

Exposure to Latent Tuberculosis Treatment During Pregnancy: the PREVENT TB and the iAdhere Trials

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Table E1. Annual Number of Tuberculosis Cases in the United States from 2000 to 2014

	Tuberculosis cases in 2000	Tuberculosis cases in 2014
Total	16,308	9,421
Women	6,105	3,578
Women in reproductive age (15–51 years of age)	3,369	1,927

Robert Pratt; Surveillance Epidemiology and Outbreak Investigations Branch. Division of Tuberculosis Elimination, Centers for Disease Control & Prevention; October 2016 (personal communication)

Table E2. Demographic Characteristics Among Participants who Reported Pregnancy (Estimated Date of Conception on or Before the Last Study Dose Date) Versus Those who did not Report Pregnancy

Characteristic		Regimen 3HP (n = 1,729)		Regimen 9H (n = 1,372)		Total (n = 3,101) n (%)
		Reported pregnancy (n = 31) n (%)	Did not report pregnancy (n = 1,698) n (%)	Reported pregnancy (n = 56) n (%)	Did not report pregnancy (n = 1,316) n (%)	
Age, median (IQR)		23 (21-30)	33 (25-42)	25 (21-29)	33 (25-42)	33 (25-42)
Enrollment Site	Brazil	2 (6.9)	120 (7.1)	1 (1.8)	122 (9.3)	245 (7.9)
	Hong Kong	0 (0)	21 (1.2)	0 (0)	0 (0)	21 (0.7)
	Peru	0 (0)	2 (0.1)	0 (0)	7 (0.5)	9 (0.3)
	South Africa	0 (0)	29 (1.7)	0 (0)	0 (0)	29 (0.9)
	Spain	0 (0)	75 (4.4)	0 (0)	32 (2.4)	107 (3.5)
	United States/Canada	29 (93.5)	1451 (85.5)	55 (98.2)	1155 (87.8)	2690 (86.8)
Race	American Indian/Alaskan Native	0 (0)	17 (1)	0 (0)	11 (0.8)	28 (0.9)
	Asian/Pacific Islander	6 (19.4)	210 (12.4)	9 (16.1)	166 (12.6)	391 (12.6)
	Black	3 (9.7)	418 (24.6)	9 (16.1)	307 (23.3)	737 (23.8)
	Other	1 (3.2)	55 (3.2)	1 (1.8)	46 (3.5)	103 (3.3)
	White	21 (67.7)	998 (58.8)	37 (66.1)	786 (59.7)	1842 (59.4)
Alcohol*	No	19 (61.3)	1023 (60.2)	33 (58.9)	805 (61.2)	1880 (60.7)
	Use	11 (35.5)	615 (36.2)	22 (39.3)	481 (36.6)	1129 (36.4)
	Abuse	1 (3.2)	57 (3.4)	1 (1.8)	28 (2.1)	87 (2.8)
	Unknown	0 (0)	3 (0.2)	0 (0)	2 (0.2)	5 (0.2)
LTBI treatment†	Contact	19 (61.3)	950 (55.9)	40 (71.4)	805 (61.2)	1814 (58.5)
	Fibrosis	2 (6.5)	18 (1.1)	1 (1.8)	17 (1.3)	38 (1.2)
	HIV positive	0 (0)	41 (2.4)	1 (1.8)	47 (3.6)	89 (2.9)
	LTBI (+)	2 (6.5)	206 (12.1)	0 (0)	0 (0)	208 (6.7)
	TST converter	8 (25.8)	483 (28.4)	14 (25)	447 (34)	952 (30.7)
Education‡	High School	19 (61.3)	1104 (65)	33 (58.9)	810 (61.6)	1966 (63.4)
	<High School	12 (38.7)	578 (34)	23 (41.1)	503 (38.2)	1116 (36)
	Unknown	0 (0)	13 (0.8)	0 (0)	3 (0.2)	16 (0.5)
Ethnic Origin	Non-United States/Canada	2 (6.5)	247 (14.5)	1 (1.8)	161 (12.2)	411 (13.3)
	United States/Canada: Hispanic	15 (48.3)	679 (40)	31 (55.4)	518 (39.4)	1243 (40.1)
	United States/Canada: non-Hispanic	14 (45.2)	772 (45.5)	24 (42.9)	637 (48.4)	1447 (46.7)

Characteristic		Regimen 3HP (n = 1,729)		Regimen 9H (n = 1,372)		Total (n = 3,101) n (%)
		Reported pregnancy (n = 31) n (%)	Did not report pregnancy (n = 1,698) n (%)	Reported pregnancy (n = 56) n (%)	Did not report pregnancy (n = 1,316) n (%)	
HIV infection	No	20 (64.5)	976 (57.5)	29 (51.8)	686 (52.1)	1711 (55.2)
	Unknown	11 (35.5)	663 (39)	26 (46.4)	574 (43.6)	1274 (41.1)
	Yes	0 (0)	59 (3.5)	1 (1.8)	56 (4.3)	116 (3.7)
IDU History [§]	No	31 (100)	1671 (98.4)	56 (100)	1284 (97.6)	3042 (98.2)
	Yes	0 (0)	25 (1.5)	0 (0)	31 (2.4)	56 (1.8)
	Unknown	0 (0)	2 (0.1)	0 (0)	1 (0.1)	3 (0.1)
Jail	No	31 (100)	1674 (98.6)	56 (100)	1297 (98.6)	3058 (98.6)
	Yes	0 (0)	24 (1.4)	0 (0)	19 (1.4)	43 (1.4)
Current Smoker	No	24 (77.4)	1378 (81.2)	47 (83.9)	1068 (81.2)	2517 (81.2)
	Yes	7 (22.6)	320 (18.8)	9 (16.1)	248 (18.8)	584 (18.8)
Unemployed	No	25 (80.6)	1439 (84.7)	51 (91.1)	1199 (91.1)	2714 (87.6)
	Yes	6 (19.4)	259 (15.3)	5 (8.9)	117 (8.9)	387 (12.5)
Homeless	No	31 (100)	1661 (97.8)	56 (100)	1286 (97.7)	3034 (97.8)
	Yes	0 (0)	37 (2.2)	0 (0)	30 (2.3)	67 (2.2)

Definition of abbreviations: 3HP = 12-dose once-weekly regimen of isoniazid (900 mg) plus rifapentine (900 mg); 9H = 9-month daily isoniazid (300 mg); HIV = human immunodeficiency virus; IDU = intravenous drug use; IQR = interquartile range; LTBI = latent tuberculosis infection; TST = Tuberculin Skin test.

* History of Alcohol not reported in 3 non-pregnant women on 3HP, and 1 non-pregnant woman on 9H.

† Subjects were counted only once in the order presented. The total number of HIV-infected persons who were enrolled in the study is listed separately in this table.

‡ Education not reported in 3 non-pregnant women on 3HP.

§ Intravenous drug use ever

|| Jail/Incarceration not reported in 1 non-pregnant woman on 3HP.

Table E3 Demographic Characteristics Among All Participants who Reported Pregnancy During Treatment or Follow-up (Estimated Date of Conception during Treatment up to 184 Days After the Last Study Dose) Versus Those who did not Report Pregnancy

Characteristic		Regimen 3HP (n = 1,751)		Regimen 9H (n = 1,388)		Total (n = 3,139) n (%)
		Reported pregnancy (n = 53) n (%)	Did not report pregnancy (n = 1,698) n (%)	Reported pregnancy (n = 72) n (%)	Did not report pregnancy (n = 1,316) n (%)	
Age, median (IQR)		25 (22-31)	33 (25-42)	24 (21-29)	33 (25-42)	33 (25-42)
Enrollment Site	Brazil	2 (3.8)	120 (7.1)	2 (2.8)	122 (9.3)	246 (7.8)
	Hong Kong	0 (0)	21 (1.2)	0 (0)	0 (0)	21 (0.7)
	Peru	0 (0)	2 (0.1)	0 (0)	7 (0.5)	9 (0.3)
	South Africa	1 (1.9)	29 (1.7)	0 (0)	0 (0)	30 (1.0)
	Spain	0 (0)	75 (4.4)	0 (0)	32 (2.4)	107 (3.5)
	United States/Canada	50 (94.3)	1451 (85.5)	70 (97.2)	1155 (87.8)	2726 (86.8)
Race	American Indian/Alaskan Native	0 (0)	17 (1)	0 (0)	11 (0.8)	28 (0.9)
	Asian/Pacific Islander	8 (15.1)	210 (12.4)	10 (13.9)	166 (12.6)	394 (12.6)
	Black	6 (11.3)	418 (24.6)	13 (18.1)	307 (23.3)	744 (23.7)
	Other	2 (3.8)	55 (3.2)	2 (2.8)	46 (3.5)	105 (3.3)
	White	37 (69.8)	998 (58.8)	47 (65.3)	786 (59.7)	1868 (59.5)
Alcohol*	No	34 (64.2)	1023 (60.2)	45 (62.5)	805 (61.2)	1907 (60.8)
	Use	17 (32.1)	615 (36.2)	26 (36.1)	481 (36.6)	1139 (36.3)
	Abuse	2 (3.8)	57 (3.4)	1 (13.9)	28 (2.1)	88 (2.8)
	Unknown	0 (0)	3 (0.2)	0 (0)	2 (0.2)	5 (0.2)
LTBI treatment†	Fibrosis	2 (3.8)	18 (1.1)	2 (2.8)	17 (1.3)	39 (1.2)
	HIV positive	0 (0)	41 (2.4)	1 (13.9)	47 (3.6)	89 (2.8)
	LTBI (+)	2 (3.8)	206 (12.1)	0 (0)	0 (0)	208 (6.6)
	TST converter	13 (24.5)	483 (28.4)	20 (27.8)	447 (34)	963 (30.7)
Education‡	High School	30 (56.6)	1104 (65)	42 (58.3)	810 (61.6)	1986 (63.3)
	<High School	23 (43.4)	578 (34)	30 (41.7)	503 (38.2)	1134 (36.1)
	Unknown	0 (0)	16 (0.9)	0 (0)	3 (0.2)	19 (0.6)
Ethnic Origin	Non-United States/Canada	3 (5.7)	247 (14.5)	2 (2.8)	161 (12.2)	413 (13.2)
	United States/Canada: Hispanic	29 (54.7)	679 (40)	39 (54.2)	518 (39.4)	1265 (40.3)
	United States/Canada: non-Hispanic	21 (39.6)	772 (45.5)	31 (43.1)	637 (48.4)	1461 (46.5)

Characteristic		Regimen 3HP (n = 1,751)		Regimen 9H (n = 1,388)		Total (n = 3,139) n (%)
		Reported pregnancy (n = 53) n (%)	Did not report pregnancy (n = 1,698) n (%)	Reported pregnancy (n = 72) n (%)	Did not report pregnancy (n = 1,316) n (%)	
HIV infection	No	30 (56.6)	976 (57.5)	36 (50.0)	686 (52.1)	1728 (55.0)
	Unknown	23 (43.4)	663 (39)	35 (48.6)	574 (43.6)	1295 (41.3)
	Yes	0 (0)	59 (3.5)	1 (13.9)	56 (4.3)	116 (3.7)
IDU History§	No	53 (100)	1671 (98.4)	72 (100)	1284 (97.6)	3080 (98.1)
	Yes	0 (0)	25 (1.5)	0 (0)	31 (2.4)	56 (1.8)
	Unknown	0 (0)	2 (0.1)	0 (0)	1 (0.1)	3 (0.1)
Jail	No	53 (100)	1674 (98.6)	72 (100)	1297 (98.6)	3096 (98.6)
	Yes	0 (0)	24 (1.4)	0 (0)	19 (1.4)	43 (1.4)
Current Smoker	No	44 (83.0)	1378 (81.2)	60 (83.3)	1068 (81.2)	2550 (81.2)
	Yes	9 (17.0)	320 (18.8)	12 (16.7)	248 (18.8)	589 (18.8)
Unemployed	No	46 (86.8)	1439 (84.7)	66 (91.7)	1199 (91.1)	2750 (87.6)
	Yes	7 (13.2)	259 (15.3)	6 (8.3)	117 (8.9)	389 (12.4)
Homeless	No	53 (100)	1661 (97.8)	72 (100)	1286 (97.7)	3072 (97.9)
	Yes	0 (0)	37 (2.2)	0 (0)	30 (2.3)	67 (2.1)

Definition of abbreviations: 3HP = 12-dose once-weekly regimen of isoniazid (900 mg) plus rifapentine (900 mg); 9H = 9-month daily isoniazid (300 mg); HIV = human immunodeficiency virus; IDU = intravenous drug use; IQR = interquartile range; LTBI = latent tuberculosis infection. TST = Tuberculin Skin test.

* History of Alcohol not reported in 3 non-pregnant women on 3HP, and 1 non-pregnant woman on 9H.

† Subjects were counted only once in the order presented. The total number of HIV-infected persons who were enrolled in the study is listed separately in this table

‡ Education not reported in 3 non-pregnant women on 3HP.

§ Intravenous drug use ever

|| Jail/Incarceration not reported in 1 non-pregnant woman on 3HP.

Table E4. Pregnancy Safety Assessment During Exposure with 3HP or 9H Treatment

	3HP		9H	
	Reported pregnancy* (n = 31) n (%)	Did not report pregnancy (n = 1,698) n (%)	Reported pregnancy* (n = 56) n (%)	Did not report pregnancy (n = 1,316) n (%)
Duration of study drug exposure, d Median (IQR)	718 20 (1-80)	119,280 78 (1-173)	2,297 32.5 (1-242)	314,577 274 (1-624)
Study drug doses received, median (range)	8 (4-12)	12 (12-12)	160 (76-241)	257 (240-270)
Completed study treatment, n (%)	9 (29)	1,417 (83.5)	14 (25)	1,007 (76.5)
Pregnancy outcome after last study dose	8 [†]	-	7 [‡]	-
Participants who reported an adverse event, n (%)	0 (0)	211 (12.4)	7 (12.5)	232 (17.6)
Discontinued due to an adverse event, n (%)	0 (0)	83 (4.9)	1 (1.8)	43 (3.3)
Toxicity grade, n (%)[§]				
Grade 1 or 2	0 (0)	143 (8.4)	6 (10.7)	177 (13.4)
Grade 3 or 4	0 (0)	74 (4.4)	1 (1.8)	70 (5.3)
Grade 5 (Death)	0 (0)	4 (0.2)	0 (0)	4 (0.3)
Adverse event classification, n (%)				
Drug related adverse event				
Hepatotoxicity only	0 (0)	8 (0.5)	1 (1.8)	37 (2.8)
Systemic drug reaction	0 (0)	74 (4.4)	0 (0)	9 (0.7)
Rash only	0 (0)	11 (0.6)	0 (0)	6 (0.5)
Other drug-related adverse event	0 (0)	41 (2.4)	3 (5.4)	29 (2.2)
Non-drug related adverse event	0 (0)	82 (4.8)	3 (5.4)	166 (12.6)

Definition of abbreviations: 3HP = 12-dose once-weekly regimen of isoniazid (900 mg) plus rifapentine (900 mg); 9H = 9-month daily isoniazid (300 mg); IQR = interquartile range

Adverse event other than pregnancy.

* Women were considered exposed to the study drug(s) during pregnancy if they took at least 1 study dose and if the estimated date of conception was on or before the last study dose date.

† Live birth (6), elective abortion (2)

‡ Live birth (6), fetal loss (1)

§ For participants reporting multiple adverse event with same toxicity, the earliest adverse event is reported.

|| Participants with multiple adverse events can be present in more than one grade toxicities and in more than one adverse event classification.