# COMPARABLE VIRAL DECAY IN DUAL AND TRIPLE DOLUTEGRAVIR-BASED ANTIRETROVIRAL THERAPY

### BACKGROUND

The PADDLE study showed that a dual therapy regimen based on dolutegravir plus lamivudine (DTG/3TC) induced a rapid viral suppression in treatment naïve patients with screening pVL <100,000 copies/mL (EACS 2015). Our objective is to compare differences between plasma viral load (pVL) change at each time point with a dual therapy regimen (DTG/3TC,) to DTG-based triple therapy regimens used in the SPRING-1 (DTG 50 mg +2NRTIs) and SINGLE study (DTG plus abacavir/lamivudine), in patients with baseline (BL) pVL < 100,000 copies/mL.

#### METHODS

In PADDLE (n=20), pVL was tested at baseline, days 2, 4, 7, 10, weeks 2, 4, 8, 12, 24 and thereafter. Four patients with BL pVL > 100,000 copies/mL in PADDLE were excluded in this analysis. In SINGLE (n=280) pVL was measured at BL, wk 2, 4, 8, 12, 16, 24 and thereafter. In SPRING-1 (n=39) pVL was measured at BL, wk 1, 2, 4, 8, 12, 16, 20, 24 and thereafter. Change in pVL vs. baseline was calculated only for time points with data for the three studies (Weeks 2, 4, 8, 12 and 24). Differences in change from baseline at W4 between PADDLE, SPRING-1 and SINGLE were analyzed by One-way ANOVA. Common Standard Deviation was obtained as the square root of the Mean Square Error term. 95% Confidence Intervals (95%CI) for the differences between PADDLE-SPRING-1 and PADDLE-SINGLE were calculated. Evaluation of equivalence was performed by following the Schuirmann approach. Briefly, two t-tests were employed to statistically test the difference between each limit of the 95%CI (i.e. superior and inferior) and the maximal difference considered equivalence, which in this case was set at -0.5 to 0.5 log viral load. Normalization was achieved by adding to the means at each time point for each treatment, the difference between the baseline value for each treatment with the baseline mean.

## RESULTS

Baseline pVL (Mean+SD) was 4.43 (0.50), 4.30 (0.45) and 4.31 (0.52) for PADDLE, SINGLE and SPRING-1 respectively. Rapid decline in viral load was observed in the three regimens. Average effects of treatment in PADDLE, SPRING-1 and SINGLE were -2.75±0.45 (Mean ±SD), -2.53±0.49 and -2.61±0.48 log10 respectively. Viral load decay for the three treatments did not reveal any differences between treatments (F2,238=1.24, p=0.29) and is shown in Fig 1. Mean difference in viral load decay and (95% CIs) at Week 4 for PADDLE-SPRING-1 was -0.21 (-0.47; 0.06) and for PADDLE-SINGLE was -0.12 (-0.34; 0.10). For PADDLE-SPRING-1, 95%CI was inside the equivalence margin (-0.5; 0.5) and Schuirman's two t-tests were significant (<0.01). Similarly, PADDLE-SINGLE 95%CI was inside the equivalence margin and both t-test were significant. In an attempt to account for the differences observed at baseline in viral load, viral load decay was normalized to such differences (Figure 2). ANOVA failed to find any difference between treatments at Week 4 (F2,238=0.57, p=0.56). Mean (95%CI) difference between PADDLE-SINGLE at Week 4 was -0.09 (-0.35, 0.18) and for PADDLE-SPRING-1 it was 0.01 (-0.21, 0.23). In both cases equivalence could be declared based on the fact that neither 95%CI included -0.5 or 0.5 and that the results of the two t-tests (Schuirmann's approach) were <0.001.

## CONCLUSIONS

Viral load decay with DTG/3TC was similar to that with DTG-based triple therapy regimens in patients with pVL < 100, 000 copies/mL. These results, albeit encouraging, should be interpreted with caution, as the analysis is based on a cross-study comparison of mean values and PADDLE is a small pilot study. Fully powered, randomized studies are planned to evaluate DTG/3TC as a valid option for first line therapy.

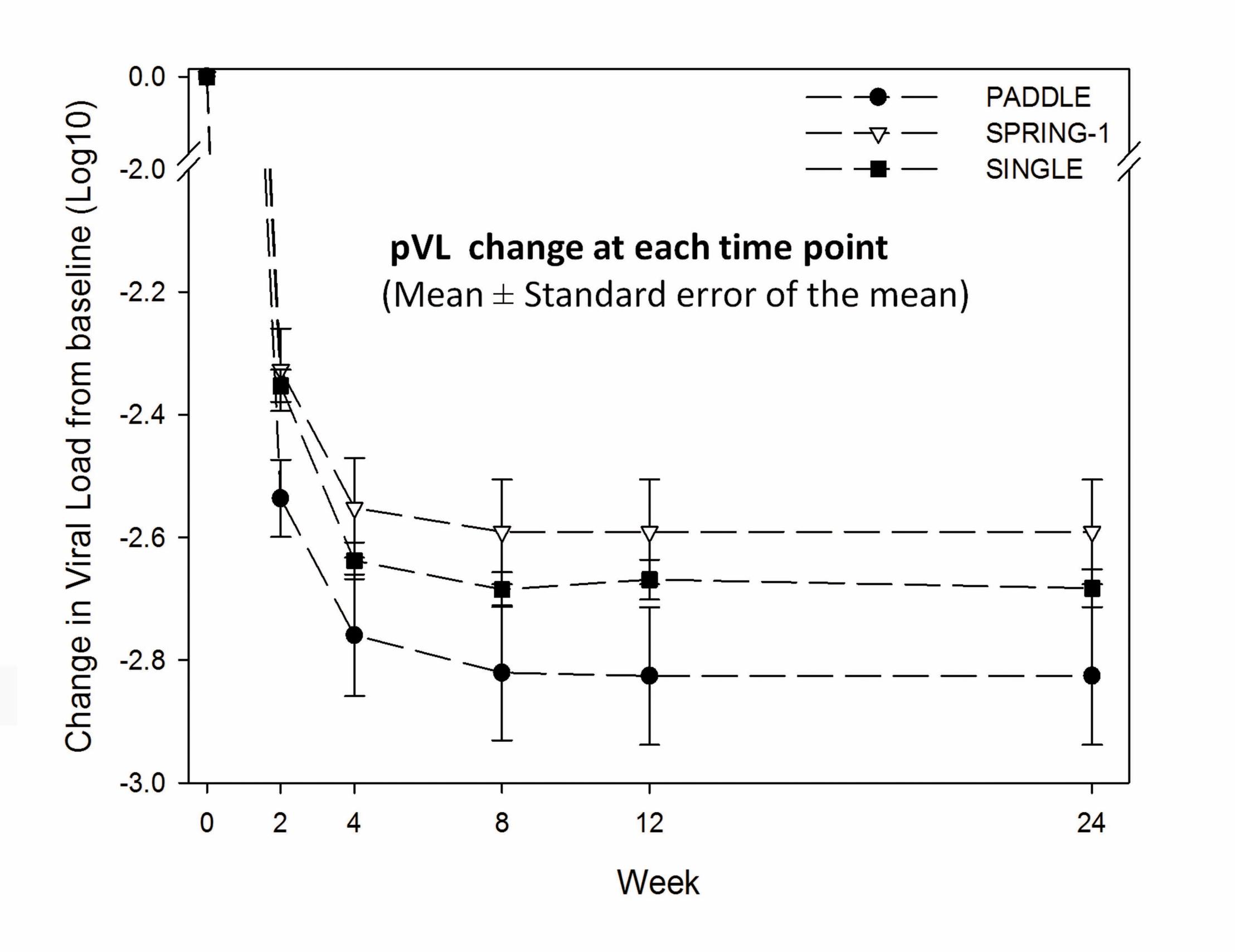


FIGURE 1: pVL change at each timepoint (Mean= standard error of the mean)

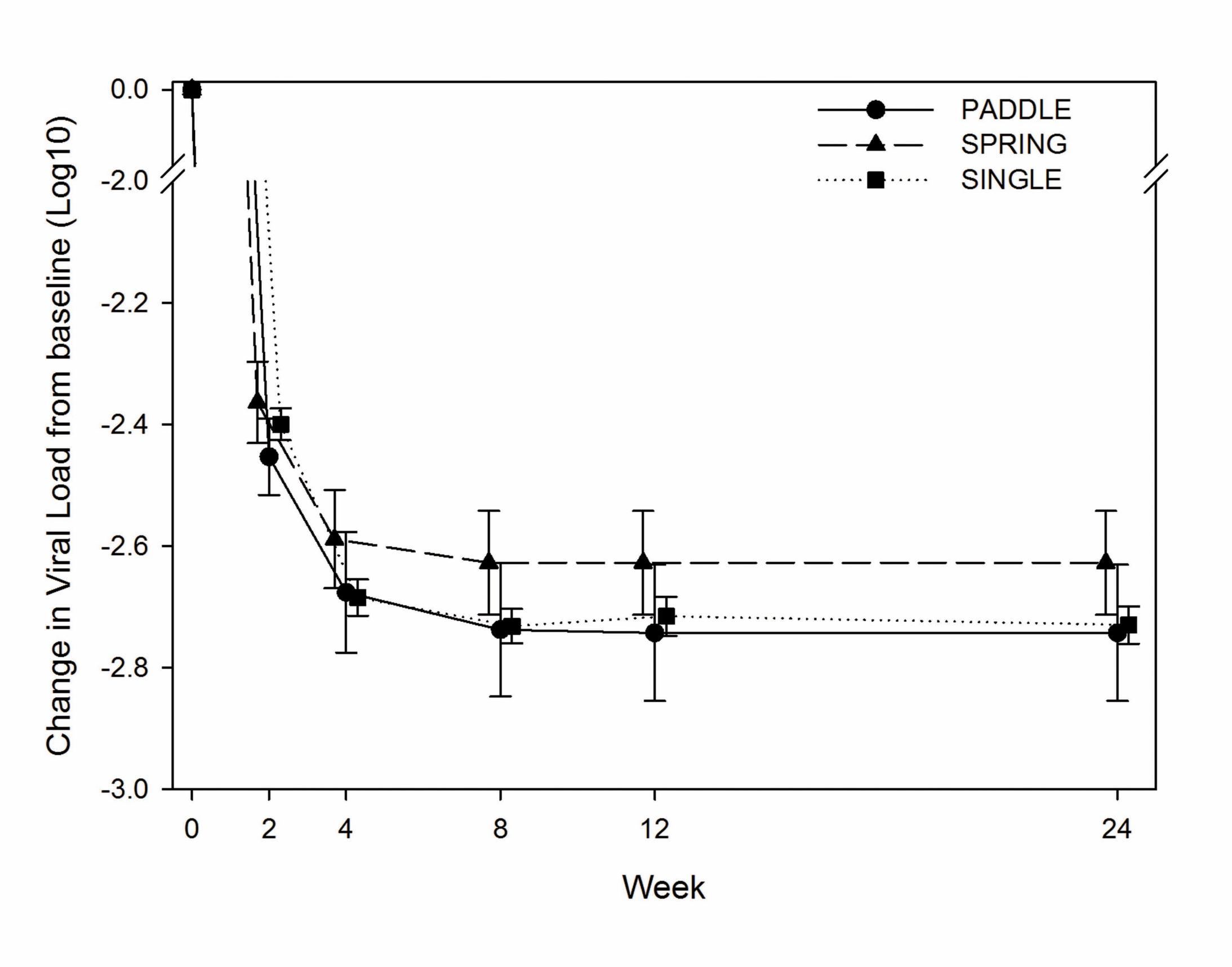


FIGURE 2: pVL change at each timepoint (Mean= standard error of the mean), normalized per baseline pVL





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