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Incidence and Predictors of Pregnancy in Women Enrolled in Large Multi-National HIV Treatment Trials of the AIDS Clinical Trials Group

Short Title: Incident Pregnancy and Predictors in Large ACTG Trials

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BACKGROUND

In 2020, 53% of all people living with HIV globally were women and girls [1]. It is vital that we obtain high-quality data on the efficacy and safety of new drugs in pregnant women with HIV [2, 3] and there is growing consensus that it is neither acceptable nor equitable to exclude women of reproductive potential from interventional trials [4, 5]. Unfortunately, women are often under-represented in clinical trials in part because trials have traditionally required confirmation that women of reproductive potential do not wish to become pregnant and will use protocol-mandated forms of contraception throughout the trial. Incident pregnancy during trial participation occurs for a range of reasons including evolving desire (by the participant or her partner or family) for children over time or inconsistent contraception use [6]. Pregnancy intent may be ambivalent [7]; women may become pregnant on-study regardless of pregnancy intent expressed at trial enrollment, which can have implications for the participant's health and for study power (if women who become pregnant stop study drug or study participation) and for interpretation of data. It is thus important to understand more about the frequency and predictors of pregnancy occurring among women enrolled in interventional trials. Despite the importance of this issue, few studies have evaluated the frequency of pregnancy in women participating in HIV clinical drug trials [6, 8-11].

We sought to determine the incidence and predictors of pregnancy in people participating in completed multi-national HIV treatment trials conducted by the AIDS Clinical Trials Group (ACTG) that enrolled people of reproductive potential and required use of contraception for study participation.

METHODS

Objectives:

Among people of reproductive potential living with HIV who participated in ACTG trials that mandated that participants intend not to become pregnant and required use of effective contraception during study treatment, to 1) determine the incidence of pregnancy occurring on study treatment, and 2) explore baseline predictors of occurrence of pregnancy on study treatment.

Study and data selection

We included completed multi-national HIV antiretroviral treatment trials conducted by the ACTG between 2005 and 2019 that enrolled at least 100 females living with HIV; enrolled in more than one country; followed for at least 6 months; and included the following inclusion criteria at the time of enrollment, for female participants of reproductive potential:

1. Do not intend to become pregnant during the study treatment period
2. Agree to use effective contraception (type stipulated by each protocol) while on-study. Acceptable methods recommended across all the selected studies were condoms, diaphragm or cervical cap, intrauterine device (IUD) and hormonal options (oral or injectable, vaginal rings or implants).

Trials that were conducted in only one country were excluded to improve the generalizability of findings.

ACTG trials used language similar to the following text, with regard to pregnancy intention and contraception inclusion/exclusion criteria for women of reproductive potential: “Participants must be willing to refrain from participating in a conception process (i.e., active attempt to become pregnant or in vitro fertilization) and, if participating in sexual activity that could lead to pregnancy, the participant/partner must use reliable form(s) of contraception.” Reproductive potential was typically defined in ACTG studies as women who have reached menarche and who have not been post-menopausal for at least 24 consecutive months (i.e., who have had menses within the preceding 24 months), and have not undergone surgical sterilization (e.g. hysterectomy, bilateral oophorectomy, salpingotomy, or tubal ligation).

Data extraction and analysis

Four ACTG trials met criteria and were selected for this analysis: A5175 (enrolled May 2005 – Jul 2007), A5208 (enrolled Nov 2005 – Feb 2008), A5234 (enrolled Apr 2009 – Sep 2011) and A5273 (enrolled Mar 2012 – Oct 2013), [12-15]. For the selected clinical trials, the study population for this analysis included all females aged 18 - 55 years (inclusive) at study entry who were of reproductive potential (all were ≥18 years of age with no upper age limit, although some protocols permitted enrollment of younger women, according to local IRB guidelines).

We extracted individual participant-level data for the study population in each of the selected clinical trials which included occurrence and dates of pregnancy during study participation and key potential predictors at study entry of incident pregnancy on study-provided antiretroviral treatment (ART), including age, country of enrollment, CD4 count, HIV-1 RNA, and randomized study-provided ART regimen. These potential predictors were selected because they

either have been associated with incidence of pregnancy in observational studies of people with HIV (e.g. CD4 count, HIV-1 RNA), or might be expected to be associated (e.g. antiretroviral regimen) [16]. Other potential predictors of interest, such as education, marital status, obstetric history, contraception methods used and other potential drug interactions were not consistently available by participants across trials. Date of pregnancy was defined as estimated date of conception based on the best available method (last menstrual period, ultrasound, maternal physical examination, or a combination of these measurements).

Follow-up after discontinuation of study-provided ART was excluded as contraceptive use was stipulated by protocols for the period of study-provided ART and a maximum of 12 weeks thereafter. If a woman had more than one pregnancy reported during follow-up, then only the first pregnancy on study-provided ART was included in the analysis. The Kaplan-Meier method was used to estimate the cumulative proportion of females who became pregnant over time from start of study-provided ART with censoring at the time of discontinuation of study-provided ART. Logrank tests and multivariable proportional hazards models were used to evaluate the potential predictors of incident pregnancy on study-provided ART.

RESULTS

Overview of selected trials

Table 1 summarizes key aspects of the trials that were included. Of note, the A5175 eligibility criteria and informed consent required women of reproductive potential to agree to use at least one reliable method of contraception when receiving study-provided ART that did not include EFV and two reliable methods of contraception while receiving EFV-containing study-provided

ART (if participating in sexual activity that could lead to pregnancy). These trials all enrolled participants in low- and middle-income countries (LMICs); A5175 also enrolled participants in the United States.

Participant characteristics

Table 2 summarizes key characteristics of the 1,626 females of age ≤55 years and of reproductive potential who were included in this analysis: 583 from A5175, 717 from A5208, 111 from A5234, and 215 from A5273.

Females in the A5175 and A5208 trials of first-line ART were younger (median 32 and 33 years, respectively) than in the A5234 and the A5273 trials of second-line ART (39 and 36 years, respectively). Participants enrolled in 14 countries; the majority (78%) enrolled in Africa, while 8% enrolled in Asia, 8% in South America and 6% in North America. South Africa (25%), Malawi (15%) and Zimbabwe (13%) accounted for more than half of the total participants included in this analysis. The median baseline CD4 count was 150 cells/uL (median was below 200 cells/uL in all studies) and median baseline viral load was 93,200 copies/mL; median baseline viral load was higher for women in the A5175 and A5208 first-line ART trials (90,774 and 142,194 copies/mL, respectively) and lower for women in the A5234 and A5273 trials of second-line ART (19,091 and 27,704 copies/mL, respectively).

The antiretroviral study agents used varied between protocols as summarized in Table 2. The majority (900 or 55%) took a protease inhibitor and 1,077 (67%) women took TDF/FTC as part of their regimen.

Pregnancy incidence on study

The median duration of follow-up on study-provided ART through to either first pregnancy or end of study, whichever occurred first, was 28 months, ranging from 12 months in A5234 to 42 months in A5175. The total follow-up time on study-provided ART was 6458 person-years. In total, 143 (9%) women became pregnant during study follow-up (Table 3). We found an overall pregnancy incidence of 2.2 pregnancies/100 person-years. The largest number of pregnancies occurred in the A5208 trial: 74 (10%) of 717 women became pregnant during 2508 person-years of follow-up on study-provided ART (incidence = 3.0 pregnancies/100 person-years). Fifty-eight (10%) of 583 women in the A5175 trial became pregnant during 3221 person-years of follow-up on study-provided ART (incidence = 1.8 pregnancies/100 person-years). In this study, the observed pregnancy incidence was higher for women randomized to ATV-containing ART (2.3 pregnancies per 100 person-years) than among women randomized to the two EFV-containing regimens (1.5 pregnancies per 100 person-years). Ten (5%) of 215 women became pregnant in A5273 (incidence = 1.8 pregnancies/100 person-years) over 544 person-years of follow-up on study-provided ART and only one (1%) of 111 women in A5234 became pregnant during 185 person-years of follow-up on study-provided ART (incidence = 0.5 pregnancies/100 person-years). The incidence rate of pregnancy was similar over time following enrolment, regardless of trial, study arm, or treatment duration (i.e., the incidence of pregnancy did not appear to change significantly over the course of follow-up) (Figure 1a).

Predictors of incident pregnancy

Only A5175 and A5208 had a sufficient number of pregnancies occurring during follow-up on study-provided ART to allow analysis of baseline predictors of pregnancy. We present analyses of pregnancy predictors separately for these two studies, given the different ART regimens used, some differences in contraceptive requirement, and differences in study location and calendar years of study conduct.

Potential baseline predictors evaluated in univariable and multivariable analyses were age, country, CD4 count, HIV-1 RNA. Because of the difference in contraception requirements in A5175 for EFV- versus ATV-containing regimens, we adjusted in both studies for type of regimen (EFV- versus ATV-containing in A5175 and NVP- versus LPV/r-containing in A5208). The strongest predictor of pregnancy occurring while on study-provided ART was younger age, with women <25 years experiencing the highest pregnancy incidence, and women 45 years or older the lowest pregnancy incidence (Figures 1b, S1and S2). In A5175, but not A5208, there was significant variation among countries in pregnancy incidence (Figures S3 and S4). In A5175, which was conducted across multiple continents, pregnancy incidence was highest in the African continent compared to South America, North America and Asia (Figure S5). Baseline CD4 and HIV-1 RNA were not associated with pregnancy incidence in either trial. In multivariable analysis including baseline age, type of regimen and country as predictor variables, younger age remained the strongest predictor of incident pregnancy ($p<0.0001$ adjusted for country and ART regimen type for both A5715 and A5208). In A5175 (but not in A5208), ART regimen type was also significantly associated with pregnancy incidence in multivariable analysis after controlling for country and age ($p=0.046$), with higher pregnancy incidence in women randomized to atazanavir-based than EFV-based ART (but not in univariate analysis).

DISCUSSION

In this analysis of individual-participant data from completed large ACTG HIV clinical trials where pregnancy intent was exclusionary, we found an overall pregnancy incidence of 2.2 pregnancies/100 person-years, with a fairly stable incidence of pregnancy over time following enrollment.

A previously-completed meta-analysis of pregnancies occurring in eight HIV prevention microbicide trials reported a much higher pregnancy incidence rate of 23 per 100 woman-years [9] compared to our finding, although the incidence in the different microbicide studies analyzed ranged from 4 – 64 per 100 woman-years. Serris et al noted a pregnancy incidence of 8/100 person-years in women with HIV taking part in clinical trials in sub-Saharan Africa, which was similar to pregnancy incidence in women with HIV in non-research settings in the same region [8].

Younger age was the strongest and most consistent predictor of incident pregnancy in our analysis. This has been reported in other HIV clinical trials conducted both in Africa [10] and the US [11], with younger women more likely to become pregnant on study. Cohn et al found in the ACTG A5257 randomized trial of HIV treatment regimens that both at ART initiation and 96 weeks post initiation, about 40% of all participants expressed a desire to have children in the future, and being younger than 30 years, having a post high-school degree and having no children were predictors of desire to have children [17].

Our findings highlight that pregnancies should be anticipated in clinical trial participants, regardless of contraception requirements. Incorporation of plans for incident pregnancy during initial study design could lead to greater trial participation by women, and could also result in earlier availability of pregnancy data for drugs. For example, participants who become pregnant could be given the opportunity to consent to stay on study drug and take part in a pre-planned nested study of pregnancy pharmacokinetics and safety, as long as non-clinical data raised no safety concerns and dosing and safety in non-pregnant persons has already been established [2]. When study drug must be discontinued in participants who become pregnant, these participants would ideally still be followed on-study to assess pregnancy and neonatal outcomes.

Our findings also suggest that protocol-mandated contraception requirements may not always be effective at achieving their goal; these requirements can also infringe upon a woman's autonomy in choosing whether to take part in research and "often are out of proportion to the actual risks of study drugs or interventions" [18]. Trial contraception requirements should ideally be based upon the best assessment of maternal and fetal risk and benefit in an individual study.

In our analysis, pregnancy incidence was highest in the African continent compared to Asia and the Americas. In the A5175 trial which enrolled participants from 9 different countries (55% of participants enrolling in sub–Saharan African countries, Table 2), we found evidence of variation in pregnancy incidence between countries (and between continents) in multivariable analysis, when controlling for participant's age and randomized treatment. Women in sub-Saharan African nations have had higher fertility rates in general [19] possibly due to a desire for a large family

size [20], and were also found to have higher pregnancy incidence in another analysis of HIV clinical trials [6].

We found significantly higher incidence of pregnancy in women on ATV-based ART compared to EFV-ART in the A5175 study. This could be explained by stricter contraceptive requirements (two methods including a barrier method) and related messaging in the informed consent which were only stipulated in the A5175 trial for EFV based regimens. This approach to contraception and counseling could be considered in trials in which pregnancy should be avoided.

Our analysis had several limitations. The first was the relatively small number of trials included (four). The predictors of pregnancy were the same in each study and in an analysis pooled across studies (with age being the most important predictor and baseline CD4 count and HIV-1 RNA not being significant predictors). Another limitation is that other possible predictors of interest (such as marital status, obstetric history, income, educational status, and contraceptive methods) were not available for individual participants in all studies, nor was information about evolving pregnancy desires collected. In addition, the analysis included women who were 45 years and above (who could have been perimenopausal) and the trials were conducted during a period in which participants had less access to long-acting reversible contraception and started ART with lower CD4 and higher HIV RNA counts. Findings may not be applicable to other geographic, cultural or socioeconomic settings.

In summary, we found a substantial rate of pregnancies during study treatment among women who agreed at enrollment to refrain from becoming pregnant and to use adequate contraception during the trial, particularly among younger women. Although pregnancies are likely to occur in

trials that enroll women of reproductive age, it is imperative that women be included in clinical trials of drugs that women are likely to use. It is also important to avoid stringent pregnancy intention and contraceptive enrollment criteria in order to facilitate enrollment of women in trials and generation of pregnancy safety information sooner, unless there is specific concern from non-clinical or other data about risk of exposure in pregnancy to a particular drug.

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Supplementary Figures S1-S5-http://links.lww.com/QAI/C129

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Figure 1a: Proportion of women becoming pregnant during follow-up by study.

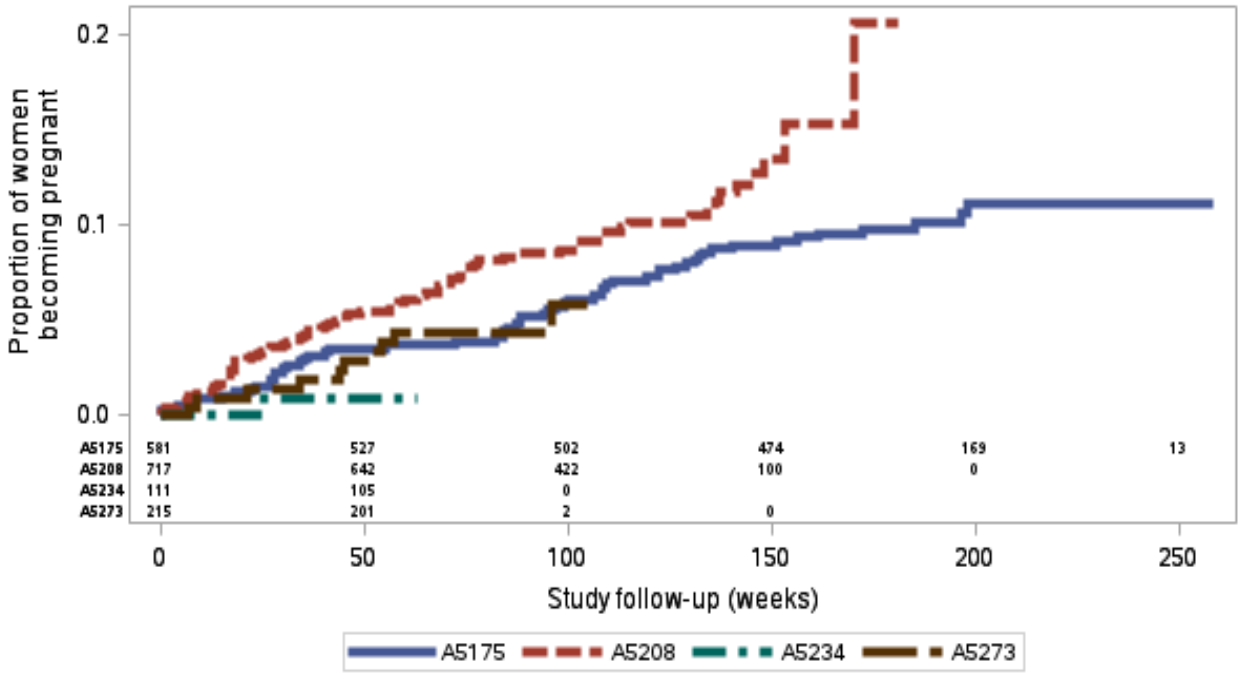

Figure Legend: The Kaplan-Meier analysis shows the proportion of women becoming pregnant over the duration on study treatment in the four clinical trials. In A5208 (red); women were censored at time of change of status to not of reproductive potential or end of study treatment. A5175 (blue), A5273 (brown) & A5234 (green); women were censored at the end of study treatment.

Table 1: Key features of trials selected for inclusion in analysis.

Studies	**# Women of reproductive potential / overall sample size**	**Location**	**Study Treatment durations**	**Study agents**	**Contraceptive requirements**
A5175 (Phase IV, Efficacy of PI- and NNRTI-based ART for in treatment-naïve adults) (NCT00084136)	583 / 1571 Enrollment period: May 2005 - Jul 2007	US & Non-US	Up to 130 weeks	3TC/ZDV + EFV FTC+DDI+ATV FTC/TDF + EFV	At least one reliable method of contraception while receiving study drug (two if on EFV), and till 6 weeks after stopping

A5208 (Phase III, efficacy of PI-based versus NNRTI 3-drug ART in treatment-naïve women) (NCT00089505)	717 / 745 Enrollment period: Nov 2005 - Feb 2008	Non-US	Up to 132 weeks	FTC/TDF + NVP FTC/TDF + LPV/RTV	At least one reliable method of contraception while receiving study drug, and till 6 weeks after stopping
A5234 (Trial of Modified Directly Observed Therapy versus self-administered therapy in individuals experiencing 1st	111 / 529 Enrollment period: Apr 2009 – Sep 2011	Non-US	Up to 52 weeks	FTC/TDF + LPV/RTV TDF + ZDV+ LPV/RTV	At least one reliable method of contraception while receiving study drug, and till 6 weeks after stopping

virologic failure on NNRTI-based ART) (NCT00608569)					
A5273 (Phase III virologic efficacy trial LPV/r-based ART in individuals failing NNRTI-based first-line ART) (NCT01352715)	215 / 515 Enrollment period: Mar 2012 – Oct 2013	Non-US	Up to 52 weeks	LPV/RTV +RAL LPV/RTV + NRTI (FTC/TDF, ABC/3TC/ZDV, or ABC/3TC)	At least one reliable method of contraception while receiving study drug, and till 12 weeks after stopping

Note: The A5175 study had the most frequent pregnancy testing (monthly for the 1st 6months). A5208, A5234 and A5273 had pregnancy testing at baseline and subsequently when suspected/indicated (monthly for women switching to EFV-ART in the A5208 study)

Abbreviations: 3TC (Lamivudine), EFV (Efavirenz), FTC (Emtricitabine), ATV (Atazanavir), TDF (Tenofovir), NVP (Nevirapine), DDI (Didanosine), ZDV (Zidovudine), LPV (Lopinavir), RTV (Ritonavir), RAL (Raltegravir), ABC (Abacavir), NRTI (Nucleoside Reverse Transcriptase Inhibitor)

Table 2: Key participant baseline demographic and HIV characteristics and ART regimens, by trial.

		Total (N=1626)	**A5175 (N=583)**	**A5208 (N=717)**	**A5234 (N=111)**	**A5273 (N=215)**
Age	Median (Q1, Q3)	33 (29, 39)	32 (27, 38)	33 (28, 37)	39 (34, 44)	36 (32, 41)
	≥18, <25	148 (9.1%)	67 (11.5%)	68 (9.5%)	4 (3.6%)	9 (4.2%)
	≥25, <35	774 (47.6%)	303 (52.0%)	370 (51.6%)	29 (26.1%)	72 (33.5%)
	≥35, <45	569 (35.0%)	172 (29.5%)	237 (33.1%)	56 (50.5%)	104 (48.4%)
	≥45, ≤55	135 (8.3%)	41 (7.0%)	42 (5.9%)	22 (19.8%)	30 (14.0%)
Race	Asian	127 (7.8%)	97 (16.6%)	0 (0.0%)	0 (0.0%)	30 (14.0%)
	Black or African American	1,380 (84.9%)	403 (69.1%)	717 (100.0%)	78 (70.3%)	182 (84.7%)
	White	41 (2.5%)	39 (6.7%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
	American Indian	1 (0.1%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Other	73 (4.5%)	39 (6.7%)	0 (0.0%)	31 (27.9%)	3 (1.4%)

		Total (N=1626)	A5175 (N=583)	A5208 (N=717)	A5234 (N=111)	A5273 (N=215)
	More than One Race	2 (0.1%)	2 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Unknown	2 (0.1%)	2 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ethnicity	Hispanic or Latino	112 (6.9%)	67 (11.5%)	5 (0.7%)	34 (30.6%)	6 (2.8%)
	Not Hispanic or Latino	1,402 (86.2%)	466 (79.9%)	650 (90.7%)	77 (69.4%)	209 (97.2%)
	Unknown	112 (6.9%)	50 (8.6%)	62 (8.6%)	0 (0.0%)	0 (0.0%)
Country	Botswana	88 (5.4%)	0 (0.0%)	87 (12.1%)	1 (0.9%)	0 (0.0%)
	Kenya	164 (10.1%)	0 (0.0%)	132 (18.4%)	0 (0.0%)	32 (14.9%)
	Malawi	250 (15.4%)	134 (23.0%)	62 (8.6%)	0 (0.0%)	54 (25.1%)
	Peru	70 (4.3%)	37 (6.3%)	0 (0.0%)	30 (27.0%)	3 (1.4%)
	South Africa	411 (25.3%)	133 (22.8%)	204 (28.5%)	15 (13.5%)	59 (27.4%)
	United States	20 (1.2%)	20 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Zimbabwe	208 (12.8%)	59 (10.1%)	114 (15.9%)	11 (9.9%)	24 (11.2%)

		Total (N=1626)	A5175 (N=583)	A5208 (N=717)	A5234 (N=111)	A5273 (N=215)
	Zambia	66 (4.1%)	0 (0.0%)	63 (8.8%)	3 (2.7%)	0 (0.0%)
	Uganda	70 (4.3%)	0 (0.0%)	55 (7.7%)	15 (13.5%)	0 (0.0%)
	Brazil	64 (3.9%)	59 (10.1%)	0 (0.0%)	4 (3.6%)	1 (0.5%)
	Haiti	76 (4.7%)	44 (7.5%)	0 (0.0%)	32 (28.8%)	0 (0.0%)
	India	90 (5.5%)	61 (10.5%)	0 (0.0%)	0 (0.0%)	29 (13.5%)
	Thailand	37 (2.3%)	36 (6.2%)	0 (0.0%)	0 (0.0%)	1 (0.5%)
	Tanzania	12 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	12 (5.6%)
Continent	Africa	1,269 (78.0%)	326 (55.9%)	717 (100.0%)	45 (40.5%)	181 (84.2%)
	South America	134 (8.2%)	96 (16.5%)	0 (0.0%)	34 (30.6%)	4 (1.9%)
	North America	96 (5.9%)	64 (11.0%)	0 (0.0%)	32 (28.8%)	0 (0.0%)
	Asia	127 (7.8%)	97 (16.6%)	0 (0.0%)	0 (0.0%)	30 (14.0%)
HIV-RNA (copies)	Median (Q1, Q3)	93,200 (27,800, 264,389)	90,774 (31,365, 226,000)	142,194 (54,929, 349,170)	19,091 (7,720, 80,915)	27,704 (7,271, 102,934)

		Total (N=1626)	A5175 (N=583)	A5208 (N=717)	A5234 (N=111)	A5273 (N=215)
CD4 (cells/uL)	Median (Q1, Q3)	150.0 (90.0, 214)	192 (127.0, 250.0)	127 (82, 173)	157 (88, 274.0)	160 (55, 295)
ARV	ATV	204 (12.5%)	204 (35.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	EFV	379 (23.3%)	379 (65.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	LPV/RTV	577 (35.5%)	0 (0.0%)	361 (50.3%)	111 (100.0%)	105 (48.8%)
	NVP	356 (21.9%)	0 (0.0%)	356 (49.7%)	0 (0.0%)	0 (0.0%)
	RAL	110 (6.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	110 (51.2%)
NRTI	3TC, ZDV	217 (14.3%)	194 (33.3%)	0 (0.0%)	0 (0.0%)	23 (22.1%)
	ABC,3TC	13 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13 (12.5%)
	ABC,3TC, ZDV	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
	DDI+FTC	204 (13.5%)	204 (35.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	TDF, FTC	177 (11.7%)	0 (0.0%)	2 (0.3%)	111 (100.0%)	64 (61.5%)
	TDF, FTC, ZDV	3 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.9%)
	TRV	900 (59.4%)	185 (31.7%)	715 (99.7%)	0 (0.0%)	0 (0.0%)

		Total (N=1626)	A5175 (N=583)	A5208 (N=717)	A5234 (N=111)	A5273 (N=215)
	# Missing	111	0	0	0	111
On RAL	yes	110 (6.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	110 (51.2%)
	no	1,516 (93.2%)	583 (100.0%)	717 (100.0%)	111 (100.0%)	105 (48.8%)

Abbreviations: ARV (Antiretrovirals) ATV (Atazanavir), ABC (Abacavir), CBV (Combivir), DDI (Didanosine), EFV (Efavirenz), FTC (Emtricitabine), LPV/RTV (Lopinavir/Ritonavir), 3TC (Lamivudine), NVP (Nevirapine), NRTI (Nucleoside Reverse Transcriptase Inhibitor), RAL (Raltegravir), TDF (Tenofovir disoproxil fumarate), TRV (Truvada), ZDV (Zidovudine)

Table 3.: Incidence rate of pregnancy.

	N	Number of events	Total person years	Rate per 100 person year (95% CI)
All	1626	143	6457.92	2.21(1.87-2.61)
A5175	583	58	3221.22	1.80(1.37-2.33)
A5175: EFV arm	379	33	2142.13	1.54(1.06-2.16)
A5175: Non-EFV arm (ATV)	204	25	1079.10	2.32(1.5-3.42)
A5208	717	74	2508.35	2.95(2.32-3.7)
A5234	111	1	184.74	0.54(0.01-3.02)
A5273	215	10	543.61	1.84(0.88-3.38)

Table 3 shows the pregnancy incidence in the four clinical trials (A5175, A5208, A5234 & A5273). The A5175 was further analyzed per arms (EFV arm versus non-EFV arm [ATV]).