The Evolving Role of Systemic Treatment in Advanced NSCLC

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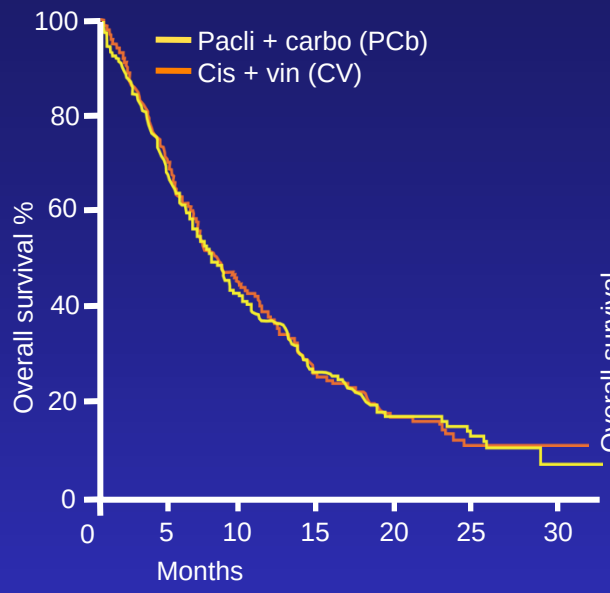
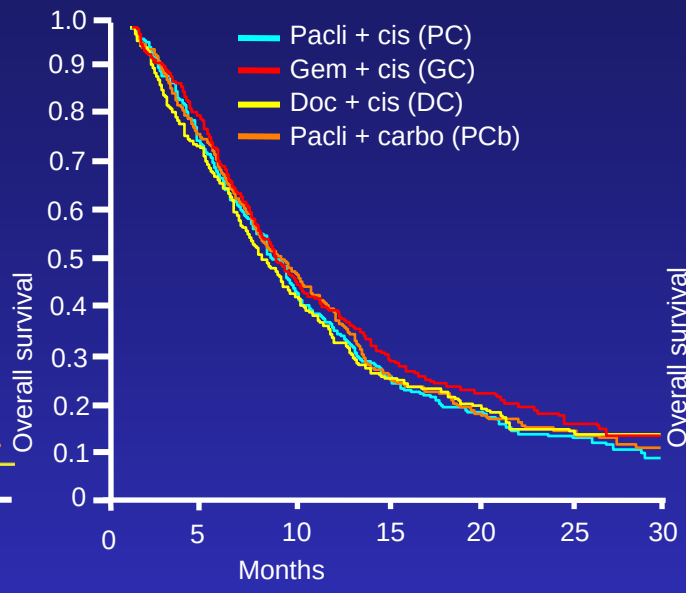
DNA instability

Immune privilege

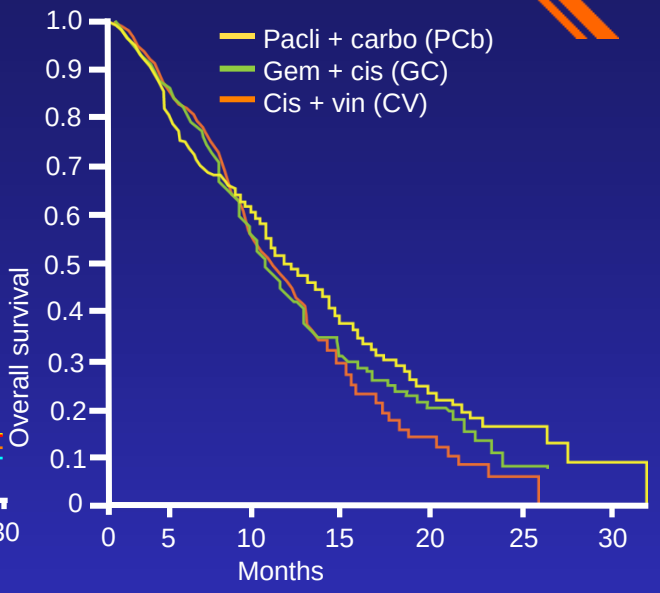
1st-line platinum-based CT: Efficacy plateau



Study arm	OS (mo)	1 year (%)
PCb	8.6	38
CV	8.1	36



Study arm	OS (mo)	1 year (%)
PC	7.8	31
GC	8.1	36
DC	7.4	31
PCb	8.1	34



Study arm	OS (mo)	1 year (%)
PCb	9.9	43
GC	9.8	37
CV	9.5	37

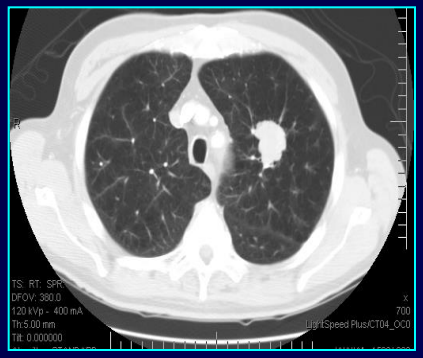
OS, overall survival

Kelly et al. JCO 2001; Schiller et al. NEJM2002; Scagliotti et al. JCO 2002

NSCLC is a Heterogeneous Disease

NSCLC

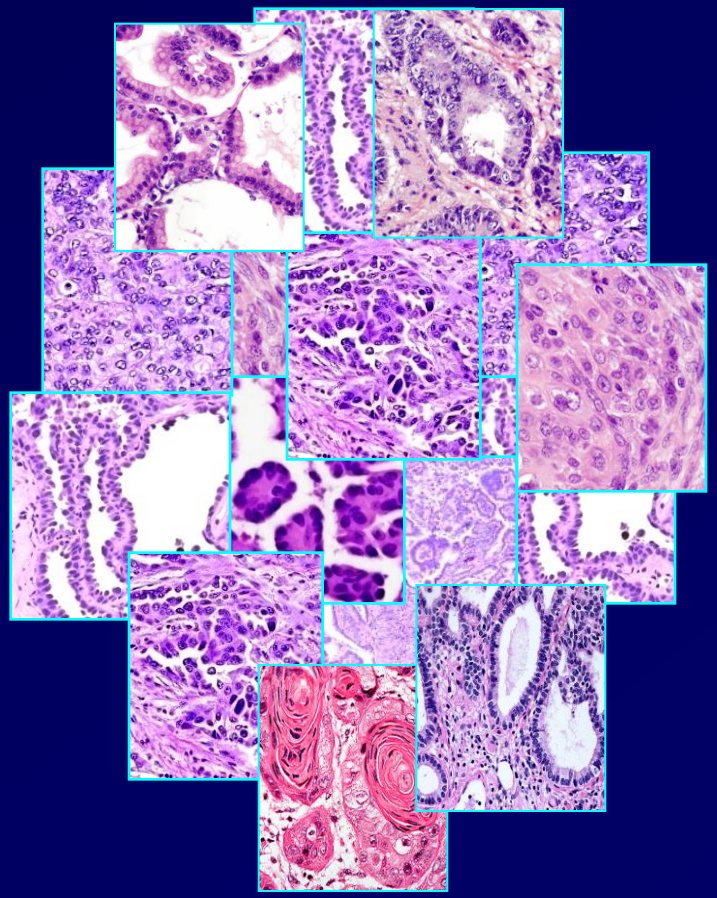
CT



Pathology Specimens

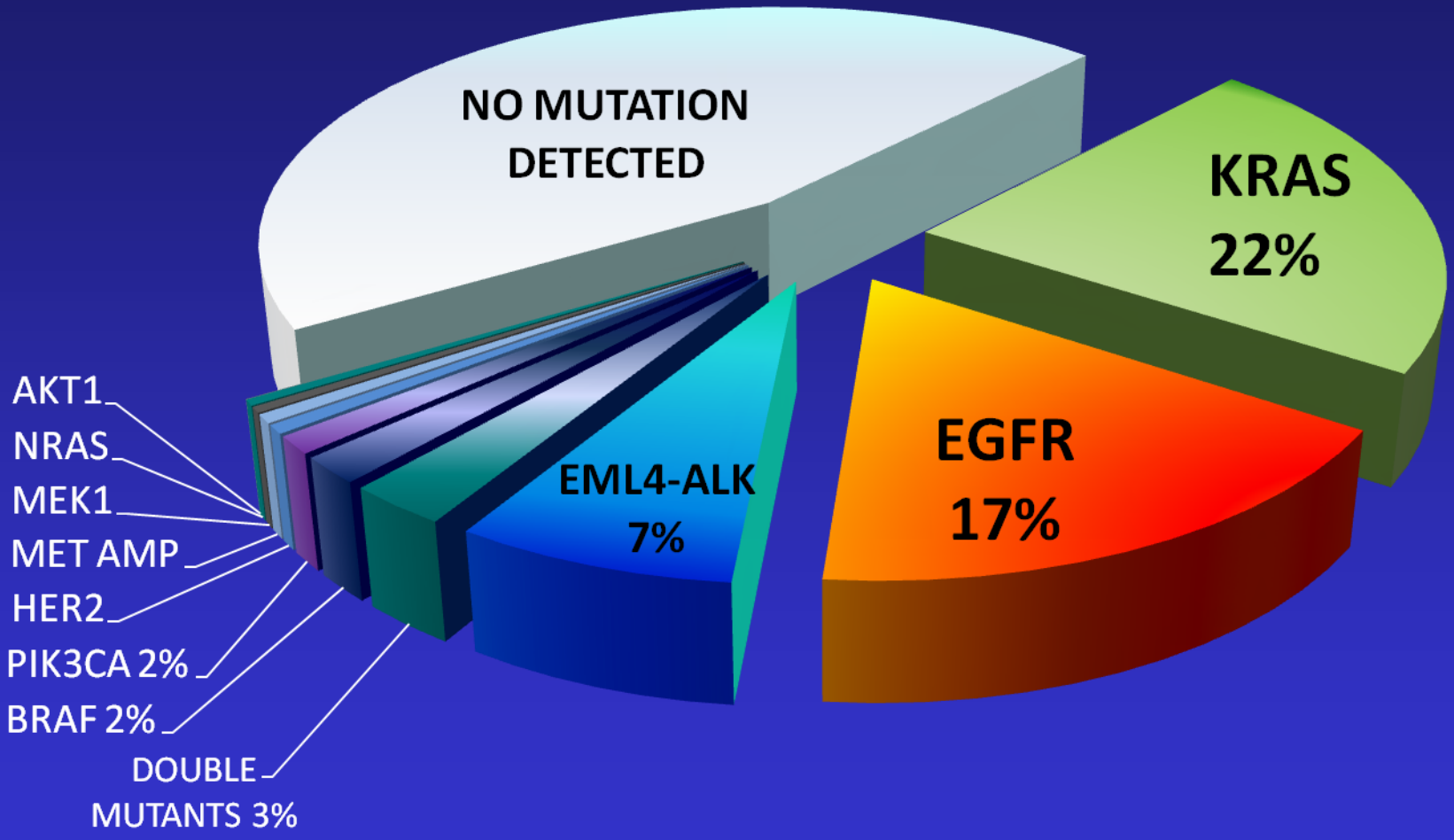
Not All Tumors are the Same

Histopathology



Lung Cancer Mutation Consortium

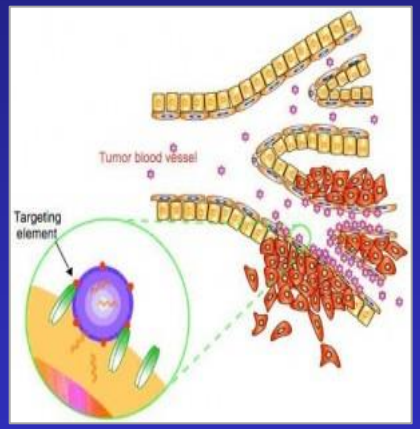
Incidence of Mutations Detected



Kris et al. ASCO 2011, Abstract 7506

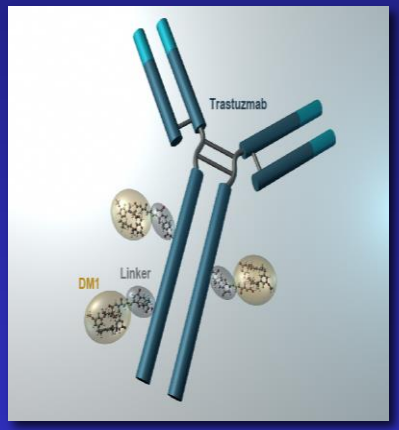
How Does This Enable Personalized Medicine?

Right Target



Genetic validation; Rare phenotypes

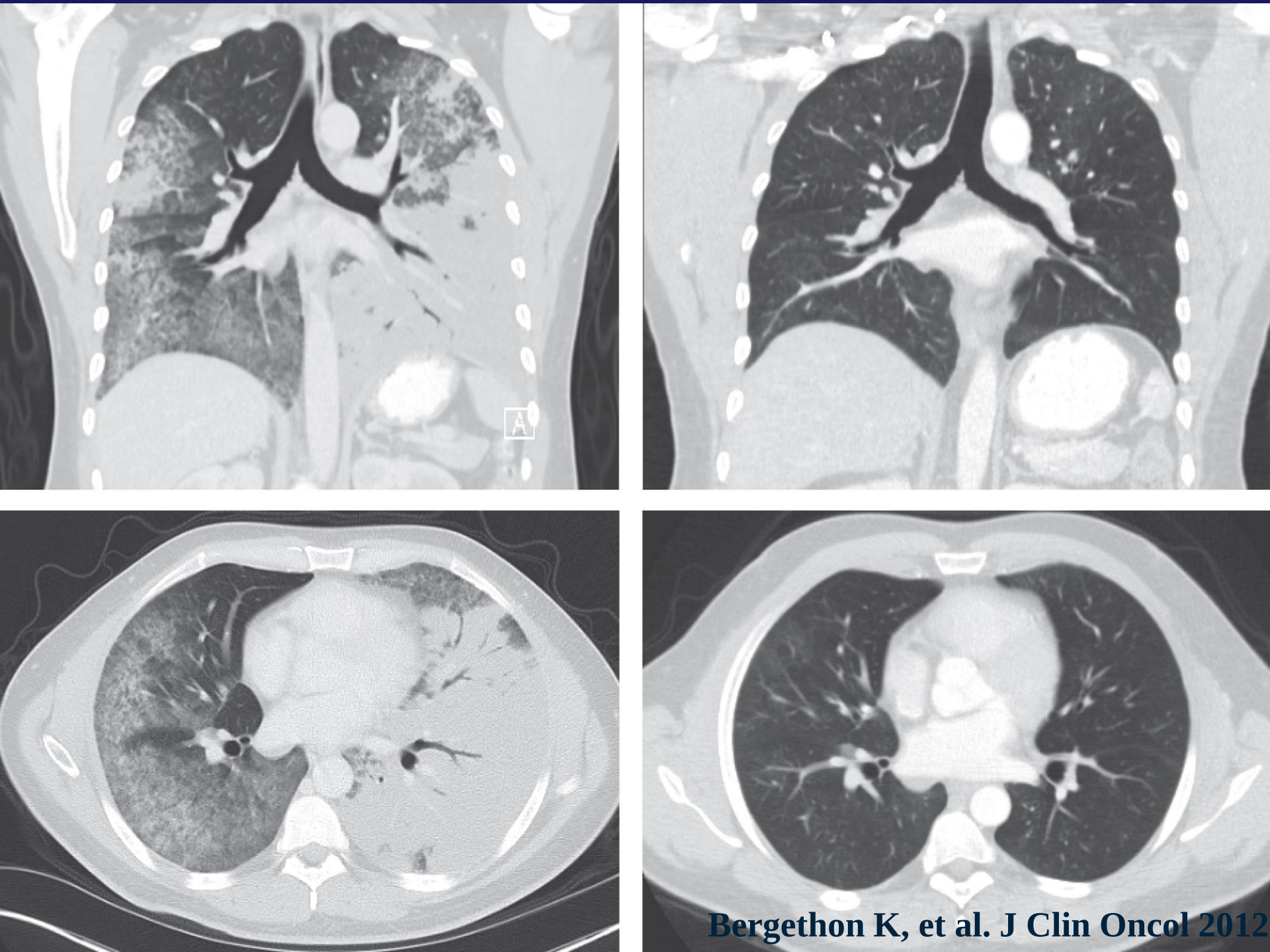
Right Drug (or Combinations)



Selective design and delivery; Combinations for complex diseases

Right Patient

Phenotyping and genotyping

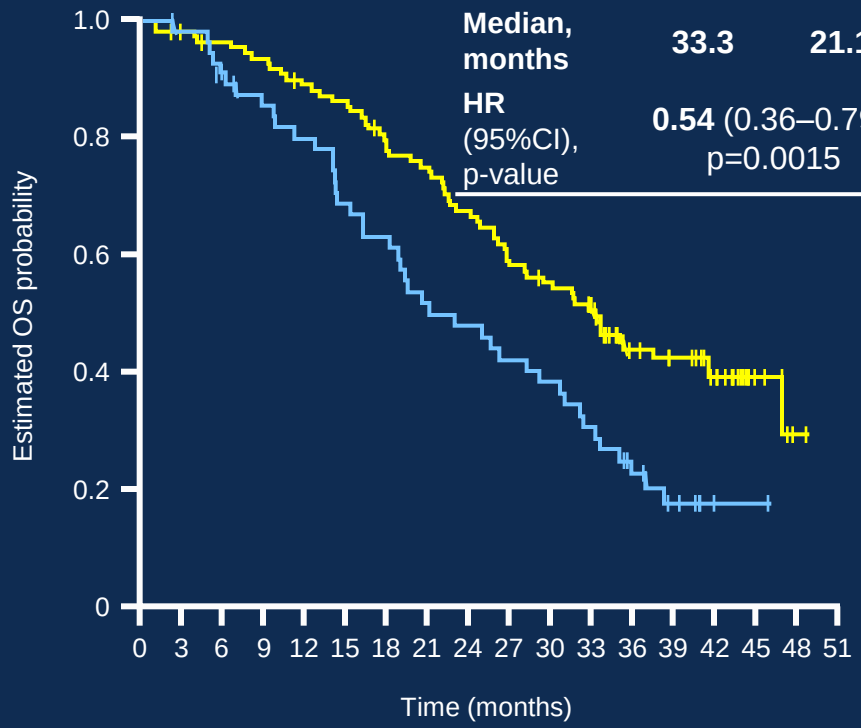


Bergethon K, et al. J Clin Oncol 2012

OS in Del19 subgroup

LUX-Lung 3

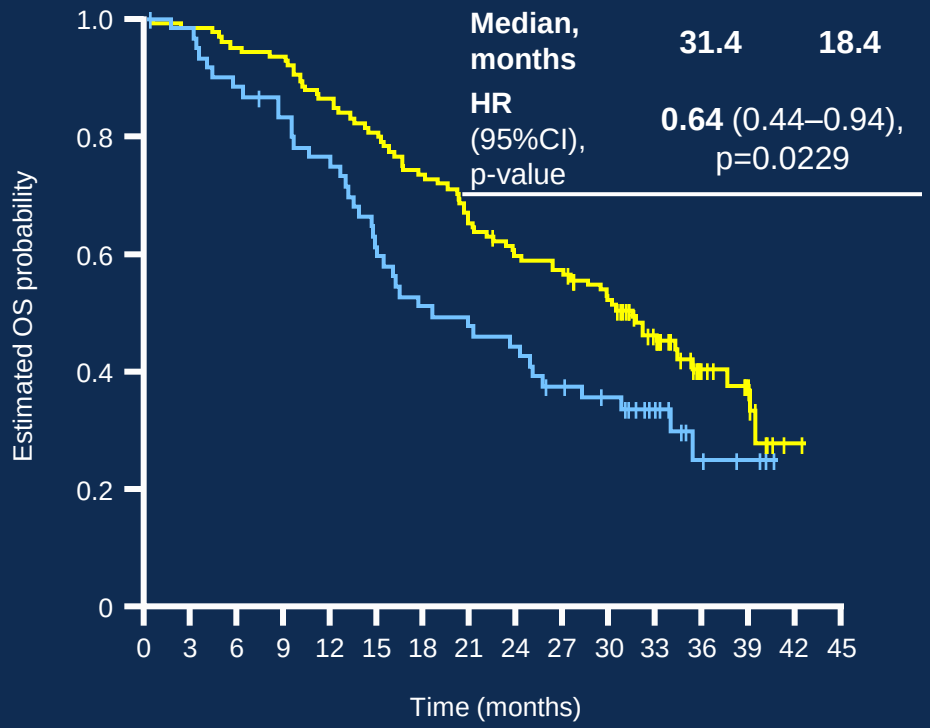
	Afatinib n=112	Pem/Cis n=57
Median, months	33.3	21.1
HR (95%CI), p-value	**0.54** (0.36–0.79), p=0.0015	



No of patients																	
Afatinib	112	108	105	102	96	93	83	80	72	62	58	51	34	30	21	6	1	0
Pem/Cis	57	55	50	46	43	37	33	27	25	22	20	16	10	6	1	1	0	0

LUX-Lung 6

	Afatinib n=124	Gem/Cis n=62
Median, months	31.4	18.4
HR (95%CI), p-value	**0.64** (0.44–0.94), p=0.0229	



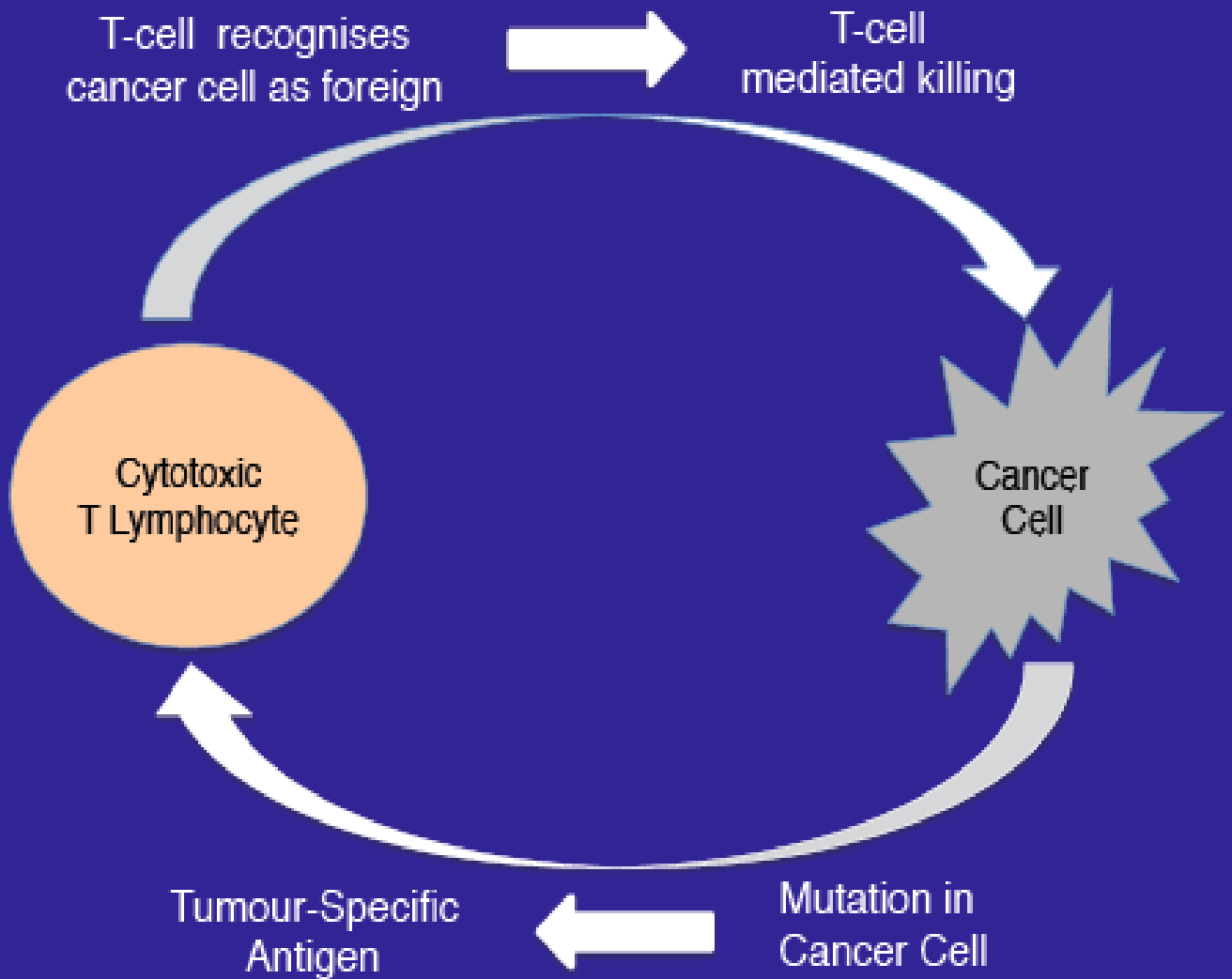
No of patients																
Afatinib	124	122	118	115	106	99	90	80	73	69	59	39	16	8	1	0
Gem/Cis	62	58	53	49	44	35	30	28	26	21	18	11	4	3	0	0

Updated Hallmarks of Cancer

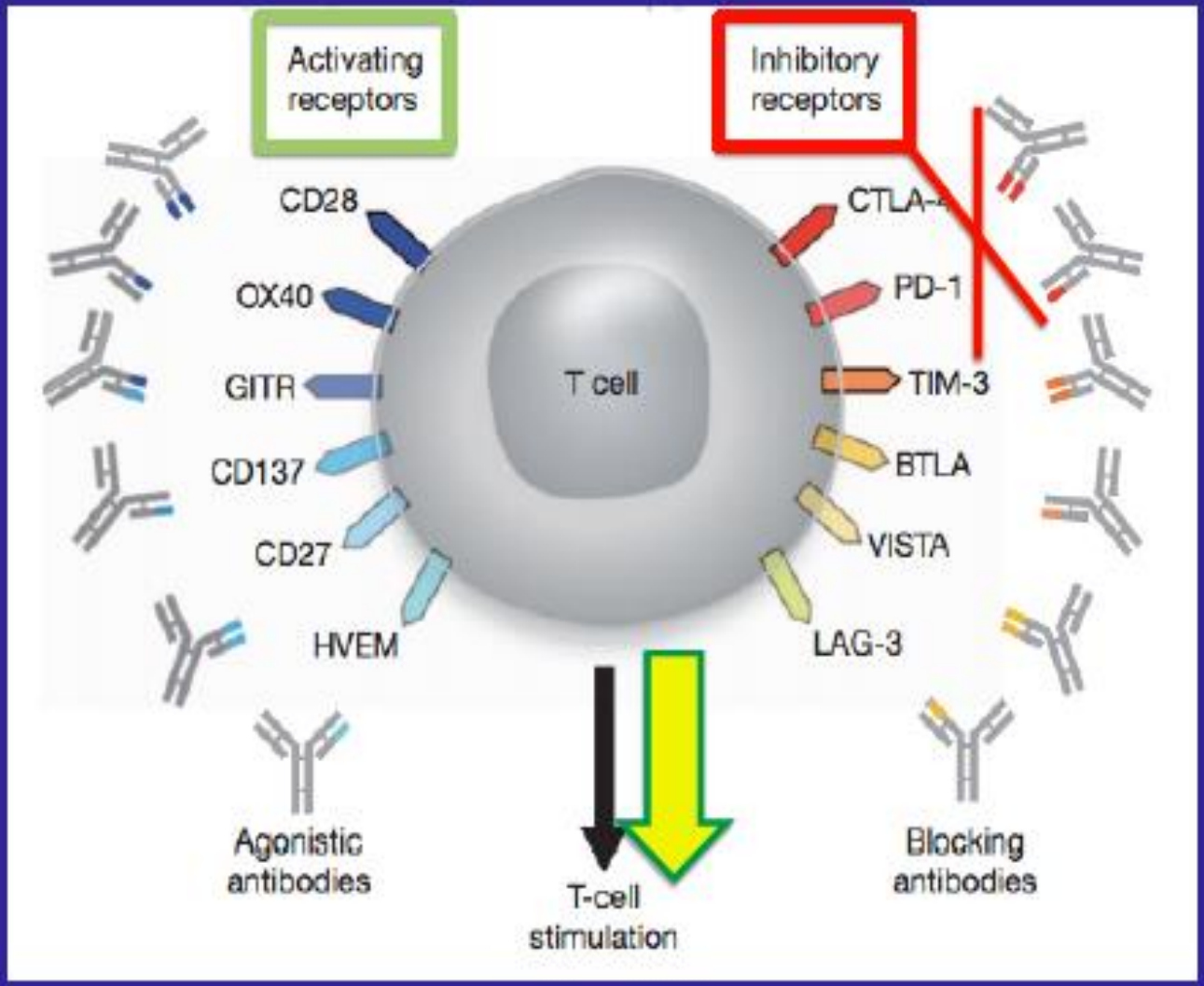
Evading Immune Attack

Hananhan & Weinberg, *Cell*, 2011

Cancer Immunology



Immune Checkpoints



Mellman et.al., *Nature*, 2011