Abstract 1641
Assessing the temporal relationship of serum neurofilament light and subclinical disease activity: Findings from APLIOS trial
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Background
Several studies showed prognostic value of serum neurofilament light chain (sNfL) in relapsing multiple sclerosis (RMS). For the first time, we explored the association of sNfL and subclinical disease activity using data from the APLIOS trial.

Objectives
To evaluate the potential of sNfL as a patient-level biomarker for monitoring subclinical disease activity in RMS patients.

Methods
In the APLIOS open-label study of ofatumumab 20 mg s.c in RMS (n=284), frequent (14 time points over 12 weeks) sNfL measurements were performed (Siemens sNfL RUO assay on ADVIA Centaur®). MRI scans were done every 4 weeks. The potential monitoring value of sNfL was examined in 3 ways: 1) Age-adjusted geometric mean sNfL over time was estimated in 3 subgroups: patients who had on-study clinical relapses (r+), patients with presence of gadolinium-enhancing T1 (GdT1) lesions at or post-baseline but no clinical relapses (GdT1−r−), and patients with neither lesions nor clinical relapses (GdT1−r−); 2) As high-frequency sampling permitted an estimation of daily sNfL levels, every report of GdT1 lesion was linked to the estimated sNfL level at the time of the scan (using a recurrent-events analysis); and 3) Patient-level predictions of GdT1 lesion were done using the last sNfL value before the corresponding scan and compared with MRI-based predictions (in terms of across-scan average area under the receiver operating characteristics curve [AUC]).

Results
Over the study course, the age-adjusted geometric mean sNfL levels in the GdT1−r− group (n=153) were low compared to other two subgroups, with 95% CIs below those of the r+ (n=15) and GdT1−r+ (n=116) groups. After adjusting for baseline age and MRI covariates, a between-patient difference of 50% higher sNfL at the time of GdT1 scan was associated with a 29% higher risk of persistent GdT1 lesion (p<0.0001). At the individual patient level, the predictive power of the last sNfL value (AUC=0.76) before scan for presence of GdT1 lesion was similar to that of baseline GdT1-count (AUC=0.77).

Conclusions
This study suggests sNfL may have utility in monitoring subclinical disease activity in RMS patients as shown by associations with GdT1 lesion activity. When frequent MRI scans are not feasible, the predictive value for subclinical disease activity may render sNfL as an alternative to MRI for standard monitoring from a resource, patient management, and convenience perspective.