CSF and Plasma JCV-DNA Changes as Prognostic Marker in Progressive Multifocal Leukoencephalopathy

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BACKGROUND

- *Context*: Progressive Multifocal Leucoencephalopathy (PML) is a severe and rapidly progressive encephalitis due to reactivation of JC virus (JCV) in the Central Nervous System (CNS) of people with immune dysfunction. Studies have shown that Cerebrospinal Fluid (CSF) JCV-DNA level at diagnosis and its variation over time may help predict PML outcome.
- *Aim*: to study the value of CSF and plasma JCV-DNA level at the time of diagnosis and relative changes at 30, 60, and 90 days of follow-up, to predict one-year survival.

Longitudinal JCV-DNA monitoring in plasma, along with CSF, seems to be a marker for outcome prediction in patients with Progressive Multifocal Leukoencephalopathy

METHODS

- *Cohort*: 114 cases from the Italian PML Registry (NCT06594614), period 1992-2024, with ≥2 sequential quantitative JCV-DNA examinations of CSF (n=98) and/or plasma (n=38), within 90 (± 14) days from diagnosis;
- *Statistics*: identification at first assessment and at 30, 60 and 90 (± 14) days of follow-up, of the best JCV-DNA cutpoints in CSF and plasma for predicting one-year survival, by maximized metric method by Youden Index, of:

1. Single point determinations (Log c/mL);
2. Slope = Log difference at each determination ÷ difference of days between each sample (Log c/mL / days)
3. Delta = Log difference between last and first determination (Log c/mL).

Figure 1. CSF and plasma JCV-DNA values as single point values at diagnosis, and at 30, 60 and 90 days of follow-up

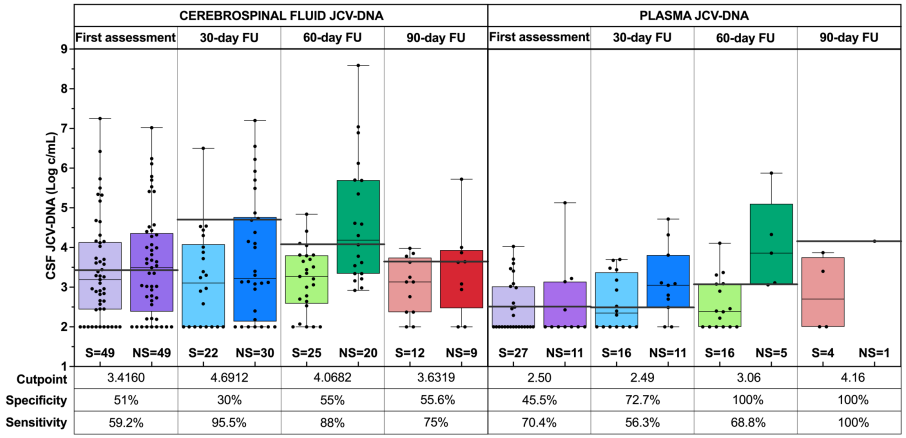


Figure 2. CSF and plasma JCV-DNA slope values at 30, 60 and 90 days of follow-up

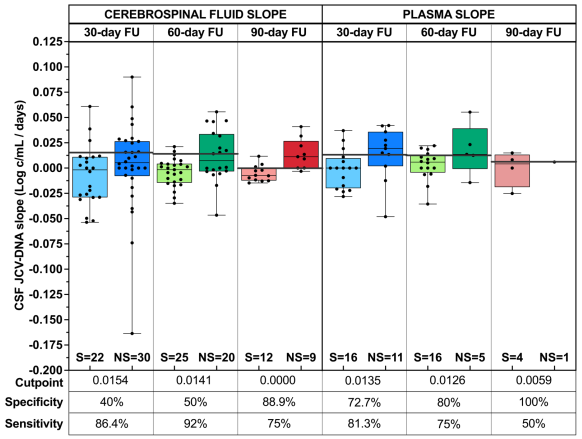
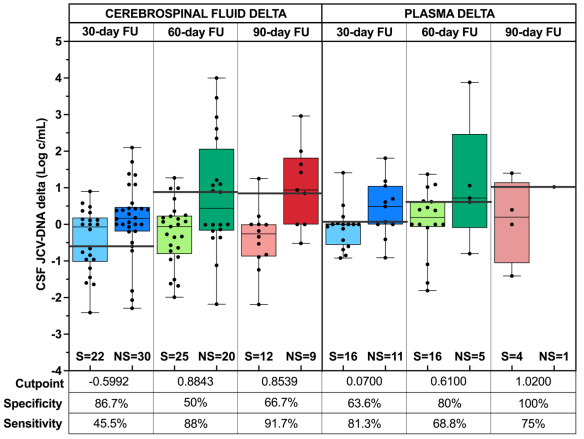


Figure 3. CSF and plasma JCV-DNA delta values at 30, 60 and 90 days of follow-up



Median and 25th-75thIQR; whiskers extend to the lowest and highest data points. The horizontal gray lines represent the cutpoints for each specific variable. FU, follow-up; S, survivors; NS, non-survivors.

RESULTS

- Underlying diseases were HIV infection (66.7%), hematological malignancies (13.3%), primary immunodeficiencies (8.6%), natalizumab-treated multiple sclerosis (5.7%), conditions not belonging to other categories (3.8%), rheumatic diseases (1.9%);
- Figure 1 (single point determinations): best predictive values observed at 60 days of follow-up for both CSF and plasma;
- Figure 2 (slope): best predictive values observed in the first 90 days of follow-up for CSF and in the first 60 days for plasma
- Figure 3 (delta): best predictive values observed in the first 90 days of follow-up for CSF and in the first 60 days for plasma.

CONCLUSIONS

Longitudinal JCV-DNA measurements in plasma, together with CSF, may provide a new non-invasive biomarker for monitoring PML course in real-time.

ACKNOWLEDGEMENTS

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