Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Full author list (with full names and degrees):
Shahin Lockman, M.D., Michael D. Hughes, Ph.D., James McIntyre, M.D., Yu Zheng, M.S., Tsungai Chipato, M.D., Francesca Conradie, M.B., Ch.B., Fred Sawe, M.D., Aida Asmelash, M.D., Mina C. Hosseinipour, M.D., Lerato Mohapi, M.D., Elizabeth Stringer, M.D., Rosie Mngqibisa, B.A., Abraham Siika, M.D., Diana Atwine, M.D., James Hakim, M.D., Douglas Shaffer, M.D., Cecilia Kanyama, M.D., Kara Wools-Kaloustian, M.D., Robert A. Salata, M.D., Evelyn Hogg, B.S., Beverly Alston-Smith, M.D., Ann Walawander, M.A., Eva Purcelle-Smith, Pharm.D.,* Susan Eshleman, M.D., James Rooney, M.D., Sibtain Rahim, M.D., John W. Mellors, M.D., Robert T. Schooley, M.D., and Judith S. Currier, M.D.

Acknowledgements and study team:

Beth Zwickl, Cissy Kityo Mutuluuza, Christine Kaseba, Charles C. Maponga, Heather Watts, Daniel Kuritzkes, Thomas B. Campbell, Lynn Kidd-Freeman, Monica Carten, Jane Hitti, Mary Marovich, Peter N. Mugyenyi, Sandra Rwambuya, Ian M. Sanne, Beverly Putnam, Cheryl Marcus, Carolyn Wester, Robin DiFrancesco, Elias Halvas, Annie Beddison, Sandra Lehrman, Francesca Aweeka, Betty Dong, Peter Ndhleni Ziba, Michael S. Saag, William C. Holmes, Scott M. Hammer.

Ms. Elizabeth Dangaiso – University of Zimbabwe-Parirenyatwa; Harare, Zimbabwe CRS (Site 30313) CTU Grant #U01AI069436

Mohammed S Rassool, MD and Josephine Tsotsotetsi - WITS HIV Research Group; Johannesburg, South Africa (Site 11101) CTU Grant #U01 AI69463-03

KMRI/Walter Reed Project Clinical Research Center; Kericho, Kenya (Site 12501) CTU Grant #IAAY1AI8374.

Charity Potani and Regina Mwausegha- UNC Project, Kamuzu Central Hospital; Lilongwe (Site 12001) CTU Grant #5 U01 AI069518

Dr. Fatima Laher and Mrs. Reinet Hen-Boisen; Soweto, South Africa ACTG CRS (Site 12301) CTU Grant # AI69453

Kipruto Kirwa and Agnes Nzioka- Moi University; Eldoret, Kenya CRS (Site 12601) CONTRACT No. AACTG. 50.5208.07, the United States Military HIV Research Program

Dr. Margaret Chibowa and Dr. Jeffrey Stringer- Centre for Infectious Disease Research, Kalingalinga; Lusaka, Zambia (Site 12801) CTU Grant #5U01AI069455-03 and # 3U01AI32775-13S5

Kagiso Sebina, Kinuthia Mburu, and Tebogo Kakhu (Gaborone Unit), Banno Moorad (Molepolole Unit), Botswana (Site 12701) CTU Grant #5U01AI069456-03

Cissy Kityo and Sandra Rwambuya, JCRC; Kampala, Uganda (Site 12401) CTU Grant #AI-069501

Drs. Farida Amod, Umesh Lalloo, and Sandy Pillay, University of Natal; Durban, South Africa (11201) CTU Grant # AI69426

SDAC (Xin Sun) FSTRF (Apsara Nair, Laura M. Smith, James Tutko, Christine Lee), Pharmaceutical Affairs Branch (Lynette Purdue, Elaine Ferguson, Ana Martinez), SSS Ops (Yvette Delph, Nikki Gettinger, Linda Berman, Linda Boone), DAIDS (Bola Adedeji).

Full inclusion/exclusion criteria for OCTANE enrollment

Inclusion criteria:

1. HIV-1 infection, documented by a rapid HIV test or any licensed ELISA test kit, and confirmed by either an ELISA, an IFA, a Western blot, or plasma HIV-1 RNA at the study-associated, DAIDS-approved laboratory. Discordant confirmatory results should be followed by plasma HIV-1 RNA determination at a DAIDS-approved laboratory for quality control purposes.

2 Women age ≥ 13 years, or who have attained the minimum age of consent, as defined by the local IRB, whichever is greater.

3 CD4 cell count <200 cells/mm^3 obtained within 90 days prior to study entry from any DAIDS-approved laboratory.

4. For participants in Trial 1, prior sdNVP MTCT prophylaxis.

   NOTE: Receipt of sdNVP more than once for any given pregnancy or in >1 pregnancy is not exclusionary.

5. For participants in Trial 1, documentation of all prior sdNVP MTCT prophylaxis.

   NOTE: Documentation of each course of prophylaxis may be the current participant report, post partum participant report, documentation of observed dose, results of post partum plasma, or any combination of the above.

6. For participants in Trial 1, the last sdNVP MTCT prophylaxis course must have been completed at least 6 months prior to study entry.

7. Plasma HIV-1 RNA quantitation using the Roche Amplicor HIV-1 Monitor Assay (version 1.5, standard not ultra sensitive) within 45 days prior to study entry from any DAIDS-approved laboratory.

8. The following laboratory values obtained within 45 days prior to study entry:
   - Absolute neutrophil count (ANC) ≥750/mm^3
   - Hemoglobin ≥7.0 g/dL
   - Platelet count ≥50,000/mm^3
   - AST (SGOT), ALT (SGPT), and alkaline phosphatase ≤2.5 x ULN
   - Total bilirubin ≤2.5 x ULN

9. Evidence of normal renal function within 45 days prior to study entry as determined by an estimated creatinine clearance of ≥60 mL/min using the Cockgroft-Gault formula

10. For participants of reproductive potential (defined as girls who have reached menarche or women who have not been post-menopausal for at least 24 consecutive months, i.e. who have had menses within the preceding 24 months), or have not undergone surgical sterilization (e.g. hysterectomy, or bilateral oophorectomy, salpingotomy, or tubal ligation) must have a negative serum or urine pregnancy test within 45 days prior to study entry.

11. For participants of reproductive potential, willingness to abstain from participation in a conception process (e.g. active attempt to become pregnant or in vitro fertilization). If participating in sexual activity that could lead to pregnancy, participants must use at least one reliable form of contraception listed below while receiving protocol-specified medications and for 6 weeks after stopping the medication.

    1) Condoms (male or female) with or without a spermicidal agent (condoms are recommended because their appropriate use is the only contraception method effective for preventing HIV transmission).
    2) Diaphragm or cervical cap with spermicide
    3) IUD
    4) Hormonal-based contraception

    Interactions of study drugs with estrogen-based contraceptives: the effectiveness of estrogen-based contraceptives when co-administered with LPV/RTV or NVP is unknown; LPV/RTV and NVP decrease plasma levels of ethinyl estradiol; therefore, estrogen-based contraceptives are not reliable for women receiving LPV/RTV and NVP, and an alternative contraception method must be used.

    NOTE: Participants who are not of reproductive potential (girls who have not reached menarche, women who have been post-menopausal for at least 24 consecutive months) girls and women who are not participating in sexual activity that could lead to pregnancy, or women who have undergone surgical sterilization, (e.g. hysterectomy, or bilateral oophorectomy, salpingotomy, or tubal ligation) are eligible without requiring the use of contraceptives. Participant report is acceptable documentation for menopause, hysterectomy, bilateral oophorectomy or tubal ligation, or sexual activity.

12. Karnofsky performance score ≥70 on at least one occasion within 45 days prior to study entry.

13. Ability and willingness of participant or legal guardian/representative to give informed consent.

14. Intent to remain in current geographical area of residence for the duration of study.

15. Willingness to attend study visits as required by the study.

Exclusion criteria:

1. Receipt of any ARV (including for purposes of occupational or sexual post-exposure prophylaxis or MTCT prevention), except as noted below, at any time prior to study entry.

   NOTE A: For participants in either trial, receipt of up to 10 weeks (cumulative) of ZDV alone, for MTCT prophylaxis or other purpose, which was completed at least 6 months prior to study entry, is not exclusionary.

   NOTE B: For participants in Trial 1, exposure to NVP, as described in 4.1.4 is not exclusionary.

2. For participants in Trial 2, any prior exposure to NVP.

3. For participants in Trial 1, any prior exposure to NVP other than the use of sdNVP for prevention of MTCT.

4. Use of systemic cancer chemotherapy, systemic investigational agents, immunomodulators (growth factors, systemic corticosteroids, HIV vaccines, immune globulin, interleukins, interferons) or rifampin within 30 days prior to study entry.

5. Breastfeeding or pregnancy.

6. Known allergy/sensitivity to study drugs or their formulations.

7. Any condition, including active drug or alcohol use or dependence that, in the opinion of the investigator, would interfere with adherence to study requirements.

8. Serious illness requiring systemic treatment and/or hospitalization until participant either completes therapy or is clinically stable on therapy, in the opinion of the investigator, for at least 30 days prior to study entry.

9. Receipt of tuberculosis (TB) treatment within 30 days prior to study entry.

10. Use of any prohibited medications listed in section 5.4.2 within 30 days prior to study entry.

11. Current compulsory detention (involuntary incarceration) in a correctional facility, prison, or jail for legal reasons or in a medical facility for treatment of either a psychiatric or physical (e.g., infectious disease) illness.

OCTANE Trial 1 Accrual by Site and Arm

Site	NVP (N=121)	LPV/r (N=120)	All Trial 1 (N=241)
Johannesburg (Witwatersrand), South Africa	13 (11%)	16 (13%)	29 (12%)
Johannesburg (Soweto), South Africa	12 (10%)	12 (10%)	24 (10%)
Durban, South Africa	10 (8%)	8 (7%)	18 (7%)
Lilongwe, Malawi	14 (12%)	10 (8%)	24 (10%)
Kampala, Uganda	8 (7%)	9 (8%)	17 (7%)
Kericho, Kenya	13 (11%)	14 (12%)	27 (11%)
Eldoret, Kenya	8 (7%)	9 (8%)	17 (7%)
Gaborone and Molepolole, Botswana	13 (11%)	12 (10%)	25 (10%)
Lusaka, Zambia	12 (10%)	12 (10%)	24 (10%)
Harare, Zimbabwe	18 (15%)	18 (15%)	36 (15%)

OCTANE Trial 1: Number and Percent of Subjects with Adherence >=95%, by Arm

Week	Drug Name	NVP (N=121)	LPV/RTV(N=120)
4	LPV/RTV	N/A	96/115 (83%)
	NVP	87/115 (76%)	N/A
	Truvada	96/115 (83%)	98/117 (84%)
12	LPV/RTV	N/A	90/115 (78%)
	NVP	83/104 (80%)	N/A
	Truvada	89/104 (86%)	100/116 (86%)
24	LPV/RTV	N/A	90/113 (80%)
	NVP	82/ 93 (88%)	N/A
	Truvada	85/ 95 (89%)	88/112 (79%)
48	LPV/RTV	N/A	75/ 95 (79%)
	NVP	64/ 73 (88%)	N/A
	Truvada	64/ 73 (88%)	79/ 95 (83%)
72	LPV/RTV	N/A	56/ 69 (81%)
	NVP	44/ 50 (88%)	N/A
	Truvada	47/ 50 (94%)	50/ 67 (75%)
96	LPV/RTV	N/A	35/ 42 (83%)
	NVP	26/ 29 (90%)	N/A
	Truvada	26/ 29 (90%)	34/ 41 (83%)

OCTANE Trial 1: Number and Percent of Subjects who Did Not Report Missing Dose in Prior Month, by Arm

Week	Drug Name	NVP (N=121)	LPV/RTV(N=120)
4	LPV/RTV	N/A	96/117 (82%)
	NVP	98/117 (84%)	N/A
	Truvada	102/117 (87%)	99/117 (85%)
12	LPV/RTV	N/A	103/119 (87%)
	NVP	96/107 (90%)	N/A
	Truvada	99/107 (93%)	108/119 (91%)
24	LPV/RTV	N/A	109/117 (93%)
	NVP	86/95 (91%)	N/A
	Truvada	89/95 (94%)	109/117 (93%)
48	LPV/RTV	N/A	88/98 (90%)
	NVP	66/74 (89%)	N/A
	Truvada	69/74 (93%)	89/98 (91%)
72	LPV/RTV	N/A	64/70 (91%)
	NVP	49/52 (94%)	N/A
	Truvada	50/52 (96%)	66/70 (94%)
96	LPV/RTV	N/A	41/43 (95%)
	NVP	31/32 (97%)	N/A
	Truvada	31/32 (97%)	41/43 (95%)

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Analysis of primary endpoint rates in NVP and LPV/r arms, Trial 1, with the addition of 18 months since sdNVP as time category

In a post-hoc analysis of the proportions of women in each treatment arm experiencing a primary endpoint among those starting ART 6 to <12, 12 to <18, 18 to <24, and ≥24 months after sdNVP exposure:

Time since most recent sdNVP dose, months	Cumulative proportions experiencing virologic failure or death, NVP arm (Number of primary endpoints/ Number of subjects)	Cumulative proportions experiencing virologic failure or death, LPV/r arm (Number of primary endpoints/ Number of subjects)	Hazard ratio (95% CI)
6 to < 12	37% (15/41)	3% (1/37)	15.8 (2.1-121)
12 to <18	29% (7/24)	12% (3/26)	3.0 (0.8-12)
18 to <24	27% (6/22)	12% (3/26)	2.6 (0.6-11)
≥24	12% (4/34)	10% (3/31)	1.3 (0.3-6.1)