Safety and Efficacy of a Simplified Fixed-Dose Combination of Stavudine, Lamivudine and Nevirapine (GPO-VIR) for the Treatment of Advanced HIV-Infected Patients: A 24-Week Study

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Objective : *To determine the efficacy and safety of the fixed-dose combination of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) in the treatment of antiretroviral na ve HIV-infected Thai adults.*
Patients And Method : *An open-label, single arm trial was conducted. Baseline clinical assessment and blood test was done on 10_1 antiretroviral na ve HIV-infected patients, who then received a fixed dose combination of d4T, 3TC and NVP (GPO-VIR , Thai Government Pharmaceutical Organization, Bangkok, Thailand). Nevirapine was given as 200 mg once daily for the first 2 weeks. The patients were followed up at 2, 4, 8, 12 and 24 weeks. A CD4 cell count and HIV-RNA assay were done at 12 and 24 weeks.*
Results : *One hundred and one patients were enrolled. The mean baseline CD4 cell count and mean HIV RNA were 58.7 (57.7) cells/mm^3 and 5.3 (0.5) log_{10} copies/mL respectively. At week 24^{th}, the mean decrease in log HIV RNA was 3.6 (0.7) log_{10} copies/mL [P < 0.001; 95% confidence interval (CI), 2.70-3.03]. Eighty one (80.2%) patients had HIV RNA < 400 copies/mL by intention-to-treat analysis (ITT) and 97.6% had HIV RNA < 400 copies/mL by on-treatment analysis (OT). Sixteen (84.2%) patients with baseline HIV RNA ≤ 100,000 copies/mL and 65 (82.3%) patients with baseline HIV RNA > 100,000 copies/mL had viral load < 400 copies/mL by ITT (P = 0.842; 95% CI, -20.9%-16.2%). Sixteen (94.1%) patients with baseline HIV RNA ≤ 100,000 copies/mL and 65 (98.5%) patients with baseline HIV RNA > 100,000 copies/mL had viral load < 400 copies/mL by OT (P = 0.295; 95% CI, -25.5%-3.8%). The mean CD4 cell count at week 24 was 155.1 (89.0) cells/mm^3 (range 13-402). The mean increase in CD4 cell count from baseline was 96.5 (63.5) cells/mm^3 (P < 0.001). A total of 12% of the patients receiving d4T + 3TC + NVP developed skin rashes. Grade 3 or 4 hepatotoxicity was recognized in 7% of the patients.*
Conclusion : *Fixed-dose combination of d4T + 3TC + NVP (GPO-VIR) is safe, well tolerated and effective in increasing CD4 cell counts and suppression of HIV RNA at 24 weeks in advanced HIV-infected patients in Thailand.*

Keywords : *Safety, Efficacy, Antiretroviral treatment, AIDS*

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During the year 2001, nearly 24,000 Thai people developed acquired immunodeficiency syndrome (AIDS) and almost 7,000 have died[1]. All patients who have contracted human immunodeficiency virus (HIV) infection will fall ill due to the disruption of the immune system during the natural course of HIV infection. The use of highly active antiretroviral therapy (HAART) has dramatically decreased morbidity and mortality in patients with HIV infection[2]. Treatment of HIV infection with a combination of three antiretroviral drugs is a cost-effective use of resources(3). The 2001 British HIV Association (BHIVA) guidelines for the treatment

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of HIV-infected adults with antiretroviral therapy and the US Department of Health and Human Services (DHHS) 2002 guidelines have recommended antiretroviral treatment for patients with serious/ recurrent HIV related illness, or AIDS, and for HIV-infected patients with CD4 cell count < 200/ L regardless of the HIV RNA concentration[4,5]. One of the antiretroviral regimens recommended by the BHIVA guidelines included nevirapine (NVP) 200 mg twice a day in combination with 2 nucleoside reverse transcriptase inhibitors (NRTIs). This concurred with the Infectious Disease Association of Thailand 2001 guidelines for HIV-infected adults. However, the 2002 US DHHS guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents recommended 2 NRTIs plus nevirapine as an alternative regimen for the treatment of adults with HIV-1 infection. Currently the cost of antiretroviral drugs is much less than in the past, particularly the locally-produced formula. However, primarily because of economic limitations, the majority of Thai HIV-infected adult patients do not have access to the antiretroviral treatment. The Thai Government Pharmaceutical Organization (GPO) has produced a new formulation of antiretroviral drugs i.e., a fixed-dose combination of 30 or 40 mg stavudine (d4T)/150 mg lamivudine (3TC)/200 mg nevirapine (NVP) [GPO-VIR] which has been available on the market since March 2002. This new combination formula makes simple dosing (one tablet twice daily) feasible. According to Thai FDA regulations, this type of new drug formula has to go through various phases of clinical trials, with an exemption of the animal toxicity study phase. However, the Thai GPO has been granted the special privilege of not needing approval by the Thai FDA for any of its products. Therefore, it is necessary to conduct a study documenting the efficacy and safety of this new formula. This prospective trial aimed to study the efficacy and safety of the fixed-dose combination of d4T/3TC/NVP. If the new fixed-dose combination of d4T/3TC/NVP is effective and safe, it may be offered to HIV-infected patients who are in the Universal Coverage Scheme.

Patients and Method

The primary objectives of this study were to evaluate the efficacy and safety of the fixed-dose combination of stavudine, lamivudine and nevirapine for the treatment of HIV infection. This was a prospective open-label single arm study. Subjects were adult HIV-infected patients who attended the HIV-clinic at Siriraj Hospital, Bangkok, Thailand. The study started in April 2002 until approximately 100 patients were enrolled. The majority of patients were insured by the Universal Coverage Scheme. However, the antiretroviral medications are not available in this public health system. The study protocol was reviewed and approved by the Ethical Committee on Research Involving Human Subjects, Faculty of Medicine Siriraj Hospital, Mahidol University. All enrolled patients had to be older than 18 years, were antiretroviral na ve, had a CD4 cell count of < 200/ L within 30 days prior to enrollment. Patients were ineligible if they were taking rifampicin, had a serum creatinine of $\geq$ 1.5X upper limit of normal (ULN), a total bilirubin of $\geq$ 2X ULN or serum alanine transaminase (ALT) and/or aspartate transaminase (AST) of $\geq$ 2X ULN or were pregnant or breast-feeding at the time of screening. Eligible patients had baseline clinical assessment and blood drawn for complete blood count (CBC), fasting blood sugar (FBS), electrolytes, AST, ALT, total bilirubin, creatinine, cholesterol, triglyceride, HDL-cholesterol, CD4 (determined by flow cytometry), HIV RNA (Roche Amplicor Monitor Standard Assay; lower limit of detection, 400 HIV RNA copies/mL) before the initiation of study drugs. The patients who were enrolled for the study received a fixed dose combination of d4T 30 mg (weight < 60 Kg) or 40 mg (weight $\geq$ 60 Kg)/3TC150 mg/NVP 200 mg orally once daily in the morning and separate antiretroviral drugs consisting of d4T 30 mg (weight < 60 Kg) or 40 mg (weight $\geq$ 60 Kg) and 3TC 150 mg orally once daily in the evening for 2 weeks and then a fixed dose combination of d4T 30 mg (weight < 60 Kg) or 40 mg (weight $\geq$ 60 Kg)/ 3TC/NVP twice daily thereafter to complete 52 weeks. The dosage of stavudine was adjusted according to the patient's current weight at each follow-up visit. The patients received prophylaxis for opportunistic infections and other standard care accordingly. The patients had follow-up visits at 2, 4, 8, 12 and 24 weeks, at which time they were assessed clinically and evaluated for adverse events. CBC, FBS, electrolytes, liver function tests (LFT), BUN, and creatinine were determined at 2, 8 and 12weeks. Blood tests for cholesterol, triglyceride, HDL-cholesterol were done at 12 weeks. CD4 cell count and HIV-RNA assay were done at 12 (HIV RNA measured by Roche Amplicor Monitor Standard Assay; lower limit of detection, 400 HIV RNA copies/mL) and 24 weeks (HIV RNA measured by Roche Amplicor Monitor Ultrasensitive Assay; lower limit of detection, 50 HIV RNA copies/

mL). Other laboratory tests were performed when clinically indicated. Treatment success was defined as the suppression of HIV RNA to below 400 copies/mL. The National Institute of Allergy and Infectious Diseases, Division of AIDS Table for Grading the Severity of Adult Adverse Events was used for reporting adverse events. This table specifies 4 grades of severity as follows: grade 1, mild; grade 2, moderate; grade 3, serious; and grade 4, life threatening. Demographic data (age, gender, weight), CD4 cell counts (at baseline, 12 and 24 weeks), HIV RNA (at baseline, 12 and 24 weeks), LFT, and the reported adverse events at each visit were recorded.

Statistical analysis

Baseline characteristics were presented as mean, standard deviation and proportions as appropriate. The efficacy analysis or treatment success (i.e., HIV RNA suppression rate to below 400 copies/mL) at 12 and 24 weeks from baseline was determined as proportions, mean $\log_{10}$ (copies/mL) change and standard deviation and analyzed by intention-to-treat (ITT) and on-treatment (OT) approach. ITT population included enrolled subjects who received at least one dose of the study drug. Patients were considered as treatment failures if either virological failure (viral load $\geq$ 400 copies/mL) or premature discontinuation of study treatment occurred. OT analysis included all patients' records on the weeks 12^{th} or 24^{th} accordingly. The mean differences of CD4 cell counts of 24 weeks from baseline were presented as proportions, mean and standard deviation. Regarding the adverse events, the data was presented as proportion. All *P* values were two-sided.

Results

One hundred and one adult HIV-infected patients who received medical care at Siriraj Hospital were enrolled in the study from April to November 2002. The baseline demographics of the patients enrolled are shown in Table 1. Mean of patients' age was 33.8 (6.8) years (range 21-53). Fifty four (54%) patients were male. Mean of baseline CD4 cell count was 58.7 (57.7) cells/mm^3 (range 0-191). Mean of baseline HIV RNA available from 98 patients was 334,671 (247,131) copies/mL (range < 400 - > 750,000) and mean of log HIV RNA was 5.3 (0.5) $\log_{10}$ copies/mL (range < 2.6 - > 5.9). At baseline 79 (80.6%) patients had HIV RNA > 100,000 copies/mL, 14 (14.1%) of whom had HIV RNA > 750,000 copies/mL.

Efficacy of treatment

Eighty four (83%) patients were available for follow-up at week 12. The mean decrease in $\log_{10}$ HIV RNA was 2.6(0.6) $\log_{10}$ copies/mL from baseline [$P < 0.001$; 95% confidence interval (CI), 2.51-2.78)]. Seventy three (72.3%) patients had HIV RNA < 400 copies/mL by intention-to-treat analysis (ITT) and 86.9% had HIV RNA < 400 copies/mL by on-treatment analysis (OT) (Table 2, Fig. 1). When stratified by baseline HIV RNA, 15 (78.9%) patients with baseline HIV RNA $\leq$ 100,000 copies/mL and 58 (73.4%) patients with baseline HIV RNA >100,000 copies/mL had a viral load < 400 copies/mL at week 12 by ITT ($P = 0.62$; 95% CI, –18.3%-22.0%) (Table 2). Fifteen (88.2%) patients with baseline HIV RNA $\leq$ 100,000 copies/mL and 58 (86.6%) patients with baseline HIV RNA > 100,000 copies/mL had a viral load < 400 copies/mL at week 12 by OT ($P = 0.856$; 95% CI, –21.7%-14.9%) (Table 2). Ten (71.4%) patients with

Table 1. Baseline demographics of 101 HIV-infected patients

Characteristic	n	Mean (SD)	Range	Median (P_5-P_{95})
Age (years)	101	33.8 (6.8)	21-53	
Sex: Male	54 (54%)			
CD4 cell count (cells/mm^3)	101	58.7 (57.7)	0-191	39.5 (1.2-1.7)
HIV RNA (copies/mL)	98	334,671 (247,131)	< 400 - > 750,000*	265,933 (33,628 - > 750,000)
$\leq$ 100,000	19 (19.4%)			
>100,000	79 (80.6%)			
log HIV RNA (copies/mL)	98	5.3 (0.5)	< 2.6 - > 5.9	5.4 (4.5 - >5.9)

* One patient had baseline HIV RNA < 400 copies/mL

Table 2. Virological responses at week 12

	Overall	HIV RNA < 400 copies/mL at week 12		95% CI for difference	*P*-value
		Baseline HIV RNA < 100,000 c/mL	Baseline HIV RNA > 100,000 c/mL		
ITT*	72.3% (73/101)	78.9% (15/19)	73.4% (58/79)	(-18.3%, 22.0%)	0.62
OT	86.9% (73/84)	88.2% (15/17)	86.6% (58/67)	(-21.7%, 14.9%)	0.856

* ITT = intention-to-treat-analysis, OT=on treatment analysis Comparison of virological response between two groups with different baseline HIV RNA HIV RNA of 3 patients were not obtained at base line

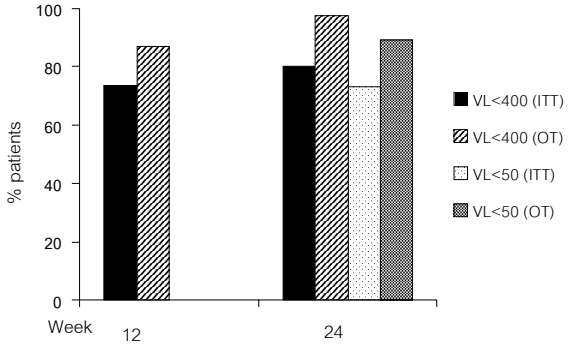
Table 3. Virological responses at week 24

HIV RNA at week 24(c/mL)		Overall	Baseline HIV RNA (c/mL)		95% CI for difference	*P*-value
			< 100,000	> 100,000		
< 400	ITT*	80.2% (81/101)	84.2% (16/19)	82.3% (65/79)	(-20.9%, 16.2%)	0.842
	OT**	97.6% (81/83)	94.1% (16/17)	98.5% (65/66)	(-25.5%, 3.8%)	0.295
< 50	ITT	73.3% (74/101)	78.9% (15/19)	74.7% (59/79)	(-19.5%, 20.7%)	0.698
	OT	89.2% (74/83)	88.2% (15/17)	89.4% (59/66)	(-24.4%, 11.7%)	0.891

* ITT = intention-to-treat-analysis, ** OT=on treatment analysis Comparison of virological response between two groups with different baseline HIV RNA HIV RNA of 3 patients were not obtained at base line

baseline plasma HIV RNA > 750,000 copies/mL had a viral load < 400 copies/mL by ITT and 83.3% had HIV RNA < 400 copies/mL by OT.

At 24 weeks, 83 (83%) patients were available for follow-up. The mean decrease in $\log_{10}$ HIV RNA was 3.6 (0.7) $\log_{10}$ copies/mL from baseline (P < 0.001; 95% CI, 3.4-3.7). Eighty one (80.2%) patients had HIV RNA < 400 copies/mL by ITT and 97.6% had HIV RNA < 400 copies/mL by OT (Table 3, Fig. 1).



VL = plasma HIV RNA load (copies/mL)
ITT = intention-to-treat analysis, OT = on-treatment analysis

Fig. 1 proportion of patients with plasma HIV RNA below a limit of detection of 400 and 50 copies/mL at 12 and 24

Seventy four (73.3%) had HIV RNA < 50 copies/mL by ITT and 89.2% had HIV RNA < 50 copies/mL by OT (Table 3, Fig. 1). By ITT, 16 of 19 (84.2%) patients with baseline HIV RNA ≤ 100,000 copies/mL and 65 of 79 (82.3%) patients with baseline HIV RNA > 100,000 copies/mL had HIV RNA < 400 copies/mL at week 24 respectively (P = 0.842; 95% CI, –20.9%-16.2%) (Table 3). Sixteen of 17 (94.1%) patients with baseline HIV RNA ≤ 100,000 copies/mL and 65 of 66 (98.5%) patients with baseline HIV RNA > 100,000 copies/mL had a viral load < 400 copies/mL at 24 weeks respectively (P = 0.295; 95% CI, –25.5%-3.8%) (Table 3). Fifteen of 19 (78.9%) patients with baseline HIV RNA ≤ 100,000 copies/mL and 59 of 79 (74.7%) patients with baseline HIV RNA > 100,000 copies/mL had HIV RNA < 50 copies/mL at week 24 by ITT respectively (P = 0.698; 95% CI, –19.5%-20.7%) (Table 3). Fifteen of 17 (88.2%) patients with baseline HIV RNA ≤ 100,000 copies/mL and 59 of 66 (89.4%) patients with baseline HIV RNA > 100,000 copies/mL had a viral load < 50 copies/mL at 24 weeks by OT respectively (P = 0.891; 95% CI, –24.4%-11.7%) (Table 3). Eleven (78.6%) patients with baseline plasma HIV RNA > 750,000 copies/mL had a viral load < 400 copies/mL by both ITT and OT. Ten (71.4%) patients with baseline plasma HIV RNA > 750,000 copies/mL had a viral load < 50

copies/mL by ITT and 90.9% had a viral load < 50 copies/mL by OT. Overall, the mean CD4 cell count was 155.1 (89.0) cells/mm^3 (range 13-402). The mean increase in CD4 cell count from baseline was 96.5 (63.5) cells/mm^3 ($P < 0.001$; 95% CI, 82.7-110.4) (Table 4). The mean $\log_{10}$ HIV RNA was 1.8 (0.4) $\log_{10}$ copies/mL (range < 1.7-4.4). Of those who had baseline HIV RNA > 750,000 copies/mL, the mean CD4 cell count was 152.6 (58.7) cells/mm^3 (range 1-175) and the mean increase in CD4 cell count from baseline was 106.4 (86.4) cells/mm^3 ($P = 0.002$; 95% CI, 48.4-164.5).

Adverse events

A total of 20 (20%) patients experienced adverse events, 15 (15%) of whom were withdrawn from the study due to the adverse events (Table 5). Six (6%) patients developed diffuse maculopapular skin rashes; 3 (3%) patients had fever with maculopapular rashes; one patient had toxic epidermal necrolysis (TEN) probably attributable to trimethoprim/sulfamethoxazole (however, TEN related to NVP cannot be excluded); 2 (2%) patients developed maculopapular rashes with grade 3 hepatotoxicity. Isolated rash was the cause of discontinuation of study drugs in all patients (6% of subjects). The overall incidence of rash was 12%. Twenty five (25%) patients developed hepatotoxicity as follows: 17 (17%) grade 1 (ALT and/or AST 1.25-2.5 X ULN), 1 (1%) grade 2 (ALT and/or AST 2.6-5 X ULN), 6 (6%) grade 3 (ALT and/or AST 5.1-10 X ULN) and 1 (1%) grade 4 (ALT and/or AST > 10 X ULN). The incidence of severe hepatotoxicity (grade 3 or 4) was 7%. Of those who developed grade 3 hepatotoxicity, 3 patients were able to continue the antiretroviral treatment. One patient had grade 3 hepatotoxicity as well as severe peripheral neuropathy; the latter was likely attributable to stavudine. Seven (7%) patients developed fever. One patient had severe hyponatremia with seizure possibly from the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Three (3%) patients were lost to follow-up. There was no significant change of blood glucose, cholesterol, triglyceride, HDL-cholesterol and calculated LDL-cholesterol. Four patients developed mycobacterial infection (2 with *M. tuberculosis*, 1 with disseminated *M. avium* complex infection and 1 with probable nontubercuous mycobacteria, 14, 14, 21 and 74 days after the start of antiretroviral treatment respectively) presumably resulting from immune reconstitution. The patient with disseminated *M. avium* complex infection died and one of the patients with tuberculosis discontinued antiretroviral treatment; the rest have remained in the study. Other adverse events such as lactic acidosis, lipoatrophy, were not observed during 6 months of antiretroviral therapy.

Table 4. Comparison of mean CD4 cell count at baseline and at week 24 (n = 83)

CD4 cell count (cells/mm^3)	Mean (SD)	95% CI	*P*-value
Baseline	58.5 (56.1)		
Week 24	155.1 (89.0) (Range 13-402)		
Change from baseline	96.5 (63.5)	(82.7-110.4)	< 0.001

Paired t-test

Table 5. Adverse events

	n (%)
Total	20 (20)
Rash	12 (12)
Isolated MP rash	6 (6)
MP Rash + fever	3 (3)
Toxic epidermal necrolysis	1 (1)
MP Rash + hepatotoxicity	2 (2)
Grade 3 or 4 hepatotoxicity	7 (7)
grade 3	6 (6)
grade 4	1 (1)
Fever	7 (7)
Neuropathy	1 (1)
Opportunistic infections	4 (4)
Severe hyponatremia + seizure	1 (1)
Death	1 (1)
Withdrawal due to adverse events	15 (15)

MP=maculopapular

Discussion

Overall virological responses (success rate) at week 12 (HIV RNA < 400 copies/mL) were 72.3% and 86.9% by intention-to-treat and on-treatment analysis respectively. There was no significant difference of success rate in patients with low (≤ 100,000 copies/mL) or high (> 100,000 copies/mL) baseline HIV RNA. The success rate at week 24 in the present study was lower than that in the study of Kaspar et al which found that 92% (23/25) of their patients had HIV RNA below 400 copies/mL at 20 weeks. A total of 25 patients in the latter study had a mean baseline CD4 cell count of 259 cells/mm^3 (which

was higher than that of the present study) and a mean viral load of 160,000 copies/mL (which was lower than that of the present study)[6]. Similarly, at week 24, 80.2% and 97.6% of patients in the present study had an undetectable viral load (< 400 copies/mL) by intention-to-treat and on-treatment analysis respectively and there was no significant difference when taking the baseline HIV RNA (low or high) into account. When the lowest cut-point HIV RNA level of < 50 copies/mL was considered, 73.3 and 89.2% of the patients had an undetectable viral load at week 24 by intention-to-treat and on-treatment analysis respectively. The authors of the present study are waiting for the results of CD4 cell counts and HIV RNA levels at 52 weeks for comparison with the 2NN study which was a head-to-head study comparing nevirapine and efavirenz. The 2NN study randomized 220 and 387 antiretroviral na ve HIV-infected patients to receive nevirapine 400 mg once daily and nevirapine 200 mg twice daily respectively together with d4T and 3TC. The results were analyzed at week 48[7]. Other studies have been done on the efficacy of the same combination of antiretroviral regimens but the outcomes were evaluated according to different measured outcomes (i.e., measurement of viral load vs CD4 cell count) and over different time-frames. Russel et al studied the efficacy of an antiretroviral regimen consisting of stavudine, lamivudine and nevirapine in 54 HIV-infected, antiretroviral-na ve patients and found that 21 out of 29 (72%) patients who had baseline viral loads below 80,000 copies/mL and 20 out of 25 (80%) who had baseline viral loads greater than 80,000 copies/mL achieved undetectable viral loads (< 500 copies/mL) at 12 months (intention-to-treat)(8). Farrell et al conducted a long-term follow-up (range 8-40 months) of 26 HIV-infected patients treated with stavudine, lamivudine and nevirapine which demonstrated that 92% had viral loads < 50 copies/mL at their last visit[9]. A study of the efficacy of generic copies of stavudine + lamivudine + nevirapine in the treatment of 226 antiretroviral-na ve patients in Lagos, Nigeria demonstrated that between baseline and week 24 the log copies of viral load decreased from 4.7 log10 RNA copies/mL to 2.7 log 10 RNA copies/mL, the median CD4 cell counts increased by 170 cells/mm^3[10]. Pujari studied the immunological effectiveness of a simplified fixed-dose combination of d4T/3TC/NVP (n = 659) or AZT/3TC/NVP (n = 335) in antiretroviral-na ve patients and found that the mean CD4 cell counts increased from 125.6 cells/mm^3 (119.8-131.3, n = 726) at baseline to 310.8 cells/mm^3 (298.1-323.5, n = 619) at 6 months[11].

The overall incidence of rash was 12% in the present study compared to 15-20% in previous studies[12]. Six percent of our patients discontinued nevirapine-containing treatment due to isolated rash compared to 4.3% in a previous report[13]. The incidence of severe (grade 3 or 4) hepatotoxicity in the present study was 7% compared to 8-21% in other studies[14,15]. Although the present study was a noncomparative trial, it demonstrated that the fixed-dose combination of d4T + 3TC + NVP (GPO-VIR) was effective for the treatment of antiretroviral na ve, advanced HIV-infected patients through 24 weeks. The study drugs were well tolerated and the adverse effects were comparable to those reported in a previous study. Long term efficacy and safety of these drugs should be followed.

Conclusion

The 24-week results from this study demonstrated that the fixed-dose combination of d4T+3TC+NVP (GPO-VIR) was safe, well tolerated and effective in increasing CD4 cell counts and suppression of HIV RNA in advanced HIV-infected patients in Thailand. However, a longer term study of the safety and efficacy should be done.

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ความปลอดภัยและประสิทธิผลของยาต้านไวรสในรูปเม็ดรวมซึ่งประกอบด้วยสตาวูดีน, ลามิวูดีน และเนวิราพีน (จีพีโอเวียร์) ในการรักษาผู้ป่วยติดเชื้อเอชไอวีระยะโรคเอดส์เต็มขั้นในประเทศไทย: ผลการศึกษาที่ 24 สัปดาห์

ถนอมศักดิ์ อเนกธนานนท์, วินัย รัตนสุวรรณ, วิชัย เตชะสาธิต, อารีเอื้อ สนใจ, สุรพล สุวรรณกูล

วัตถุประสงค์ : เพื่อศึกษาความปลอดภัยและประสิทธิผลของยาเม็ดรวมประกอบด้วยสตาวูดีน, ลามิวูดีน และเนวิราพีน (จีพีโอเวียร์) ในการรักษาผู้ป่วยติดเชื้อเอชไอวีที่เป็นผู้ใหญ่และไม่เคยได้รับยาต้านไวรัสเอชไอวีมาก่อน

วิธีการ : การศึกษาแบบเปิดในผู้ป่วยกลุ่มเดียว ผู้ป่วยติดเชื้อเอชไอวีจำนวน 101 รายซึ่งไม่เคยได้รับยาต้านไวรัสเอชไอวีมาก่อน ได้รับยาเม็ดรวมซึ่งประกอบด้วยยาสตาวูดีน, ลามิวูดีนและเนวิราพีน (2 สัปดาห์แรกผู้ป่วยได้รับยาเนวิราพีนวันละหนึ่งมื้อ) ผู้ป่วยได้รับการติดตามที่สัปดาห์ที่ 2, 4, 8, 12 และ 24 มีการตรวจจำนวนเม็ดเลือดขาวซีดี 4 และปริมาณไวรัสเอชไอวีที่สัปดาห์ที่ 12 และ 24

ผลการศึกษา : มีผู้ป่วยทั้งหมด 101 รายเข้าร่วมในการศึกษา ค่าเฉลี่ย (ค่าเบี่ยงเบนมาตรฐาน) ของจำนวนเม็ดเลือดขาวซีดี 4 และปริมาณไวรัสเอชไอวีที่ระยะพื้นฐานมีค่าเท่ากับ 58.7 (57.7) เซลล์ต่อลบ.มม. และ 5.3(0.5) log_{10} copies ต่อมล.ตามลำดับ ที่สัปดาห์ที่ 24 ค่าเฉลี่ยของ log HIV RNA ลดลง 3.6(0.7) log_{10} copies ต่อมล. ($P < 0.001$; 95% CI, 2.70-3.032) ผู้ป่วย 81 ราย (ร้อยละ 80.2) มีปริมาณไวรัสเอชไอวีต่ำกว่า 400 copies ต่อมล. โดยการวิเคราะห์แบบ intent-to-treat และร้อยละ 97.6 มีปริมาณไวรัสเอชไอวีต่ำกว่า 400 copies ต่อมล. โดยการวิเคราะห์แบบ on-treatment ผู้ป่วย 16 ราย (ร้อยละ 84.2) ซึ่งมีปริมาณไวรัสเอชไอวีที่ระยะพื้นฐานน้อยกว่าหรือเท่ากับ 100,000 copies ต่อมล.และผู้ป่วย 65 ราย (ร้อยละ 82.3) ซึ่งมีปริมาณไวรัสเอชไอวีที่ระยะพื้นฐานมากกว่า 100,000 copies ต่อมล.มีปริมาณไวรัสเอชไอวีต่ำกว่า 400 copies ต่อมล.โดยการวิเคราะห์แบบ intent-to-treat ($P = 0.842$; 95% CI, -20.9%-16.2%) ผู้ป่วย 16 ราย (ร้อยละ 94.1) ซึ่งมีปริมาณไวรัสเอชไอวีที่ระยะพื้นฐานน้อยกว่าหรือเท่ากับ 100,000 copies ต่อมล.และผู้ป่วย 65 ราย (ร้อยละ 98.5) ซึ่งมีปริมาณไวรัสเอชไอวีที่ระยะพื้นฐานมากกว่า 100,000 copies ต่อมล.มีปริมาณไวรัสเอชไอวีต่ำกว่า 400 copies ต่อมล.โดยการวิเคราะห์แบบ on-treatment ($P = 0.295$; 95% CI, -25.5%-3.8%) ค่าเฉลี่ย (ค่าเบี่ยงเบนมาตรฐาน) ของจำนวนเม็ดเลือดขาวซีดี 4 ที่ 24 สัปดาห์มีค่าเท่ากับ 155.1 (89.0) เซลล์ต่อลบ.มม. (พิสัย 13-402) ค่าเฉลี่ย (ค่าเบี่ยงเบนมาตรฐาน) ของจำนวนเม็ดเลือดขาวซีดี 4 เพิ่มขึ้นจากระยะพื้นฐานเท่ากับ 96.5 (63.5) เซลล์ต่อลบ.มม. ($P < 0.001$) ผู้ป่วยร้อยละ 12 ที่ได้รับยาสตาวูดีน, ลามิวูดีนและเนวิราพีนเกิดผื่น ผู้ป่วยร้อยละ 7 เกิดพิษต่อตับรุนแรงระดับ 3 หรือ 4

สรุป : ยาต้านไวรัสเอชไอวีชนิดเม็ดรวมซึ่งประกอบด้วยยาสตาวูดีน, ลามิวูดีนและเนวิราพีน (จีพีโอเวียร์) มีความปลอดภัย ผู้ป่วยทนต่อยาได้ดีและมีประสิทธิผลดีในการเพิ่มจำนวนเม็ดเลือดขาวซีดี 4 และลดจำนวนไวรัสเอชไอวีได้ที่ 24 สัปดาห์ในผู้ป่วยติดเชื้อเอชไอวีในระยะโรคเอดส์เต็มขั้นในประเทศไทย