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Pending availability of new HCV treatments, should HIV-HCV co-infected patients start receiving peg-interferon and ribavirin in settings where this regimen is becoming affordable?

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Introduction

In Thailand, hepatitis C virus (HCV)–infected patients with advanced fibrosis, especially those HIV co-infected, may die before new anti-HCV agents are available and affordable.

Combination therapy of pegylated interferon (peg-IFN) /ribavirin was not affordable in Thailand until 2014 and has never been evaluated in HIV-HCV co-infected patients in the context of routine HIV clinic practice.

We report here the results of the first 12 weeks of HCV treatment in the first 16 co-infected patients who received peg-IFN/ribavirin treatment in four HIV clinics in Thailand. The treatment and laboratory monitoring was provided free of charge to study participants.

Patients and Methods

➢ Population

HIV-infected adults followed within the PHPT HIV cohort study (NCT00433030) were enrolled in this HCV treatment program if they had:

- Evidence of chronic HCV infection for at least past 6 months
- Liver fibrosis stage F2/F3/F4 assessed by transient elastography (FibroScan®)
- HIV RNA< 400 copies/mL (or HIV RNA ≤ 5,000 copies/mL if no antiretroviral treatment)

The self-rated Beck Depression Inventory (BDI) was used to screen for and track depression at 2, 4, 8, and 12 weeks follow-up.

➢ HCV treatment

HCV treatment for 48 weeks was prescribed by internists, with hepatologist's advice as necessary:

- peg-interferon alpha 2-b: 1.5 microgram/kg once a week
- ribavirin for HCV genotype 1/4/5/6: dose according to weight
  for HCV genotype 2/3: 400/400mg bid regardless of weight

➢ Assessment of HCV response

- HCV RNA is assessed at 4, 12, 24, 48 and 72 weeks (Abbott RealTime HCV assay, range 1.08 – 8 $\log_{10}$ IU/mL)
- Rapid Virological Response (RVR) was defined as HCV RNA <1.08 $\log_{10}$ or 12 IU/mL at 4 weeks.
- Complete Early Virological Response (EVR) was defined as HCV RNA <1.08 $\log_{10}$ or 12 IU/mL at 12 weeks.
- Partial EVR is defined as drop HCV RNA >2 $\log_{10}$IU.

In-house IT tools for study management

Mobile-friendly Intranet tool for direct entry of laboratory results, drug dose calculations and safety alerts

Monitoring participant health status: clinical e-report for study physicians and nurses *(screen capture of an Intranet interface)*

Results

Table 1: Baseline characteristics (N=16)	N or Median (IQR)
Gender	Male: 11, Female: 5
Age (years)	44.3 (40.4 – 51.1)
Weight (kg)	59.8 (52.0 – 63.0)
Body Mass Index (kg/m^2)	21.4 (20.5 – 24.2)
Fibrosis stage (n) by Fibroscan°	F2: 1, F3: 4, F4: 11
HCV RNA load ($\log_{10}$ IU/mL)	5.95 (5.53 – 6.75)
IL28B polymorphism	CC: 13, CT: 3, TT: 0
Hemoglobin (g/dL)	14.3 (11.8 – 14.9)
WBC (cells/mm^3)	5,800 (4,600 – 7,400)
Absolute neutrophil cell count (/mm^3)	2,680 (1,740 – 4,150)

Table 2: Baseline characteristics by fibrosis stage		F2 (n=1)	F3 (n=4)	F4 (n=11)
HCV RNA ($\log_{10}$ IU/mL) median		6.37	6.99	5.69
HCV genotype*	1	1	1	7
	3	0	3	2
	6	0	0	2
IL28b	CC	1	3	9
	CT	0	1	2
Hemoglobin (g/dL) median		14.7	13.0	14.1
WBC (cells/mm^3) median		5,700	7,500	4,800
Absolute neutrophils count (cells/mm^3) median		2,700	4,300	2,200

*HCV genotype distribution: 1a: 2; 1b: 7; 3a: 5; 6a/6b: 1 and 6c-i: 1

Results

- Prior to starting HCV treatment: All patients had normal BDI score except one who had a mild mood disturbance (11 – 16) and who did not tolerate the treatment
- At week 2: of 15 patients on follow-up, one patient developed a mild mood disturbance through week 12 and one developed borderline clinical depression (17 – 20) and went back to normal at week 8 through week 12;
- At week 8: of 15 patients on follow-up, one developed borderline clinical depression which turned to a mild mood disturbance at week 12 and one had a mild mood disturbance which normalized at week 12.
- No patients were on anti-depressant therapy.

Table 3: Adverse events during the first 12 weeks of treatment (≥ Grade 3)	Number of participants experiencing ≥ 1 adverse event	
	Grade 3	Grade 4
Anemia (Hemoglobin ≤ 7.4 g/dL)	1	0
Neutropenia (Absolute neutrophils <750 cells/mm3)	3	1
Thrombocytopenia (Platelets <50,000 /mm3)	0	0

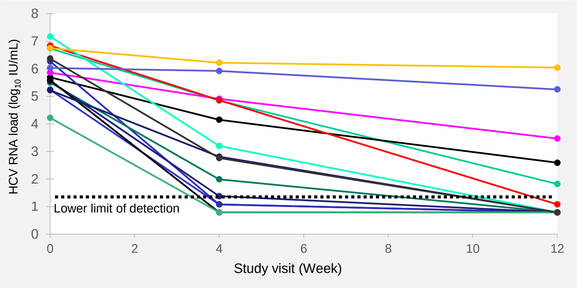
- None of the patients received EPO or GCSF.

Table 4: Proportion of participants with undetectable HCV RNA at week 12 according to HCV genotype and IL28b genotype

HCV genotype	IL28b genotype			Total
	CC	CT	TT	
1	4/7	0/2	0	4/9 (44%)
3	3/3	0/1	0	3/4 (75%)
6	2/2	0	0	2/2 (100%)
Total	**9/12**	**0/3**	**0**	**9/15 (60%)**

- None of the patients with IL-28 CT had undetectable HCV RNA at Week 12.

Figure 1: HCV RNA at Screening, Week 4, and Week 12 (n=15)



- Of 15 participants on treatment, 2 had RVR, 9 had complete EVR, 4 had partial EVR response, and 2 were non-responders.

Conclusions

In these HIV-HCV co-infected patients with favorable IL28b but advanced fibrosis, peg-IFN/ribavirin combination therapy appeared effective and relatively well tolerated after 12 weeks.

The new HCV directly acting agents are still not available in Thailand and may not be affordable soon. The classical treatment remains the only option for a significant number of patients with advanced liver disease who cannot wait longer for the new oral drugs.

In this program, several HIV specialists were able to start treating HCV co-infection with the support of their colleagues hepatologists.

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