ASSOCIATIONS BETWEEN MICROBIAL GUT TRANSLOCATION MARKERS AND AGE-RELATED CLONAL HAEMATOPOIESIS IN OLDER ADULTS WITH AND WITHOUT HIV: THE ARCHIVE STUDY

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Background:
Microbial gut translocation is increased in people living with HIV (PLHIV) compared with people without HIV and is associated with systemic inflammation and

comorbidities. We evaluated whether gut translocation markers (LBP and sCD14) are associated with clonal haematopoiesis (CH) in older adults with and without HIV.

Methods:
ARCHIVE is a prospective longitudinal cohort study that enrolled participants over 55 years with and without HIV in Sydney and Melbourne, Australia. Participants had blood samples collected at three timepoints (T1 2014-2015; T2 2017-2018; T3 2021-2022). Whole blood samples at T2 were classified as CH-positive if any CH mutation was detected using deep sequencing. Concentrations of sCD14 and lipopolysaccharide binding protein (LBP) were measured in plasma samples at all timepoints using ELISA. For each biomarker, log-transformed concentrations were analysed in a linear mixed model, adjusting for age, gender, smoking and BMI. Trajectories of median concentrations over time were estimated and tested for differences across CH and HIV status.

Results:
Among 443 participants, 96% were male, median age (T2) was 64 years [IQR 59-69], 49% had HIV, and 22% had at least one CH mutation (T2). Median LBP concentration (T2) was higher in participants with vs. without CH (p=0.032), overall and within participants with HIV (median ratio LBP in participants with:without CH=1.15 [95% CI 1.01-1.31]) and without HIV (1.13 [1.03-1.32]). Median sCD14 concentration (T2) was higher in participants with vs. without CH, but not significantly (p=0.12). Both sCD14 and LBP trajectories over time were not significantly different between those with and without CH (p=0.74 for CD14; 0.60 for LBP).

Conclusion:
To our knowledge, this is the first report of an association between markers of gut translocation and CH in people with and without HIV. Further studies should evaluate whether gut translocation may be an inflammatory driver of the emergence of CH in PLHIV.

Disclosure of Interest Statement:
Part of this work has been supported by an unrestricted grant from Gilead Sciences Pty Ltd (awarded to NJD).
MB has received funding from Gilead Sciences and ViiV Healthcare for lecturing, travel to scientific meetings and medical advisory boards.
DAB has received funding, travel grants and served on advisory boards for ViiV Healthcare and Gilead.
BE has received consultation fees from ViiV and Gilead Sciences for unrelated work.
DES has received consultancy fees and lecturing honorarium from ViiV Healthcare and Gilead Sciences.
JFH's institution has received reimbursement for her participation in Advisory Boards for Gilead Sciences and ViiV Healthcare.
IW has worked as an investigator on commercial and investigator-initiated studies with funding to institutions from Gilead, ViiV, MAS, Moderna and CSL. IW has worked on advisory boards.
GVM has received research funding from Gilead, Abbvie, Janssen, and ViiV, has served on advisory boards for Astra Zeneca and ViiV, and has provided consultancy and received travel support from Gilead.

MNP has received research funding from ViiV, Janssen, Gilead (awarded to institution), research support (in kind) from ViiV, Janssen, BMS, Verastem, ASTEX, Grifols, CSL Behring, Takeda, Emergent (in kind, to institution), and has served on the advisory board for AstraZeneca and Gilead.
KP has received unrestricted research funding from ViiV healthcare Australia and Gilead Health Sciences.
PY has received speaker honoraria from Astellas Pharmaceuticals, Novartis and Johnson and Johnson for unrelated projects.
None of the other authors have any Competing Interests to declare.

Acknowledgement of Funding
This work was supported by funding from the Royal Australasian College of Physicians Foundation, the University of New South Wales, and Gilead Sciences Pty Ltd.