[^{89}Zr]Df-crefmirlimab PET/CT imaging to assess the *in vivo* biodistribution of CD8^{+} T-cells in hospitalized COVID-19 patients

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Introduction

The initial site of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) encounter is the mucosa of the upper respiratory tract [1], from where it may spread to the lower respiratory tract and eventually distant organ sites [2]. Early recognition and clearance of the virus by the adaptive immune system in the mucosa of the URT is crucial to control viral load [3] and avoid tissue destruction during later stages of infection [4]. In response to the continuously exposition to inhaled pathogens, mucosal immunity in the respiratory tract has developed into a complex system that requires response of both local and systemic lymphoid compartments [5].

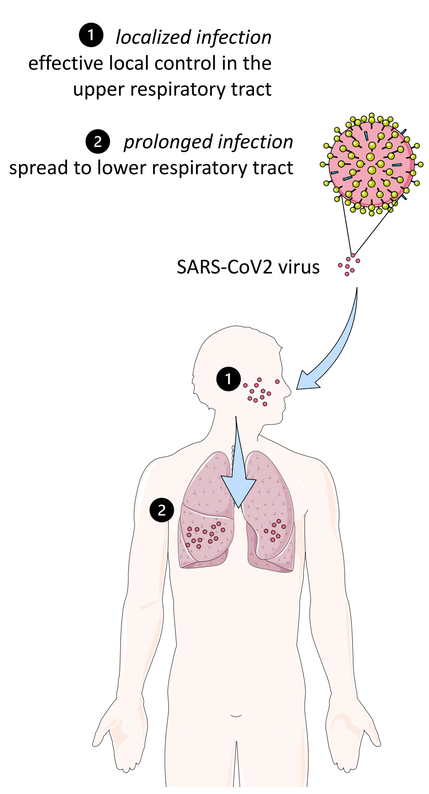
This case series describes the *in vivo* distribution of CD8+ T-cells in patients during active SARS-CoV-2 infection using PET imaging

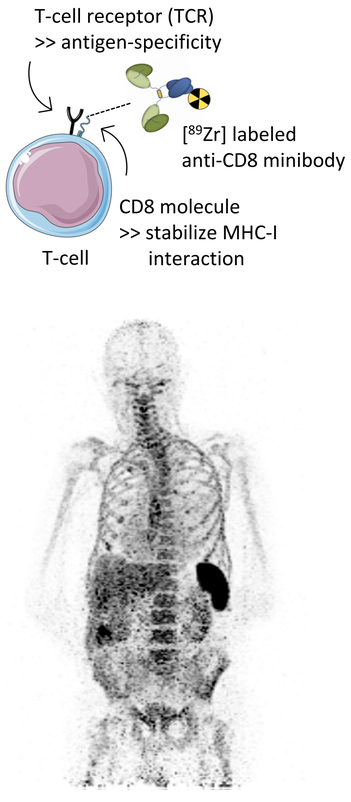
Patient characteristics

		TAN001	TAN002	TAN003
age	years	89	83	79
sexe	m/f	m	m	m
co-morbidities		COPD, cardio-vasc	T2D, HT, chronic ITP	COPD
onset of symptoms	days	10	2	4
admission duration	days	22	8	6
vaccination status		2x, plus booster	2x, plus booster	not vaccinated
SARS-CoV2 variant		delta	delta	delta
treatment		dexamethasone 6mg	IVIG 1g, platelet infusion	prednison 30mg
SaO_2	%	90, with 4L oxygen	96, w/o oxygen	94, w/o oxygen
C-reactive protein	mg/L	81	70	17
lymphocyte count	x 10^9/L	0.22	1.34	0.44

Methods

This is a prospective, observational non-randomized pilot study in hospitalized patients of >50 years with microbiologically proven SARS-CoV-2 infection. The prior use of immune suppressive medication was an exclusion criterion. Whole body [^{89}Zr]Df-crefmirlimab PET/CT scan were acquired at 24 hrs after i.v injection of 1.5mg protein dose labelled with 37 MBq (1 mCi) ^{89}Zr. Peripheral blood samples were collected for multi-color flowcytometry phenotyping of CD8+ T-cells, including homing receptors and immune senescence markers.





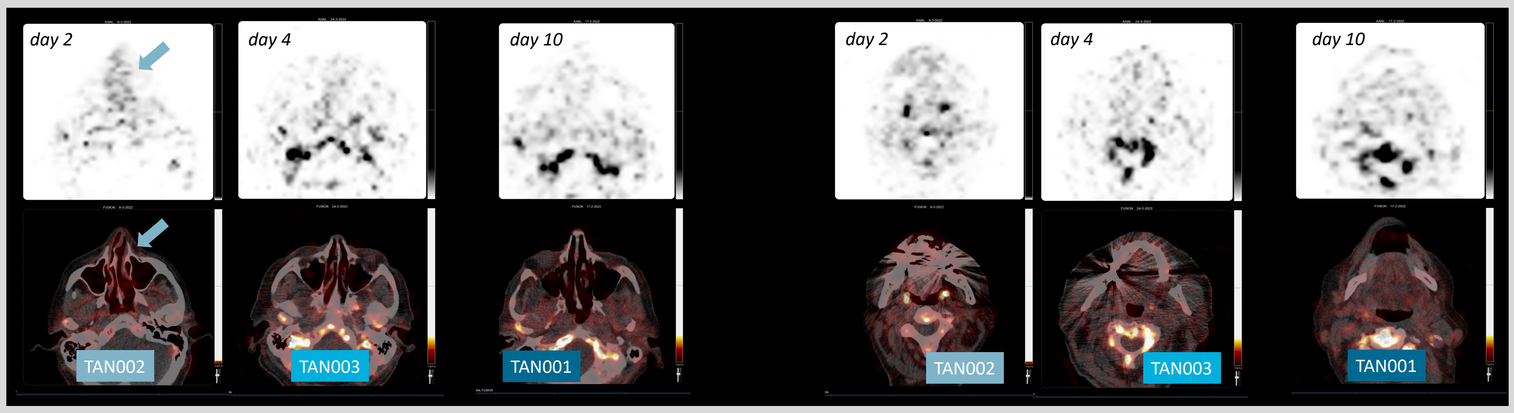
Conclusion

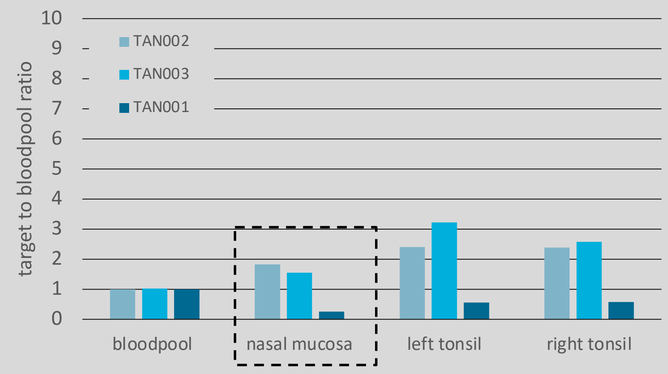
Imaging CD8+ T-cells in hospitalized COVID-19 patients reveals distinct patterns of CD8+ T-cell distribution during course of disease and underscores the importance of early local viral control in the upper respiratory tract.

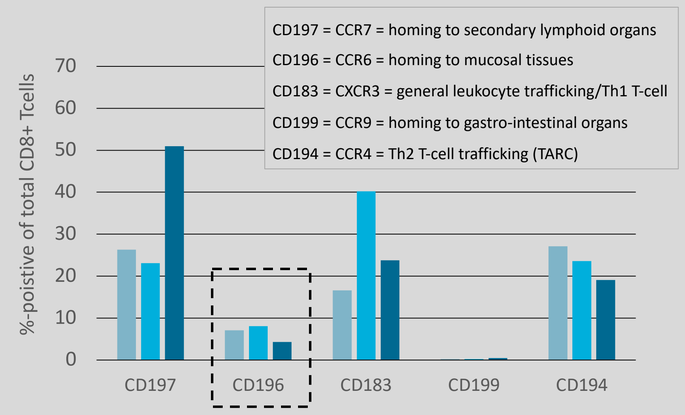
This case series highlights PET imaging with immune cell specific tracers as a potential imaging biomarker complementing immunological assays with spatial and dynamic data on CD8+ T-cell behavior *in vivo*.

Results

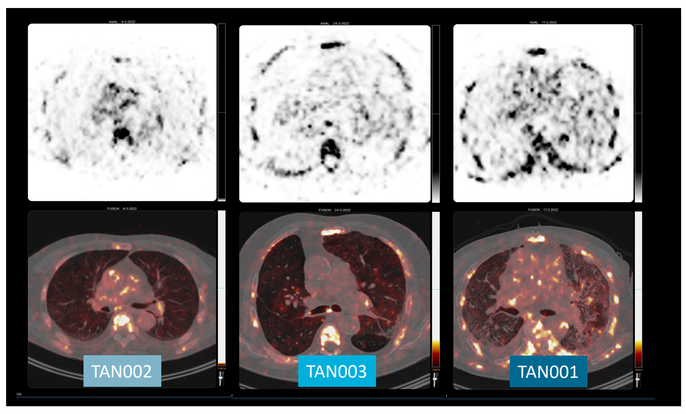
1 *tracer uptake in nasal mucosa correlates with higher expression of mucosa-homing recepter CD196 (CCR6)*

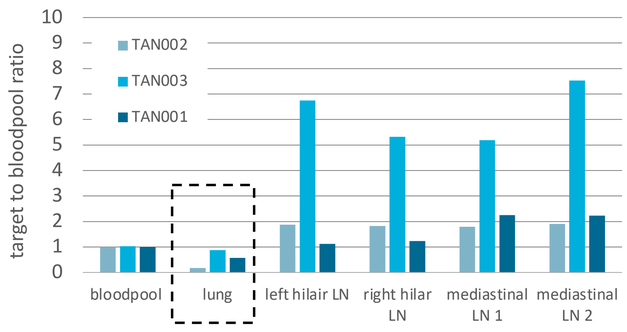


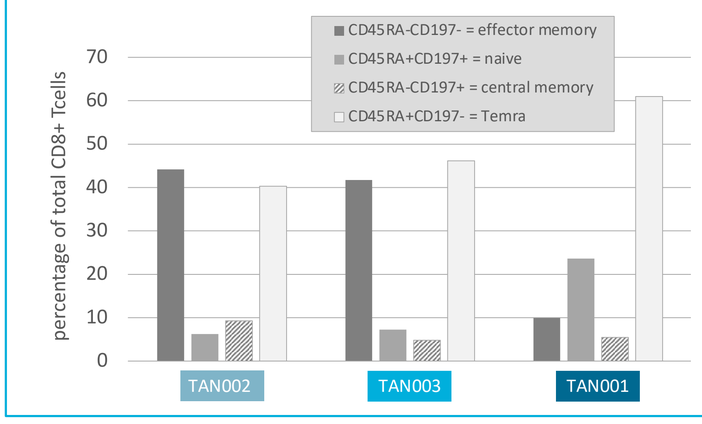


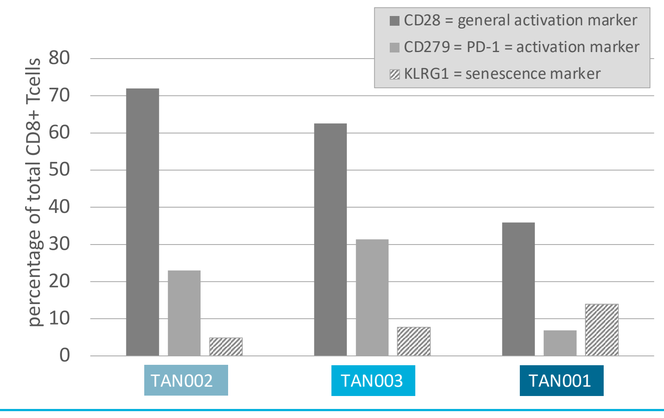


2 *increased CD8+ Temra populations and senescence phenotypes in prolonged COVID-19*









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