Therapeutic vaccination with Tat restores immune homeostasis, promotes proviral DNA decay and induces cross-clade neutralizating antibodies in patients on HAART: results from phase II clinical trials in Italy and South Africa

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Tat is a key regulatory protein and virulence factor of HIV playing major roles in virus gene expression, replication and transmission. Tat is also key for virus reactivation, maintenance of the virus reservoir and in immune dysregulation, all unmet needs of HAART. In addition, by binding Env spikes, Tat forms an entry complex promoting an integrin-mediated infection of DCs, and efficient virus transmission to T cells (*Monini, PLoS ONE 2012*). By binding Env, Tat shields HIV from Env neutralizing antibodies (Abs); conversely, anti-Tat Abs, which are infrequently produced in natural infection, restore HIV neutralization. This provides a strong rationale for using Tat in HIV/AIDS vaccine development (*Ensoli, Frontiers in Immunology 2014*).
Results from two phase II trials in Italy (ISS T-002, Clinicaltrials.gov: NCT00751595) and South Africa (ISS T-003, Clinicaltrials.gov: NCT01513135) in 168 and 200 anti-Tat Ab-neg subjects under effective HAART (Ensoli, PLoS ONE 2010, Retrovirology 2015 and submitted), respectively, indicated that vaccination with Tat was safe and immunogenic and reverted signs of AIDS progression, since it reduced immunoactivation, increased T ($CD4^+$), B lymphocyte and NK cell number, and restored $CD4^+$ and $CD8^+$ central memory subsets, independently from CD4 nadir and particularly in the most immunocompromised patients. Remarkably, proviral DNA load progressively decreased in vaccinees. Reduction correlated with anti-Tat Ab titers and neutralization of Tat-mediated entry of Env in DCs. Further, vaccination induced cross-clade neutralizing anti-Tat Abs and protected patients noncompliant to therapy from $CD4^+$ T cell decay and viral load increase. Phase III studies are planned for vaccine registration.

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Biography

Barbara Ensoli (MD, PhD) is the Director of the NAC. She spent over 10 years at NIH. Back in Italy in 1996, she initiated an HIV Tat-based vaccine program, currently in advanced clinical phase. She has coordinated national and international research programs in Europe and Developing countries. She has also coordinated 7 clinical trials and 7 observational studies in Italy and South Africa. She was Vice President of the National AIDS Committee for 8 years. She is a member of

EMBO and of the European Research Council (*ERC*). She has over 300 publications in peer-reviewed international journals.

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