PRESS RELEASE

HIV/AIDS: INTERIM ANALYSIS OF PHASE II TRIAL OF TAT VACCINE IN HIV-INFECTED PATIENTS

The results of a 48-weeks interim analysis of a randomized phase II clinical trial suggest that the Tat vaccine can normalize, in a specific and selective manner, the immune functions of HIV-infected patients being treated with antiretroviral drugs.

These are the key findings of the study conducted by the team of Dr. Barbara Ensoli, Director of the National AIDS Center of the Istituto Superiore di Sanità, and President Prof. Enrico Garaci, which are published today in the journal *PLoS ONE* (www.plosone.org). The Tat vaccine has already shown to be safe and capable of inducing specific antibody and cellular immune responses in preclinical studies in monkeys and in previous phase I trials, and now appears to be a promising tool to improve immune functions in HIV-infected subjects treated with antiretroviral drugs (HAART).

"The results published today in *PLoS ONE* demonstrate that it was worth it to pursue the Tat vaccine strategy – says the President Enrico Garaci -. The improvement of the immunological parameters upon vaccination of patients being treated with antiretroviral drugs represents a key milestone. This is - concludes the President – a first possible indication for use of this vaccine that, today, thanks to the ad interim results of the phase II trial, we are even more determined to move forward".

The interim results of the randomized phase II trial, conducted in 87 HAART-treated patients, 48 weeks after vaccination indicate that not only is the Tat vaccine safe and capable of inducing specific antibody and cellular immune responses, but it also has a key and novel role in reducing immune system alterations observed in HIV infection, which usually persist even under successful HAART. Further, those patients who are the most immunocompromised may benefit the most from Tat vaccination.

This interim analysis shows that vaccinated patients have a significant increase of both B cells and $CD4^+$ T cells (key players of the immune system hit hardest by HIV), as compared to non-vaccinated HAART-treated subjects. Moreover, vaccinated patients show a significant recovery of immune functions (an increase of regulatory and memory T cells) and a reduction of immune activation (CD38 expression on $CD8^+$ T cells and biochemical markers), which is considered to be the primary cause of the clinical manifestations of HIV infection, even under successful antiretroviral therapy.

"These results, obtained with the precious support of the clinical centers involved in the study – says Dr. Barbara Ensoli – suggest that therapeutic vaccination with the Tat vaccine, combined with HAART, can significantly improve the recovery of the immune system in patients with HIV".

The phase II trial is presently ongoing in 11 Italian clinical centers. It has been amended to increase the number of vaccinated patients from 128 to 160 and to include more immunocompromised individuals. Patients fulfilling the inclusion criteria will receive 3 or 5 intradermal administrations of either 7.5 or 30 μg of the Tat vaccine at monthly intervals.

The sites involved in the conduction of the clinical trial are the following: Division of Infectious Diseases, University Policlinic of Modena (Prof. R. Esposito, Prof. C. Mussini), Clinic of Infectious

Diseases, Amedeo di Savoia Hospital, Turin (Prof. G. Di Perri), Division of Infectious Diseases, S. Raffaele Hospital, Milan (Prof. A. Lazzarin), Institute of Tropical and Infectious Diseases, University of Milan L. Sacco Hospital (Prof. M. Galli), Division of Tropical and Infectious Diseases, Spedali Civili, Brescia (Prof. G. Carosi), Division of Infectious Diseases, San Gerardo Hospital, Monza (Dr. A. Gori), Unit of Infectious Diseases, University Hospital of Ferrara (Dr. L. Sighinolfi), Unit of Infectious Diseases, S.M. Annunziata Hospital, Florence (Prof. F. Mazzotta), Department of Infectious Dermatology, San Gallicano Hospital, Rome (Prof. G. Palamara), Department of Infectious Diseases, S. Maria Goretti Hospital, Latina (Dr. Mercurio), Division of Infectious Diseases, Policlinic Hospital, University of Bari (Prof. G. Angarano).

The Istituto Superiore di Sanità is the sponsor of the trial, which is being conducted with special funds from the Italian Ministry of Health. Official information on Tat vaccine and Dr. Ensoli's research program can be found at the website http://www.hiv1tat-vaccines.info/index.php and http://www.iss.it/aids, or by calling the AIDS Toll Free Number of the Istituto Superiore di Sanità (Tel. +39.800.86.10.61, from 1.00 p.m. to 6.00 p.m.). From November 12 until December 10, 2010, the AIDS Toll Free Number will extend its opening time from 10.00 a.m. to 6.00 p.m. Furthermore, from 10.00 a.m. to 4.00 p.m. information will be provided also in English.

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