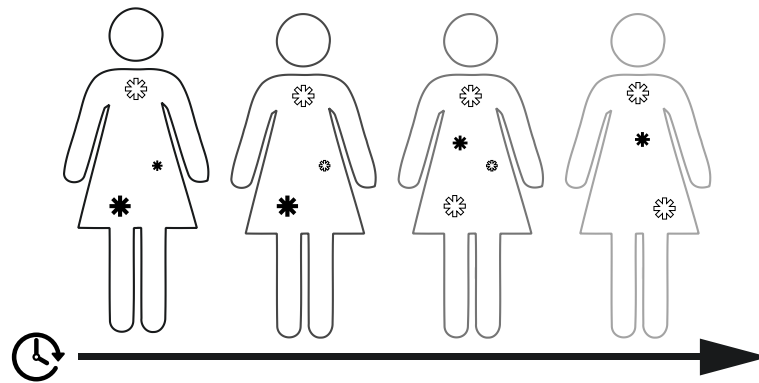


Diagnostics of immune exclusion: Molecular imaging with PET:

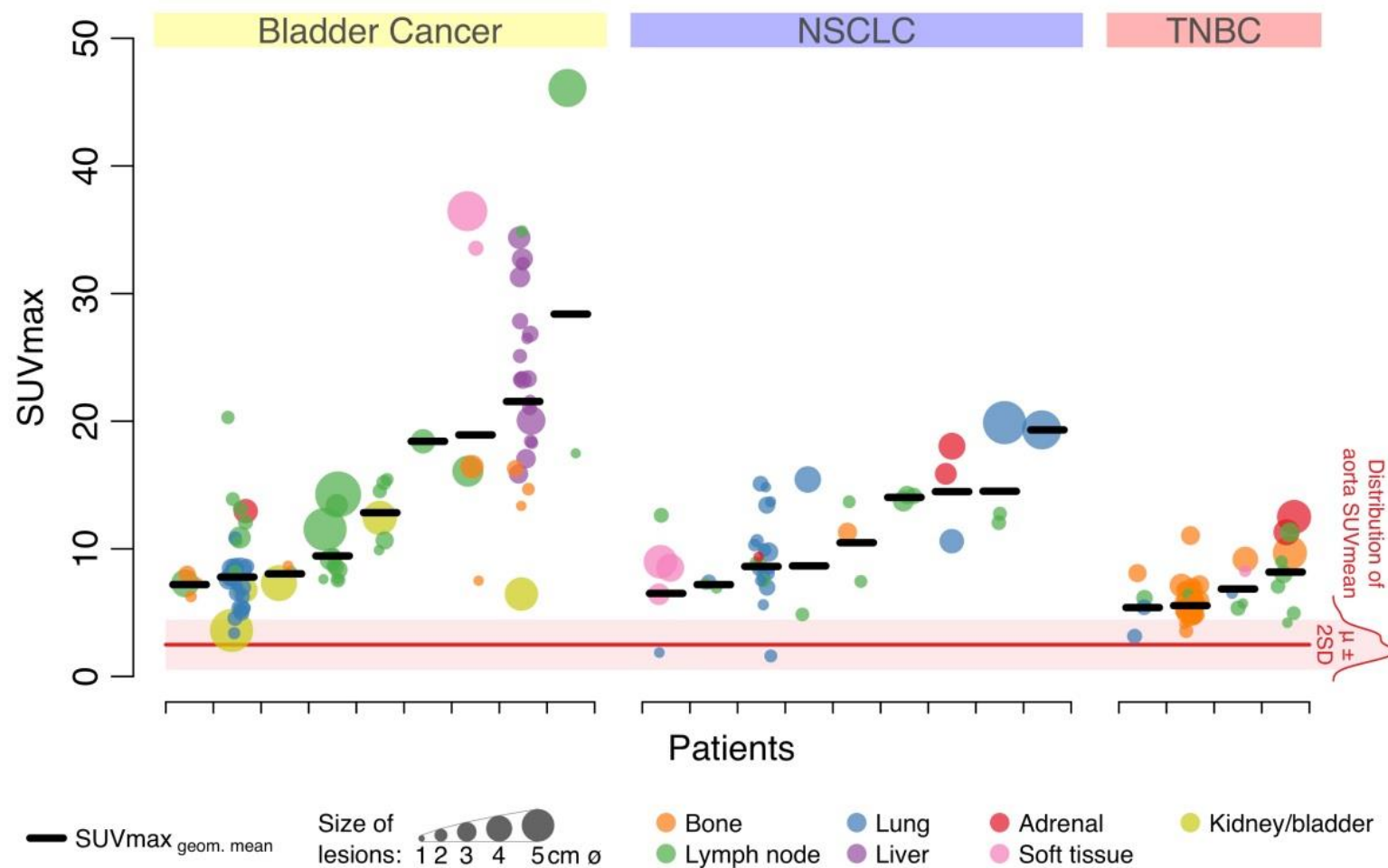
Elisabeth de Vries, UMCG, Groningen

Information on:

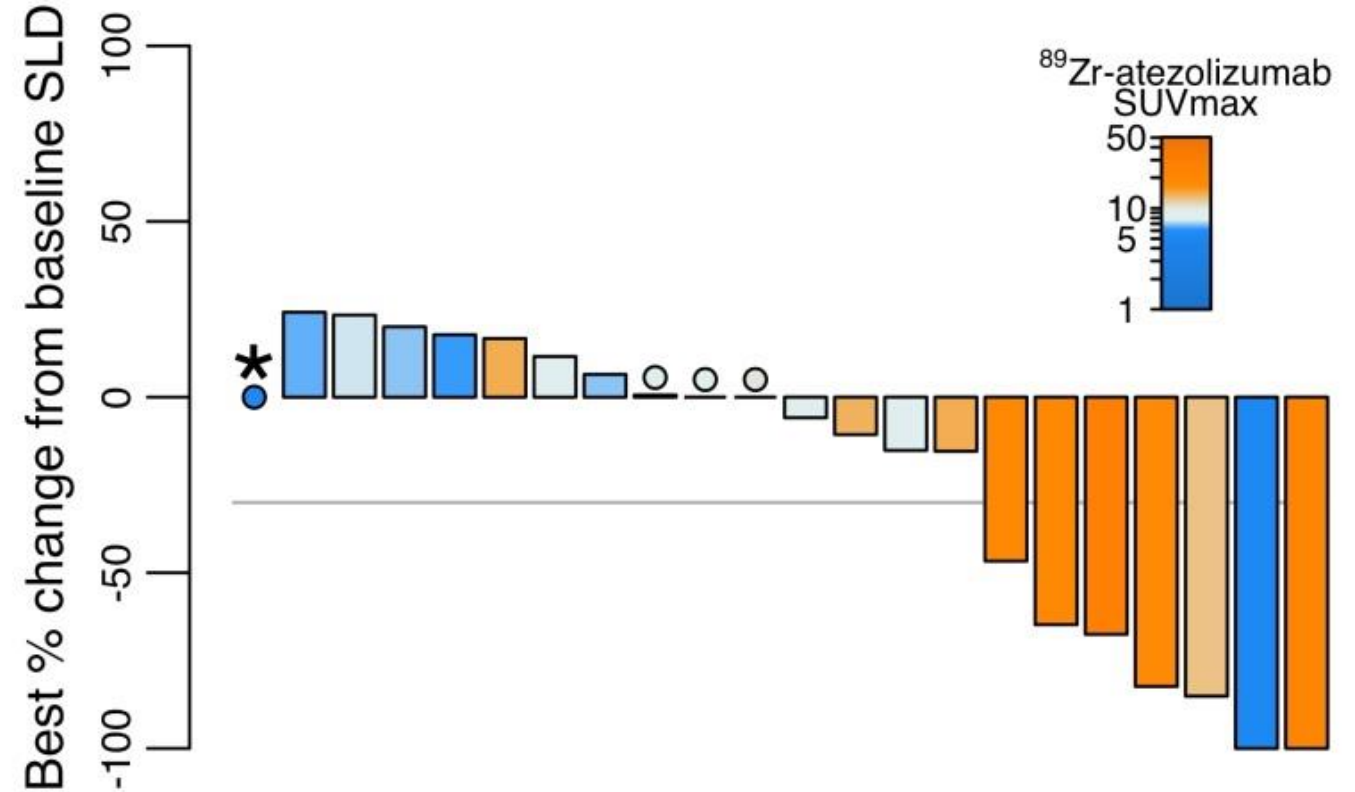
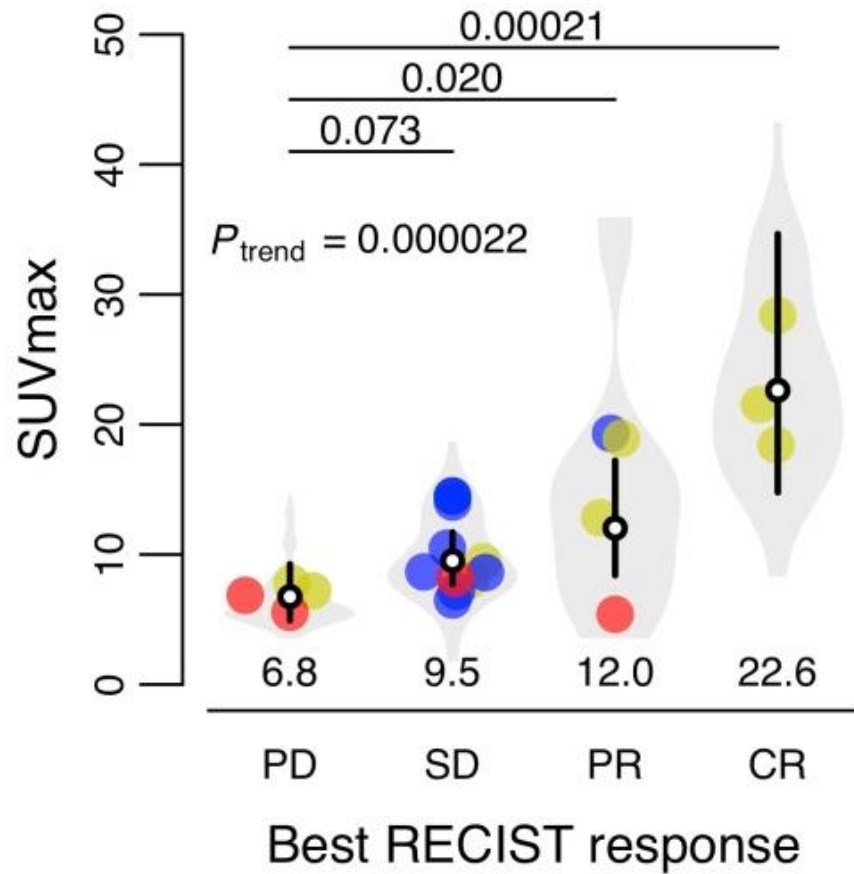
- PD-L1, and CD8 targeting tracer uptake in tumor lesions and the immune system
- Drug distribution
- Spatial and temporal heterogeneity within a patient



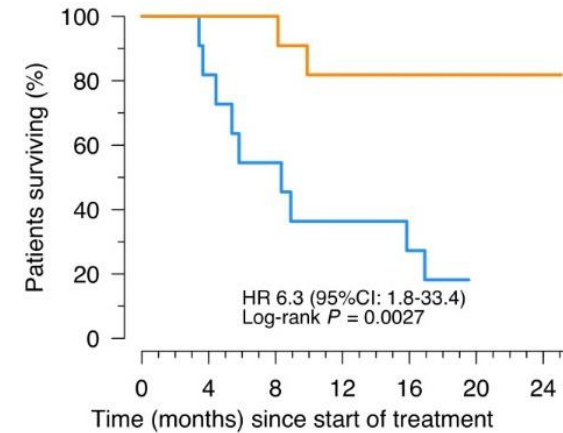
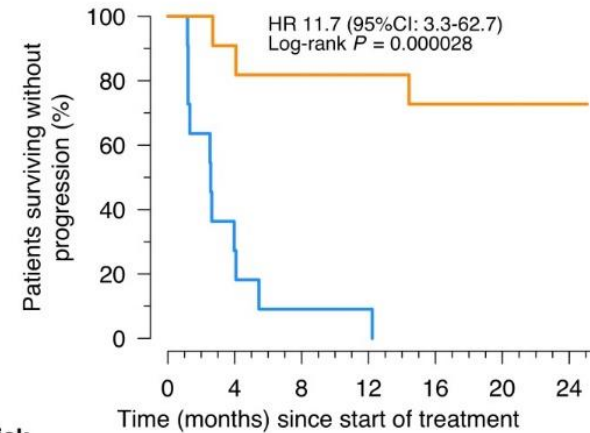
Heterogeneity in ^{89}Zr -atezolizumab tumor uptake per patient per tumor type (Day 7)



Tumor response on atezolizumab treatment related to ^{89}Zr -atezolizumab mean tumor uptake day 7 per patient

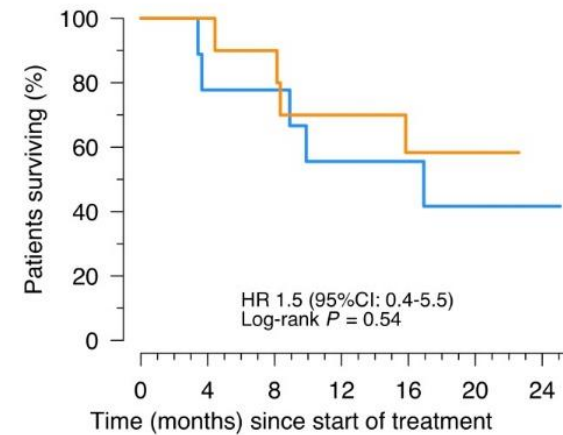
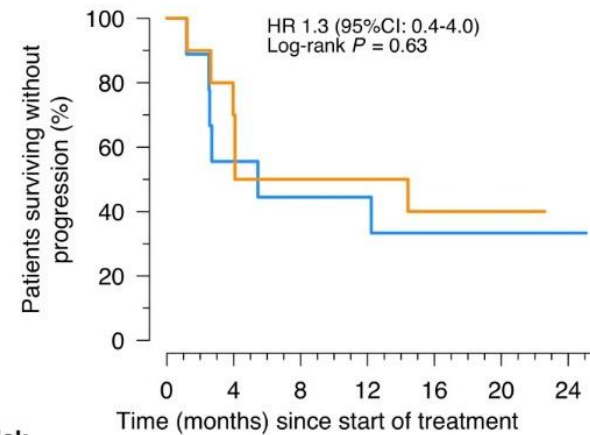


Geometric mean ^{89}Zr -atezolizumab tumor uptake predicts survival following start atezolizumab treatment, IHC does not



Number at risk

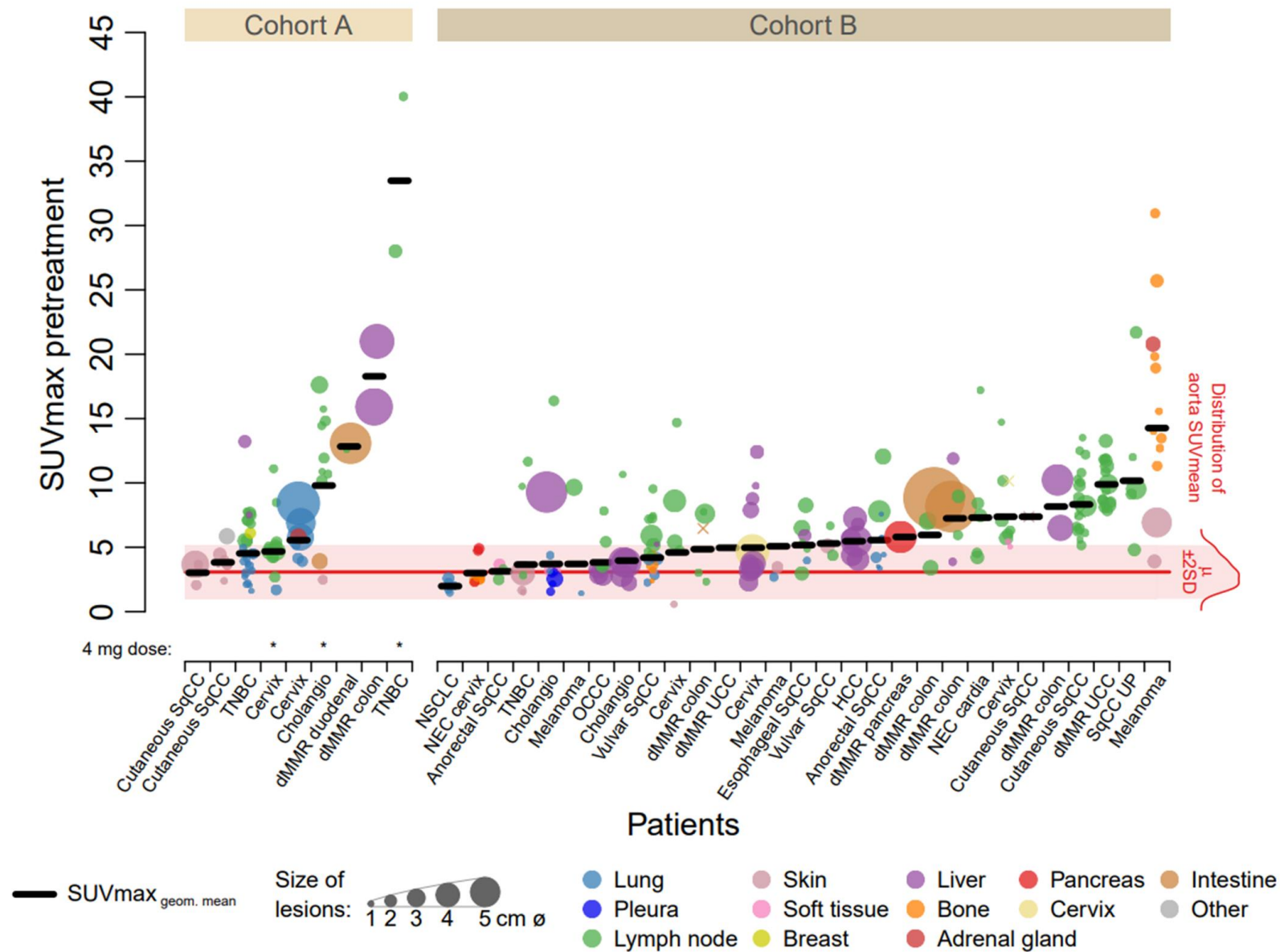
— SUVmax _{geom. mean} ≥ 9.0	11	10	9	9	8	6	1
— SUVmax _{geom. mean} < 9.0	11	3	1	1	0	0	0



Number at risk

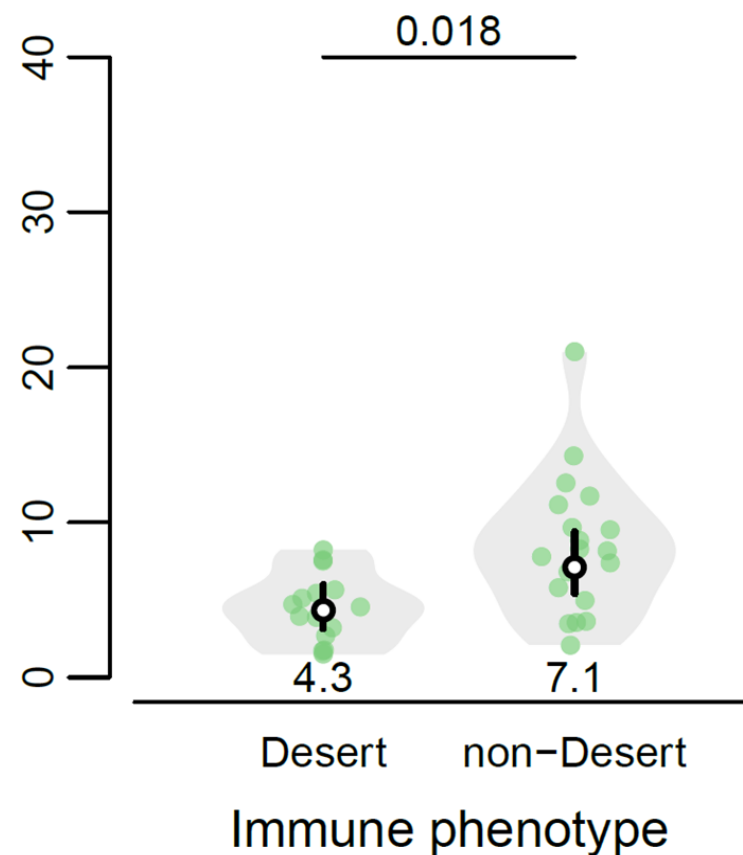
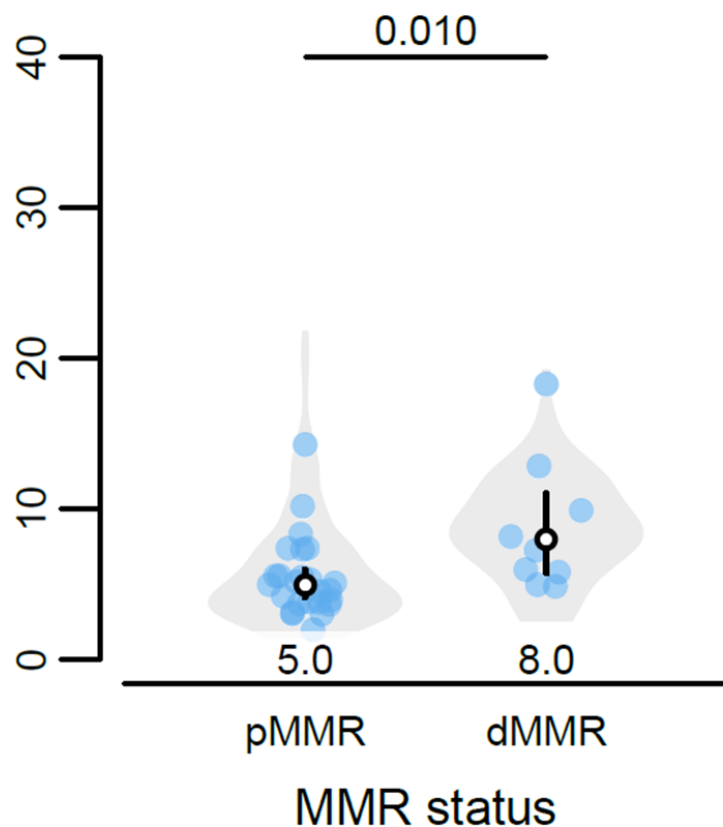
— SP142 IHC 1 or 2	10	7	5	5	4	3	0
— SP142 IHC 0	9	5	4	4	3	2	1

Pretreatment ⁸⁹ZED88082A (CD8 one-armed antibody) tumor uptake day 2

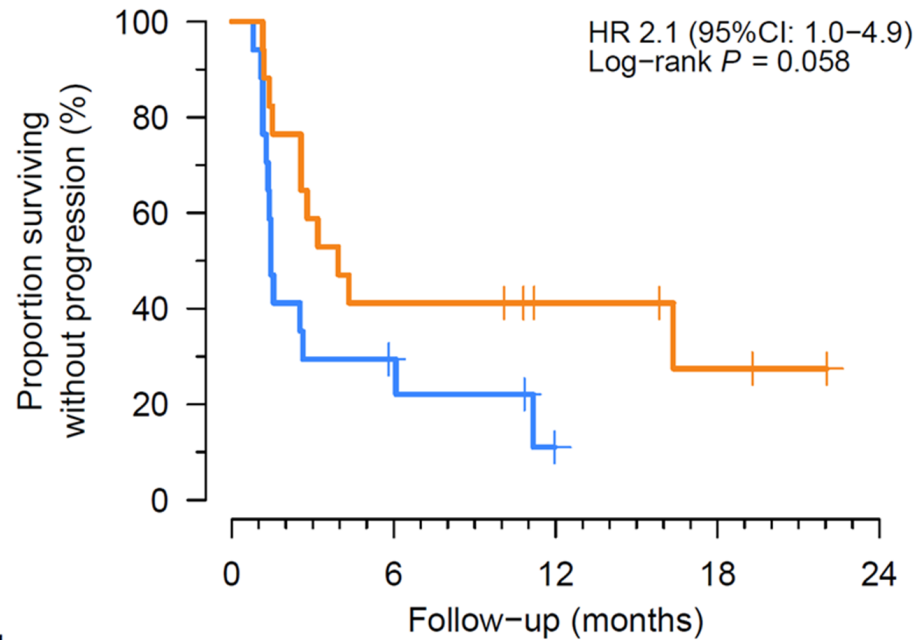


SUVmax ⁸⁹ZED88082A PET in patients with pMMR < dMMR tumors

SUVmax in lesions with desert < non-desert phenotype



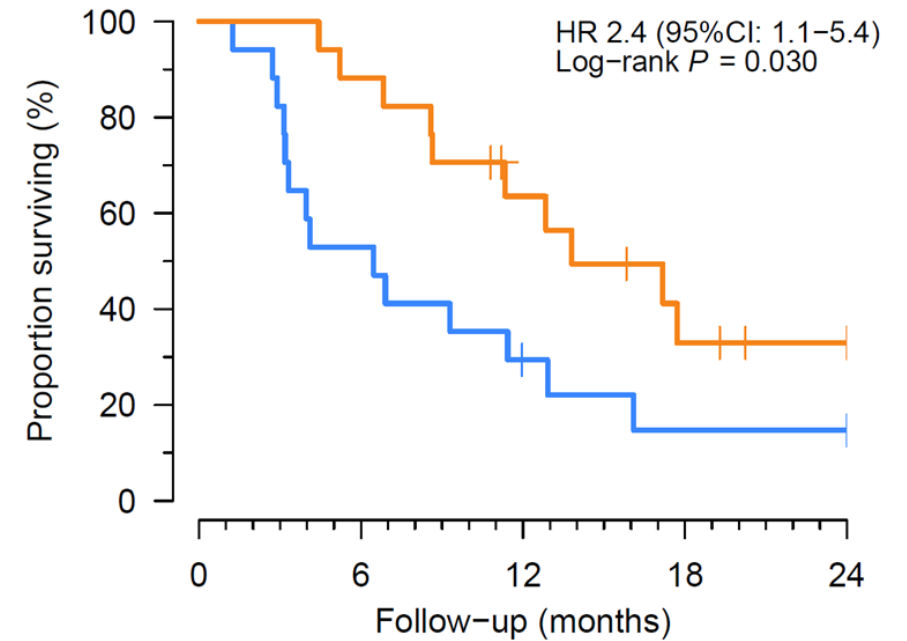
⁸⁹ZED88082A-uptake related to PFS and OS since start ICI, according to baseline geometric mean SUV_{max} below & above the median



Number at risk

— SUVmax geom. mean < 5.2
— SUVmax geom. mean ≥ 5.2

17	4	0	0	0
17	7	4	2	0

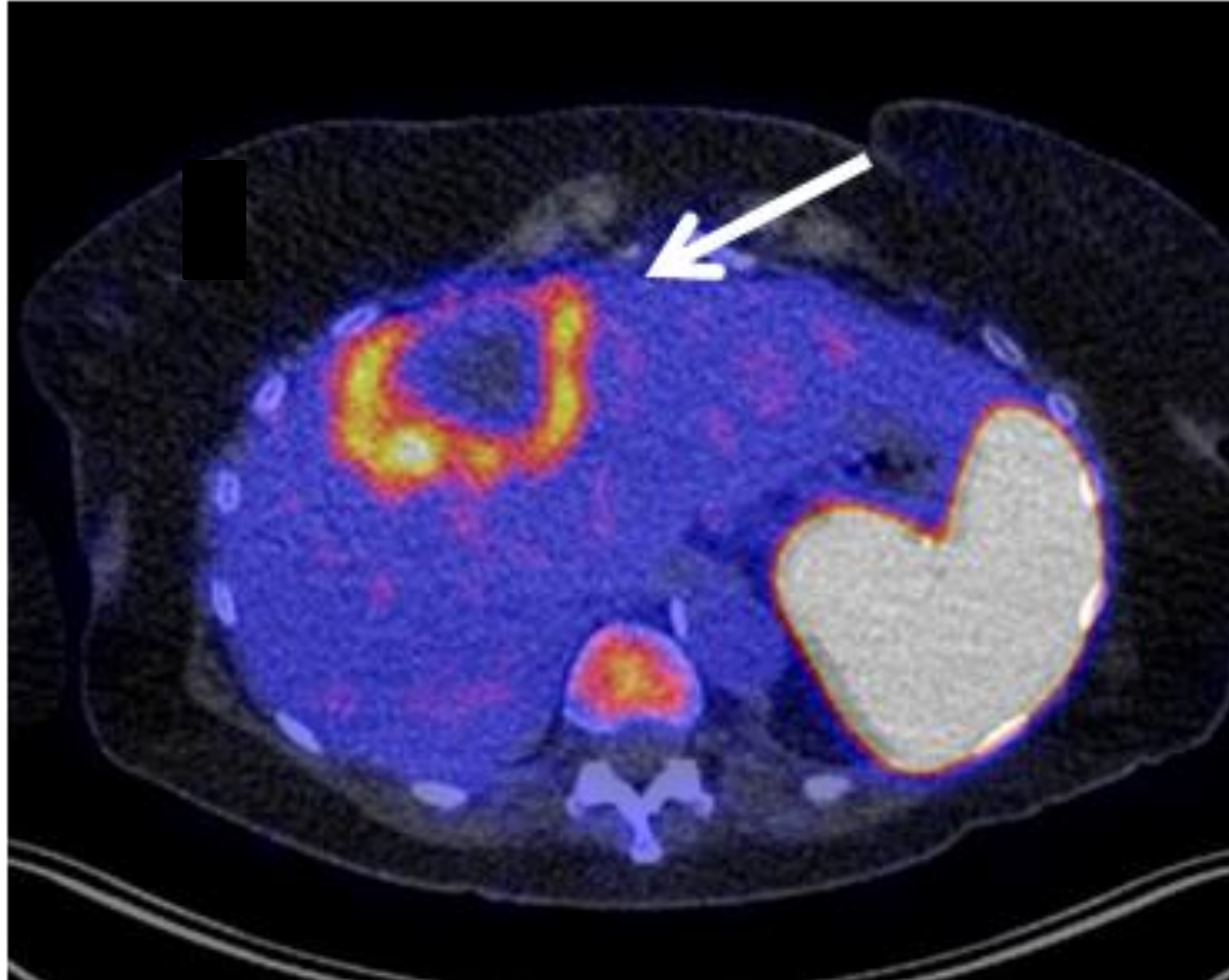


Number at risk

— SUVmax geom. mean < 5.2
— SUVmax geom. mean ≥ 5.2

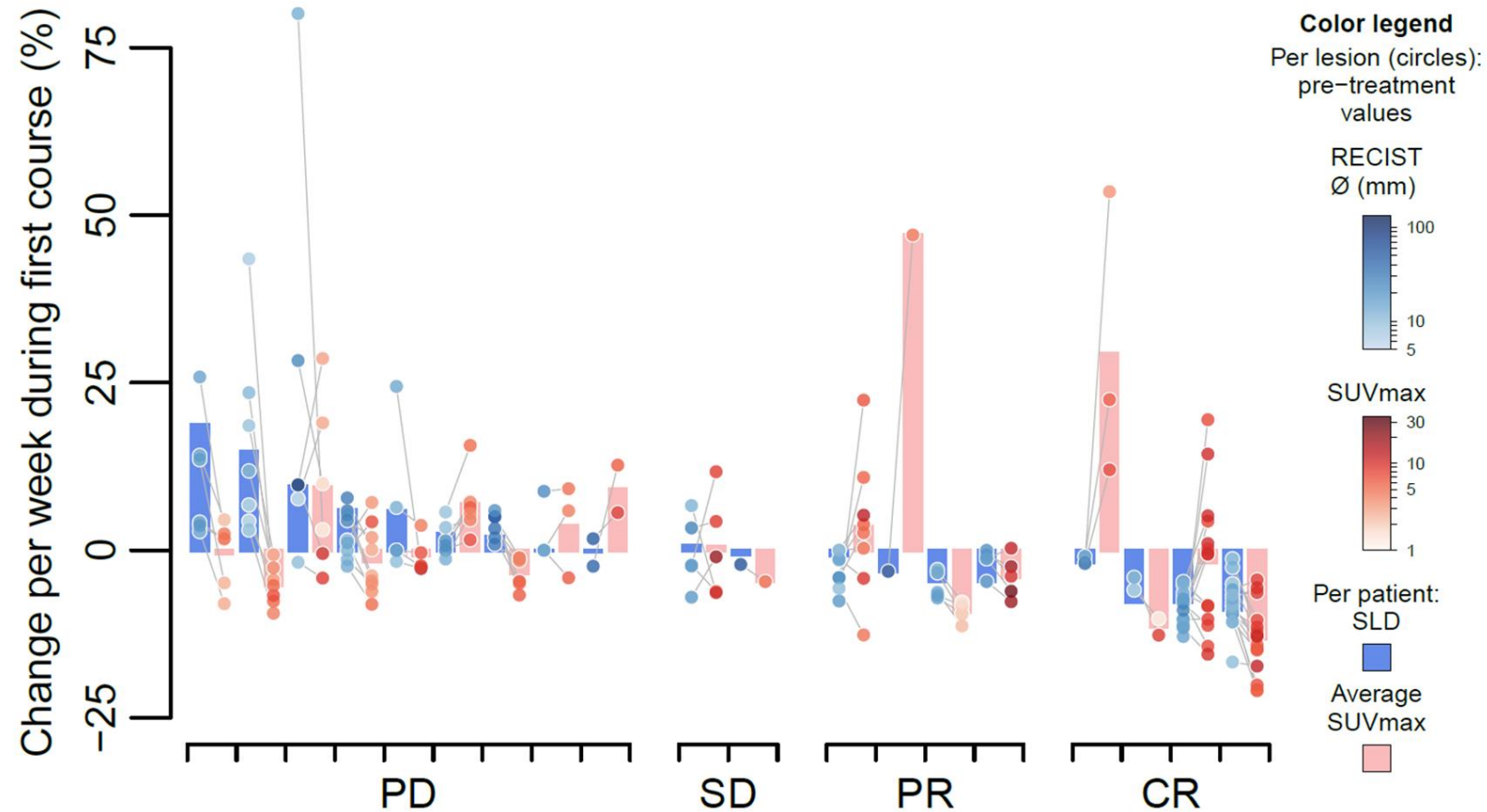
17	9	4	2	2
17	15	9	4	2

High ^{89}Zr D88082A uptake in liver metastasis rim in a patient with dMMR colorectal cancer



$^{89}\text{ZED88082A}$ -uptake and tumor response to ICI in 19 patients

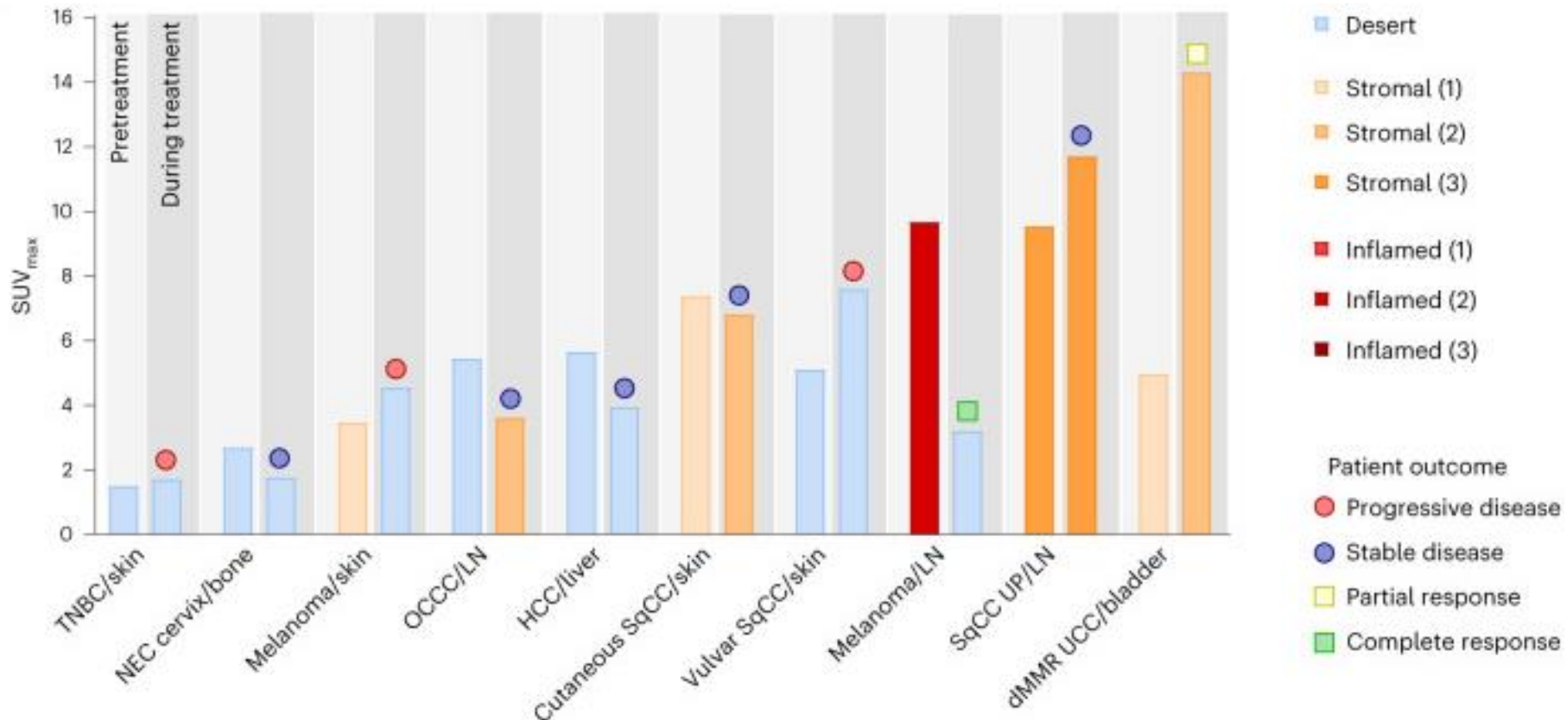
Changes in tracer tumor uptake and anatomic size during repeated imaging



Best RECIST response

Dots are individual lesions ($n = 111$) with their data points for size (●) and uptake (●) connected by grey lines

SUV_{max} and CD8 IHC expression pattern (density score) in lesions with corresponding paired biopsy samples before and during ICI treatment (n=10)



Conclusions role PET imaging

- Whole body drug distribution, tumor characteristics, and immune system visualization
- Predicts tumor response, PFS, and OS (small studies)
- Provides insight into
 - Tumor heterogeneity
 - Pharmacodynamic effects on the tumor
 - Immune system