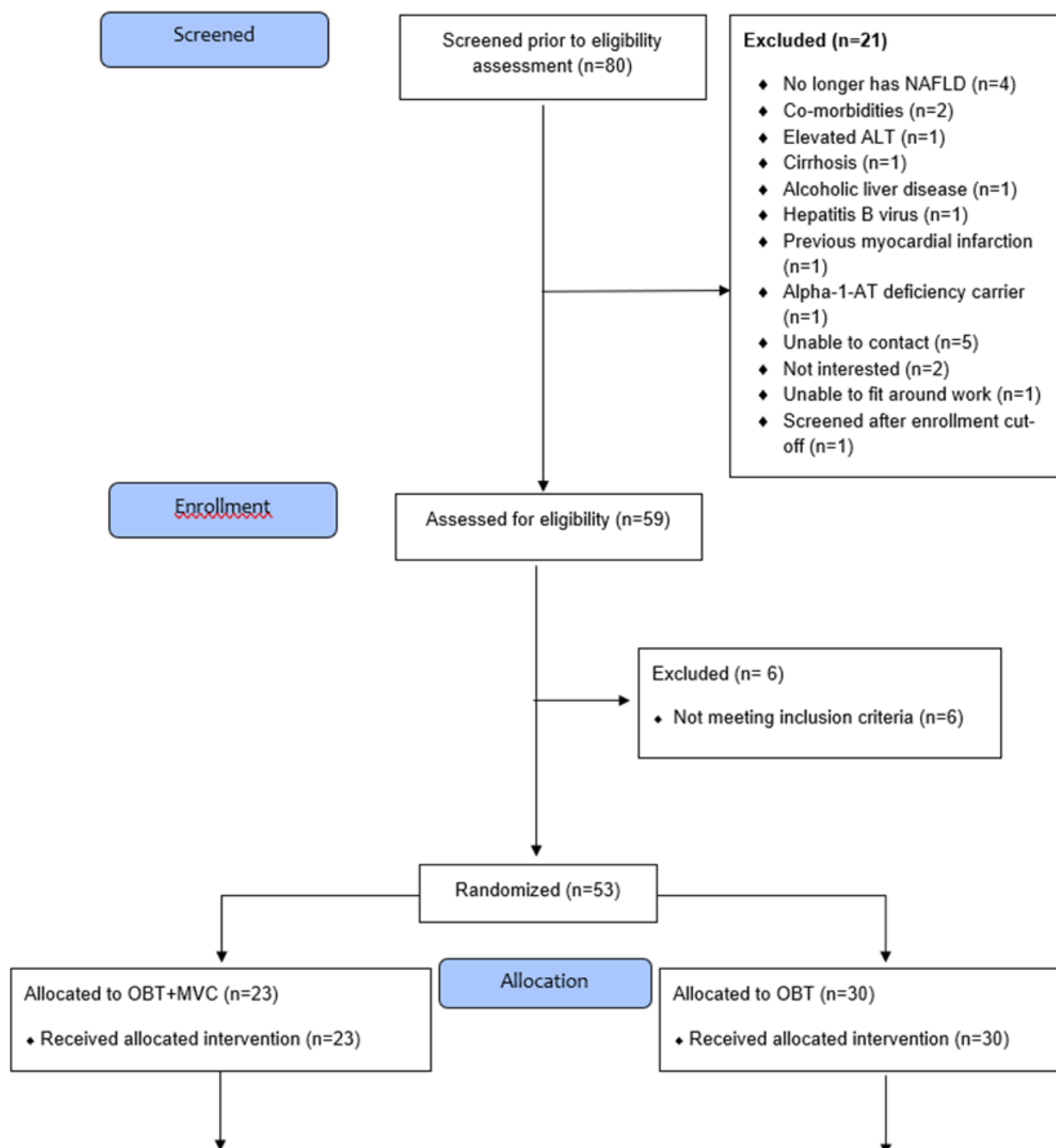
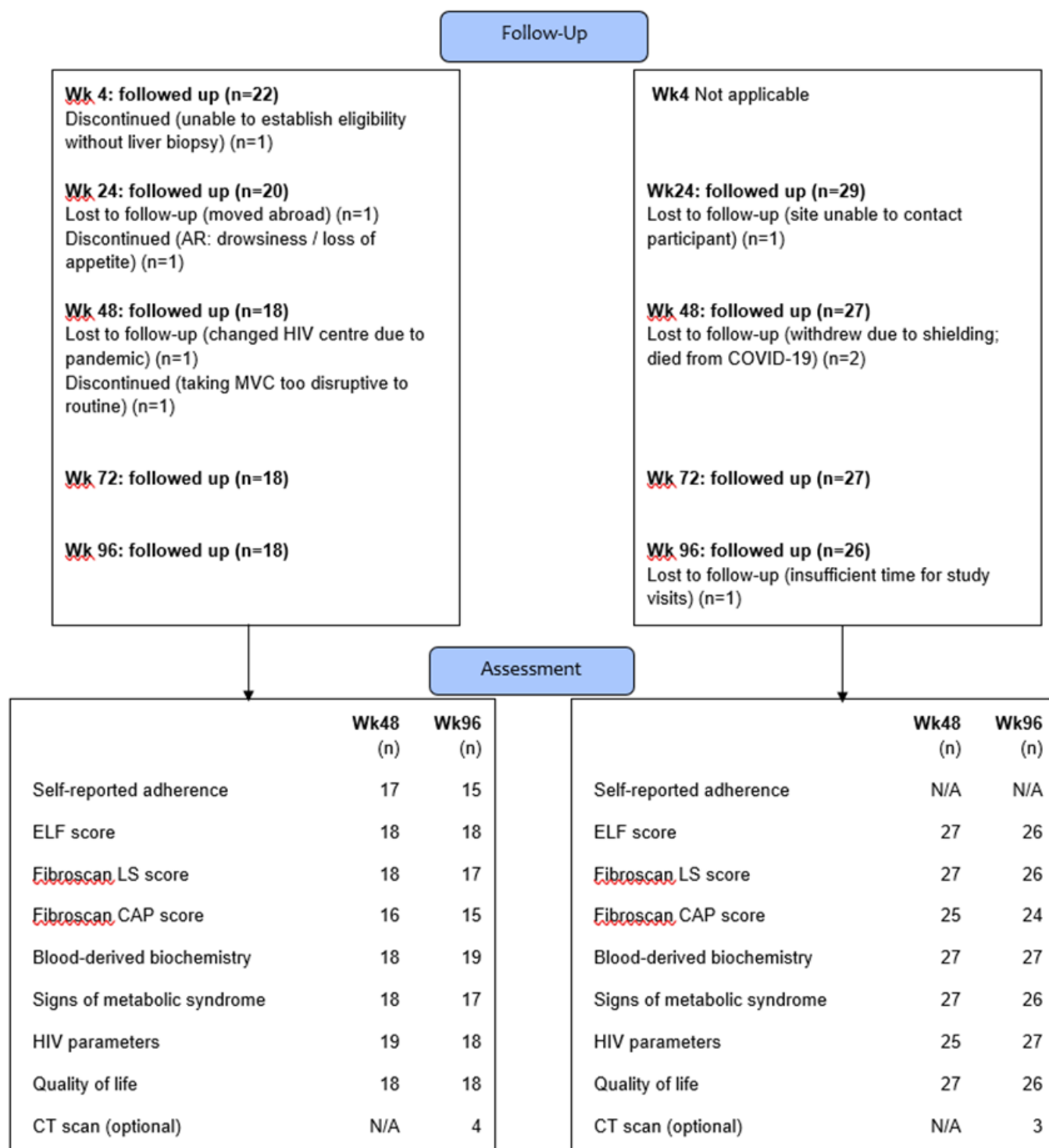


Participant flow

Figure 1. CONSORT flow diagram





Note. In the MVC+OBT group, one participant who discontinued follow up before week 48, permitted inclusion of their HIV / biochemistry parameters collected under standard care at week 48 / 96 timepoints, respectively. In the OBT group, one participant, who discontinued follow up between weeks 72 and 96, permitted inclusion of their HIV and biochemistry parameters collected under standard care, at the week 96 timepoint.

Baseline characteristics

	OBT+MVC (N=23)		OBT (N=30)		Total (N=53)	
	Med/n	IQR/%	Med/n	IQR/%	Med/n	IQR/%
Age, years	51	38 to 59	55	49 to 61	54	47 to 60
Male	20	87%	27	90%	47	89%
White	19	83%	28	93%	47	89%
BMI, Kg/m ²	28	26 to 32	31	26 to 35	30	26 to 35
Waist circumference, cm	102	95 to 113	108	96 to 116	106	95 to 115
Systolic blood pressure, mmHg	129	124 to 136	132	121 to 141	130	123 to 140
Antihypertensive therapy	4	17%	7	23%	11	21%
Lipid lowering therapy	9	39%	14	47%	23	43%
Glucose lowering therapy	2	9%	4	13%	6	11%
Duration HIV infection, years	16	12 to 23	14	9 to 22	15	11 to 22
CCR5 tropic*	12	80%	20	83%	32	82%
CD4 count, cells/mm ³	702	546 to 1007	745	514 to 1055	702	545 to 1035
HbA1c, mmol/mol	38	32 to 42	39	35 to 45	38	33 to 43
ALT, U/L	45	31 to 62	44	29 to 69	44	31 to 69
AST, U/L	32	24 to 39	33	23 to 58	32	24 to 44
GGT, U/L	45	33 to 97	41	26 to 58	42	30 to 72
Fasting LDL cholesterol, mmol/L	2.8	2.3 to 3.3	2.8	1.8 to 3.1	2.8	2.1 to 3.3
Fasting HDL cholesterol, mmol/L	1.2	1 to 1.5	1.1	0.9 to 1.2	1.1	0.9 to 1.3
Fasting Triglycerides, mmol/L	1.7	1.2 to 3	1.7	1.3 to 2.5	1.7	1.3 to 2.5
Metabolic syndrome	11	48%	16	53%	27	51%
Fibroscan median LS, kPa	6.4	4.9 to 8.9	5.7	4.5 to 7.3	6.2	4.6 to 7.8
Fibroscan CAP score, dB/m	335	235 to 349	313	267 to 347	320	267 to 347
ELF score	9.2	8.5 to 9.5	9.0	8.7 to 9.6	9.1	8.6 to 9.6
NNRTI-based cART	9	39%	8	27%	17	32%
INSTI-based cART	10	43%	18	60%	28	53%
PI-based cART	4	17%	4	13%	8	15%
TAF	5	22%	10	33%	15	28%

*Tropism testing from HIV proviral DNA sequencing was successful for 39/53 (74%)

cART combination antiretroviral therapy, CAP controlled attenuation parameter, INSTI integrase strand transfer inhibitor, LS liver stiffness, MVC maraviroc, NNRTI Non-nucleoside reverse transcriptase inhibitor, OBT optimised background therapy, PI protease inhibitor, TAF tenofovir alafenamide

Primary outcome measures

1. Proportion of eligible individuals approached who are successfully recruited using MACRO electronic case report form at week 96	100%
2. Monthly participant recruitment rate	2.9 participants / month
3. Participant retention collected through eCRF completion in the study at 48 and 96 weeks in the maraviroc and non-maraviroc assigned groups	48 weeks: 45/53 (85%, 95% CI (72%, 93%)) 96 weeks: 44/53 (83%, 95%CI (70%, 92%))
4. Proportion of participants for whom there is missing data collected by eCRF at 48 and 96 weeks in the maraviroc and non-maraviroc assigned groups	48 weeks: 6% 96 weeks: 4%
5. Proportion of participants reporting adverse reactions collected by eCRF at 48 and 96 weeks	48 weeks: (22%, 95% CI (5%, 49%)) 96 weeks: no new adverse reactions
6. Level of self-reported adherence to the study drug as collected by patient questionnaire at 48 and 96 weeks in those allocated to the maraviroc group	48 weeks & 96 weeks: 92% (SD 7%) [Adherence based on pill count as self reported adherence data not usable.]

Secondary outcome measures

Difference in change from baseline in metabolic and liver parameters for the maraviroc + OBT versus OBT group with bootstrapped 95% confidence intervals

	Week	Number of participants	Difference between groups in change from baseline	95% LCL	95% UCL
BMI, kg/m ²	48	45	-0.2	-1.0	0.6
	96	45	-0.2	-0.8	0.4
Waist circumference, cm	48	43	2.7	-5.1	11
	96	42	1.3	-7.3	9.9
CD4 cell count, cells/mm ³	48	45	70	-35	175
	96	44	-47	-135	41
Fasting glucose, mmol/L	48	44	-0.1	-0.8	0.7
	96	42	0.8	-0.4	2.1
HbA1c, mmol/mol	48	45	-2.3	-6.6	2.1
	96	45	2.5	-3.0	8.0
AST, U/L	48	43	-0.5	-7.2	6.1
	96	38	7.0	-3.4	17
ALT, U/L	48	44	-5.7	-22	10
	96	45	0.5	-19	20
Fasting triglycerides, mmol/L	48	44	0.7	-0.1	1.4
	96	46	-0.2	-1.0	0.6
Fasting LDL, mmol/L	48	40	0	-0.5	0.4
	96	41	0	-0.4	0.5
Fasting HDL, mmol/L	48	44	0	-0.2	0.2
	96	46	0.1	-0.1	0.3
Fasting HDL: total chol. ratio	48	44	0.3	-0.6	1.1
	96	46	-0.3	-1.0	0.4
Fasting total chol., mmol/L	48	44	0.1	-0.4	0.6
	96	46	0.1	-0.4	0.7
Fibroscan median LS, kPa	48	43	-1.7	-3.8	0.4
	96	41	-0.2	-2.0	1.6
Fibroscan CAP score, dB/m	48	41	-15	-56	25
	96	39	-5.8	-41	30
ELF score	48	43	0.3	0	0.6
	96	42	0.1	-0.3	0.4

LCL, lower confidence limit; UCL upper confidence limit

Difference in change from baseline in quality of life outcomes for the maraviroc + OBT versus OBT group with bootstrapped 95% confidence intervals

Outcome	Week	N	Difference between groups in changes from baseline	95% LCL	95% UCL
CLDQ-NAFLD	48	45	-0.3	-1.0	0.4
	96	44	-0.5	-1.3	0.2
SF36					
Physical function	48	45	-1.7	-11	7.6
	96	44	-1.1	-11	8.7
Role physical	48	44	1.4	-17	20
	96	44	13	-8.2	34
Role emotional	48	44	-0.6	-28	27
	96	44	-15	-36	6.9
Energy/fatigue	48	43	-20	-11	10
	96	43	-1.8	-12	7.9
Emotional wellbeing	48	43	6.0	-3.3	15
	96	43	2.6	-8.2	13
Social function	48	44	-4.1	-16	7.3
	96	44	-4.9	-19	9.0
Bodily pain	48	43	-1.3	-15	13
	96	43	-7.5	-20	5.0
General health	48	45	2.9	-7.4	13
	96	44	1.5	-6.7	9.7
WPAI:SHP					
% Work time missed	48	25	-11	-26	4.8
	96	25	-8.2	-23	6.3
% Impairment while working due to NAFLD	48	29	-2.6	-21	16
	96	30	-7.2	-21	6.7
% Overall work impairment due to NAFLD	48	25	-5.5	-27	16
	96	25	-14	-30	2.7
% Activity impairment due to NAFLD	48	43	1.3	-10	13
	96	43	0.1	-12	13

LCL, lower confidence interval, UCL upper confidence interval

CLDQ-NAFLD Chronic Liver Disease Questionnaire for NAFLD, SF36 36-item Short Form Survey, WPAI:SHP Work Productivity and Activity Impairment: Specific Health Problem

Other secondary outcome measures

- No cases of virological failure were observed. Blips, defined as a single VL 50-1000 c/ml followed by a VL<50c/ml, were seen in 5/23 (22%) and 3/30 (10%) individuals in the MVC+OBT versus OBT group respectively.
- CT liver: spleen attenuation results were excluded from the main analysis due to low numbers of participants with paired scans (n=7)

Adverse Events

Adverse Reactions (AR) to maraviroc

Participant	Type of AR	Grade	No. days post BL	AR duration (days)	Caused by MVC?	Outcome	Discontinued MVC?
A	Generalised rash	Mild	3	5	Possibly	Resolved	No
A	Vomiting	Mild	7	8	Possibly	Resolved	No
B	Dizziness	Mild	1	7	Definitely	Resolved	No
C	Worsening of restless legs	Moderate	32	557	Possibly	Resolved	Yes
D	Dizziness	Mild	2	21	Possibly	Resolved	No
E	Drowsiness	Moderate	28	182	Probably	Resolved	Yes
E	Loss appetite	Moderate	28	182	Probably	Resolved	Yes

AR Adverse Reaction, BL baseline visit, MVC maraviroc

All adverse events in the MVC+OBT group

Adverse Event	Grade	Relatedness	Outcome	Treated	SAE
Generalised rash	Mild	Possibly	Resolved	No	No
Vomit	Mild	Possibly	Resolved	No	No
Vomit	Mild	Possibly	Resolved	No	No
Urinary tract infection	Moderate	Not related	Resolved	Yes	No
Acute kidney injury	Moderate	Not related	Resolved	Yes	No
Community acquired pneumonia	Severe	Not related	Resolved	Yes	Yes
Impaired renal function (Post Acute Kidney Injury)	Moderate	Not related	Ongoing	No	No
Osteoporosis L2-4 spine	Moderate	Not related	Ongoing	Yes	No
Diarrhoea	Mild	Not related	Resolved	Yes	No
Osteoarthritis left knee	Moderate	Not related	Ongoing	Yes	No
Abdominal pain - unexplained	Mild	Not related	Resolved	Yes	No
Hearing loss right ear	Moderate	Not related	Ongoing	Yes	No
Lower respiratory tract infection	Mild	Not related	Resolved	Yes	No
Left shoulder pain	Mild	Not related	Ongoing	No	No
Headaches	Mild	Not related	Ongoing	Yes	No
Dizziness	Mild	Definite	Resolved	No	No
Diabetes mellitus Type 2	Moderate	Not related	Ongoing	No	No
Haemorrhoids	Moderate	Not related	Ongoing	No	No
Constipation	Moderate	Not related	Resolved	Yes	No
Anaemia	Mild	Not related	Resolved	No	No
Rectal Lymphogranuloma Venereum	Mild	Not related	Resolved	Yes	No
Trauma right foot	Moderate	Not related	Resolved	Yes	No
Cold	Mild	Not related	Resolved	No	No

Diarrhoea + vomiting	Mild	Not related	Resolved	No	No
Throat Gonorrhoea	Mild	Not related	Resolved	Yes	No
Worsening of restless legs	Moderate	Possibly	Resolved	No	No
Shoulder pain	Moderate	Not related	Resolved	Yes	No
Perianal fissures/pile	Moderate	Not related	Ongoing	Yes	No
Tooth infection	Moderate	Not related	Resolved	Yes	No
Rash query cause on torso	Moderate	Not related	Ongoing	Yes	No
Right shoulder pain	Moderate	Not related	Resolved	Yes	No
Perineal abscess	Moderate	Not related	Resolved	Yes	No
Left knee meniscal injury	Moderate	Not related	Ongoing	Yes	No
Vitamin D deficiency	Moderate	Not related	Ongoing	Yes	No
Left sciatica	Moderate	Not related	Resolved	No	No
Menopause symptoms	Moderate	Not related	Ongoing	No	No
Poor diabetic control	Mild	Not related	Resolved	No	No
'Cold'	Mild	Not related	Resolved	No	No
Tooth ache	Moderate	Not related	Ongoing	Yes	No
Worsening diabetic control	Moderate	Not related	Ongoing	No	No
Folliculitis	Mild	Unlikely	Resolved	No	No
Dizziness	Mild	Possibly	Resolved	No	No
Common Cold	Mild	Not related	Resolved	No	No
Peripheral neuropathy worsening in lower extremities	Moderate	Not related	Ongoing	No	No
Chronic Obstructive Pulmonary Disease	Moderate	Not related	Ongoing	Yes	No
Loss of consciousness	Moderate	Not related	Resolved	No	No
Panic Attack	Mild	Not related	Resolved	No	No
Common cold	Mild	Not related	Resolved	No	No
Bloating	Mild	Not related	Resolved	No	No
Sleeping difficulties	Mild	Not related	Ongoing	No	No
Acid reflux and vomiting	Severe	Not related	Resolved	Yes	Yes
Raised Blood Cholesterol Levels	Moderate	Not related	Ongoing	Yes	No
Raised Blood Triglyceride level	Severe	Not related	Ongoing	Yes	No
Drowsiness	Moderate	Probably	Resolved	No	No
Loss of appetite	Moderate	Probably	Resolved	No	No
Anaemia	Mild	Not related	Ongoing	No	No
Raised HbA1C	Mild	Not related	Ongoing	No	No
Raised Fasting Glucose	Mild	Not related	Ongoing	No	No
Elevated HIV viral Load	Mild	Not related	Resolved	No	No
Exacerbation of osteoarthritis	Mild	Not related	Resolved	Yes	No
Left submandibular lymphadenopathy	Mild	Not related	Unknown	No	No
Covid 19	Mild	Not related	Resolved	Yes	No
Raised Lipids	Mild	Not related	Ongoing	No	No
Cold symptoms	Mild	Not related	Resolved	Yes	No
Low mood	Moderate	Unlikely	Ongoing	No	No
Anxiety	Moderate	Unlikely	Unknown	Yes	No
Episode of Psychosis	Moderate	Not related	Resolved	Yes	No
Genital warts	Mild	Not related	Resolved	Yes	No
Flu like symptoms	Mild	Not related	Resolved	No	No
Elevated HbA1c	Mild	Not related	Ongoing	No	No

Elevated GGT	Mild	Not related	Ongoing	No	No
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All adverse events in the OBT group

Adverse Event	Grade	Relatedness	Outcome	Treated	SAE
Penile sore	Mild	Not related	Resolved	Yes	No
Raised ALT	Severe	Not related	Resolved	No	No
Impaired glucose tolerance	Moderate	Not related	Ongoing	No	No
Diverticular disease	Moderate	Not related	Ongoing	No	No
Type 2 diabetes	Moderate	Not related	Ongoing	No	No
Hyperlipidaemia	Moderate	Not related	Ongoing	Yes	No
Probable Covid-19	Moderate	Not related	Resolved	Yes	No
Sciatica	Moderate	Not related	Ongoing	Yes	No
Ankle swelling	Mild	Not related	Resolved	No	No
Poorly controlled diabetes	Moderate	Not related	Ongoing	No	No
Looser bowel motions	Moderate	Not related	Resolved	No	No
Fatigue	Moderate	Not related	Resolved	No	No
Chest infection	Moderate	Not related	Resolved	Yes	No
Query contact dermatitis	Moderate	Not related	Ongoing	Yes	No
Aubergine allergy	Moderate	Not related	Resolved	No	No
Right wrist pain	Moderate	Not related	Resolved	Yes	No
Left shoulder musculoskeletal pain	Moderate	Not related	Ongoing	Yes	No
Coryzal illness	Mild	Not related	Ongoing	Yes	No
Excision of right epididymal lesion	Moderate	Not related	Resolved	Yes	No
Worsening of asthma	Moderate	Not related	Resolved	Yes	No
Gastric reflux	Moderate	Not related	Resolved	Yes	No
Worsening of asthma	Moderate	Not related	Ongoing	Yes	No
Gastric Reflux	Moderate	Not related	Ongoing	Yes	No
Depression	Moderate	Not related	Ongoing	No	No
Chronic Obstructive Pulmonary Disorder	Moderate	Not related	Ongoing	No	No
Bronchitis	Moderate	Not related	Resolved	Yes	No
Dizziness	Moderate	Not related	Resolved	No	No
Insomnia	Moderate	Not related	Resolved	No	No
Common cold	Mild	Not related	Resolved	Yes	No
Post Vaccine syndrome	Moderate	Not related	Resolved	No	No
Common Cold	Mild	Not related	Resolved	Yes	No
Excessive sweating	Mild	Not related	Ongoing	No	No
Back Pain	Moderate	Not related	Ongoing	No	No
Rectal bleeding/Likely haemorrhoids	Mild	Not related	Ongoing	Yes	No
Hospital admission for retention of urine	Severe	Not related	Resolved	Yes	Yes
Listeria Meningitis	Severe	Not related	Resolved	Yes	Yes
Raised Creatine Kinase	Mild	Unlikely	Resolved	No	No
Worsening Liver Function Tests	Moderate	Unlikely	Ongoing	No	No
Suicidal ideation	Moderate	Not related	Resolved	Yes	Yes

Elevated HbA1c	Mild	Not related	Ongoing	No	No
Rectal polyp	Mild	Not related	Ongoing	No	No
fungal rash	Mild	Not related	Resolved	Yes	No
Raised HbA1C	Mild	Not related	Ongoing	No	No
Covid 19	Mild	Not related	Resolved	No	No
Trigger finger	Mild	Not related	Unknown	Yes	No
Possible Bechet's disease	Mild	Not related	Ongoing	Yes	No
Anxiety	Mild	Not related	Ongoing	No	No
Cold	Mild	Not related	Resolved	Yes	No
Raised cholesterol	Mild	Not related	Ongoing	No	No
Neurosyphilis	Mild	Not related	Resolved	Yes	No
Microscopic haematuria on urine dip	Mild	Not related	Ongoing	No	No
Elevated Triglycerides	Mild	Not related	Ongoing	No	No
Community Acquired Pneumonia - Covid 19	Severe	Not related	Unknown	Yes	Yes
Shingles eye socket	Mild	Not related	Resolved	Yes	No
Lichen sclerosis	Mild	Not related	Ongoing	Yes	No
Covid 19	Moderate	Not related	Resolved	No	No
HIV viral Load detectable	Mild	Not related	Resolved	No	No
Chest pain radiating down left arm	Mild	Not related	Ongoing	Yes	No
Bell's Palsy	Mild	Not related	Ongoing	Yes	No
Cough/Chest Infection	Moderate	Not related	Resolved	Yes	No
Fever and Flu like symptoms	Moderate	Not related	Resolved	No	No
Chest Infection	Moderate	Not related	Resolved	Yes	No