ASCO analyst and investor meeting

1 June 2013, Chicago, IL

AstraZeneca

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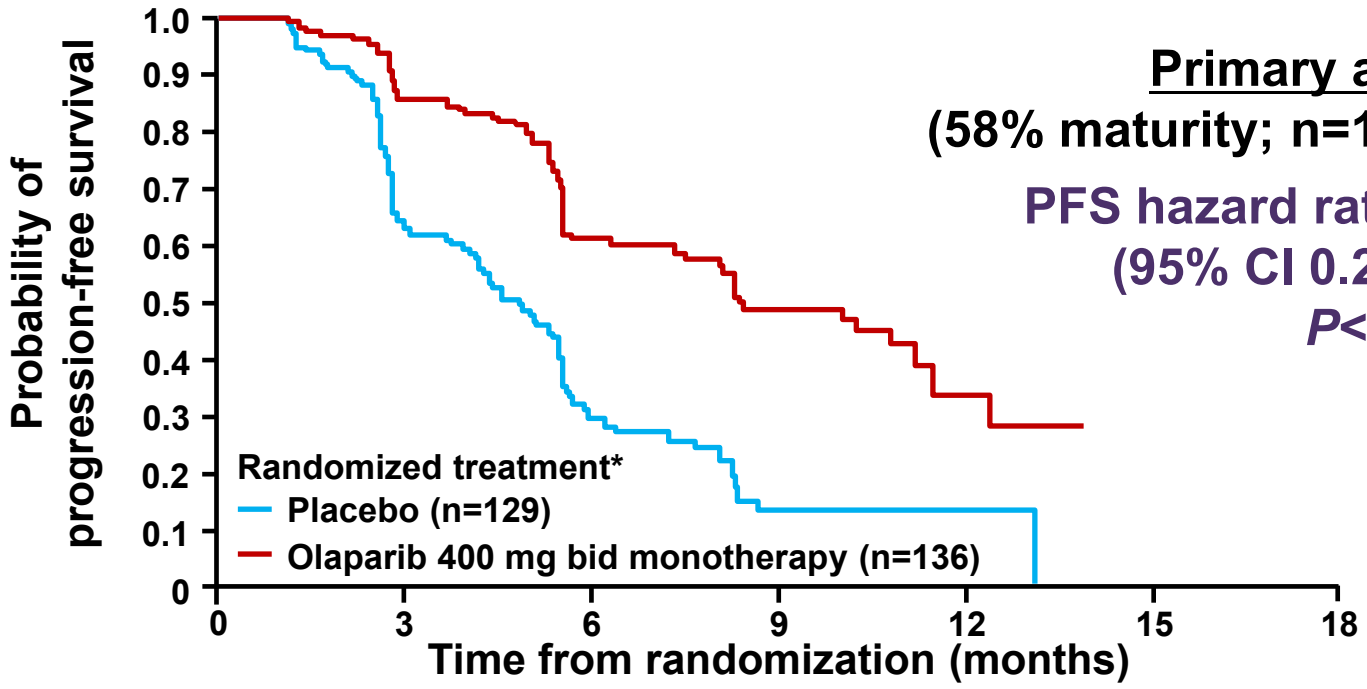
Agenda

6:30pm	Welcome and Introduction	
6:35pm	Olaparib update	Jane Robertson VP Global Product Development
6:45pm	Selumetinib update	Donna Francher VP Global Product Development
6:55pm	Q&A	Jane Robertson Donna Francher Susan Galbraith Head of Innovative Medicines Oncology IMED Ed Bradley Head of MedImmune Oncology IMED Antoine Yver Head of Oncology Global Medicines Development
7:30pm	Close	

Olaparib update

Jane Robertson
VP Global Product Development

Study 19: Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer



- Patients were randomized after response to platinum-based chemotherapy
- Interim OS analysis (38% maturity): HR=0.94; 95% CI 0.63–1.39; *P*=0.75

HR, hazard ratio; OS, overall survival; PFS, progression-free survival
Ledermann J *et al*. *N Engl J Med* 2012;366:1382–1392
*Patients were treated until disease progression

Methods: BRCAm testing

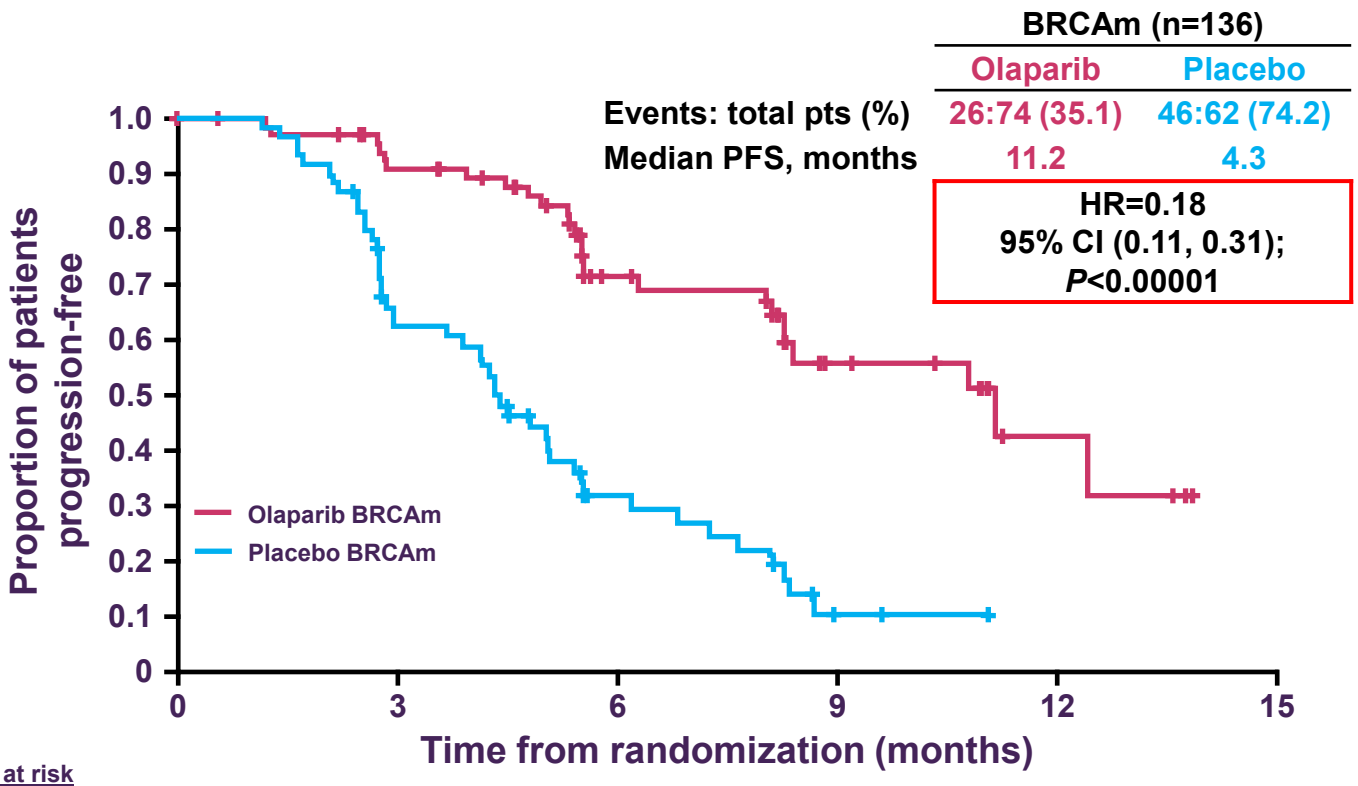
Germline BRCAm (gBRCAm) status was determined retrospectively in an additional 121 patients (218 in total)

- The diagnostic assay (Myriad Genetics) used blood samples collected before randomization from consenting patients

Since patients without an inherited gBRCAm can develop somatic mutations, tumour BRCAm (tBRCAm) status was also determined in 209/265 patients

- Archival tumour samples were analyzed by Foundation Medicine

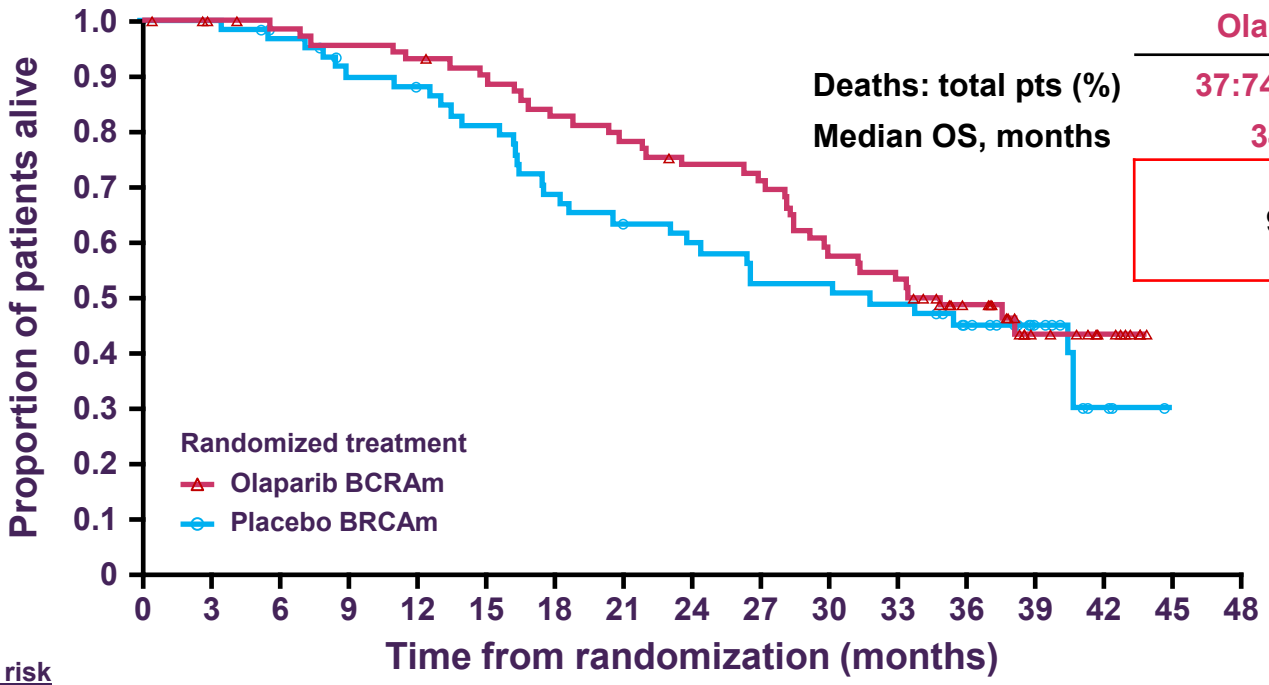
PFS by BRCAm status



82% reduction in risk of disease progression or death with olaparib

AZ data on file

OS in BRCAm patients



BRCAm (n=136)	Olaparib	Placebo
Deaths: total pts (%)	37:74 (50.0)	34:62 (54.8)
Median OS, months	34.9	31.9

HR=0.74
95% CI (0.46, 1.19)
P=0.208

Number at risk															
Olaparib BRCAm	74	71	69	67	65	62	57	54	50	48	39	36	26	12	7
Placebo BRCAm	62	62	58	52	50	46	39	36	33	29	29	27	21	12	4

OS in BRCAwt patients: HR=0.98; 95% CI 0.62–1.55; *P*=0.946

- Median OS: olaparib, 24.5 months; placebo, 26.2 months

14/62 (22.6%) placebo patients switched to a PARP inhibitor

AZ data on file

Olaparib development plan 2013

BRCA-mutated ovarian cancer

- Platinum-sensitive, relapsed maintenance study with ENGOT
- High-risk, first-line ovarian maintenance with GOG

BRCA-mutated breast cancer

- Metastatic disease with Breast Cancer Alliance
- Neoadjuvant (combination with paclitaxel) with Breast International Group
- Adjuvant treatment post-chemotherapy with Breast International Group

Gastric cancer

- Second-line combination with paclitaxel: Asia study

Prostate cancer

- Phase II combination with abiraterone
- Phase I combination with AZD5363 (AKTi)

ENGOT, European Network of Gynaecological Oncological Trial Groups; GOG, Gynecologic Oncology Group

Selumetinib update

Donna Francher
VP Global Product Development

Monotherapy activity in uveal melanoma (GNAQ)

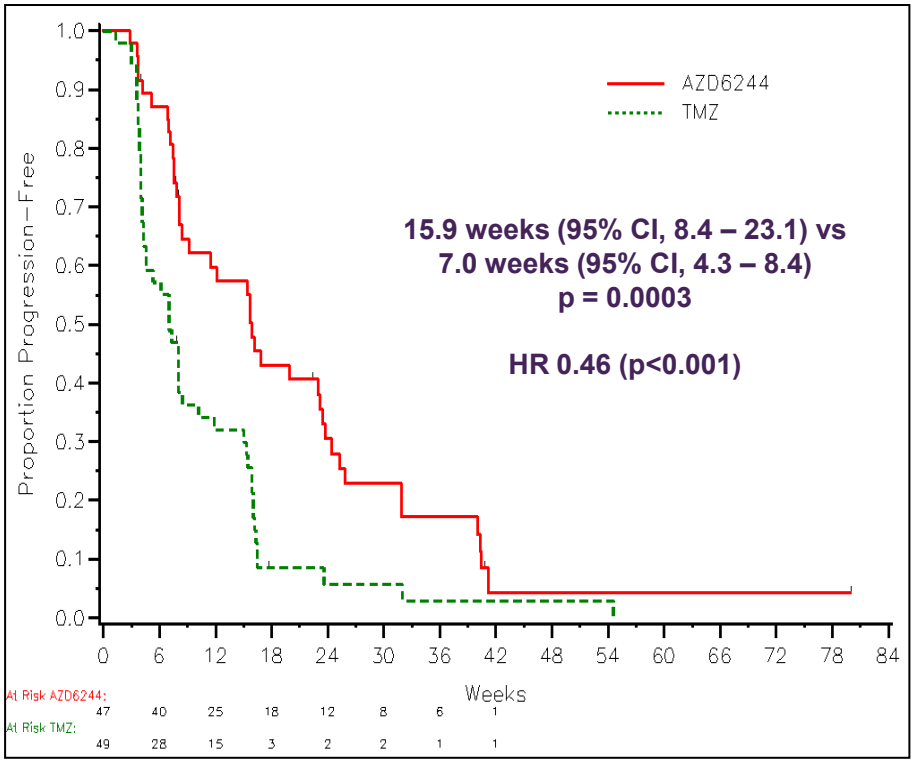
Scientific / Clinical Context

- In contrast to melanomas, uveal melanomas rarely exhibit NRAS / BRAF activation
- **Commonly possess mutation of GNAQ**. Provides an alternate route to MEK-ERK activation[1]
- No effective standard of care
- Trametinib did not warrant taking forward after single-arm study

Implications

- This is the largest Phase II trial in uveal melanoma
- We are discussing options for moving forward

Selumetinib vs. temozolomide in uveal melanoma



Cross over on progression for TMZ treated patients

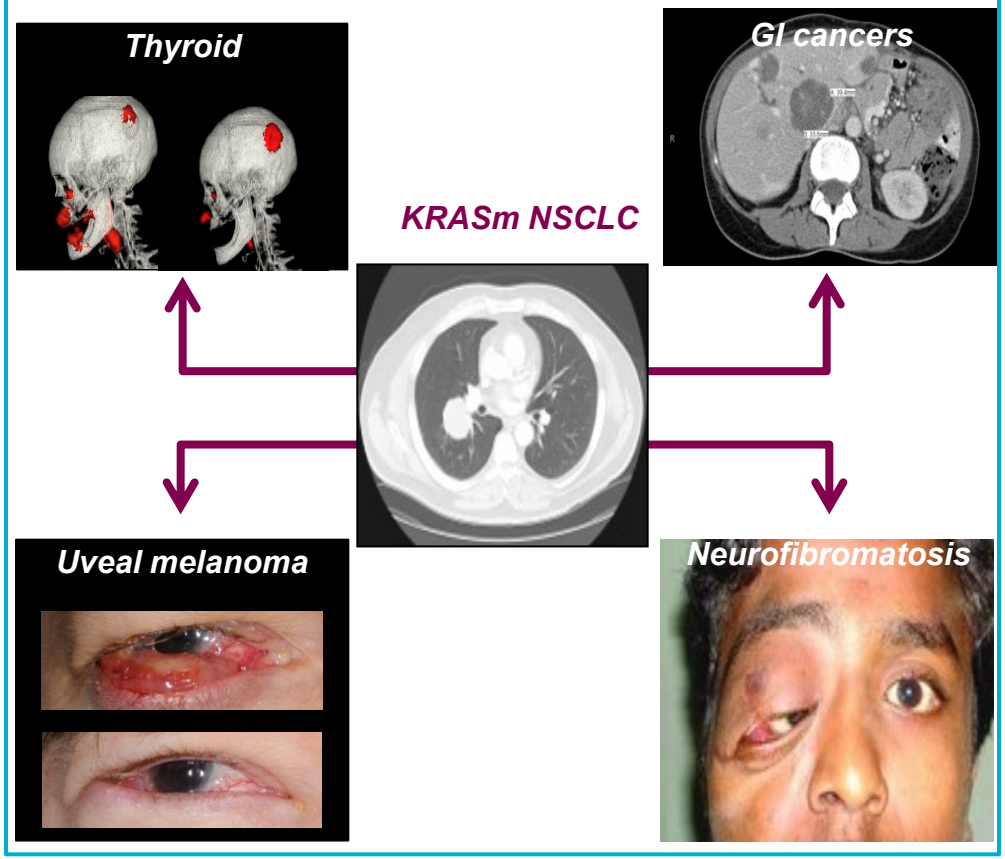
Van Raamsdonk et al., *Nature* 2009;457:599-602

Accelerating multiple opportunities with selumetinib

Starting pivotal trials 2013

- Effective and well-tolerated as monotherapy
- Induces ‘re-differentiation’ in thyroid cancer
- Active in combination with chemo in multiple tumour types
- Opportunity to lead in high unmet need indications with MEK-dependence
- 2H13 trial starts – 2L KRASm NSCLC (Phase III – planned); thyroid (pivotal Phase IIB)

Selumetinib in MEK-driven tumours



Images: NF – Klaus D. Peter, Gummersbach, Germany (Creative Commons license);
GI – courtesy of Deirdre Cohen and Howard Hochster, Yale University, USA;
Lung – courtesy of E. Cortell, Harvard Vanguard Medical Associates, USA
NSCLC – non-small cell lung cancer

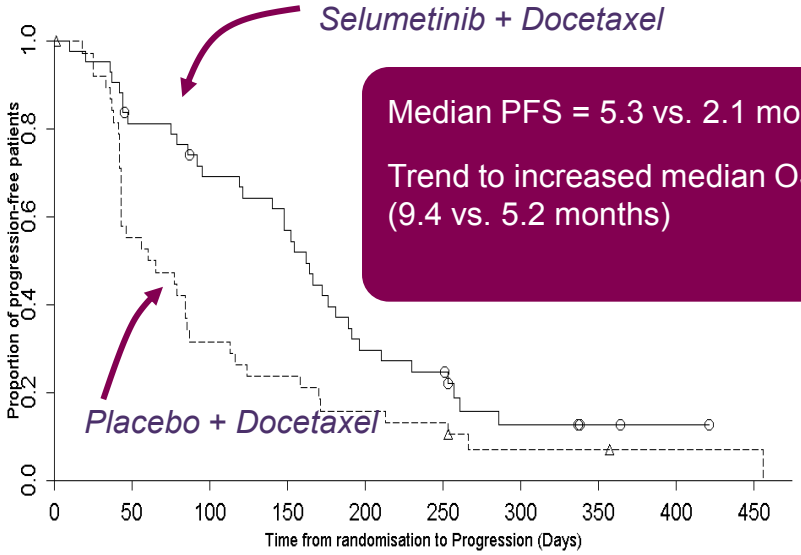
Selumetinib combination with chemo in NSCLC

Active in combination with chemotherapy

- High and durable response rate in segment with poor response to docetaxel alone
- Improved PFS
- Tolerated in combination with doublet chemotherapy
- KRASm NSCLC opportunity – ~25K 2nd-line; ~45K 1st-line[1]
- Pivotal study to start October 2013

Evidence in 2nd-line KRASm NSCLC[2]

	Selumetinib + Docetaxel[3] (N=43)	Placebo + Docetaxel[3] (N=40)
Response	16 (37%)	0
Non-response	27 (63%)	40 (100%)



Median PFS = 5.3 vs. 2.1 months[4]

Trend to increased median OS (9.4 vs. 5.2 months)

[1] G7 only – Kantar Health, internal AZ estimates
[2] Jänne et al., Lancet Oncol 2013; 14:38-47
[3] Selumetinib 75 mg BD; docetaxel 75 mg/m^2
[4] HR 0.58, 80% CI (0.42, 0.79), p = 0.0138
PFS – progression free survival

Originally presented at ASCO 2012

Q&A