Final Report
17 October 1996 through
31 March 1999

The HIV Postexposure Prophylaxis Registry

Registry of Health-Care Workers Receiving
Postexposure Prophylaxis
After Occupational Exposure to
Human Immunodeficiency Virus

The HIV Postexposure Prophylaxis Registry is jointly sponsored by:

The Centers for Disease Control and Prevention
Glaxo Wellcome Inc **Merck & Co., Inc.**

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Acknowledgement

The HIV Postexposure Registry Sponsors and Coordinating Center Staff wish to thank the health-care providers and health-care workers who participated in the Registry and have made the program a success. As providers, we greatly appreciate your interest in this important public health issue and for taking the time from busy schedules to provide us with the information required to complete the program.

The Centers for Disease Control and Prevention
Glaxo Wellcome Inc.
Merck & Company, Inc.

PharmaResearch Corporation

POLICY FOR PRESENTATION OF DATA

The sponsors of the HIV Postexposure Prophylaxis Registry (Registry) encourage the responsible sharing of the information contained in this report with health-care providers who might benefit from it. In an attempt to standardize dissemination and interpretation of the data from this final Registry report, the HIV Postexposure Prophylaxis Registry consensus statement must be included with any presentation of these data, including emphasis on the limitations of information collected from voluntary registries such as this one.

The HIV Postexposure Prophylaxis Registry reported aggregate data; no site-specific information is presented in this report or in any other presentation of these data. Institutions are not identified as participants without their expressed consent.

Please contact the Centers For Disease Control and Prevention, HIV Hospital Infections Branch at 404-639-6425 with any questions.

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FOREWORD

The HIV Postexposure Prophylaxis (PEP) Registry, as you may know, has been in existence since October 1996. This program has been very successful thanks to your participation. Because of health-care professionals such as you, the goals and objectives of the Registry have been met. The Registry data showed that health-care workers for whom HIV PEP was prescribed reported widely recognized toxicities to these treatments and suggest that careful counseling regarding drug toxicity may be necessary to improve compliance with PEP among exposed health-care workers. Continuation of the Registry now appears redundant with other ongoing surveillance programs. Therefore, on December 31, 1998 the Registry was closed to new enrollments.

Closure of the Registry does not mean interest in this important public health issue has also ended. There are other surveillance activities currently in existence which will continue to monitor occupational exposures to HIV, as well as, other bloodborne pathogens. The NaSH (National Surveillance System for Hospital Health Care Workers) is one such program. (For information on this program contact Centers for Disease Control and Prevention at 404-639-6425.)

This final report describes the cumulative data from the HIV PEP Registry surveillance of health-care workers who received PEP following an occupational HIV exposure. The report includes information collected from initiation of the Registry on October 17, 1996 through March 31, 1999. The Registry was closed to new enrollments on December 31, 1998, with collection of follow-up information through March 31, 1999.

The HIV PEP Registry Advisory Committee was established to review data and Registry activities. The members of the Advisory Committee are listed alphabetically below.

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1. SUMMARY

From October 17, 1996 through March 31, 1999, the HIV Postexposure Prophylaxis (PEP) Registry included data on 492 prospectively enrolled health-care workers (HCWs). The enrolled HCWs were 71% female, with an overall median age of 37 years. The median time from exposure to treatment was 1.75 hours. The majority (63%) of PEP regimens were composed of three or more drugs.

Of the 449 HCWs for whom 4-6 week follow-up data were available, the median therapy duration for at least one of the PEP drugs prescribed was 28 days. Forty-three percent (n=195) of HCWs completed all of the drugs in their PEP regimens as initially prescribed. Forty-four percent (n=197) of HCWs discontinued all PEP drugs and did not complete a PEP regimen. Nine percent (n=39) discontinued one or more drugs and/or modified drug dosage and/or added a drug but did complete a course of PEP. The remaining 4% (n=16) completed modified regimens, which did not involve discontinuation of any of the drugs in the original regimen. Of the 197 HCWs who discontinued all PEP drugs, 48% (n=95) did so because the source patient tested HIV negative.

Overall, 76% of HCWs with 4-6 week follow-up reported some symptoms or adverse events. The most frequently cited symptoms were nausea (57%), fatigue/malaise (38%), headache (18%), vomiting (16%), and diarrhea (14%). Only 8% of HCWs were reported to have laboratory abnormalities, but review of the reported abnormalities revealed that most were not significant. Of those HCWs who discontinued all PEP drugs, 50% cited symptoms or adverse events as a reason for discontinuation. The median time from start of PEP to onset of the five most frequently reported symptoms was 3 to 4 days. Serious adverse events were reported to the Registry for six HCWs; all but one of these resolved by the 6-month follow-up visit.

The tables, beginning on page 7, summarize the prospective cohort of HCWs enrolled in the Registry. The tables include information on demographics, treatment regimens, with reasons for modification/discontinuation, number of hours from HIV exposure to initiation of PEP, and duration of treatment. Also included is a frequency table of the most commonly reported adverse experiences at 4-6 week follow-up and a summary of serious adverse events.

There was one episode of a late occurring HIV infection, which could not be confirmed as being related to the occupational exposure nor could the possibility of other risk factors be ruled out.

Limitations of these data due to potential biases in data collected by voluntary registries should be recognized.

Consensus Statement

Cumulative data were reviewed by the HIV PEP Registry Advisory Committee (Committee). The data included observations from the HIV PEP reports to the Registry. The Committee concluded that the goals of the Registry were met and that there are other programs in place which can provide further information on this important public health issue. Through the Registry the Committee was able to observe the antiretroviral treatment regimens used for HIV PEP following an occupational exposure to HIV, in addition to identifying the adverse events HCWs exhibited while on these regimens. For this reason it is reasonable for the Registry to be closed and a final report of the findings summarized.

It is the consensus of the Committee that there is not adequate power in this study to draw any definitive conclusions on rates of occurrence of toxicity nor is it possible to correlate toxicity with any particular drug. The Registry data may, in fact, reflect over-reporting of occurrences of toxicity, since there appeared to be a trend toward more reporting of adverse events when enrollment occurred later than 3 days following the exposure. Even though side effects were reported frequently, these limited data suggest that toxicity was not generally severe/serious. (See section 3.4 for description of serious and severe). In addition, the reported adverse events appeared to be consistent with those listed in the product labeling (package insert) for each respective agent.

2. INTRODUCTION

In 1996, information suggesting that zidovudine (ZDV) HIV PEP may reduce the risk of HIV transmission following an occupational exposure to HIV-infected blood prompted a federal interagency working group*, with expert consultation, to develop an update [1] to a previous statement on management of occupational exposure to HIV [2]. In a case-control study among HCWs, the use of ZDV after percutaneous exposure to HIV-infected blood reduced the risk of HIV infection by approximately 79% [3]. Other studies have shown that administration of ZDV to HIV-infected mothers and their infants may have contributed to a reduction in perinatal HIV transmission [4,5]. In some animal studies, PEP also prevented or ameliorated retroviral infection [6,7]. However, failures of ZDV PEP have been known to occur [8].

In the June 7, 1996 *Morbidity and Mortality Weekly Report*, the U.S. Public Health Service recommended the use of combinations of antiretroviral agents as PEP following certain occupational HIV exposures [1]. It was anticipated that many hundreds, and possibly thousands, of HCWs might take these drugs following occupational HIV exposures. Except for ZDV, there is little information on the use or toxicity of antiretroviral drugs in persons not infected with HIV.

The HIV PEP Registry was an observational, exposure-registration study developed to collect information about the safety and outcome of using antiretroviral drugs in HCWs who received PEP for occupational HIV exposure. By collecting data on blood exposures, antiretroviral drugs taken, symptoms experienced by the HCW while on PEP, and laboratory findings, this Registry's intent was to help clarify the safety of PEP use. The Registry confidentially collected data on HCWs who took HIV PEP and who agreed to enroll in the Registry through their health-care providers (providers). Providers included physicians, infection control practitioners, occupational health nurses, etc., who managed HCWs after occupational HIV exposures.

The HIV PEP Registry was established in October 1996 and continued enrollment through December 31, 1998. Follow-up information through 6-weeks post-exposure was sought from all HCWs enrolled. The Registry was sponsored by the Centers for Disease Control and Prevention, Glaxo Wellcome Inc., and Merck & Co., Inc. An Advisory Committee for the Registry included members from each of these organizations, as well as from the Food and Drug Administration, and from several academic medical institutions. Members of the Advisory Committee provided their expertise in a biannual review of the Registry activities and of data collected.

* The interagency working group comprised representatives of Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration, and the National Institutes of Health.

3. METHODS

3.1 Overview

The HIV PEP Registry was a collaborative project managed by the Centers for Disease Control and Prevention (CDC) and two pharmaceutical companies, Glaxo Wellcome Inc., and Merck & Co., Inc. A designated third party, PharmaResearch Corporation, was responsible for registration and follow-up and served as the data coordinating center.

Participation in the Registry was voluntary. Providers who managed occupational HIV exposures enrolled HCWs who were prescribed PEP and consented to participate in the Registry. An enrolled HCW was followed for a 6-month observation period through December 31, 1998 when enrollment was discontinued. After the end of 1998, follow-up only through the 6-week follow-up was systematically sought. Epidemiologic and laboratory data was sent to the Registry at baseline, at approximately 6 weeks (post-treatment initiation), and at 6 months postexposure.

3.2 Eligibility Criteria

HCWs, for the purposes of this Registry, included persons working in health-care settings as well as public safety workers and emergency workers, such as emergency medical technicians and first responders, in the United States and its outlying areas including dependencies, possessions, and independent nations in free association with the U.S. HCWs were eligible for enrollment in this Registry if all of the following criteria were met:

1. Had signed and dated a consent form for release of medical information
2. Had a known or presumed occupational exposure to HIV
3. Was started on a regimen of HIV PEP (e.g., any combination of ZDV, 3TC, and IDV, or any other licensed antiretroviral agent)
4. Was presumed to be HIV-antibody negative at baseline
5. Agreed to report safety, HIV-antibody test results, and other information to the Registry

Providers who managed occupational HIV exposures of HCWs could enroll HCWs in this Registry. Providers were responsible for obtaining a signed consent for release of medical information from HCWs for data collection, for registering exposed HCWs at their respective institutions, and for prospectively evaluating exposed HCWs for the duration of the observation period.

3.3 Enrollment and Follow-up

Registration was voluntary. To protect the identity of exposed HCWs participating in this Registry, no personal identifiers were collected by the Registry. Each enrolled HCW was assigned a unique Registry number used for communication with the provider. The provider was responsible for maintaining the link between the exposed HCW and Registry number and for protecting the confidentiality of the HCW's identity and test results. The Registry did not have access to the link between the HCW's identity and Registry number.

At the time of HCW enrollment, the provider completed and returned a Registration Form which requested data on the exposure and the PEP regimen prescribed. Providers were encouraged to enroll HCWs into the Registry as soon after the exposure as possible and no later than 2 weeks after completion of HIV PEP. At the 6-week follow-up (post-HIV PEP), the Registry sent a Follow-Up Form #1 to the provider to obtain information on any adverse events experienced by the HCW while on PEP, as well as abnormal laboratory test results, which resulted in modification or discontinuation of HIV PEP. At the 6-month follow-up, the Registry sent Follow-Up Form #2 to the provider to obtain results of HIV-antibody testing. Serious adverse experiences were to be reported on a FDA *MedWatch* form to the HIV PEP Registry Office within 24 hours of detection.

3.4 Classification of Adverse Experiences

Adverse experiences were initially coded using CoSTART, version 5. Once the initial coding was complete, the terms inconsistent with those reported by Tokars, et al [8] were recoded appropriately. Therefore, myalgia and arthralgia were reported together; asthenia, somnolence, malaise were reported as "fatigue or malaise"; migraine headache was coded to "headache"; and the term "bloating" included bloating, abdominal bloating, and abdominal distention.

A serious adverse experience was defined as any event which was fatal, life–threatening, permanently disabling, required or prolonged hospitalization, resulted in a congenital anomaly, required intervention to prevent permanent impairment or damage, overdose, or any other serious event. Using this definition, events which were considered by the reporter as severe in intensity, may or may not be considered a serious adverse experience.

3.5 Data Analysis and Management

Data were analyzed to provide descriptive demographic information, treatment regimens, and duration of treatments, in addition to the incidence of specific adverse events which occurred during the period of HIV PEP. Data were maintained and analysis conducted by the Coordinating Center. The data were analyzed collaboratively by the sponsor pharmaceutical companies and by professional staff of the HIV Infections Branch, Hospital Infections Program (HIP) with assistance provided by the Statistics and Information Systems Branch, HIP at the CDC. The Registry Advisory Committee provided input into the analyses and reviewed reports before dissemination of results.

In reviewing the Registry results, care was taken to consider the limitations of the data obtained through this Registry. A general limitation of any exposure-registration study is that risks of drug-associated adverse events cannot be extrapolated to reflect true risk in the potential target population. Because reports of exposure are voluntary, they are subject to numerous potential selection biases.

- In this Registry, under the criteria for a prospective case, most HCWs were enrolled after starting PEP, as opposed to before or at the time of initiation of PEP. Because of this there may have been a bias toward reporting of cases with adverse events over those who were treated and experienced no adverse events. Therefore, the risk of overall and specific adverse experiences may not reflect a true risk.
- The study attempted to capture some of the dimensions or reasons why HCWs did not comply with the PEP regimen prescribed. It is important to recognize that many factors influence the decision to discontinue therapy such as psycho-social and economic characteristics and level of education that were not captured in this study.
- A discontinuation was defined as a discontinuation of one or more of the drugs in the PEP regimen, e.g., an HCW could discontinue one drug, but complete the other drug(s) as prescribed. Likewise, a modification was defined as any change, e.g., dose, excluding discontinuation of one or more of the drugs in PEP regimen.

Data were summarized and reported periodically at scientific meetings and in articles submitted for scientific publication. In addition, participating Providers were sent a newsletter or interim reports which summarized findings of the Registry.

TABLES

Table 1: Summary of Demographics

	Overall
Subjects Enrolled	492
Age	
N	492
Mean (Standard Error)	37.6 (0.44)
Median (Interquartile Range)	37 (14.00)
Min - Max	18-74
Sex	
Female	351 (71%)
Male	141 (29%)
Pregnancy Status (Females)	
Pregnant Females	3 (00.85%)
Non-Pregnant Females	348 (99%)
By year	
1996 [1]	22 (4.5%)
1997	208 (42.3%)
1998	262 (53.3%)

[1] The Registry began enrollment in October 1996.

Table 2: Summary of HIV PEP Regimens

	# Enrolled	# Completed 4-6 weeks Follow-up Forms	# Completed 6 Months Follow-up Forms
ZDV mono	5 /492 (1%)	5 /5 (100%)	4 /5 (80%)
3TC, ZDV combination	177 /492 (36%)	161 /177 (91%)	88 /177 (50%)
D4T, DDI combination	1 /492 (0%)	1 /1 (100%)	0 /1 (0%)
IDV, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, D4T, IDV combination	1 /492 (0%)	1 /1 (100%)	0 /1 (0%)
3TC, D4T, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, DDI, IDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, IDV, ZDV combination	239 /492 (49%)	219 /239 (92%)	173 /239 (72%)
3TC, NFV, ZDV combination	15 /492 (3%)	11 /15 (73%)	6 /15 (40%)
3TC, NVP, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, SQV, ZDV combination	25 /492 (5%)	23 /25 (92%)	14 /25 (56%)
D4T, DDI, IDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
D4T, DDI, NFV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
D4T, NFV, NVP combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
DDC, NVP, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
DDI, IDV, ZDV combination	2 /492 (0%)	2 /2 (100%)	2 /2 (100%)
3TC, D4T, DDC, SQV, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, D4T, DDI, IDV, NVP, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, D4T, IDV, ZDV combination	2 /492 (0%)	2 /2 (100%)	2 /2 (100%)
3TC, D4T, NFV, NVP, SQV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, D4T, NFV, SQV, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
3TC, DDI, IDV, ZDV combination	2 /492 (0%)	2 /2 (100%)	0 /2 (0%)
3TC, IDV, NFV, ZDV combination	2 /492 (0%)	1 /2 (50%)	0 /2 (0%)
3TC, IDV, NVP, ZDV combination	5 /492 (1%)	5 /5 (100%)	2 /5 (40%)
3TC, IDV, SQV, ZDV combination	2 /492 (0%)	2 /2 (100%)	1 /2 (50%)
D4T, DDI, NFV, NVP combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
D4T, DDI, NFV, ZDV combination	1 /492 (0%)	1 /1 (100%)	1 /1 (100%)
Any 1 drug for PEP mono	5 /492 (1%)	5 /5 (100%)	4 /5 (80%)
Any 2 drugs for PEP combination	179 /492 (36%)	163 /179 (91%)	89 /179 (50%)
Any 3 or more drugs for PEP combination	308 /492 (63%)	281 /308 (91%)	213 /308 (69%)
Overall	492	449 /492 (91%)	306 /492 (62%)

DDI=(VIDEX®, didanosine), DDC=(HIVID®, zalcitabine), D4T=(ZERIT®, stavudine), IDV=(CRIXIVAN®, indinavir), NFV=(VIRACEPT®, nelfinavir), NVP=(VIRAMUNE®, nevirapine), SQV=(INVIRASE®, saquinavir), ZDV=(RETROVIR®, zidovudine, AZT), 3TC=(EPIVIR®, lamivudine)

Note: HIV PEP combination therapies listed as reported on the Registration Form. All drugs in the combinations listed may not have been taken concurrently (e.g., some drugs may have been discontinued and others started).

Table 3: Exposure To Treatment and Enrollment Time

	Overall
Subjects Enrolled	492
Number of Hours - Exposure to Treatment	
N	491
Mean (Standard Error)	10.27 (1.52)
Median (Interquartile Range)	1.75 (2.75)
Min - Max [1]	0.00-343.00
Missing [2]	1
Number of Days Between Exposure & Enrollment [3]	
N	492
Mean (Standard Error)	8.88 (0.47)
Median (Interquartile Range)	5.00 (13.00)
Min - Max	0 - 58
Missing	0

[1] Eleven cases initiated treatment 5-10 days following exposure.
[2] Missing at least 1 value necessary for calculation.

Table 4: Summary of the Type of Exposure and Exposure Medium

	Overall
Subjects Enrolled	492
Type of Exposure [1]	
Percutaneous	413 (84.0%)
Mucous Membrane	46 (9.3%)
Skin	41 (8.3%)
Exposure Medium [2]	
Blood/Blood Products	347 (71.0%)
Visibly Bloody Products	65 (13.0%)
Concentrated HIV	12 (2.4%)
Unknown	61 (18.0%)
Other [3]	44 (8.9%)
Medication	12 (27%)
Bodily Fluid	14 (32%)
Tissue	12 (27%)
Instrument	6 (14%)

[1] Types of exposure not mutually exclusive.
[2] Exposure mediums not mutually exclusive.
[3] Other exposure media included medication exposures (e.g., from IV/IM injection); bodily fluids, not obviously bloody; tissue; instrument, questionable contamination (e.g., surgical instrument cleaned in hypochlorite).

Table 5: Summary of Exposures Due to Percutaneous Injuries

	Overall
Subjects Enrolled - Percutaneous Injury	413
Percutaneous Injury Device	
Hollow-bore Needle	287 (69%)
Suture Needle	45 (11%)
Glass	7 (2%)
Scalpel	19 (5%)
Other (Not specified)	55 (13%)
If device is hollow-bore needle, was it used for blood withdrawal or venous access?	
Yes	186 (65%)
No	73 (25%)
Unknown	28 (10%)
Was source patient's blood visible on device [1]	
Yes	169 (41%)
No	89 (22%)
Unknown	101 (24%)
Missing	54 (13%)
Depth of injury	
Superficial Surface Scratch	89 (22%)
Moderate - Penetrated Skin	185 (69%)
Deep Puncture or Wound	39 (9%)

[1] Question added to data form, revision date, March 3, 1997.

Table 6: Summary of Compliance and Reasons for Discontinuation of HIV PEP

	Overall
Subjects With Follow-up at 4-6 Weeks	449
Initial PEP Regimen Was	
Completed as Prescribed [1]	195 (43%)
Modified:	16 (4%)
Completed with Modified Dose	16 (100%)
Completed with Additional Drug	0 (0%)
Discontinued:	238 (53%)
Discontinued at Least One Drug:	39 (16%)
Completed Others as Prescribed	35 (90%)
Completed Others-Modified Dose	3 (8%)
Completed Others-Additional Drug	1 (3%)
Disc. All Drugs-Completed Add. Drug	2 (1%)
Discontinued All Drugs	197 (83%)
Reasons[2] PEP was discontinued (All Drugs)	
Symptoms	99 (50%)
Lab Test Results	4 (2%)
Source Patient HIV Negative [3]	95 (48%)
Subject Choice	62 (31%)
Regimen Too Complicated	3 (5%)
Drug Holiday	0 (0%)
Other	58 (94%)
Unknown	0 (0%)
Health Care Provider Judgment	25 (13%)
Other	9 (5%)

[1] Included one case where drug was inadvertently stopped for three days and then resumed.
[2] Reasons for discontinuation of treatment were not mutually exclusive.
[3] This question was new on revised forms (March 3, 1997). However, if on the old form 'Other specify' was 'Source patient not HIV positive' this field was checked instead.

Table 7: Frequency of Subjects Experiencing Any Adverse Event [1,2,3]

	Overall
Subjects With Follow-up at 4-6 Weeks	449
Subjects with Any Event	340 (76%)
NAUSEA	258 (57%)
FATIGUE OR MALAISE	171 (38%)
HEADACHE	80 (18%)
VOMITING	73 (16%)
DIARRHEA	64 (14%)
MYALGIA OR ARTHRALGIA	28 (6%)
ABDOMINAL PAIN	22 (5%)
ANOREXIA	22 (5%)
DYSPEPSIA	18 (4%)
DIZZINESS	16 (4%)
INSOMNIA	15 (3%)
RASH	14 (3%)
TASTE PERVERSION	14 (3%)
FEVER	11 (2%)
FLANK PAIN	9 (2%)
PAIN	9 (2%)
PARESTHESIA	8 (2%)
HEMATURIA	7 (2%)
KIDNEY CALCULUS	6 (1%)
BACK PAIN	5 (1%)
BLOATING	5 (1%)
EPISTAXIS	5 (1%)
MACULOPAPULAR RASH	5 (1%)
THINKING ABNORMAL	5 (1%)
AMNESIA	4 (1%)
ANXIETY	4 (1%)
CHILLS	4 (1%)
DYSPNEA	4 (1%)
EMOTIONAL LABILITY	4 (1%)
PRURITIS	4 (1%)

[1] More than one event may have be reported for a subject, but only one occurrence of an individual event was reported for a subject.
[2] Events were included regardless of whether or not they were attributed to the PEP Regimen.
[3] Only events which occurred in 4 or more subjects.

Table 8: Time (Days) from Start of PEP to Onset of Most Common Adverse Events

	Overall
Subjects With Follow-up at 4-6 Weeks	449
Total Number of Recorded Events	1033
Subjects with at least 1 Event	340 (76%)
# of Days to Onset of Adverse Event: [2]	
Nausea	
Median (IQR)	3 (4)
Min - Max	1 - 44
Number of observations (# missing) [3]	253 (5)
Fatigue Or Malaise	
Median (IQR)	3 (6)
Min - Max	1 - 44
Number of observations (# missing) [3]	167 (4)
Headache	
Median (IQR)	3 (5)
Min - Max	1 - 44
Number of observations (# missing) [3]	79 (1)
Vomiting	
Median (IQR)	4 (9)
Min - Max	1 - 37
Number of observations (# missing) [3]	71 (2)
Diarrhea	
Median (IQR)	3 (4)
Min - Max	1 - 34
Number of observations (# missing) [3]	61 (3)

[1] More than one event may have been recorded for a subject, but only the first occurrence of an individual event was reported for a subject. Events were included whether or not they were attributed to the PEP Regimen.
[2] 5 most frequently occurring adverse events.
[3] Date of onset missing for some observations.

Table 9: Listing of HIV PEP-Related Serious Adverse Events by HIV PEP Regimen

Treatment	Sub-ject	PEP Event	Days from PEP [2]	Inten-sity	PEP Change Required	6 Months Attrib to PEP	6 Months Return to Normal
3TC, D4T, NFV, NVP, SQV	1	HIGH FEVER	12	Severe	Discont	Yes	Yes
		RASH	12	Severe	Discont	Yes	Yes
3TC, IDV, ZDV	8	RENAL CALCULI	3	Severe	R/D [1]	Yes	Yes
		FLANK PAIN	3	Severe	R/D [1]	Yes	Yes
		HEMATURIA	3	Severe	R/D [1]	Yes	Yes
	47	R URETERAL LITHIASIS COLIC	23	Mild	Discont	Yes	Yes
			23	Mild	Discont		
3TC, SQV, ZDV	36	"ALMOST INTRACTABLE VOMITING"	3	Severe	Discont	Yes	Yes
	37	NAUSEA	4	Severe	No Change	Yes	Yes
	38	INVOLUNTARY MUSCLE MOVEMENTS EYES DO NOT FOCUS-CAN SEE LIGHT ONLY LASTS <1 MIN. OCCURS ABOUT 10-12 X A DAY	2	Severe	No Change	Yes	No

[1] R/D = IDV, ZDV doses reduced day 5, on day 7 PEP was discontinued.
[2] Day from start of treatment to onset of the event.

Notes:
1) A serious adverse experience was defined as any event which was fatal, life-threatening, permanently disabling, required or prolonged hospitalization, resulted in a congenital anomaly, required intervention to prevent permanent impairment or damage, overdose, or any other serious event. Using this definition, events which were considered by the reporter as severe intensity, may or may not have been considered a serious adverse experience.
2) HIV PEP combination therapies listed as reported on the Registration Form. All drugs in the combinations listed may not have been taken concurrently (e.g., some drugs may have been discontinued and others started).

Table 10: Frequency of Severe Adverse Events [1,2,3,4]

	Overall
Subjects With Follow-up at 4-6 Weeks	449
Subjects with Any Event	83 (18%)
NAUSEA	40 (9%)
VOMITING	22 (5%)
FATIGUE OR MALAISE	18 (4%)
HEADACHE	12 (3%)
ABDOMINAL PAIN	9 (2%)
DIARRHEA	9 (2%)
ANOREXIA	4 (1%)
FLANK PAIN	4 (1%)
HEMATURIA	4 (1%)
KIDNEY CALCULUS	4 (1%)
MYALGIA OR ARTHRALGIA	4 (1%)
DIZZINESS	3 (1%)
FEVER	2 (0%)
INSOMNIA	2 (0%)
RASH	2 (0%)
TASTE PERVERSION	2 (0%)
ANXIETY	1 (0%)
BACK PAIN	1 (0%)
BLOATING	1 (0%)
DRY SKIN	1 (0%)
EMOTIONAL LABILITY	1 (0%)
EYE DISORDER	1 (0%)
HEMATEMESIS	1 (0%)
RECTAL BLEEDING	1 (0%)
SWEAT	1 (0%)
TARDIVE DYSKINESIA	1 (0%)
THINKING ABNORMAL	1 (0%)
URINARY TRACT INFECTION	1 (0%)
URTICARIA	1 (0%)
WEIGHT GAIN	1 (0%)
WEIGHT LOSS	1 (0%)

[1] More than one event may have been reported for a subject, but only one occurrence of an individual event was reported for a subject.
[2] Events were included regardless of whether or not they were attributed to the PEP Regimen.
[3] Of those subjects who experienced a severe adverse event 41% had no change in their HIV PEP Regimen, 3% interrupted treatment or had a dose reduction, and 55% discontinued one or more HIV PEP drug. All events had resolved by 6 month follow-up, but one (Table 9).
[4] The intensity of adverse events was recorded as reported by the health-care provider (i.e., the provider reported these events as “severe” in intensity).

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