towards an HIV cure
people focused science driven
2015 Towards an HIV Cure Symposium
Abstract Book | Poster Exhibition

PE61

Vacc-4x/lenalidomide increases naïve CD4 T-cells in well controlled patients on ART with low preART CD4 counts and poor immune reconstitution

J. van Lunzen[1], G. Pantaleo[2], K. Arastéh[3], G. Fätkenheuer[4], D. Schürmann[5], J. Zeldis[6], D. Jolliffe[7], K. Krogsgaard[8], A. Mørk[9], M.A. Sommerfelt[9]

[1]University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [2]University of Lausanne, Lausanne, Switzerland, [3]EPIMED, Vivantes Auguste-Viktoria-Klinikum, Berlin, Germany, [4]University of Cologne, Cologne, Germany, [5]Charité-Universitätsmedizin, Berlin, Germany, [6]Celgene, Summit, United States, [7]S-Cubed Ltd, Abingdon, United Kingdom, [8]KLIFO, Copenhagen, Denmark, [9]Bionor Pharma ASA, Oslo, Norway

Background: A randomized, exploratory, double-blind phase I/II placebo-controlled clinical study was conducted to determine whether the immune modulator, Lenalidomide, in combination with Vacc-4x therapeutic vaccination, could improve CD4 counts in persons with low pre-ART CD4 nadir which often experience incomplete immune reconstitution despite effective ART (Study ID: NCT01704781).

Methods: The study was conducted at 3 sites in Germany from 10.2012 - 08.2014 and included study participants with CD4 T-cell counts >200 and < 500 cells/µL on ART. Part A was a Lenalidomide dose escalation study (5mg n=3; 10mg n=3; 25mg n=6) in combination with 4 weekly intradermal (id) Vacc-4x immunizations (1.2mg) using rhuGM-CSF (60µg) as local adjuvant. Part B used 6 id Vacc-4x immunizations and rhuGM-CSF on ART at weeks 1, 2, 3, 4, 12 and 13 in combination with 25mg Lenalidomide tablets (n=12) or placebo (n=12). Lenalidomide/placebo was administered once daily two days before and on the day of each immunization with follow up until week 26. A two-sample 2-sided t-test (Satterthwaite) compared mean change in CD4 counts from baseline (BL) to week 26 between the two groups. A paired T-test compared change in mean CD4 counts at baseline with week 26 within each group.

Results: In the part B ITT population (n=24), Vacc-4x/Lenalidomide and Vacc-4x/placebo had mean pre-ART CD4 counts of 141 and 99, and mean BL CD4 counts of 365 and 304 cells/µl respectively. A significant mean CD4 increase of 91 cells/µl (p=0.009) was observed between BL and week 26 in the Vacc-4x/Lenalidomide group (n=12). The Vacc-4x/placebo group had a corresponding mean CD4 increase of 42 cells/µl (p=0.100). CD4 increases compared between the two groups, were not statistically significant (p=0.201). Mean naïve CD4 T-cells increased in Vacc-4x/Lenalidomide and Vacc-4x/placebo groups (48 and 21 cells/µl). Other T-cell phenotypes e.g. Treg remained unchanged. CD4 increases were most pronounced between the last immunization (week 13) and study end (week 26). The Vacc-4x/Lenalidomide combination was well tolerated with only one serious adverse event (abcess) deemed unrelated to treatment.

Conclusions: Immune restoration by Lenalidomide in combination with Vacc-4x antigen-specific immune stimulation, warrants further study in populations on ART with low CD4 nadir as well as in HIV "functional cure" strategies.

95