

Clinical impact of Immunosenescence in lung cancer

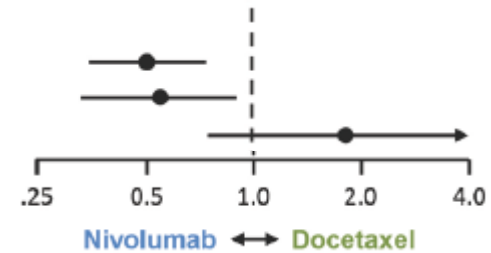
YMO Biomarkerprojekt

Dr. med. J. Kuon

NSCLC Immunotherapy

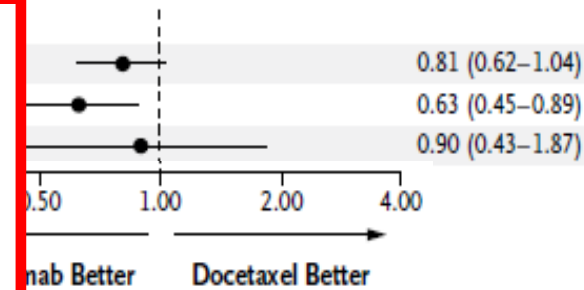
Checkmate 017
„squamous“

Age			
<65 years	152	0.52 (0.35, 0.75)	
→ ≥65 and <75 years	91	0.56 (0.34, 0.91)	
→ ≥75 years	29	1.85 (0.76, 4.51)	



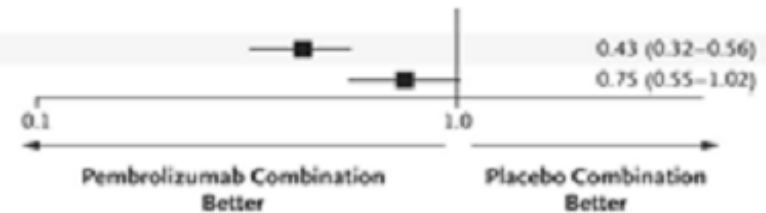
Checkmate 057
„non-squamous“

**Unmet need:
IO evidence
in patients >70 y**



Keynote 189

Age	
<65 yr	224/312
→ ≥65 yr	186/304



**Mean age 65 yo
Only 35 pts > 74 y!**

T-cell function in aging and cancer

Aging → **Immunosenescence**

- **Decrease in peripheral blood naive CD8⁺ T-cells**
- **Increase in terminally differentiated T-cells (CD8⁺ CD28⁻)**
- Relative deficit in the number and proportion of B cells

→ Increased cancer incidence ("inflammaging")

Cancer progression → **Immune dysregulation**

- Downregulation of CD28 and CD247
- Expansion of hyporesponsive populations (e.g. CD28⁻ CD57⁺)
- T-cell exhaustion (PD1⁺, LAG3⁺ ...)

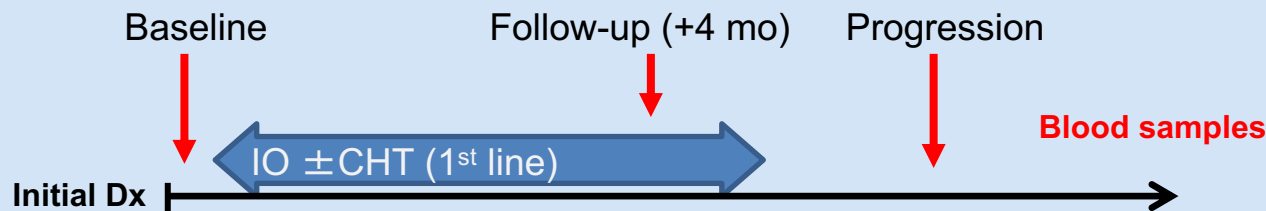
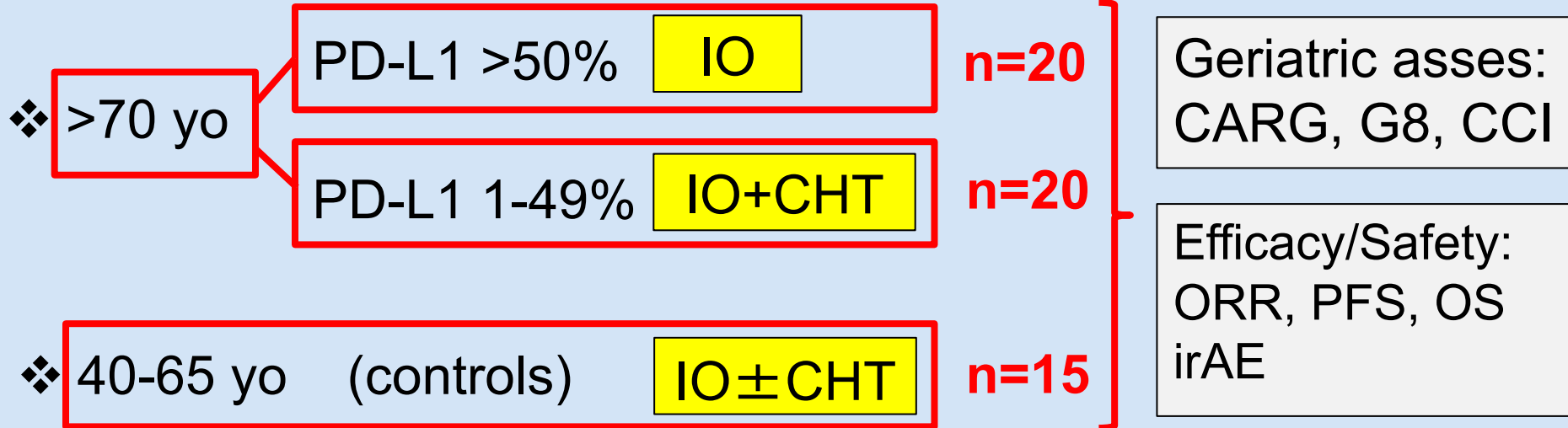
T-cell senescence and exhaustion markers for prediction of response to checkpoint inhibitors

Prospective IO cohort

Systematic material collection since Q2 2017 (Ethik Votum S-145/2017)

- Translational Research Unit of the Thoraxklinik Heidelberg
- Lungenbiobank Heidelberg

Characterization of immunosenescence in NSCLC*



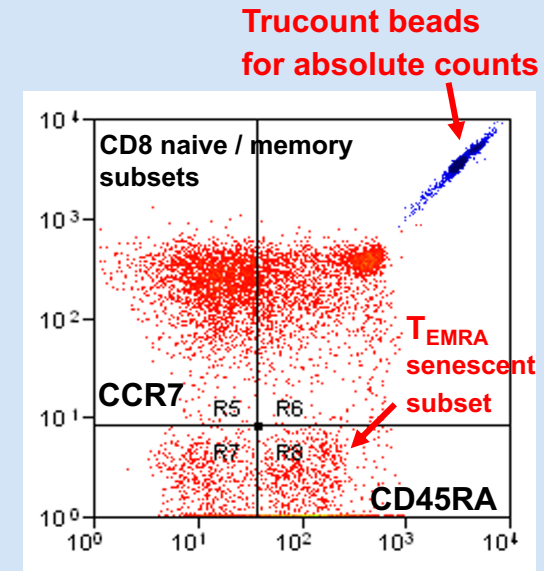
- * planned expansion:
- St. II-III (OP/CRT)
 - SCLC

Experimental readout

Absolute quantification of immune cell subsets (FCM)

- ❖ CD4/CD8, activated, naive/central/peripheral memory/ T_{EMRA}
- ❖ Th1/Th2/Th17/Treg
- ❖ senescent and exhausted T cells

- * single-platform absolute cell counts (Trucount)
- * lyse-no-wash staining, 12-color panel including:
CD45RA, CCR7, CD28, CD57, PD-1, KLRG-1, LAG-3, Tim-3,
CXCR3, CXCR6, TIGIT, BTLA, CD31, CD95, CD11a, CD25, FOXP3

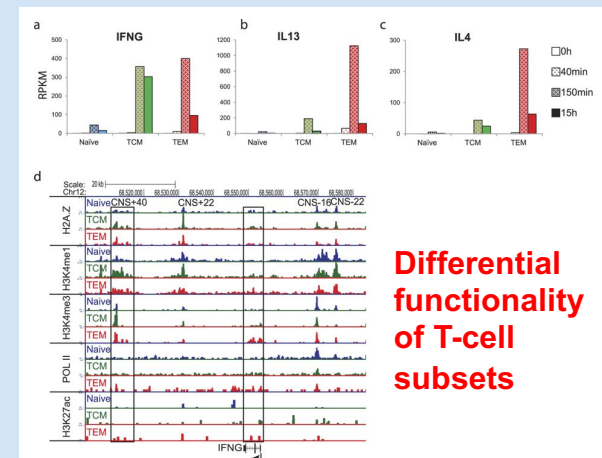


T-cell function after polyclonal *in vitro* stimulation (aCD3/aCD28)

"untouched" isolated CD4 cell subsets (MACS)

- ❖ cytokine production (Fireplex 17x immunoassay)
- ❖ TCR-repertoire
- ❖ single-cell function and polyfunctionality

- * single-cell RNA profiling (scRNA-seq)
- * single-cell cytokine profiling (FCM/Isoplexis)



Vielen Dank für Ihre Aufmerksamkeit!