

## The Evolving Role of Molecular Markers in Managing Non-Small Cell Lung Cancer: Q & A Session

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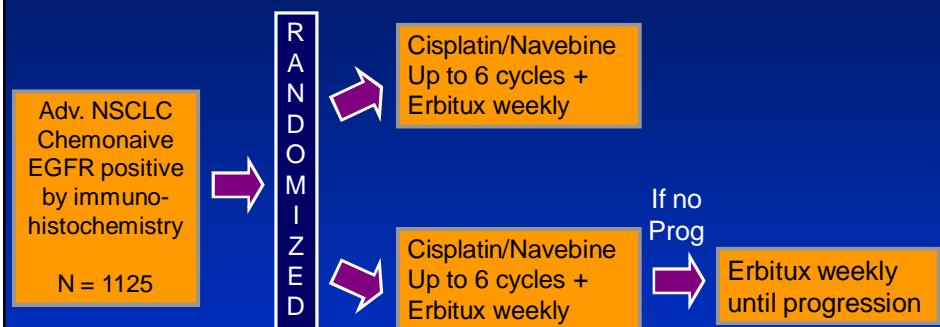
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Does KRAS mutation status, or another molecular marker, correlate with outcomes on anti-EGFR monoclonal antibody therapy?



## FLEX Trial: First Line Chemo +/- Erbitux (Cetuximab) in EGFR-Expressing NSCLC



Primary Endpoint: Overall Survival



Pirker, Lancet 2009

## KRAS Mutations: Lung Cancer vs CRC

KRAS mutations predict benefit to EGFR inhibitors in colon cancer, but not NSCLC

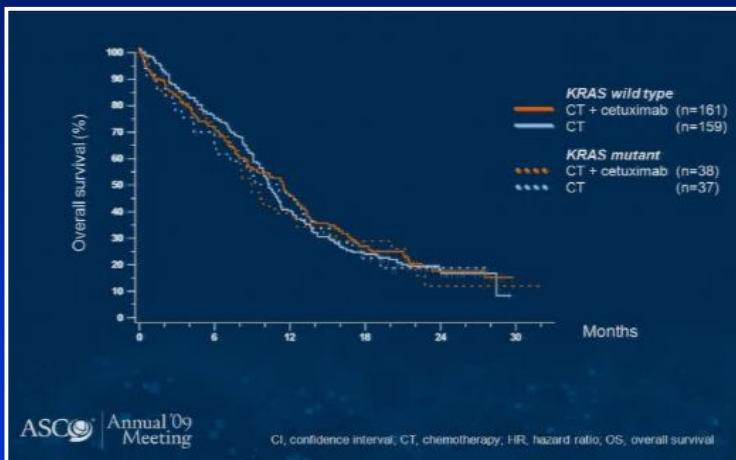
Trial	Regimen	N	PFS		ORR	
			Wild Type	Mutant	Wild Type	Mutant
<b>Colo-rectal Cancer</b>						
CRYSTAL	FOLFIRI + Cetuximab	277	9.9 mos*	7.6 mos*	59%	36%
OPUS	FOLFOX4 + Cetuximab	168	7.7 mos*	5.5 mos*	61%	33%
Amado, 2008	Panitumumab	208	2.9 mos*	1.7 mos*	17%	0%
<b>NSCLC</b>			<b>OS</b>		<b>ORR</b>	
BMS-099	Taxane/Cb + Cetuximab	202	9.7 mos	16.8 mos	33%	31%
INTEREST	Gefitinib	114	7.5 mos	7.8 mos	10%	0%
BR.21	Erlotinib	206	7.5 mos	3.7 mos	10%	5%

\*Statistically significant.



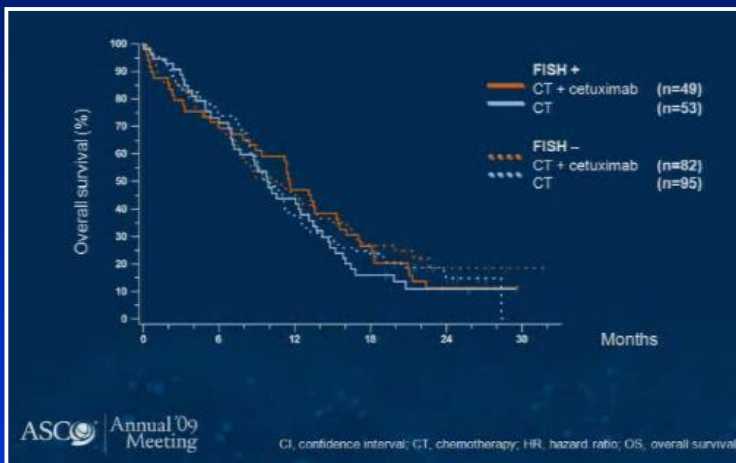
Van Cutsem. ASCO. 2008 (abstr 2); Bokemeyer. ASCO. 2008 (abstr 4000); Amado. *J Clin Oncol.* 2008;26:1626; Douillard. ASCO. 2008 (abstr 8001); Zhu. *J Clin Oncol.* 2008;26:4268; Khambata-Ford. 2008 Chicago Multidisciplinary Symposium in Thoracic Oncology.

## FLEX Trial: KRAS Mutation Status and Overall Survival



O'Byrne, ASCO 2009

## FLEX Trial: EGFR Gene Amplification by FISH Testing and Overall Survival



O'Byrne, ASCO 2009

Is there a value in testing for  
molecular markers in anyone  
who has already received first  
line treatment for advanced  
NSCLC?

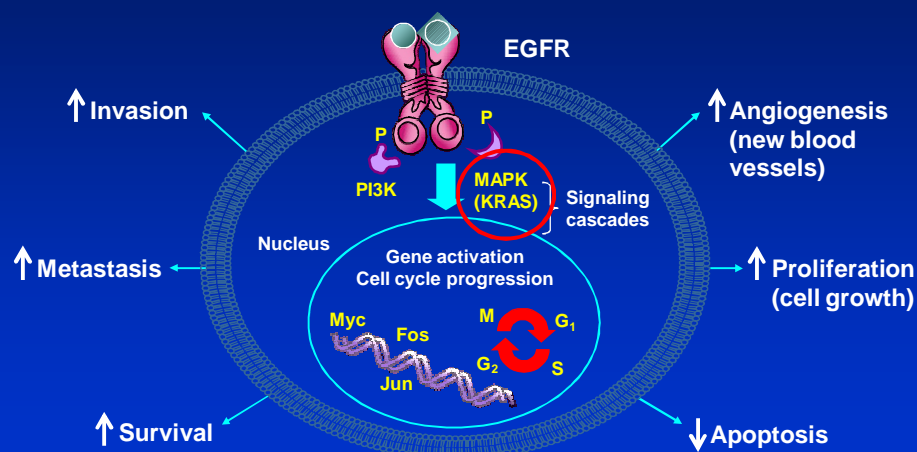


How will more individualized,  
molecularly defined treatment  
plans for patients with advanced  
NSCLC affect designs for clinical  
trials in this setting?



Are there treatments still early in development looking promising in combination with selection of the right patient population by molecular markers?

As RAS is downstream of EGFR, activating RAS mutations take EGFR "out of the loop"



How are anti-angiogenic inhibitors sorafenib and sunitinib looking in lung cancer, and are there molecular markers associated with clinical benefit with this class?



Are there treatments still early in development looking promising in combination with selection of the right patient population by molecular markers?



Can patients who are shown to **not** have an EGFR mutation early on develop one later on in their clinical course?



What is the value in doing EGFR mutation, ALK rearrangement, or other molecular marker testing in patients relatively unlikely to have the marker?



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