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Long-term Follow-up Report

Version 1.0

27. Mar 2024

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Revision History

Version	Author	Date	Reason for Revision
0.1	W Stöhr	24-Apr-2023	First full draft
0.2	W Stöhr	24-Apr-2023	Minor corrections by Sarah Pett
0.3	W Stöhr	24-Mar-2024	Changes accepted; added SOC for SAEs; clarified that no notable pregnancy outcomes; added background.
0.4	W Stöhr	27-Mar-2024	Reviewed again by Sarah Pett. All changes accepted; added table with characteristics at randomisation.
1.0	W Stöhr	27-Mar-2024	Made version 0.4 to version 1.0

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1 BACKGROUND

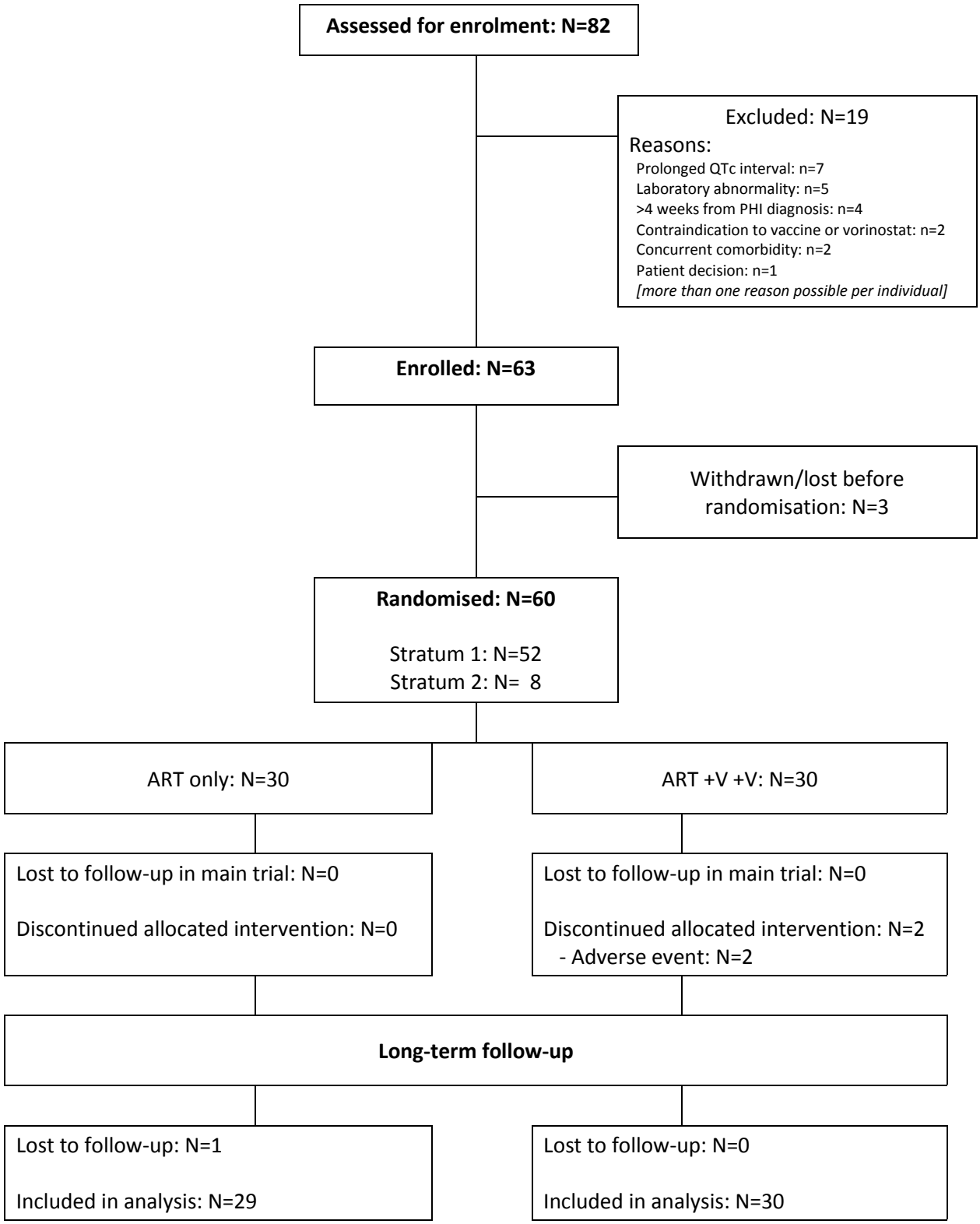
Long-term Follow-up

All participants were to be followed annually for 5 years following the end of the interventional phase of the study, through retrospective data collection from participant medical records.

The purpose of long-term follow-up was to annually gather safety information specifically for vorinostat – as the mechanism of action of vorinostat is gene modification this may carry unforeseen long-term consequences beyond the timeframe of the main study. Specific safety related questions asked included:

- Any Notable Events:
  - Vaccine related events
  - Cancers
  - Pregnancy outcome in female partners – reportable within 1 year of completing the course of vorinostat
- Any event that meets the following criteria:
  - Results in death
  - Is life-threatening
  - Requires hospitalisation or prolongation of existing hospitalisation
  - Results in persistent or significant disability or incapacity
  - Consists of a congenital anomaly or birth defect
  - Other important medical condition
- AIDS-defining illness (ADI) or serious non-AIDS (SNA) events (Diabetes mellitus, Renal Failure, Cardiovascular disease (CAD) i.e. Myocardial Infarction, Heart Failure, Angina, Stroke and Thromboembolic events including Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

2 CONSORT FLOW DIAGRAM



Control: ART only
Intervention: ART +V +V: ART plus ChAdV63.HIVconsv prime and MVA.HIVconsv boost vaccines; followed by a 28-day course of vorinostat (10 doses in total).

3 DESCRIPTION OF LONG-TERM FOLLOW-UP

Table 1. Description of long-term follow-up

	ART only N=30	**ART +V+V** N=30	**Total** N=60
Any annual CRF received?			
no	1 (3%)	0 (0%)	1 (2%)
yes	29 (97%)	30 (100%)	59 (98%)
# of annual CRFs			
0	1 (3%)	0 (0%)	1 (2%)
2	0 (0%)	2 (7%)	2 (3%)
3	3 (10%)	0 (0%)	3 (5%)
4	2 (7%)	2 (7%)	4 (7%)
5	24 (80%)	26 (87%)	50 (83%)
Annual form 1 received			
no	1 (3%)	1 (3%)	2 (3%)
yes	29 (97%)	29 (97%)	58 (97%)
Annual form 2 received			
no	1 (3%)	2 (7%)	3 (5%)
yes	29 (97%)	28 (93%)	57 (95%)
Annual form 3 received			
no	1 (3%)	1 (3%)	2 (3%)
yes	29 (97%)	29 (97%)	58 (97%)
Annual form 4 received			
no	5 (17%)	1 (3%)	6 (10%)
yes	25 (83%)	29 (97%)	54 (90%)
Annual form 5 received			
no	5 (17%)	3 (10%)	8 (13%)
yes	25 (83%)	27 (90%)	52 (87%)
Last follow-up last participant	20/09/2022	22/11/2022	22/11/2022
Months from PR-18* to last annual follow-up	61 (60, 65)	61 (60, 66)	61 (60, 65)
Months from randomisation to last annual follow-up	66 (64, 69)	66 (64, 70)	66 (64, 70)

Note: * PR-18 was the last study visit in main RIVER trial. Results are N (%) or median (IQR).

4 CHARACTERISTICS AT RANDOMISATION

Table 2. Participants' characteristics at randomisation

	ART only N=29	**ART +V+V** N=30	**Total** N=59
Age (years)	31 (30, 38)	35 (28, 44)	32 (28, 40)
Sex			
Male	29 (100%)	30 (100%)	59 (100%)
Ethnicity			
White	16 (55%)	26 (87%)	42 (71%)
Asian	1 (3%)	1 (3%)	2 (3%)
Hispanic/Latino	2 (7%)	2 (7%)	4 (7%)
Black	4 (14%)	0 (0%)	4 (7%)
Mixed	5 (17%)	1 (3%)	6 (10%)
Other	1 (3%)	0 (0%)	1 (2%)
Mode of HIV infection			
MSM	25 (86%)	29 (97%)	54 (92%)
MSW	1 (3%)	1 (3%)	2 (3%)
unknown	1 (3%)	0 (0%)	1 (2%)
MSM+IDU	2 (7%)	0 (0%)	2 (3%)
CD4 at randomisation (cells/mm^3)	712 (561, 844)	710 (579, 759)	712 (566, 790)
HIV RNA at randomisation (copies/ml)			
<50	28 (97%)	30 (100%)	58 (98%)
50 - <200	1 (3%)	0 (0%)	1 (2%)
eGFR (ml/min/1.73 m^2)	105 (99, 119)	111 (105, 120)	110 (100, 120)
Weeks since PHI diagnosis (at enrolment)			
<=1 week	1 (3%)	0 (0%)	1 (2%)
>1 - 2 weeks	3 (10%)	3 (10%)	6 (10%)
>2 - 3 weeks	7 (24%)	7 (23%)	14 (24%)
>3 - 4 weeks	14 (48%)	16 (53%)	30 (51%)
>4 weeks	4 (14%)	4 (13%)	8 (14%)
Weeks since PHI diagnosis (at randomisation)	28 (27, 31)	28 (27, 34)	28 (27, 34)

Note: Results are number (%) or median (IQR). MSM=men who have sex with men; MSW=men who have sex with women; IDU=injection drug use. PHI=Primary HIV infection.

5 ADVERSE EVENTS

5.1 SAES & NOTABLE EVENTS

Table 3. Summary of serious adverse events and notable events reported during long-term follow-up

	ART only N=29	ART +V+V N=30	Total N=59
SAE/SAR/SUSAR or notable event			
no	25 (86%)	25 (83%)	50 (85%)
yes	4 (14%)	5 (17%)	9 (15%)
SAE/SAR/SUSAR			
no	25 (86%)	28 (93%)	53 (90%)
yes	4 (14%)	2 (7%)	6 (10%)
SAE			
no	25 (86%)	29 (97%)	54 (92%)
yes	4 (14%)	1 (3%)	5 (8%)
Number of SAEs per participant			
0	25 (86%)	29 (97%)	54 (92%)
1	3 (10%)	1 (3%)	4 (7%)
2	1 (3%)	0 (0%)	1 (2%)
SAR			
no	29 (100%)	30 (100%)	59 (100%)
SUSAR			
no	29 (100%)	29 (97%)	58 (98%)
yes	0 (0%)	1 (3%)	1 (2%)
Notable cancer event			
no	29 (100%)	28 (93%)	57 (97%)
yes	0 (0%)	2 (7%)	2 (3%)
Notable vaccine event			
no	29 (100%)	28 (93%)	57 (97%)
yes	0 (0%)	2 (7%)	2 (3%)
Notable pregnancy outcome			
no	29 (100%)	30 (100%)	59 (100%)

Table 4. Line listing of SAEs / SUSARs reported during long-term follow-up

Participant ID	Randomisation arm	SAE type	Why serious?	Body system (MedDRA SOC)	Diagnosis (MedDRA LLT)	Status
R03302P	ART +V+V	SAE	Hospitalisation	Infections and Infestations	Appendicitis	Resolved
R03604S	ART +V+V	SUSAR	Other	Neoplasms benign, malignant and unspecified	Hodgkin's lymphoma [a]	Resolved
R03618N	ART only	SAE	Hospitalisation	Infections and Infestations	Quinsy	Resolved
R04405W	ART only	SAE	Hospitalisation	Psychiatric disorders	Psychosis	Ongoing
R04405W	ART only	SAE	Hospitalisation	Injury, poisoning and procedural complications	Drug overdose	Resolved
R05501S	ART only	SAE	Hospitalisation	Injury, poisoning and procedural complications	Other, multiple and fractures of lower limb	Resolved
R05504A	ART only	SAE	Hospitalisation	Infections and Infestations	Parainfluenza virus infection	Resolved

Table 5. Line listing of notable events reported during long-term follow-up

Participant ID	Randomisation arm	Notable event type	Diagnosis (MedDRA LLT)	SAE or SUSAR?
R03604S	ART +V+V	Cancer	Hodgkin's lymphoma [a]	yes
R04403H	ART +V+V	Cancer	Melanoma right arm	no
R01204T	ART +V+V	Vaccine-related	Diabetes mellitus type I	no
R05519R	ART +V+V	Vaccine-related	Grave's or Basedow's disease	no

Note: [a] same event

5.2 OTHER ADVERSE EVENTS

Table 6. Summary of other events reported during long-term follow-up

	ART only N=29	**ART +V+V** N=30	**Total** N=59
Ever other adverse event			
no	29 (100%)	29 (97%)	58 (98%)
yes	0 (0%)	1 (3%)	1 (2%)
Ever diabetes?			
no	29 (100%)	29 (97%)	58 (98%)
yes	0 (0%)	1 (3%) [a]	1 (2%)
Ever renal event?			
no	29 (100%)	30 (100%)	59 (100%)
Ever Cardiovascular disease (CAD)?			
no	29 (100%)	30 (100%)	59 (100%)
Ever myocardial event?			
no	29 (100%)	30 (100%)	59 (100%)
Ever heart failure?			
no	29 (100%)	30 (100%)	59 (100%)
Ever angina?			
no	29 (100%)	30 (100%)	59 (100%)
Ever stroke?			
no	29 (100%)	30 (100%)	59 (100%)
Ever thromboembolic event?			
no	29 (100%)	30 (100%)	59 (100%)
Ever AIDS defining illness?			
no	29 (100%)	30 (100%)	59 (100%)

Note: [a] also a notable event, see table above

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