

LUNG CANCER **UPDATES**

AACR HIGHLIGHTS

29 MARZO - 3 ABRIL 2019



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Iniciativa científica de:



Grupo Español de Cáncer de Pulmón
Spanish Lung Cancer Group



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New BMK and LT Survivals

Dr. Santiago Ponce

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Results – cfDNA Concordance and Positive Predictive Value

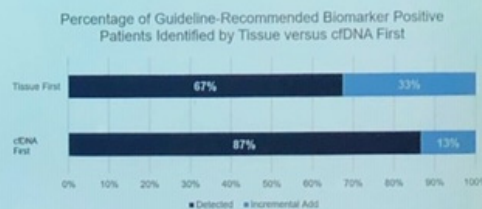
- For genes with FDA-approved targeted therapy (*EGFR*, *ALK*, *ROS1*, and *BRAF*) concordance of tissue and cfDNA results was >98.2%
- EGFR*, *ALK*, and *BRAF* had 100% positive predictive value for cfDNA versus tissue (34/34)
- Modifications to the cfDNA bioinformatics pipeline, including in fusion calling and discrimination of focal copy number amplification
 - Re-analysis of samples improved *ALK* fusion sensitivity

FDA Approved Targets		Tissue +	Tissue -	Tissue Not Assessed/ QMS	Total		
EGFR Exon 19 del	cfDNA+	18	0	1	19	Sensitivity	81.8%
	cfDNA-	4	201	44	249	PPV	100.0%
	cfDNA cancelled / TND	0	11	3	14	Specificity	100.0%
	Total	22	212	48	282	NPV	98.0%
						Concordance	98.2%
EGFR L858R	cfDNA+	9	0	2	11	Sensitivity	90.8%
	cfDNA-	1	213	43	257	PPV	100.0%
	cfDNA cancelled / TND	0	11	3	14	Specificity	100.0%
	Total	10	224	48	282	NPV	98.9%
						Concordance	99.3%
ALK Fusion (ORIGINAL)	cfDNA+	5	0	1	6	Sensitivity	82.8%
	cfDNA-	3	207	52	262	PPV	100.0%
	cfDNA cancelled / TND	1	11	2	14	Specificity	100.0%
	Total	9	218	55	282	NPV	98.6%
						Concordance	98.6%
ALK Fusion (Re-analysis)	cfDNA+	6	0	1	7	Sensitivity	78.6%
	cfDNA-	2	207	52	261	PPV	100.0%
	cfDNA cancelled / TND	1	11	2	14	Specificity	100.0%
	Total	9	218	55	282	NPV	99.0%
						Concordance	99.1%
ROS1 Fusion	cfDNA+	0	0	0	0	Sensitivity	-
	cfDNA-	2	151	115	268	PPV	-
	cfDNA cancelled / TND	0	8	6	14	Specificity	100.0%
	Total	2	159	121	282	NPV	98.7%
						Concordance	98.7%
BRAF V600E mutation	cfDNA+	2	0	0	2	Sensitivity	100.0%
	cfDNA-	0	90	176	266	PPV	100.0%
	cfDNA cancelled / TND	0	3	9	14	Specificity	100.0%
	Total	2	93	185	282	NPV	100.0%
						Concordance	100.0%

TND = tumor not detected

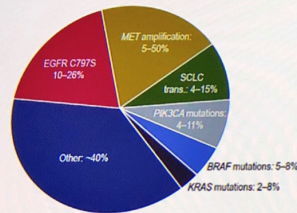
Results – cfDNA Testing versus Tissue Testing First

- Utilizing tissue testing first would have identified 67% of the 89 patients with a guideline-recommended biomarker
 - 33% of patients identified on reflex cfDNA testing
- If cfDNA was the first genomic testing modality, significantly more patients would be identified (87%) ($p < 0.0001$)
 - 13% of patients identified on reflex tissue testing



Acquired EGFR C797S mutation mediates resistance to osimertinib

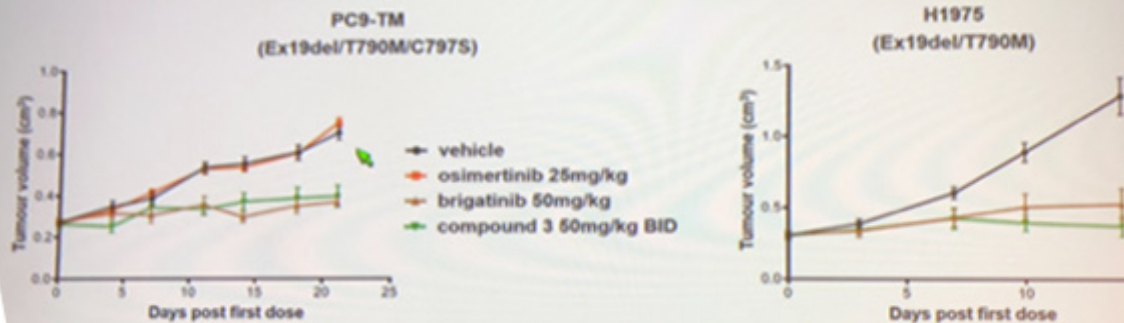
- C797S mutation is a major mechanism for resistance to osimertinib in second line of therapy (EGFR Ex19/L858R NSCLC T790M+ve)



Composite pie chart restricted to analyses with >15 patients*

C797S has been identified post first line osimertinib therapy (TKI naive EGFR Ex19/L858R NSCLC)

Compound 3 induces tumor growth inhibition *in vivo*



Compound	PC9-TM %TGI	H1975 %TGI
Compound 3	52	87
brigatinib	71	86

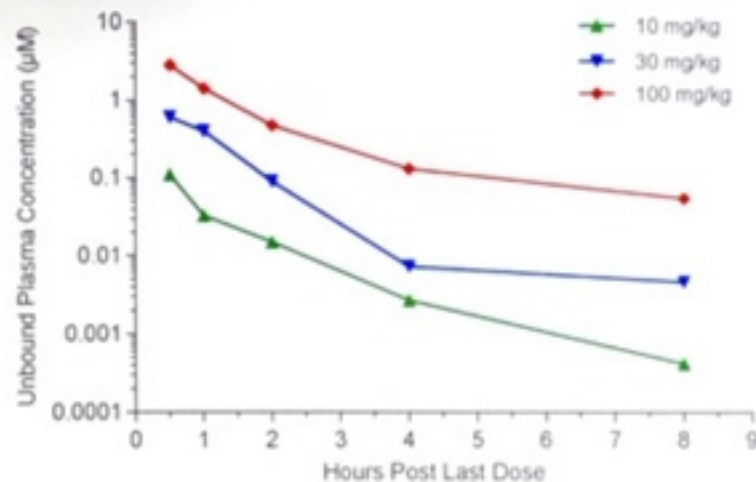
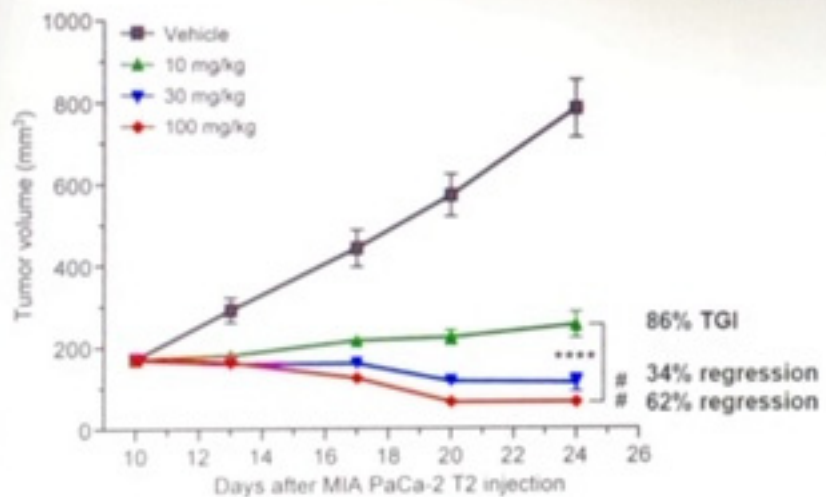
- 52% tumour growth inhibition with AZ7608 monotherapy in PC9-TM

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AMG 510 DOSED ORALLY ONCE DAILY RESULTS IN REGRESSION OF *KRAS P.G12C* TUMOR XENOGRAPHS



CTC and Immune Cell Imaging

A. CTC staining



B. Immune cell staining

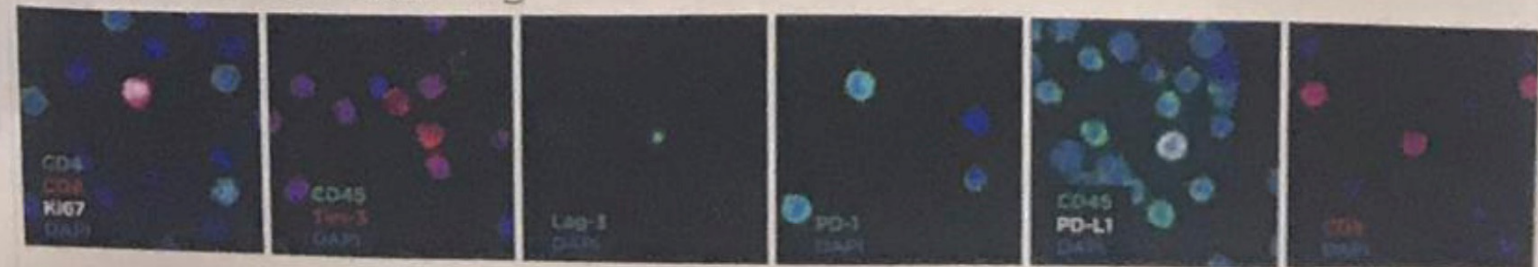


Figure 3. OS with nivolumab vs docetaxel by tumor PD-L1 expression in CheckMate 017/ 057^a

