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**HOW CAN WE UNDERSTAND
AND DEFINE RE-CHALLENGE IN THE
TREATMENT OF METASTATIC COLORECTAL
CANCER?**

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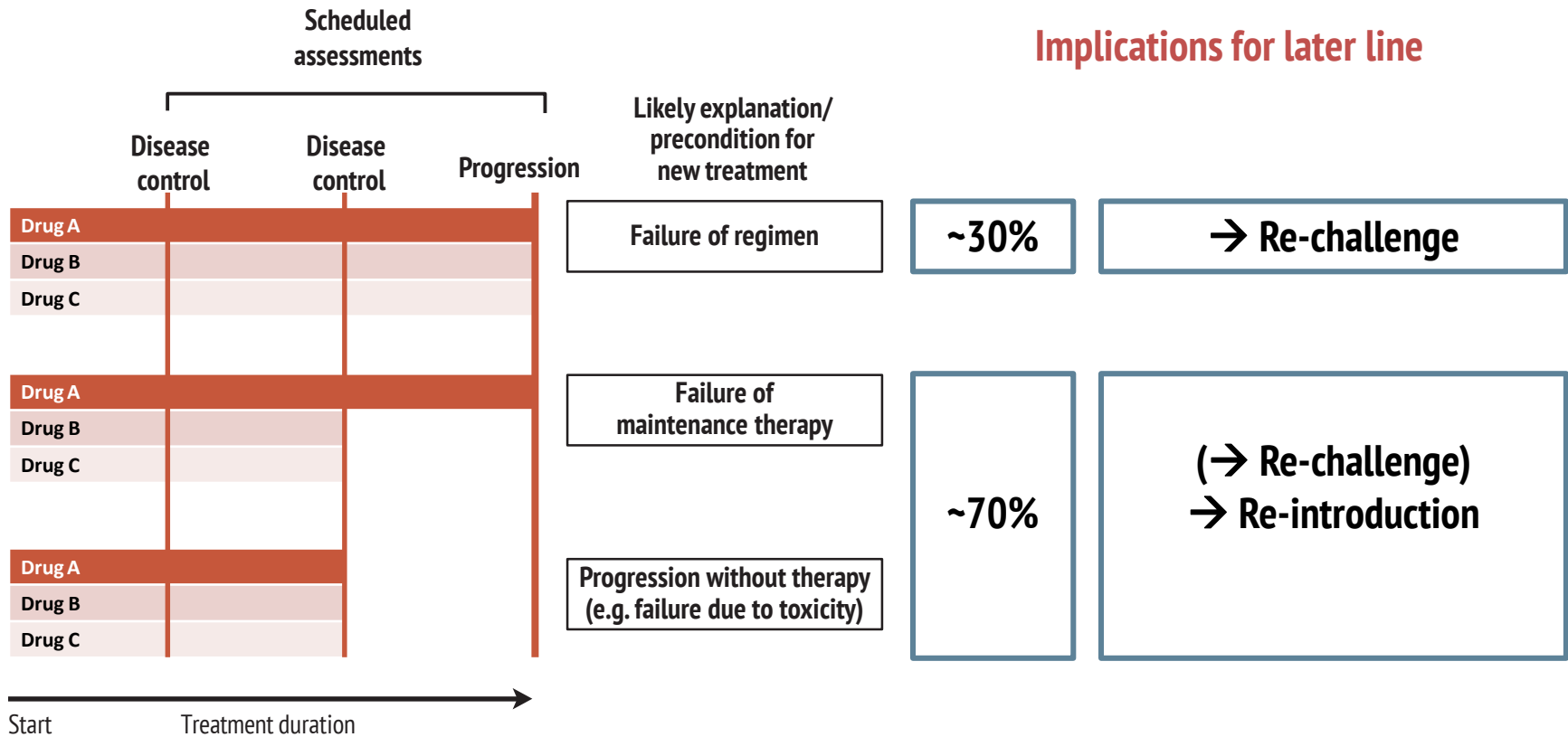
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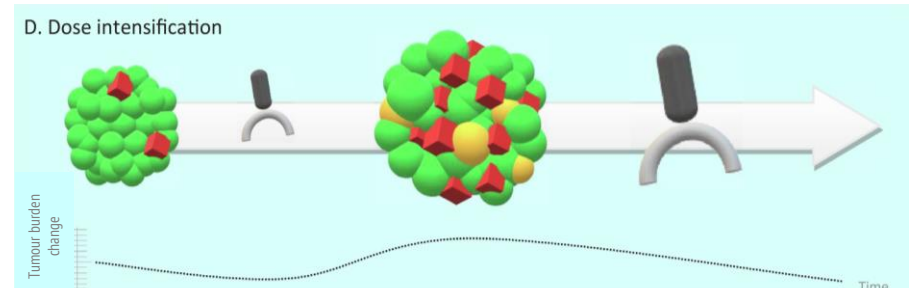
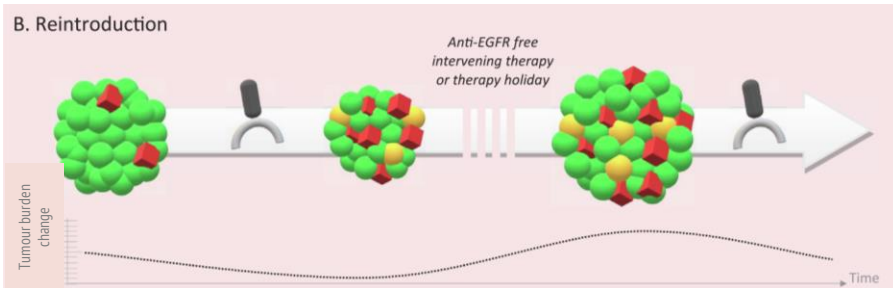
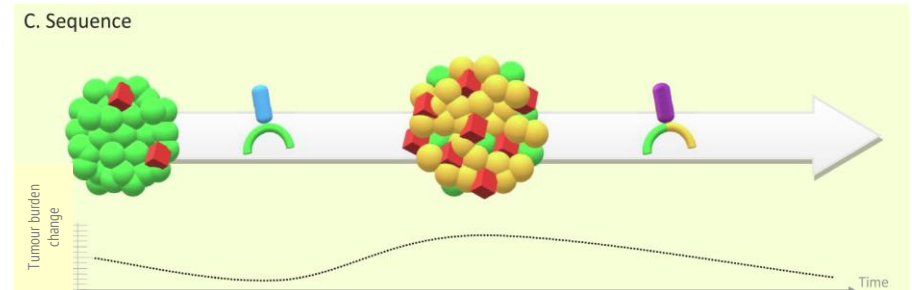
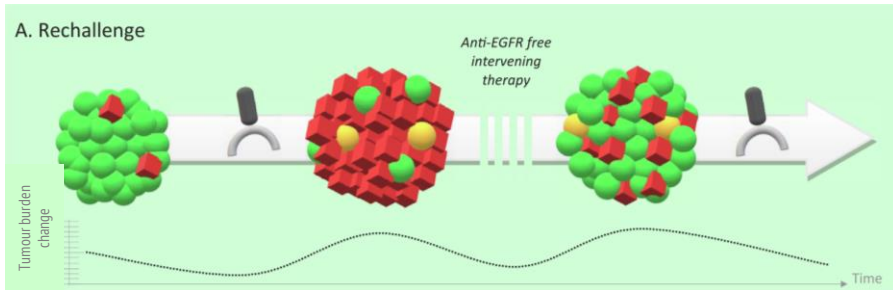
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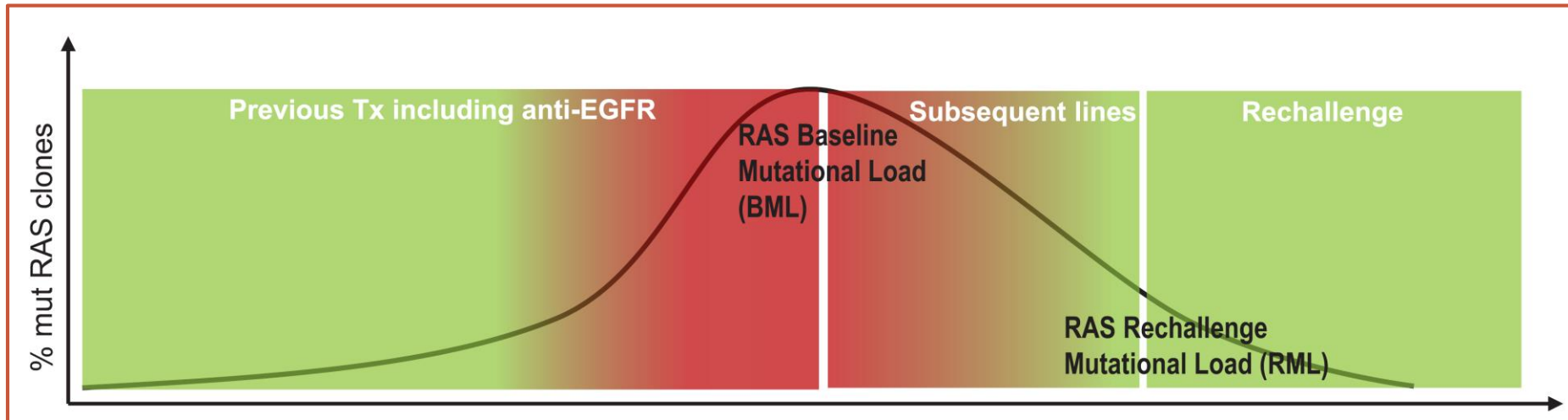
CLINICAL UNDERSTANDING OF RE-TREATMENT



MOLECULAR UNDERSTANDING OF RE-TREATMENT



MOLECULAR RATIONAL OF RE-CHALLENGE



BML, baseline mutational load; EGFR, epidermal growth factor receptor; mut, mutant; RAS, retrovirus-associated DNA sequences; RML, rechallenge mutational load; Tx, treatment

Mauri G et al. Cancer Treat Rev 2019; 73:41-53

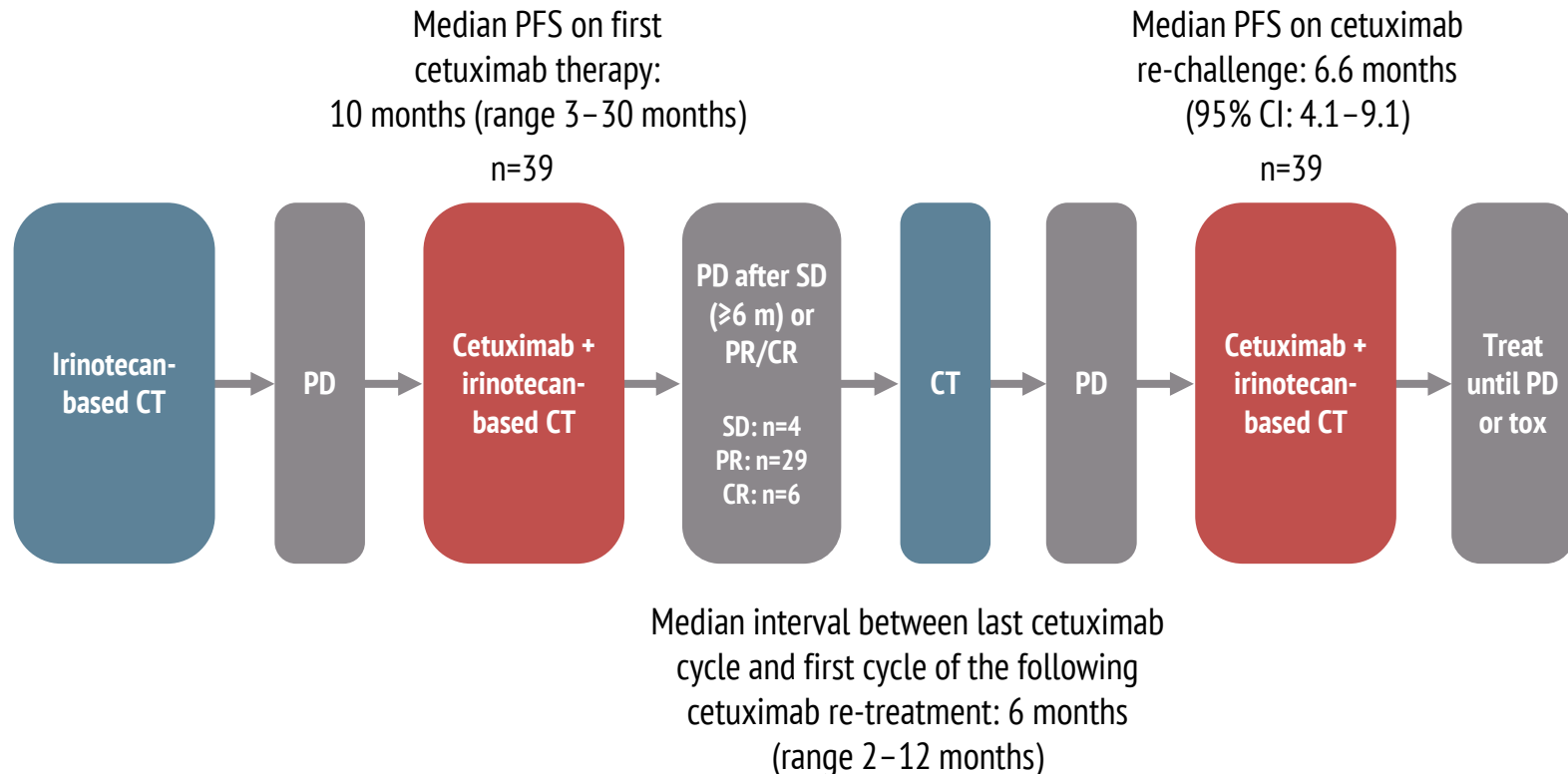
CONCORDANCE BETWEEN TUMOUR TISSUE ASSESSMENT AND ctDNA-ANALYSIS (N=95)

		Tissue analysis					
Accuracy	KRAS	Mutant	WT	Sensitivity	Specificity	Accuracy	
cfDNA - Analysis	Mutant	36	1	92%	98%	96%	
	WT	3	55				
	total	39	56				
		BRAF	Mutant	WT	Sensitivity	Specificity	Accuracy
cfDNA - Analysis	Mutant	5	0	100%	100%	100%	
	WT	0	90				
	total	5	90				
		All Mutations	Mutant	WT	Sensitivity	Specificity	Accuracy
cfDNA - Analysis	Mutant	41	1	93%	98%	96%	
	WT	3	50				
	total	44	51				

cfDNA, circulating free DNA; ctDNA, circulating tumour DNA; WT, wild type

CLINICAL EVIDENCE

PFS AFTER CETUXIMAB TREATMENT AND RE-CHALLENGE: STUDY DESIGN

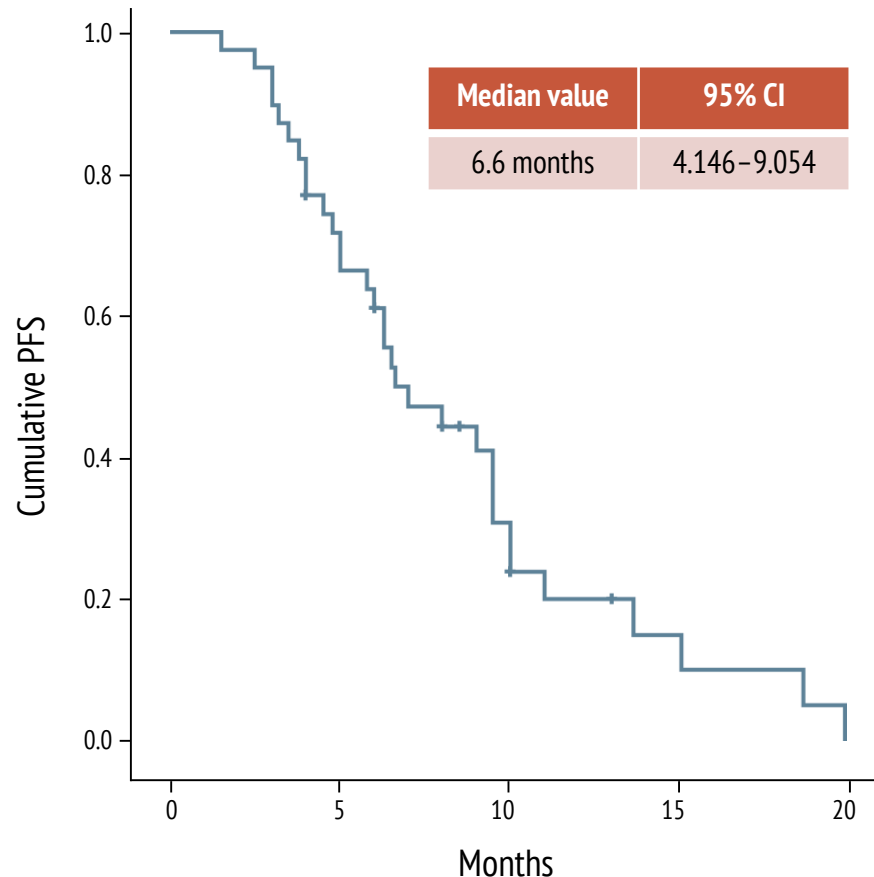


Median number of therapy lines before cetuximab re-challenge: 4 (range 3–7)

RE-CHALLENGE WITH CETUXIMAB: KEY RESULTS

Clinical response after 1st cetuximab-based therapy and 2nd cetuximab-based therapy in 39 patients

Best response 1 st cetuximab	Best response rechallenge	No. of patients	Total no. (%)
PR	CR	1	2 (5)
CR		1	
SD	PR	1	19 (49)
PR		14	
CR		4	
SD	SD	3	14 (36)
PR		10	
CR		1	
PR	PD	4	4 (10)

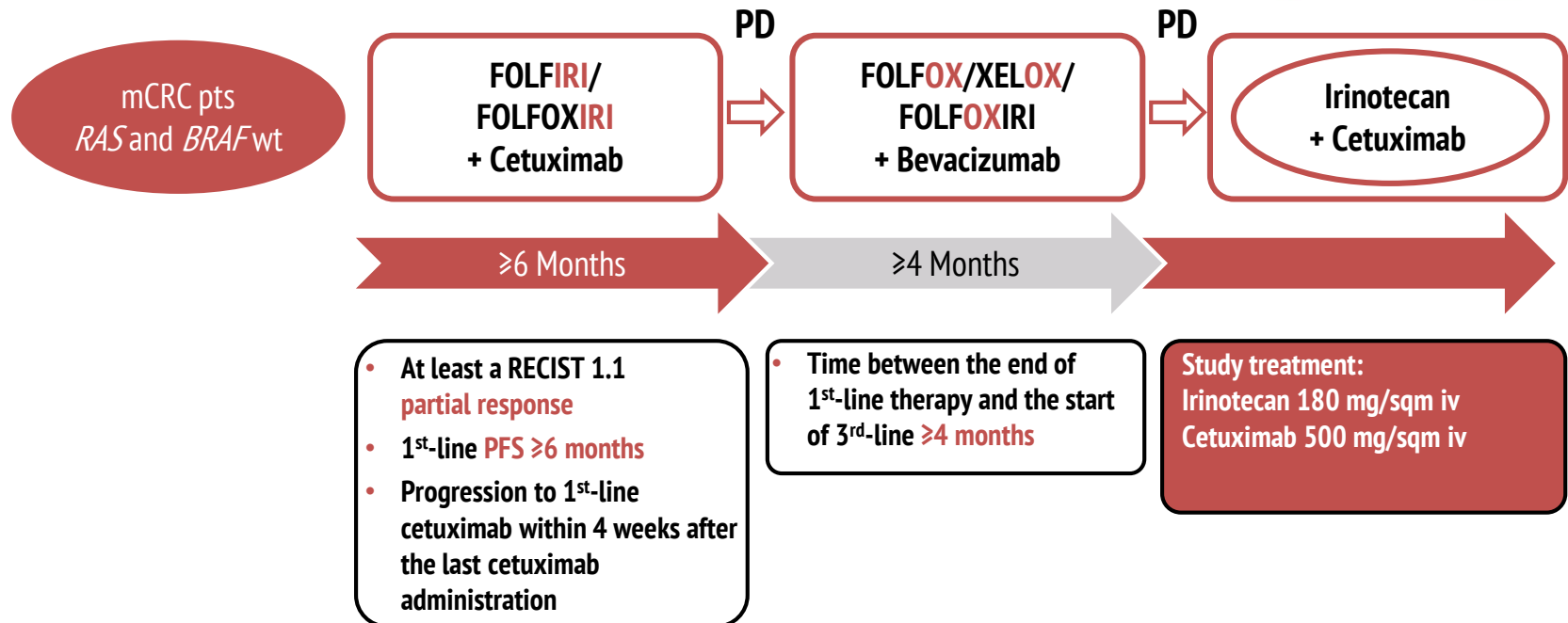


CI, confidence interval; CR, complete response; PD, progression of disease; PFS, progression-free survival; PR, partial response; SD, stable disease; tox, toxicity

PHASE II NON-COMPARATIVE CRICKET STUDY: STUDY DESIGN

Phase II non-comparative study
Target accrual: 27 pts

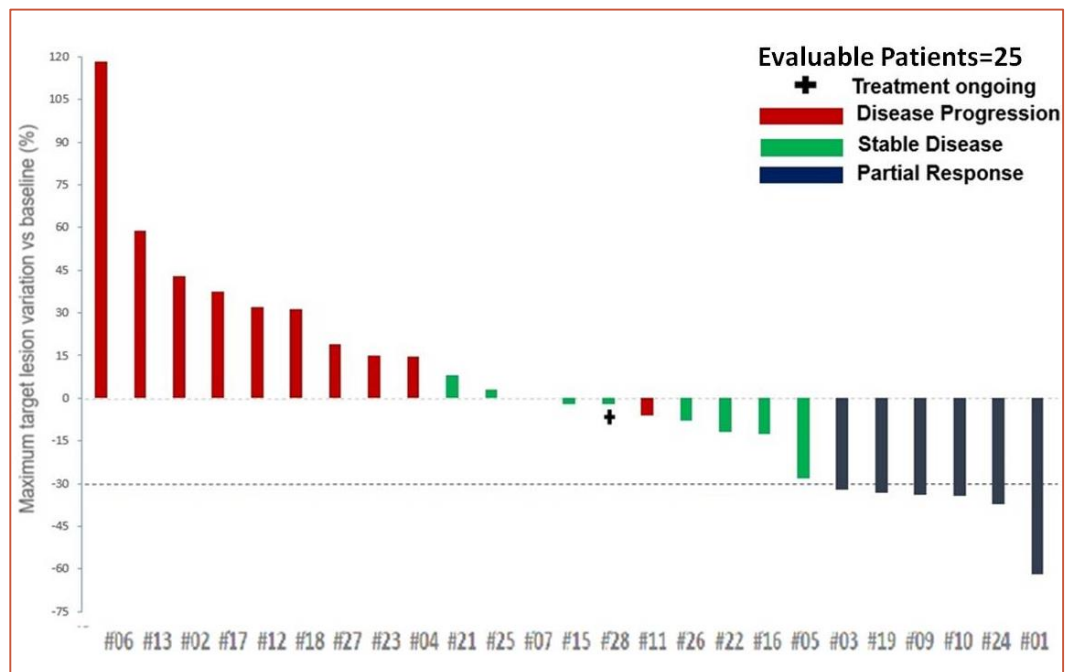
CRICKET



Cetuximab was administered every 2 weeks, which is an off-label regimen

PHASE II NON-COMPARATIVE CRICKET STUDY: BEST RESPONSE

	Study population N=28 No (%) [95% CI]
Partial response	6 (21.5%)
• Confirmed partial response	4 (14.3%)
• Unconfirmed partial response	2 (7.1%)
Stable disease	9 (32.1%)
Progressive disease	13 (46.4%)
• Radiological PD	10 (35.7%)
• Clinical PD	3 (10.7%)
Response rate	6 (21.5%) [10-40%]
Disease control rate	15 (53.6%) [36-70%]



CI, confidence interval; PD, progression of disease

Presented By Daniele Rossini at 2018 ASCO Annual Meeting

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