Experience in Using Antiretroviral Therapy in Cross-border Areas along the Mekong River

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Abstract Chiang Saen Hospital has provided antiretroviral therapy (ART) to people infected with HIV, especially the Burmese and Laotians residing in Thailand or in their own countries. The guidelines of the country program were applied. The cohort study design measured ART adherence, survival rate, clinical outcomes, result of the prevention approach and psychological support as outcome indicators. Data were collected and analyzed using FUCHIA software. The Kaplan-Meier method was conducted for survival analysis. The results revealed that 73 non-Thai PLHA (people living with HIV/AIDS) who received ART from July 2004 to June 2007 (19 Laotians, 16 of whom resided in their own country; 51 Burmese, 20 of whom resided in their own country, and three minority people residing in Chiang Saen. Mean ART adherence was more than 98.2 per cent. Mean survival time in months was 41 (95% CI 39.0-43.2). Survival at 36 weeks was 96 percent. Three cases died after ART, two from AIDS and one from the adverse effects of ART. No case had been lost to follow-up or stopped treatment. Thirty per cent of the patients needed to change individual drugs due to adverse effects. The health of those on treatment improved. Access to ART increased the uptake of service in the prevention approach. Eleven cases received vocational loans and one case received an education fund. It is one model of how the disadvantaged can access ART in cross-border areas and how Thailand can support its neighbors. However, the effectiveness and the sustainability of the program still need to be considered.

Key words: *antiretroviral, cross-border program, Chiang Saen Hospital*

บทคัดย่อ **ประสบการณ์การใช้ยาต้านไวรัสรักษาผู้ติดเชื้อเอชไอวีในพื้นที่ชายแดนเลียบแม่น้ำโขง**

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**โรงพยาบาลเชียงแสน จังหวัดเชียงราย*

ที่โรงพยาบาลเชียงแสนได้ให้การรักษาผู้ติดเชื้อเอชไอวีชาวพม่าและชาวลาวด้วยยาต้านเอชไอวี โดยใช้แนวทางโครงการของประเทศไทย. การศึกษาออกแบบการเก็บข้อมูลไปข้างหน้า. ตัวชี้วัดผลลัพธ์คือการวัดความร่วมใจในการรักษาด้วยยาต้านเอชไอวี, อัตราการรอดชีวิต, ผลลัพธ์ทางเวชกรรม และผลการดำเนินโครงการ เก็บข้อมูลและวิเคราะห์ผลทางสถิติโดยใช้โปรแกรมฟูเชีย (FUCHIA Program), วิเคราะห์การรอดชีวิตโดยวิธีของเคพแลน-ไมเออร์. ผลพบว่ามีผู้ติดเชื้อเอชไอวีที่มิใช่ชาวไทย จำนวน ๗๓ รายได้รับยาต้านเอชไอวีตั้งแต่เดือนกรกฎาคม ๒๕๔๗ จนถึงเดือนมิถุนายน ๒๕๕๐ มี

Chiang Saen Hospital, Chiang Rai Province

ผู้ป่วย ๑๙ รายเป็นชาวลาว (๑๖ รายอาศัยอยู่ในประเทศของตน), ผู้ป่วย ๕๑ รายเป็นชาวพม่า (๒๐ อาศัยอยู่ในประเทศของตน) และอีก ๓ รายเป็นชนกลุ่มน้อยที่อาศัยอยู่ในเชียงแสน ค่าความร่วมใจในการรักษาด้วยยาต้านเอชไอวีเฉลี่ยสูงกว่าร้อยละ ๙๘.๒. ระยะเวลาการรอดชีวิตเฉลี่ย ๔๑ เดือน (ร้อยละ ๙๕ ของค่าความเชื่อมั่น ๓๙.๐ - ๔๓.๒). การรอดชีวิต ณ สัปดาห์ที่ ๓๖ ร้อยละ ๙๖. ผู้ป่วยจำนวน ๓ รายเสียชีวิตภายหลังการรักษาด้วยยาต้านเอชไอวี (๒ รายเสียชีวิตจากโรคระยะเอดส์ และ ๑ รายเสียชีวิตจากผลไม่พึงประสงค์จากการรักษาด้วยยาต้านเอชไอวี). ไม่มีผู้ป่วยรายใดที่ขาดการติดตามหรือหยุดการรักษา. ร้อยละ ๓๐ ของผู้ป่วยจำเป็นต้องเปลี่ยนยาตัวใดตัวหนึ่งจากเหตุการณ์ไม่พึงประสงค์. สุขภาพของผู้ป่วยที่ได้รับการรักษาดีขึ้น การเข้าถึงการรักษาด้วยยาต้านเอชไอวีเพิ่มการเข้าร่วมกิจกรรมต่าง ๆ ที่อยู่ในแนวทางการป้องกัน. ผู้ป่วยจำนวน ๑๑ รายได้รับเงินทุนกู้ยืมในการประกอบอาชีพและผู้ป่วยจำนวน ๑ รายได้รับเงินทุนการศึกษา. โครงการดังกล่าวเป็นรูปแบบหนึ่งของการที่ผู้ด้อยโอกาสสามารถเข้าถึงการรักษาด้วยยาต้านเอชไอวีในบริเวณพื้นที่ชายแดนและเป็นรูปแบบหนึ่งที่ประเทศไทยสามารถให้การสนับสนุนประเทศเพื่อนบ้าน. ผลประโยชน์แท้จริงและความยั่งยืนของโปรแกรมคงจำเป็นที่จะต้องพิจารณาต่อไป.

คำสำคัญ: *ยาต้านเอชไอวี, พื้นที่ชายแดนเลียบแม่น้ำโขง, โรงพยาบาลเชียงแสน*

Background and rationale

The World Health Organization (WHO) reported the number of people living with HIV/AIDS (PLHA) in 2006 as being 39.5 million, with 2.9 million having died from the complications of AIDS[1]. Thailand is one of the countries facing the threat of HIV/AIDS. A report from the Department of Disease Control, Ministry of Public Health (MOPH), says that the estimated number of PLHA in Thailand is 309,653 and 85,870 have died from AIDS[2]. Of the living cases, 91,520 of them have access to antiretroviral therapy (ART)[3]. National access to antiretroviral drugs for PLHA is called the NAPHA (National Access to Care for People Living with HIV/AIDS) Program, which was established in 1993. Some generic antiretrovirals (ARVs) are manufactured under the Program. Since mid-2005, every Thai in need of ART has been able to receive it free of charge through the government health-care system. Unfortunately, the NAPHA Program is not serving the needs of many people from neighboring countries who cross the border into Thailand for work and trade.

In response to the “3 by 5 policy”, the Chiang Saen Cross-border ART Program was launched in 2004 in cooperation with the Thai Ministry of Public Health, various community programs of the 15th International AIDS Conference in Bangkok in 2006, Medecins Sans Frontieres (MSF) and the Population and Community Development Association (PDA). The Program has been partly funded by the European Union (EU) with grant of 100,000 euros, which is aimed at providing the opportunity for the cross-border population to access ART. The Program was launched in Maesai and Chiang Saen districts in Chiang Rai Province, the northernmost province of Thailand, since the two districts had already established ART programs supported by strong PLHA peer groups. Furthermore, although the districts border different countries (Myanmar and the Lao People’s Democratic Republic) they are only some 30 kilometers apart, thus facilitating supervision, exchange of experiences, and mutual support.

Mobile and marginalized populations in Chiang Saen border area

Chiang Sean district shares a common border with Bor Kaew district, Lao PDR, along the Mekong River for about 30 km, with Myanmar along the Raung River for a similar distance. This area is called “The Golden Triangle”. Currently, Chiang Saen is being promoted as one part of an economic quadrangle, established for increasing trade among those coun-

tries with China via the Mekong River. The district has also become an attractive place for cross-border migrants. There are now approximately 1,480 registered, and 1,830 non-registered people living in the district, 90 percent of whom are Burmese, 10 percent Laotian and a few Chinese and minority people.[4] Non-registered people do not have identification (ID) cards or health insurance. The non-Thai population in the Chiang Saen border area comprises migrants, mobile populations who come primarily from neighboring countries (Lao PDR and Myanmar) for trade and work, and so-called hilltribe people. Although they are of different nationality, defined by the State, historically they share a common language and culture. Most work in tobacco-curing houses or factories, or work as manual laborers or hired workers. Female migrants usually work in restaurants and massage parlors which often provide illicit sexual services. Assessing the extent of HIV prevalence among the marginalized population at the Chiang Saen border area is difficult owing to the lack of data and questionable sporadic surveillance. Most of them still do not have enough knowledge about HIV/AIDS to care for themselves, and most of them cannot read or write Thai. This makes it more difficult to care for them compared with the general population.

The PLHA and HIV Clinic in Chiang Saen Hospital is a 60-bed district hospital. It is responsible for 64,380 members of the National Health Coverage Insurance scheme in two districts, Chiang Saen and Doi Luang.[5] The number of PLHA in Chiang Saen that have been recorded since 1988 totals 1,471 cases to date. Of them, 650 have already died. The hospital has provided ART since 2002, and currently provides ART to 420 Thai patients (399 adults and 21 children) via the NAPHA Program and to 73 non-Thai patients via the Chiang Saen Cross-border ART Program. Clients attend with different regularities according to clinical stage (serving over 250 HIV patients per month). The Chiang Saen HIV Clinic provides a comprehensive package of HIV/AIDS services that includes counseling, support, prophylaxis, treatment of opportunistic infections, ART and referrals where necessary. The services range from the expansion of voluntary counseling and testing (VCT), the development of tuberculosis (TB) screening, and the availability of care for the prevention of mother-to-child transmission (PMTCT). A community-based educational program, incorporating basic HIV/AIDS education and a treatment literacy component explaining the value and use of ARV medications, is also one component that complements treatment in this Program. The hospital has integrated the approaches of Western and Eastern medicine to care for its patients. The clinic, which is linked with seven sub-district health stations, provides care to PLHA through a cross-functional team consisting of one physician, two professional nurses, two pharmacists, two lab technicians, three health workers, and one aide, with the assistance of 11 well-trained PLHA volunteers. The PLHA volunteers were trained and now assist the hospital team in carrying out primary counseling and adherence. A semi one-stop service, of which only drug-dispensing is provided separately, is held every Tuesday at the PLHA peer office, which is located in Chiang Saen Hospital. There are monthly support group meetings, which involve many activities including prevention, health promotion focus on alternative methods, psychosocial support, and promoting families and community participation.[6]

Chiang Saen Cross-border ART Program

Initial design of the Program. At the beginning, funds were available to assure that some 60 people would receive ART for two years (30 in Chiang Saen and 30 in Mae Sai) as well as treat any underlying opportunistic infections that would otherwise seriously affect the health of the persons starting ART. When the treatment program started at Chiang Saen Hospital in July 2004, the program was operated through the HIV clinic at the hospital. Treatment is free of charge for ART and anti-opportunistic medication, as is laboratory testing.

Treatment protocols and guidelines. To ensure that the additional workload on already busy staff is kept to a minimum, the treatment protocols and guide-

lines used would be identical to those of the NAPHA Program. This would ensure that the beneficiaries receive a standard of treatment and care identical to that currently offered to Thai nationals by the Chiang Saen Hospital. Moreover, data collection would also be the same as that in the NAPHA Program. In this way, the Program would integrate the non-registered population into the existing ART program in the hospitals.

Eligibility criteria for Cross-border ART Program

With a limited quota at the beginning of the Program, initiating ART in a mobile population with a high prevalence of infection and limited resources necessitated a process of patient selection. Patient selection potentially challenges equity in the delivery of the services and, therefore, requires clearly defined and transparent procedures. The assessment was carried out by a selection committee consisting of a Chiang Saen cross-functional team, representatives of PDA and Thai PLHA volunteers in Chiang Saen. Eligibility for the Program is determined by criteria that combine an assessment of the clinical and social conditions of the candidates, their anticipated ability to adhere to therapy, as well as the need of the patients to be cases of AIDS, or asymptomatic HIV with CD4 cell counts of less than 250/mm^3, or symptomatic HIV with CD4 cell counts of less than 200/mm^3. After the patient has been counseled about ART, PLHA volunteers assess the social and support structures available by conducting a home visit which verifies the person's family environment and disclosure to at least one person who will act as a treatment assistant. PLHA volunteers could play a supportive role by bringing potential beneficiaries to the hospital and acting as their friend or "buddy". Preference has been given to PLHA based on their number of dependants (such as mothers versus single men), health status (very sick versus meeting the clinical criteria), disclosure and activism (being open about HIV status and/or active in community organizations versus refusing to disclose). Other factors considered in the decision to initiate ART are history of alcohol abuse and geographical mobility. In the initial phase of this Program, beneficiaries should come from one of the ethnic minority groups or be a national of Myanmar or Lao PDR who resides within the district in order to enable easy follow-up and the possibility of home visits by volunteers or NGO staff.

Enrolment process

Enrolment was begun in a step-wise fashion to allow for a rapid launch of the Program and so as not to place too great a burden on hospital staff. Potential beneficiaries were introduced to the hospital staff by the PLHA groups or by self referral.

Candidates' anonymous dossiers are presented to a Chiang Saen Cross-border ART Committee who make the final decision on enrolment, based on the clinical, social and adherence criteria.

Treatment regimen

Standardized triple therapy regimens are used. Initially the vast majority of patients were started on GPO-Vir, a local generic fixed-dose combination of stavudine, lamivudine and nevirapine, which costs only US$1 per day. The choice of first-line therapy between efavirenz and nevirapine considers whether the person is receiving tuberculosis treatment, has abnormal liver function (in which case efavirenz is preferred) or is pregnant (in which case nevirapine is preferred), in accordance with WHO guidelines.

Outcome indicator

The outcome indicators of this program are ART adherence, survival rate (Kaplan-Meier method), patients' clinical outcomes, and results of the Program.

Patient follow-up

Before initiation of ART, patients attend a group session led by a specialized nurse and PLHA volunteers as counselors, who explain the nature of treatment and other HIV issues, such as transmission. A pharmacist explains the related medications and im-

portance of adherence. One week later, a second, individual counseling session takes place. The patient is asked what they remember from the first session and, if considered to have gained enough understanding, they receive a two-week supply of drug therapy. At follow-up visits, the patient's remaining pill stocks are counted, and health staff ask the patient about any problems he or she may have in taking the medicines. The PLHA volunteer team conducts systematic home visits during the first weeks of the ART regimen to ensure adherence to treatment from pill counts at the time of consultation. There is no access to systematic viral load testing for this patient group. In terms of clinical follow-up, the frequency of visits is adapted to the patient's clinical condition. During the first trimester following the start of treatment, all patients receive medical consultations. After the first trimester, a nurse assesses the need for and frequency of medical consultations. In general, patients who have stabilized and are doing well on treatment are seen every two months by a medical doctor when they come to collect their prescription refills. At the same time, they receive adherence counseling from the pharmacists if adherence problems are identified. Currently, all patients undergo a CD4 cell count every six months. Until now, there has been no access to viral load testing at Chiang Saen Hospital. Diagnosing treatment success has relied on detecting change in the CD4 cell count and on clinical symptoms.

Adherence support

ART requires good adherence to achieve sustained suppression of viral replication and to prevent the onset of resistance. Because ART is a life-long treatment, it requires commitment and a responsible attitude. To achieve good adherence to ART, the Program has combined several components.

Simplify dosage regimens Combining simplified regimens with a low pill burden of one pill twice a day makes it easier to initiate more patients on treatment. Use of fixed-dose combinations (GPO-vir or GPO-Z), which simplifies the treatment regimen, reduced the time needed for patient education and generally facilitated adherence to treatment.

Material support People in therapy are provided with pillboxes and daily drug schedule records and educational materials explaining the importance of ART adherence.

Individual support A solid, patient-centered educational approach and a comprehensive individual support program are implemented to ensure a good understanding of the treatment by the patients and a strong support system. Everyone who enrolled in the Program is required to identify a treatment assistant. The treatment assistant is usually someone living in the household, aware of the person's status and willing to assist with medication as necessary. PLHA volunteers (trained in HIV/AIDS and ART) are available in the clinic to help PLHA with individualized adherence plans that respond to their specific needs. A pharmaceutical self-reported evaluation, pill count, interview and one-by-one counseling take place on every visit to the dispensing unit of the Pharmacy Department. PLHA volunteers conduct one home visit per month per person to follow-up on adherence by re-checking the pharmacists' record of their drug regimen with the number of pills remaining, discussing their regimen and teaching them more about health care. In case PLHA fail to come for their appointments, PLHA volunteers will follow-up on them and forward data to the health-care providers at Chiang Saen Hospital.

Peer support Once a month, the HIV Clinic hosts self-help support group meetings, attended exclusively by people on ART in the Day Care Center at Chiang Saen Hospital, on the third Thursday of each month, as well as monthly group meetings in Day Care Centers at the sub-district level. Participants discuss barriers to adherence, adverse events, disclosure and other psychosocial issues that affect them. PLHA volunteers, as counselors, regularly perform adherence workshops in the support groups. Every six months, group meetings for self-evaluation on ART adherence and outcome are organized to share the patients' experiences on how to adhere to a program of long-

term drug intake.

Communication and transportation

Most of the mobile population in the Chiang Saen border areas can speak the local Thai language. Also, the cultures of these people are similar. A few cases need interpreters, who also are in the Program, to communicate. In the second year of the Program, since the population is mobile, the people returned to their own countries. As a result, the Program expanded in order to provide ART for patients who reside in Myanmar or Lao border sites. Therefore, follow-up and monitoring have become more challenging. Communication and follow-up for the people in the Myanmar and Lao sites are carried out through relatives in Thai border areas, and river-crossing speed boat drivers, as well as by using mobile phones and pamphlets printed in their own languages. Home visits were done through PLHA volunteers or the MSF staff, crossing the border into the Lao or Myanmar sites. Work in Myanmar is more difficult than in Lao PDR. Currently, there are two Burmese patients in the program who are healthier and who work as PLHA volunteers in Myanmar sites, and link with Thai PLHA volunteers. Both of them were well-trained at Chiang Saen Hospital to care for PLHA in their community within Myanmar. The affordability of transportation across the border, the distance and costs involved, are big issues for those residing in neighboring countries. However, Norwegian Church Aid (NCA) and MSF supported these costs, and the hospital makes appointments with participants all on the same day so they could travel together more cheaply.

Psycho-social support

Apart from regular psychosocial support as Thai PLHA, participants in the Program have an opportunity to receive micro-credit loans from PDA. The project called “Buddy” or Pa “Tong Go” is to support loans for PLHA not in excess of 16,000 Baht as a one-time loan to a pair comprising an HIV-positive migrant and an HIV-negative Thai. This aims to decrease the problem of HIV/AIDS in the minds of the community. The loans are directed toward starting a business, such as selling mobile phone cards or raising pigs. The interest of 0.5 percent per month is placed in a revolving fund for PLHA activities.

METHODOLOGY

Study design This study applied a descriptive cohort design to assess the outcome of the Program which provided ART to non-Thai PLHA in border areas through Chiang Saen Hospital, Ministry of Public Health, Chiang Rai Province, Thailand.

Inclusion criteria The inclusion criteria were as follows: adult, non-Thai HIV patients (aged more than 15 years) who were diagnosed with AIDS, or symptomatic HIV with a CD4 cell count less than or equal to 250 cells/mm^3, or asymptomatic HIV with a CD4 cell count less than 200 cells/mm^3; and enrolled in the cross-border ART Program at Chiang Saen Hospital in Chiang Rai Province from July 1, 2004 to June 30, 2007, whose treatments were supported by MSF exclusively.

Data collection To monitor the Program, everyone on ART in the Chiang Saen cross-border program were assessed clinically: weekly for the first two weeks, then monthly thereafter. Once people were stable on therapy, they could be assessed every two months. At all visits, patient data were recorded on the hospital Out-Patient Department (OPD) card and FUCHIA (Follow Up and Clinical of HIV Infection and AIDS)[7] form. The starting date was counted from the start of ART in the Program until June 30, 2007 (the end date of the present study). CD4 cell count and weight value were taken from a database with 90 days of precision (i.e. ± 90 days valued at six monthly intervals). If the CD4 cell count value was missing at the start of ART, the available result within six months before ART was taken as the baseline CD4 cell-count value.

Data analysis Medical information from standardized FUCHIA forms were fed into an MSF/Epicentre-designed data management system of the FUCHIA Program. The system produced standardized reports, including key outcome indicators. De-

scriptive statistics were used to describe the patients' characteristics, percentage of adherence, mean CD4 gain, mean weight gain, treatment changes and adverse effects. A Kaplan-Meier survival analysis was performed to determine the survival rate of the patients, increasing the number of patients who undertook activities in the Program. Patients who received psychological support were also determined. Data were presented in number and/or percentage forms.

Ethical consideration The study was conducted under the patient rights regulations of Chiang Saen Hospital. The case record forms were treated anonymously.

RESULTS

Extending and expanding the Program

The second-year Program (July 1, 2005 - June 30, 2006). In May 2005, MSF extended and expanded the Program for Chiang Saen Hospital. The quota depended on the workload Chiang Saen Hospital could handle. This enabled the Program to be up and running. An MSF doctor and a nurse had a joint Chiang Saen Team to care for the cross-border ART group monthly at the HIV clinic in Chiang Saen Hospital. Owing to the unlimited quota in the second-year Program, selection of eligible applicants was changed from being the responsibility of the selection committee to that of the medical doctor, to make the assessment and decide on inclusion.

The third-year Program (July 1, 2006 - June 30, 2007). In the third-year Program, Chiang Saen Hospital limited the number to 80 patients due to the workload involved.

The cumulative number of patients in the Chiang Saen Cross-border ART Program has increased rapidly from 19 to 56 and then 76 patients in the first, second and third years of the Program, respectively. ART enrolments by Chiang Saen Hospital are shown in Table 1.

Patient characteristics and clinical measures at baseline. An analysis of those receiving treatment between July 2004 and June 2007 included 73 adults, prior to ART in the Chiang Saen Cross-border ART Program. The median age at baseline was 33 years [range 16-64]. The majority were females (55%), mar-

Table 1 ART enrollments, by Chiang Saen hospital (1 July 2004 - 30 June, 2007)

Residence	Number of patients started on ART			
	Laotian	**Myanmar**	**Minority**	**Total**
July 1, 04 - June 30, 05 (31 cases)				
Thailand	2	16	1	19
Homeland	4	8	-	12
Total	**6**	**24**	**1**	**31**
July 1, 05 - June 30, 06 (25 cases)				
Thailand	1	9	1	11
Homeland	5	9	-	14
Total	**6**	**18**	**1**	**25**
July 1, 06 - June 30, 07 (17 cases)				
Thailand	-	6	1	7
Homeland	7	3	-	10
Total	**7**	**9**	**1**	**17**
Grand total	**19**	**51**	**3**	**73**

ried (78%), illiterate (76%) and of Myanmar nationality (69.9%). Half of them were farmers (58%). Almost all were Buddhists (99%). Forty-three percent of their partners had already been infected but a certain number were asymptomatic (38%). Seventy-nine percent were ART naïve. The median CD4 cell count at the time of initiating ART was quite low (median CD4 cell count, 81). Thirty-six percent were already in stage III, and 12 percent in stage IV at the time of starting ARV (tuberculosis, 12 cases; *Pneumocystis carinii* pneumonia; eight cases; Cryptococcal meningitis, four cases; Penicillosis, three cases; and toxoplasmosis, one case). These reflected the fact that many people initiated ART at a very advanced stage of disease progression. For patients that had a baseline body mass index (BMI) (33 cases), some were normal, with a BMI of more than 18.5 (37%).

Results of adherence. Beneficiaries of the Program showed high levels of adherence to the medication. All of them came for the services regularly. The average ART adherence rates at the first, the second and the third years were 98.2, 99.1 and 99.4 percent, respectively.

Survival. The estimated mean survival time was 41 months (95% confidence interval 39.0-43.2). Survival at 36 weeks was 96% (Figure 1). Three patients died after ART. Of them, two deaths were attributed to AIDS and one died due to a serious adverse effect (Steven Johnson Syndrome) from ARV medication. All the deaths occurred before the patients had completed three months on treatment, with no mortality after this time.

Clinical outcome. Ninety-six percent (70/73 cases) were still alive and taking treatment. Fifty-eight percent (42/73 cases) had been on ART for more than a year. No cases had been lost to follow-up or had stopped treatment. The median follow-up time was two months. After initial ART, the frequency of opportunistic infections declined dramatically. Summaries of patient outcome on CD4 cell count and weight gain up to June 2007 are shown in Figure 2 and Figure 3, respectively.

Treatment changes and adverse events. Seventy percent (51/73 cases) tolerated the GPO-vir regimen well. Liver function test rate was low at 6 percent. This indicated good follow-up. Thirty percent (22/73 cases) of patients needed to change an individual drug due to adverse effects (four cases from nevirapine, nine cases had lipodystrophy from D4T, eight cases had numbness from D4T, and one case changed to a second-line regimen due to drug intol-

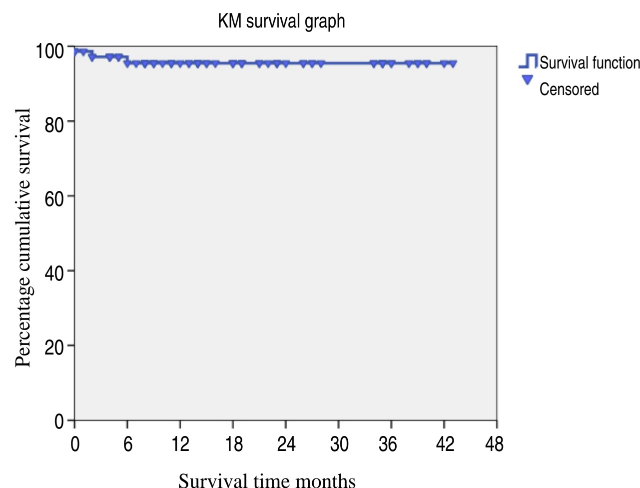

Fig. 1 Kaplan-Meier survival graph of patients on ART. Mean CD4 cell count gain from baseline (cells-cm^3).

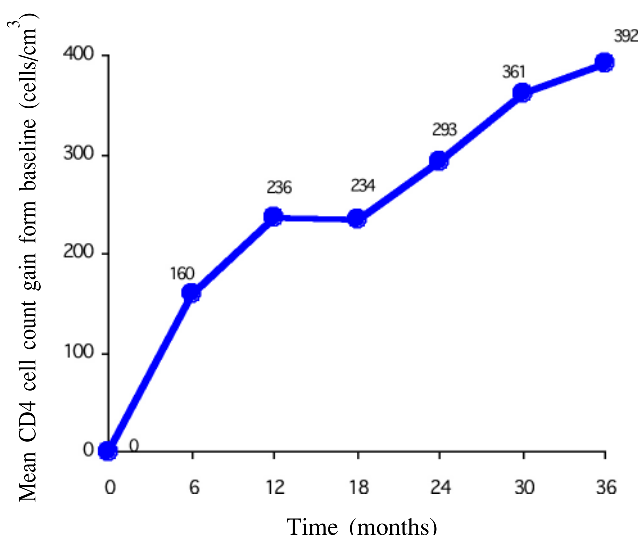

Fig. 2 Mean C4 cell count gain from baseline of patients on ART.

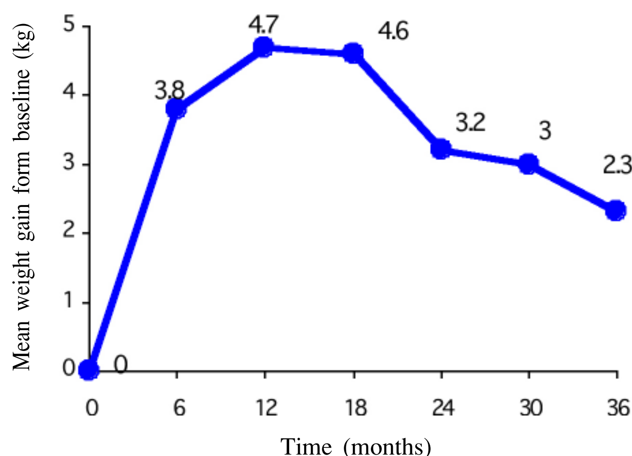

Fig. 3 Mean weight gain from baseline of patients on ART.

erance from nevirapine and efaviranz). To date, 23.3 percent (17/73 cases) of the patients changed to the triple fixed-dose combination of zidovudine, lamivudine and nevirapine (GPO-Z), due to adverse effects from long-term use of D4T.

Result of the prevention approach in the Program. The Program is part of an increasing number of initiatives in the Chiang Saen cross-border area responding to HIV/AIDS. Before the Program existed, few non-Thai PLHA there were aware of their status and even fewer were willing to disclose it. This difference can be attributed largely to the comprehensive approach to HIV/AIDS care for non-Thai PLHA, and critically to the inclusion of ART, which has seen an increase in the uptake of VCT in Chiang Saen Hospital from 80 HIV tests in 2004 to 122, 138 and 126 in 2005, 2006 and the first six months of 2007, respectively. TB screening increased from 12 in 2004 to 28, 32 and 30 in 2005, 2006 and the first six months of 2007, respectively. PMTCT provided motivation for non-Thai pregnant women to be tested for HIV (1, 1, 2 and 1 cases in 2004, 2005, 2006 and the first six months of 2007, respectively). Condom distribution increased from 2,400 pieces in 2004 to 3,600, 4,800 and 4,200 pieces in 2004, 2005, 2006 and the first six months of 2007, respectively. It was found that the target group increased the desire to join a day-care center and AIDS activities during the Program.

Results of the psychosocial support. At the start of treatment, most non-Thais who had received ART in the Program met with pain and discomfort, anxiety and depression. Over time, the health of those on treatment improved in all domains. Many cases were prepared to help new cases with the same problems as theirs. Of the 73 non-Thai ART patients, 11 had applied for and received vocational loans, which had played a very significant role in ensuring economic autonomy and improving self-confidence. One case, a 16-year-old female, had received some educational funding from both PDA and NCA; now she receives support from the Baan Chivit Mai Foundation in Chiang Rai Province.

DISCUSSION

Patient outcome. The results of the study showed that patient outcome under this Program has been positive. Survival at 36 weeks was 96 percent, which is better than the reference survival rate in the United States (80%)[8]. Mean CD4 cell count gain and mean weight gain were strong. Mean CD4 cell count gain after one year of treatment is higher than the reference value obtained from Hopkins Clinic and Kampala Clinic (236 cells/cm^3 compared with 110 and 72 cells/cm^3, respectively[9]. Mean CD4 cell count gain is still increasing at the end of the three-year treatment. Although there was a dramatic weight increase up to one year after treatment, weight started to decrease after 18 months of treatment. It is most likely due to lipodystrophy. All cases are healthy and have a better quality of life and look forward to the future with hope. When they have the chance to access ART, receive care at Chiang Saen Hospital, and join others who have HIV, whether Thai, Laotian or Burmese, they are all seen as equals in receiving care. They understand each other, provide moral support, and help each other like members of a family. This helps give them strength, both physically and mentally, knowing that they are not alone; it gives them the energy to work and raise income for themselves. These findings indicate that ART is producing good results for the patients in the Program.

Availability of ART is important for prevention of HIV/AIDS. The availability of the Chiang Saen Cross-order ART Program has demonstrated that treatment is important for prevention because it provides motivation for non-Thai PLHA to be aware of their status; without treatment as an option, knowledge that one is HIV-positive can be seen as offering little more than stigmatization. Community participation as well as dialogue that fosters trust between care providers and receivers is absolutely necessary. The Program helps migrants in the Chiang Saen border area to have trust and faith in the hospital and public health care. This Program promotes openness and reduces stigma, as HIV is no longer an inevitable death sentence for non-Thai people. It can fuel educational initiatives supported by a pool of non-Thai PLHA about their status. By providing effective treatment for opportunistic infections and ART for those in the late stages of AIDS, the clinic provides an incentive for others to be tested. The combination of prevention activity initiatives has helped to create an environment where non-Thai people feel cared for. This has positively affected prevention, promoting openness and decreasing the stigma around HIV/AIDS in the Chiang Saen cross-border area.

Sustainability of the Program. At the beginning, the Program was planned only as a two-year project. The Chiang Saen Team envisaged that, once the Program was up and running, further funding could be secured to expand and extend the life of the Program. In the second-year Program, MSF supported the Program without limiting the duration and the number of cases. However, Chiang Saen Hospital staff do not have the capacity to handle more than 80 cases of non-Thai ART owing to their workload and the fact that ART is a life-long treatment. In the provision of ART, if attention is given only to funding in terms of support for the drugs, there is the chance of negative rather than positive outcomes owing to the many, various and related factors which would make the model Program a feasible success. The effectiveness and sustainability of the Program should be considered. Ideally, all Program partners should play a role to ensure the long-term sustainability of the Program, with the Ministry of Public Health taking a leading role in this matter. The sustainability of providing people from other countries with access to ART should not be the sole responsibility of Thailand. The hospital has thus made an effort to organize joint programs between Thailand and neighboring countries to facilitate better holistic care and to establish facilities within their communities, with the intention that they will eventually be self-run.

Essential key components supporting the cross-border ART program. The experience of the Chiang Saen Cross-border ART Program yields several lessons. In the most severely affected border areas, this can be achieved with many components, as follows:

Policy. The policy of related countries in border areas should be clear and concrete enough to be put into action. Leaders at both the central and local levels should provide enough support for implementation.

Service organization structure. The structure of the service system regarding health and other aspects, which include governmental organizations (GOs) and non-governmental organizations (NGOs), have to be linked in order to ensure holistic and comprehensive care. The structure of a system disbursing power down to the district level makes the work easier. Good relationships and links with other ministries will also help the Program receive more support.

Attitude and willingness of health-care providers "No boundaries" is the condition that should have been set for the Cross-border ART Program, because, no matter where people come from, they should all have the right to health care. In these conditions, the attitude and willingness of all those involved in the work of this Program are important components for ensuring that the aim is achieved together. That is, PLHA can live normally and happily in society with good health and quality of life, the same as others, without regard for ethnicity or religion but as people of the world.

Teams and volunteers. Service teams among

primary, secondary and tertiary care settings should develop service plans together for each PLHA receiving services. The referral system, for both the formal and informal approaches has to be organized and regularly reviewed. Good collaboration among health-care settings of countries and NGOs are important. Multidisciplinary teams, including PLHA network-based care with a major emphasis on psychosocial support, utilizes available resources and ensures holistic management of HIV/AIDS. Identifying potential beneficiaries of the HIV/AIDS patient-care team is the role not only of the health-care providers and PLHA peer support groups, but also migrant health workers, who are already active in Chiang Saen district. Because of the challenge in reaching and maintaining a relationship with the non-Thai population, this Program relies on a team that stretches beyond the hospital's doors. Trained PLHA volunteers share the workload of health providers. Most of the prevention and promotion activities in the communities are led by the PLHA leaders. Home visits by PLHA volunteers are another important component of community support

Effective communication and empowering PLHA to take care of themselves. The Program has empowered PLHA, with some having become role models for others in the Program. Migrants may know how to prevent HIV, but the social conditions are not in place to empower them to achieve good health. Effective communication empowering PLHA to take care of themselves is needed to ensure long-term adherence to ART.

Mobilizing the community. The Team developed HIV care alongside strong civil society pressure and a community-based education program. This approach mobilizes the community to be aware of HIV in a comprehensive response. The Team educated many in the community about HIV/AIDS, prevention and ART. In the Chiang Saen cross-border area, the link between education and treatment can best be described as a new social contract. The clinics provide effective HIV/AIDS care and life-saving treatment, and the community breaks the silence, fights stigma and discrimination and, through education, promotes understanding and prevention. Emphasis on spiritual care was achieved through community gatherings at local temples.

NGOs support. It was necessary to rely on support from various NGOs since, in Thailand, ART is not serving the needs of non-Thai people. We have contacted many NGOs for assistance, such as Norwegian Church Aid (NCA), focusing on community-bases Programs; the International Organization for Migration (IOM), focusing on primary care, and the Research Institute Tuberculosis/Japan Foundation AIDS Program (RIT/JFAP) supporting a tuberculosis offensive, which is an important problem that cannot be separated from the AIDS problem. RIT/JFAP funded the community program, including religious and spiritual care to support this ART Program.

Families and communities. The key players in providing holistic care include not just the hospital staff. Therefore, the Chiang Saen Hospital, with the PLHA network, has recognized the need for strong patient and family participation since the project began.

Simplified approach. Simple regimens with standardized clinical guidelines sequencing the use of a triple fixed-dosed regimen, such as GPO-vir or GPO-Z, and managing adverse events encourage ease of adherence for the patient and follow-up for the health-care professionals.

Resources management. With limited resources, GOs and NGOs should adjust their way of thinking and be stronger together so that they can work in the same direction. Various resources, including personnel, funding and time from many organizations should be integrated in order to decrease repetitiveness and loss of resources, and to gain the most benefit for the target group. In late 2005, in response to staff shortages and the heavy workload of existing staff, not having enough medical doctors and nurses available to play this role, MSF sent a doctor and a nurse to help in HIV clinics once a month. The Program has therefore had to draw on a mix of local and supplemental staff from MSF to provide di-

rect medical services, technical assistance and training. Adherence counseling sometimes now takes place in groups, in order to reach more patients with the same human resources.

Future challenges. The study suggests that a future study should involve a bigger sample size to compare clinical outcome and survival rate. For the Chiang Saen Cross-border ART Program, many challenges remain ahead as the Program extends into future years of treatment provision. These include the following points.

The first challenge is the sustainability of the Program. From July 2007, care for Laotian PLHA receiving ART is being extended to people in Lao PDR. HIV clinics for Laotians have been planned for three hospital facilities in Lao border sites (Ton Pueng District Hospital, Bor Kaew Provincial Hospital and Laueng Nam Ta Provincial Hospital) instead of exclusively at the Chiang Saen Hospital. Lao cases at Chiang Saen Hospital will be transferred to hospital facilities in the Lao border area in the fourth-year program (from 1 July 2007). The plan is to transform Chiang Saen Hospital into a referral center that can provide care for complicated cases. Training activities targeting clinical staff in their countries are needed to ensure that an HIV/AIDS patient is properly cared for from an early stage. Now, the Program has already offered additional training for medical staff of Lao sites on diagnosis, treatment of opportunistic infections and ART follow-up for their patients so that more patients could be handled in their countries. It is hoped that, with initial NGO funding, ART access will soon become a part of the national plans fo Lao PDR. For Myanmar, the work is more difficult than in Lao PDR due to the political situation and cultural differences. Carrying out an offensive in Myanmar border areas for ART access is less feasible than in the Lao border site. Initial work was done through a Christian group. In addition, Chiang Saen Hospital encouraged two PLHA in the Program to become volunteers in Myanmar and help care for PLHA there. At this time, the sustainability of the Program still remains the big question for Myanmar PLHA.

The second challenge is human resources and training, since it is already planned that the Laotian cases will be transferred to three hospital facilities in the Lao border site, the clinical algorithms and the referral system between countries need to be developed urgently to enable health personnel in Lao PDR working in isolated locations to follow patients within existing structures and resources.

The third challenge is addressing the specific challenges of pediatric HIV. In July 2007, there were four Lao children with HIV/AIDS in need of ART. Chiang Saen Hospital has no specialist doctor for ART in pediatrics. In addition, currently available formulations for pediatric HIV care hardly include any fixed-drug combination, which complicates administration and thus adherence. These aspects pose problems of adjusting and measuring dosages. On the psychosocial component, pediatric HIV requires specific adherence support programs to address the challenges faced by care givers and children. These issues are currently being explored in Chiang Saen.

For the fourth challenge, although the adherence-support program used in the Chiang Saen Cross-border ART Program up to now has proven to be effective in achieving high levels of adherence and increasing CD4 levels, later stages of treatment might require a different approach to adherence-support as patients begin to feel healthier and more distanced from the negative effects of their illness. Counselors in Chiang Saen Hospital are implementing separate support groups to respond specifically to the issues affecting patients with regard to treatment for one year or longer.

For the fifth challenge, under the Program there are plans to offer more prevention activities by providing more effective information, education and communication on safe sex, commercial sex workers, as well as PMTCT. Next is an effective intervention to address TB and HIV, which necessitates an exploration of the possibility of integrating both services for non-Thai people. Planning HIV/AIDS strategies for Chinese groups residing in Chiang Saen is another challenge. This group of people lack an organization

that cares for their health problems, which is a problem when they have risky behavior. Now, the Chiang Saen Team is trying to find a way to support this issue. Finally, related to the policy level, in the coming years the Program will face the challenge of growing numbers of non-Thai HIV patients failing to use first-line treatment. There is therefore an urgent need to advocate lower prices for second-line drugs and the development of a new triple-fixed-dose regimen.

CONCLUSIONS

The Chiang Saen Cross-border ART Program was initiated to demonstrate that treating HIV/AIDS with antiretroviral drugs in a Chiang Saen cross-border health-care setting and in a resource-limited environment is feasible. Although the Program is still evolving, and treatment systems and points of care continue to be modified, the Program has already shown that, when treatment is adapted to local conditions and is supported by human and financial resources, cross-border health systems can effectively provide comprehensive HIV/AIDS care. The Program mobilizes the public health system-related HIV/AIDS issues and provides unprecedented opportunities for a more effective response by involving non-Thai PLHA in cross-border areas, their families and communities. It also provides care and strengthened HIV prevention by increasing awareness, and health education, creating a demand for testing and counseling, and reducing stigma and discrimination. Seventy-three patients are now on ART in this Program and patients' clinical outcomes have been positive. The experience in Chiang Saen reveals that effective implementation of cross-border services relies on several components. The Program improves the morale of health-care workers who can offer something beyond temporary treatment for opportunistic infections, and helps to keep families intact and economically stable, thereby protecting the most vulnerable (women and children) and minimizing at-risk populations. The Program also provides examples of how such challenges are being overcome in the growing number of cross-border areas in which the ART Program is under way. This was envisioned as a Thai endeavor to help neighboring countries to access ART following the "3 by 5 policy". The case studies and analyses in this series show how governments, civil society organizations, NGOs, corporations and others are successfully providing ART and care to non-Thai PLHA. In documenting this pioneering Program, the author hopes that Chiang Saen's experiences will both inform and inspire everyone who is working to make access to ART a reality.

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