AstraZeneca
What science can do

ASCO 2016 Investor Science Event

Chicago, IL, USA
6 June 2016

Forward-looking statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement:

This document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; effects of patent litigation in respect of IP rights; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions, including licensing and collaborations, will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure of outsourcing; the risks associated with manufacturing biologics; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the risk that new products do not perform as we expect; failure to achieve strategic priorities or to meet targets or expectations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the risk of misuse of social medial platforms and new technology; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the risks from pressures resulting from generic competition; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; economic, regulatory and political pressures to limit or reduce the cost of our products; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; and the risk of failure of information technology and cybercrime. Nothing in this presentation / webcast should be construed as a profit forecast.

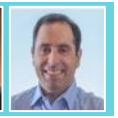
Agenda

Welcome

Oncology strategy and commercial update

DNA damage response (DDR)

Immuno-oncology:
Late- & early-stage development

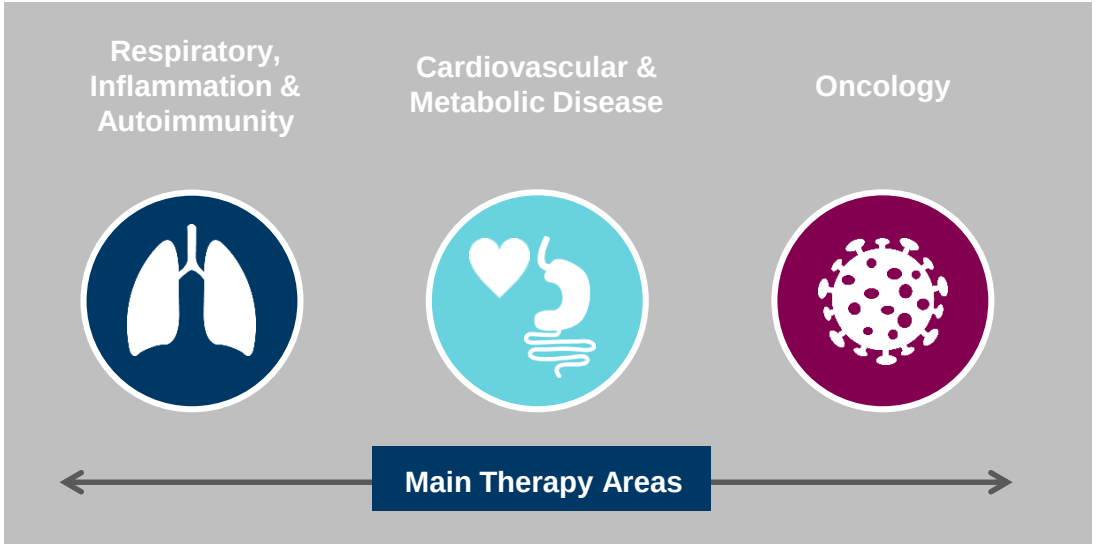


Haematology

Summary and Q&A

Focused strategy

Three therapy areas



Commitment to further focus the portfolio

Delivering the late-stage pipeline

saxa/dapa
submission EU
(type-2 diabetes)

brodalumab
submission US, EU
(psoriasis)

Tagrisso
approval US,EU,JP
(lung cancer)

durvalumab
Breakthrough US
(bladder cancer)

benralizumab
Phase III positive
(severe asthma)

saxa/dapa
positive opinion EU
(type-2 diabetes)

cediranib
submission EU
(ovarian cancer)

saxa/dapa
CRL US
(type-2 diabetes)

Iressa
approval US
(lung cancer)

Brilinta/Brilique
Phase III miss
(stroke)

CAZ AVI
positive opinion EU
(serious infections)

Lynparza
Phase III miss
(gastric cancer)

Faslodex
Phase III positive
(breast cancer 1L)

2015-2016: Great progress for patients and science

***Faslodex* 500mg**
approval CN
(breast cancer 2L)

selumitinib
Phase III miss
(uveal melanoma)

Zurampic
approval US, EU
(gout)

tremelimumab
Phase II miss
(mesothelioma)

Lynparza
Breakthrough US
(prostate cancer)

Bevespi
approval US
(COPD)

selumetinib
Orphan Drug US
(thyroid cancer)

***Bydureon* Pen**
approval JP
(type-2 diabetes)

Brilinta/Brilique
approval US, EU
(post/prior MI)

acalabrutinib
Orphan Drug EU
(blood cancers)

MEDI-551
Orphan Drug US
(neuromyelitis optica)

AZD3293
Phase III un-gating
(Alzheimer's disease)

ZS-9
submission EU

CRL US
(hyperkalaemia)

Illustrative timeline of 2015 and 2016 main late-stage pipeline newsflow Favourable Unfavourable

Key late-stage medicines & lifecycle

Phase III trials or under regulatory review*

Respiratory, Inflammation, Autoimmunity	Cardiovascular & Metabolic Disease	Oncology	Infection, Neuroscience (opportunistic)
brodalumab* (psoriasis)	**ZS-9*** (hyperkalaemia)	**cediranib*** (ovarian cancer)	**CAZ AVI*** (serious infections)
benralizumab (severe asthma, COPD)	**roxadustat** (anaemia)	**selumetinib** (lung cancer)	**AZD3293** (Alzheimer's disease)
tralokinumab (severe asthma)	***BrilintalBrilique*** (heart disease)	**durvalumab** (multiple cancers)	
PT010 (COPD, asthma)		**durva + treme** (multiple cancers)	
anifrolumab (lupus)		**acalabrutinib** (blood cancers)	
		moxetumomab (leukaemia)	
		Lynparza (multiple cancers)	
		Tagrisso (lung cancer)	

Status as of 29 April 2016 (Q1 2016 Results) New medicine with larger potential

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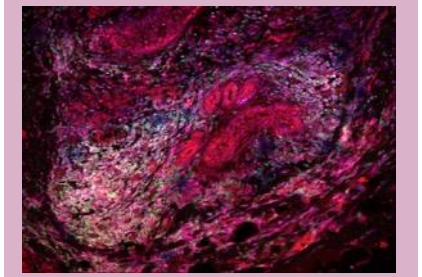
Oncology strategy and commercial update

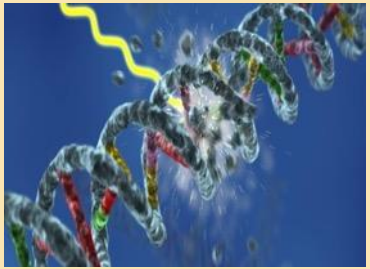
Mondher Mahjoubi
Senior Vice President, Global Product Strategy Oncology

Oncology: Scientific leadership around four key platforms

Personalised healthcare as key driver



Tumour drivers and resistance



DNA damage response (DDR)

Immuno-oncology (IO)

Antibody conjugates

Oncology: Aiming for first or best in class

Deliver six new medicines to patients by 2020

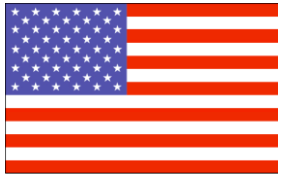
2013 - 2015	2016 - 2018	2019+
1st PARP inhibitor	Beyond BRCA and ovarian cancer	Leader in DDR
1st EGFR-T790M inhibitor	Earlier lines and combinations	Leader in EGFRm
	Best-in-class BTK inhibitor	IO in haematology
	Lead with IO/IO combination	Leader in IO
		Next wave of innovation

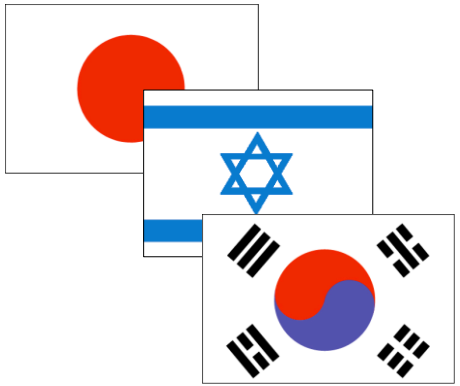
Tagrisso: Fastest development time

Rationally-designed and targeted treatment

March 2013 ↯ **November 2015** **February 2016** **March 2016** **H2 2016**

First in human



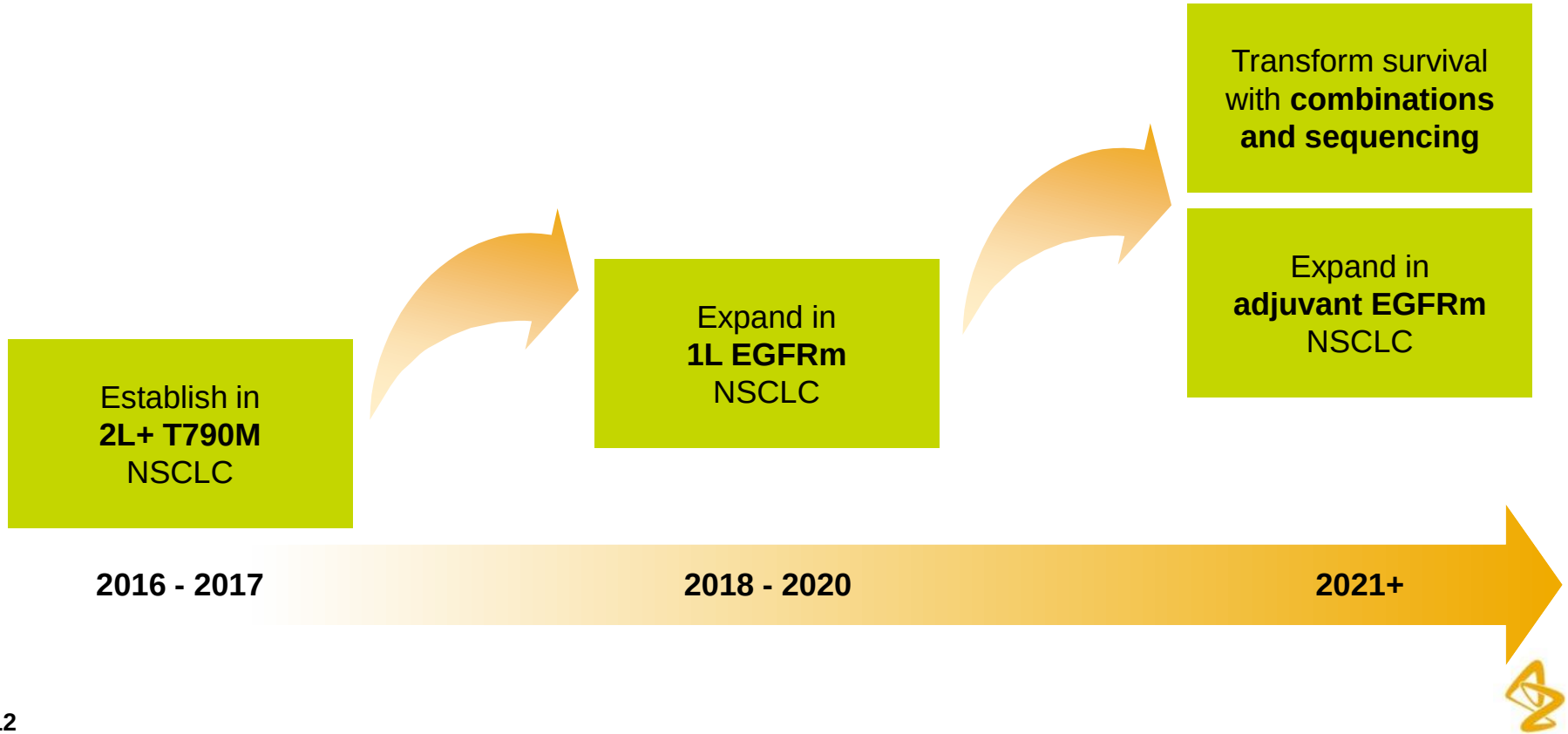


Multiple markets globally

- 32 months from first in human to first approval; leapfrogged competition
- US, EU, Japan approved within six months
- Aggressive development plan, including China

Tagrisso: Reaching more patients through life cycle

Transforming outcomes for patients with EGFRm lung cancer

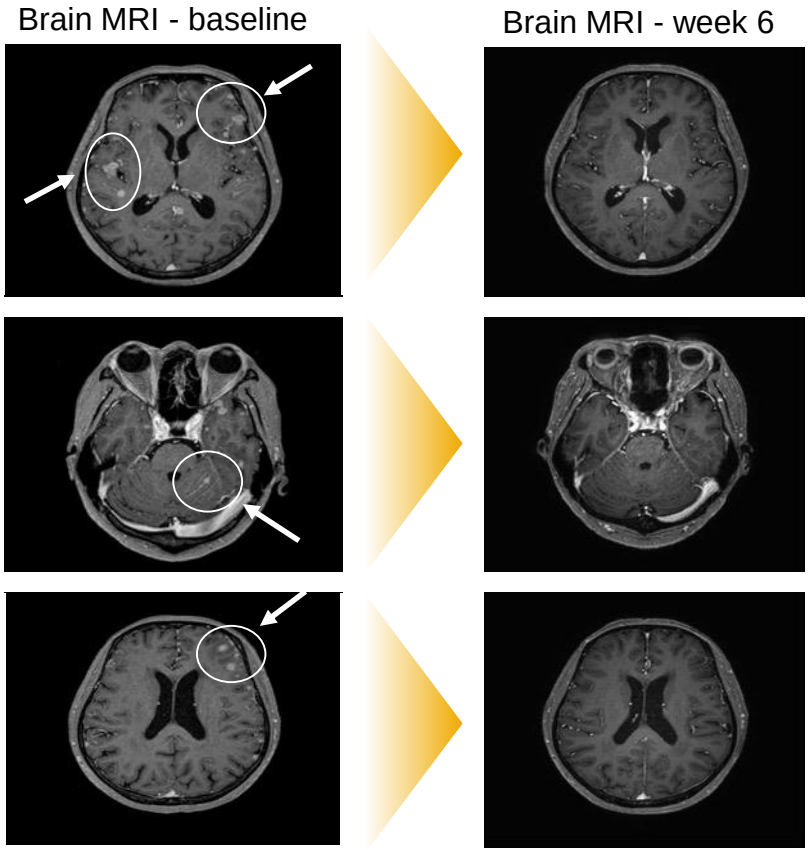


Tagrisso: Patient example

BLOOM trial effective in CNS

Diagnosis of advanced NSCLC June 2013 with most-recent disease progression March 2015

- Prior therapy included *Iressa* (March 2013-May 2015) and whole-brain radiotherapy (April 2013-May 2015)
- *Tagrisso* 160mg once daily started 20 May 2015
- Response ongoing from week 6. Week 12 images not presented as minimal changes were observed during weeks 6-12
- Stable extracranial disease since week 6; partial response since week 12
- Normal neurological function since baseline



Source: ASCO 2016, abstract 9002

Tagrisso: Potential in 1L EGFRm NSCLC

Early, but very promising data from Phase I

Tony Mok
Discussion of *Tagrisso* data at ELCC - Geneva, 13 April 2016

60 ← Number of EGFRm +ve patients who received *Tagrisso* in 1L setting

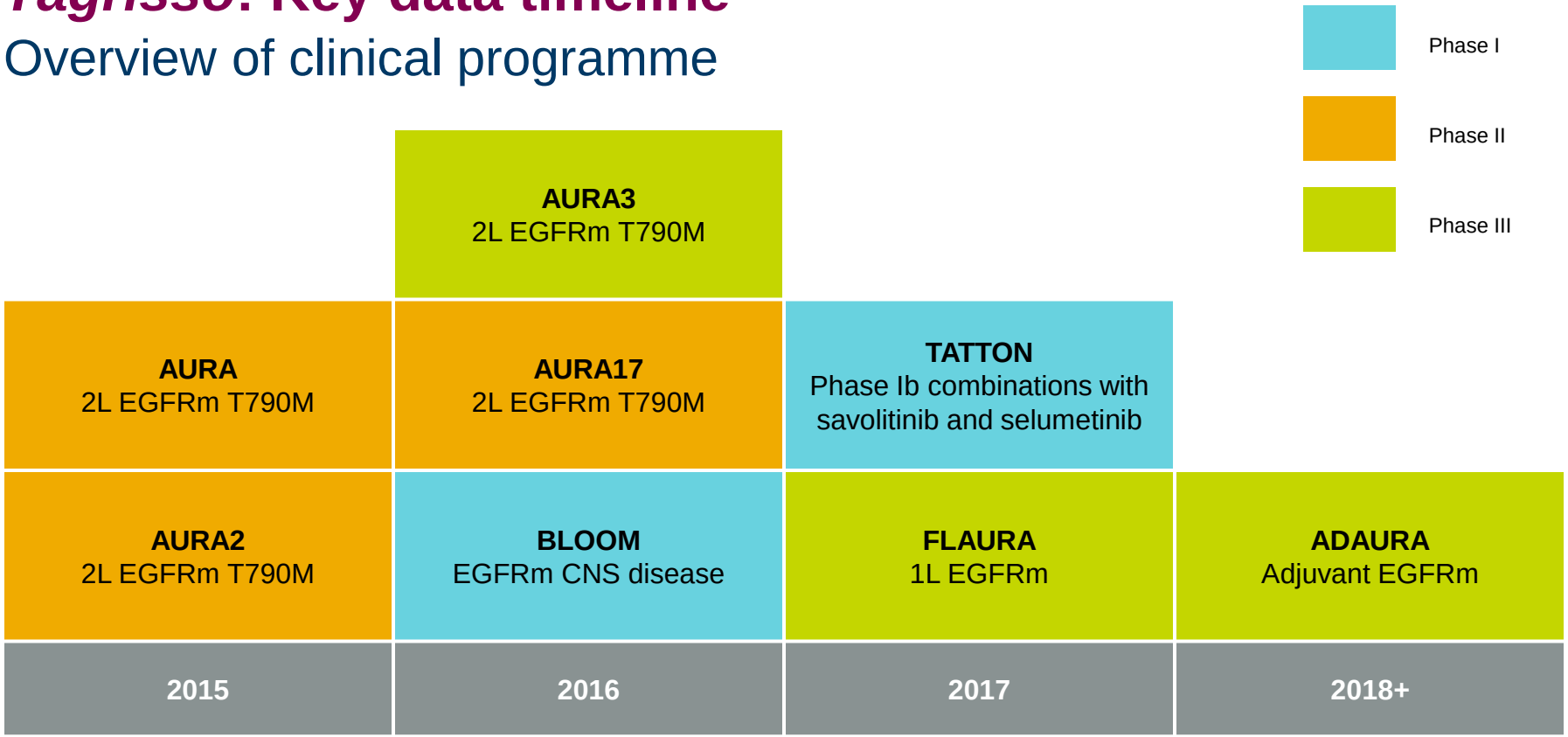
Percentage of patients who attained partial response → **77**

19.3 ← Median number of months of PFS in 1L setting

Source: ELCC 2016, AstraZeneca data on file

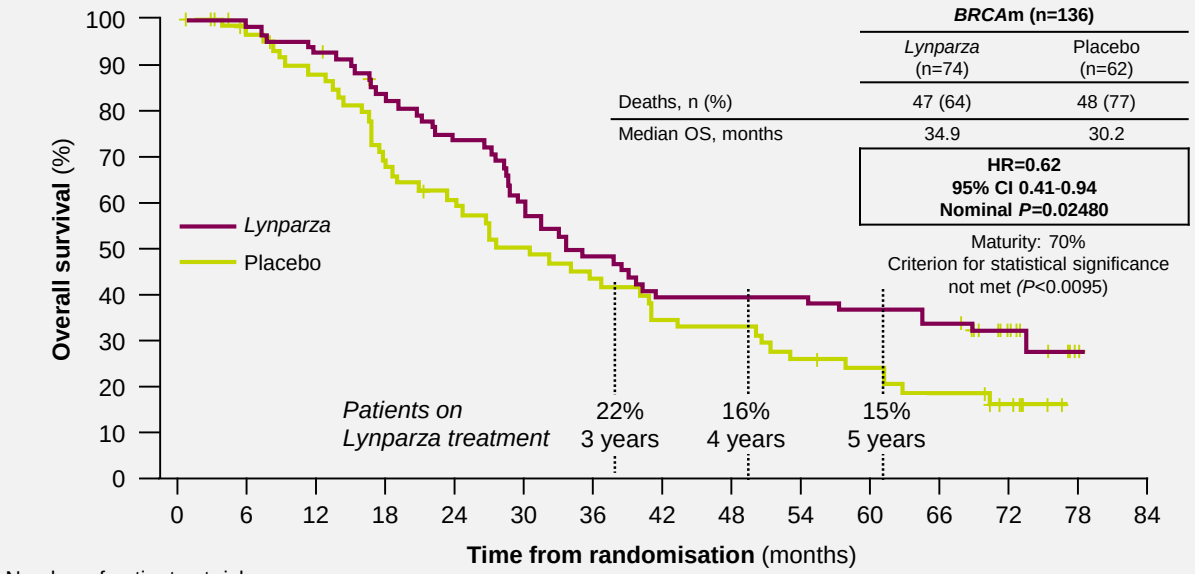
Tagrisso: Key data timeline

Overview of clinical programme



Lynparza: Ovarian cancer

Long-term survival benefit in BRCAm patients

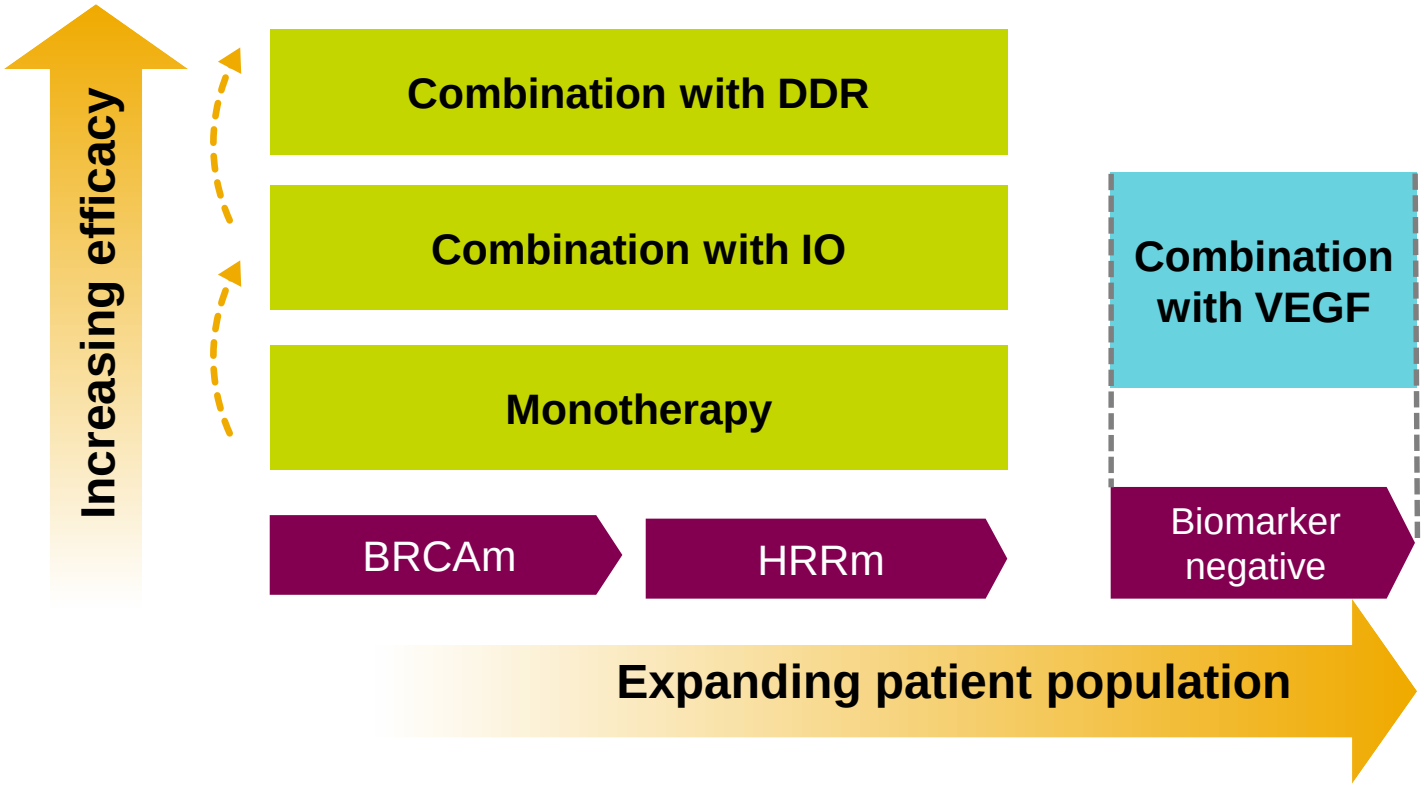


- First PARPi to show **long-term OS data**
- Long-term responders indicate IO-like benefit with **15% of patients on treatment for five years**
- sBRCA patients show similar benefit to gBRCA
- Future patient selection to be based on HRRm test, including BRCAwt/HRRm patients (~8% of all ovarian cancer patients)

Source: ASCO 2016, abstract 5501

Lynparza: Expanding beyond BRCA

Two dimensions driving life-cycle programme



Lynparza: Future newsflow

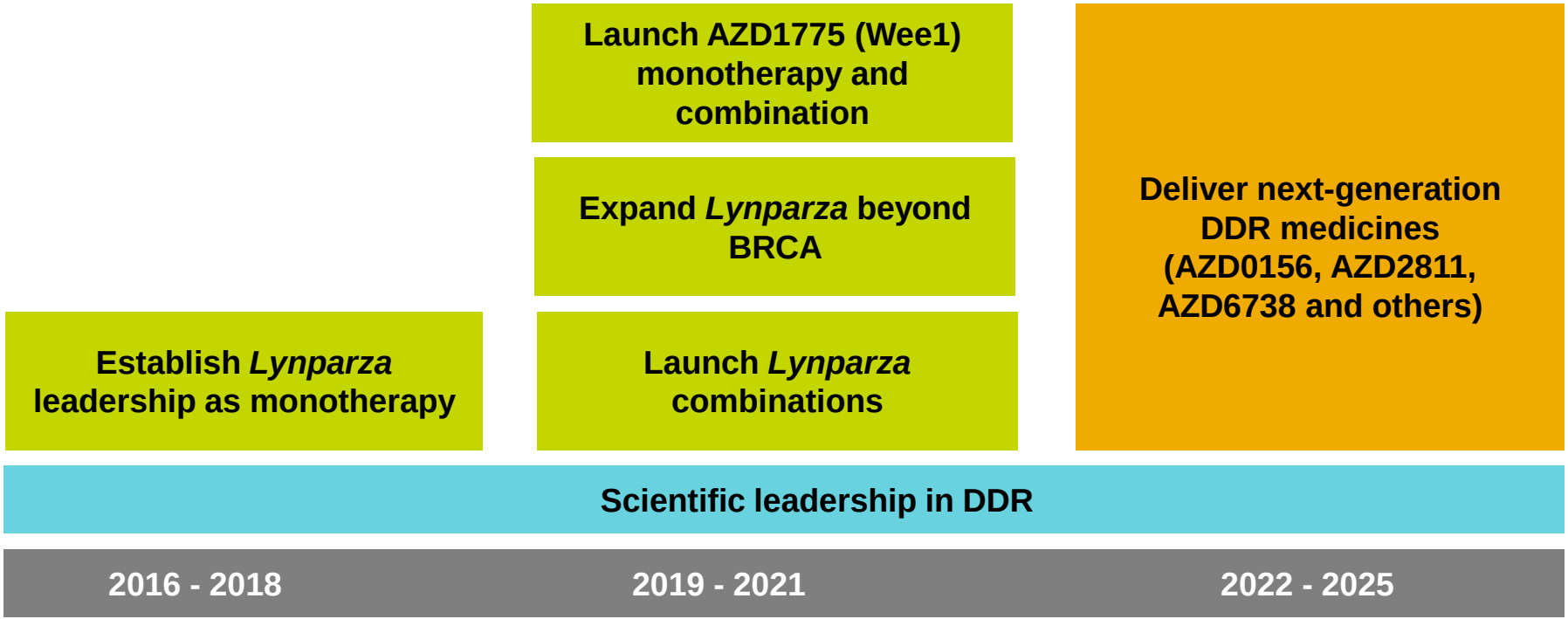
Expected regulatory submissions

2017	2018+
	Study 8 (prostate cancer)
	PAOLA bevacizumab combination (ovarian cancer)
SOLO-1 (1L BRCAm ovarian cancer)	**OlympiA** (adjuvant BC)
SOLO-2 (2L BRCAm PSR ovarian cancer)	**POLO** (pancreatic cancer)
OlympiAD (advanced breast cancer)	**SOLO-3** (3L+ gBRCAm PSR ovarian cancer)

Phase II Phase III

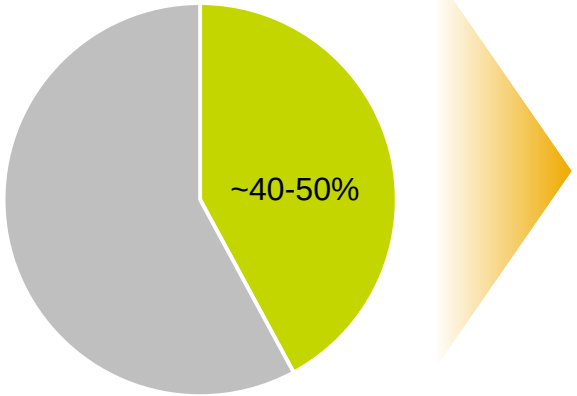
Beyond *Lynparza*: DDR

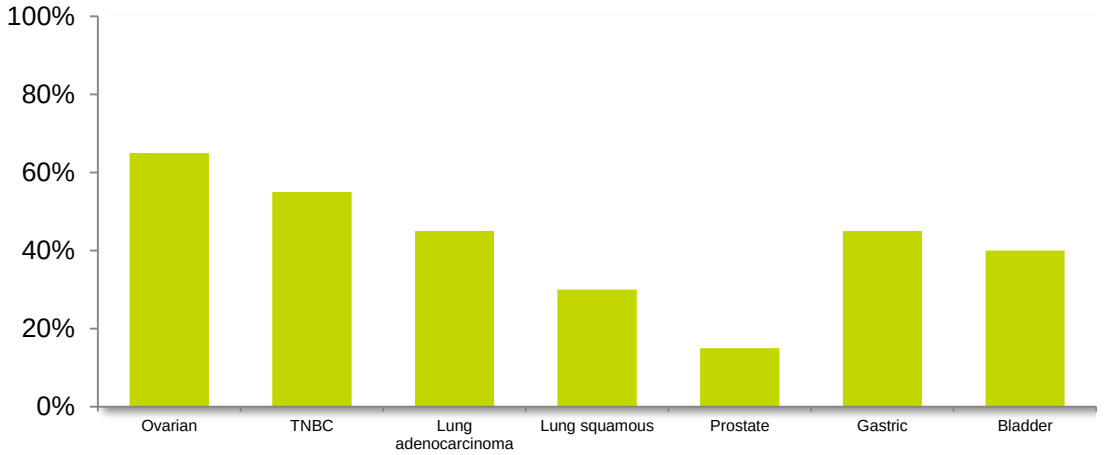
Developing chemo-free regimen, extending survival



DDR abrogation is frequent across multiple cancer types

Cancer patients with targetable DDR defects





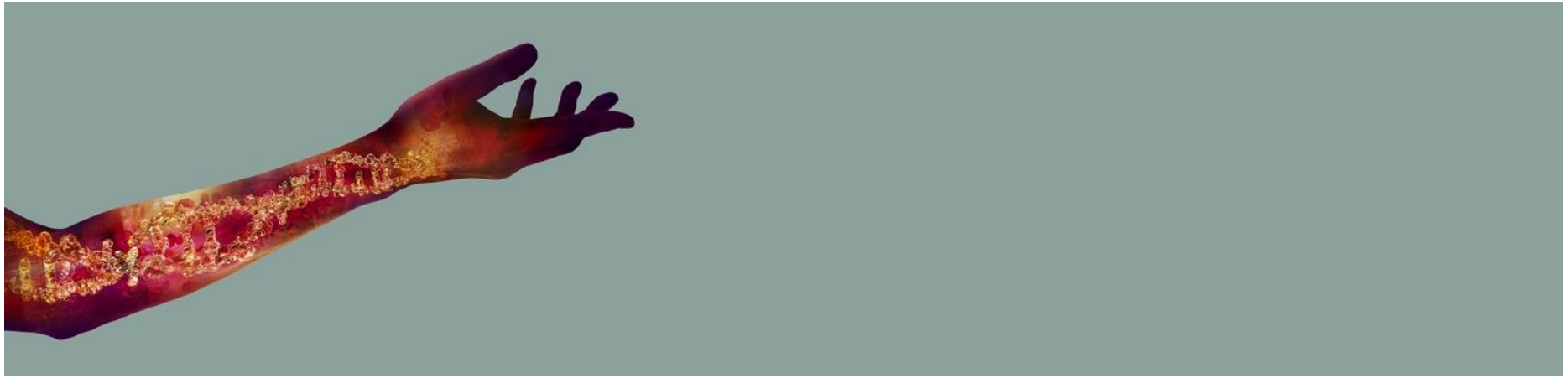
DDR abrogations include:

Cell cycle, oncogenic driver and homologous recombination repair

Source: AstraZeneca data on file

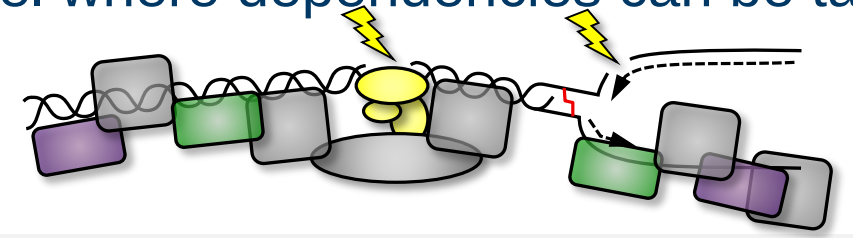
DDR

Susan Galbraith
Senior Vice President, Head of Oncology, IMED Biotech Unit



Targeting DNA damage response (DDR)

An Achilles heel where dependencies can be targeted selectively

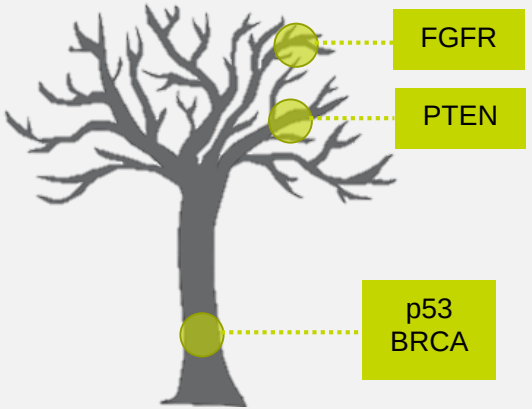


DDR deficiency is an early (truncal) event leading to:

- *Deep responses:* Homogeneity across tumours with all cancer cells targeted
- *High response rates:* Reduced opportunity for innate resistance
- *Wide therapeutic index:* Selective sensitivity to DDR drugs (unlike chemotherapies)

DDR engages the immune response

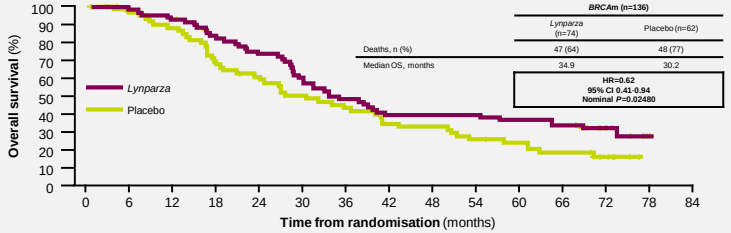
- Synergistic opportunities with IO agents



Emerging evidence: DDR provides potential for cure

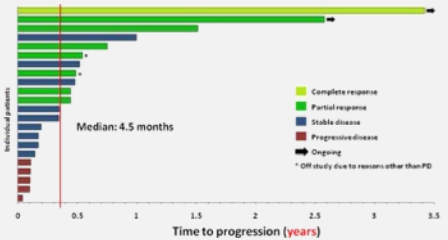
Lynparza in BRCAm ovarian cancer

- Patients still alive after eight years+
- ~25% patients are long-term responders (≥two years)



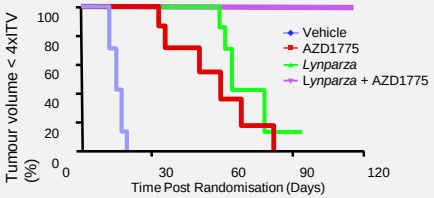
AZD1775 + carboplatin in platinum-resistant ovarian cancer

- 42% ORR in combination with platinum chemotherapy
- 3/22 patients showed responses lasting one to three years



Lynparza + AZD1775 in pre-clinical SCLC PDX model

- Five/seven cures after only 21 days of treatment with mice alive after more than one year



Source: ASCO 2016, abstract 5501; AstraZeneca data on file

Patient selection

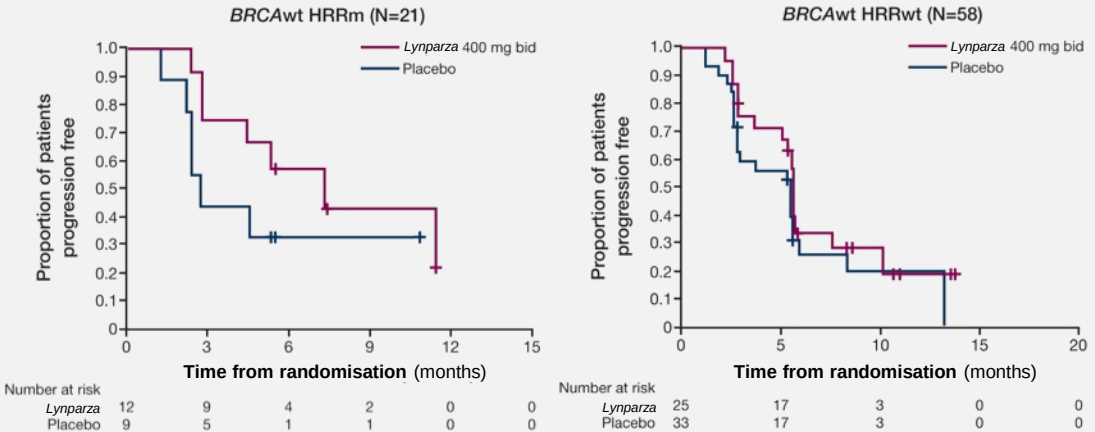
Critical component of delivering medical benefit

Reason to believe HRD LOH is NOT the right patient selection

- BRCAwt/HRD +ve patients in Study 19: No statistically-significant benefit
- HRD score cut-off base currently being refined

Reason to believe HRRm test is better in identifying BRCAwt patients likely to benefit from *Lynparza*

Study 19



Source: ECC 2015, Hodgson et al.

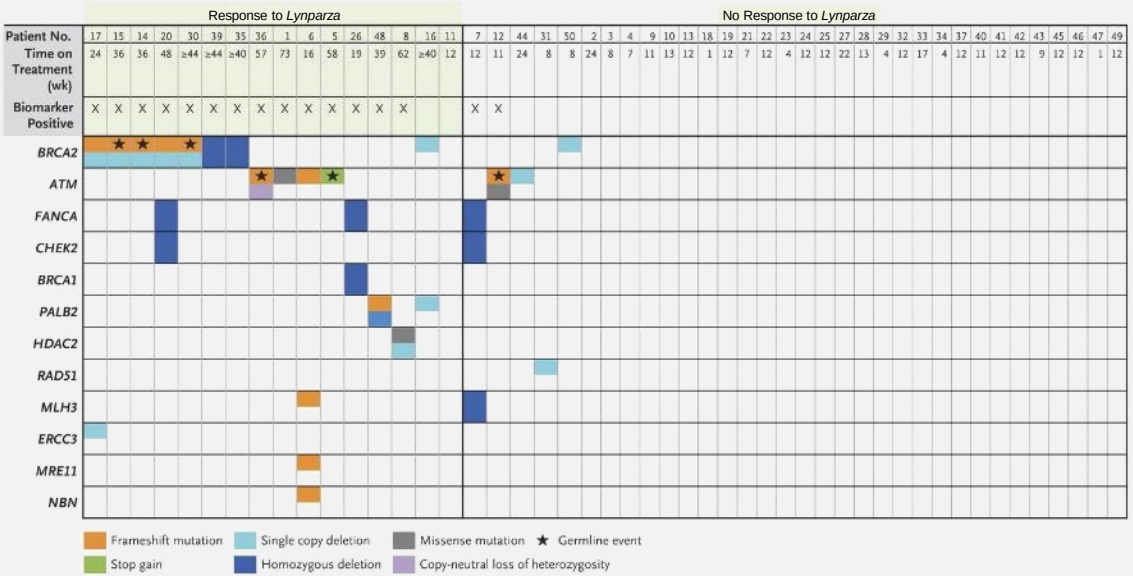
Patient selection

Example in prostate cancer

AstraZeneca HRR 15 gene panel

BRCA1	FANCL
BRCA2	FANCN(PALB2)
ATM	BARD1
RAD51B	CHEK1
RAD51C	CHEK2
RAD54L	CDK12
RAD51D	PPP2R2A
FANCJ/BRIP1	

Genomic aberrations in DNA repair in patients with mCRPC*



Source: J. Mateo et al. The New England Journal of Medicine, 2015; 373:1697-1708

Next-generation sequencing

Platform transforming accessibility to patients

Hot-spot activating mutation for a **single gene**	Multiple deficiencies for **two genes**	Multiple deficiencies for **multiple genes**	Multiple deficiencies for multiple genes and **multiple DDR mechanisms**
			Cell-cycle deregulation + Oncogenic driver or HRR
e.g. EGFR	e.g. BRCA1/2 (PARPi sensitive)	Homologous Recombination Repair (HRR) (broader PARPi sensitivity)	Broad DDR test
Approved	**Approved**	**In validation**	**In translation**
Roche	myriad	FOUNDATION MEDICINE	

DDR engages the immune response

Mechanisms

Generate immune-cell diversity through V(D)J recombination

Inflammatory response

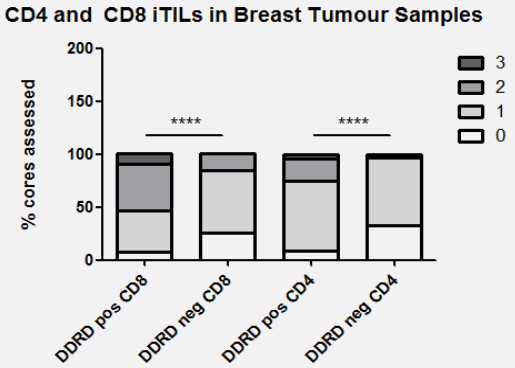
DDR

Generate neo-antigens through mutational control (MMR)

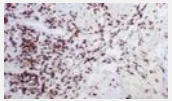
CDK1 regulation required for immune-mediated cell killing

'Anti-viral' early warning system / immune priming

Biomarker evidence

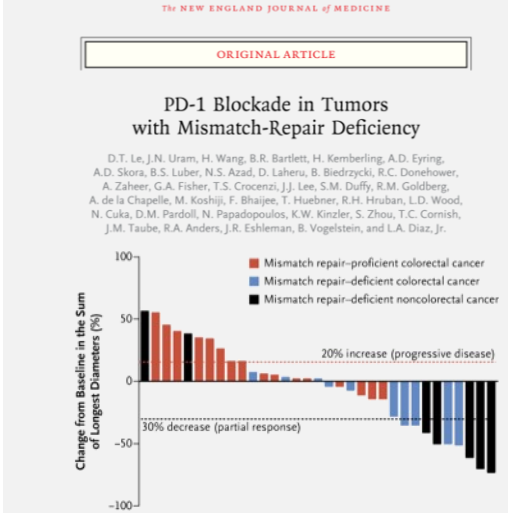


DDRD negative core
No lymphocytes



DDRD positive core
Profuse lymphocytic infiltration

Clinical evidence



MSI-H is caused by MMR deficiency, but also impacts DNA double-strand break-repair capability due to microsatellite deletions in ATM gene

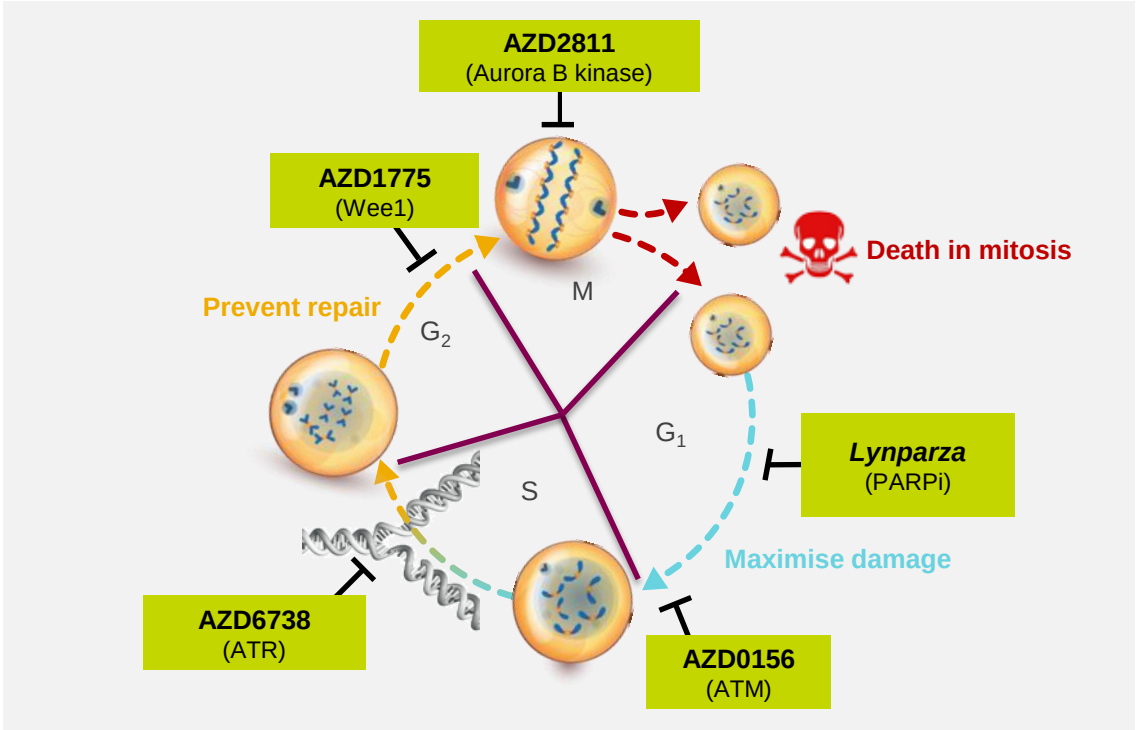
Source: AstraZeneca data on file; NEJM

DDR portfolio

Emergence of a new cancer-treatment paradigm

40-50% with DDR defects

- Loss of one of more DNA repair pathways
- Increased levels of endogenous DNA damage
- DNA replication stress
- Genomic instability

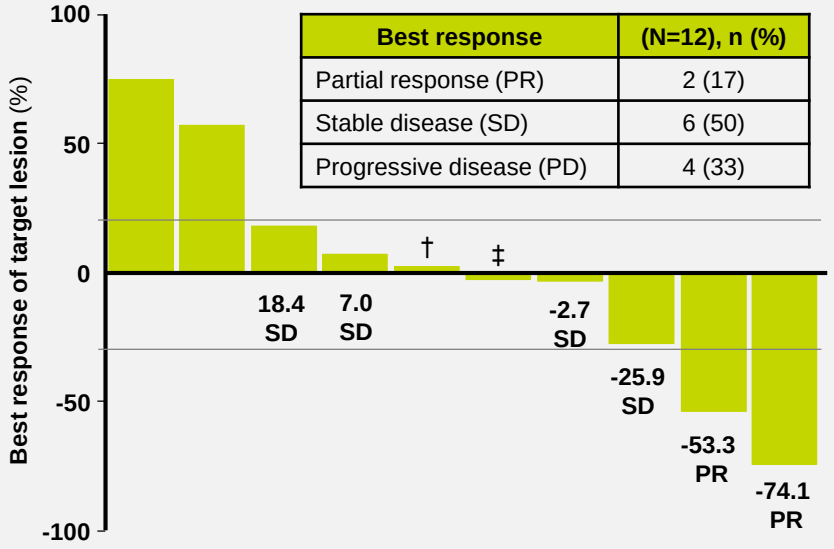


Source: AstraZeneca data on file

AZD1775

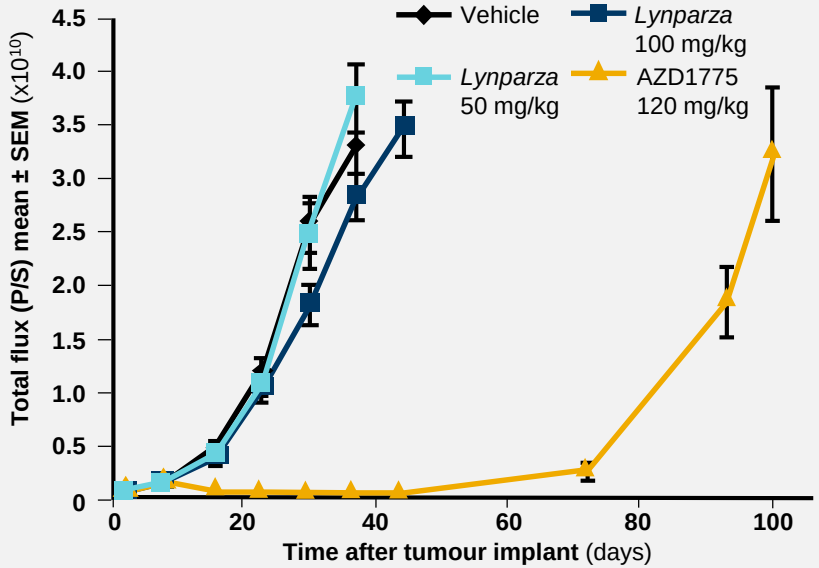
Potential for monotherapy post PARPi

Monotherapy
Best percentage change tumour size*



Best response	(N=12), n (%)
Partial response (PR)	2 (17)
Stable disease (SD)	6 (50)
Progressive disease (PD)	4 (33)

9/12 ovarian patient-derived tumour models resistant to *Lynparza* respond to AZD1775 single agent

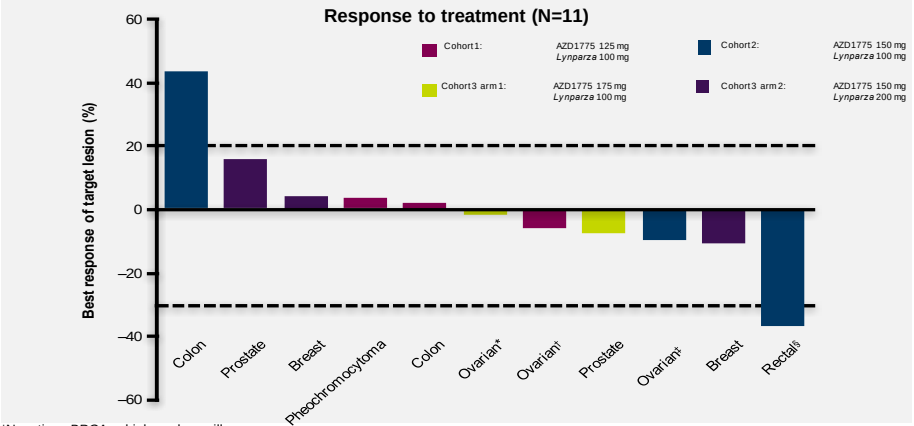


* Two additional patients with stable disease had evaluable, but not measurable, disease; †Patient had clinical progression; ‡Patient had new lesion

Source: AACR 2016

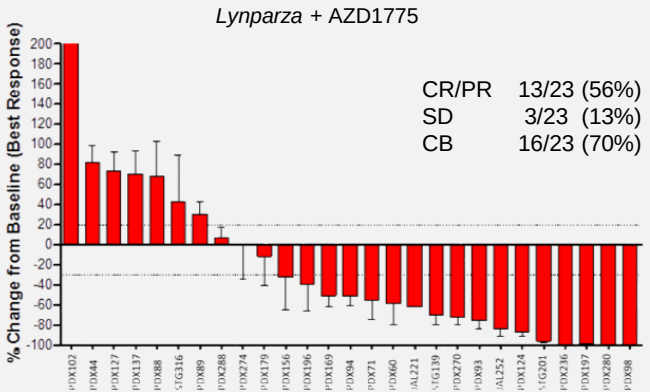
Lynparza + AZD1775 combination

Phase I clinical data



*Negative g*BRCA*m; high grade papillary serous;
†Negative g*BRCA*m; high grade undifferentiated;
‡*BRCA* polymorphism R504 (1630 G>A); high grade papillary serous;
§*BRCA*m; poorly differentiated squamous cell carcinoma

Pre-clinical data
Lynparza + AZD1775 in TNBC patient-derived tumour models show improved activity vs *Lynparza* monotherapy



Lynparza + AZD1775 combination in Phase I to identify dose/schedule

Phase II 2016

- Ovarian (30 patients) (15 gBRCA, PARPi failures)
- SCLC (30 patients) (15 MYC amplified)
- TNBC (30 patients) (15 CCNE1 amplified)

Source: AstraZeneca data on file; AACR 2016, O'Connor; ASCO 2016, abstract 5562

AZD0156 (ATM) and AZD6738 (ATR)

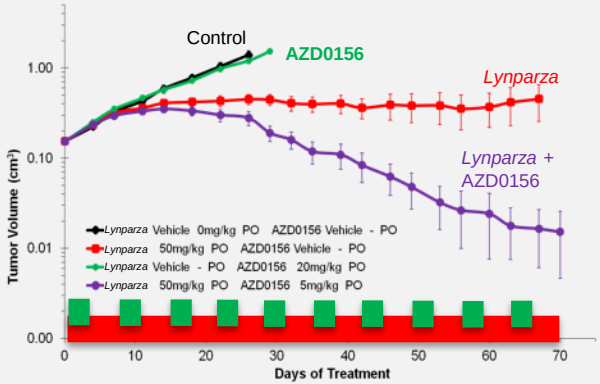
Combinations with *Lynparza* in Phase I

Maximising DNA damage in S-phase

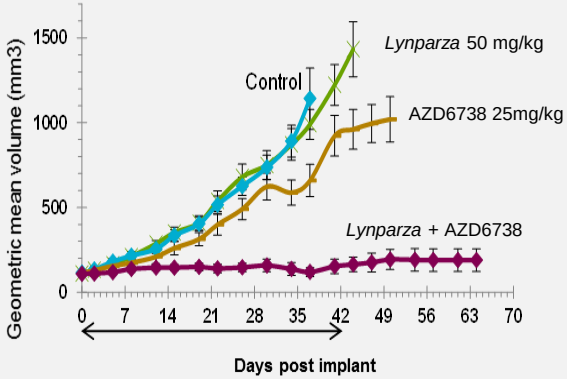
- **ATM** coordinates the repair of double-strand breaks (DSBs)
- **ATR** is required to repair stalled DNA replication forks
- **PARP** detects and triggers the repair of single-strand breaks (SSBs). Inhibition of PARP causes stalled replication forks and a build up of SSBs which convert to DSBs

Lynparza + AZD0156 and *Lynparza* + AZD6738 in two breast-cancer models

***Lynparza* + AZD0156 induce tumour regression in a TNBC patient-derived xenograft model (BRCA-2 mut)**



***Lynparza* + AZD6738 in breast primary explant xenograft**



Source: AstraZeneca data on file

Summary

1	DDR deficiencies are common in multiple cancers (40-50%)
2	Targeting DDR deficiencies is clinically validated and a subset of patients experience long-term benefit
3	Patient selection is critical. NGS test development is underway for HRR panel for *Lynparza* and AZD1775
4	There is a significant scientific rationale and clinical evidence that DDR and immune responses are linked and potentially synergistic
5	AstraZeneca portfolio of DDR-targeting agents is the broadest with multiple agents in proof-of-concept studies

AstraZeneca
What science can do

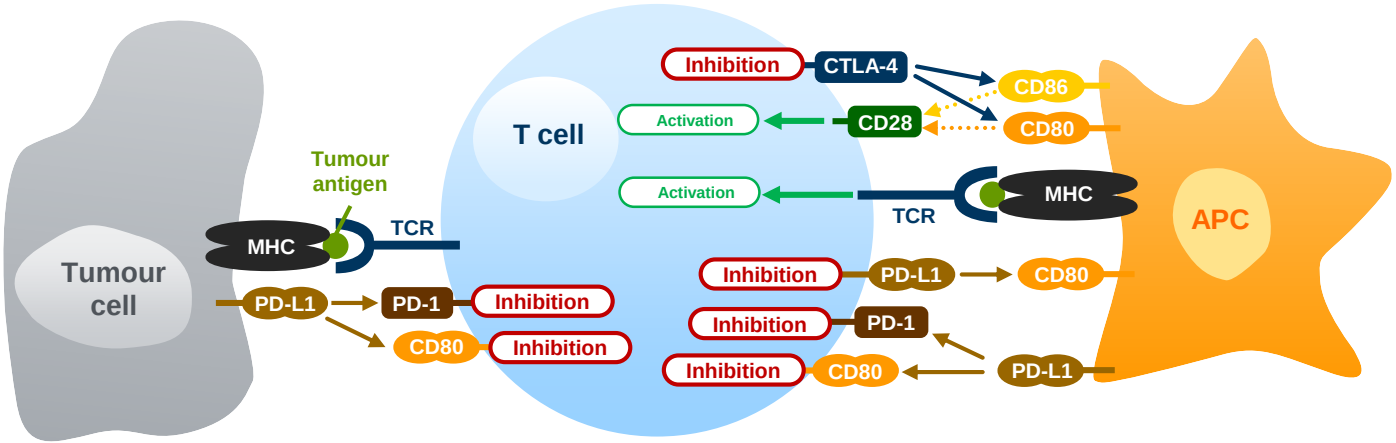
IO: Late-stage development

Rob Iannone, MD, MSCE
Senior Vice President, IO, Global Medicines Development

CTLA-4 and PD-L1

IO strategy built on fundamental checkpoints in anti-cancer immunity

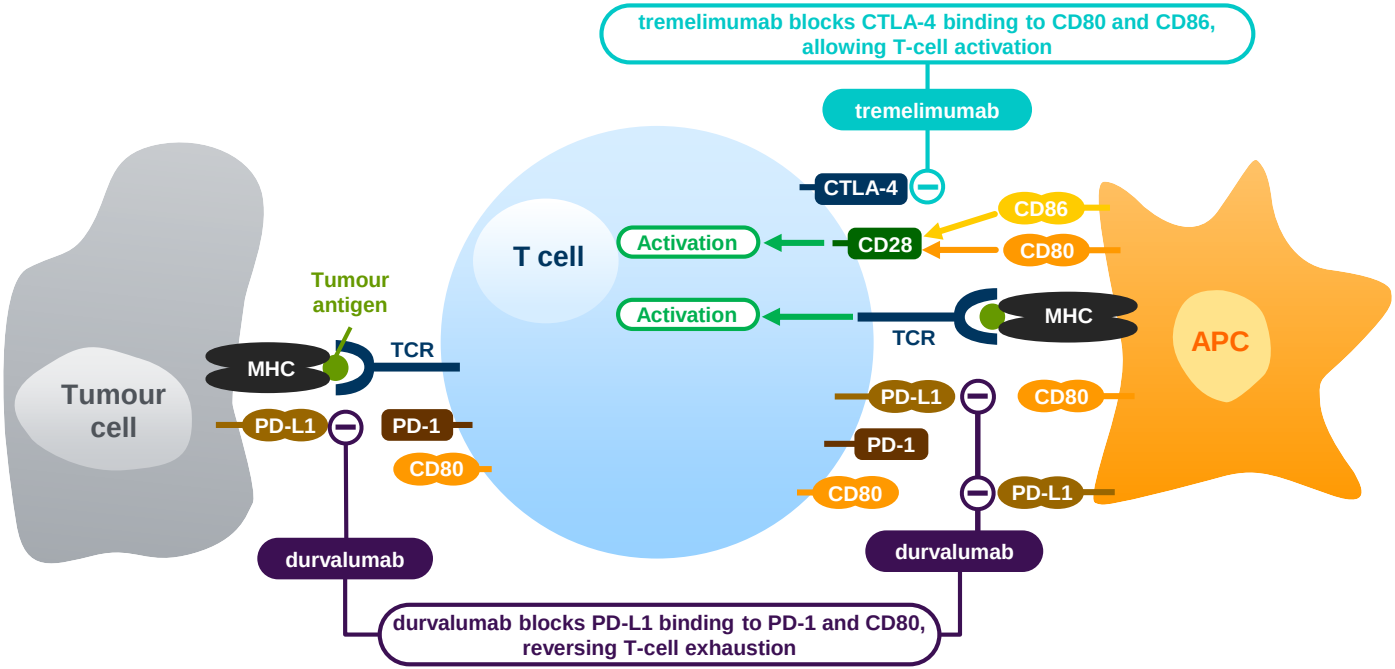
CTLA-4: 'Hard-wired' negative regulator of T-cell activation



PD-L1: Adaptive resistance; induces T-cell exhaustion

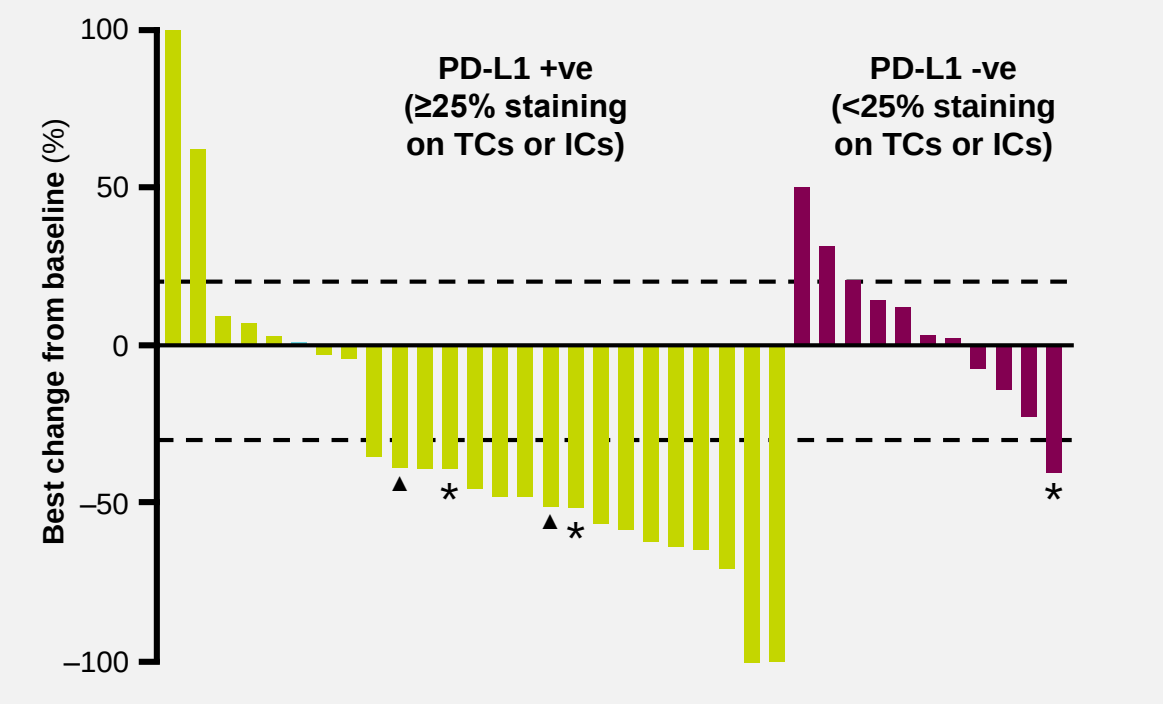
CTLA-4 and PD-L1

IO strategy built on fundamental checkpoints in anti-cancer immunity



Durvalumab monotherapy: 2L urothelial bladder cancer

Breakthrough Therapy Designation granted



Subgroup
PD-L1 +ve 76% (19/25) had a reduction in tumour size (RECIST 1.1 ORR = 46%)
PD-L1 -ve 36% (4/11) had a reduction in tumour size (RECIST 1.1 ORR = 0%)

* Unconfirmed response (all other patients with best tumour shrinkage ≥30% had confirmed responses); ▲Unconventional response
Response evaluable population (n = 42); patients who initiated trial therapy ≥12 weeks prior to DCO and had ≥1 follow-up scans

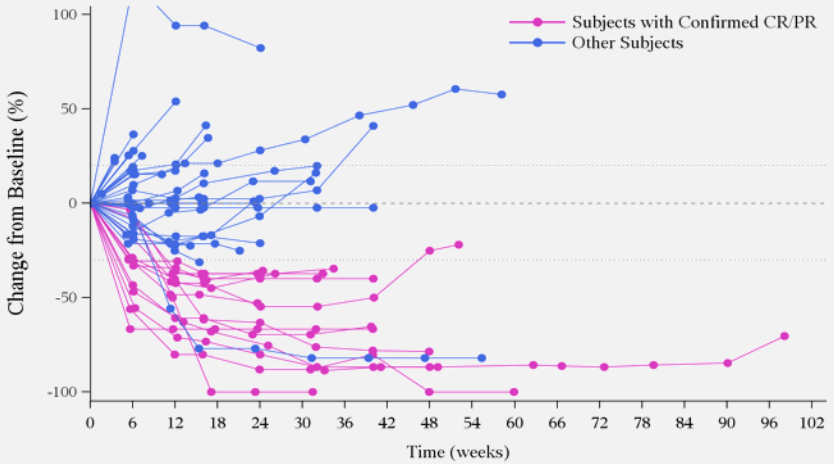
Source: ASCO 2016, abstract 4502

Durvalumab monotherapy: 1L NSCLC

1L cohort from Study 1108 (Phase I/II)

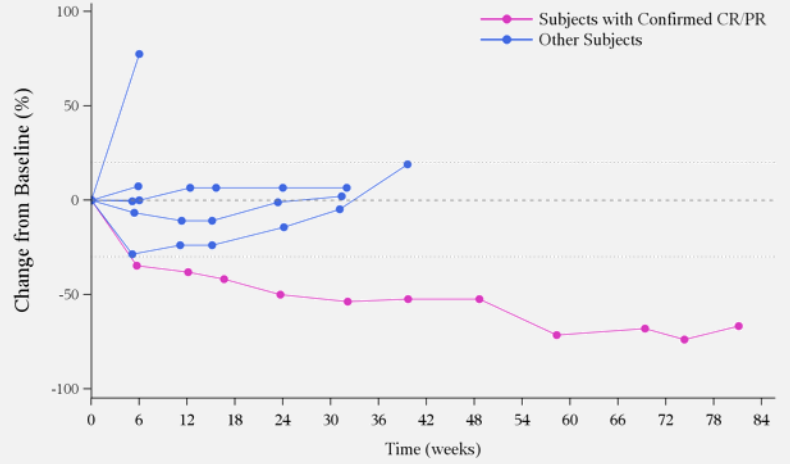
PD-L1 +ve: Durvalumab monotherapy

29% ORR (95% CI: 17 - 43) in PD-L1 +ve tumours



PD-L1 -ve: Durvalumab monotherapy

11% ORR (95% CI: 0 - 48) in PD-L1 -ve tumours



* Response-evaluable population = patients with ≥24 weeks follow up

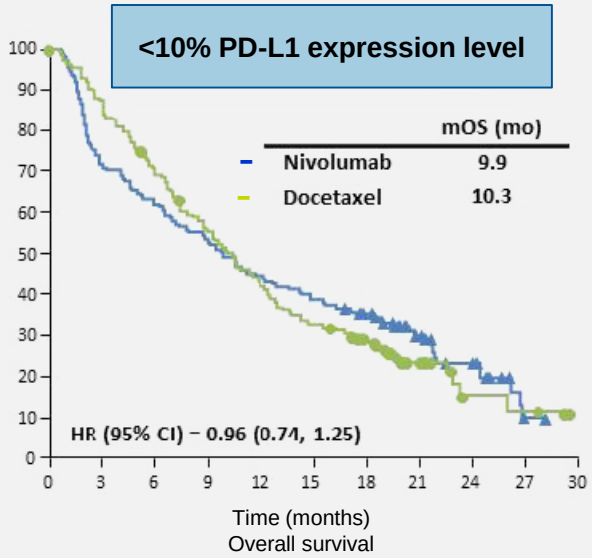
** PD-L1 +ve defined as ≥25% tumour cells stained for PD-L1 at any intensity

*** PD-L1 -ve defined as <25% tumour cells stained for PD-L1 at any intensity

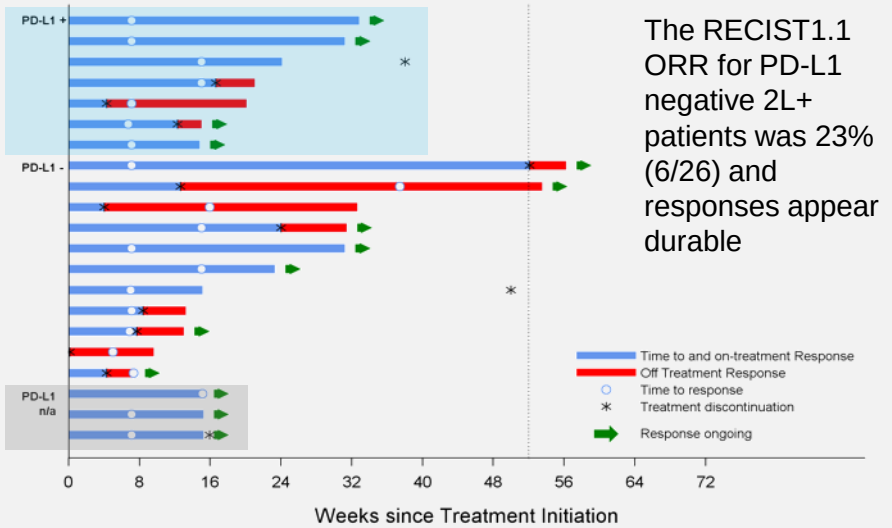
Source: ASCO 2016, abstract 9029

Durva + treme: Clinical activity in PD-L1 low/-ve NSCLC

60-70% of patients below 10% PD-L1 expression level



Durva + treme combinations address large unmet need: PD-L1 low/-ve tumours in lung cancer



The RECIST1.1 ORR for PD-L1 negative 2L+ patients was 23% (6/26) and responses appear durable

Source: H. Borghaei 2015. Nivolumab vs docetaxel in advanced non-squamous non-small-cell lung cancer. The New England Journal of Medicine, EJM, 373, 1627-39; AstraZeneca data on file

Durva and durva + treme clinical programmes

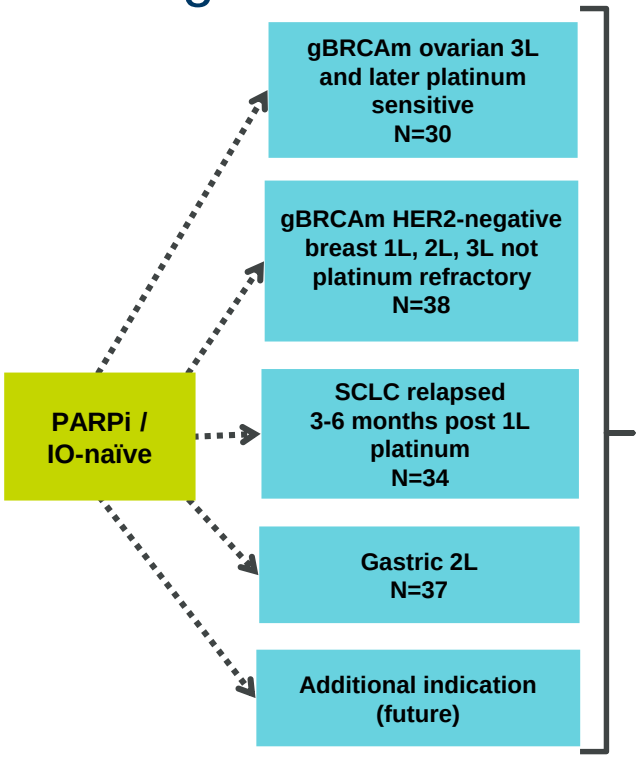
Leading in **early** and **first-line** settings in key cancers

	ADJUVANT	PACIFIC	MYSTIC	NEPTUNE	Chemotherapy combination	KESTREL	DANUBE
Trial design	Phase III (randomised)	Phase III (randomised)	Phase III (randomised) EGFR/ALK wt Non-sq/sq Arms: durvalumab durva + treme SoC	Phase III (randomised) EGFR/ALK wt Non-sq/sq Arms: durva + treme SoC	Phase III (randomised) EGFR/ALK wt Non-sq Arms: durva + chemo durva + treme + chemo SoC	Phase III (randomised) Arms: durvalumab durva + treme SoC	Phase III (randomised) Cis-eligible Cis-ineligible Arms: durvalumab durva + treme SoC
Primary endpoints	PFS	PFS	PFS OS	OS	TBD	PFS OS	PFS
Data readout	2020	H1 2017	H1 2017 (PFS) 2018 (OS)	2018	TBD	2018	2018
	Non-small cell lung cancer					**Head & neck cancer**	**Bladder cancer**

First line

Lynparza + durvalumab (MEDIOLA trial)

Leading with novel anti-PDL1 plus targeted-therapy combinations



Baseline tumour biopsy and blood

Repeat tumour biopsy and blood

Repeat tumour biopsy and blood: C2D1

***Lynparza* monotherapy** (4w run-in)

Combination *Lynparza* + durvalumab (to progression)

Key features:

- Phase II proof-of-concept basket trial
- Dose finding established in National Cancer Institute (NCI) D081KC00001
- Rigorous translational science

Source: ASCO 2016, abstract 3015

AstraZeneca
What science can do

IO: Early-stage development

David Berman
Senior Vice President, R&D Oncology, MedImmune

Building on anti-PD1/L1 cornerstone with new MOAs

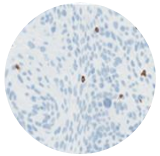
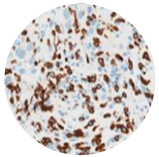
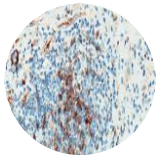
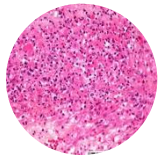
1) PD-1/L1 blockade is highly active, but not every patient responds
2) Some tumours are insensitive to PD-1/L1 blockade

Our strategy

- Identify mechanisms by which tumors evade immune system
- Develop IO combinations to address multiple mechanisms
- Identify patients most likely to benefit

Broad clinical-stage IO pipeline

Enhancement of anti-tumour immunity

	1. No effective anti-tumour immunity	2. sub-optimal or exhausted anti-tumour immunity	3. anti-tumour immunity suppressed by TME	**Goal**: Highly active anti-tumour immunity
Immune status	 "Cold' tumour	 Example: PD-L1+ tumour	 Example: CD73+ tumour	
Therapeutic aim	**Prime new response**	**Potentiate existing response**	**Reverse tumour immuno-suppression**	**Eliminate tumour**
Clinical pipeline	**TLR 7/8** **NME** **DNA vaccine**	**PD-L1** **CTLA-4** **PD-1**	**hOX40** **GITR** **NKG2A**	**CD73** **CXCR2** **STAT3**

Unlocking the power of IO combinations

Multiple ongoing IO combinations based on complementary MOAs

Durvalumab combination (sponsored)
CTLA-4
hOX40
CD73
NKG2A
PD-1
STAT3
CXCR2

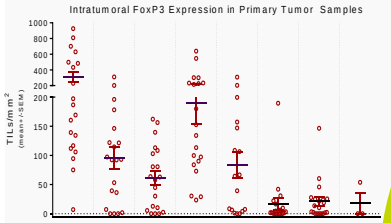
Durvalumab combination (clinical collaboration)
IDO
HDAC
IMCgp100
CSF-1R
TGFβR-1
CD19-CART
CCR4
HPVE7

Tremelimumab combination
hOX40

Develop the science

Guiding the IO portfolio and identification of new targets

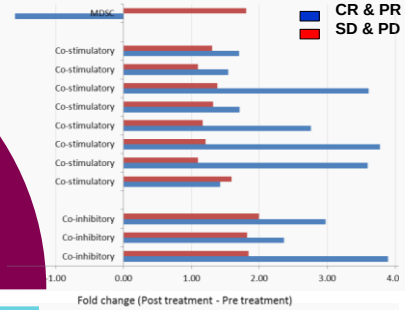
MOA-based prioritisation



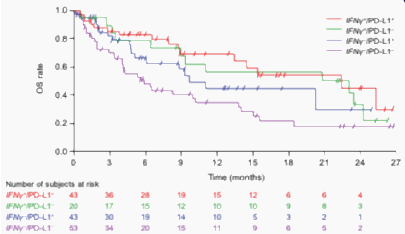
Identify which tumours to study

Pre- vs. post-therapy biopsies

Identify markers of adaptive resistance



IFNγ



Identify which patients may respond

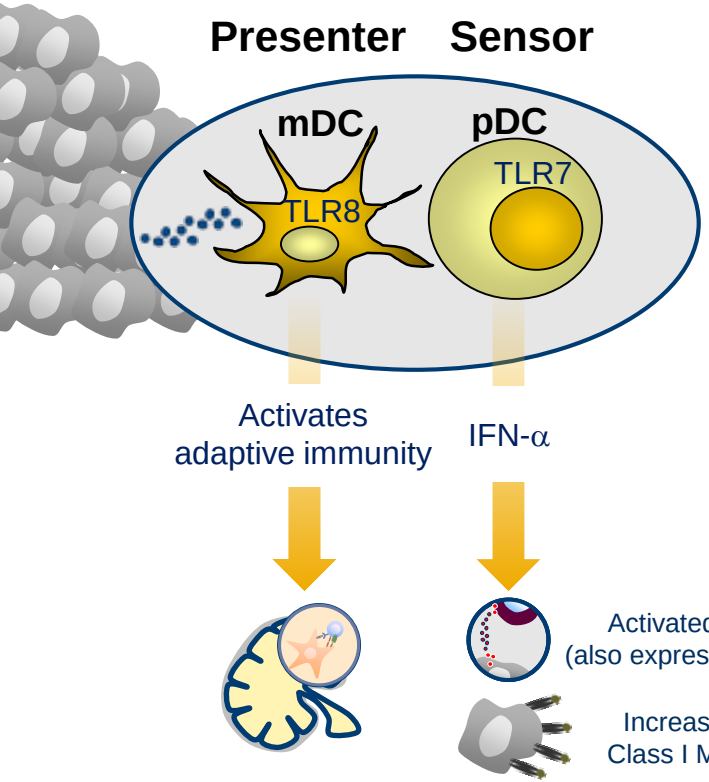
Understand immune landscape of tumours

DEFINIENS®
the tissue phenomics company

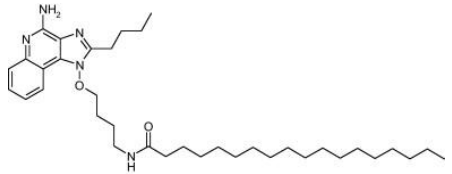
Source: ASCO 2016, abstract 3036

TLR 7/8 (MEDI9197) primes new immune response

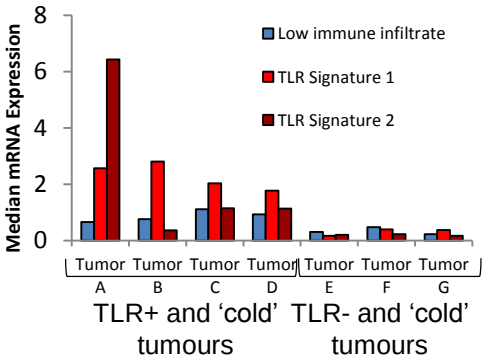
Activates ‘sensor’ and ‘presenter’ dendritic cells (DC)



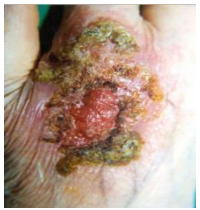
Lipid tail increases tumour retention

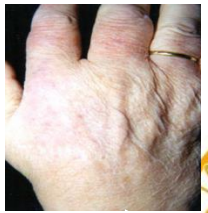


Developing predictive signature



Imiquimod validates TLR7



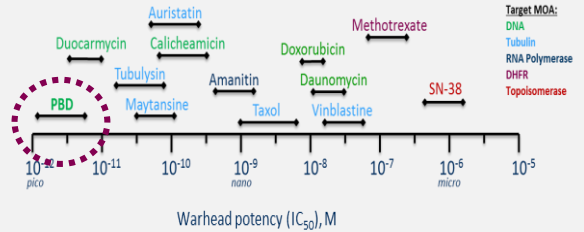


Oster-Schmidt C. J Dtsch. Dermatol Ges 2005;3:705

Source: ASCO 2016, abstract TPS3095

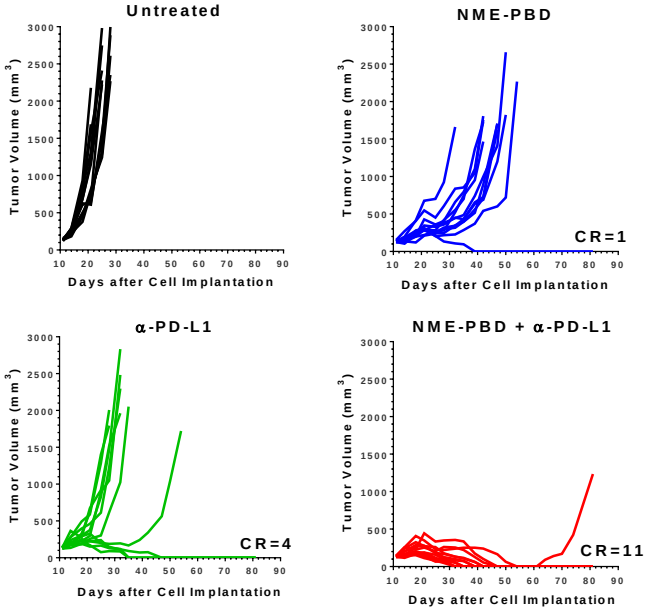
IO synergy with antibody conjugates

Highly potent warhead
(pyrrolobenzodiazepine, PBD)



- Clinically validated
- Cross-links DNA & induces apoptosis in dividing and resting cells
- Kills cancer stem cells
- Synthetic lethality with BRCA & other DNA-repair defects

Synergy with anti-PDL1

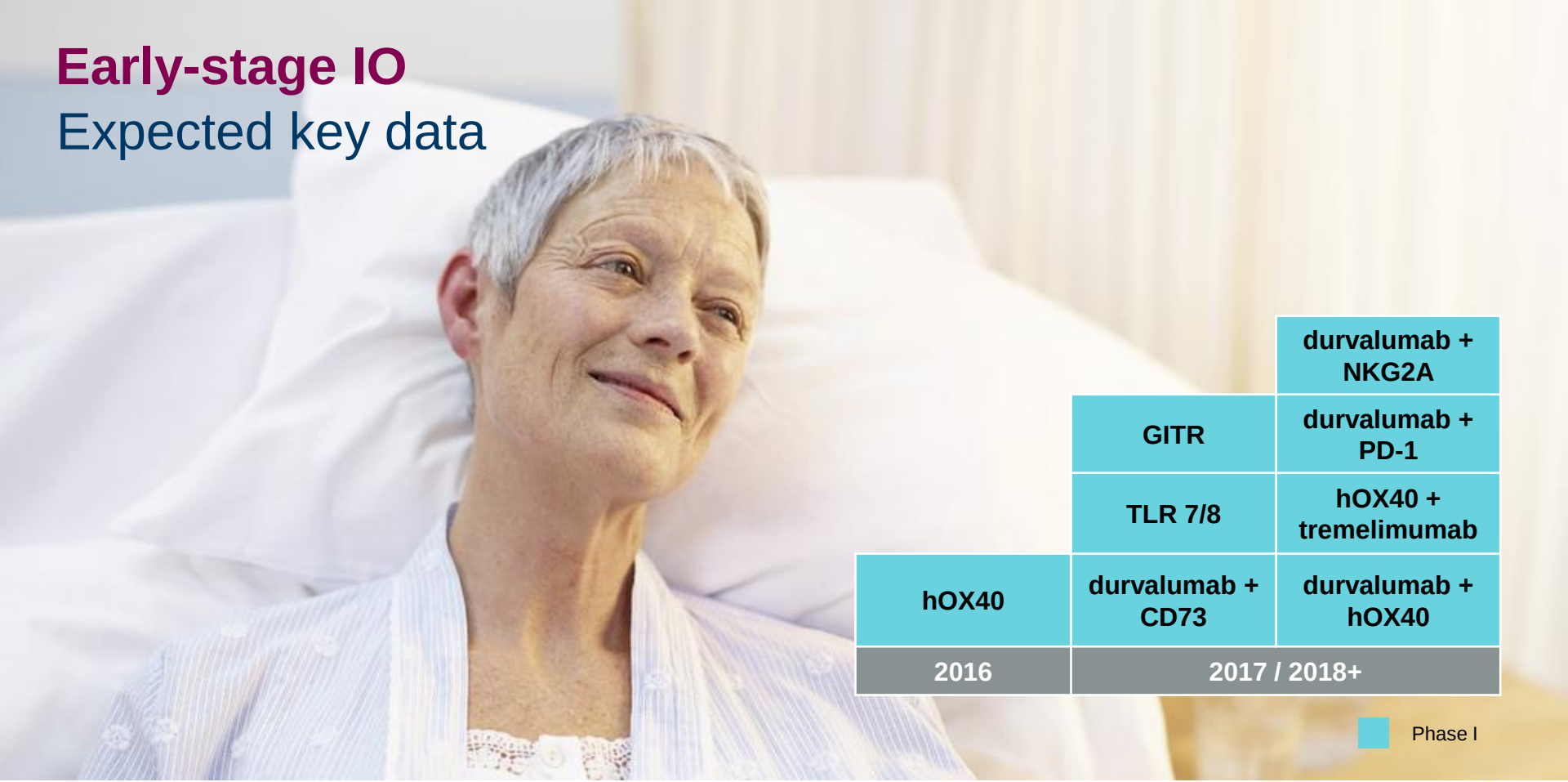


Novel antibody engineering

- Bi-paratopic technology, induces higher order lattice clustering to drive internalisation
- Proprietary site-specific conjugation
- Alternative scaffold technology
- Half-life extension technology
- Non-natural amino acid technology

Source: AstraZeneca data on file

Early-stage IO
Expected key data



		durvalumab + NKG2A
	GITR	durvalumab + PD-1
	TLR 7/8	hOX40 + tremelimumab
hOX40	durvalumab + CD73	durvalumab + hOX40
2016	2017 / 2018+	

Phase I

AstraZeneca
What science can do

Haematology

Sean Bohen
Executive Vice President, Global Medicines Development & Chief Medical Officer

Complementary strategies

Establish leadership in haematology

Elevating the standard of care in B-cell cancers

- Acalabrutinib has opportunity to become SoC in CLL and NHL
- Acerta as Haematology Centre of Excellence

Acerta Pharma
A member of the AstraZeneca Group

Driving towards a cure in multiple haematological-disease states

- Immediate access to a portfolio of effective small-molecule medicines
- Aspiration to cure patients with durvalumab combinations in areas of high unmet medical need

Celgene

Leverage breadth of portfolio and clinical-trial opportunities to become the partner of choice in haematology and transform care

AstraZeneca: Potential haematology leadership

Driven by access to rich portfolio across two growth platforms

Acalabrutinib

Acerta Pharma
A member of the AstraZeneca Group

- Non-Hodgkins Lymphoma
- Mantle Cell Lymphoma
- Waldenström's Macroglobunaemia
- Chronic Lymphocytic Leukaemia

Durvalumab

Celgene · MedImmune · AstraZeneca · FUSION TRIAL PROGRAM

- Non-Hodgkins Lymphoma
- Hodgkins Lymphoma
- Multiple Myeloma
- Chronic Lymphocytic Leukaemia
- Acute Myeloid Leukaemia / Myelodysplastic Syndrome

Further indications and combinations to be determined

BTK inhibitor class

Cornerstone of treatment for B-cell malignancies

- **Long treatment duration** drives market growth ($19bn G7 market by 2024[1])
- **Continuous BTK inhibition is critical** to improving treatment outcomes[2]
- **Tolerability is key** to maintaining dose intensity and ability to combine with other treatments for improved efficacy
- Ibrutinib is the **only approved medicine** in the BTK-inhibitor class
- **Off-target activity** can lead to rash, diarrhoea, arthralgia/myalgia, severe bleeding and atrial fibrillation[3]

Acalabrutinib has the potential to become a best-in-class BTKi

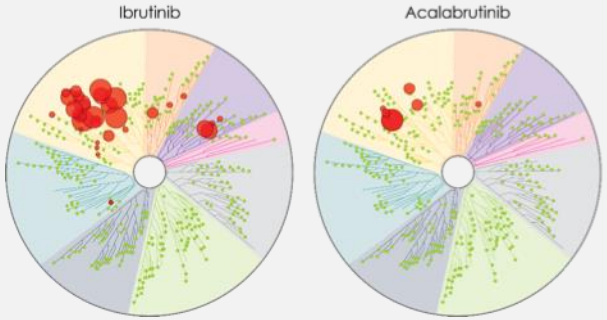
1 Decision Resources, NHL report Nov 2015
2 Dose adherence and baseline exposure analysis of the ibrutinib 420mg dose administered to patients with previously treated CLL; ASCO 2015 abstract 7012
3 P. Jain 2015. Outcomes of patients with chronic lymphocytic leukemia after discontinuing ibrutinib. Blood. 125(13):2062-2067
K.J. Maddocks 2014. Etiology of Ibrutinib Therapy Discontinuation and Outcomes in Patients With Chronic Lymphocytic Leukemia. JAMA. Oncol.doi:10.1001/jamaoncol.2014.218
M. Farooqui 2015. Atrial Fibrillation in CLL/SLL Patients on Ibrutinib; ASH abstract 2933

Acalabrutinib

Designed to deliver differentiated clinical profile, best-in-class potential

Highly-potent and selective BTK inhibition

Minimal effects on TEC, EGFR, or ITK signaling



Kinase inhibition IC_{50} (nM)

Kinase	acalabrutinib	ibrutinib
BTK	5.1	1.5
TEC	93	7.0
BMX	46	0.8
TXK	368	2.0
ERBB2	~1000	6.4
EGFR	>1000	5.3
ITK	>1000	4.9
JAK3	>1000	32
BLK	>1000	0.1

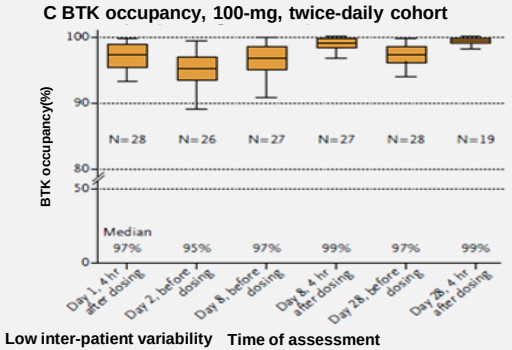
Covey AACR 2015, abstract 2596

Improved safety and tolerability potential

+

Continued BTK inhibition

Short half-life prevents plasma accumulation and enables complete 24-hr BTK coverage (≥97%)[1]



Optimal disease-control potential

Source: Byrd et al. 2016

Acalabrutinib

ASCO 2016: Compelling efficacy in front-line CLL

R/R CLL*: ASH 2015	
n (%)	**All cohorts (N=60)†**
CR	0 (0)
PR	51 (85)
PR+L	6 (10)
SD	3 (5)
PD	0 (0)
ORR (CR + PR)	**51 (85%)**
ORR (CR + PR + PRL)	57 (95%)

FL CLL*: ASCO 2016	
n (%)	**All cohorts (N=72)**
CR	0 (0)
PR	63 (88)
PR+L	7 (10)
SD	2 (3)
PD	0 (0)
ORR (CR + PR)	**63 (88%)**
ORR (CR + PR + PRL)	70 (97%)

PR+L = Partial Response with Lymphocytosis
ORR in del17p: 100%
†30 Sept 2015; ASH 2015 data; best overall response assessment; median time to last response assessment = 11 months
‡Includes two SD patients (100 mg BID) with all nodes <1.5 cm at baseline CT
*Based on modified IWCLL 2008., *investigator assessed

PRL, PR with lymphocytosis
aEfficacy-evaluable patients had at least one response assessment after first dose of trial drug
* investigator assessed
Source: ASH 2015; ASCO 2016, abstract 7521

Acalabrutinib

Favourable safety profile

R/R CLL: ASH 2015

Reported in ≥ 15% of patients (N=61)

Adverse event	All Grades, n (%)	Grades 3/4, n (%)
Headache	26 (43)	0
Diarrhea	24 (39)	1 (2)
Weight increased	16 (26)	1 (2)
Pyrexia	14 (23)	2 (3)
Upper respiratory tract infection	14 (23)	0
Fatigue	13 (21)	2 (3)
Oedema peripheral	13 (21)	0
Hypertension	12 (20)	4 (7)
Nausea	12 (20)	0
Contusion	11 (18)	0
Arthralgia	10 (16)	1 (2)
Petechiae	10 (16)	0
Weight decreased	10 (16)	0

FL CLL: ASCO 2016

Reported in ≥ 15% of patients (N=74)

Adverse event	All Grades, n (%)	Grades 3/4, n (%)
Headache	30 (41)	1 (1)
Diarrhea	26 (35)	0
Arthralgia	16 (22)	1 (1)
Nausea	13 (18)	2 (3)
Increased weight	13 (18)	1 (1)
Contusion	13 (18)	0
Rash	12 (16)	1 (1)

Multiple occurrences of the same event for a given subject were counted once for each system organ class and each preferred term

There were no cases of atrial fibrillation or acalabrutinib-associated major bleeding

Source: ASH 2015; ASCO 2016, abstract 7521

Acalabrutinib clinical development

Haematological malignancies represent first registration opportunity

Indication	Trial design and line of therapy	Phase
CLL	acalabrutinib vs. ibrutinib CLL relapsed/refractory	III
	acalabrutinib + obinutuzumab vs. obinutuzumab + chlorambucil vs. acalabrutinib CLL front/first line	III
	acalabrutinib CLL relapsed/refractory, ibrutinib-intolerant	II
MCL	acalabrutinib MCL relapsed/refractory	II
WM	acalabrutinib WM relapsed/refractory	Ib/II

- Early monotherapy and combination trials ongoing in Richter's transformation, DLBCL, FL, MM
- Monotherapy and combination trials ongoing in multiple solid tumours (pancreatic, bladder, ovarian cancers and NSCLC, HNSCC and GBM)

Closing

Sean Bohen
Executive Vice President of Global Medicines Development and Chief Medical Officer

Key takeaways

1	*Lynparza* and *Tagrisso* - encouraging launches and strong bases for further approvals
2	DDR - significant potential across multiple tumour types. AstraZeneca portfolio of DDR-targeting medicines is the broadest and leading the field
3	IO: Late-stage development - opportunities across a wide range of combination therapies with key data points in H1 2017
4	IO: Early-stage development - building on the anti-PD1/L1 cornerstone with OX40 next
5	Haematology - potential leadership driven by access to rich portfolio of assets across two growth platforms

Please press *1 on your phone if you wish to ask a question

- Pascal Soriot, moderator
- Sean Bohen
- Mondher Mahjoubi
- Susan Galbraith
- David Berman
- Rob Iannone
- Other members of the AstraZeneca Oncology team

Investor science event expected to end at 8:30 PM CDT

AstraZeneca
What science can do

ASCO 2016 Investor Science Event

Chicago, IL, USA
6 June 2016