A Ph I/II Study of Oral Selective AXL Inhibitor Bemcentinib (BGB324) with Docetaxel in pts with Previously Treated NSCLC

UTSouthwestern

Medical Center



dynamic changes of plasma pro-

The top right quadrant repre-

sents markers that are signifi

down-regulated after 1 cycle of

Shown are screen levels of os-

teopontin in patients responding

to combination treatment versus

those that show no benefit from

quadrant those that are

bemcentinib + docetaxel.

predict benefit:

tein markers following 1 cycle of

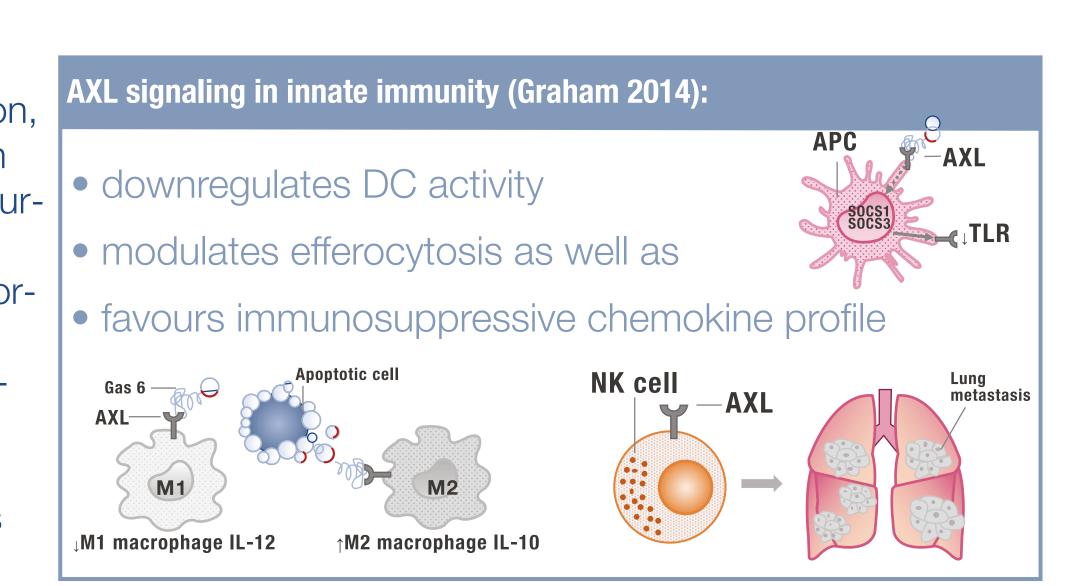
(1) Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, (2) BerGenBio ASA

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Background & objective

RTK AXL drives therapy resistance and negatively regulates innate immunity

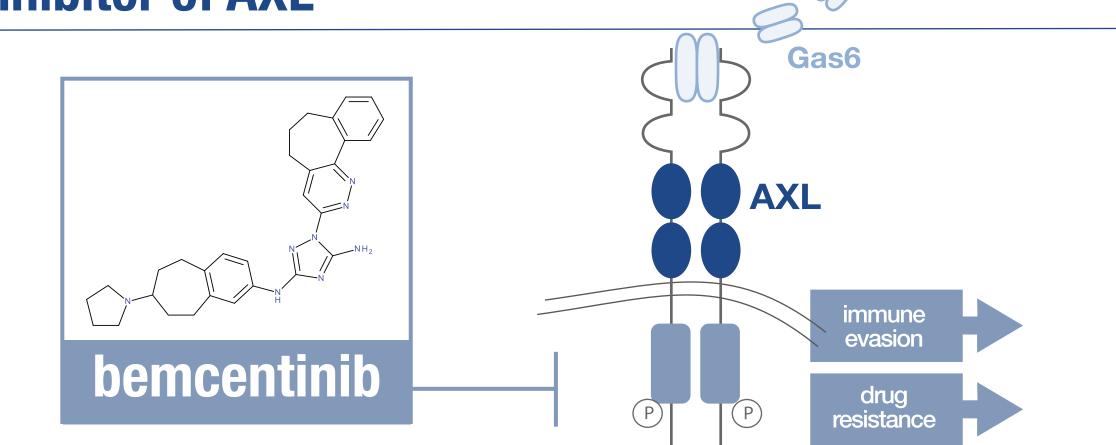
AXL is a member of the TAM family of receptor tyrosine kinases that regulate multiple cellular responses including cell survival, proliferation, and migration. AXL expression is associated with a variety of human cancers including NSCLC, and is predictive of poor patient overall survival. AXL is associated with epithelial-to-mesenchymal transition (EMT) and is required to maintain invasiveness and metastasis. Importantly, AXL confers resistance to both chemotherapeutic agents as well as EGFR tyrosine kinase inhibitors. Activation of the receptor tyrosine kinase AXL has a profound suppressive effect on the innate immune system. AXL is overexpressed on multiple cell types in the tumour immune microenvironment including dendritic cells, NK cells and tumour-associated macrophages.



Bemcentinib - selective, oral small molecule inhibitor of AXL

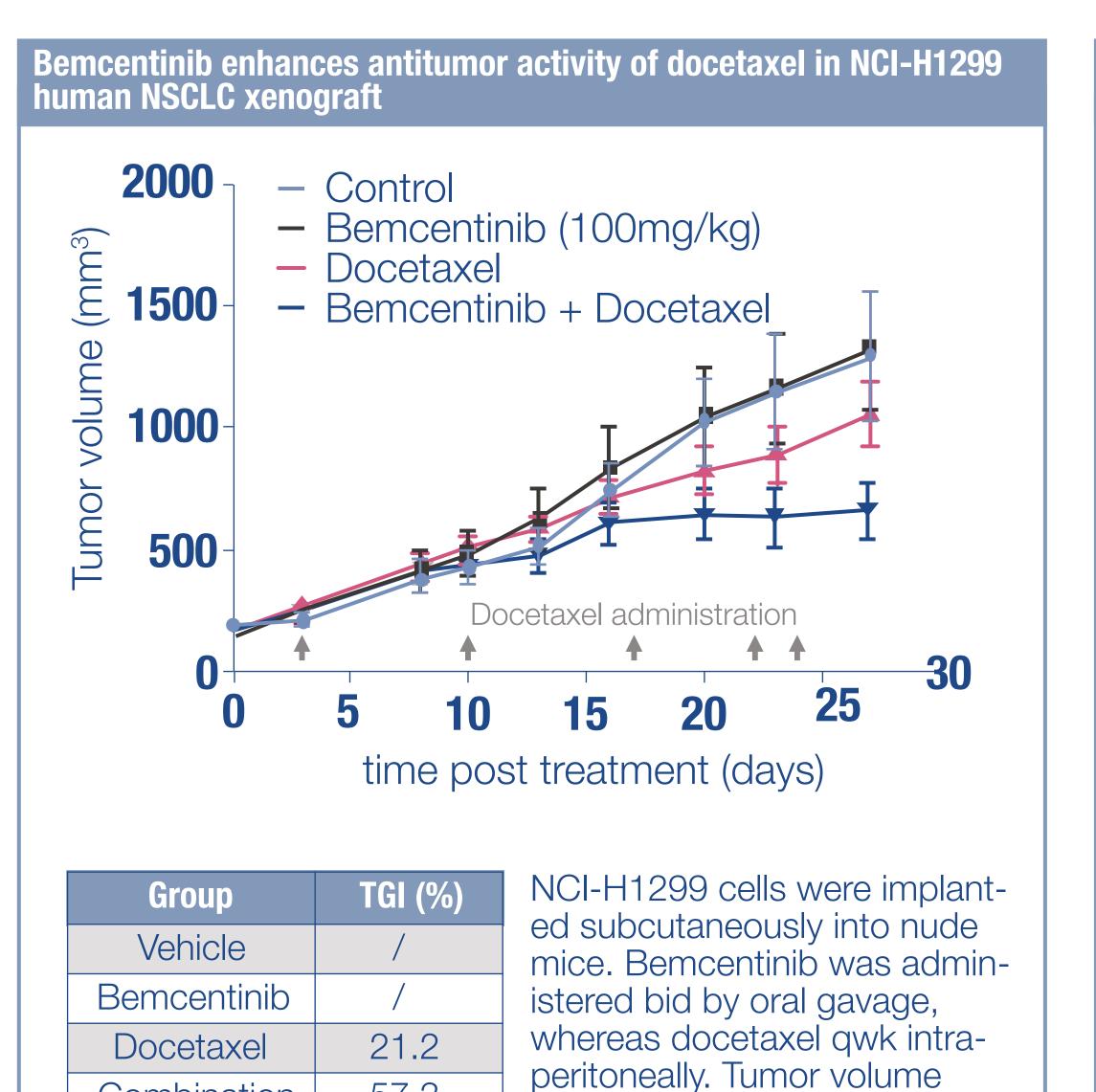
Bemcentinib selectivity profile										
	Kinome Scan (Kd)		Kinase Profiler (IC50)		Fluorescence Polarization (IC ₅₀)		Receptor Cross- Linking (IC ₅₀)			
Kinase	nM	Fold	nM	Fold	nM	Fold	nM	Fold		
4xI	0.4	1	4.6	1	14	1	14	1		
Mer	100	250	12.5	2.7	220	16		50		
Tyro	>1000	>1000	413	89				>100		

NCT02424617: bemcentinib + erlotinib

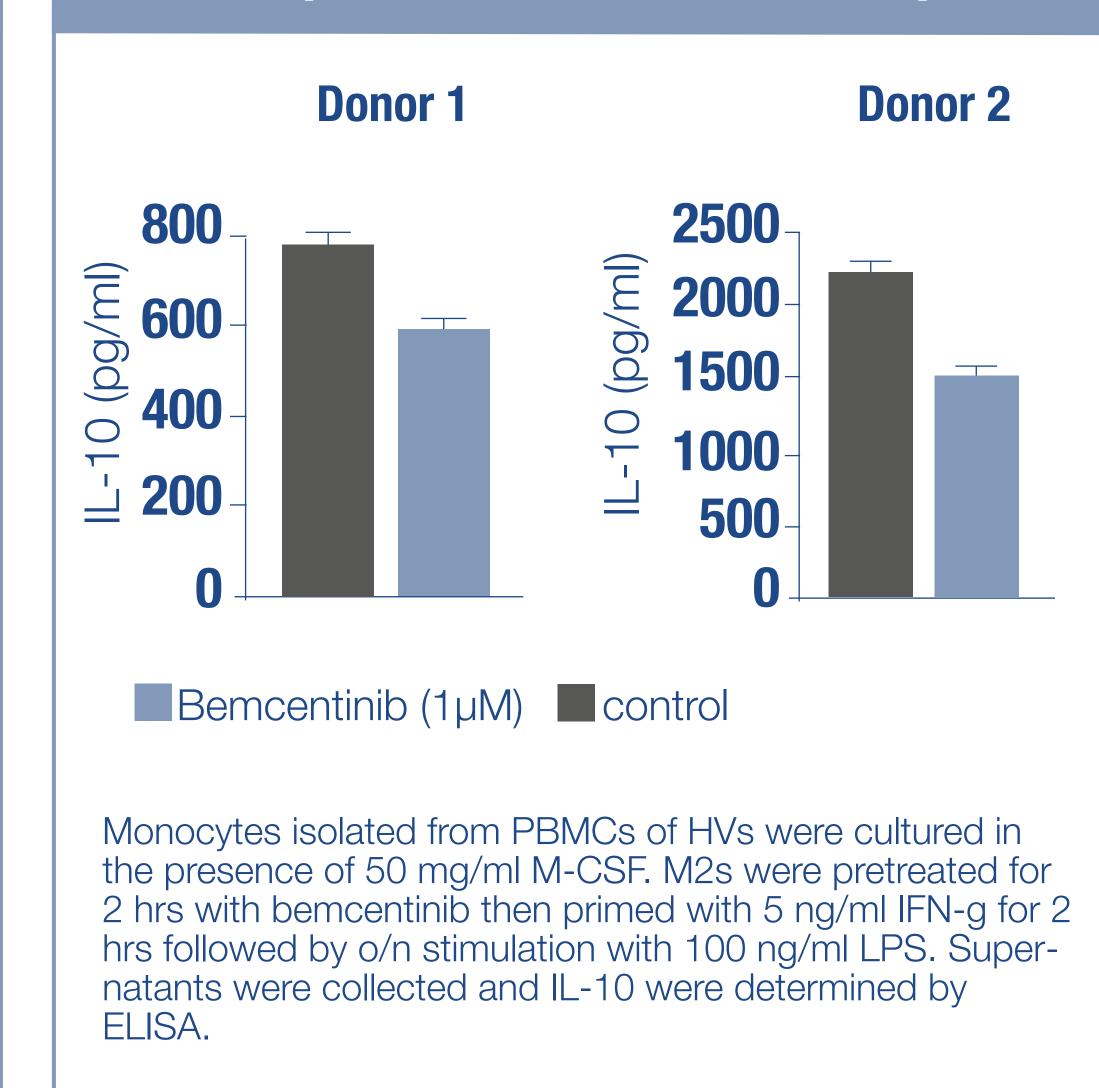


AML/MDS NCT02488408: bemcentinib single agent or + decitabine or cytarabine Melanoma NCT02872259: bemcentinib + pembrolizumab or dabrafenib/trametinib

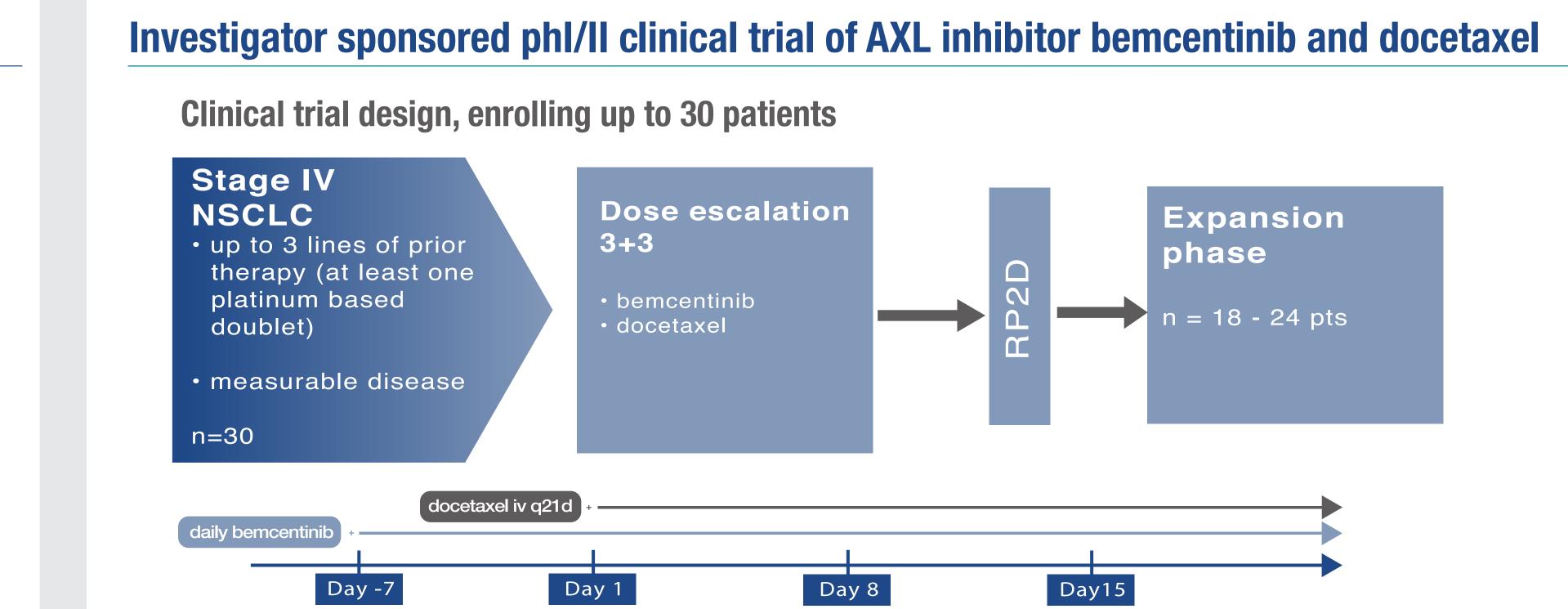
Bemcentinib enhances antitumor activity of docetaxel & stimulates innate immunity



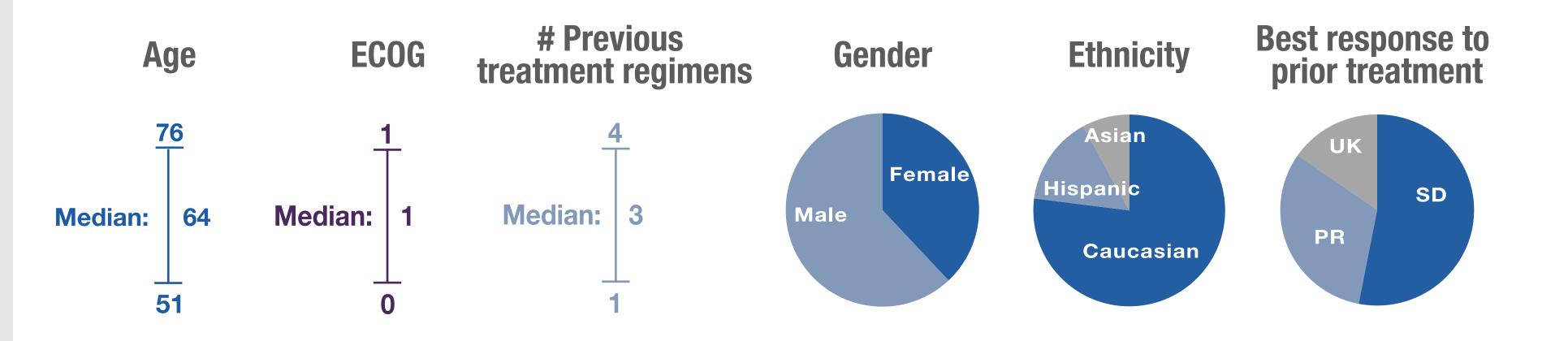
was measured twice a week.



Results



Demographics



Cycle 1 + (21 days)

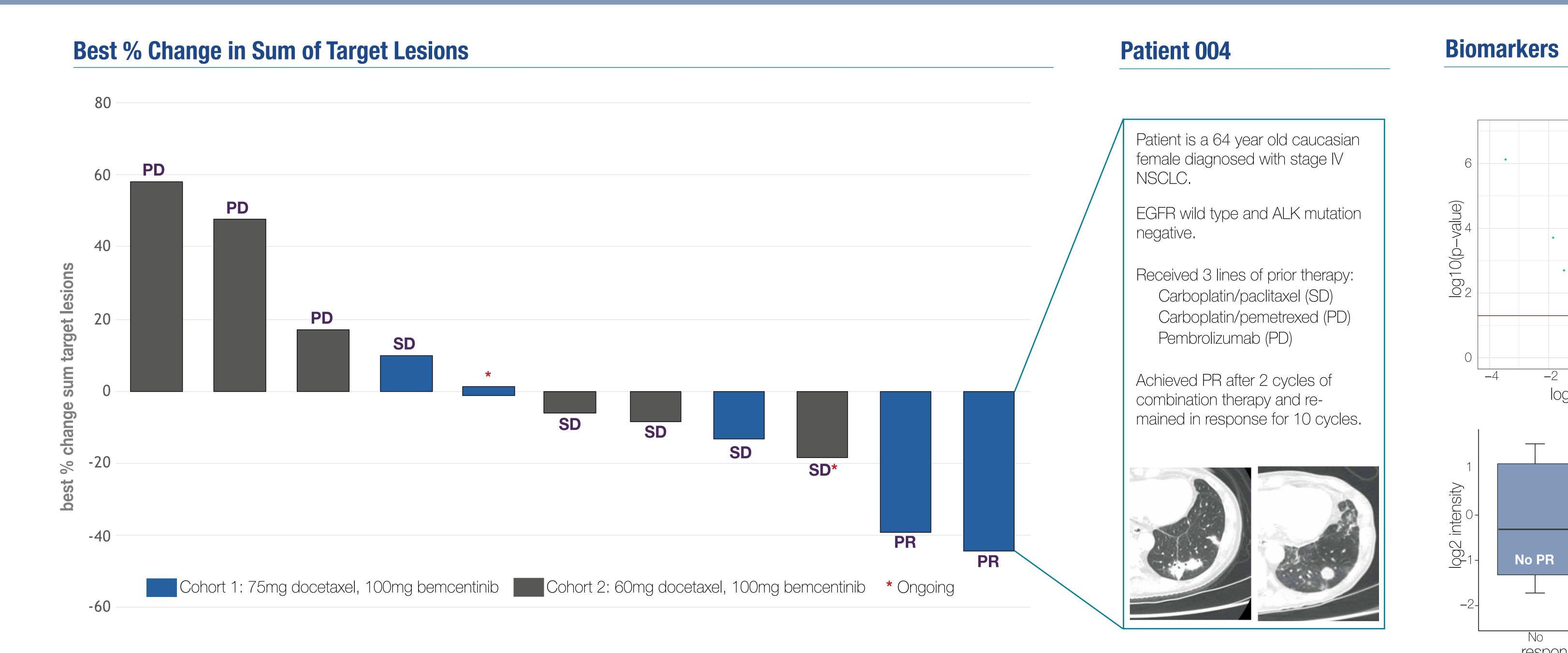
Methods

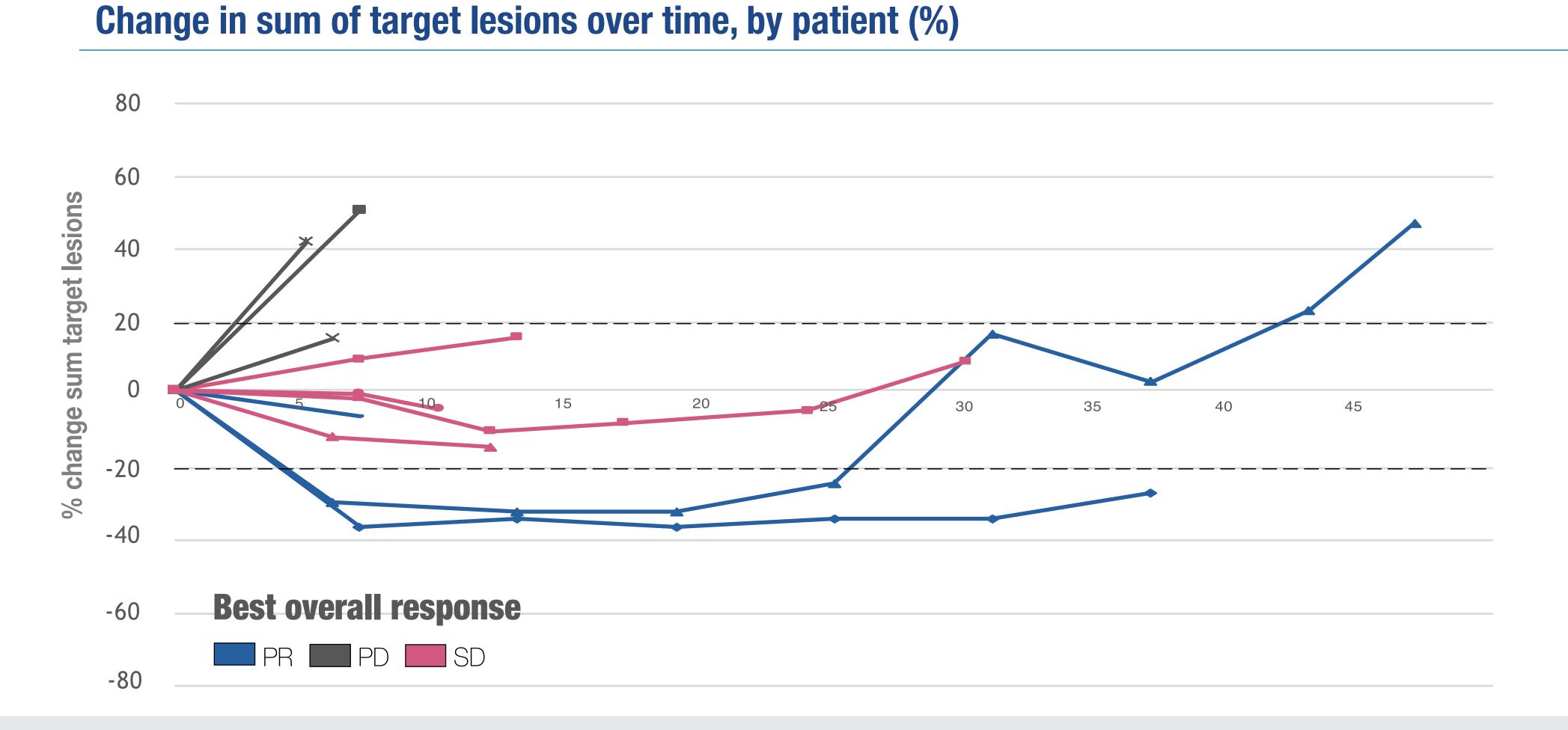
		SAEs n (%) E: 8 (67) 15	
	Grade 2	Grade 3	Grade 4
Blood and lymphatic system disorders			
Febrile neutropenia		3	1
Gastrointestinal disorders			
Constipation	1		
General disorders and administration site conditions			
Pyrexia	1		
Infections and infestations			
Pneumonia		1	
Metabolism and nutrition disorders			
Hypercalcaemia	1	1	
Nervous system disorders			
Syncope		1	
Psychiatric disorders			
Confusional state	1		
Hallucination	1		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome	1		
Pleural Effusion		1	
Pneumonitis		1	

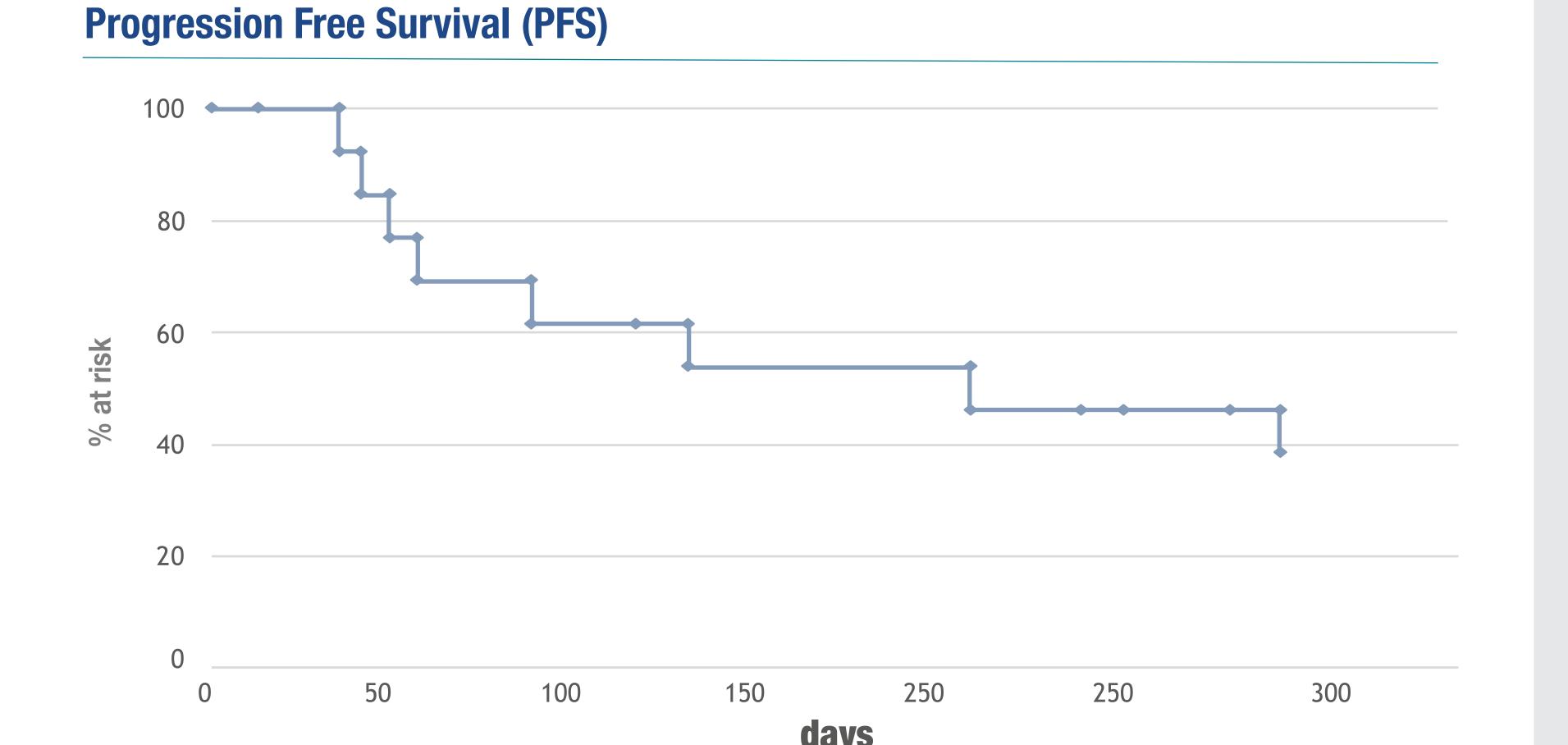
biomarkers: Plasma protein biomark er levels were measured using the DiscoveryMap v3.3 panel (Myriad RBM) at pre-dose and at C2D1. Bi oinformatics analysis was carried out by Fios Genomics. Comparisons were performed on the QC-passed and normalised Myriad

Tumor assessments: Sum target lesions were assessed as per RECIST v1.1. Scans were carried out every

were assessed by CTCAE v4.03.







log2 (fold-change)

Contact

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Conclusions

The combination of bemcentinib and docetaxel is active in pts with advanced NSCLC who progressed on chemotherapy, targeted therapy as well as CPIs