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Supporting Online Material for

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

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Materials and methods

In April 2008, a CAPRISA 004 participant was found to be co-enrolled in another microbicide trial (*1*). A detailed investigation of all enrolled women at both study sites identified 135 women who had co-enrolled in CAPRISA 004 while still in follow-up in another microbicide trial and another 50 women who had participated in another microbicide trial within 12 months prior to CAPRISA 004. These 185 women, all from the urban clinic, were withdrawn from the study. Their exclusion from the primary analysis was based on criteria objectively assessed in all participants based on information collected prior to randomization and irrespective of treatment assignment, which is consistent with International Conference on Harmonization guidelines(*2*). Of the remaining 11 women not included in the primary analysis, one was under-age at enrolment, eight were in the window period of HIV infection at enrollment, and two had no post-randomization follow-up. The remaining 889 women were included in the analysis.

References

S1. S. S. Abdool Karim, Inadvertent enrollment of ineligible participants in CAPRISA 004. Available from: www.caprisa.org (accessed June 2010). *CAPRISA Newsletter* **7**, 2 (2008).

S2. ICH E9 Expert Working Group, Statistical principles for clinical trials (ICH E9): an introductory note on an international guideline. *Stat Med* **18**, 1903-1942 (1999).

Table: Comparison of baseline and follow-up cumulative renal, bone and hepatic laboratory parameters and severity grading according to the Division of AIDS Table for Grading Adult and Pediatric Adverse Events, 2004 in the CAPRISA 004 tenofovir gel trial

Parameter	Number of participants		Within normal limits		Grade 1 (mild)		Grade 2 (moderate)		Grade 3 (severe)		Grade 4 (potentially life-threatening)	
	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo
Low total serum calcium (mmol/L)												
Baseline	443	443	435	428	8	14	0	0	0	0	0	0
Month 3	408	402	397	395	10	5	0	2	0	0	0	0
Month 12	364	340	362	336	0	1	0	1	0	0	0	0
Month 24	115	109	115	108	0	1	0	0	0	0	0	0
Exit	426	431	423	429	3	1	0	0	0	0	0	0
Elevated creatinine (umol/L)												
Baseline	443	444	442	442	1	2	0	0	0	0	0	0
Month 3	408	402	407	402	1	0	0	0	0	0	0	0
Month 12	364	340	363	339	1	1	0	0	0	0	0	0
Month 24	115	109	115	109	0	0	0	0	0	0	0	0
Exit	426	431	425	431	0	0	1	0	0	0	0	0
Low serum phosphate (mmol/L)												
Baseline	443	443	420	429	0	0	21	12	2	2	0	0
Month 3	408	402	376	382	0	0	25	15	7	5	0	0
Month 12	364	340	348	324	0	0	13	15	3	1	0	0
Month 24	115	109	108	106	0	0	5	3	2	0	0	0
Exit	426	431	402	405	2	0	19	22	3	4	0	0
Low serum potassium (mmol/L)												
Baseline	443	444	377	387	60	53	4	1	0	0	0	0
Month 3	408	402	355	360	53	41	0	1	0	0	0	0
Month 12	364	340	324	305	38	33	2	1	0	0	0	0
Month 24	114	108	110	104	3	4	1	0	0	0	0	0
Exit	426	431	404	412	22	18	0	0	0	0	0	0
Low serum sodium (mmol/L)												
Baseline	443	443	415	422	27	18	0	0	0	1	0	0
Month 3	408	402	388	389	19	13	0	0	0	0	0	0
Month 12	364	340	348	331	16	8	0	0	0	0	0	0
Month 24	115	109	112	105	3	3	0	0	0	0	0	0

Parameter	Number of participants		Within normal limits		Grade 1 (mild)		Grade 2 (moderate)		Grade 3 (severe)		Grade 4 (potentially life-threatening)	
	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo
Exit	426	431	411	414	14	17	0	0	1	0	0	0
High serum sodium, (mmol/L)												
Baseline	443	443	415	422	1	2	0	0	0	0	0	0
Month 3	408	402	388	389	1	0	0	0	0	0	0	0
Month 12	364	340	348	331	0	0	0	0	0	0	0	1
Month 24	115	109	112	105	0	1	0	0	0	0	0	0
Exit	426	431	411	414	0	0	0	0	0	0	0	0
Low serum albumin (g/L)												
Baseline	443	444	433	429	10	14	0	0	0	1	0	0
Month 3	414	418	399	408	15	10	0	0	0	0	0	0
Month 12	365	341	350	332	14	6	1	3	0	0	0	0
Month 24	116	109	109	107	6	0	1	2	0	0	0	0
Exit	426	431	397	402	23	25	6	4	0	0	0	0
Elevated alkaline phosphatase (IU/L)												
Baseline	443	444	407	420	36	24	0	0	0	0	0	0
Month 3	414	418	382	393	32	24	0	1	0	0	0	0
Month 12	365	341	341	333	24	8	0	0	0	0	0	0
Month 24	116	109	111	104	5	5	0	0	0	0	0	0
Exit	426	431	393	413	33	18	0	0	0	0	0	0
Elevated total bilirubin (umol/L)												
Baseline	443	443	434	439	9	4	0	0	0	0	0	0
Month 3	414	418	405	406	8	10	1	1	0	1	0	0
Month 12	365	341	357	333	8	8	0	0	0	0	0	0
Month 24	116	109	114	108	2	1	0	0	0	0	0	0
Exit	426	431	421	426	5	5	0	0	0	0	0	0
Elevated Aspartate aminotransferase (AST) (IU/L)												
Baseline	443	444	438	436	3	6	1	2	1	0	0	0
Month 3	414	418	406	403	7	12	1	2	0	1	0	0
Month 12	365	341	361	335	3	3	1	1	0	1	0	1
Month 24	116	109	111	106	4	1	0	2	0	0	1	0
Exit	426	431	414	419	10	10	1	1	0	1	1	0

Parameter	Number of participants		Within normal limits		Grade 1 (mild)		Grade 2 (moderate)		Grade 3 (severe)		Grade 4 (potentially life-threatening)	
	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo
Elevated Alanine transaminase (ALT) (IU/L)												
Baseline	443	444	435	433	6	9	1	2	0	0	1	0
Month 3	414	418	397	400	14	11	2	5	1	2	0	0
Month 12	365	341	356	328	7	9	0	1	1	2	1	1
Month 24	116	109	110	106	4	2	1	1	0	0	1	0
Exit	426	431	416	415	7	12	2	4	0	0	1	0