Prevalence of depression among postpartum women on Isoniazid-Preventive Therapy and Efavirenz-based treatment for HIV—An exploratory objective of the IMPAACT P1078 randomized trial

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Background

- IMPAACT P1078 was a Phase IV, randomized, double-blind, placebo-controlled non-inferiority study
  - Evaluated the safety of isoniazid (INH) preventative therapy initiated during pregnancy (Immediate) or 12 weeks postpartum (Deferred) in pregnant women living with HIV
- Patient Health Questionnaire 9 (PHQ-9) was added partway through study implementation to systematically evaluate depression symptoms
  - Included in protocol Version 2.0 in response to a concern for INH/efavirenz (EFV) interaction
- Exploratory analysis to investigate possible depression symptoms in postpartum women on HIV treatment

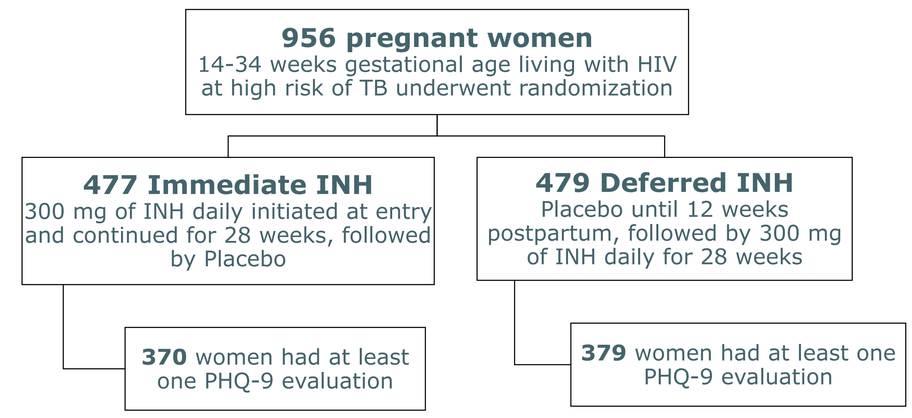

Figure 1. Randomization and analysis population, PHQ-9 assessment was added to protocol Version 2.0

There was **no difference** in the frequency of depression symptoms between postpartum women on Efavirenz alone and those on Efavirenz plus Isoniazid

Methods

- Summarized percentages of women with depression symptoms at postpartum weeks 4, 12, 24, 36, and 48
- Assessed association of 11 risk factors of probable depression (PHQ-9 ≥10) at 36 weeks postpartum using exact logistic regression, adjusted for gestational age stratum
  - Week 36 was selected *post-hoc* because it had a high prevalence
  - Risk factors included study arm, EFV-containing regimen at study entry, Hepatitis B surface antigen status, Hepatitis C serology status, Country, CD4 count at screening, HIV viral load at screening, age, Body Mass Index, INH acetylation status, EFV acetylation status, and Cotrimoxazole use at study entry
- Evaluated study arm effect modification by EFV use

Table 1. Baseline characteristics

Characteristic	Immediate INH (N=370)	Deferred INH (N=379)	Overall (N=749)
Age (years) Median (Q1, Q3)	29.0 (25.0, 33.0)	29.0 (24.0, 34.0)	29.0 (24.0, 33.0)
Black African/Black of African origin	344 (93%)	347 (92%)	691 (92%)
Gestational age 14 - <24 weeks	130 (35%)	136 (36%)	266 (36%)
Cotrimoxazole use	179 (48%)	164 (43%)	343 (46%)
EFV regimen	313 (85%)	327 (86%)	640 (85%)
Undetectable HIV viral load	226 (61%)	241 (64%)	467 (62%)

Table 2. Summary of depression symptoms by study arm and postpartum study visit

Postpartum Week	Number of Women Evaluated	Depression Symptoms: Minimal (PHQ-9: 1-4)	Mild (PHQ-9: 5-9)	Moderate (PHQ-9: 10-14)	Moderately severe, severe (PHQ-9: 15-27)	Probable Depression (PHQ-9 ≥ 10): Immediate INH	Deferred INH
4	136	28 (20.6%)	8 (5.9%)	0 (0%)	2 (0.7%)	0/64 (0%)	2/72 (2.8%)
12	229	57 (24.9%)	24 (10.5%)	4 (1.7%)	1 (0.4%)	2/111 (1.8%)	3/118 (2.5%)
24	378	91 (24.1%)	29 (7.7%)	3 (0.8%)	3 (0.8%)	3/186 (1.6%)	3/192 (1.6%)
36	539	117 (21.7%)	26 (4.8%)	9 (1.7%)	2 (0.4%)	7/270 (2.6%)	4/269 (1.5%)
48	689	127 (18.4%)	25 (3.6%)	4 (0.6%)	1 (0.1%)	3/342 (0.9%)	2/347 (0.6%)

Results

- Of 956 women enrolled, 749 (78%) women had ≥1 PHQ-9 evaluation(s)
- At study entry, 691/749 (92%) women were Black African/Black of African origin, with median (Q1, Q3) age of 29 years (24, 33) and gestational age of 26 weeks (22, 30)
- Most women were at WHO Clinical Stage I (88%), on an EFV-containing regimen (85%), and had undetectable HIV RNA levels (63%), with median CD4 count of 499 cells/mm^3 (355, 689).
- Across postpartum visits, probable depression was reported in 0.7-2.2% of women
- Cotrimoxazole use was associated with increased odds of probable depression at Week 36 [adjusted odds ratio (95% confidence interval): 9.45 (1.32, 413.68)]
- There was no evidence of study arm differences in odds of probable depression, nor treatment effect modification by EFV use.

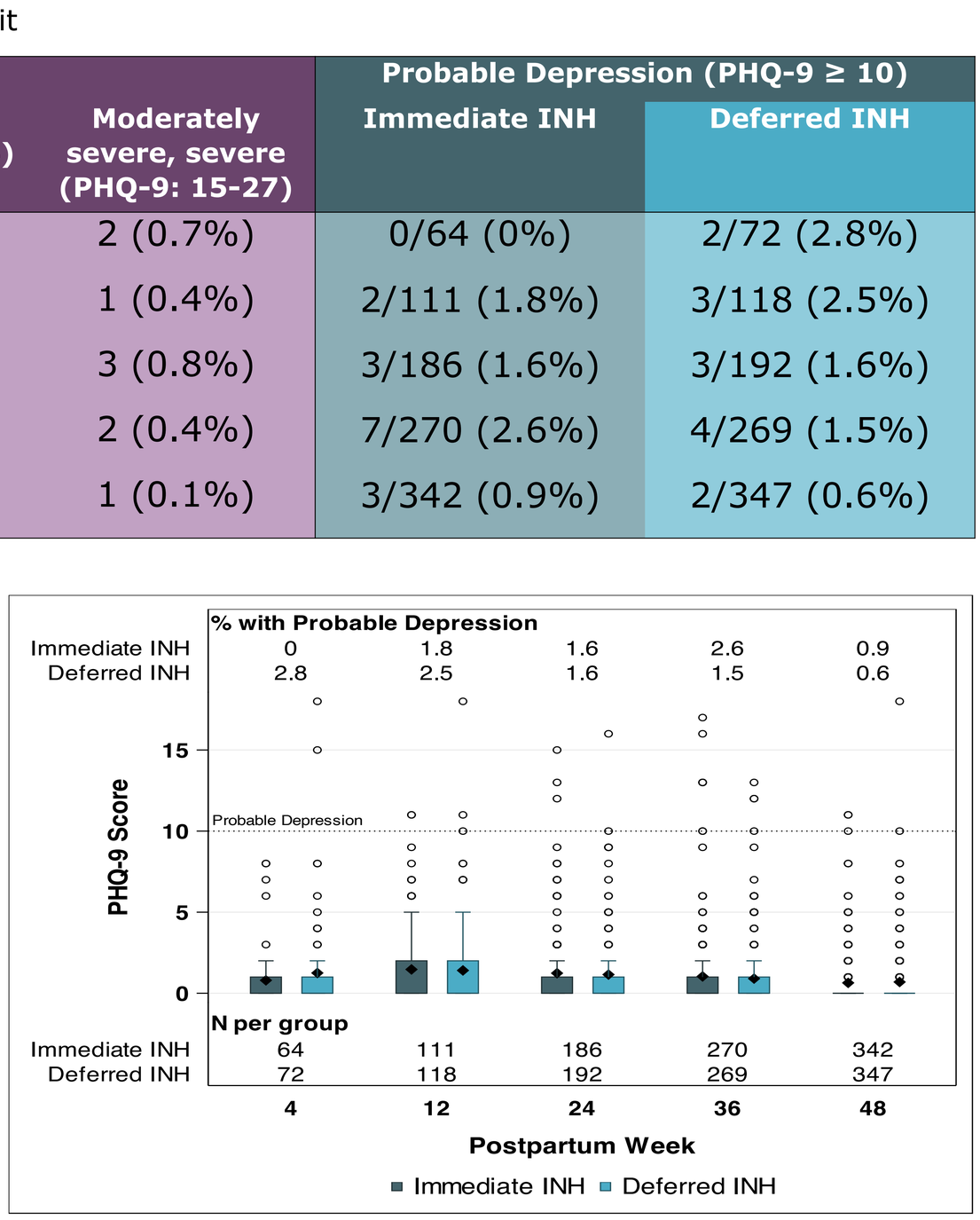

Figure 2. Distribution of PHQ-9 scores by study arm

Conclusions

- Timing of IPH initiation was not associated with probable depression
- Further study is advised to formally assess associations of risk factors with probable depression

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