2019 San Antonio Breast Cancer Symposium
Roche Analyst Audio Webcast

16 December, 2019

SAN ANTONIO BREAST CANCER SYMPOSIUM®

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Agenda

Welcome
Karl Mahler, Head of Investor Relations

HER2+ Franchise Overview
Alan Sandler, M.D., Head of Oncology – Solid Tumors, Global Product Development

HR+/HER2- and TNBC Franchise Overview
Elena Bernedo Arzac, M.D., Head of Oncology, Global Product Strategy

Key early stage data presented at SABCS 2019: PI3K, SERD
Stuart Lutzker, M.D., Ph.D., Head of Oncology, Early Clinical Development

Q&A

Welcome

Karl Mahler | Head of Investor Relations

2019: a year of achievements

Key Late Stage News Flow

Positive Ph 3 / Pivotal Data	
Tecentriq + Avastin	*1L HCC (IMbrave150)*
Tecentriq + chemo	*1L mUC (IMvigor130)*
Tecentriq + Zelboraf + Cotellic	*1L BRAFm Melanoma (IMspire150)*
Gazyva + Venclexta	*1L unfit CLL (CLL14)*
Risdiplam	*SMA type 2/3 (SUNFISH)*
Herceptin + Perjeta FDC	*HER2+ Breast Cancer (FeDeriCa)*

Regulatory Filing	
Satralizumab	*NMOSD*
Risdiplam	*SMA type 1/2/3*
Gazyva + Venclexta	*1L unfit CLL*
Xofluza	*High-risk influenza*

Approval	
Rozlytrek	*ROS1+ NSCLC*
Rozlytrek	*NTRK+ pan tumor*
Polivy	*R/R DLBCL*
Tecentriq + chemo	*1L PD-L1+ TNBC*
Tecentriq + chemo	*1L SCLC*
Kadcyla	*Adj. HER2+ BC*
Gazyva + Venclexta	*1L unfit CLL*

3 molecules advancing into pivotal studies

- Gazyva — Lupus Nephritis
- GDC-0077 (PI3K) — 1L HR+ mBC
- GDC-9545 (SERD) — 1L HR+ mBC

HER2+ Breast Cancer

Alan Sandler | Alan Sandler, M.D., Global Head Product Development Oncology, Solid Tumors

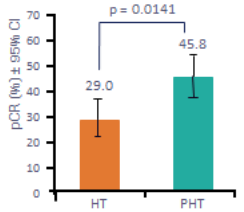
Roche has established the standard of care across HER2+ BC

Early Breast Cancer — *Metastatic Breast Cancer*

Neoadjuvant

Herceptin + PERJETA pertuzumab

NeoSphere ✓

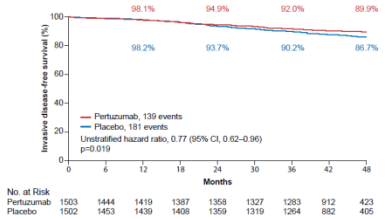


2013

Adjuvant

Herceptin + PERJETA pertuzumab

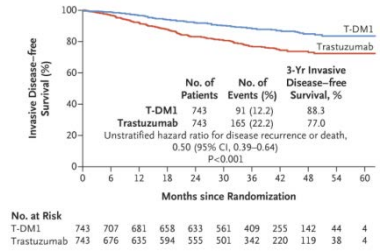
APHINITY ✓



2017

Kadcyla ado-trastuzumab emtansine for injection

KATHERINE ✓

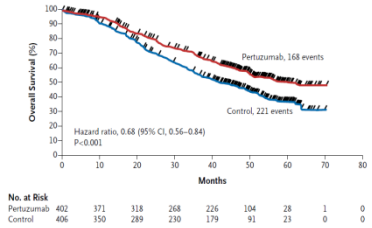


2019

1L mBC

Herceptin + PERJETA pertuzumab

CLEOPATRA ✓

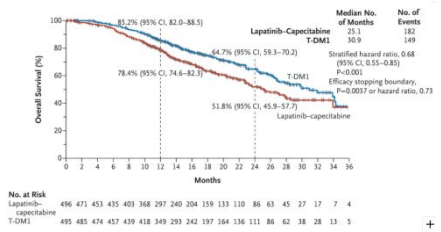


2012

2L mBC

Kadcyla ado-trastuzumab emtansine for injection

EMILIA ✓



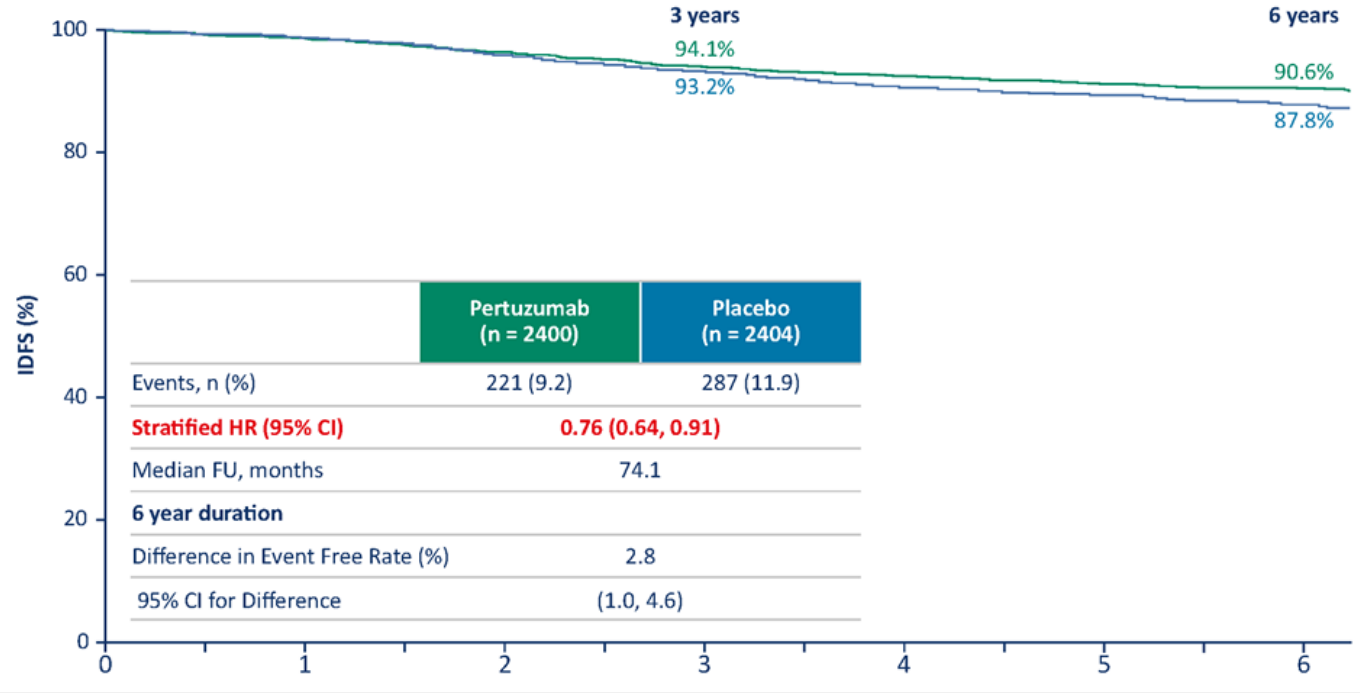
2013

mBC= Metastatic Breast Cancer

APHINITY: IDFS curves continue to separate over time

Herceptin + PERJETA pertuzumab

IDFS: ITT Population



Perjeta + Herceptin demonstrates iDFS of >90% after 6 years of follow-up

- The benefit of Perjeta in HER2+ eBC has continued to improve over time, with additional separation of the curves
- Fewer deaths were seen in the Perjeta + Herceptin arm, however OS remains immature with ~95% of patients alive at 6 years (HR: 0.85)
- Incidence of primary cardiac events remains <1% in both arms

Piccart M., et al, SABCS 2019; primary analysis (2017): median follow-up 45.4 months, Updated Analysis (2019): median follow-up 74.1 months
IDFS= invasive disease free surival; eBC = early breast cancer

APHINITY: updated data by key patient subgroups

Herceptin + PERJETA pertuzumab

Updated IDFS by nodal status and HR-status

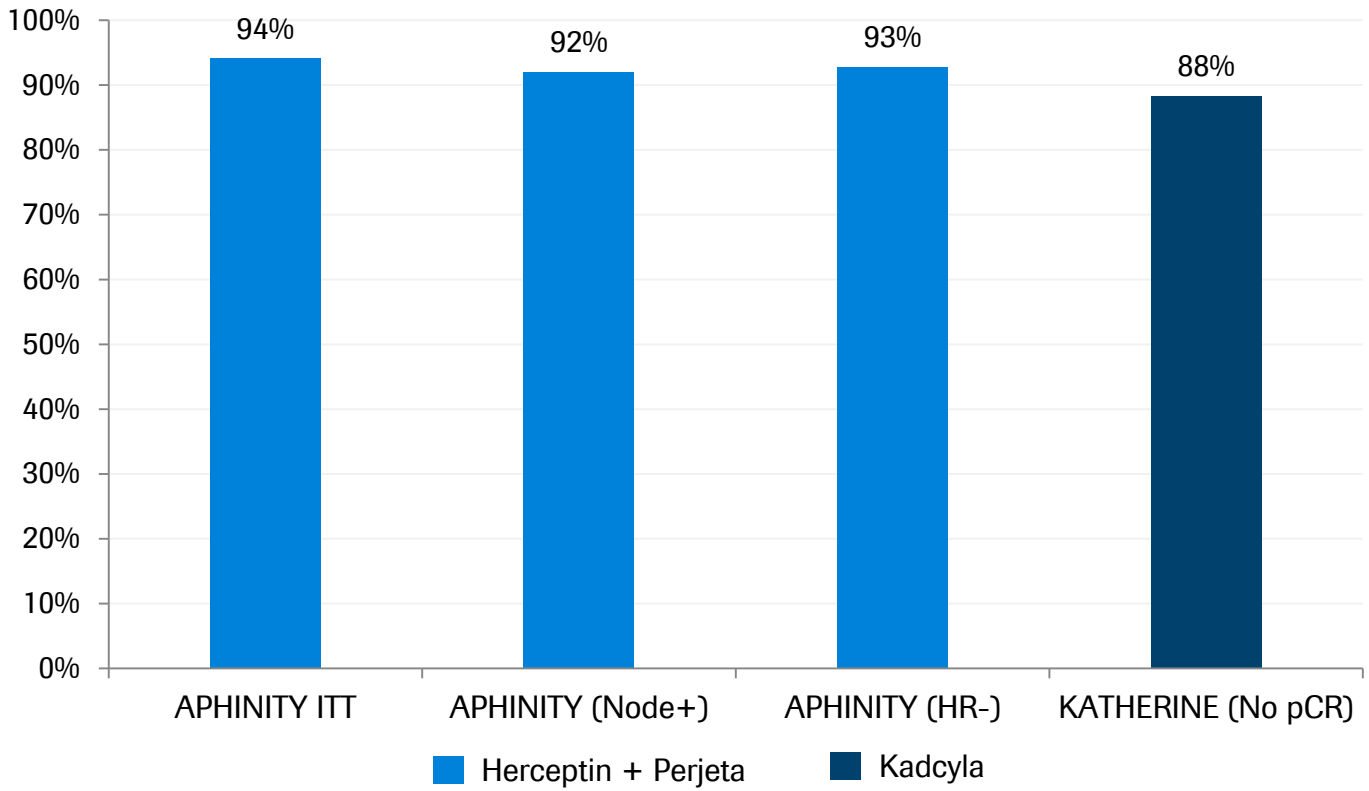
IDFS Hazard Ratio			6-yr IDFS rate		
Population	**Primary Analysis**	**Updated Analysis**	**Perjeta + Herceptin**	**Herceptin**	**Absolute benefit**
ITT	**0.81** (0.66-1.00)	**0.76** (0.64-0.91)	90.6%	87.8%	**+2.8%**
LN-positive	**0.77** (0.62-0.96)	**0.72** (0.59-0.87)	87.9%	83.4%	**+4.5%**
LN-negative	**1.13** (0.68-1.86)	**1.02** (0.69-1.53)	95.0%	94.9%	**+0.1%**
HR-positive	**0.86** (0.66-1.13)	**0.73** (0.59-0.92)	91.2%	88.2%	**+3.0%**
HR-negative	**0.76** (0.56-1.04)	**0.83** (0.63-1.10)	89.5%	87.0%	**+2.5%**

- The node + cohort continues to derive clear benefit from the addition of Perjeta
- Treatment benefit of Perjeta is now seen in both HR+ and HR- cohorts

Piccart M., et al, SABCS 2019; primary analysis (2017): median follow-up 45.4 months, Updated Analysis (2019): median follow-up 74.1 months
IDFS= invasive disease free surival; eBC = early breast cancer; LN = lymph node; HR = hormone receptor

High bar set in adjuvant disease

3-yr iDFS in APHINITY and KATHERINE



1. High efficacy bar established

- Long term disease free survival established in both ITT and high-risk pts

2. Strong safety profile

- APHINITY and KATHERINE regimens well tolerated, with low discontinuation rate

3. Robust trial design

- APHINITY trial: 4,800 patients and ~5.5 years from FPI to primary endpoint

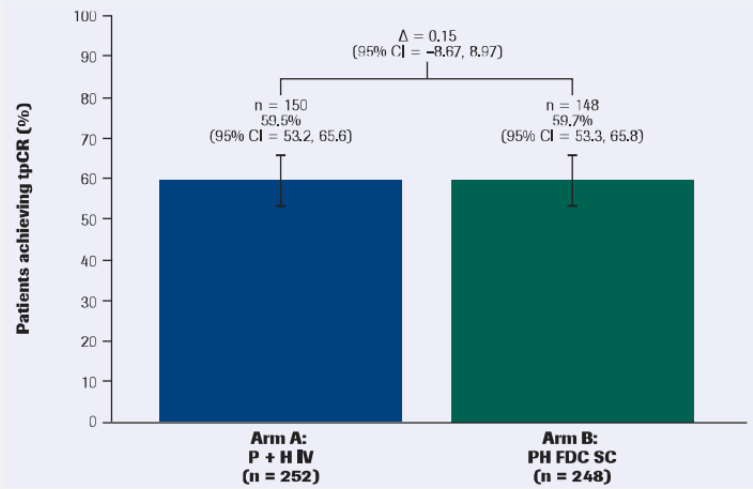
Future trials in HER2+ adjuvant disease likely to be designed around high-risk patient subgroups or deescalation of therapy

FPI= first patient in; pCR= pathogenic complete response

Ph 3 FeDeriCa trial of Perjeta+Herceptin SC FDC positive

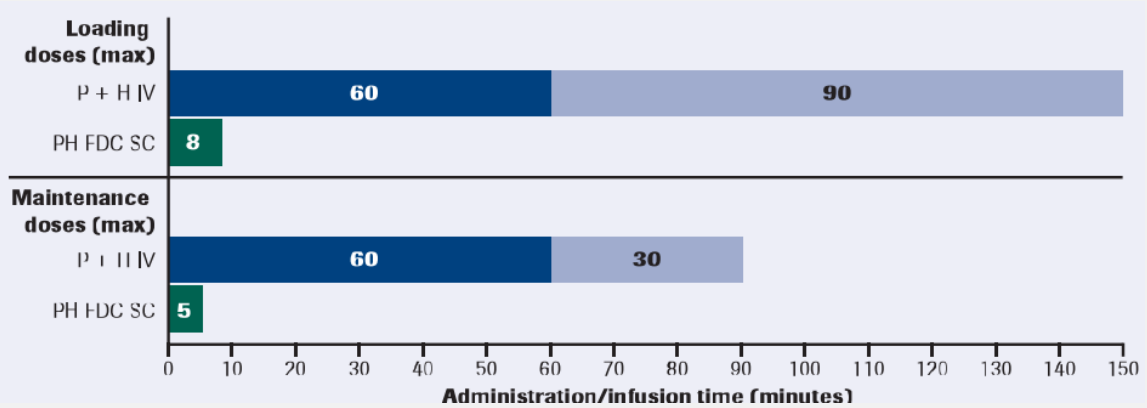
Herceptin + PERJETA pertuzumab

tpCR rates nearly identical between IV and SC



- PH FDC SC was non-inferior to P+H IV based on pre dose cycle 8 P and H C_{trough} concentrations
- tpCR nearly identical and in-line with data from prior studies
- Safety was comparable between arms

FDC reduces administration and observation time



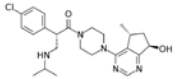
- PH FDC SC is administered in 5-8 minutes (compared to up to 2.5 hours for H+P IV)
- Strong patient preference for H+P FDC SC administration
- US/EU filing in early 2020

Tan, A.R., et al, SABCS 2019 *Ranges driven by differences in loading and maintenance dose; H+P FDC SC in collaboration with Halozyme
H=Herceptin; P=Perjeta; FDC=fixed dose combination; SC=subcutaneous; IV=intravenous; tpCR=total pathogenic complete response

HR+/HER2- and TNBC strategy

Elena Bernedo Arzac | M.D., Head of Oncology, Global Product Strategy

Largest breast cancer portfolio
Expanding beyond HER2+ disease

	 *mAb*	 *Small Molecule*	 *ADC*	 *CPI*	 *Bispecific*
HER2+ BC 20%	Herceptin ✓ PERJETA pertuzumab ✓		Kadcyla ado-trastuzumab emtansine for injection ✓	TECENTRIQ atezolizumab	RG6194
HR+/HER2- BC 65%		ipatasertib (AKTi) GDC-0077 (PI3Ki) GDC-9545 (SERD) VENCLEXTA venetoclax tablets			
TNBC 15%		ipatasertib (AKTi)		TECENTRIQ atezolizumab ✓	

✓ = approved

mAB=monoclonal antibody; ADC=antibody drug conjugate; CPI=checkpoint inhibitor; TNBC=triple negative breast cancer; Venclexta in collaboration with Abbvie

TNBC treatment landscape

TNBC is not one disease, but a constellation of diseases

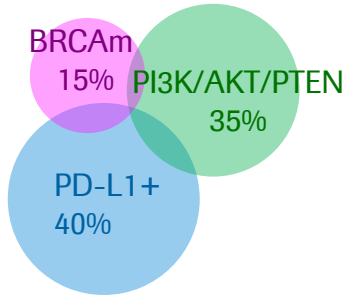
Historical standard of care

1L mBC

Chemotherapy

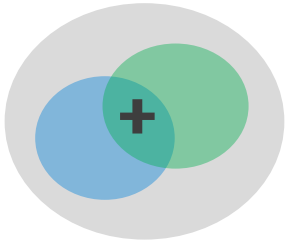
TNBC patients defined by lack of actionable targets

2020 (PHC approach)



Treatment algorithm defined by relevant biomarkers

Future (NME combinations)



All-comers benefit observed with Tecentriq + ipatasertib combination

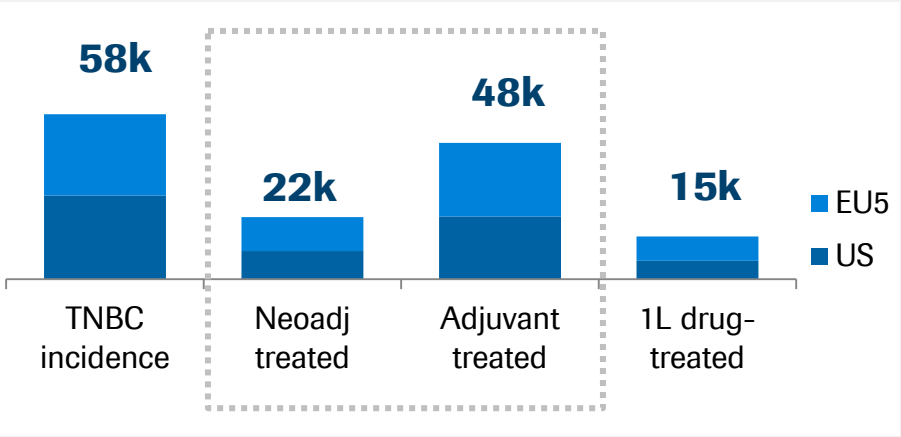
Tecentriq + chemo	IMpassion130	1L TNBC (PD-L1+)	✔
Tecentriq + chemo	IMpassion131	1L TNBC (PD-L1+)	
Tecentriq + chemo	IMpassion132	1L TNBC (PD-L1+)	
ipatasertib + chemo	IPATUNITY130	1L TNBC (PI3K/AKT/PTENm)	
ipatasertib + Tecentriq + chemo	IPATUNITY170	1L TNBC	

- **Tecentriq is the first new agent approved in TNBC in ~15 years**

TNBC=triple negative breast cancer; mBC = metastatic breast cancer; PHC = personalized healthcare; NME = new moleculear entity
PIK3CA/AKT/PTEN includes any of the three mutations

Expanding into early TNBC

Significant opportunity in early TNBC



- 4.5x more patients treated with neoadjuvant/adjuvant disease than metastatic disease
- Number of neoadjuvant treated patients expected to increase further with new treatments

TECENTRIQ
atezolizumab

IMpassion031 (Neoadjuvant)

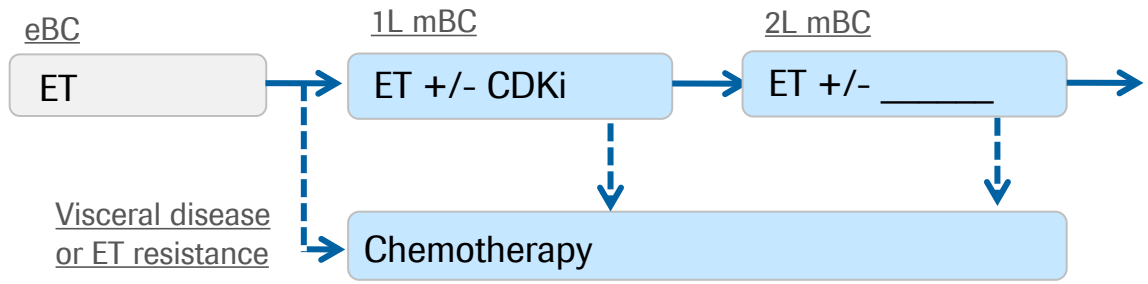
Trial passed futility analysis.
Readout expected 1H 2020

Tecentriq	IMpassion031	Neoadjuvant TNBC
	IMpassion030	Adjuvant TNBC
	GEPARDOUZE	Neoadj/Adj TNBC

TNBC=triple negative breast cancer

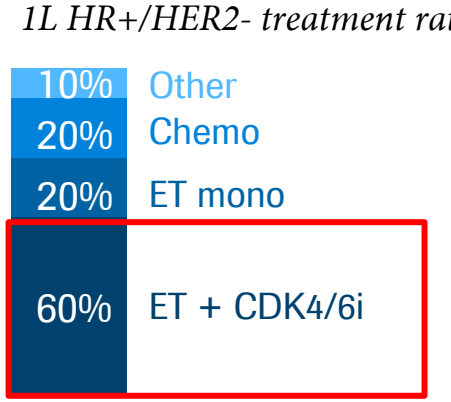
HR+/HER2- breast cancer: current treatment landscape

Endocrine therapy is the backbone of HR+/HER2- treatment



- HR+/HER2- patients treated with Endocrine Therapy (e.g. letrozole, fulvestrant) as monotherapy or combination until resistance develops or visceral disease present
- High unmet need remains: despite the effectiveness of available therapies, many patients ultimately relapse or develop resistance

ET + CDK4/6i combination is SOC in 1L



- Most common 1L regimen for metastatic patients is combination of CDK4/6i + ET

ET=endocrine therapy; HR+ = hormone receptor positive

HR+/HER2- breast cancer treatment landscape

Goal to combine with or replace 1L standard of care in HR+ breast cancer

ET + CDK4/6i + ⬇

Replace ET with GDC-9545 (SERD)

⬇

Add-on ipatasertib (AKT) or GDC-0077 (PI3K)

Chemotherapy + ⬇

Add-on ipatasertib (AKT)

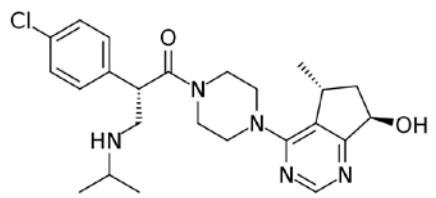
ipatasertib + chemo	IPATUNITY130	1L HR+ mBC (PIK3CA/AKT/PTENm)
ipatasertib + ET + CDKi	IPATUNITY150	1L HR+ mBC
GDC-0077 + ET + CDKi	Ph 3	1L HR+ mBC (PIK3CAm)
GDC-9545 + CDKi	Ph 3 planned	1L HR+ mBC

Potential for future development in eBC

ET=endocrine therapy; HR+ = hormone receptor positive; eBC = early breast cancer; ipatasertib in collaboration with Array BioPharma
*AKT diagnostic (PI3K/AKT/PTEN mutation), GDC-0077 diagnostic (PI3K mutation only)

Ipatasertib

Highly selective AKT inhibitor

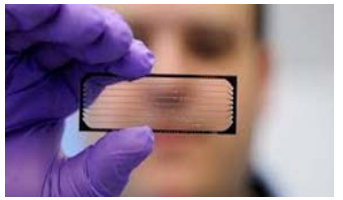


- Oral, highly specific inhibitor of all three activated isoforms of AKT
- Clinical development in tumors with high frequency of PI3K/AKT/PTEN mutations (TNBC, HR+ mBC, CRPC)

Ph 3 program

Ph 1	Ph 2	Ph 3	Approved
IPATunity130	1L TNBC 1L HR+ mBC		Data 2020
IPATential150	1L mCRPC		Data 2020
IPATunity150	1L HR+ mBC		
IPATunity170	1L TNBC		

FOUNDATIONONE CDx™



PI3K/AKT/PTEN diagnostic used for IPATunity130

- **Three readouts in 2020 across 1L TNBC, 1L HR+ mBC, and 1L mCRPC**
  - IPATunity130: ipat + chemo 1L TNBC (dx+)
  - IPATunity130: ipat + chemo 1L HR+ mBC (dx+)
  - IPATential150: ipat + abiraterone 1L CRPC
- **New combinations advanced to Ph 3**
  - IPATunity150: ipat+fulv+palbo 1L HR+ mBC
  - IPATunity170: ipat+Tecentriq+chemo 1L TNBC

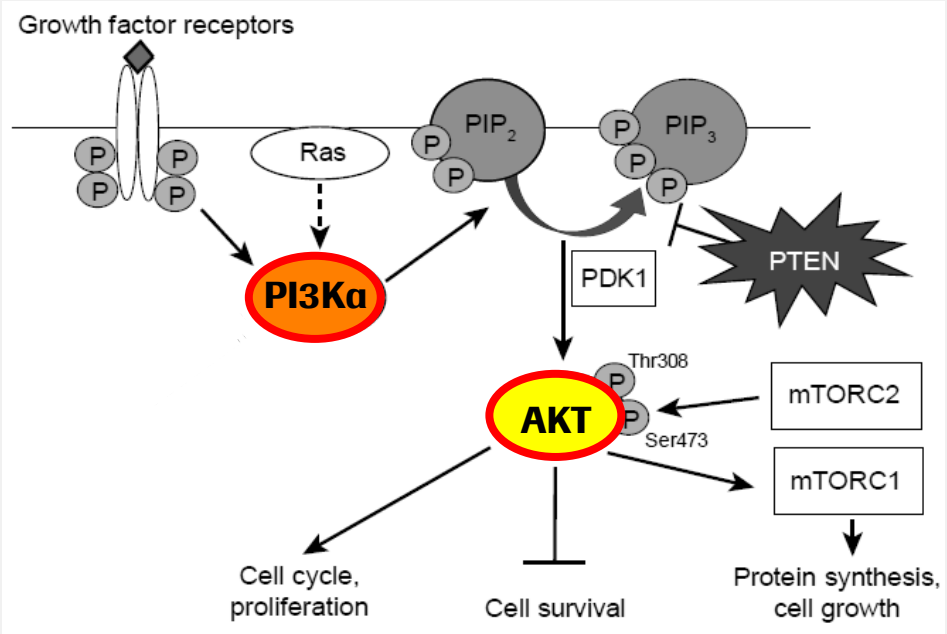
TNBC=triple negative breast cancer; HR=hormone receptor; BC=breast cancer; CRPC=castration resistant prostate cancer
Breast cancer diagnostic (PI3K/AKT/PTEN mutation), CRPC diagnostic (PTEN-low); ipatasertib in collaboration with Array BioPharma

Key early stage data presented at SABCS 2019: PI3K, SERD

Stuart Lutzker | M.D., Ph.D. Head of Oncology, Early Clinical Development

PI3K/AKT is the most frequently altered pathway in cancer

PI3K pathway



Frequency of PI3K mutations across tumor types

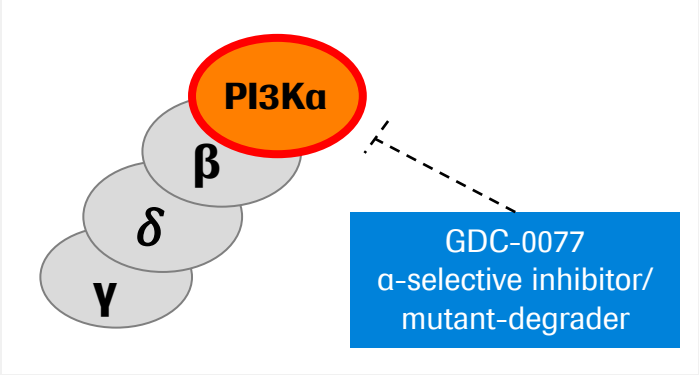
Tumor type	*PIK3CA* mutation
HR+ Breast Cancer	~40%
Ovarian	~33%
Endometrial	~25%
HER2+ Breast Cancer	~25%
Colon	~20%
Bladder	~20%
Cervix	~20%
HNSCC	~15%
TNBC	~8%
Gastric	~7%

14 million cancer patients diagnosed annually world wide, ~17% are *PIK3CA* mutant ~2.4M patients

HR+ = hormone receptor positive; HNSCC= head and neck squamour cell carcinoma; TNBC = triple negative breast cancer

GDC-0077 in *PIK3CA*-mutant HR+/HER2- mBC

GDC-0077



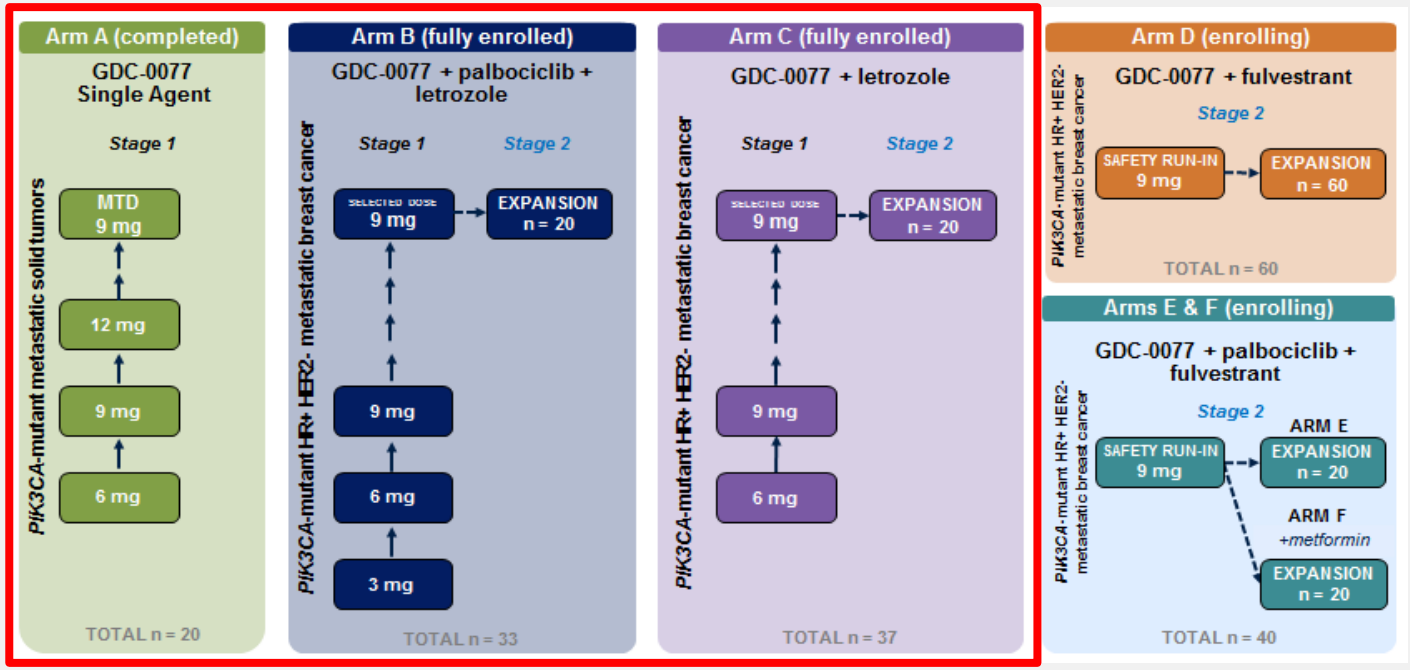
Best in-class molecular properties:

- More selective for PI3Kα
- Degradation of mutant PI3Kα
- Greater, more durable target inhibition

Potential for clinical differentiation:

- Increased efficacy
- Greater safety margins
- Combination with CDK4/6i + ET

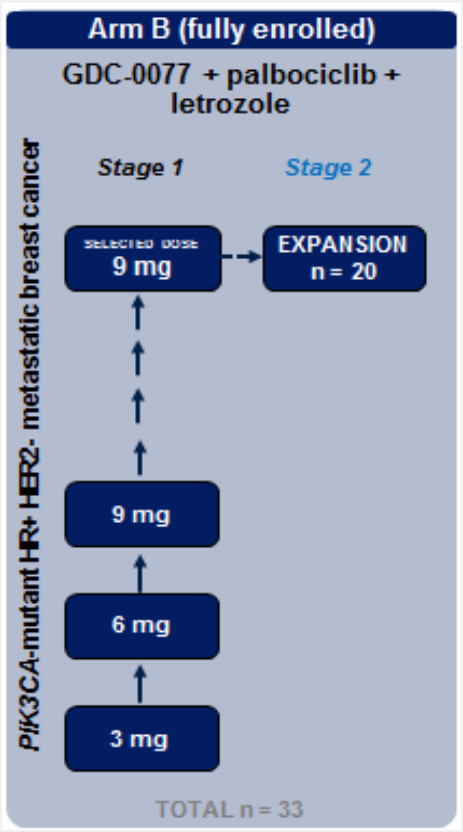
Ph 1 development program

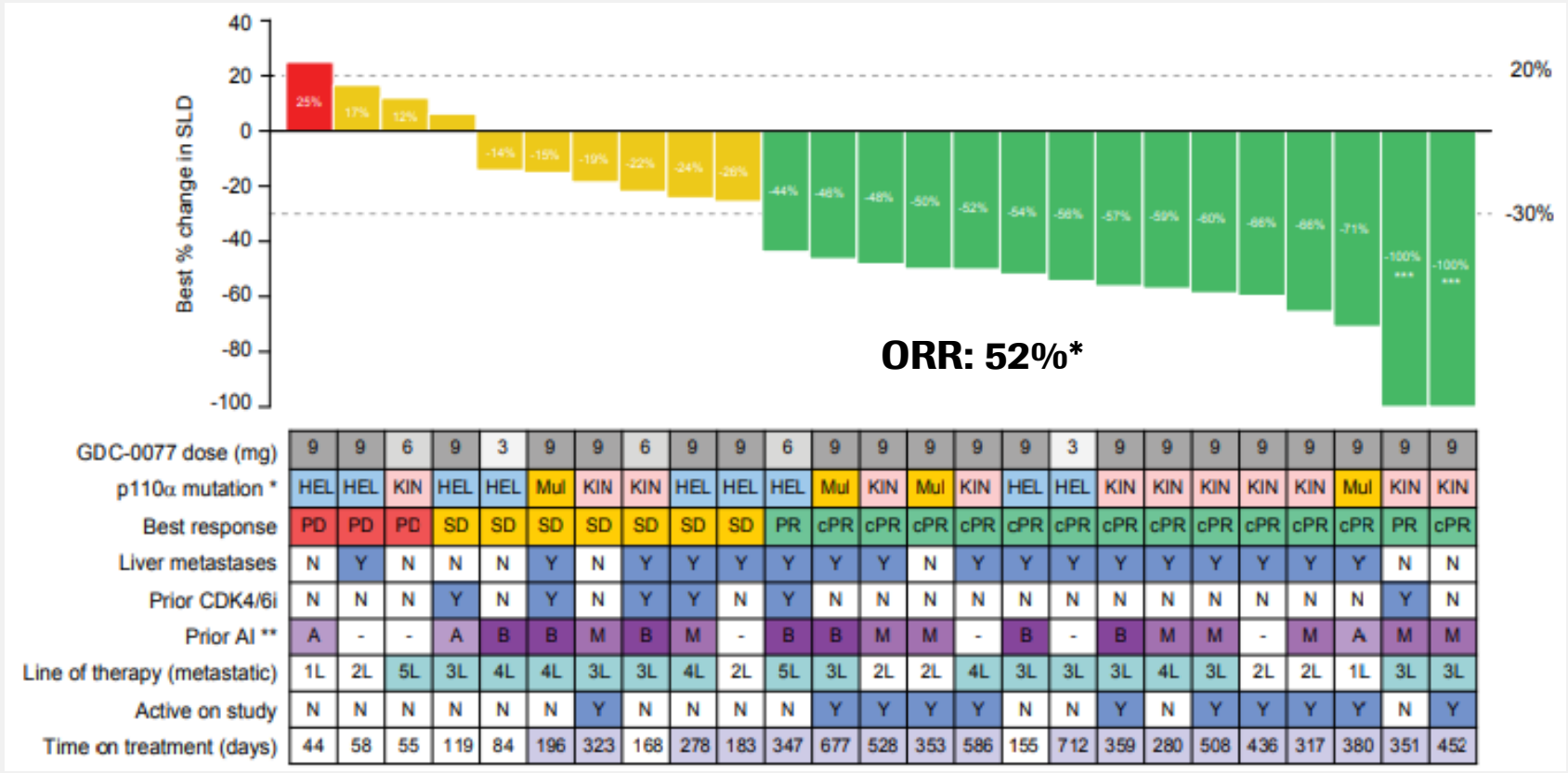


Dose escalation data from single agent GDC-077 and combinations with letrozole and palbociclib + letrozole presented at SABCS 2019

HR=hormone receptor; BC=breast cancer ; ET=endocrine therapy

GDC-0077 + CDK4/6i + ET demonstrates encouraging activity





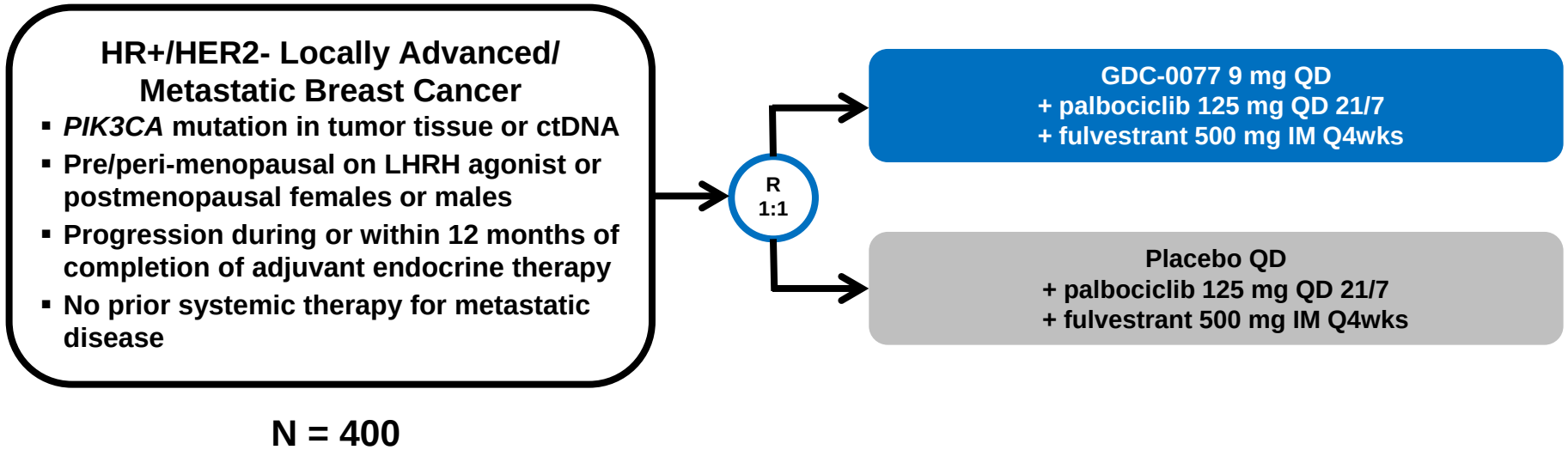
GDC-0077 dose (mg)	9	9	6	9	3	9	9	6	9	9	6	9	9	9	9	9	3	9	9	9	9	9	9	9	9
p110α mutation *	HEL	HEL	KIN	HEL	HEL	Mul	KIN	KIN	HEL	HEL	HEL	Mul	KIN	Mul	KIN	HEL	HEL	KIN	KIN	KIN	KIN	KIN	Mul	KIN	KIN
Best response	PD	PD	PD	SD	SD	SD	SD	SD	SD	SD	PR	cPR	cPR	cPR	cPR	cPR	cPR	cPR	cPR	cPR	cPR	cPR	cPR	PR	cPR
Liver metastases	N	Y	N	N	N	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N
Prior CDK4/6i	N	N	N	Y	N	Y	N	Y	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	N
Prior AI **	A	-	-	A	B	B	M	B	M	-	B	B	M	M	-	B	-	B	M	M	-	M	A	M	M
Line of therapy (metastatic)	1L	2L	5L	3L	4L	4L	3L	3L	4L	2L	5L	3L	2L	2L	4L	3L	3L	3L	4L	3L	2L	2L	1L	3L	3L
Active on study	N	N	N	N	N	N	Y	N	N	N	N	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	Y	N	Y
Time on treatment (days)	44	58	55	119	84	196	323	168	278	183	347	677	528	353	586	155	712	359	280	508	436	317	380	351	452

GDC-0077 can safely combine at its single agent recommended Ph 2 dose with palbo + letrozole at standard approved doses

Jhaveri, K., et al, SABCS 2019 *Confirmed ORR in patients with measurable disease; HR=hormone receptor; BC=breast cancer; ORR=overall response rate

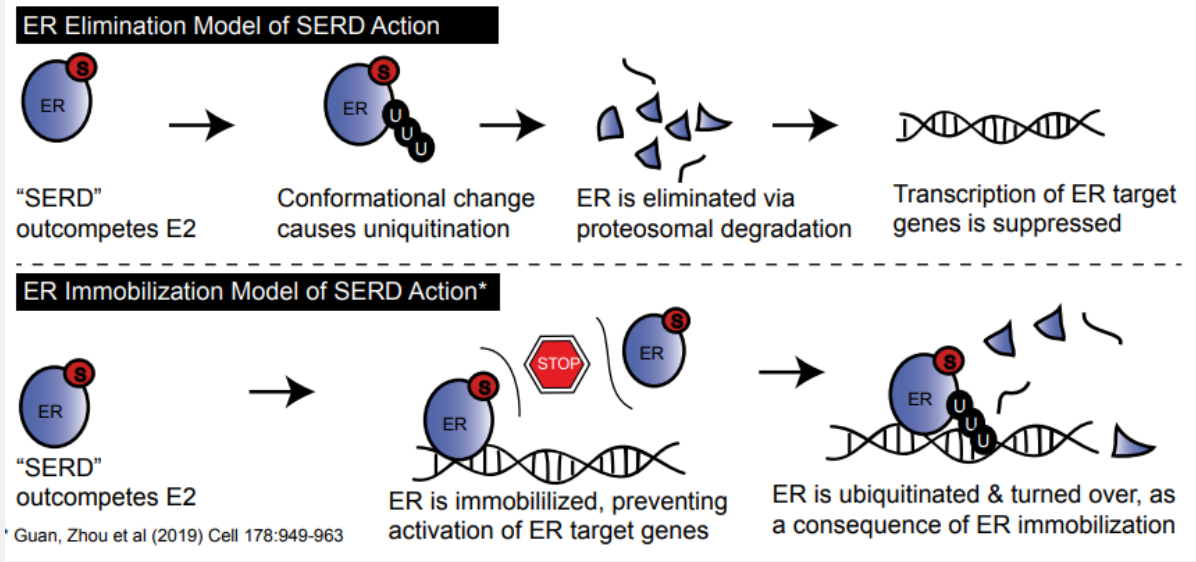
GDC-0077 in *PIK3CA*-mutant HR+/HER2- mBC

Ph III study in 1L *PIK3CA*-mutant HR+/HER2- mBC



HR=hormone receptor; mBC=metastatic breast cancer; Ph 1 combination data with palbociclib + fulvestrant not yet presented

GDC-9545 (SERD) in HR+/HER2- mBC



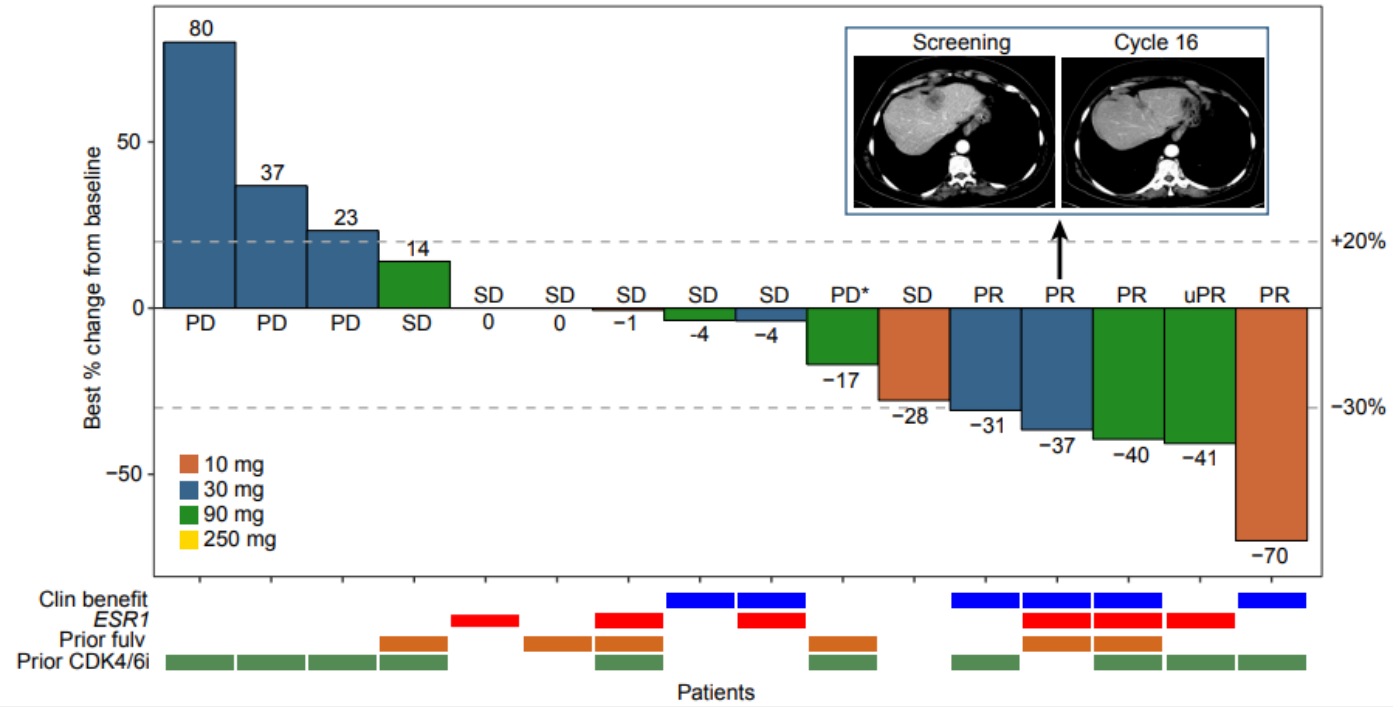
GDC-9545 has best-in-class potential

- Oral route of administration
- Highly potent and improved efficacy *in vivo* vs. other SERDs
- Full ER pathway blockade
- Superior PK results in efficacy at low doses in vivo
- Wide nonclinical safety margins

Jhaveri, K., et al, SABCS 2019
HR=hormone receptor; mBC=metastatic breast cancer; ER=estrogen receptor; PK=pharmacokinetics

GDC-9545 (SERD) in HR+/HER2- mBC

Ph 1 dose escalation: tumor responses



- Responses observed in pts with prior CDK4/6i and fulvestrant, and in pts with *ESR1*m
- Dose expansion cohorts with or without palbociclib are ongoing

Safety

	AEs related to GDC-9545	
	Grade 3	All Grades
Nausea	0	6 (21%)
Arthralgia	0	6 (21%)
Constipation	0	3 (10%)
Diarrhea	0	5 (17%)
Fatigue	0	6 (21%)
Hot flush	0	3 (10%)
Bradycardia[a]	0	3 (10%)
ALT increased	0	3 (10%)
Dyspepsia	0	3 (10%)
Gastroesophageal reflux	0	3 (10%)

- Treatment related AEs were all Gr 1-2
- No patients withdrew or reduced dose due to AE
- Bradycardia was all Gr 1, asymptomatic, reversible

Program advancing to Ph 3; trial design in progress

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Doing now what patients need next