Conclusion: These results suggested that BIC/FTC/TAF was safe and effective in rapid ART.

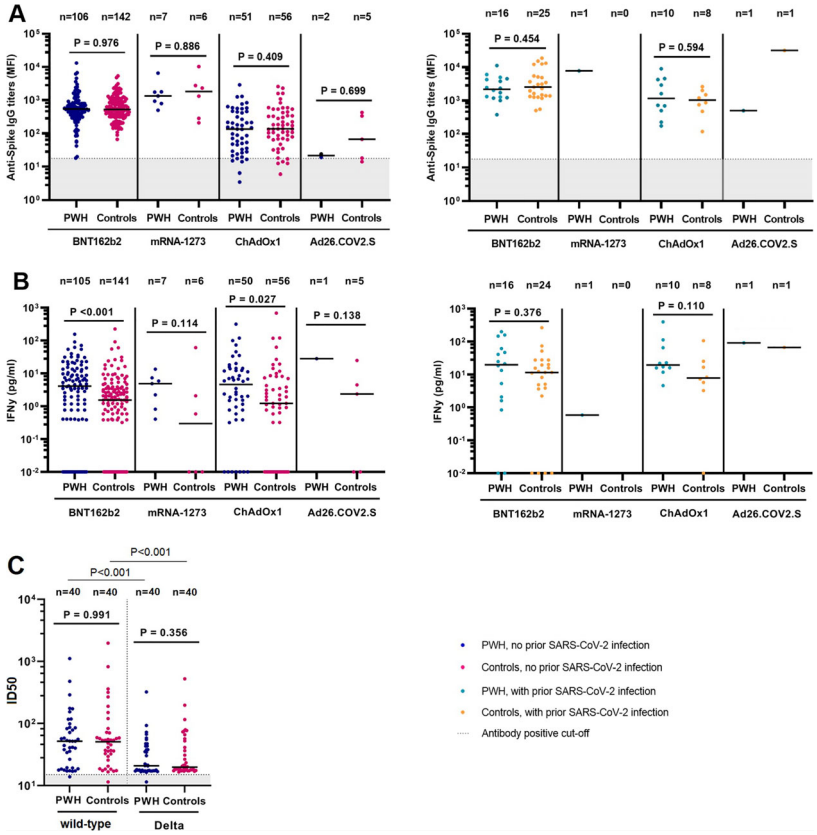
HIV Clinical Challenges (II)

O31

Older people with well-controlled HIV have similar antibody and higher T-cell responses after vaccination against SARS-CoV-2 compared to demographically and lifestyle-comparable people without HIV

M Verburgh[1], L van Pul[2], M Grobben[3], A Boyd[4], F Wit[1], A van Nuenen[2], K van Dort[2], K Tejjani[3], J van Rijswijk[3], M Bakker[3], L van der Hoek[3], M Schim van der Loeff[5], M van der Valk[1], M van Gils[3], N Kootstra[2], P Reiss[1]

[1]Infectious Diseases, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; [2]Experimental Immunology, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; [3]Medical Microbiology and Infection Prevention, Laboratory of Experimental



Abstract O31 – Figure 1. Post-vaccination SARS-CoV-2 IgG spike-antibody titers, T-cell responses and neutralisation against wild-type and Delta variants in participants of the AGEhIV COVID-19 substudy. P-values, comparing people with HIV (PWHIV) and HIV-negative controls, were calculated using Wilcoxon rank-sum test. (A) Post-vaccination SARS-CoV-2 IgG spike-antibody titers in participants without (left panel) and with (right panel) prior SARS-CoV-2 infection, by HIV-status and vaccine type. Resulting values are expressed as the median fluorescence intensity (MFI) of at least 50 beads per antigen. The dotted line represents the antibody non-response cut-off value (IgG S-antibody titer <17.8 MFI). (B) Post-vaccination SARS-CoV-2 T-cell responses in participants without (left panel) and with (right panel) prior SARS-CoV-2 infection, by HIV-status and vaccine type. Resulting values are expressed as the IFNγ release (in pg/mL, lower detection limit 0.09 pg/mL). (C) Post-vaccination virus-neutralisation against SARS-CoV-2 wild-type and Delta variants in 40 PWHIV and 40 controls (1:1 matched on age, sex and vaccine type). Resulting values are expressed as the serum dilution at which 50% of the infectivity was inhibited (ID50).

Virology, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; [4]Infectious Diseases, HIV Monitoring Foundation, Amsterdam, Netherlands; [5]Infectious Diseases, Public Health Service of Amsterdam, Amsterdam, Netherlands

Background: Studies comparing humoral and cellular SARS-CoV-2 vaccine responses in people with HIV (PWHIV) and demographically and lifestyle-comparable HIV-negative controls are scarce.
Methods: SARS-CoV-2-spike(S)-IgG antibody (custom Luminex immunoassay) and T-cell responses (IFNγ release upon S-peptide stimulation) were measured in last available stored samples prior to vaccination and 4 to 13 weeks after completing primary vaccination from PWHIV and HIV-negative Amsterdam AGEhIV COVID-19 substudy participants [1]. A positive nucleocapsid-antibody test (INgezim IgA/IgM/IgG) or self-reported positive PCR defined prior SARS-CoV-2 infection. Factors associated with post-vaccination IgG S-titers and T-cell responses were assessed by multivariable linear and tobit regression, respectively, grouping vaccines as mRNA- or vector-based. In 2 x 40 age-/sex-/vaccine type-matched PWHIV and controls without prior SARS-CoV-2, virus-neutralisation (wild-type and Delta variants) was determined on VeroE6 cells by cytotoxicity-assay.
Results: Characteristics of 195 enrolled PWHIV and 246 controls include a similar distribution of vaccines received (Table 1). Both pre- and post-(Figure 1A) vaccination IgG S-titers, regardless of vaccine type, did not significantly differ between groups. Pre- and post-(Figure 1B) vaccination T-cell responses were higher in PWHIV. HIV-status was not associated with IgG S-titer. Prior SARS-CoV-2 infection (β = 0.77), mRNA vaccine (β = 0.56), female sex

Abstract O31 – Table 1. Characteristics of 441 included participants in the AGEhIV COVID-19 substudy (at the time of 4 to 13 weeks after last dose of a COVID-19 vaccine), by HIV-status. All values are n (%) or median (interquartile range). A) Last available data prior to receiving last vaccine dose of the primary vaccination course. B) HIV-1 viral load missing in 1/195 PWHIV.

	People with HIV (n = 195)	Controls (n = 246)	p
Age, yr	63.3 (58.7 to 68.3)	61.6 (58.0 to 67.5)	0.145[a]
Male sex at birth	184 (94.4%)	211 (85.8%)	0.003[b]
Ethnic origin - Caucasian - African - Asian	- 190 (97.4%) - 5 (2.6%) - 0 (0.0%)	- 237 (96.4%) - 4 (1.6%) - 5 (2.0%)	0.109[c]
BMI, kg/m^2 (A) - Underweight (<18.5) - Normal weight (18.5 to 24.9) - Overweight (25.0 to 29.9) - Obese (30.0)	- 1 (0.5%) - 101 (51.8%) - 72 (36.9%) - 21 (10.8%)	- 0 (0.0%) - 118 (48.0%) - 97 (39.4%) - 31 (12.6%)	0.608[c]
Total comorbidities (A) - 0 comorbidities - 1 to 2 comorbidities - 3 to 7 comorbidities	- 79 (40.5%) - 96 (49.2%) - 20 (10.3%)	- 154 (62.6%) - 78 (31.7%) - 14 (5.7%)	<0.001[b]
Current CD4 count, cells/mm^3 (A)	640 (500 to 850)	810 (650 to 1010)	<0.001[a]
Current CD4 count (A) - <350 cells/mm^3 - 350 to 499 cells/mm^3 - 500 to 749 cells/mm^3 - 750 cells/mm^3	- 19 (9.8%) - 26 (13.3%) - 77 (39.5%) - 73 (37.4%)	- 3 (1.2%) - 21 (8.5%) - 72 (29.3%) - 150 (61.0%)	<0.001[c]
Current CD8 count, cells/mm^3 (A)	750 (500 to 990)	410 (300 to 560)	<0.001[a]
Current CD8 count (A) - <350 cells/mm^3 - 350 to 499 cells/mm^3 - 500 to 749 cells/mm^3 - 750 cells/mm^3	- 22 (11.3%) - 24 (12.3%) - 50 (25.6%) - 99 (50.8%)	- 88 (35.8%) - 73 (29.6%) - 42 (17.1%) - 43 (17.5%)	<0.001[c]
Current CD4/8 ratio (A)	0.86 (0.65 to 1.22)	1.87 (1.32 to 2.56)	<0.001[a]
Current CD4/8 ratio (A) - <0.50 - 0.50 to 0.99 - 1.0	- 21 (10.8%) - 98 (50.2%) - 76 (39.0%)	- 0 (0.0%) - 21 (8.5%) - 225 (91.5%)	<0.001[c]
Time since HIV diagnosis, yr	22.6 (17.1 to 27.9)	NA	…
Time since first starting ART, yr	19.8 (13.9 to 24.7)	NA	…
CD4 nadir, cells/mm^3	180 (70 to 260)	NA	…
Undetectable HIV-1 viral load (A, B)	193 (99.5%)	NA	…
COVID-19 vaccine type - BNT162b2 - mRNA-1273 - ChAdOx1 - Ad26.COV2.S - ChAdOx1+BNT162b2	- 122 (62.6%) - 8 (4.1%) - 61 (31.3%) - 3 (1.5%) - 1 (0.5%)	- 167 (67.9%) - 6 (2.4%) - 64 (26.0%) - 6 (2.4%) - 3 (1.2%)	0.491[c]
Only one dose of BNT162b2, mRNA-1273 or ChAdOx1 due to prior SARS-CoV-2 infection	2 (1.0%)	8 (3.3%)	0.284[c]
Days between pre-vaccination sample and first vaccine dose	44 (26 to 67)	45 (28 to 74)	0.702[a]
Days between first and second vaccine dose - BNT162b2 - mRNA-1273 - ChAdOx1 - ChAdOx1 + BNT162b2	- 35 (35 to 36) - 28 (28 to 32) - 77 (63 to 77) - 88 (88 to 88)	- 36 (35 to 36) - 32 (28 to 36) - 76 (68 to 77) - 65 (33 to 113)	- 0.096[a] - 0.459[a] - 0.538[a] - 0.655[a]
Days between last vaccine dose and post-vaccination sample	64 (46 to 76)	70 (43 to 77)	0.262[a]
Prior SARS-CoV-2 infection - prior to pre-vaccination sample - between pre- and post-vaccination sample	- 20 (10.3%) - 8 (4.1%)	- 25 (10.2%) - 9 (3.7%)	0.877[b]

BMI, body mass index; NA, not applicable; yr, in years.
[a]Wilcoxon rank-sum test;
[b]Pearson $\chi 2$ test;
[c]Fisher's exact test.

(β = 0.24) and fewer days between last vaccination and sampling (β = 0.07) were significantly associated with higher, and a CD4/8 ratio<1.0 with lower (β = -0.39) IgG S-titers, without significant interactions between HIV-status and any of these factors. Prior SARS-CoV-2 infection (β = 0.97), HIV-positive status (β = 0.63) and fewer days between last vaccination and sampling (β = 0.10) were associated with higher T-cell responses, after adjusting for pre-vaccination levels. SARS-CoV-2-neutralisation was not significantly different between the subgroup of PWHIV and controls, but significantly reduced for the Delta variant in both groups (Figure 1C).

Conclusions: Total and neutralising antibody responses to SARS-CoV-2 vaccines did not differ significantly, whereas the T-cell response was increased in these older PWHIV with well-controlled HIV compared to demographically and lifestyle-similar individuals without HIV. Factors affecting the height of response were similar in both groups. Interestingly, this included a lower CD4/8 ratio being associated with an overall lower antibody response in both PWHIV and controls. Further analyses will explore potential relationships with immune senescence and functionality of the T-cell response.

Reference

1. Verburgh ML, Boyd A, Wit FWNM, Schim van der Loeff MF, van der Valk M, Bakker M, et al. Similar risk of severe acute respiratory syndrome coronavirus 2 infection and similar nucleocapsid antibody levels in people with well-controlled human immunodeficiency virus (HIV) and a comparable cohort of people without HIV. J Infect Dis. 2022;225:1937-47.

O32

External validation of the Dat'AIDS score for predicting 5-year mortality among elderly people with HIV in the Swiss HIV Cohort Study

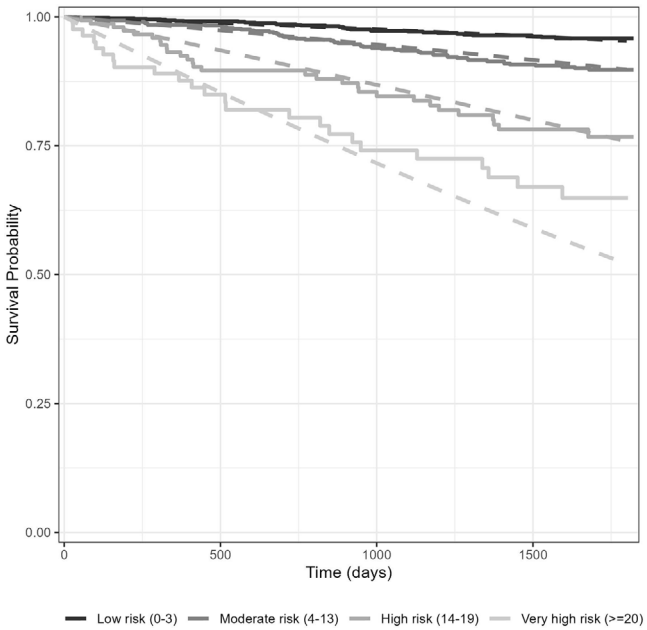
M Hentzien[1], J Frossard[1], R Kouyos[2], V Prendki[3], J Damas[4], E Hofmann[5], D Braun[6], P Schmid[7], E Bernasconi[8], S Ragozzino[9], O Efthimiou[10], C Delpierre[11], C Allavena[12], F Bani-Sadr[13], A Calmy[1]
[1]HIV/AIDS Research Unit, Geneva University Hospitals, Geneva, Switzerland; [2]Institute of Medical Virology, University of Zurich, Zurich, Switzerland; [3]Division of Internal Medicine for the Aged, Geneva University Hospitals, Geneva, Switzerland; [4]Infectious Diseases Service, University Hospital Lausanne, University of Lausanne, Lausanne, Switzerland; [5]Department of Infectious Diseases, Bern University Hospital, University of Bern, Bern, Switzerland; [6]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland; [7]Division of Infectious Diseases, Cantonal Hospital St. Gallen, St. Gallen, Switzerland; [8]Division of Infectious Diseases, Ospedale Regionale di Lugano (Ente Ospedaliero Cantonale), and University of Southern Switzerland, Lugano, Switzerland; [9]Department of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Basel, Switzerland; [10]Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland; [11]Unité Mixte de Recherche (UMR) 1027, Institut National de la Santé et de la Recherche Médicale, Toulouse, France; [12]Infectious Diseases Department, Institut National de la Santé et de la Recherche Médicale (INSERM), Equipe d'Accueil (EA) 1413, Centre Hospitalier Universitaire, Nantes, France; [13]Department of Internal Medicine, Clinical Immunology and Infectious Diseases, Reims University Hospital, Reims, France

Background: People living with HIV (PLWHIV) are ageing and adapted mortality prognostic indexes are needed in this future predominant population. The Dat'AIDS score includes age, comorbidities (non-HIV related cancer, cardiovascular diseases, estimated glomerular filtration rate, cirrhosis and anaemia), low body mass index and HIV-specific variables (CD4 cell count). It has been derived and internally validated in PLWHIV aged 60 years and over and allows the discrimination of four risk groups ranging from low to very high risk with the very high risk group having an expected 54% probability of 5-year survival. The score showed good discrimination and calibration in a single French cohort but has never been externally validated.

Methods: The Dat'AIDS score was calculated at the first follow-up after 1 January 2015 for all PLWHIV aged ≥60 years actively followed in the Swiss HIV Cohort Study. Survival times were evaluated until 1 January 2020. The score's prognostic capacity was evaluated by fitting a Cox model. Its discrimination capacity was first assessed using the Harrell C-statistic on the selected population and subgroups by gender, age, HIV viral load, CD4 and CD4 nadir strata, and then by calculating hazard ratios between adjacent risk groups. Calibration was assessed by comparing observed and expected survival.

Results: Among 2212 PLWHIV (1801 males; 411 females) included, 144 deaths were recorded. Mean CD4 cell count was 621±296 /mm^3; 92.7% had a baseline HIV viral load <50 copies/mL. Mean observed Dat'AIDS score was 5.1±6.5 and ranged from 0 to 46. Using the validation dataset, the Cox model on the Dat'AIDS score confirmed good prognostic capacities (hazard ratio 1.09; 95% CI 1.07 to 1.11; p < 0.001). Discrimination was good, as the overall Harrell C-statistic was 0.73 (95% CI 0.69 to 0.77), similar to the derivation dataset, and ranged from 0.71 to 0.78 across subgroups. Hazard ratios across pre-defined risk groups showed a higher probability of death for higher predicted risk (Table 1) as well as good calibration (Figure 1).

Conclusion: The Dat'AIDS score showed good external validity to predict the 5-year survival, with an excellent discrimination and calibration, and will allow careful clinical monitoring in the most fragile patients.



Abstract O32 – Figure 1. Calibration of the Dat'AIDS score in the validation dataset. Expected (dashed lines) versus observed (solid lines) survival probability.

Abstract O32 – Table 1. Hazard ratios across risk groups of the Dat'AIDS score.

Characteristic	HR	95% CI	p-value
Moderate (4 to 13 points) vs low risk (0 to 3 points)	2.53	1.65 to 3.88	<0.001
High (14 to 19 points) vs moderate risk (4 to 13 points)	2.55	1.63 to 3.98	<0.001
Very high (≥20 points) vs high risk (14 to 19 points)	1.72	1.00 to 2.96	0.048

HR, hazard ratio.

O33

COCOVIH study: impact of comorbidities on the over-mortality of people living with HIV

F Prevoteau du Clary[1], C Majerholc[2], D Zucman[3], J Livrozet[4], B Guigui[5], A Vallee[6], C Laurendeau[7], S Bouee[7]
[1]Centre de Santé Sexuelle, La Grave Hospital, University Hospital Toulouse, Toulouse, France; [2]Medecine Interne, University Hospital Toulouse, Toulouse, France; [3]Medecine Interne, Foch Hospital, Suresnes, France; [4]Service de Maladies Infectieuses et Tropicales, Edouard Herriot Hospital, Lyon, France; [5]Departement de Medecine Generale, Université Paris Cité, Paris, France; [6]Department of Epidemiology - Data - Biostatistics, Foch Hospital, Suresnes, France; [7]Public Health and Epidemiology, CEMKA-EVAL, Bourg La Reine, France

Background and objectives: Efficacious treatments prevent immunodeficiency and opportunistic infection in people living with HIV (PLWHIV). However, PLWHIV have more frequent other chronic conditions such as cardiovascular diseases, cancer, due to the infection itself or to side effects of antiviral treatments. Moreover, some patients remain untreated because of unknown reasons. The objectives of this study were to estimate mortality of PLWHIV and the impact of other conditions on the over-mortality.
Methods: COCOVIH draws upon anonymised records from the national health database SNDS, which includes >90% of the French population registered in CNAM (National Health Insurance Fund). A cohort of PLWHIV and age- and gender-matched controls was extracted from the French National Healthcare System Database (SNDS). PLWHIV were identified between 2006 and 2019 and followed up until 2019. The incidence of deaths was estimated and compared between both groups. Comorbidities were identified through classical algorithms used in this database (ICD-10 codes, specific drugs or procedures etc.). A Cox model was used to estimate the increased risk of deaths. Impact of comorbidities was estimated by adjusting on them.
Results: 173 712 PLWHIV and controls were followed up 8 years on average. Mean age at inception was 42 years and 66% were males. Significant increase of death rates was found in PLWHIV with a HR of 2.1 (CI 95% 2.0 to 2.2). This HR was 1.961 (CI 95% 1.898 to 2.027) for men and 2.966 (CI 95% 2.767 to 3.180) for women. The HR was higher in young PLWHIV: 3.5 (18 to 30-year-old subjects), 3.7 (30 to 40), 2.9 (40 to 50), 1.7 (50 to 60), 1.5 (60 to 70), 1.4 (70 to 80). Infectious diseases had the higher impact on the over-mortality: the HR decreased from 2.1 to 1.6 after adjusting on infectious diseases, hence an attributable risk (AR) of 50%. The other conditions were: hepatitis C (AR 30%), psychiatric diseases (AR 16%), hepatitis B (AR 6%), coronary diseases (4%), and phlebitis/pulmonary embolism (4%). Other studied diseases had ARs below 3% (Table 1).
Conclusion: HIV infection doubles the risk of death and infectious diseases explain half of this over-mortality. The relative over-mortality is higher among women and young patients.

Abstract O33 – Table 1. Hazard ratio (HR) in different categories of subjects according to age, gender and adjusted on comorbidities.

		HR	CI 95%	CI 95%
CRUDE HR	Overall	2.1	2.0	2.2
CRUDE HR	Male	1.961	1.898	2.027
CRUDE HR	Female	2.966	2.767	3.180
CRUDE HR	[18-30] years	3.517	2.704	4.574
CRUDE HR	[30-40] years	3.664	3.331	4.03
CRUDE HR	[40-50] years	2.896	2.75	3.05
CRUDE HR	[50-60] years	1.705	1.61	1.806
CRUDE HR	[60-70] years	1.483	1.375	1.600
CRUDE HR	[70-80] years	1.379	1.246	1.527
CRUDE HR	≥80 years	1.691	1.4	2.041
HR Adjusted on comorbidities	Infectious diseases	1.587	1.538	1.638
HR Adjusted on comorbidities	Hepatitis C	1.791	1.736	1.847
HR Adjusted on comorbidities	Psychiatric diseases	1.950	1.893	2.009
HR Adjusted on comorbidities	Coronary diseases	2.086	2.025	2.149
HR Adjusted on comorbidities	Hepatitis B	2.063	2.002	2.126
HR Adjusted on comorbidities	Phlebitis/pulmonary embolism	2.089	2.028	2.152
HR Adjusted on comorbidities	Peripheral artery disease	2.105	2.043	2.168
HR Adjusted on comorbidities	Kidney diseases	2.134	2.072	2.199
HR Adjusted on comorbidities	All above comorbidities (multivariate model)	1.333	1.290	1.377