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)

Bensch et al. Nat Med 2018
Tumor response on atezolizumab treatment related to $^{89}\text{Zr}$-atezolizumab mean tumor uptake day 7 per patient

$P_{\text{trend}} = 0.000022$

Bensch et al. Nat. Med. 2018
Geometric mean $^{89}$Zr-atezolizumab tumor uptake predicts survival following start atezolizumab treatment, IHC does not
Pretreatment $^{89}$ZED88082A (CD8 one-armed antibody) tumor uptake day 2

Kist de Ruijter et al Nat Med 2022
SUVmax $^{89}$ZED88082A PET in patients with pMMR < dMMR tumors
SUVmax in lesions with desert < non-desert phenotype
$^{89}\text{ZED88082A}$-uptake related to PFS and OS since start ICI, according to baseline geometric mean $\text{SUV}_{\text{max}}$ below & above the median.
High $^{89}$ZED88082A uptake in liver metastasis rim in a patient with dMMR colorectal cancer
ZED88082A-uptake and tumor response to ICI in 19 patients
Changes in tracer tumor uptake and anatomic size during repeated imaging

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

Best RECIST response
Per lesion (circles): pre-treatment values
RECIST Ø (mm)
SUVmax
$SUV_{\text{max}}$ 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