Although ART can reduce plasma viral load to non-detectable levels, HIV persists in reservoir cells and rapidly rebounds after cessation of therapy. In the CNS, the HIV reservoir is predominantly perivascular macrophages. In SIV and HIV infection, increased CSF1R expression is a marker of infected perivascular macrophages. We have shown that treating SIV infected macaques with the CSF1R inhibitor BLZ-945 selectively ablates SIV-infected macrophages in the CNS. As monocytes can function as precursor cells to macrophages, and CSF1R is thought to regulate maturation of monocytes to macrophages, we sought to characterize changes in monocyte populations in SIV-infected macaques treated with BLZ-945. We find that the number of total monocytes were significantly lower between ART+BLZ animals vs. ART controls (p < 0.001), driven by decreases in the numbers of classical monocytes (p < 0.001) and nonclassical monocytes (p < 0.0001). After treatment cessation, animals that had received ART+BLZ-945 had significantly greater rebound in total monocyte numbers (p < 0.001), driven by rebounding classical monocytes (p < 0.001) and nonclassical monocytes (p < 0.001). Kinetically, it appeared that classical monocytes emerged, followed by intermediate, then nonclassical monocytes in animals that received BLZ-945. Overall, these data are consistent with the notion that BLZ-945 decreases the numbers of monocytes by reducing the number of classical monocytes produced and inhibiting monocyte maturation from classical to nonclassical phenotypes. The sequential rebound of classical and nonclassical monocytes after BLZ-945 are consistent with replenishment of macrophages from increased production of classical monocytes, which differentiate into intermediate then nonclassical monocytes in the blood. It will be interesting to see whether greater rebound of CD16+ monocyte populations in BLZ-945 treated macaques after treatment cessation replenishes SIV reservoirs.

**Total monocyte number**

A graph showing the number of lines

Description automatically generated with medium confidence

A graph of lines and dots

Description automatically generated

A graph of different points and lines

Description automatically generated with medium confidence

**Classical monocytes, absolute**

A graph of a graph showing the number of the same numbers

Description automatically generated with medium confidence

A graph of lines and dots

Description automatically generated

A graph of a graph with lines and dots

Description automatically generated with medium confidence

**Intermediate monocytes, absolute**A graph of a graph showing the number of lines

Description automatically generated with medium confidence

A graph of a graph with lines and dots

Description automatically generatedA graph of a graph of a graph

Description automatically generated with medium confidence

**Nonclassical monocytes, absolute**

A graph of a graph showing the value of a stock market

Description automatically generated with medium confidence

A graph of a graph with lines and dots

Description automatically generated with medium confidence

A graph of a graph of a line

Description automatically generated with medium confidence

**%BrdU**

A graph of a graph with lines and dots

Description automatically generated

A graph of a number of objects

Description automatically generated with medium confidenceA graph of a graph

Description automatically generated