Comparing STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV Tests in RRMS to Assess PML Risk

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Breakthrough research in Autoimmune and Neurodegenerative diseases

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INTRODUCTION

The risk of developing progressive multifocal leukoencephalopathy (PML), a rare but potentially fatal opportunistic infection of the central nervous system caused by the J.C. virus (JCV), remains a primary concern associated with natalizumab therapy in the clinical management of patients diagnosed with multiple sclerosis (MS).

Branded natalizumab (Tysabri ®) has a well-established risk stratification algorithm and monitoring protocol that includes testing with STRATIFY JCV™ DxSelect™. At the same time, the biosimilar Tyruko ® introduces a new testing method, IMMUNOWELL™ JCV, for assessing JCV antibody status.

AIM

Our study focuses on the **simultaneous collection** of samples for both STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV antibody

tests from patients treated with natalizumab (as Tysabri®).

By analyzing samples collected on the same day with both methodologies, we aimed to **determine the comparability of these tests** in **classifying PML risk** during treatment.

METHODS

This was an independent retrospective cohort study. Patients diagnosed with Relapsing Remitting MS (RRMS) according to revised McDonald criteria who were actively followed at two Italian MS centers (Foggia and Frosinone), treated with Natalizumab (Tysabri®) and clinically stable were eligible for enrollment.

The dataset contained patient characteristics and treatment histories, including the number of natalizumab administrations, previous immunosuppressive therapy, extended dose regimen, and test results for both STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV antibody tests colected on the same date.

Risk categories were defined as follows:

RESULTS

A total of 69 patients, mean age of 39±10.3 years, were enrolled (Table 1). In this cohort, 56 (56/69; 81.2%) tested negative with STRATIFY JCV™ DxSelect™, and 45 (65.2%) tested negative with IMMUNOWELL™ JCV (χ^2=3.69, p=0.0546).

The level of agreement for risk stratification between the two tests was 85.5%. In detail, the intermediate and high-risk categories showed discordances (p<0.05), and the most common type of discordance was between low and intermediate risk (77.8%), followed by low/high classification discordance (22.2%).

The radar chart highlighted the distribution of risk changes, emphasizing the tendency of IMMUNOWELL™ JCV to classify patients into higher risk categories (Fig. 1). The heatmap (Fig. 2) confirms these results. STRATIFY JCV™ DxSelect™ test categorized the majority of patients (91.3%) as low risk, with equal distributions (4.3%) in both intermediate- and high-risk categories.

Total Cohort (n=69)	
Race, n(%) Caucasian	69 (100)
Age (years), mean ± SD	39 ± 10.3
Age at MS diagnosis (years), mean ± SD	28.2 ± 9.3
Sex, n (%)	Female: 53 (76.8); Male: 16 (23.2)
EDSS at NTZ prescription, median (IQR)	3.00 (2.0–4.0)
EDSS, median (IQR)	3.00 (2.5–4.0)
Patients with MRI activity in the last year, n(%)	0
Number of Relapses in the last two years	0.2 ± 0.5
Patients with >24 administrations, n(%)	47 (68.1)
Patients on EID regimen, n(%)	21 (30.4)
Patients previously exposed to immunosuppressive* drugs	4 (5.8)
Naïve to any DMT, n(%)	27 (39.1)
N. of NTZ Administrations, mean ± SD	46.7 ± 45.7
Time on NTZ (months), mean ± SD	68.7 ± 180.3

*Table 1. Characteristics of the enrolled cohort. SD, standard deviation; IQR, interquartile range; n, number; EDSS, Expanded Disability Status Scale; EID, extended interval dose; MS, multiple sclerosis; NTZ, natalizumab; MRI, magnetic resonance imaging; DMT, disease modifying therapy. Note: *in our cohort: alemtuzumab, cladribine, azathioprine.*

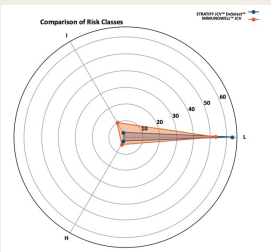

Figure 1. Radar chart for the distribution of risk classes (Low, Intermediate, High) for both STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV tests. Blue lines= STRATIFY JCV™ DxSelect™, orange lines= IMMUNOWELL™ JCV. L=Low; I=Intermediate; H=High.

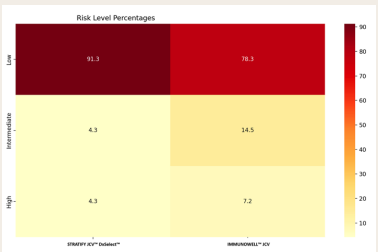

Figure 2. The heatmap displays the percentage distribution of PML risk levels as assessed by STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV tests. The X-axis shows test types, Y-axis indicates risk levels (Low, Intermediate, High). Color intensity corresponds to the percentage of patients in each risk category, with darker colors representing higher percentages. Cell values show the percentage of patients in each category, rounded to one decimal place. n = 69 patients.

In contrast, IMMUNOWELL™ JCV classified 78.3% as low risk while identifying higher proportions in both intermediate- (14.5%)and high-risk (7.2%) categories. Hence, compared to STRATIFY JCV™ DxSelect™, **IMMUNOWELL™ JCV antibody test tended to categorize more patients as higher risk**. No significant association was found between discordance and prior use of immunosuppressant drugs and >24 doses of natalizumab. **The agreement between tests, assessed with the weighted Cohen's Kappa coefficient, was substantial (κ=0.6222).**

CONCLUSIONS

Compared to the STRATIFY JCV™ DxSelect™, **the IMMUNOWELL™ JCV test tends to place more patients in higher risk categories.** Further, longitudinal studies are needed to evaluate the clinical impact of these differences in PML risk assessment.

REFERENCES

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DISCLOSURES

The authors have nothing to disclose.

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