AstraZeneca
What science can do

Hyatt Conference
Columbus2018

ASCO 2018 investor event; breakout 3: Next-gen DNA damage response and tumour drivers

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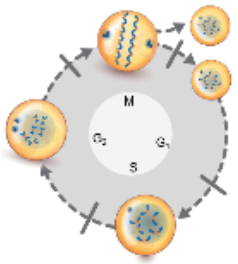
DNA damage response: *Lynparza* and beyond

Developing chemo-free regimens, extending survival

Launch AZD1775 (WEE1) / AZD6738 (ATR) *Lynparza* combinations

Expand *Lynparza* beyond *BRCA* (Study 08, prostate cancer)



Deliver next-generation DDR medicines: AZD0156, AZD1390 (ATM inhibitors), AZD2811 (aurora kinase B inhibitor), DNA-PK

Establish *Lynparza* leadership as monotherapy

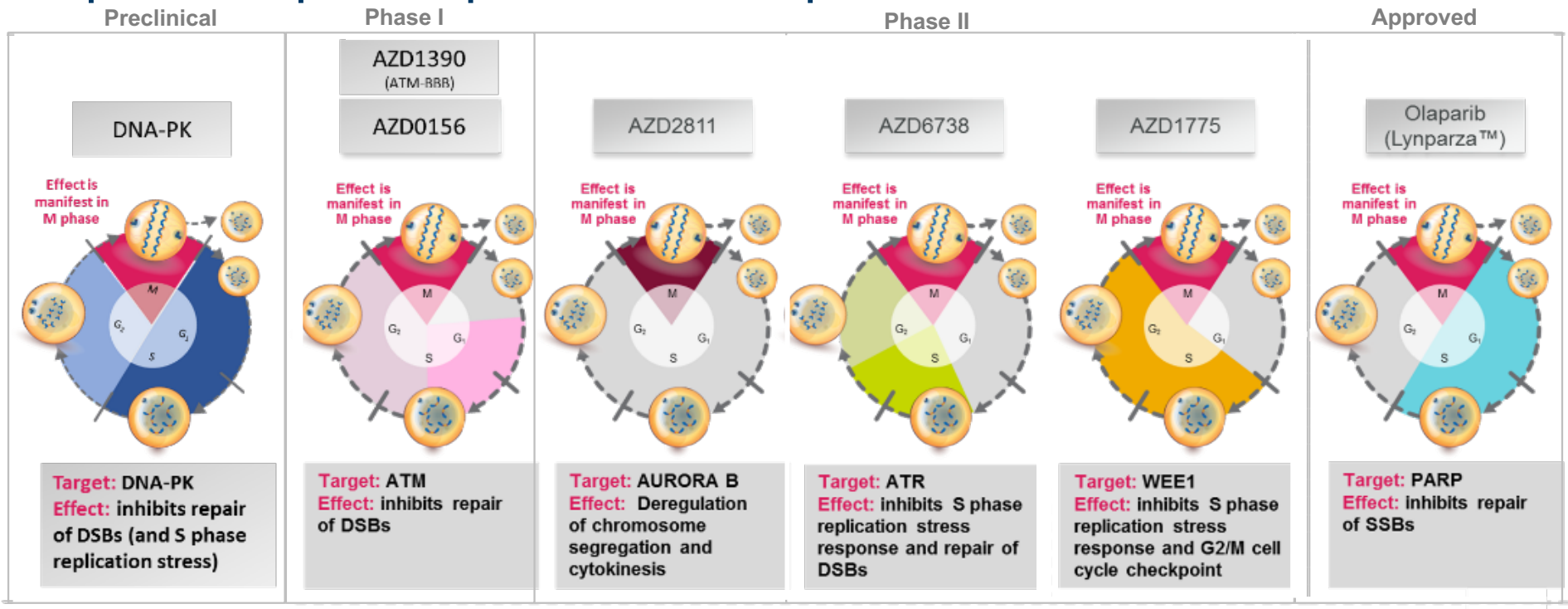
Launch *Lynparza* combinations (VEGF, IO)

Scientific leadership in DDR

2016 - 2018	2019 - 2021	2022 - 2025

AstraZeneca portfolio targets distinct aspects of DDR

Deep development portfolio from preclinical to launch



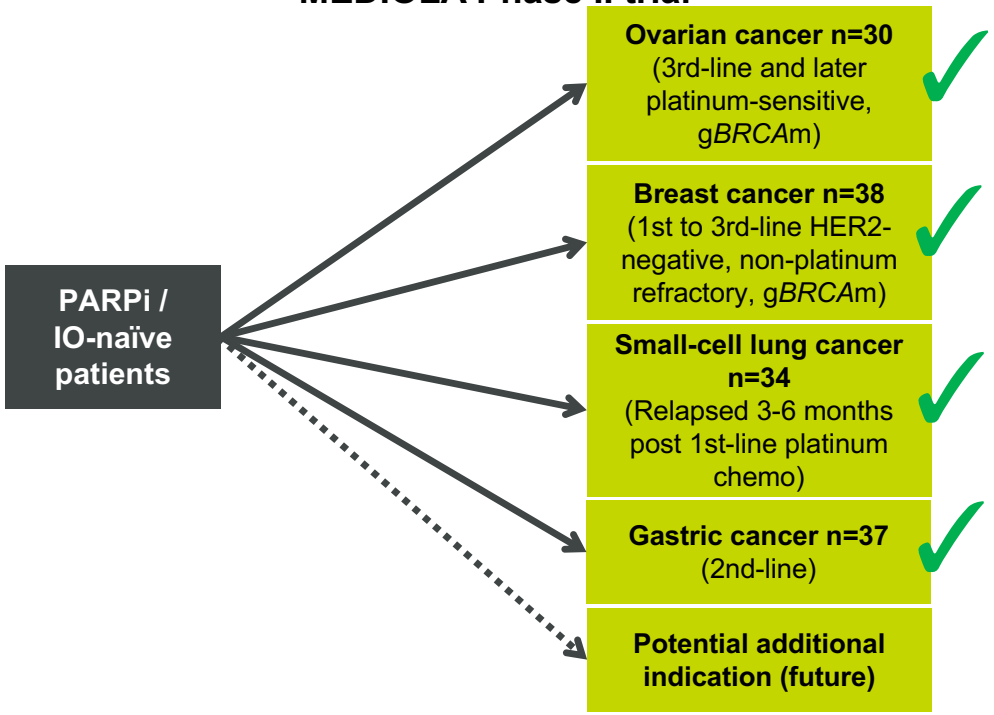
One launched medicine, four clinical and two preclinical projects: uniquely placed to exploit the full range of therapeutic opportunities afforded by DDR

ATM = ataxia-telangiectasia mutated; ATR = ataxia-telangiectasia and Rad3-related; DNA-PK = DNA-dependent protein kinase; DSB = double strand break; PARP = poly ADP-ribose polymerase; SSB = single-strand break.

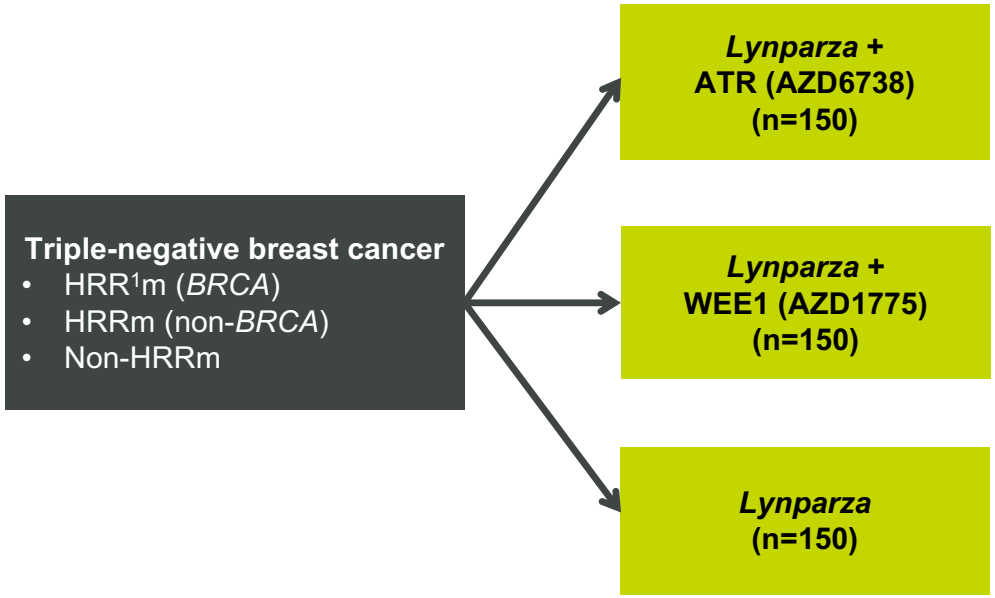
Lynparza: IO and DDR

Next-generation combinations underway

Lynparza* + *Imfinzi
MEDIOLA Phase II trial



***Lynparza* + novel DDR**
VIOLETTE Phase II trial



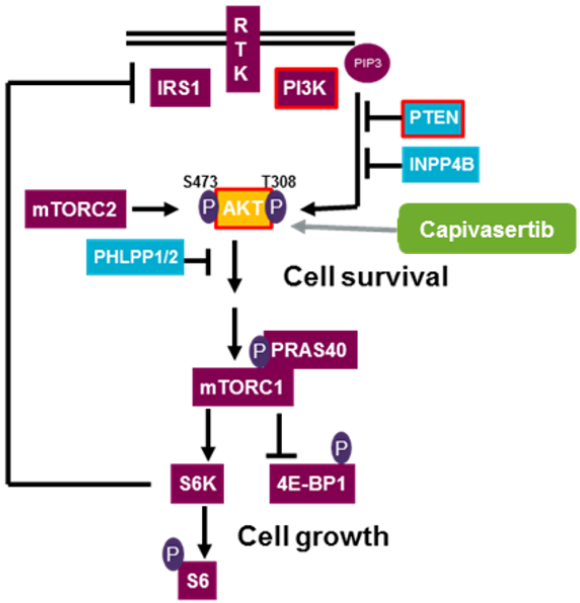
1. Homologous recombination repair mutation.

Broad DDR portfolio; deep scientific understanding is driving combination approach

Company	Target	Medicine	Pre-clinical	Phase I	Phase I/II	Phase II	Phase III	Launched
AstraZeneca	PARP	*Lynparza*						
AstraZeneca	Wee1	AZD1775						
AstraZeneca	ATR	AZD6738						
AstraZeneca	AKB	AZD2811						
AstraZeneca	ATM	AZD0156						
AstraZeneca	ATM	AZD1390						
AstraZeneca	DNA-PK	AZD7648						
Clovis	PARP	rucaparib						
Tesaro		niraparib						
Medivation (Pfizer)		talazoparib						
AbbVie		veliparib						
Eli Lilly	Chk 1/2	LY 2606368						
Genentech		GDC-0575						
Merck		MK-8776						
Eli Lilly		LY 2603618						
Novartis		CHIR-214						
Cancer Research UK		CCT241533						
Pfizer	ATM	CP 466722						
Merck-Serono		M3541						
Merck-Serono	DNA-PK	MSC 2490484A						
Vertex Pharma/Merck-Serono		VX 984						
Vertex Pharma/Merck-Serono	ATR	VX 970						

Capivasertib (AZD5363): targeting AKT

AKT pathway



Hypothesis

- AKT is a key node in the PI3K-AKT network: common oncogenic pathways converge
- AKT is key driver of resistance to multiple therapies, including hormonal therapies and chemotherapy
- Genetic alterations in the PI3K-AKT network are common in a number of tumours

Opportunity

Combinations:

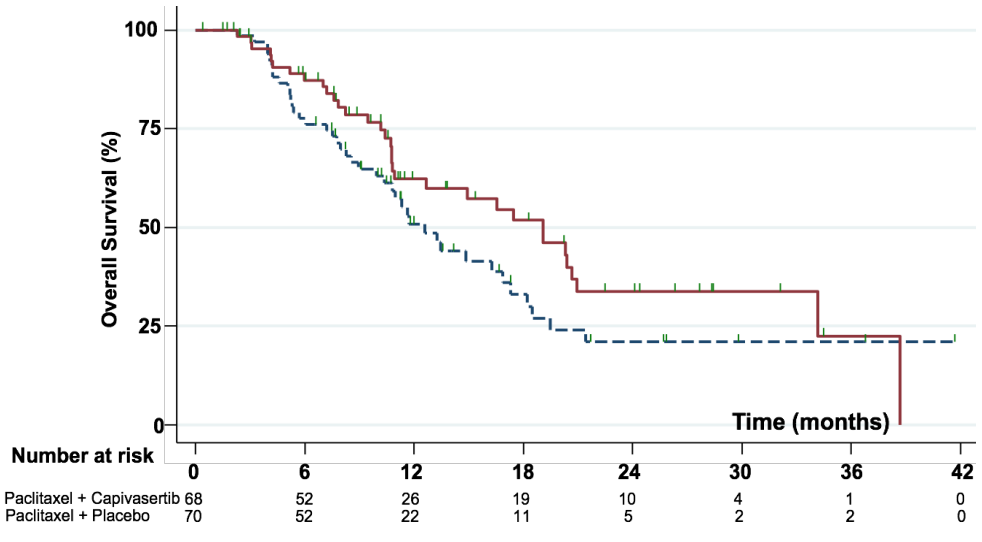
inhibition of AKT to prevent early adaptation and feedback responses

Patient selection:

genetic alterations in the network (AKT1, PTEN, PIK3CA, etc.)

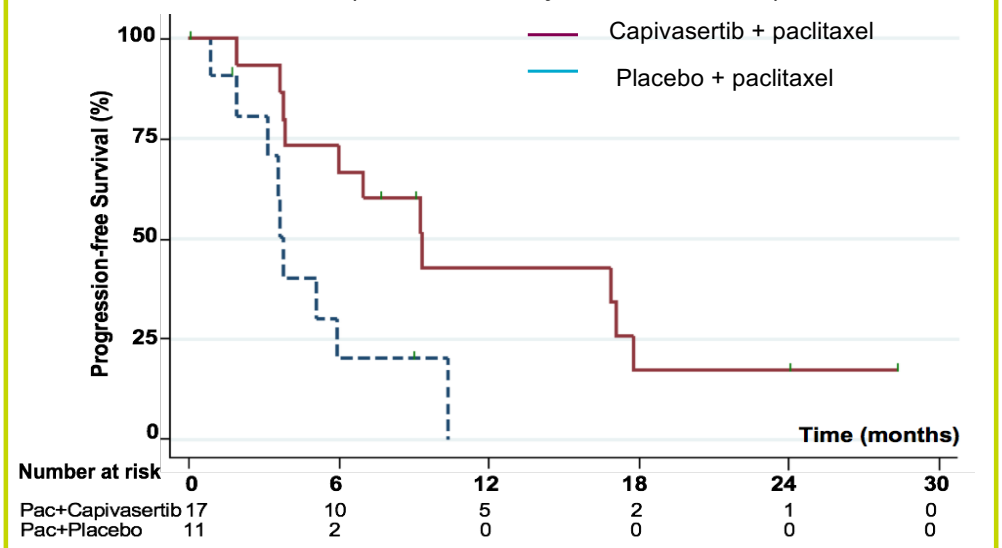
Capivasertib: PAKT randomised Phase IIb; 1st-line TNBC[1]

PAKT overall survival: ITT population



Median OS (95% CI) 19.1m vs. 12.6m
HR (95% CI)) 0.61 (0.37, 0.99)

PAKT progression-free survival: PI3KCA/AKT/PTEN altered (aberrations by NGS on FFPE)



Median PFS (95% CI) 9.26m vs. 3.75m
HR (95% CI) 0.30 (0.11, 0.79)

1. Triple-negative breast cancer.
Source: ASCO 2018, abstract #1007.

Q&A

Use of AstraZeneca conference call, webcast and presentation slides