Survival Time of AIDS Patients in Bamrasnaradura Institute

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A retrospective cohort study compared the survival time of AIDS patients, or HIV infected patients who had a CD4 count less than 200 cell/mm^3, who had Thailand's local triple anti-retroviral drugs regimen (GPO-VIR) with original triple anti-retroviral therapy without protease inhibitor in Bamrasnaradura Institute. The result proved that survival time in patients who had local anti-retroviral drugs was the same as patients who had original triple anti-retroviral therapy without protease inhibitor (log rank p-value = 0.9617). In conclusion, local anti-retroviral drugs can be used to prolong patients' survival time as much as original triple anti-retroviral therapy without protease inhibitor.

Keywords: *AIDS, Survival time, GPO-VIR*

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World Health Organization (WHO) reported global epidemiology from 1982 until 2003, the estimated number of patients who live with HIV-infection is 42 million, and more than 3 million died from AIDS. Thailand is one of the countries that are faced with HIV/AIDS situation. A report from the Department of Disease Control, Ministry of Public Health (MOPH), the estimated the number of patients who live with HIV-infection in Thailand is 362,768 and 86,923 have died from AIDS[1-3].

Many factors affect the survival time in this group of patients such as genetic marker, opportunistic infections, CD4+ count, and anti-retro viral drug[4,5]. From a previous study, most Thai patients whose disease progress to AIDS will be dead in 24 months and mean survival time is 9 months[6,7]. It is now proved that Highly Active Anti-Retroviral Therapy (HAART) can prolong patients' survival time significantly. Many original HAART regimens are now available in Thailand, but the cost of the original drug is more than 10,000 baht per month. In order to deal with the financial constraint, the Thai Government Pharmaceutical Organization (GPO) has introduced a cheaper local triple anti-retroviral drugs regimen, GPO-VIR.GPO-VIR which is a combination of triple drugs, 3TC, d4T, and Nevirapine[8]. There is a one-year descriptive clinical study of GPO-VIR in Thailand that demonstrated that GPO-VIR could improve CD4+ count and reduce opportunistic infections in HIV infected patients[9]. From evaluation of rapid expansion of the national ART program in Thailand shows that the local fixed dose regimen is safe and reduces the risk of dying from HIV infection[10,11]. The present research shows that the survival time of AIDS patients or HIV infected patients who had a CD4 count less than 200 Cell/mm^3, treated with GPO-VIR had at least an equally prolonged survival time compared to the original triple Anti-Retroviral Therapy without Protease inhibitor.

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Hypothesis

Survival time in AIDS patients or HIV infected patients, who had a CD4 count of less than 200 Cell/mm^3 who had Thailand's local Triple anti-retroviral drugs regimen (GPO-VIR) was the same for those who had the original triple Anti-Retroviral Therapy without Protease inhibitor

Objectives

To compare the survival time of AIDS patients, or HIV infected patients who had a CD4 count of less than 200 Cell/mm^3, with those who had Thailand's local

Triple anti-retroviral drugs regimen (GPO-VIR) rather than with the original triple Anti-Retroviral Therapy without Protease inhibitor.

Material and Method

This is a retrospective cohort study from patients' records in Bamrasnaradura Infectious Institute, Ministry of Public Health. Samples were AIDS patients or HIV infected patients who had a CD4 count of less than 200 Cell/mm^3 in Bamrasnaradura Infectious Institute. The present study retrieved data of AIDS patients who attended OPD from 1 January 2002 until reaching the required number of samples. Starting date was counted from the diagnosis of AIDS or had CD4 of less than 200 Cell/mm^3 until 1 July 2004 (the end date of the present study).

Sample size was calculated by the formula for time to event study based on log-rank test

$$\text{Sample size per group (n)} = \frac{(Z_{\alpha/2} + Z_{\beta})^2 (h + 1)^2}{(2 - P_1 - P_2)(h - 1)^2}$$

$Z_{\alpha/2}(\alpha = 0.05) = 1.96$ $\quad P_1 = P_2 = 0.75$ (% of survival at time end)

$Z_{\beta}(\beta = 0.9) = 1.28$ $\quad h = \frac{\ln(P_1)}{\ln(P_2)} = \frac{\ln(0.75)}{\ln(0.75)} = 1$

Therefore, the number of samples per group was 123 (actual numbers of samples in the present study are as follows:

1. Number of patients who had GPO-VIR was 131.

2. Number of patients who had the original triple Anti-Retroviral Therapy without Protease inhibitor was 136.

Inclusion criteria

1. Adult patients (aged more than 15 years old) who were diagnosed with AIDS or HIV-infection with a CD4 count less than 200 Cell/mm^3.

2. Received GPO-VIR or original triple Anti-Retroviral Therapy without Protease inhibitor.

Exclusion criteria

1. Patients who were pregnant before or in the present study period.

2. Patients whose data or record forms were not complete for data collection, such as that which cannot be defined the starting time.

Statistical analysis

Data were presented in number and percentage. Pearson Chi-square test was used to find out the association between sociodemographic data and the two groups of patients, by Kaplan-Meier survival analysis and log rank test. A p-value of less than 0.05 was considered significant.

Ethical Consideration

The present study was conducted under the supervision and regulations of the Bamrasnaradura Infectious Institute research committee. The case record forms were treated anonymously.

Results

Total number of patients enrolled in this study is 267. Number of patients who had GPO-VIR is 131. Number of patients who had original triple Anti-Retroviral Therapy without Protease inhibitor is 136. They were similar in their profile, marital status, residential province (p-value > 0.05). There were more males in this study than females (p-value = 0.052). Most of the patients worked in the private sector (p-value = < 0.01). Most of the patients were enrolled because of CD4+ count of less than 200 cells/cumm (p-value = 0.074) (Table 1).

Most patients were still alive at the end of the present study. The proportion of surviving patients in both groups was the same at the end of the present study (p-value = 0.675) (Table 2).

Kaplan-Meier survival analysis

Kaplan-Meier survival analysis was performed to compare survival time between the two groups of patients; patients who had local anti-retroviral drugs (GPO-VIR), patients who had the original triple Anti-Retroviral Therapy without Protease inhibitor. Log rank analysis, there was no difference in the survival time between both treatment groups (Log rank p-value = 0.9617) (Fig. 1, Table 3).

Discussion

A study by Dr. Ruxrungtham showed that median survival time in Thai AIDS patients who had no treatment is about nine months and most of them died within two years[12]. The present study showed that local anti-retroviral drugs can be used to prolong patients' survival time as much as the original triple Anti-Retroviral Therapy without Protease inhibitor (p-value = 0.9617). The limitation of the present study is that it is a retrospective cohort study, resulting in a

Table 1. Patients' profile (n = 267)

Socio-demographic data		GPO-VIR Group	Triple therapy Group	Chi-square (p-value)
Sex	Male	79 (60.30)	98 (72.10)	4.125 (0.052)
	Female	52 (39.70)	38 (27.90)	
Marital status	Single	49 (37.40)	44 (32.40)	3.03 (0.551)
	Married	66 (50.40)	76 (55.90)	
	Widow	11 (8.40)	10 (7.40)	
	Divorce	5 (3.80)	4 (2.90)	
	No record	0 (0)	2 (1.50)	
Occupation	No work	25 (19.10)	19 (14.00)	19.044 (<0.01)
	Private sector	84 (64.10)	78 (57.40)	
	Public sector	9 (6.90)	34 (25.00)	
	No record	13 (9.90)	5 (3.70)	
Residential province	Bangkok	54 (41.20)	53 (39.00)	0.816 (0.665)
	Nontaburi	22 (16.80)	19 (14.00)	
	Other provinces	55 (42.00)	64 (47.10)	
Criteria including in this study	CD4 < 200	75 (57.30)	91 (66.90)	11.493 (0.074)
	TB	24 (18.30)	28 (20.60)	
	PCP	20 (15.30)	7 (5.10)	
	Cryptococcal meningitis	11 (8.40)	8 (5.90)	
	Herpes Zoster	0 (0.00)	1 (0.70)	
	Toxoplasmosis	1 (0.80)	0 (0.00)	
	Histoplasmosis	0 (0.00)	0 (0.00)	
	CMV retinitis	0 (0.00)	1 (0.70)	
	Total	131 (100)	136 (100)	

Table 2. Patients' status at the end of the present study (1 July 2004)

Status	GPO-VIR Group	Triple therapy Group	Chi-square (p-value)
Alive	129 (98.50)	134 (98.50)	0.01 (0.675)
Dead	2 (1.50)	2 (1.50)	
Loss F/U	0 (0.00)	0 (0.00)	
Total	131 (100)	136 (100)	

Table 3. Log rank test compares the survival time between patients who had GPO-VIR compared with patients who had the original triple Anti-Retroviral Therapy without Protease inhibitor

Type of ARV	Total patients	Number of events	Number of censored	Log rank test (p-value)
GPO-VIR	131	2	129	0.00 (0.9617)
Original HAART	136	2	134	

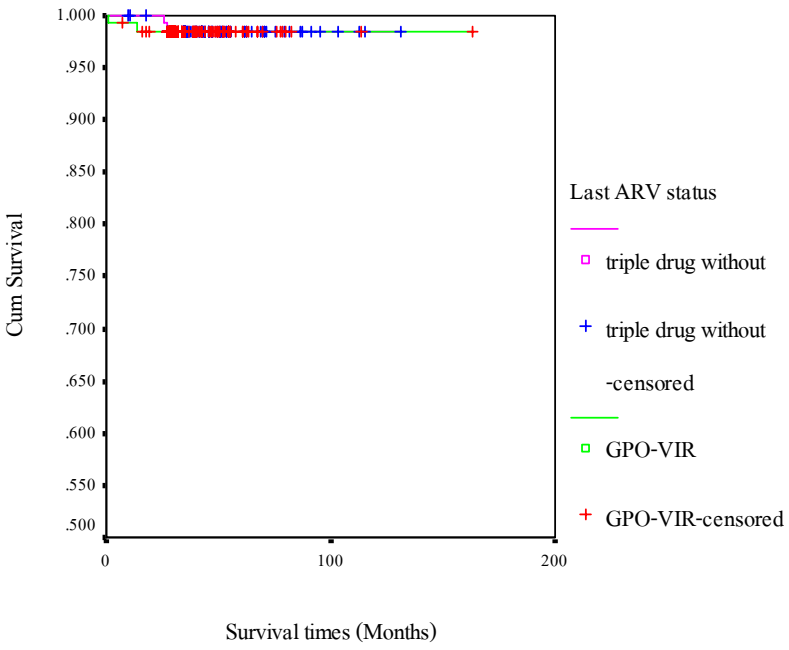

Fig. 1 Kaplan-Meier survival curve in patients who had GPO-VIR compared with patients who had the original triple Anti-Retroviral Therapy without Protease inhibitor

lot of censored cases losing the power of prediction. Secondly, the present study did not compare other aspects between the two groups of drugs such as price, side effects, complaint, etc[13,14]. From the present study, TB and Cryptococcal meningitis were the top two opportunistic infections in patients, which was the same as other studies in Thailand[15,16].

Conclusion

HIV infected patients who had anti-retroviral therapy lived longer than patients who did not receive any treatment. Most of them lived longer than 5 years and most of the patients in the no-treatment group were dead within two years. The present study showed that local anti-retroviral drugs could be used to prolong patients' survival time as much as the original triple Anti-Retroviral Therapy without Protease inhibitor. The authors recommend that future study be a cohort and compare other aspects of drugs such as price, side effects, complaints, etc.

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การศึกษาระยะเวลารอดชีวิตของผู้ป่วยโรคเอดส์ที่สถาบันบำราศนราดูร

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การศึกษาข้อมูลจากเวชระเบียนเพื่อเปรียบเทียบระยะเวลารอดชีวิตในผู้ป่วยที่มีอาการของโรคเอดส์ หรือ เริ่มมีเม็ดเลือดขาวแบบซีดีสี่ต่ำกว่า 200 ตัวต่อลูกบาศก์มิลลิเมตร ที่ได้รับยาต้านไวรัสสูตรสามตัวที่ผลิตในประเทศไทยโดยองค์การเภสัชกรรม (GPO-VIR) เปรียบเทียบกับยาสูตรสามตัวแบบมาตรฐานโดยไม่รวมผู้ที่ได้รับยา protease inhibitor ผลการศึกษาพบว่า ระยะเวลารอดชีวิตในผู้ป่วยไม่แตกต่างกันในผู้ป่วยทั้งสองกลุ่ม (p-value = 0.9617) สรุปได้ว่าการใช้ยาต้านไวรัสสูตรสามตัวที่ผลิตในประเทศไทย โดยองค์การเภสัชกรรม (GPO-VIR) ในผู้ป่วยที่มีอาการของโรคเอดส์ หรือ เริ่มมีเม็ดเลือดขาวแบบซีดีสี่ต่ำกว่า 200 ตัวต่อลูกบาศก์มิลลิเมตรมี อัตราการรอดชีวิตไม่ต่างจากยาสูตรสามตัวแบบมาตรฐานที่ผลิตโดยไม่รวมผู้ที่ได้รับยา protease inhibitor