

 #ECPUPDATES

Iniciativa científica de:



LUNG CANCER
UPDATES
ECP HIGHLIGHTS

7-11 DE SEPTIEMBRE 2019



Con la colaboración de:





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TMB como biomarcador. ¿Listo para su uso?

Federico Rojo

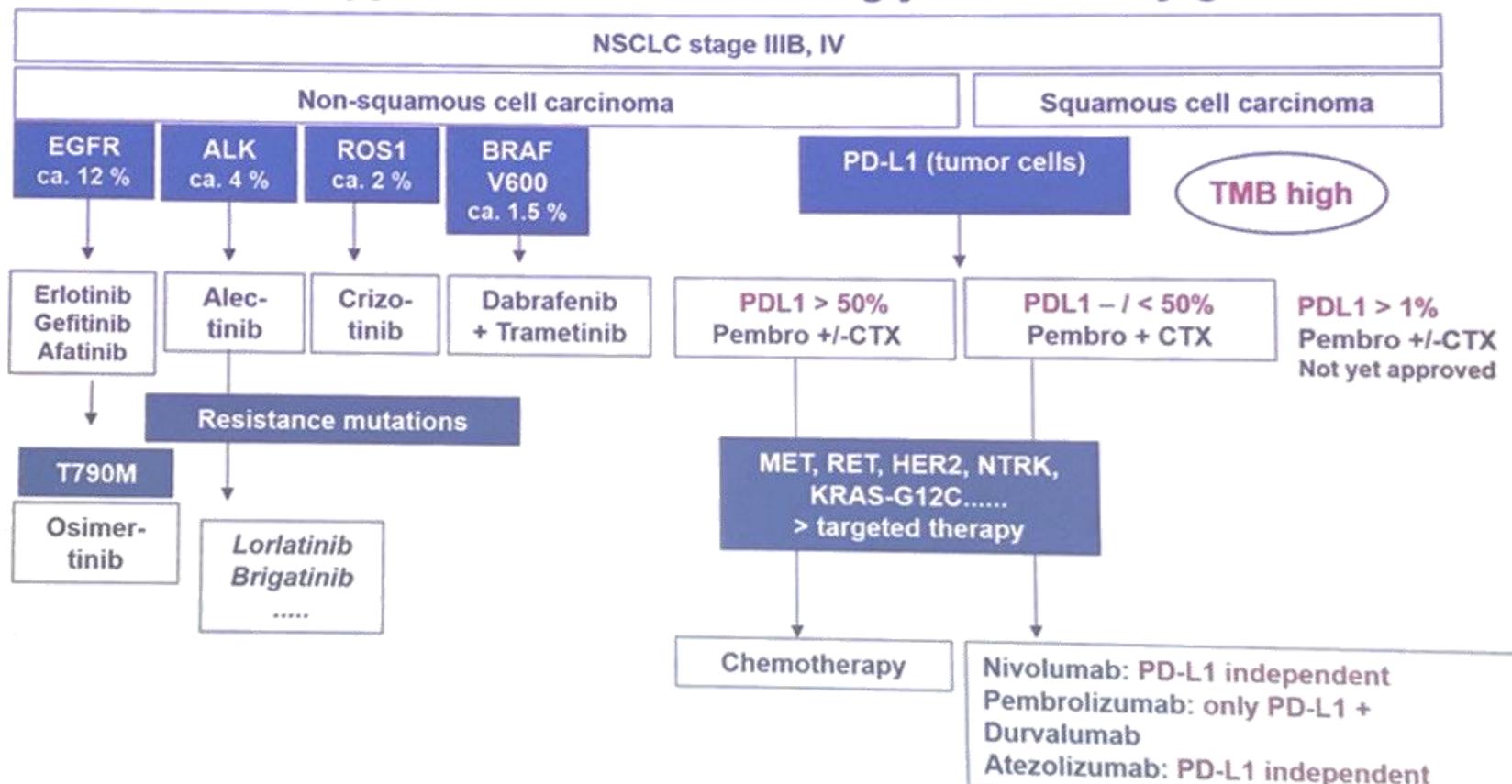
Con la colaboración de:



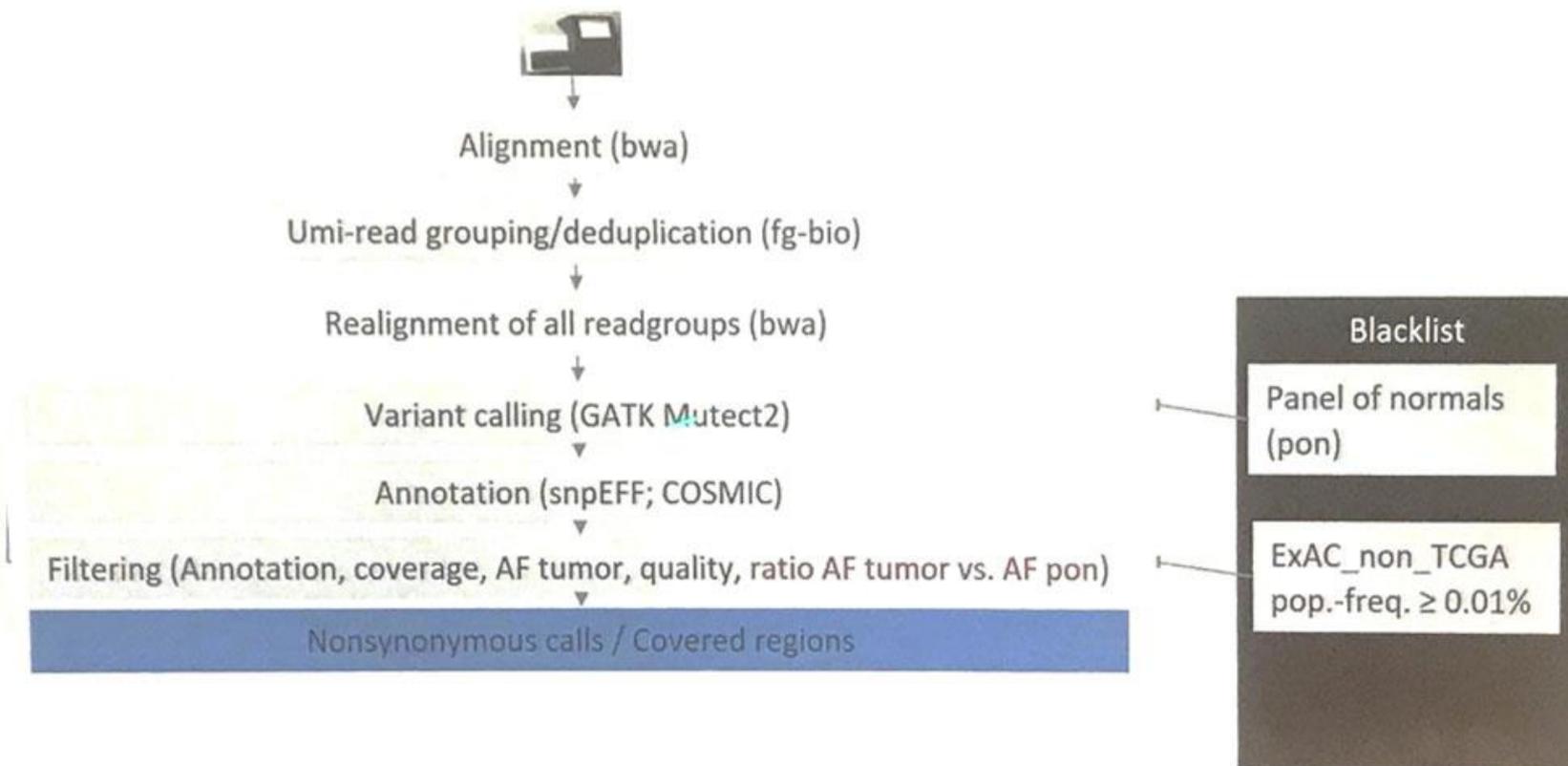
Panel testing or single gene testing: is there an optimal approach?

Reinhard Buettner. University Hospital and Center for Integrated Oncology, Cologne

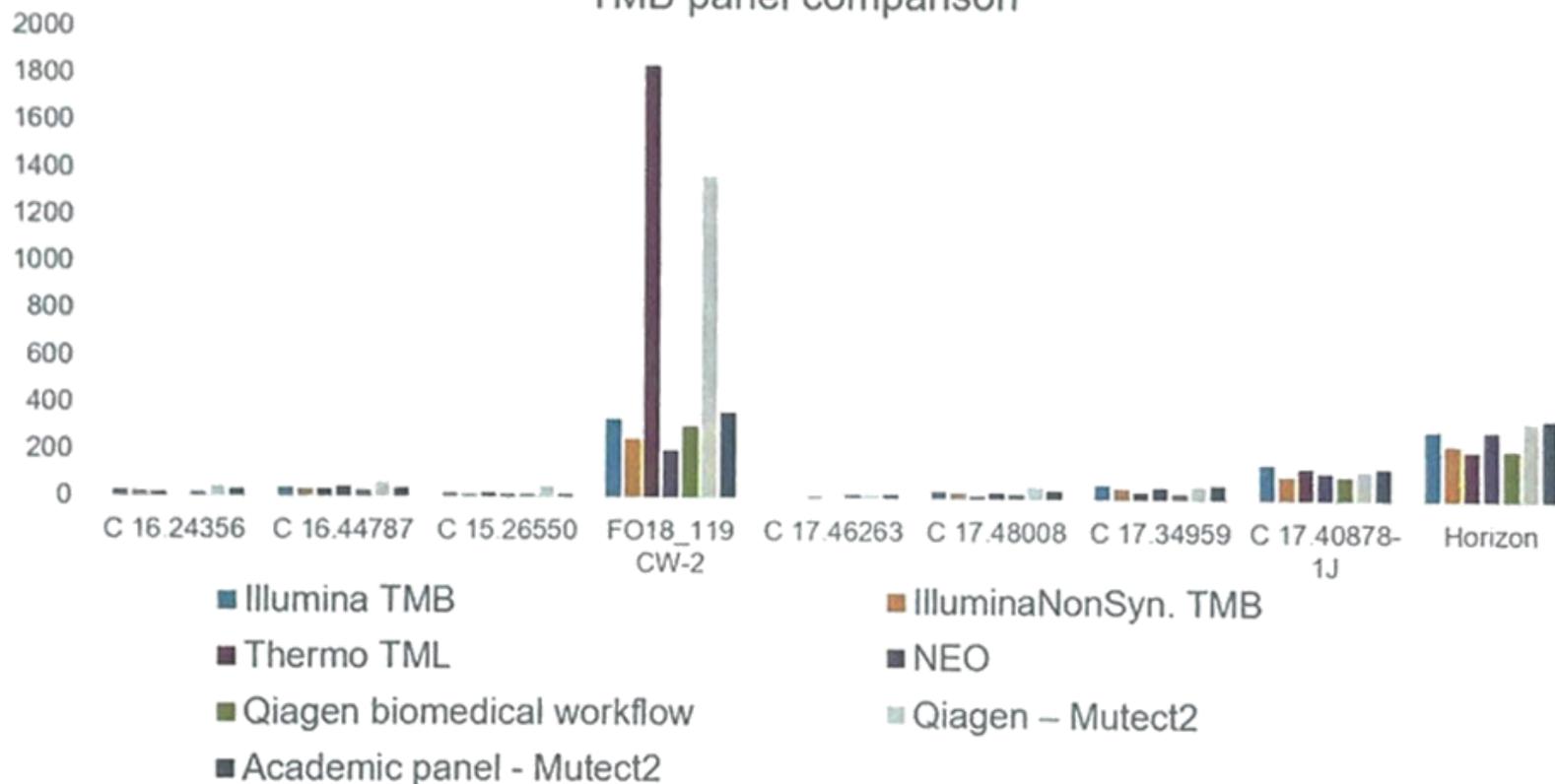
Systemic therapy of NSCLC is increasingly molecularly guided



Mutect2-Pipeline



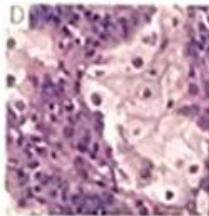
TMB panel comparison



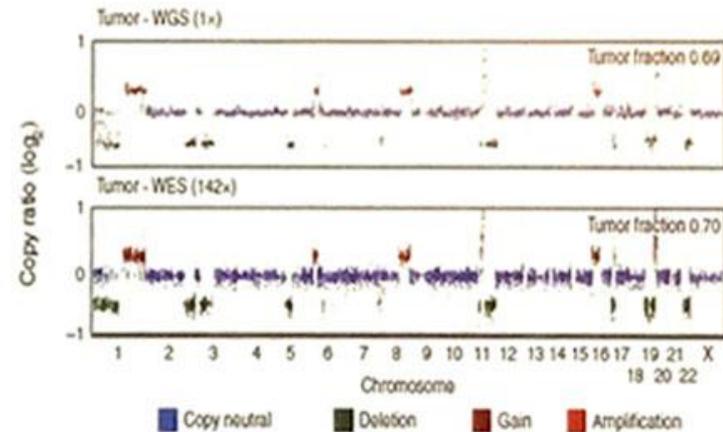
Are you prepared for routine TMB analysis in NSCLC?

Paul Hofman. Cote Azur University, Nice

Factors that impact TMB: Pre-analytical conditions



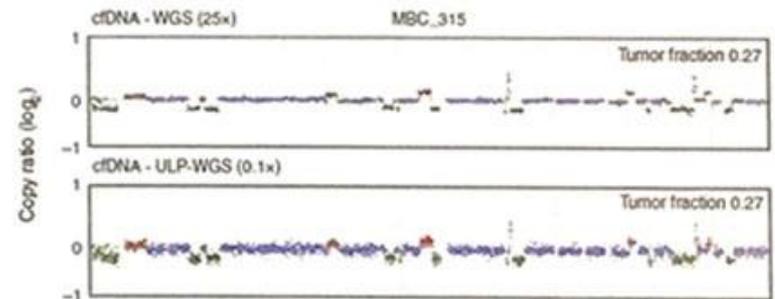
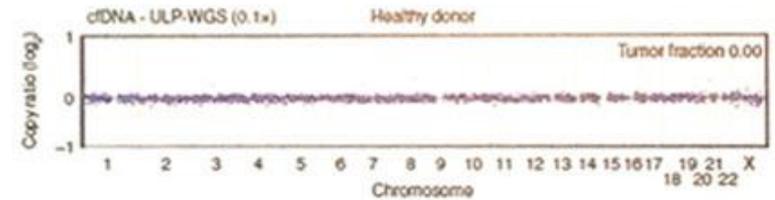
Sample type	FFPE samples may harbor artefactual deamination alterations that may impact mutation calling and TMB calculation
Tumor purity	Infiltration of tumor with immune or TME cells may impact TMB score (lower tumor purity is associated with reduced sensitivity)



Factors that impact TMB: Pre-analytical conditions



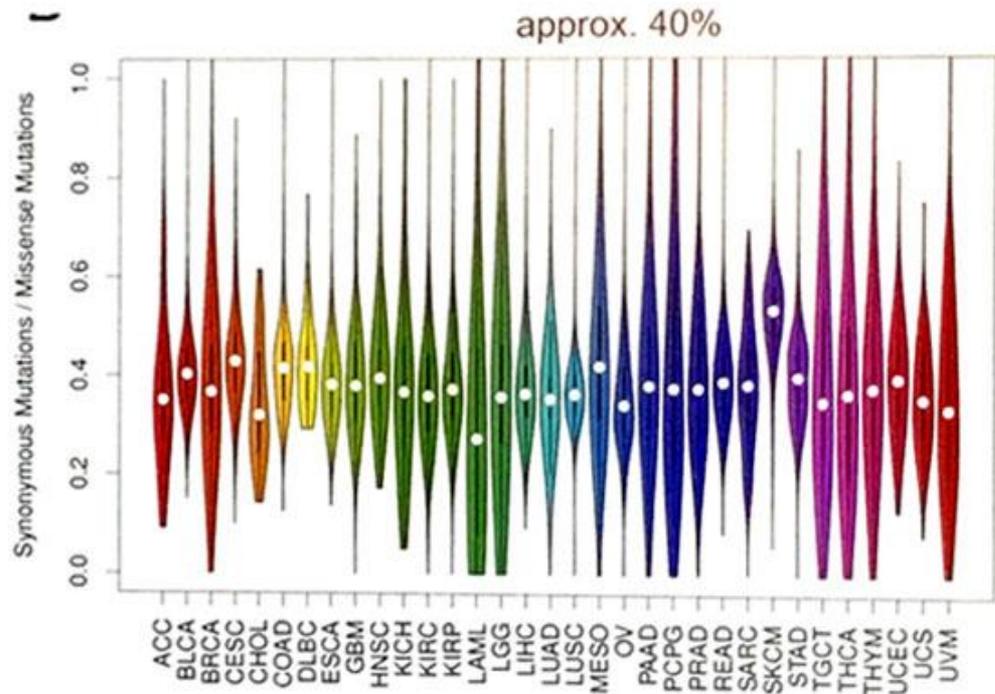
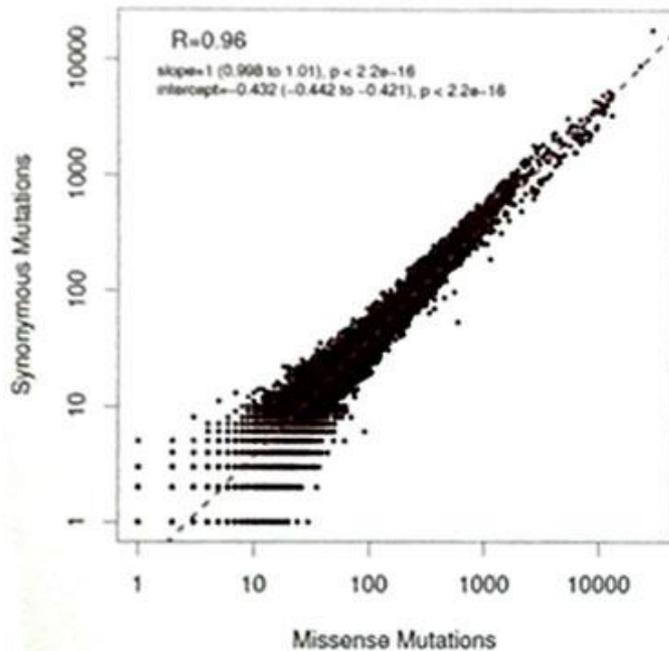
Sample type	<p>Low amount of ctDNA High amount of normal cfDNA ⇒ Evaluation of its % using CNA evaluation ⇒ Low ctDNA amount is associated with reduced sensitivity Small fragments (around 150pb)</p>
Immune cells	<p>Presence of immune cells Hematopoietic clonality</p>



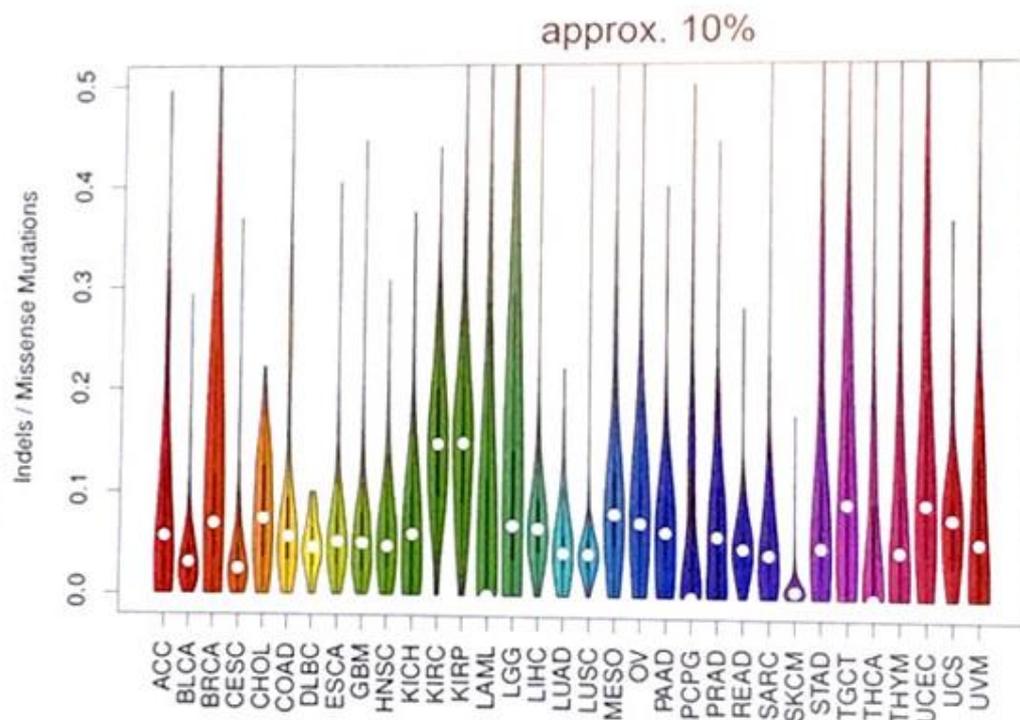
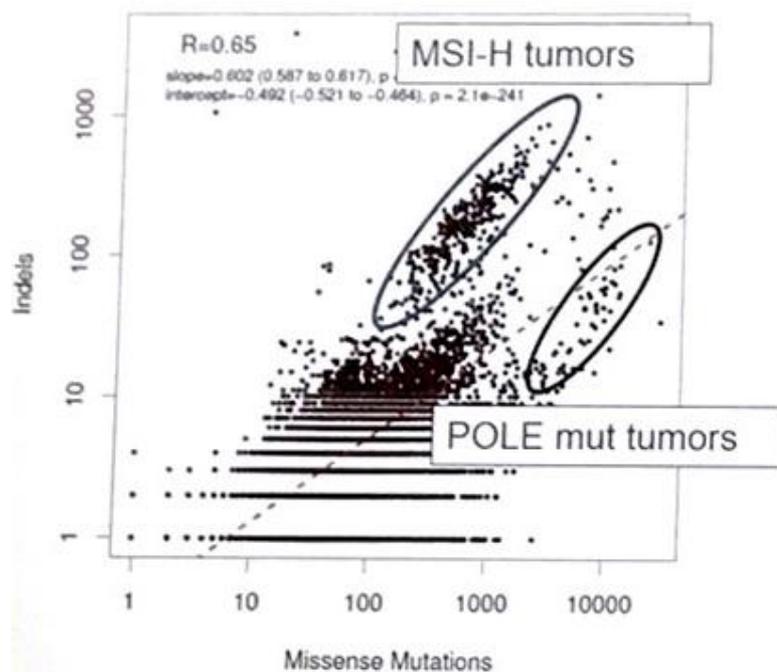
TMB standardisation and harmonisation: recommendations for consistent TMB assessment across assays and centres

Albrecht Stenzinger, Insitute of Pathology Heidelberg

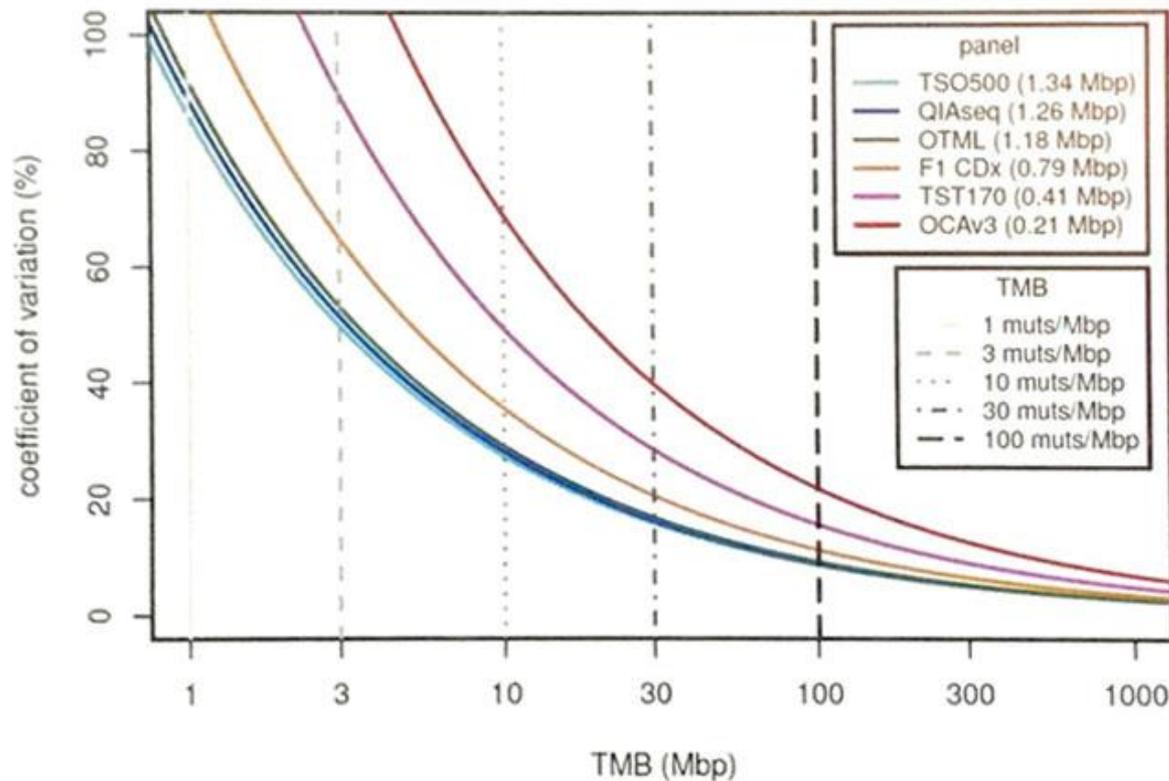
Synonymous mutations vs. missense mutations



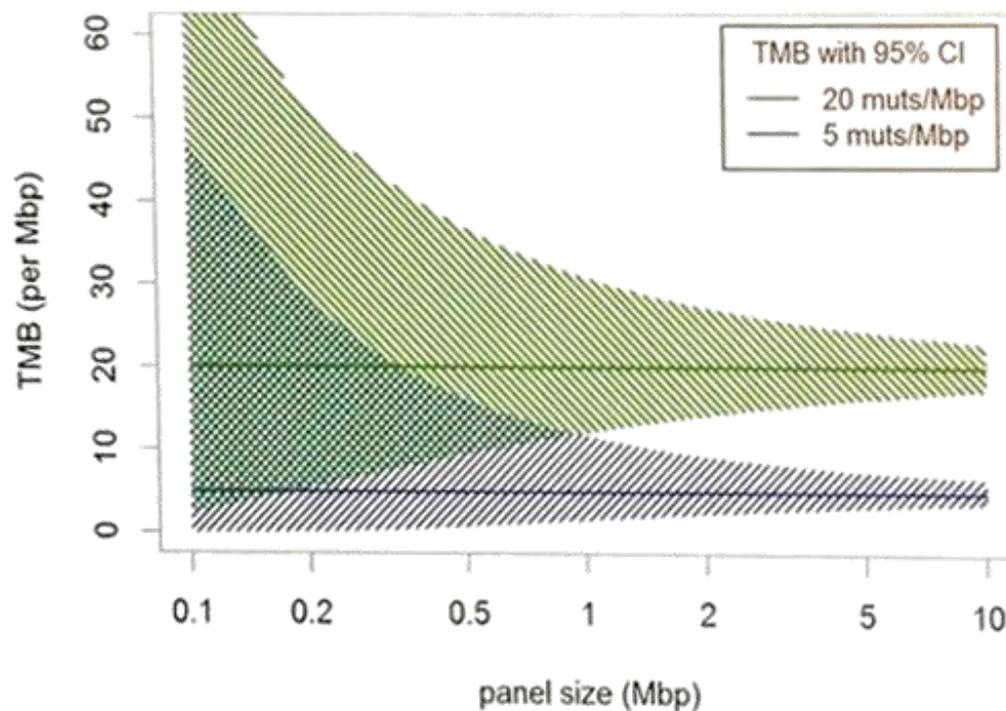
Indels vs. missense mutations



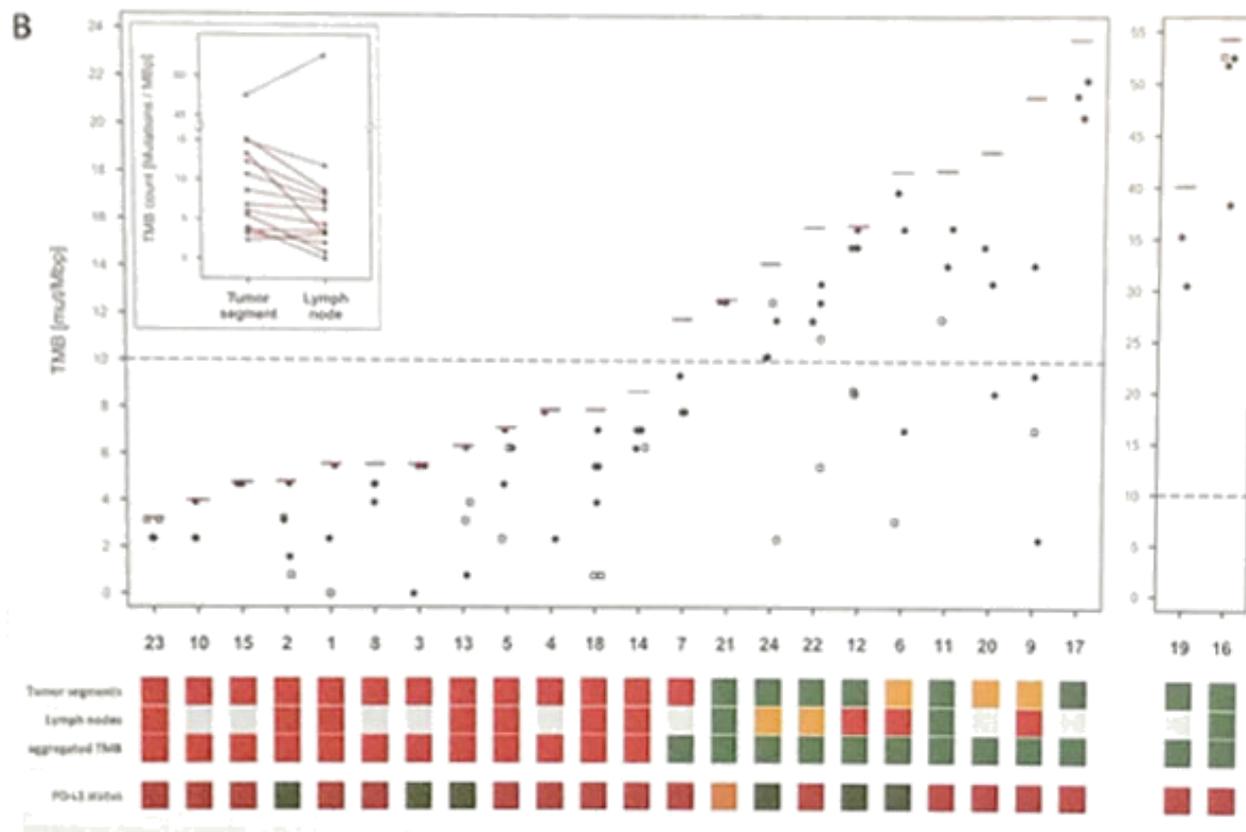
CV decreases proportionally to square root of TMB level



Separation of a tumor with TMB=20 muts/Mbp from a tumor with TMB=5 muts/Mbp



Spatial TMB heterogeneity: Multi-regional analysis



Overall TMB range:
0 - 52.55 mut/Mbp

29% with ITH of ≥ 5 mut/Mbp;
max. diff. 14.13

*varying tumor cell content (4/7)
*distinct mutational profiles (3/7)

13 cases with region specific mutations -> simulation of pooled sample as aggregated TMB

17% patients with divergent TMB states

TMB in lymph nodes lower ($p=0.02$)

Independent of PD-L1 expression

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