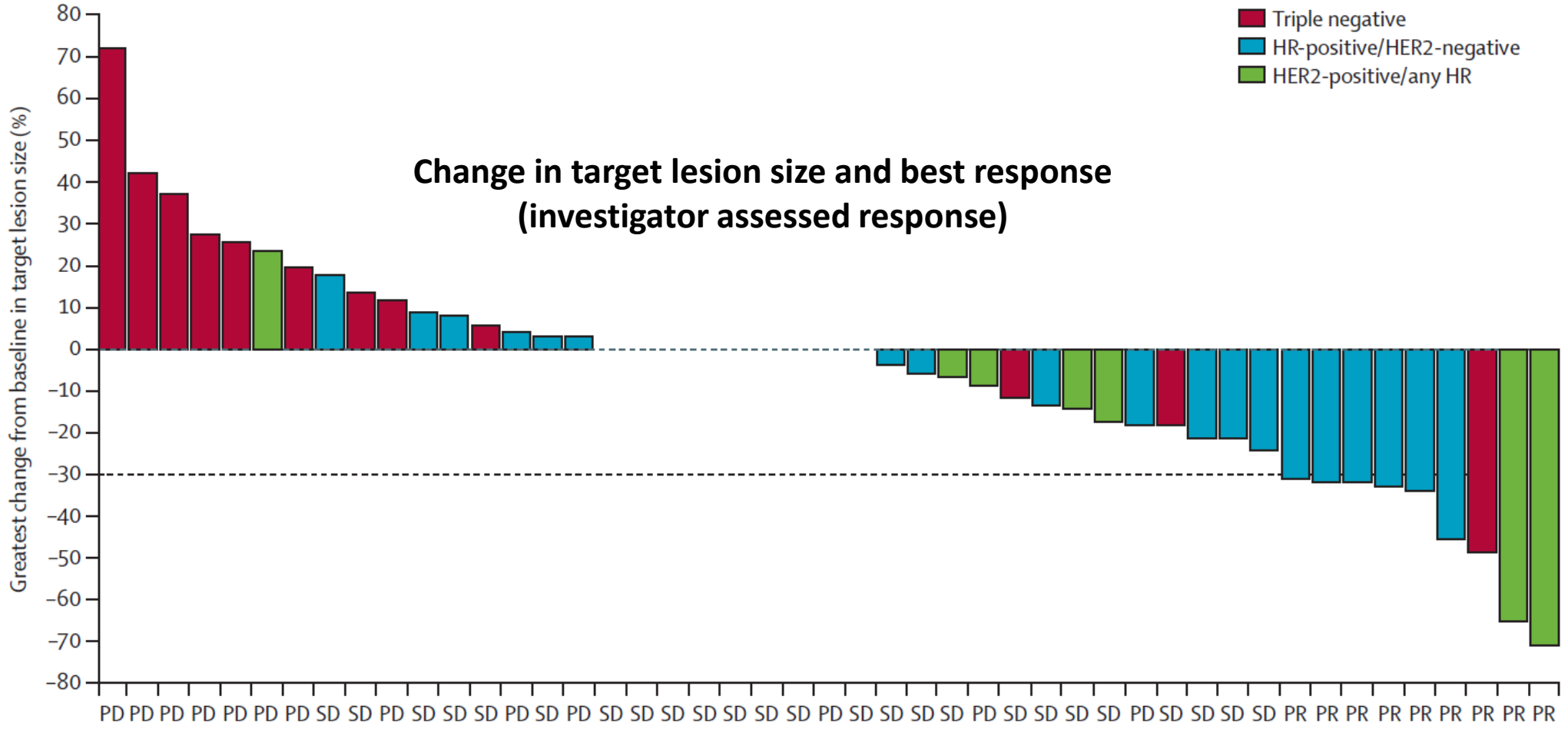
Data are either number of patients (%) (95% CI), or median (95% CI), unless otherwise stated. For the breast cancer subgroup, numbers of patients were too small to calculate 95% CIs. *Safety population. †All were partial responses. . ‡ These two patients had the only hormone receptor-negative tumors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

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

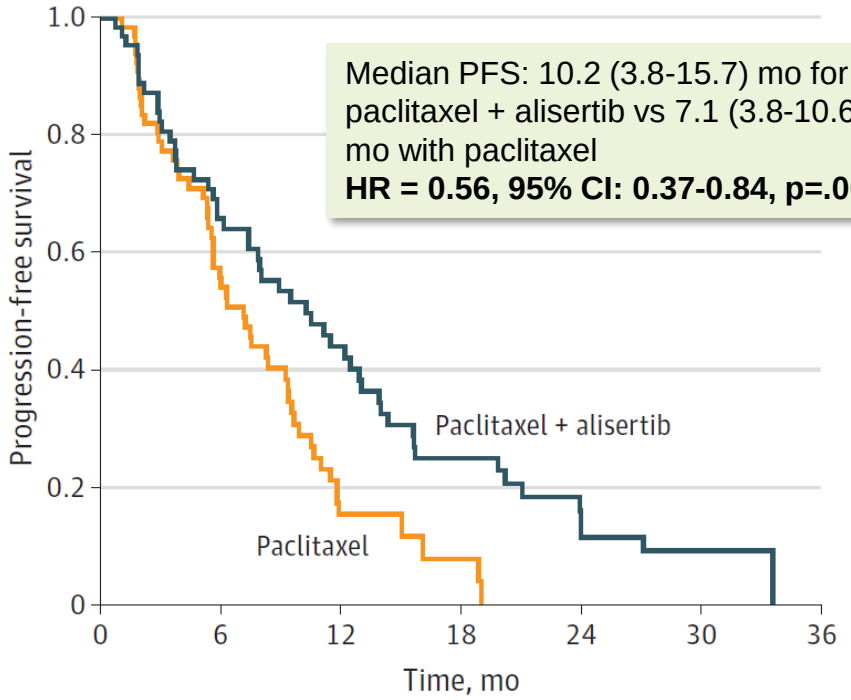
Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

- 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

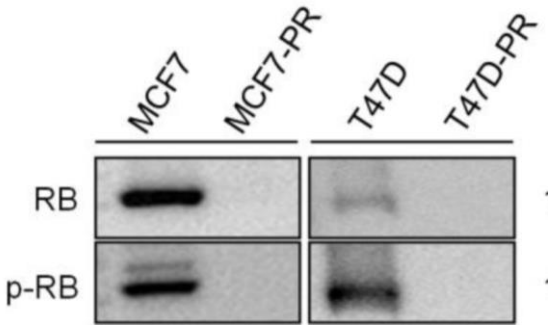
Efficacy in patients pretreated with palbociclib (n=30)

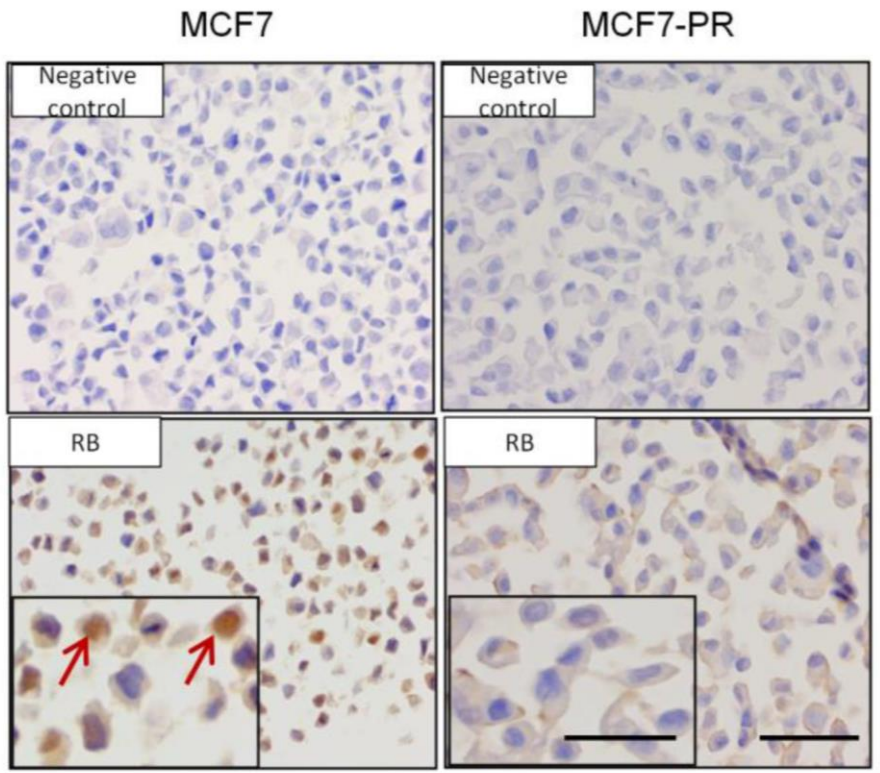
- Median PFS: 13.9 (5.6-15.6) mo (14 pts) w/ paclitaxel + alisertib vs 5.6 (3.0-10.6) mo (16 pts) w/ paclitaxel alone (HR, 0.58; 95%CI, 0.26-1.32; *P* = .19)
- CBR: 61.5% w/ paclitaxel + alisertib (95%CI,31.6%-86.1%) vs 37.5% (95%CI, 15.2%-64.6%) w/ paclitaxel alone

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

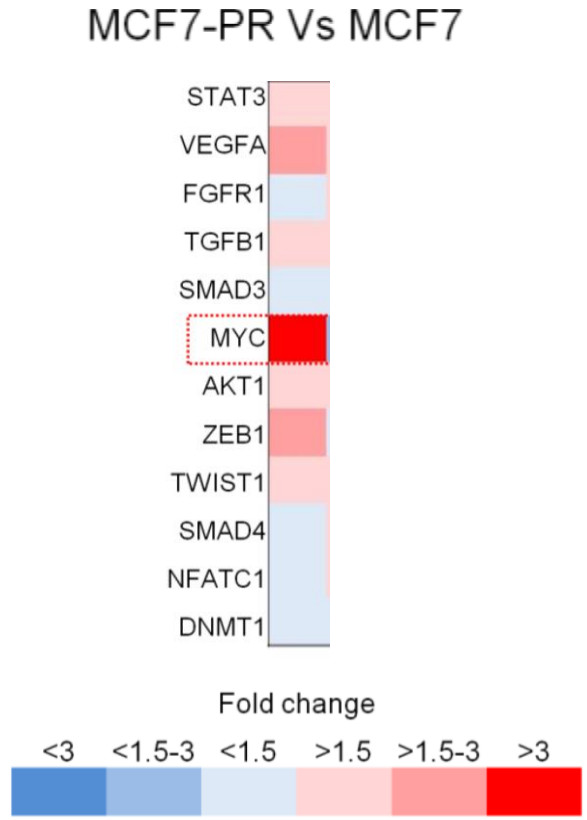
Both RB1 loss and MYC upregulation were observed in palbociclib-resistant HR+ breast cancer cell lines, supporting a role for alisertib in this setting

RB1 Loss





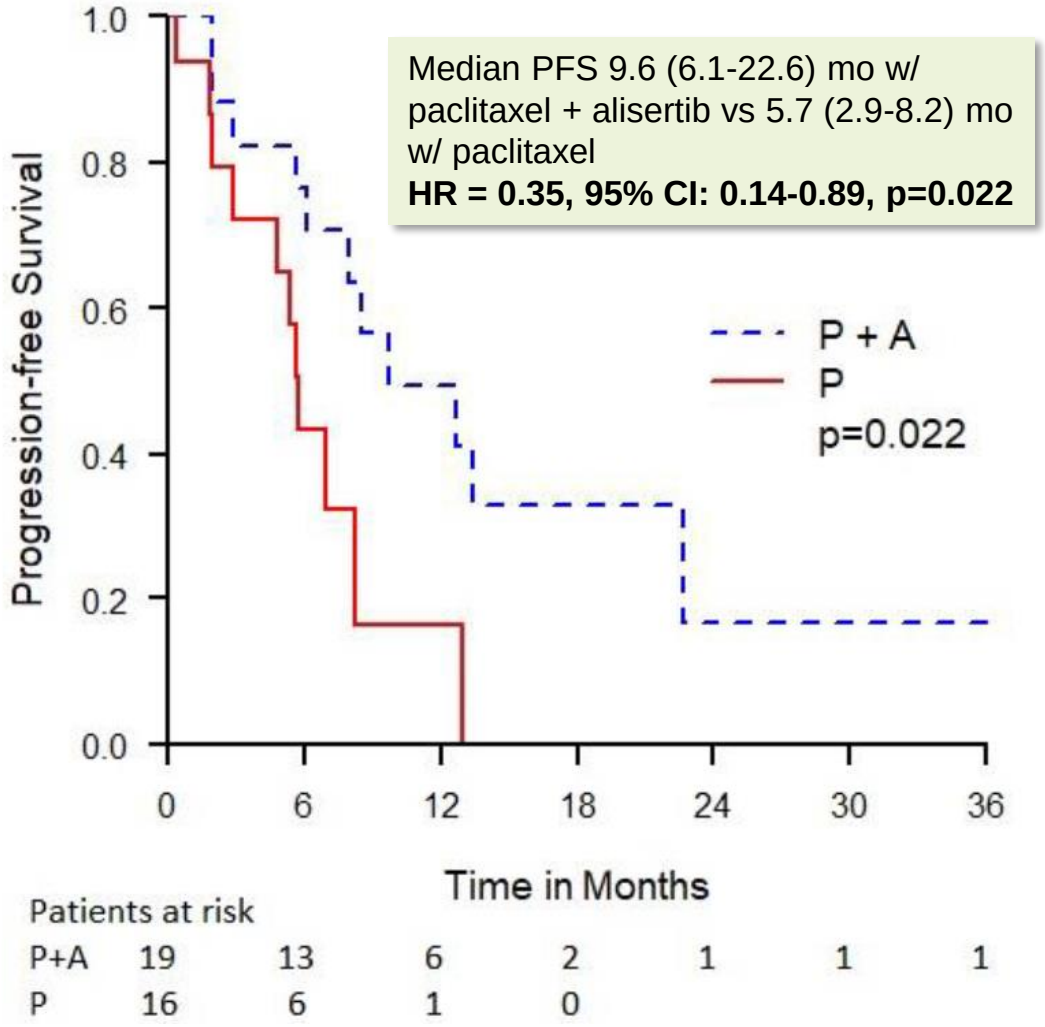
C-Myc Upregulation



Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

- Efficacy in TNBC Cohort

PFS in TNBC ITT



Median PFS 9.6 (6.1-22.6) mo w/ paclitaxel + alisertib vs 5.7 (2.9-8.2) mo w/ paclitaxel

HR = 0.35, 95% CI: 0.14-0.89, p=0.022

Median OS: 16 (9.6-34.0) mo w/ paclitaxel + alisertib vs 12.7 (6.8-23.5) mo w/ paclitaxel alone (HR, 0.51; 95%CI, 0.23-1.13; *P* = .09)

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Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

- Safety for ER+/HER2- MBC & TNBC (both cohorts combined)

Table 3. Treatment-Related Toxic Effects in Both Cohorts

	Patients, No. (%)									
	Paclitaxel plus alisertib (n = 66)					Paclitaxel (n = 70)				
Reported term	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 1	Grade 2	Grade 3	Grade 4	Total
Neutropenia	3 (3.6)	4 (4.8)	27 (32.1)	23 (27.4)	57 (67.9)	1 (1.2)	3 (3.5)	11 (12.9)	3 (3.5)	18 (21.2)
Anemia	8 (9.5)	6 (7.1)	8 (9.5)	0	22 (26.2)	5 (5.9)	5 (5.9)	1 (1.2)	0	11 (12.9)
Leukopenia	0	3 (3.6)	5 (6.0)	2 (2.4)	10 (11.9)	2 (2.4)	1 (1.2)	2 (2.4)	0	5 (5.9)
Thrombocytopenia	3 (3.6)	0	0	0	3 (3.6)	0	0	0	0	0
Febrile neutropenia	0	0	0	1 (1.2)	1 (1.2)	0	0	0	0	0
Diarrhea	17 (20.2)	22 (26.2)	9 (10.7)	0	48 (57.1)	9 (10.6)	2 (2.4)	0	0	11 (12.9)
Nausea	24 (28.6)	11 (13.1)	0	0	35 (41.7)	19 (22.4)	4 (4.7)	1 (1.2)	0	24 (28.2)
Mucositis oral	7 (8.3)	7 (8.3)	9 (10.7)	0	23 (27.4)	4 (4.7)	0	0	0	4 (4.7)
Stomatitis	6 (7.1)	4 (4.8)	4 (4.8)	0	14 (16.7)	7 (8.2)	0	0	0	7 (8.2)
Fatigue	21 (25.0)	17 (20.2)	4 (4.8)	0	42 (50.0)	26 (30.6)	6 (7.1)	2 (2.4)	0	34 (40.0)
Neuropathy	7 (10.6)	4 (6.1)	1 (1.5)	0	12 (18)	9 (12.9)	8 (11.4)	8 (11.4)	0	25 (35.7)
Dizziness	7 (8.3)	2 (2.4)	0	0	9 (10.7)	2 (2.4)	0	0	0	2 (2.4)
Headache	9 (10.7)	2 (2.4)	0	0	11 (13.1)	4 (4.7)	1 (1.2)	0	0	5 (5.9)

One pt receiving paclitaxel + alisertib died of sepsis

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 H2 2022/H1 2023

Clinical Milestones

- Biomarker data from Phase 2 randomized trial of alisertib plus fulvestrant vs alisertib alone in hormone receptor-positive, HER2-negative advanced breast cancer (Q4 2022)

- Biomarker data from Phase 2 randomized trial of paclitaxel plus alisertib vs paclitaxel alone in patients with hormone receptor-positive, HER2-negative advanced breast cancer (H1 2023)

- Presentation of data from an ongoing investigator sponsored Phase 1/2 trial of alisertib plus pembrolizumab for the treatment of patients with Rb-deficient head and neck squamous cell cancer (2023)

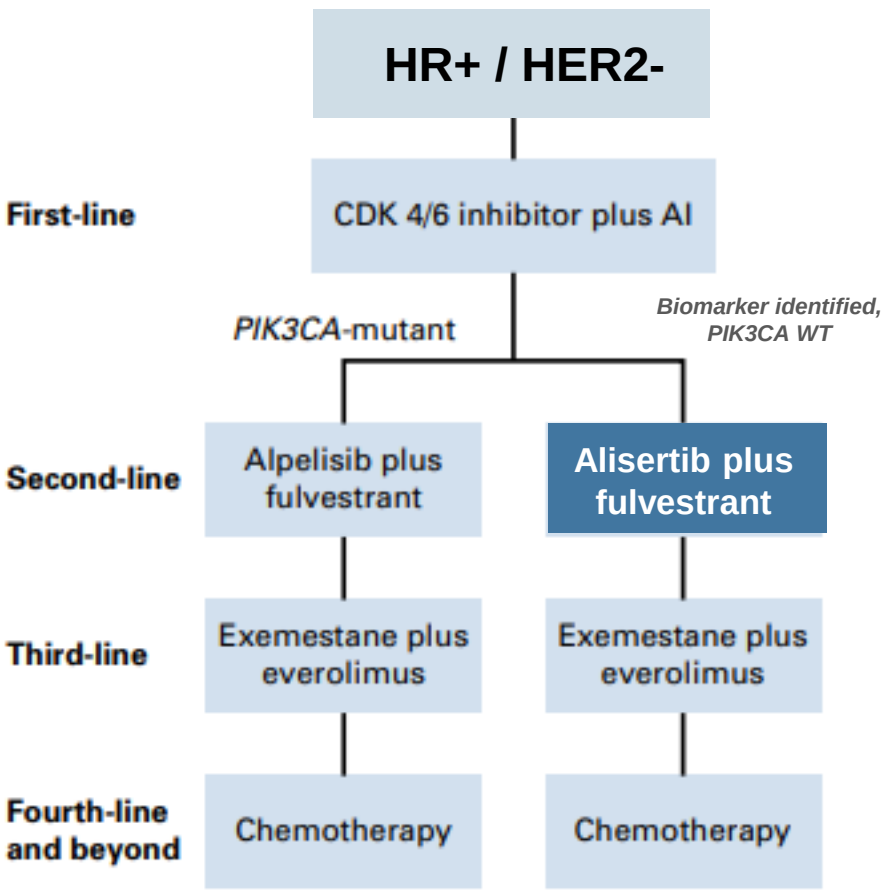
Treatment Landscape

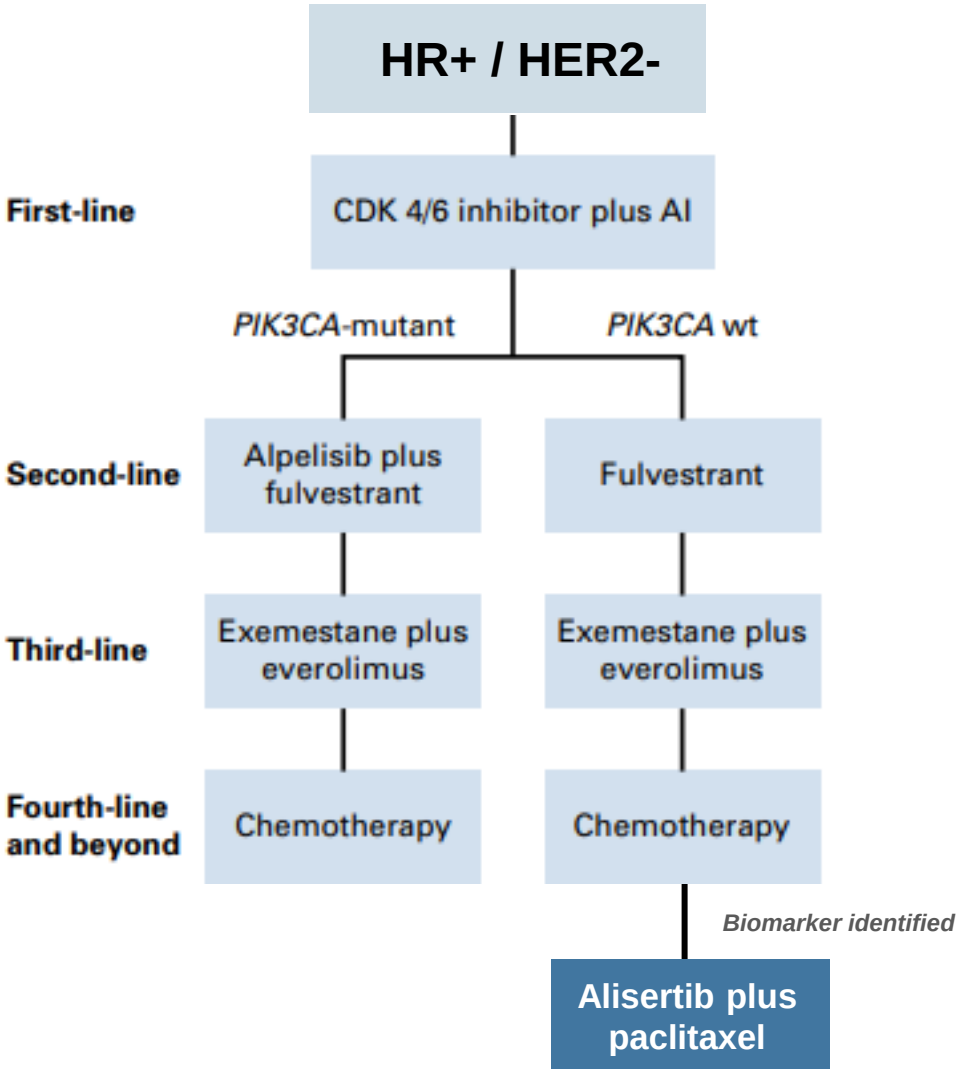
HR-positive HER2-negative Breast Cancer in US

- US Incidence: ~40,000 patients[1]
- US Deaths: ~29,770[2]
- Estimated approximately 50% of HR-positive breast cancer patients have elevated c-Myc levels
- Estimated approximately 2%-9% of HR-positive HER2-negative patients have *RB1* mutations at the time of the development of drug resistance to CDK4/6 inhibition

1. Kantar Health, 2. Assumes 43,780 breast cancer deaths (Cancer.net) and 68% are ER-positive, HER2-negative (SEER), 3. Green Br J Cancer 2016, 4. Asghar JCO Precis Oncol 2022

Proposed Schema of Management of HR+/HER2- MBC





Small Cell Lung Cancer Market in US

- US Incidence: ~31,000-33,000 patients[1]
- US Deaths: ~17,000-18,000[2]
- Estimated approximately 72% small cell lung patients have elevated c-Myc levels[3]
- Estimated approximately 60-80% of small cell lung cancer patients have *RB1* mutations[3]

1. Assumes 236,740 newly diagnosed lung cancer patients (Cancer.net) and 13-14% are SCLC (Cancer.net), 2. Assumes 130,180 lung cancer deaths (Cancer.net) and 13-14% are SCLC (Cancer.net), 3. Owonikoko J Thorac Oncol 2020

Limited Agents Currently Under P2/3 Development for SCLC

- Most recent immunotherapies and ADCs for the treatment of SCLC have either failed their confirmatory study or failed to show improvement in OS (e.g., nivolumab, ipilimumab, pembrolizumab, rovalpituzumab tesirine, tremelimumab)

- Only 2 immunotherapies demonstrated OS improvement and received full approval from FDA (atezolizumab and durvalumab) in 1st line ES-SCLC in combo with a platinum agent plus etoposide

- Lurbinectedin, received accelerated approval for patients with SCLC who progressed on prior platinum-based chemotherapies (2nd line) in June 2020 based on ORR and DOR
  - currently conducting a P3 study to confirm OS benefit in combo with doxorubicin in 2nd line ES-SCLC pts who progressed on prior platinum-based chemotherapies

TECENTRIQ USPI, IMFINZI USPI, ZEPZELCA USPI, https://www.clinicaltrials.gov

Licensing Agreement Terms

- $7 million up front
- $287.3 million upon Puma’s achievement of certain regulatory and commercial milestones
  - No milestone payments during clinical development
- Tiered royalty payments for any sales of alisertib
- No Impact to Puma’s R&D budget or expense guidance for 2022

Alisertib Summary

- Clinical activity demonstrated in Phase 2 clinical trials in HR-positive, HER2-negative breast cancer, Triple Negative Breast Cancer (TNBC), Small Cell Lung Cancer (SCLC)
- Synergy with Puma’s existing Nerlynx franchise
- Large potential addressable market
- Differentiated mechanism of action
- Potential for novel biomarker directed commercial opportunities compared to other marketed drugs and drugs in development