First-in-human immunoPET imaging of COVID-19 convalescent patients using dynamic total-body PET and a CD8-targeted minibody

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Abstract

With the majority of $CD8^+$ T cells residing and functioning in tissue, not blood, developing noninvasive methods for *in vivo* quantification of their biodistribution and kinetics in humans offers the means for studying their key role in adaptive immune response and memory. This study is the first report on using positron emission tomography (PET) dynamic imaging and compartmental kinetic modeling for *in vivo* measurement of whole-body biodistribution of $CD8^+$ T cells in human subjects. For this, a ^{89}Zr-labeled minibody with high affinity for human CD8 (^{89}Zr-Df-Crefmirlimab) was used with total-body PET in healthy subjects (N=3) and in COVID-19 convalescent patients (N=5). The high detection sensitivity, total-body coverage, and the use of dynamic scans enabled the study of kinetics simultaneously in spleen, bone marrow, liver, lungs, thymus, lymph nodes, and tonsils, at reduced radiation doses compared to prior studies. Analysis and modeling of the kinetics was consistent with T cell trafficking effects expected from immunobiology of lymphoid organs, suggesting early uptake in spleen and bone marrow followed by redistribution and delayed increasing uptake in lymph nodes, tonsils, and thymus. Tissue-to-blood ratios from the first 7 h of CD8-targeted imaging showed significantly higher values in the bone marrow of COVID-19 patients compared to controls,

with an increasing trend between 2 and 6 months post-infection, consistent with net influx rates obtained by kinetic modeling and flow cytometry analysis of peripheral blood samples. These results provide the platform for using dynamic PET scans and kinetic modelling to study total-body immunological response and memory.

Competing Interest Statement

RD Badawi and SR Cherry are principal investigators on a grant funded by United Imaging Healthcare. UC Davis has a research agreement and a sales-based revenue sharing agreement with United Imaging Healthcare. This research was supported by ImaginAb. I Wilson serves as CEO of ImaginAb. K Schmiedehausen serves as VP of Medical Affairs at ImaginAb.

Clinical Trial

IND 153492

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Author Declarations

I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.

Yes

The details of the IRB/oversight body that provided approval or exemption for the research described are given below:

Ethics committee/IRB of University of California Davis gave ethical approval for this work.

I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals.

Yes

I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance).

Yes

I have followed all appropriate research reporting guidelines, such as any relevant EQUATOR Network research reporting checklist(s) and other pertinent material, if applicable.

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