

RECRUITMENT UPDATE

1245 participants were recruited into START by the end of April 2011, of which 169 were recruited during the months of February, March and April. Table 1 shows, accrual by country, with sites in South Africa, Brazil and Chile performing exceptionally well. Congratulations to these sites for their success!

Table 1: Accrual Summary by Country

Country	No. of patients recruited		
	By 31-Mar-11	From 01-Feb to 30-Apr-11	Per site in 3 months*
USA	187	19	0.66
Germany	182	15	0.88
Brazil	88	31	15.5
Spain	79	5	1
France	75	7	0.64
UK	73	12	2.4
Argentina	69	8	1.14
Thailand	59	7	3.5
South Africa	59	16	16
Belgium	54	7	3.5
Peru	52	10	3.33
Australia	45	4	0.66
Poland	39	7	7
Chile	35	11	11
Greece	27	0	0
Mali	24	1	1
Denmark	23	0	0
Morocco	22	6	6
Switzerland	17	1	0.33
Finland	15	2	2
Italy	11	0	0
Israel	10	1	1

* Only sites that are open for recruitment have been included.

We would like to thank all sites for their hard work so far and for their efforts in identifying new potential study participants. A particular thank you goes to our top 10 recruiters, namely:

1.	Desmond Tutu HIV Foundation, Cape Town, South Africa	59 patients
2.	Hospital Escola Sao Francisco de Assis, Rio De Janeiro, Brazil	58 patients
3.	Chulalongkorn University Hospital, Bangkok, Thailand	39 patients
4.	Wojewodzki Szpital Zakazny, Warszawa, Poland	39 patients
5.	Fundacion Arriaran, Santiago, Chile	35 patients
6.	Asociacion Civil Impacta Salud y Educacion, Lima, Peru	35 patients
7.	Instituto de Infectologia Emilio Ribas, Sao Paulo, Brazil	31 patients
8.	Institute of Tropical Medicine, Antwerp, Belgium	30 patients

9.	Johann Wolfgang Goethe University Hospital, Frankfurt, Germany	27 patients
10.	Hopital Saint-Louis, Paris, France	26 patients

CENTRAL DRUG REPOSITORY (CDR) UPDATE

Various activities are underway at the CDR to accommodate new sites and countries and newly available drug. The following activities were completed so far or are currently ongoing:

1. Updating of the Clinical Trial Agreements (CTAs) between the pharmaceutical companies and the University of Minnesota (Sponsor); the last CTA was executed at the end of April.
2. Translation, approval, and printing of START drug labels to cover expanded availability of ARVs to both pilot and definitive phase sites; the label booklets are currently being printed.
3. Shipment of fresh drug to the depots, ready for order and shipment to new countries; this activity can only be completed once the drugs with the new label booklets are available. Drug labeling will commence this month (May).

New sites in countries that participated in the Pilot Phase of START are able to order drug from the CDR as soon as site registration and training have been completed and pharmacy plans have been approved; however, raltegravir will only be available in June and only in countries where it is commercially licensed.

New sites in countries that did not participate in the Pilot Phase must also complete site registration and training and obtain START pharmacy plan approvals before ordering START drug. In addition, the newly-labeled study drug must be available at the depots serving these sites. We expect that the CDR will open for most of these sites in June; however, as the initial import of drug into some countries may require more time this may not be possible.

Please do not hesitate to contact your SCC or ICC if you have any questions with regard to drug availability. We are happy to help.

NOTE REGARDING RITONAVIR

The START CDR to date has only provided ritonavir soft-gel capsules, which require refrigeration. The new tablet formulation for ritonavir, which can be kept at room temperature, will be added to the CDR in 2012.

NEW START SUBSTUDY: LIVER FIBROSIS

A new START substudy examining the effect of HIV, Hepatitis C virus (HCV) and ART on the rates of liver fibrosis progression (LFP) among HIV-infected individuals with or without hepatitis is currently being developed. More details about the substudy will follow soon.

SUBSTUDY ENROLMENT

Accrual into all START substudies has been progressing well in recent months. Co-enrollment into the Genomics, Neurology and Arterial Elasticity substudies is above 70%, while co-enrollment into the Pulmonary Substudy has risen to almost 50% and is with the addition of new sites expected to increase further.

Table 3: Co-enrolment into START Substudies

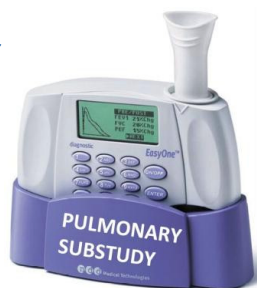
	Overall Co-enrolment in %*
Genomics Substudy	95.4%
Neurology Substudy	71.6%
Arterial Elasticity Substudy	74%
Pulmonary Substudy	45.8%

* Data as of 03 May 2011

High co-enrolment rates are important, because substudy enrollment needs to be completed by the time the main START study has accrued the planned 4000 participants. Therefore, we encourage all sites to co-enroll as many participants as possible into the START substudies. Please contact your SCC/ICC as soon as possible if you encounter any issues with substudy recruitment. The substudy protocol teams may wish to explore options with you in greater detail.

FEATURED SUBSTUDY: PULMONARY SUBSTUDY

Chronic obstructive pulmonary disease (COPD) is a debilitating lung disease that will soon become the third leading cause of global death.



Compared to HIV-uninfected patients, patients with HIV infection are at higher risk of COPD, whether

they are smokers or non-smokers. The reasons for this are not known, but untreated HIV infection is associated with abnormal inflammation (CD8+ lymphocytes) in the lungs. Antiretroviral therapy (ART) reduces this inflammation, which would usually be a desirable effect. However, some data also suggest that ART may worsen airflow obstruction in the lungs.

The START Pulmonary Substudy will determine whether ART is good or bad for lung function, with a primary outcome of rate of lung function decline over time. The substudy seeks to co-enroll 1000 START participants. It will be one of the largest studies to ever follow lung function in patients with HIV infection. It will be the only study using a randomized ART design to determine ART effects on lung function.

Patients who enroll in this substudy are asked to perform a short test of lung function (spirometry) and to complete a respiratory health status questionnaire. Substudy tests are performed at baseline and annually. The INSIGHT website has a video demonstration of spirometry, narrated slide sets, and other educational material for site technicians and investigators. The substudy co-chairs are readily available by e-mail, phone, and Skype videoconferencing for questions.

The Pulmonary substudy protocol team extends its utmost thanks to the 38 sites that have co-enrolled over 150 patients to date, and we welcome our 40+ new sites who will be joining our effort to shed important new light on lung disease in patients with HIV infection.

Here is a comment from one of our sites, 621-003, Institute of Tropical Medicine, Belgium:

“We think this study is a unique opportunity to review an important & interesting question. These are the arguments we use when speaking to the patients:

- Not so time consuming, not frequent.
- They receive a pulmonary evaluation for free at regular interval.
- It may be interesting for a broad range of patients and for different reasons (sportsmen, smokers, patients with chronic lung problems)
- Scientifically sound
- Harmless”

UPCOMING MEETINGS

NEXT INSIGHT INVESTIGATOR MEETING

An INSIGHT investigator meeting is scheduled in conjunction with the IAS conference in Rome, Italy on Sunday, 17th July from 1 pm to 3:30 pm. The meeting agenda and registration information will be provided closer to the time.