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Prof. Steven Deeks

Steven G. Deeks, MD, is a professor of medicine in residence at the University of California, San Francisco (UCSF), and a faculty member in the Positive Health Program (AIDS Program) at San Francisco General Hospital. He received his undergraduate degree from the University of California, Berkeley, and his medical degree from UCSF. He served as an intern and resident in the Department of Medicine at UCSF prior to joining the faculty of the Department of Medicine in 1993. He has been engaged in both HIV research and clinical care since that time.

Dr. Deeks is a recognized expert in the immunopathogenesis of HIV and works from a clinical perspective to identify how the virus and host interact to cause disease and how to translate information learned from such studies into the clinic. He currently directs a large research program dedicated to the investigation of the immunopathogenesis of antiretroviral-treated HIV infection. Recently he expanded his research interests to include those rare individuals who are able to control HIV replication in the absence of therapy. He has published over 150 peer-reviewed articles and editorials on these and related topics.

Dr. Deeks co-directs the Population and Clinical Sciences Core of the UCSF-GIVI Center for AIDS Research and the UCSF SCOPE cohort. He is a member of the American Society for Clinical Investigation. In addition to his clinical and translational investigation, Dr. Deeks maintains a large primary care clinic for HIV-infected patients and is a member of the Department on Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents.

INSIGHT (International Network for Strategic Initiatives in Global HIV Trials) has been funded to conduct HIV treatment trials since 2006 by the National Institute of Allergy and Infectious Diseases, a component of the National Institutes of Health.
Since then, INSIGHT's scope has broadened and now the network also conducts several influenza studies. Our mission is to define optimal strategies for the management of HIV and other infectious diseases through a global clinical research network. INSIGHT conducts studies worldwide.
INSIGHT is currently conducting the START study. Further analyses are ongoing on data from studies that were previously coordinated by the Terry Beirn Community Programs for Clinical Research on AIDS and the ESPRIT Group.
START (Strategic Timing of AntiRetroviral Treatment) is investigating the optimal time to begin antiretroviral therapy (ART) in over 200 sites around the globe. Further information is available on this website, and at START Study Public Website, which includes a video presentation featuring current and past research participants, as well as START investigators, explaining the purpose of the trial and its importance to advancing HIV medicine.
The International Network for Strategic Initiatives in Global HIV Trials (INSIGHT) was created in 2006 by merging two existing National Institutes of Health-funded clinical research trial groups: The Evaluation of Subcutaneous Proleukin® in a Randomized International Trial (ESPRIT) and the Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA).
The synergy and success of the INSIGHT organization can be best demonstrated by the enrollment of the two largest HIV treatment trials to date, the Strategies for Management of Anti-Retroviral Therapy (SMART) study and ESPRIT. In 2009, INSIGHT commenced recruitment to the START (Strategic Timing of AntiRetroviral Therapy) study.
Subsequent to the unblinding of the SMART findings in 2006, multiple successful projects have been completed, providing a better understanding of why intermittent provision of antiretroviral therapy (ART) was associated with excess morbidity and mortality. A similar exercise has been initiated for ESPRIT, the results of which were unblinded in January 2009.
ESPRIT, SMART and START aim to provide definitive evidence to a clinical research question. By design, these studies have included several thousand study participants followed within the trial over several years. Follow-up included as a priority careful ascertainment of relevant clinical endpoints.
Additionally, INSIGHT has performed or coordinated several other studies with less ambitious aims. These studies have been launched by INSIGHT because they address an intriguing research question that warrants investigation as a prelude to the design and execution of definitive trials. As such, these types of studies can be viewed as Vanguard Studies.
The STALWART study was a vanguard study which included 250 patients to assess the extent to which interleukin-2 affects a surrogate for immune function (CD4+ lymphocytes) over 24 weeks among patients not taking ART. Had STALWART (and other research) supported the notion that IL-2 may be able to prolong the time to commencement of ART in the course of the chronic HIV infection (and ESPRIT shown that CD4+ lymphocyte count increases on IL-2 were associated with clinical benefit), a trial providing definitive evidence hereof may have been conducted.
INSIGHT is conducting two international observational studies on the pandemic influenza virus (H1N1v): FLU 002 (H1N1v Outpatient Study) and FLU 003 (H1N1v Hospitalization Study).

FLU 002 aims to describe the prevalence and risk factors for hospital admission for patients seeking health care with influenza-like symptoms during ongoing community epidemic spread of the H1N1v influenza virus. FLU 003 assesses the characteristics and outcomes over a 60 days period from complicated or severe influenza infection requiring hospital admission. As of April 2010, 707 patients are enrolled in FLU 002 and 276 in FLU 003. The studies are planned to continue at least until the seasonal influenza season is completed in the southern Hemisphere in October 2010, and likely until the influenza season in the northern Hemisphere is also completed in April 2011.
These observational studies provide information on characteristics of persons particularly affected by H1N1v in different countries. This will assist in determining the type of patients to include, and sample size requirements, for influenza treatment trials. INSIGHT intends to perform prospective observational studies as Vanguard-type trials to inform the planning of its overall research programme.

Stefano Rusconi:

We are here with Prof Steve Deeks from UCSF. One question for him: there is considerable evidence of HIV-mediated inflammation and systemic diseases. In your opinion, which are the most striking?

Prof. Deeks:

Well, you have to look at both untreated HIV disease and treated HIV disease. With regard to untreated HIV disease, there's no question that the immune system is characterized by one of heightened T-cell activation and chronic inflammation. In fact, this was actually observed in the first paper in 1981 on PCP; and if you look at that paper on this small group of patients who had PCP, as published in the New England Journal of Medicine back in the early 1980s, that's the first thing they noticed – that all the cells were activated. So from that point on, through the mid-1990s, a fair amount of data was generated showing that T cells are activated in a context of untreated disease, and it predicts what happens next. But that's of less interest these days because, of course, we get rid of most of that T-cell activation by putting people on therapy. And when you put people on therapy, the amount of T-cell activation, the amount of chronic inflammation plummets. But it does not normalize. And here we look at the data primarily from the large cohorts in the INSIGHT network, which I think are the strongest sets of data, which have collectively shown that among people who go on therapy, achieve good control of their virus, that when you measure some of the inflammatory markers that have been well validated in the general population, particularly Interleukin 6, D-Dimers, now some of the macrophage markers, like soluble CD14, soluble CD163; and study after study, these markers in a treated person are higher than in an HIV uninfected person. The effect is subtle; it's not dramatic; but it is consistent. The other finding which is very consistent and is very important that comes from those same studies is that these subtle elevations are stable over time. So if you have a doubling or a tripling compared to a normal VLR 6, that level, as long as you remain on therapy, tends to remain high for years and years. Third finding, also from that same family of studies, is that these subtle increases – again, not dramatic, you know, not like tenfold above normal, but just two or three times higher than what might be expected as normal - having such elevation is associated with excess risk of cancer, cardiovascular disease and mortality. The trends have been seen in multiple different cohorts, including our own, but the strongest evidence - if you ask me what the strongest evidence is - it primarily comes from the Smart Study, and the INSIGHT Network.

The other piece of evidence, which is less direct, that something is going on, is of course the evidence that multi-morbidity, cardiovascular disease, cancers, and so forth are more common in people with HIV than without, and that many of these beings have a potentially inflammatory component to it. But collectively, you know, there's a lot of controversy as to how real this is. And I would agree. You know, nothing is really definitive. There are lots of descriptive studies, lots of associations, not all of them all that consistent. In order to truly figure out whether inflammation is a problem for our patient population, what the field needs to do now is to come up with this series of interventions, identify something that can reduce this inflammation in a reproducible manner, that is safe, and then move forward with a clinical end-point study. And that's where the field is now. There are dozens of these proof-of-concept studies going on across the world. Many have been finished; some were just presented at CROI, which are identifying potential interventions, which will precisely intervene, block chronic inflammation. And if we can identify something that alters the biomarkers of interest, and which we think is safe, and can be combined with combination therapy, then the next step will be to do this study that will prove once and for all whether inflammation is a problem. And that'll be taking five thousand or so people on therapy, half get the intervention, half do not, follow them for 5 to 7 years, and see what happens.

Stefano Rusconi:

Great. Thank you, Steve.