P0135
Paper Poster Session
Cellular immunity as marker of viral infection

Long-term immune recovery and viral reservoir dynamics in advanced HIV infected patients

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Background: The aim of this study was to assess the effect of CART on long-term immune recovery, bacterial translocation, inflammation and coagulation markers and the viral reservoir in patients with very low CD4+ T-cell counts.

Material and methods: The ADVANZ trial was a randomized study comparing the efficacy of first-line ART with efavirenz (EFV) vs. indinavir/r + Combivir® in ART-naïve patients with CD4+ counts <100 cells/mm^3 and wildtype HIV-1 at study entry. Those patients who had maintained virologic suppression for 9 years were included in the study. Determinations of CD4 and CD8 T-cell count, immune activation (CD8+CD38+/DR), immune senescence (CD8+CD28- and CD8+CD28-CD57+), specific HIV antigens response (against p24/gp 160)], inflammation (IL-6, TNF-alfa, usCRP), coagulation (D-dimer), bacterial translocation (sCD14), and total and integrated HIV-1 DNA were performed. Baseline, 1- and 9-year results were compared.

Results: Eight patients (11%) were included in the sub-study. All subjects were MSM; median (IQR) age at study entry was 52 (39-55) years and 6/8 (75%) received EFV-based CART. Median (IQR) baseline CD4+ cell count and HIV-RNA were 55 (20-69) cells/mm^3 and 406K (179.5K-810K) copies/mL. After a median (IQR) follow up of 9 (8.8-9.4) years from baseline, patients reached a median (IQR) CD4+ T-cell count of 710 (445-1052) cells/mm^3 ($p<0.001$), the percentage of CD4+ cells rose from 5.3% (2.5-9.5) to 22.9% (19.8-32.4) [$p<0.0001$], and the CD4/CD8 ratio rose from 0.11 (0.05-0.31) to 0.66 (0.42-1.01) [$p<0.001$]. The **table** shows baseline, 1- and 9-year results for immune activation, senescence, coagulation and viral reservoir. Neither a significant decrease in inflammation or bacterial translocation markers nor a significant increase in specific response to viral antigens (p24 and gp160) was observed during the follow-up.

Conclusions: Very advanced patients starting CART and maintaining viral suppression for a median period of 9 years were able to restore acceptable values of CD4+ T-cell count and to achieve a

significant reduction in immune activation, immune senescence and coagulation markers. Viral reservoir only decreased during the first year. Conversely, inflammation and bacterial translocation markers did not decrease and response to specific viral proteins remained poor.

Variable	Baseline (BL)	1-year	9-year	*p*-value (BL/1-yr)	*p*-value (1 yr/9-yr)
CD8+CD38+ (%)	85(83-93)	49 (36-65)	36 (26-42)	**<0.05**	**n.s.**
CD8+CD38+HLA-DR (%)	34 (23-47)	6 (3-10)	8 (7-9)	**<0.001**	**n.s.**
CD8+CD28+ (%)	26 (15-45)	25 (18-42)	52 (42-72)	n.s.	**<0.05**
CD8+CD28-CD57+ (%)	58 (37-63)	59 (46-67)	31 (18-49)	n.s.	**<0.05**
D-dimer (pg/mL)	670 (295-1240)	260 (160-317)	235 (157-307)	**<0.05**	n.s.
Total HIV-1 DNA (cp/10^6 PBMC)	5795 (2469-11776)	832,3(280,6-1453)	669,3(329,7-1085)	**<0.05**	**n.s.**

Table. Baseline, 1- and 9-year results for immune activation, immune senescence, coagulation and viral reservoir. Values are expressed in median (IQR). **n.s**., not significant p-value. **PBMC**, peripheral blood mononuclear cells.