ABX464 Decreases the Total HIV Reservoir and HIV Transcription Initiation in vivo

Sara Moron-Lopez1,2, Silvia Bernal-Santantessa3,4, Jean-Marc Steens5, Joseph K. Wong1,2, Javier Martinez-Picado4,6, Steven A. Yukl1,2
1 University of California San Francisco, San Francisco, CA, USA; 2 San Francisco VA Medical Center, San Francisco, CA, USA; 3 AIDS Research Institute InCiDA, Badalona, Spain; 4 University of Vic, Vic, Spain; 5 Abivax S.A., Paris, France; 6 Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain
*These authors contributed equally to this work

BACKGROUND
• Antiretroviral treatment (ART) intensification and disruption of latent HIV infection (reversal or silencing) have been suggested as strategies to eradicate HIV
• ABX464 (AbiVax) is a novel antiviral that binds to the capsid binding complex, interfering with splicing and Rev-mediated export of newly transcribed HIV RNA
• ABX464 has been shown to inhibit HIV RNA biogenesis in vitro and delayed viral rebound in two humanized mouse models [1-5]

AIMS: To investigate the effect of ABX464 on the HIV transcription profile and total and intact HIV DNA in circulating CD4+ T cells from ART-suppressed participants enrolled in the ABIVAX-005 clinical trial (NCT02990325)

METHODS
Study design and sample processing

CONCLUSIONS
After ABX464 treatment we observed:
1. A significant decrease in total HIV DNA (median [wk4/wk0]=0.8), and a similar trend for intact HIV DNA (median [wk4/wk0]=0.8). However, intact HIV DNA increased significantly after stopping ABX464 (wk4 vs wk8).
2. A significant decrease in initiated HIV transcripts per million CD4+ T cells and provirus (median [wk4/wk0]: 0.7, 0.5), and a similar trend for 5'-elongated and unspliced HIV transcripts (median [wk4/wk0]: 0.6, 0.7; 0.5, 0.6). However, no significant change was observed in polyadenylated or multiply-spliced HIV transcripts.

RESULTS
1. Characteristics of the study participants

2. Effect of ABX464 on total and intact HIV DNA

3. Effect of ABX464 on HIV transcription

In this substudy, treatment with ABX464 decreased total HIV DNA (and possibly intact proviruses) and decreased HIV transcription initiation