



Early Treatment Trial Planning Moves Forward

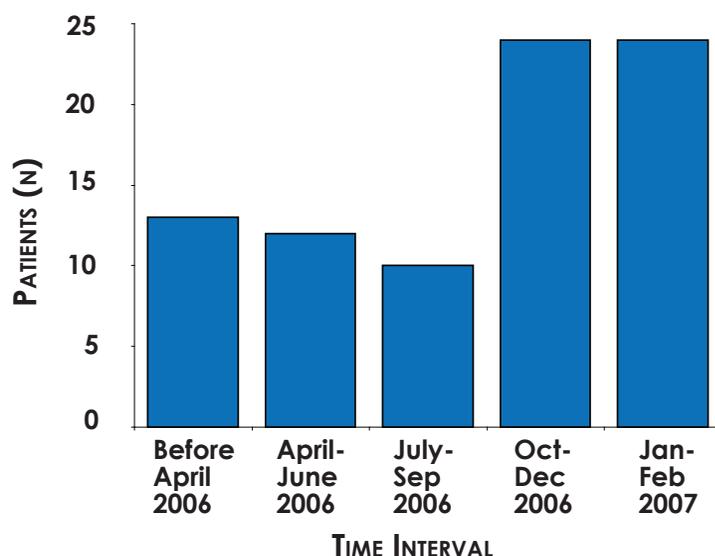
The INSIGHT Executive Committee has been directed by the Division of AIDS (DAIDS), at the National Institute of Allergy and Infectious Diseases, to work with DAIDS on workshops, cohort analyses, and pilot studies that would lay the groundwork for a new clinical trial on early treatment of HIV/AIDS. This early treatment trial would focus on the impact of antiretroviral therapy on the incidence of serious non-AIDS disease as well as traditional opportunistic diseases in patients with CD4+ counts that exceed current treatment guideline thresholds.

Approval from DAIDS for this planning effort culminates a process that was initiated in the summer of 2006 to formulate new INSIGHT science proposals. In November, the INSIGHT International Steering Committee met in London to review three concepts (early treatment, strategies for patients with limited treatment options, and new alternatives for initial regimens of combination therapy). Following that meeting, consultations with DAIDS, and the appointment by DAIDS of a Strategic Working Group (SWG) to review new research proposals, the Executive Committee decided in December to bring an early treatment proposal to the first meeting of the SWG on 17-18 January 2007. The proposal, "Strategic Timing of AntiRetroviral Treatment (START)," consisted of two trials: START 500 (designed for patients with CD4+ counts ≥ 500 cells/mm³) and START 350 (designed for patients with CD4+ counts of 350-499 cells/mm³). The proposals included collaboration with a number of other groups, including IMPAACT, HPTN, ATN, PENTA, ANRS, and Project PHIDISA.

Further details and next steps will be discussed at the Executive Committee meeting and Joint Scientific Session scheduled in conjunction with the Conference on Retroviruses and Opportunistic Infections this February. The goal is to agree on the timing of workshops, cohort analyses, SMART follow-up analyses, and pilot studies that will lead to submission of a trial proposal to the SWG in January 2008.

STALWART Enrollment Climbs

STALWART enrollment doubled in the last quarter, climbing from 40 participants in November to 85 by mid-February. STALWART opened in December 2005 with an enrollment goal of 480, but initial uncertainty about insurance coverage and new regulatory requirements for local labs significantly delayed site registration. Though 35 of 65 proposed sites have still not completed registration, recently opened sites in Argentina and Thailand have helped boost the accrual rate. Highest enrollments to date, by Site Coordinating Center, are in Argentina (n=26), Australia (n=24), Thailand (n=8), and the United Kingdom (n=13). Additional sites in Germany and Spain are expected to open by the end of February.



INSIGHT Website Goes Live

The INSIGHT website (www.insight-trials.org) will go live to all investigators, as well as the public, at the end of February 2007. The website, which has been in development and testing for several months, includes both protocol-specific information for all open studies and networkwide information of interest to investigators, participants, and the public. Also available are protocol overviews and materials; protocol-specific and networkwide reports; community group resources; slide presentations; abstracts; papers; newsletters; contact information; and links to International Coordinating Center (ICC) websites, other DAIDS-funded networks, and journals.

The website provides important functions for the ICCs, such as online randomization, document uploads, and access to case report forms; additional functions are being developed. Although most of the website is open to the public, these functional areas are password-protected. Please contact your ICC if you have any questions about obtaining a password.

Community Partners Group Formed

Community Partners is the DAIDS community group with representation from the six funded clinical trials networks: INSIGHT, ACTG, IMPAACT, MTN, HVTN, and HPTN. (See www.studysource.org/networks for a full description of each network.) The purpose of Community Partners is to have a group of community advocates working together to make decisions and solve problems across the community groups of all the networks. Examples of cross-network issues might include educational training, recommendations for community participation in clinical trials, and solving problems regarding language translation.

Four experienced community representatives, one from each of the ICCs, will represent INSIGHT on Community Partners: Jo Watson (Sydney ICC), Simon Collins (London ICC), Siegfried Schwarze (Copenhagen ICC), and Dave Munroe (Washington ICC). In addition to the ICC community representatives, Claire Rappoport will be the INSIGHT staff person assigned to work with Community Partners. Ms. Rappoport is INSIGHT's community liaison and has a long history working as a community representative in AIDS research. Her office is located at the University of California – San Francisco and is funded by the INSIGHT leadership grant.

Community Partners is funded by DAIDS and administered by the HIV/AIDS Network Coordination (HANC) group, based at the Fred Hutchinson Cancer Resource Center in Seattle. For more information about the workings of Community Partners, see their website (www.studysource.org). If you have questions regarding INSIGHT's participation in Community Partners, please contact Ms. Rappoport (crappoport@php.ucsf.edu).

DSMB Reviews: ESPRIT, STALWART, and SMART

ESPRIT. In its eighth review of ESPRIT on 6 November 2006, the Data and Safety Monitoring Board (DSMB) stressed the importance of continued cycling. The DSMB recognized the difficulties inherent in recycling, but urged ESPRIT investigators to make every effort to increase recycling rates. The DSMB also expressed concern over the increasing lost-to-follow-up rate (5.9%) and encouraged investigators to be vigilant in following patients. Finally, the DSMB communicated its strong endorsement of this study and commended investigators for their efforts.

STALWART. The first DSMB review of interim data also occurred on 6 November 2006. The DSMB expressed concern over the very slow rate of site registration and enrollment. Although the study has been open to enrollment for over a year, at the time of the DSMB meeting only 40 patients had been enrolled. (See "STALWART Enrollment Climbs" on page 1 of this newsletter for an update on STALWART enrollment.) The DSMB recognized that there were many hurdles to overcome in the site registration process, but urged the team to work quickly to open remaining sites and increase the rate of enrollment. The DSMB endorsed the STALWART protocol team's recommendations for monitoring genotypic resistance and encouraged timely shipping of plasma specimens so that genotypic data can be reviewed at the next DSMB meeting.

The next DSMB reviews of ESPRIT and STALWART will take place in September or October 2007.

SMART. The DSMB met on 4 January 2007 for its seventh review of SMART data. This was the first review since 11 January 2006 when enrollment was stopped and antiretroviral therapy-experienced patients in the DC group were encouraged to restart therapy.

The DSMB expressed concern about the number of participants in the DC group who had not restarted antiretroviral therapy. As of the data cutoff for the DSMB meeting (10 November 2006), 23% of DC patients who were on antiretroviral therapy at baseline had not resumed therapy. Attendees described the efforts that had been made to contact all patients regarding the study findings and their implications. The DSMB recommended that the Executive Committee consider gathering data from sites on the reasons for DC patients not restarting antiretroviral therapy. The DSMB was also concerned about the increased number of patients lost to follow-up. As of 11 January 2006, 73 (1.3%) patients were lost to follow-up. This number has increased to 206 (3.8%).

No consideration of early stopping, based on safety, was indicated.

Upcoming Meetings

The INSIGHT/SILCAAT Joint Scientific Session for investigators will follow the Executive Committee meeting on Sunday afternoon, 25 February 2007, in conjunction with the 14th Conference on Retroviruses and Opportunistic Infections in Los Angeles, California.