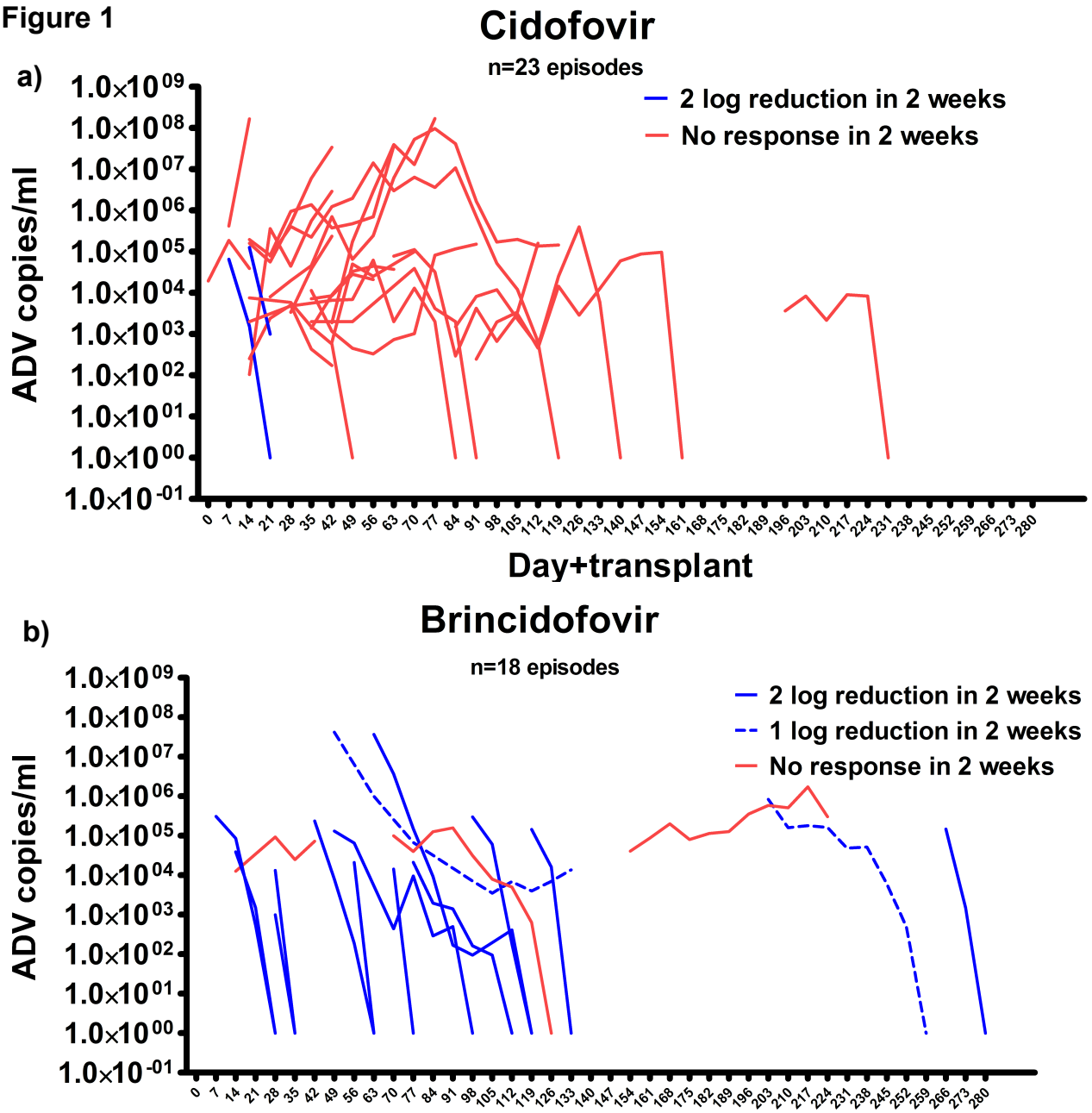
Figure 1



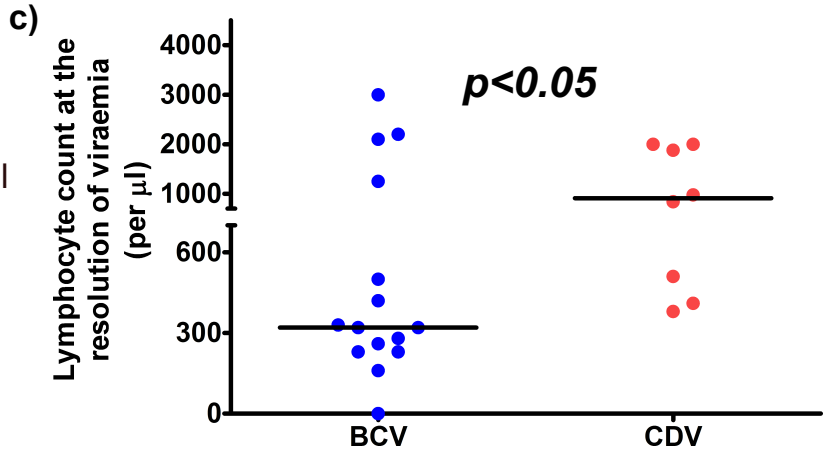
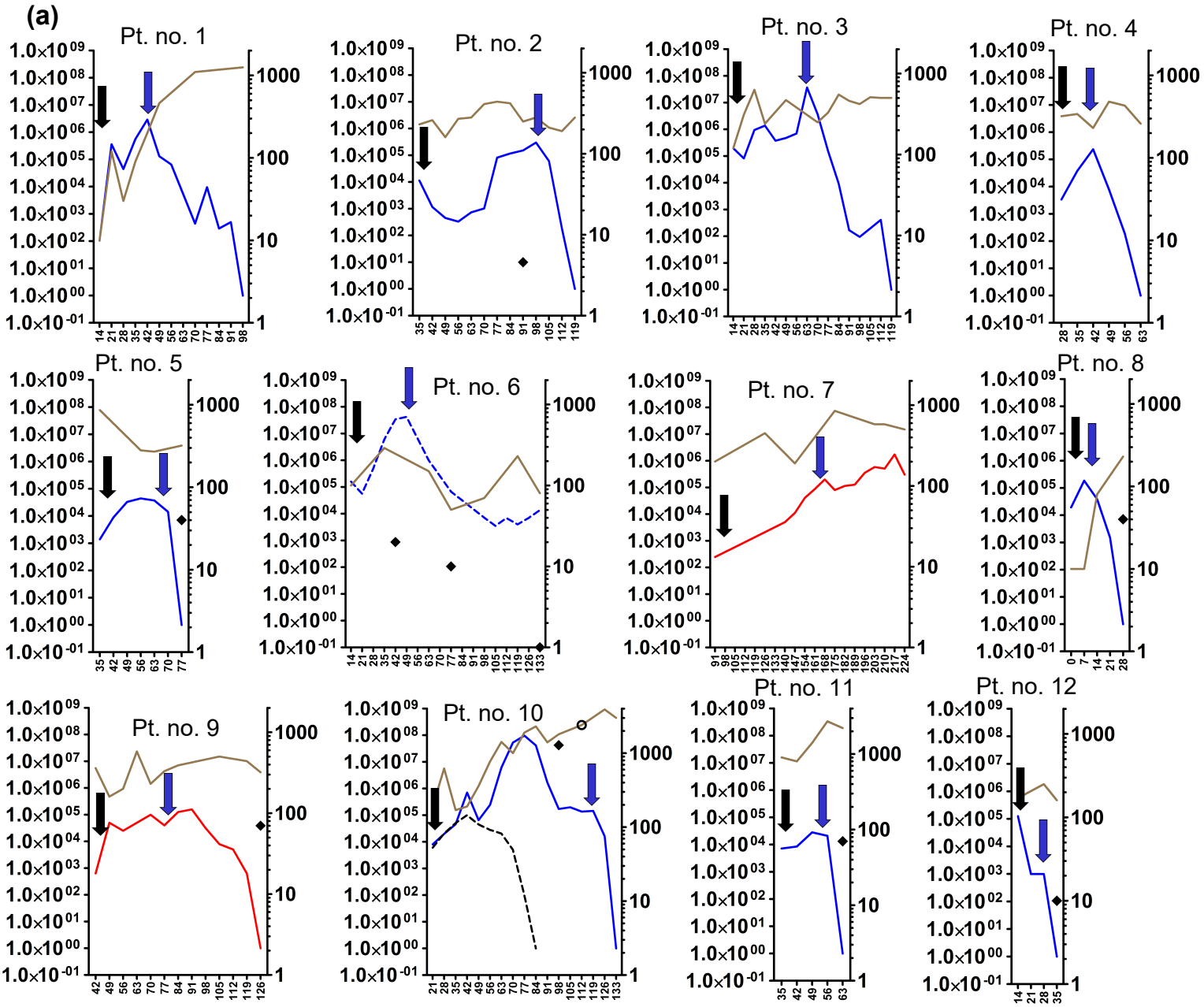


Figure 1 a) and b) shows kinetics of adenoviremia after treatment with Cidofovir and Brincidofovir respectively. Viral load (log_{10} copies/ml) are plotted on y-axis and days after HCT are plotted on x-axis. Cidofovir mediated major virological responses (2 log reduction in 2 weeks) in 2 of 23 episodes. In contrast, 13 of 18 episodes demonstrated major virological responses with Brincidofovir (*p<0.0001*). The majority of responses to Brincidofovir were major. Minor responses (1 log reduction in 2 weeks) were observed only in two episodes. Brincidofovir mediated complete responses in 13 patients (80%) and Cidofovir mediated complete responses in 8 patients (35%) (*p<0.01*). Figure 1 c) compares the lymphocyte count at the resolution of viremia following treatment with Brincidofovir (n=15) and Cidofovir (n=8). The median lymphocyte count at the resoluton of viremia after Brincidofovir versus Cidofovir was 320/microlitre versus 910/microlitre respectively. The resolution of viremia occurred in the Brincidofovir group despite signficant lymphopenia of > 300/microlitre. In contrast, resolution of viremia occured in the Cidofovir group when lymphocyte count was > 300/microlitre (*p<0.05*)

Figure 2



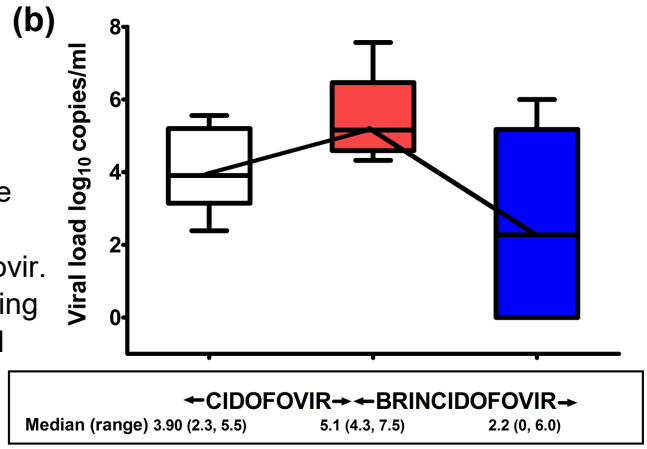


Figure 2 a) shows kinetics of adenoviremia (plotted on left y-axis) and corresponding lymphocyte count (plotted on right y-axis) in 12 episodes treated with Cidofovir followed by Brincidofovir. Days after HCT are plotted on x-axis. Black arrows indicate start of Cidofovir and blue arrows indicate start of Brincidofovir. Major (shown as blue line) and minor responses (shown as interupted blue line) were observed in 9 of 11 episodes unresponsive to Cidofovir. No response in 2 weeks is shown as red line. The circulating lymphocyte count is shown as brown line and CD4+ T-cell count (where available) is shown as black diamond. The median circulating lymphocyte count at complete response was 300/microlitre (160 - 3000). In patient number 10, coexistent CMV viremia (shown as interuppted black line) resulted in T-cell expansion and resolution of CMV viremia. However, adenoviremia and gut adenoviral disease continued despite CD4+ T cell reconstitution. Adenovirus-specific T-cell response was absent despite CD4+ T-cell expansion (shown as black circle). In the remaining 7 patients who had lymphocyte subsets measured, CD4+ T-cells were < 100/ microlitre. Figure 2 b) shows change in adenovirus load between Cidofovir and Brincidofovir in patients unresponsive to Cidofovir (n=11). The median change in log10 viral load on Cidofovir treatment was +1.2 (range, 0.3 to 2.3). In contrast, median change in log10 viral load after 2 weeks of Brincidofovir treatment was -2.9 (range: -5.1 to 0.6; p<0.005). The solid lines represent median and interquartile range and whiskers represent minimum and maximum values.