

Cautionary statement regarding 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 presentation contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group. 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 presentation 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 patents, marketing exclusivity or trade marks, or the risk of failure to obtain patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions 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 failure by third parties to supply materials or services; the risk of failure to manage a crisis; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to observe ongoing regulatory oversight; the risk that new products do not perform as we expect; the risk of environmental liabilities; the risks associated with conducting business in emerging markets; the risk of reputational damage; the risk of product counterfeiting; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; and the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation.

Nothing in this presentation should be construed as a profit forecast.



Agenda

Immuno-Oncology (PD-L1 mono & PD-L1 + CTLA-4 combo focus)
Rachel Humphrey

AZD9291 in lung cancer
Susan Galbraith

Q&A



3

Immuno-Oncology (IO)

Rachel Humphrey
Head, Immuno-Oncology, Global Medicines Development

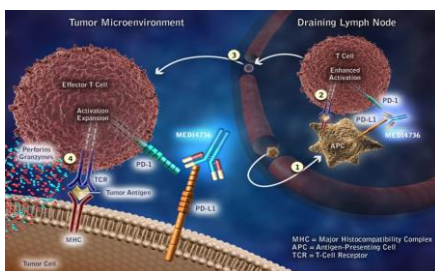


Anti-PDL1 (MEDI4736)

Potent anti-cancer agent with potential for differentiation



MEDI4736: An engineered anti-PDL1 antibody



Uniquely engineered human IgG1κ mAb

- No binding to PD-L2¹
- No immunogenicity impacting PK-PD at phase III dose 10 mg/kg q2w to date²
 - 2/196 patients treated at 10 mg/kg showed anti-drug antibodies (ADA) that did not impact PK-PD
- Sustained exposure through dosing interval (>1 year)
- Triple mutation in Fc domain removes ADCC activity³

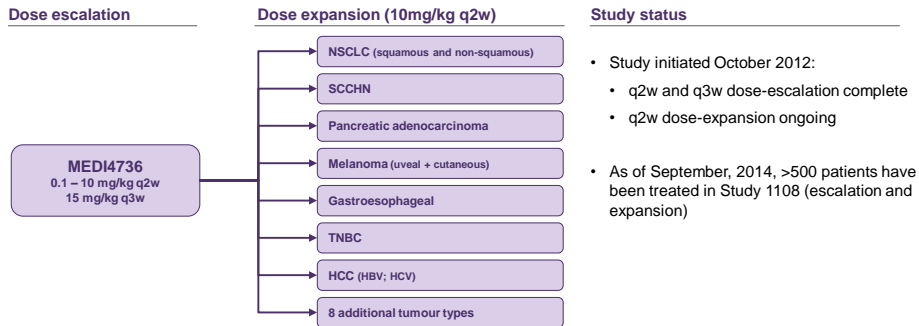
**>600 patients treated
(monotherapy and in combination)¹**



¹Data on file, MedImmune/AstraZeneca; ²Fairman D, et al. Poster presentation at ASCO 2014, Abstract 134334
³Oganesyan V, et al. *Acta Crystallogr D Biol Crystallogr* 2008;64:700-4



Study 1108: Phase I/II dose escalation and expansion in multiple tumour types



7

Anti-PDL1 monotherapy safety: No colitis, no high grade pneumonitis, no drug-related deaths

		MEDI4736 10 mg/kg q2w N = 408 ^a	
System organ class	Selected drug-related events	All grades n (%)	Grade 3/4 n (%) ^a
Constitutional – General	Fatigue	64 (16)	6 (2)
	Pyrexia	13 (3)	0
Gastrointestinal	Vomiting	24 (6)	2 (1)
	Diarrhoea	26 (6)	1 (0.2)
	Abdominal pain	8 (2)	0
	Colitis	0	0
Endocrine	Hypothyroidism	13 (3)	1 (0.2)
	Hyperthyroidism	9 (2)	0
	Hyperglycaemia	2 (1)	1 (0.2)
Skin	Rash/pruritus	26/18 (6/4)	0/1 (0/0.2)
Respiratory	Dyspnoea	16 (4)	0
	Pneumonitis	5 (1)	0
Laboratory investigations	AST/ALT elevation	11/11 (3/3)	2/2 (1/1)
Nervous system	Peripheral neuropathy	3 (1)	0



Causality assigned by the investigator. ^aIncluding six patients from dose escalation; AST, aspartate aminotransferase; ALT, alanine aminotransferase.



8

Anti-PDL1 safety: Similar safety profile across tumour types with AEs leading to discontinuation reported in 1%

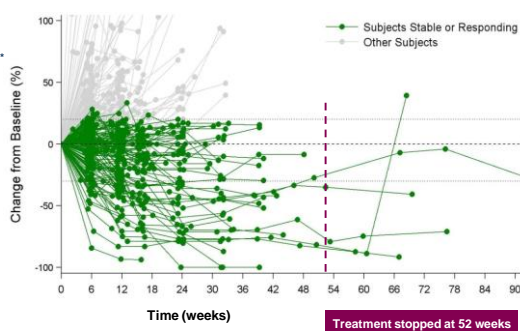
Select drug-related AEs	MEDI4736 10 mg/kg q2w								
	Total ^a n (%)	NSCLC ^b n (%)	SCCHN n (%)	Pancreatic n (%)	CM n (%)	UM n (%)	GE n (%)	TNBC n (%)	HCC n (%)
Any AE	189 (46)	70 (39)	32 (53)	20 (65)	9 (39)	9 (38)	22 (54)	14 (54)	13 (62)
Grade 3/4 AE	30 (7)	5 (3)	4 (7)	7 (23)	1 (4)	0	7 (17)	4 (15)	2 (10)
Serious AE	10 (3)	2 (1)	1 (2)	3 (10)	0	0	1 (2)	2 (8)	1 (5)
AEs leading to discontinuation	5 (1) ^d	2 (1)	0	2 (7)	0	0	0	1 (4)	0
AEs leading to death	0	0	0	0	0	0	0	0	0



Data cut-off: 21 August, 2014. ^aIncluding 6 patients from dose escalation; ^bSquamous and non-squamous; ^cCausality assigned by the investigator; ^dn=1, pneumonitis (Grade 2), n=1, AST elevation (Grade 3), n=1 LFT elevation (Grade 3), n=1 ataxia (Grade 3), n=1 hyperthyroidism and tachycardia (both Grade 2)



Anti-PDL1 monotherapy efficacy: Early and durable activity across multiple tumour types^{*}



Total study population
(10 mg/kg q2w)

Ongoing Responders

Total* 92% (33/36)

RECIST Response

PD-L1+ 22% (18/81)

PD-L1- 5% (12/233)

Total* 10% (36/352)

Disease Control Rate at 12 weeks

PD-L1+ 47% (38/81)

PD-L1- 28% (64/233)

Total* 33% (115/352)

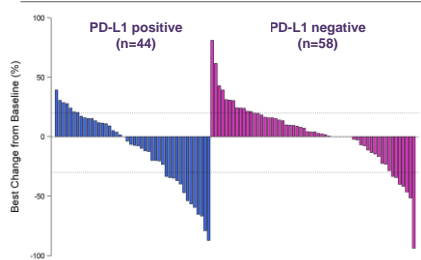


*Changes >100% are truncated; [†]Patients with baseline and ≥1 on-treatment scan; Disease assessment at 6 weeks, 12 weeks, 16 weeks, and then every 8 weeks
Data cut-off: 21 August, 2014.



Anti-PDL1 in NSCLC: Encouraging anti-tumour activity

Best Change in Tumour Size by PD-L1 status (n=102)*



	NSCLC (All doses)	NSCLC (10mg/kg q2w)
Ongoing responders		
Total*	88% (23/26)	96% (22/23)
RECIST Response		
PD-L1+	25% (12/48)	26% (12/47)
PD-L1-	10% (7/74)	10% (7/74)
Total*	16% (26/162)	15% (23/150)
Disease Control Rate at 12 weeks		
PD-L1+	48% (23/48)	47% (22/47)
PD-L1-	42% (31/74)	42% (31/74)
Total*	41% (66/162)	39% (59/150)



* PD-L1 status not available for n=33 patients; Changes represent target lesions; Disease assessment at 6 weeks, 12 weeks, 16 weeks, and then every 8 weeks (MEDI4736 all dose levels). PD-L1 status defined by VENTANA assay. Data cut-off: 21 August, 2014.



11

Enrichment based on PD-L1 expression in 2/3 line lung cancer: Key driver of response in monotherapy

Agent	ORR PDL1+	ORR PDL1-	Source
Pembrolizumab	23% (36/159)	9% (3/35)	2014 ASCO
Nivolumab	15% (5/33)	14% (5/35)	2014 ASCO
MPDL3280A	46% (6/13)	15% (6/40)	2014 ASCO
MEDI4736¹	26% (12/47)	10% (7/74)	2014 ESMO



¹Patients treated < 12 wks prior to the data cut were censored, dose 10 mg/kg q2w



12

Anti-PDL1 in SCCHN: No colitis, no high grade pneumonitis, no drug-related deaths

		MEDI4736 10 mg/kg q2w n=61	
System organ class	Selected drug-related events	All grades n (%)	Grade 3/4 n (%) ^a
Constitutional – General	Fatigue	5 (8)	1 (2)
	Pyrexia	4 (7)	0
Gastrointestinal	Vomiting	1 (2)	0
	Diarrhoea	5 (8)	0
	Abdominal pain	0	0
	Colitis	0	0
Endocrine	Hypothyroidism	2(3)	0
	Hyperthyroidism	0	0
	Hyperglycaemia	0	0
Skin	Rash/pruritus	3/3 (5/5)	0/0
Respiratory	Dyspnoea	1 (2)	0
	Pneumonitis	2 (3)	0
Laboratory investigations	AST/ALT elevation	2/0 (3/0)	0/0
Nervous system	Peripheral neuropathy	0	0



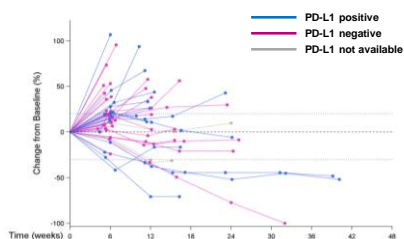
Causality assigned by the investigator; ^aOther Grade 3/4 events were: n=1 gamma-glutamyltransferase elevation, n=1 oncologic complication, n=1 not yet coded; ALT = alanine transaminase.



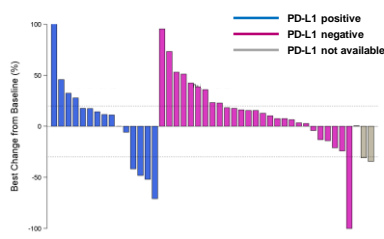
13

Anti-PDL1 in SCCHN: Encouraging anti-tumour activity supporting accelerated late stage development

Tumour Shrinkage by PD-L1 Status (n=45)[†]



Best Change in Tumour Size by PD-L1 status (n=45)[†]



[†]Data cut-off: August 21, 2014; Patients with baseline and ≥ 1 on-treatment scan. Disease assessment at 6 weeks, 12 weeks, 16 weeks, and then every 8 weeks. PD-L1 status defined by VENTANA assay



14

Anti-PDL1 in SCCHN: Increased objective response & disease control in PD-L1 positive patients†

	MEDI4736 10 mg/kg q2w ¹		
	Total population	PD-L1+	PD-L1-
DCR12w	28% (15/53)	35% (6/17)	21% (7/33)
RECIST Response (ORR)	11% (6/53)	24% (4/17)	3% (1/33)
Ongoing responders	100% (6/6)	100% (4/4)	100% (1/1)



¹Data cut-off: August 21, 2014; Patients with baseline and ≥ 1 on-treatment scan. Disease assessment at 6 weeks, 12 weeks, 16 weeks, and then every 8 weeks. PD-L1 status defined by VENTANA assay



15

Anti-PDL1 + Tremelimumab Phase I dose escalation in refractory NSCLC



Anti-PDL1 (MEDI4736) combines well with tremelimumab

MEDI4736 + tremelimumab: Dose escalation

Cohort	Anti-PDL1 (mg/kg)	Tremelimumab (mg/kg)
1	3	1
2	10	1
3a	15	1
3b	10	3
4a	15	3
5	15	10
Current Cohort 5a	20	3

Nivolumab + ipilimumab: Dose escalation

Cohort	Nivolumab (mg/kg)	Ipilimumab (mg/kg)
1	0.3	3
2a	1	3
2	3	1
3	3	3
4	10	3
5	10	10

Maximum tolerated dose

Dose escalation continues



17

Anti-PDL1 + tremelimumab in NSCLC: Emerging safety profile supports continued development

Cohort	n	Anti-PDL1 (mg/kg)	Tremelimumab (mg/kg)	DLT	Events leading to Discontinuation	Related Grade 3-4*	Related Grade 5
1	3	3	1	0	0	0	0
2	3	10	1	0	1	2	1 (myasthenia)
3a	3	15	1	0	0	2	0
3b	3	10	3	0	1	1	0
4a	3	15	3	0	0	0	0
5	6	15	10	0	1	1	0
5a	3	20	3	0*	0*	0*	0
Total	24	NA	NA	1	3/24* (13%)	6/24* (25%)	1/24 (4%)

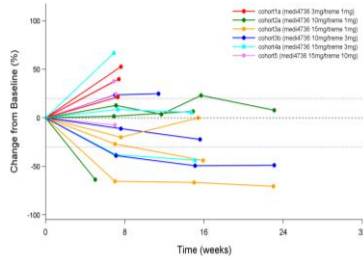
*Post data cut-off, n=1 patient in cohort 5a with asymptomatic grade 3 AST/ALT elevation that was deemed a DLT. Transaminitis reversed with systemic steroids. All Grade 3-4 events were rapidly responsive to steroids



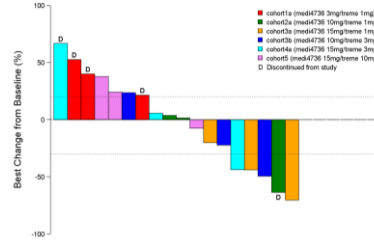
18

Encouraging efficacy for anti-PDL1 + tremelimumab combination in NSCLC

Tumour Shrinkage by dose cohort (n=18)



Best Change in Tumour Size by dose cohort (n=18)



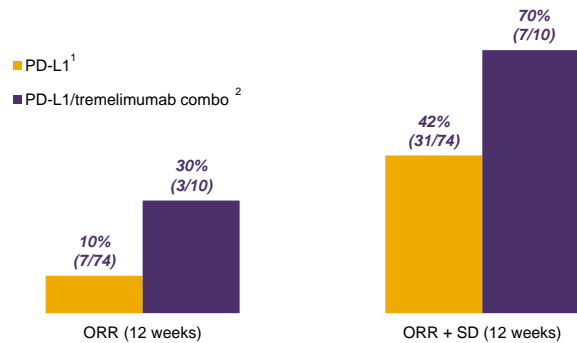
All patients	ORR	Stable Disease
MEDI4736 + tremelimumab	28% (5/18)	28% (5/18)



19

PD-L1 negative tumours: Potentially better response with anti-PDL1 + tremelimumab combination

PD-L1 negative patients in NSCLC



¹Monotherapy: ORR 10% (7/74), 95%CI (3.9%, 18.5%) SD≥12weeks 32.4% (24/74), 95%CI (22.0%, 44.3%)
²Combination: ORR 30% (3/10), 95%CI (6.7%, 65.2%) SD≥12weeks 40% (4/10), 95%CI (12.2%, 73.8%)



20

Summary: Anti-PDL1 and tremelimumab (anti-CTLA-4)

Anti-PDL1

- Encouraging safety profile, consistent across programme
- Active at all doses in multiple tumour types
- Consistent response rates with other PD-1 and PD-L1 agents
- Ongoing responses in ~90% of treated patients

Anti-PDL1 + tremelimumab

- Manageable safety profile – dose escalation continues
- Early signs of anti-tumour activity
- Encouraging activity for combination in PD-L1 negative NSCLC
- Pivotal studies to start in NSCLC & SCCHN 2014



21

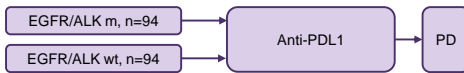
Clinical Plan

Speed, Differentiation, Leadership



Anti-PDL1 development in NSCLC: Fast to market for monotherapy and combination

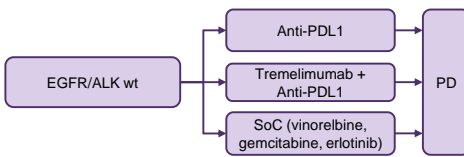
ATLANTIC: 2-cohort, uncontrolled, Ph II 3L NSCLC, PD-L1 positive



Potential registrational study

Primary end-point: ORR
 First subject-in: Q1 2014
 Primary data readout: 2015
 Each arm can be analyzed separately

ARCTIC: Randomised, controlled Ph III 3L NSCLC



First combo registrational study

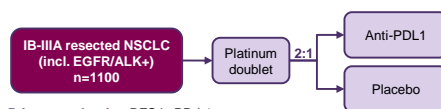
Co-Primary end-points: PFS/OS
 First subject-in: Q4 2014
 Primary data readout: 2017



23

Anti-PDL1 development in NSCLC: First mover advantage in early stage

ADJUVANT: Randomised, controlled Ph III NSCLC

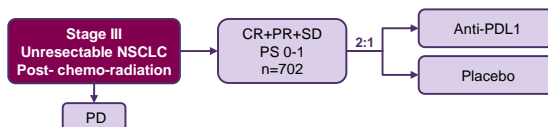


Primary end-point: DFS in PD-L1+
 Secondary end-points: DFS & OS by biomarker status
 First subject-in: 1Q 2015
 Primary data readout: 2020

Rationale to advance into adjuvant NSCLC

- Monotherapy clinical activity in patients who failed on all available therapies, including chemo & TKIs
- Safety data >400 patients with well tolerated safety profile and no treatment related deaths
- Low level of high grade adverse events manageable and reversible in monotherapy

PACIFIC: Ph III, Stage 3 unresectable NSCLC



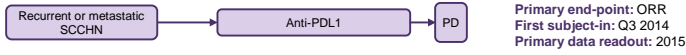
Co-primary end-points: PFS/OS
 First Subject-in: Q2 2014
 Data readout: 2017



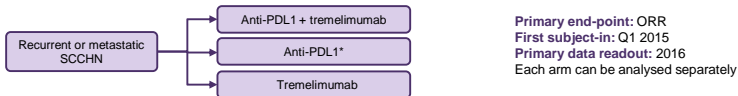
24

Anti-PDL1 development in SCCHN: Fast to market for monotherapy and combination

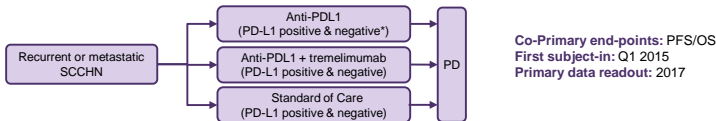
Phase II: PD-L1 positive patients



Phase II: PD-L1 negative patients



Phase III: Randomised, open-label

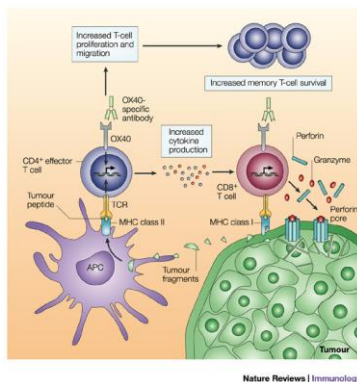


* Enrolment of PD-L1 -ve patients in phase III may be stopped based on phase II data



25

Targeting OX40: Driving potent Anti-tumour T cell Immunity



Our OX40 portfolio leverages aspects of T cell biology to effectively promote anti-tumour immunity

- Targeting the OX40 pathway:
 - Induces T cell activation and migration
 - Drives antigen specific T cell proliferation
 - Supports effector T cell survival
 - Increases antigen specific T-cell memory
 - Potently drives anti-tumour immunity



26

Multiple approaches to OX40-mediated immunity

Murine OX40 MEDI6469

- 1st OX40 agonist in clinic
- Combination with:
- PD-L1 / OX40 combo - ongoing
 - PD-L1 / CTLA4 / rituximab

Humanized anti-OX40 MEDI6383

- Monotherapy dose-escalation
- First subject dosed in Sep 2014

Humanized anti-OX40 MEDI0562

- Monotherapy dose-escalation
- FSI expected early Q1 2015

Multipronged approach to define the best biology to maximize patient benefit



27

Immuno-oncology combinations

Ongoing combination studies

PD-L1 + tremelimumab	Ph I	NSCLC
PD-L1 + tremelimumab	Ph I	solid tumours
PD-L1 + BRAF + MEK	Ph I	Melanoma
PD-L1 + Iressa	Ph I	EGFR M+ NSCLC
PD-L1 + PD-1	Ph I	solid & haems
PD-L1 + AZD9291	Ph I	EGFR M+ NSCLC
PD-L1 + mOX40	Ph I/II	solid tumours
Tremelimumab + Iressa	Ph I	EGFR M+ NSCLC
Tremelimumab + ANG-2	Ph I	Melanoma
Tremelimumab + TACE/RFA	Ph I	HCC
Seq. AZD9291/Selumetinib + docetaxel/Iressa/CTLA-4 & PD-L1	Ph II	NSCLC

Planned combination studies

PD-L1 + radiation	Ph I	solid tumours
PD-L1 + tremelimumab	Ph I	haematological
PD-L1 +/- tremelimumab	Ph I/II/III	SCCHN
PD-L1 + tremelimumab	Ph III	3L NSCLC
PD-L1 + INCB024360 (IDO1)	Ph I/II	solid tumours
PD-L1 + mogamulizumab (CCR4)	Ph I/II	solid tumours
Tremelimumab + mogamulizumab (CCR4)	Ph I/II	solid tumours
PD-L1 + ADXS-HPV	Ph I/II	HPV-cervical & H&N
mOX40 + rituxan	Ph I/II	haematological
mOX40 + tremelimumab	Ph I/II	solid tumours

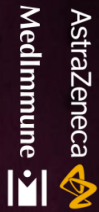


28



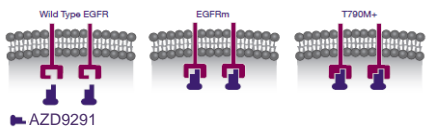
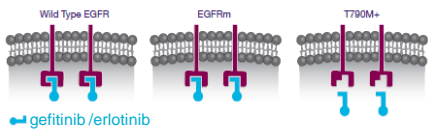
AZD9291

Susan Galbraith
 Head, Oncology, Innovative Medicines & Early Development



AZD9291: Irreversible selective double mutant inhibitor

Designed to inhibit EGFR Exon19 del, L858R, T790M



Key differentiation features

- Increased potency towards EGFRm/T790M
 - Large selectivity margin vs. wild-type EGFR / IGFR
 - >600 patients dosed in 1st line EGFRm & ≥2nd line T790M
-
- Confirmed ORR 70% in T790M patients at 80 mg QD, promising but still immature PFS
 - ORR 63% (confirmed and unconfirmed) in 1st line EGFRm patients
 - Potential to sustain longer efficacy
 - Reduced EGFR wt toxicity, no hyperglycemia concern



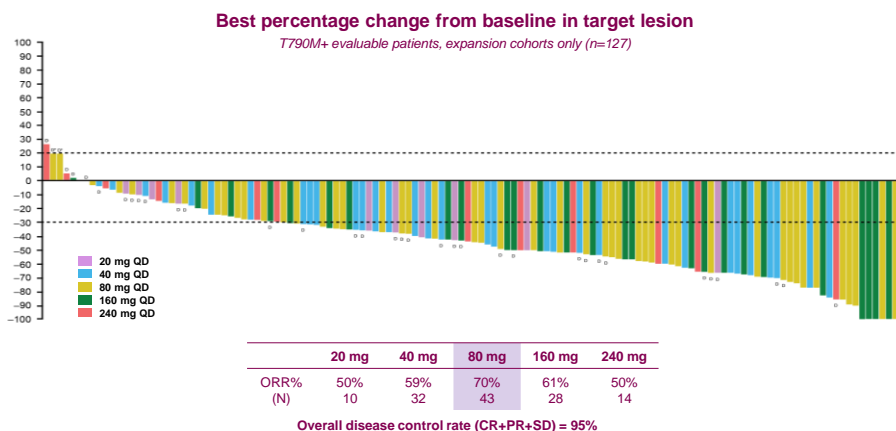
AZD9291: Balanced patients characteristics will allow for relevant generalisation of benefit:risk

Characteristic		Expansion n=222
Race	Caucasian	37% (82/222)
	Asian	60% (134/222)
	Other	3% (6/222)
Prior EGFR-TKIs, Number of regimens	1	49% (108/222)
	2	34% (75/222)
	≥3	17% (38/222)
Immediate prior EGFR-TKI	Yes	62% (137/222)
	No	38% (84/222)



31

AZD9291: Confirmed overall response rate* 61% in T790M+; Longest response > 11 months and ongoing

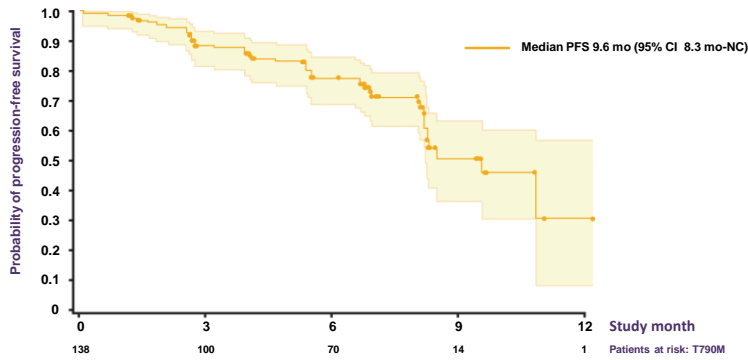


ORR, overall response rate; PR, partial response; SD, stable disease. *Patients who discontinued treatment.
 Data cutoff 1 August 2014



32

AZD9291: Promising PFS for patients with T790M, but still immature (30%)



33

AZD9291: Well tolerated at all dose levels tested and a non-tolerated dose has not been defined

Patients with an AE, %	20 mg (N=21)		40 mg (N=58)		80 mg (N=90)		160 mg (N=63)		240 mg (N=21)	
	Any Gr n (%)	Gr ≥3 n (%)	Any Gr n (%)	Gr ≥3 n (%)	Any Gr n (%)	Gr ≥3 n (%)	Any Gr n (%)	Gr ≥3 n (%)	Any Gr n (%)	Gr ≥3 n (%)
AE by preferred term, occurring in at least 15% of patients overall										
Diarrhoea	5 (24)	0	24 (41)	1 (2)	30 (33)	1 (1)	43 (68)	1 (2)	16 (76)	1 (5)
Rash (grouped terms)	5 (24)	0	13 (22)	0	29 (32)	0	40 (63)	2 (3)	15 (71)	0
Nausea	3 (14)	1 (5)	10 (17)	0	16 (18)	0	19 (30)	0	7 (33)	0
Decreased appetite	7 (33)	1 (5)	11 (19)	0	14 (16)	1 (1)	16 (25)	0	6 (29)	0
Dry Skin	2 (10)	0	9 (16)	0	10 (11)	0	25 (40)	0	5 (24)	0
Pruritus	2 (10)	0	11 (19)	0	15 (17)	0	12 (19)	0	7 (33)	0
Fatigue	4 (19)	1 (5)	15 (26)	0	9 (10)	0	11 (17)	0	5 (24)	1 (5)
Paronychia	2 (10)	0	5 (9)	0	11 (12)	0	18 (29)	1 (2)	6 (29)	0
Constipation	1 (5)	0	13 (22)	0	15 (17)	0	10 (16)	0	1 (5)	0
Cough	3 (14)	0	9 (16)	0	12 (13)	0	13 (21)	0	0	0
Select AEs of interest										
Hyperglycemia	0	0	1 (2)	0	3 (3)	0	2 (3)	0	0	0
QT prolongation	0	0	2 (3)	0	4 (4)	1 (1)	4 (6)	0	1 (5)	0
Pneumonitis-like event ^a	0	0	0	0	2 (2)	2 (2)	4 (6)	2 (3)	0	0



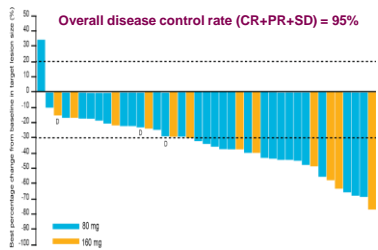
^aAs of 12th Sept, out of more than 620 patients across all studies dosed with AZD9291, pneumonitis grouped term events have been reported in 2.09% of patients (13 events). Of these events, seven were Grade 1-2, three were Grade 3, and one Grade 5 event (0.16%); two have no CTCAE grade reported yet.



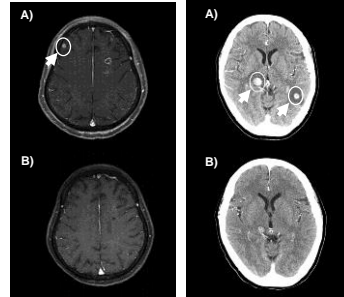
34

AZD9291: Encouraging early efficacy in 1st line EGFRm & preliminary evidence of activity in NSCLC brain mets*

Best % change from baseline in 1st line EGFRm



Preliminary evidence of activity in NSCLC brain mets



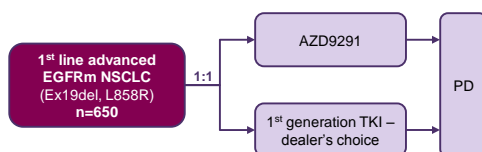
*Clinical activity of AZD9291 in brain mets has been observed in a Phase I study in patients with acquired resistance to current EGFR-TKIs.



35

AZD9291: H2H vs 1st generation TKI in 1st line EGFRm NSCLC

FLAURA: Randomised, controlled, Ph III 1st line EGFRm NSCLC H2H vs 1st generation TKI



Phase III 1st line study

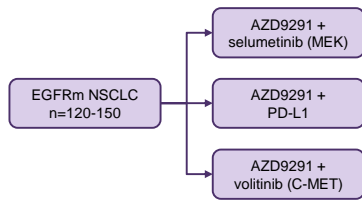
Primary end-point: PFS
 Secondary end-points: OS, ORR, HRQoL
 First subject-in: Q4 2014
 Primary data readout: 2017
 Sized to provide robust subgroup data



36

AZD9291: Multiple combinations synergies to be explored

Phase Ib, multi-arm, open-label combo study



Status of combination studies

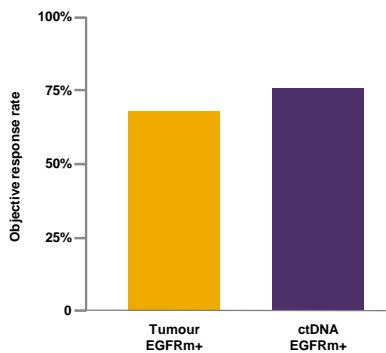
- Pre-clinical and clinical data supports that combining EGFR TKIs with molecularly targeted agents and immunotherapeutics has the potential to address acquired resistance or prevent emergence of resistance across lines of therapy.
- First subject dosed Q3 2014 in all three combinations in Phase Ib study to explore potential to address or prevent resistance



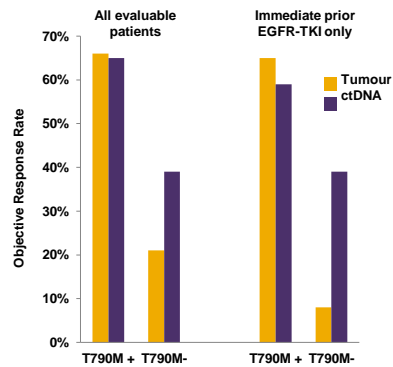
37

CT DNA: CHMP positive opinion for inclusion in Iressa label for EGFRm; evaluation for AZD9291 ongoing

ORR for IRESSA in EGFRm determined by either ctDNA or tumour biopsy



ORR for AZD9291 in EGFRm/T790M determined by either ctDNA or tumour biopsy



IFUM: Douillard et al. (2014) British Journal of Cancer 110: 55-62

Thress et al. (2014) ESMO Poster 1270



38

AZD9291: Continued rapid progress 1st line EGFR M+ H2H to start Q4 2014

Impressive clinical efficacy

- Unprecedented confirmed response rate 70% & DCR 95% in T790M+ patients at 80mg QD
- Promising PFS in T790M+ patients - but still immature
- Evidence of activity in brain mets
- Encouraging 63% response rate and DCR 95% in 1st line EGFRm NSCLC, pre-clinical data supports potential for sustained durability vs gefitinib

Encouraging tolerability profile

- No IGFR inhibition: no hyperglycemia concern
- No HERG liability: no QTc concern

Speed of development

- 1st line H2H vs 1st generation TKI FSI Q4 2014, data readout 2017



39

Q&A

Mondher Mahjoubi, Rachel Humphrey & Susan Galbraith

MedImmune
AstraZeneca