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ESPRIT Closure Plans Finalized

ESPRIT participant follow-up is slated to end on 15 November 2008. By that date, study statisticians and the INSIGHT Executive Committee project that the goal of accruing 320 primary events will have been reached. SILCAAT also will close to follow-up on 15 November. The common closing date for both studies will allow for a joint unblinding of these IL-2 studies early in 2009.

ESPRIT

Closes to last follow-up visit: 15 November 2008

Administrative payments end: 15 February 2009

Visit/closeout form reimbursements end: 15 February 2009

To date, ESPRIT's median follow-up has reached 80 months (6.6 years), with a lost-to-follow-up rate of 7.8%. INSIGHT's Quality Oversight and Performance Evaluation Committee will augment its usual review of study metrics in preparation for the closure, focusing particularly on missing endpoints, completion of outstanding work in documenting visits and events, resolving form queries, and shipping specimens.

To ensure that ESPRIT study results can be quickly communicated to investigators, a simple closeout process is planned. While details are still forthcoming, participants will continue to be seen according to their visit schedules until the closure date. As soon as possible after 15 November, sites will complete a one-page closeout form for each participant, verifying their event status during the study.

In an effort to reduce the current lost-to-follow-up rate, site investigators have already been asked to broaden activities undertaken to locate participants who have not been seen in the past year, to report and document clinical events as soon as possible after they occur, and to send specimens stored at the site to the ESPRIT repository.

As the study nears its end, the site clinicians and the 4150 volunteer participants deserve to be recognized for their long-standing contributions and their continued diligence in seeing ESPRIT through to its successful completion.

STALWART Enrollment Ends

Following recommendations from the STALWART protocol team, the INSIGHT Executive Committee closed the study to enrollment on 30 June 2008. Participant follow-up will close on 28 February 2009 to ensure each participant is followed for a minimum of 32 weeks. Enrollment concluded with 267 participants. In June 2008, the final month of enrollment, 38 participants were randomized, more than double the previous high for monthly enrollment.

STALWART

Closes to last follow-up visit: 28 February 2009

Administrative payments end: 31 March 2009

Visit reimbursements end: 31 March 2009

During the last two and a half years, the Data and Safety Monitoring Board (DSMB) regularly reviewed STALWART and determined that it should continue, despite the slow accrual; however, the DSMB concurred with the team's recommendation to halt enrollment. The STALWART team and investigators are confident that the information and specimens collected during follow-up will contribute to research efforts addressing the efficacy and management of IL-2 in persons with HIV and may complement results from the ESPRIT and SILCAAT studies, which will be unblinded early next year.

START Plans Advance

Work on the START study protocol has now been completed, and regulatory and medical officer sign-offs at the Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID), are expected shortly. Following approval, the protocol will be translated, and sites can initiate the process of obtaining institutional review board/ethics committee approvals preparatory to study registration.

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START Plans Advance (continued from page 1)

Activities in other areas are well underway. The number of sites participating in the pilot phase of START has expanded as other groups have sought to join the study and collaborative interest has grown. In addition to the 65 sites that are fully funded by DAIDS, 24 sites will be wholly or partially funded by other groups, including France's Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (ANRS), Germany's Bundesministerium für Bildung und Forschung (BMBF), the U.S. National Institutes of Health (NIH) Clinical Center, and the U.S. Department of Defense (DoD). Other institutes at NIH, including the National Institute of Mental Health and the National Institute of Neurological Disorders and Stroke have committed funds for START; applications are pending at the National Institute of Diabetes and Digestive and Kidney Diseases and the National Heart, Lung and Blood Institute.

Sites Participating in Pilot Phase of START

ICC	Country	Number of Sites
Copenhagen		
DAIDS Funded	Belgium	2
	Denmark	2
	Finland	1
	Poland	1
	Spain	5
Externally Funded in Whole or Part	Germany (BMBF)	5
London		
DAIDS Funded	Italy	1
	Greece	3
	Morocco	1
	Switzerland	3
	United Kingdom	5
Externally Funded in Whole or Part	France (ANRS)	12
Sydney		
DAIDS Funded	Argentina	8
	Australia	3
	Chile	1
	Israel	1
	Singapore	1
	Thailand	2
Washington		
DAIDS Funded	Brazil	2
	Peru	2
	South Africa	1
	United States	20
Externally Funded in Whole or Part	Mali (NIH)	1
	United States (DoD)	5
	United States (NIH)	1
Total		**89**

A central START antiretroviral therapy repository will stock licensed antiretrovirals donated by five pharmaceutical companies: Abbott, Bristol-Meyers Squibb, Gilead, GlaxoSmithKline, and Merck. INSIGHT has contracted with Almac in Durham, North Carolina, to label, package, and distribute the drugs to participating clinical sites. Although sites can prescribe from their own pharmacies, most sites that are funded by INSIGHT through DAIDS are expected to order drug from the START repository. Externally funded sites may rely on their own drug suppliers.

The specimen repository for START will be located at Advanced BioMedical Laboratories (ABML) in Cinnaminson, New Jersey, where other INSIGHT study specimens are currently stored. Sites will either ship blood and urine specimens directly to ABML or ship the specimens to intermediate repositories at various international locations for consolidation before sending them on to ABML.

START is expected to begin enrolling participants in the United States and Australia before the end of 2008. Most international sites are expected to begin accrual early in 2009.

SMART Papers In Press

Data from SMART continue to be analyzed. Look for these papers, which were recently accepted for publication, in the coming months:

Episodic antiretroviral therapy increases HIV transmission risk compared to continuous therapy: Results of a randomized controlled trial by W Burman, B Grund, J Neuhaus, J Douglas Jr, G Friedland, E Telzak, R Colebunders, N Paton, M Fisher, C Rietmeijer (*J Acquir Immun Defic Syndr*).

Opportunistic disease and mortality in patients co-infected with hepatitis C virus and/or hepatitis B virus in the SMART (Strategic Management of Antiretroviral Therapy) Study by the SMART Study Group (E Tedaldi, L Peters, J Neuhaus, M Puoti, J Rockstroh, MB Klein, GJ Dore, A Mocroft, V Soriano, B Clotet, JD Lundgren) (*Clin Infect Dis*).

Pneumonia in HIV-infected persons: Increased risk with cigarette smoking and treatment interruption by FM Gordin, MP Roediger, P-M Girard, J Lundgren, JM Miro, A Palfreeman, MC Rodriguez-Barradas, MJ Wolff, PJ Easterbrook, K Clezy, LN Slater (*Am J Respir Crit Care Med;* available now as epublication).

Risk for opportunistic disease and death after reinitiating continuous antiretroviral therapy in HIV patients previously receiving episodic therapy by the SMART Study Group (WM El-Sadr, B Grund, J Neuhaus, A Babiker, CJ Cohen, J Darbyshire, S Emery, JD Lundgren, A Phillips, JD Neaton) (*Ann Int Med*).

Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the SMART study by the SMART/INSIGHT and the D:A:D Study Groups (JD Lundgren, J Neuhaus, A Babiker, D Cooper, D Duprez, W El-Sadr, S Emery, F Gordin, J Kowalska, A Phillips, RJ Prineas, P Reiss, C Sabin, R Tracy, R Weber, B Grund, JD Neaton) (*AIDS*).

Viral re-suppression and detection of drug resistance following interruption of a suppressive NNRTI-based regimen by Z Fox, A Phillips, C Cohen, J Neuhaus, J Baxter, S Emery, B Hirschel, K Huppler Hullsiek, C Stephan, J Lundgren (*AIDS*).

Upcoming Meetings

The next INSIGHT/SILCAAT Joint Scientific Session for investigators will be held in Mexico City, Mexico on 3 August 2008, in conjunction with the XVII International AIDS Conference, at the Sevilla Palace Hotel, Murillo Room, from 12:00 to 17:00.