

Figure S1 Association between CLA and composite disability progression in the absence of ALA for natalizumab. CLA in (B) non-SELs and (C) CNT2 lesions but not (A) SELs remained associated with composite disability progression in the absence of ALA in SPMS patients treated with natalizumab. However, a consistent directional trend was observed in SELs. Absence of acute lesion activity was defined as no baseline and postbaseline T1 gadolinium-enhancing and no postbaseline new/enlarging T2 lesions. Composite progression was confirmed at 24 weeks and end of study on one or more of the EDSS, Timed 25-Foot Walk, or 9-Hole Peg Test. In these box-and-whisker representations, the box spans the interquartile range, the median is marked by the horizontal line inside the box, and the whiskers are the two lines outside the box that extend to the highest and lowest observations. *p* values by Van Elteren test; stratified by baseline EDSS score (≤ 5.5 or ≥ 6.0) and baseline T2 lesion volume category based on tertiles (≤ 6908.79 mm³, >6908.79 – 18818.49 mm³, and >18818.49 mm³). ALA, acute lesion activity; CNT2, chronic nonenhancing T2; CLA, chronic lesion activity; EDSS, Expanded Disability Status Scale; SEL, slowly expanding lesion; SPMS, secondary progressive multiple sclerosis; T1LV, T1-hypointense lesion volume.

