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Nintedanib + pemetrexed/cisplatin in malignant pleural mesothelioma: Phase II biomarker data from the LUME-Meso study

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Disclosures

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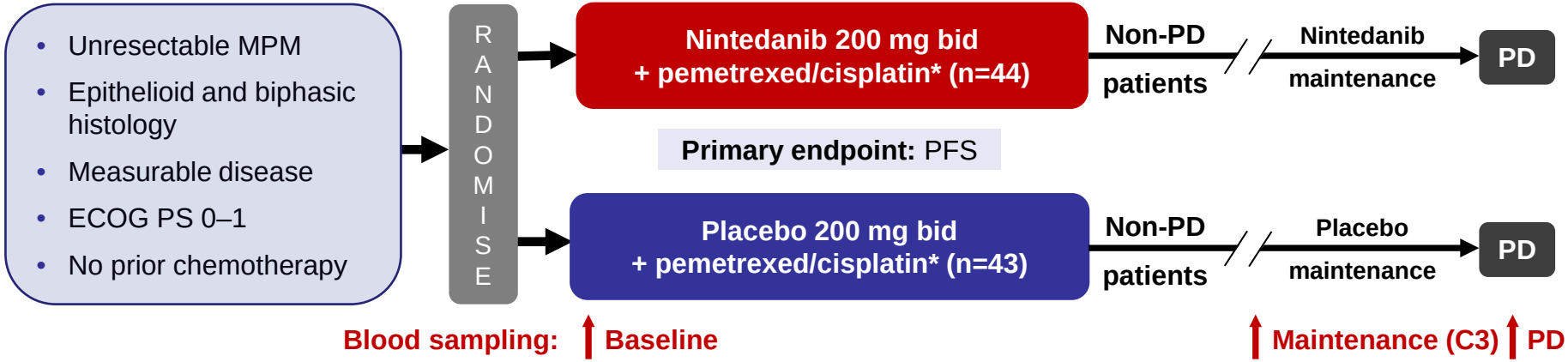
LUME-Meso (NCT01907100): Phase II design and results[1]



- Clinically meaningful 3.7-month improvement in median PFS (HR=0.54; 95% CI: 0.33–0.87; p=0.010†)
- Trend for longer OS (HR=0.77; 95% CI: 0.46–1.29; p=0.319†)
- Efficacy most pronounced in patients with epithelioid tumours

1. Grosso F, et al. J Clin Oncol 2017.

*Pemetrexed 500 mg/m^2 + cisplatin 75 mg/m^2 iv, every 21 days for maximum treatment duration of 6 cycles; †Results for the overall population.
bid, twice daily; C3, Cycle 3; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; iv, intravenous; MPM, malignant pleural mesothelioma; OS, overall survival; PD, progressive disease; PFS, progression-free survival.

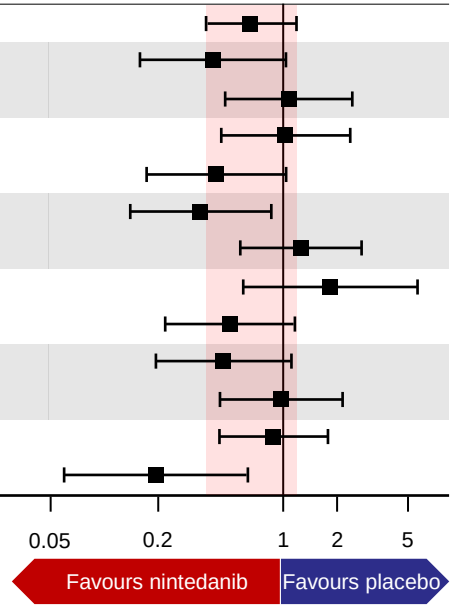
Exploratory biomarker analyses

- Biomarkers
  - Plasma levels of 58 angiogenic factors (Human AngiogenesisMAP® panel, Myriad RBM)
  - SNPs in genes for mesothelin (MSLN), VEGFR1 (FLT1) and VEGFR3 (FLT4)
  - Microvessel density: CD31 IHC assessment of archival biopsy samples
- Statistics
  - Predictive and prognostic analyses performed for OS and PFS
  - Cox regression modelling used for categorical markers
  - p values corrected by FDR adjustment
  - All analyses exploratory and considered hypothesis generating
- Analyses reported for the epithelioid population

FDR, false discovery rate; IHC, immunohistochemistry; SNP, single-nucleotide polymorphism; VEGFR, vascular endothelial growth factor receptor.

Angiogenic factor levels at baseline: predictive analyses (OS)

Angiogenic factor	Subgroup	Events, n/N		HR (95% CI)	Interaction p value	
		Nintedanib	Placebo		Unadjusted	FDR-adjusted
Total	N/A	23/37	25/34	0.66 (0.37–1.17)	N/A	N/A
ANG-1	<Median	8/17	13/16	0.41 (0.16–1.03)	0.097	0.956
	≥Median	15/19	10/15	1.08 (0.48–2.43)		
CEACAM1	<Median	16/21	9/14	1.03 (0.45–2.36)	0.120	0.956
	≥Median	7/16	16/20	0.42 (0.17–1.04)		
Endoglin	<Median	9/18	12/15	0.35 (0.14–0.86)	0.023	0.720
	≥Median	14/19	13/19	1.25 (0.57–2.73)		
IGFBP-2	<Median	15/24	4/11	1.83 (0.60–5.59)	0.054	0.723
	≥Median	8/13	21/23	0.51 (0.22–1.16)		
PDGF-BB	<Median	11/22	11/13	0.46 (0.20–1.10)	0.179	0.962
	≥Median	12/15	14/21	0.97 (0.44–2.14)		
VEGF-D	<BLQ	16/26	17/24	0.88 (0.44–1.77)	0.036	0.720
	≥BLQ	7/11	8/10	0.20 (0.06–0.63)		



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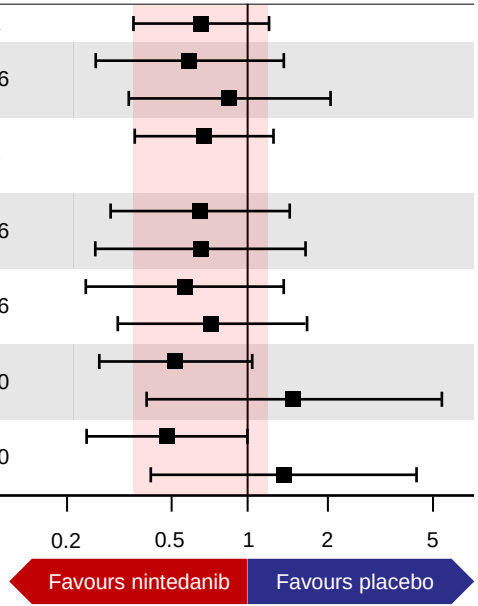
ANG, angiopoietin; BLQ, below the limit of quantitation; CEACAM, carcinoembryonic antigen-related cell adhesion molecule; IGFBP, insulin-like growth factor-binding protein; N/A, not applicable; PDGF, platelet-derived growth factor; VEGF, vascular endothelial growth factor.

SNPs: predictive analyses (OS)

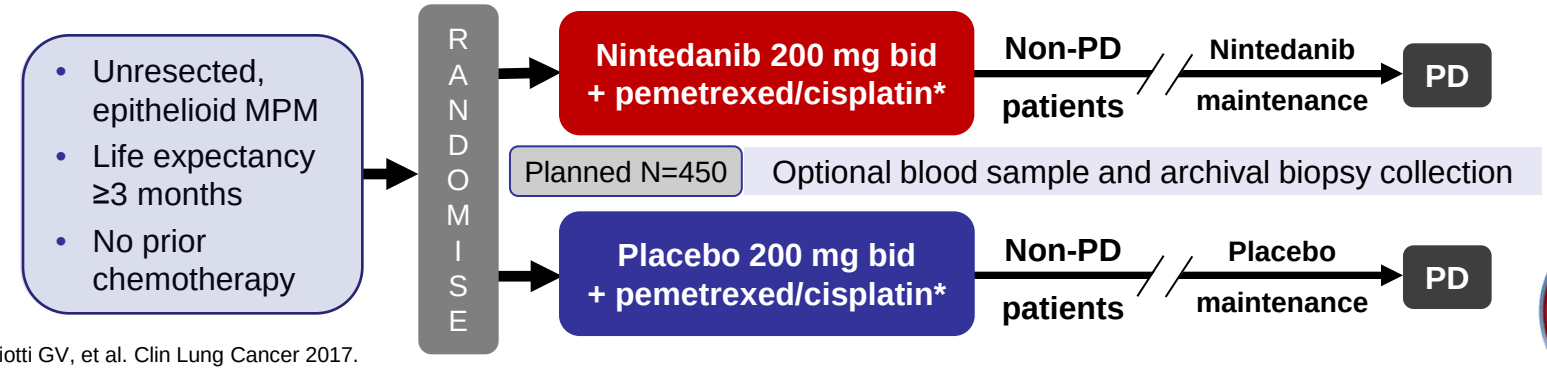
Gene (SNP)	Genotype subgroup	Events, n/N		HR (95% CI)	Interaction p value	
		Nintedanib	Placebo		Unadjusted	FDR-adjusted
Total	N/A	21/35	22/32	0.66 (0.36–1.20)	N/A	N/A
MSLN (rs3764247)	A/A	13/23	10/16	0.59 (0.26–1.38)	0.586	0.926
	C/C or A/C	8/12	12/16	0.85 (0.35–2.08)		
MSLN (rs74002893)	C/C	20/33	21/31	0.68 (0.36–1.26)	N/C	N/C
	C/T*	1/2	1/1	N/C		
VEGFR1 (rs7993418)	A/A	13/21	12/19	0.65 (0.29–1.46)	0.926	0.926
	G/G or A/G	8/14	10/13	0.65 (0.25–1.68)		
VEGFR1 (rs9582036)	A/A	10/16	11/15	0.57 (0.23–1.38)	0.783	0.926
	C/C or A/C	11/19	11/17	0.73 (0.31–1.70)		
VEGFR3 (rs307821)	G/G	16/28	18/25	0.52 (0.26–1.04)	0.140	0.350
	T/T or G/T	5/7	4/7	1.50 (0.40–5.65)		
VEGFR3 (rs307826)	A/A	14/25	17/21	0.49 (0.24–1.00)	0.117	0.350
	G/G or A/G	7/10	5/11	1.38 (0.42–4.53)		



*No patients with T/T genotype were identified; N/C, not calculable.

Take-home messages

- No biomarkers showed clear association with treatment benefit
- There were potential signals for greater treatment effect in patients with low plasma endoglin (OS and PFS) and major homozygous VEGFR3 genotypes (OS only)
- Analyses were limited by small sample size; none were significant after FDR adjustment
- These findings will be evaluated further in the Phase III part of the study:[1]



1. Scagliotti GV, et al. Clin Lung Cancer 2017.

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