

John Cunningham Virus (JCV) serostatus discrepancy by two different tests: impact on the clinicians and patients choices in a cohort of Multiple Sclerosis patients treated with Natalizumab

INTRODUCTION

JCV serostatus is crucial in evaluating the risk-benefit ratio of Natalizumab therapy in Multiple Sclerosis. Two different JCV antibody tests are now available: the **Stratify® JCV test** (Unilabs) for the originator and the **ImmunoWELL® JCV test** (GenB) for the biosimilar. We collected clinical data on both tests in a cohort of MS patients treated with NTZ.

OBJECTIVES/AIMS

- **Comparison of anti-JCV antibody results** obtained from the two tests in patients receiving natalizumab.
- **Evaluation of potential discrepancies** between the two testing methods in clinical practice and treatment decisions.

METHODS

We included MS patients treated with NTZ who had undergone initial JCV testing with Stratify® test, followed by a subsequent ImmunoWELL test. Patients were then re-tested using the Stratify® test.

Clinical decisions following test results, based on both clinicians' and patients' preferences, were recorded.

RESULTS

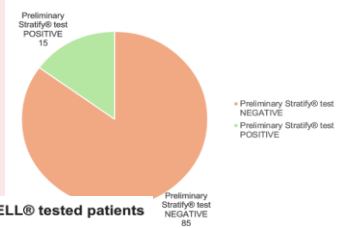
Total enrolled patients	100 patients
Mean age	39.2 years
Median EDSS	2.0
Mean NTZ treatment duration	62.3 months

Table 1 – Enrolled patients' data.

Out of the 100 enrolled patients, **85** had tested **negative** for JCV antibodies with the Stratify test in the previous six months. Among the patients tested with the ImmunoWELL® JCV IgG test (fig. 2), **54.9% turned positive** (mean index: 0.569; 75% had a low index < 0.8, 18% had an intermediate index 0.8-1.4, and only 7% had a high index > 1.4). **All samples from formerly Stratify® positive patients were confirmed positive with the ImmunoWELL® test.**

All, except two, of the 37 patients who tested negative to the ImmunoWELL® test were confirmed negative with the Stratify® retest; the two positive results from the Stratify® retest were considered real JCV seroconversion episodes.

Fig 1 - Results of preliminary JCV Stratify® test in NTZ patients.



Index in JCV ImmunoWELL® tested patients

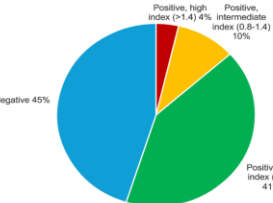


Fig. 2 - JCV index in ImmunoWELL® tested patients

On the other hand, out of the ImmunoWELL® positive patients, **77.8%** then resulted negative to the Stratify® retest; among the others that were confirmed positive by the retest, 2 presented high index, 2 intermediate index, and 6 low index (fig. 3).

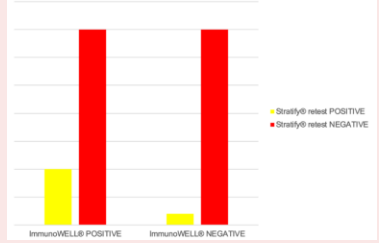
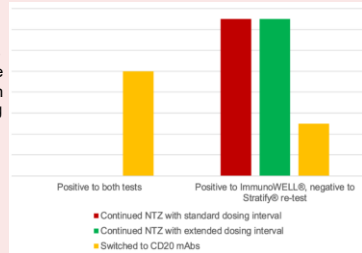


Fig.3 Distribution of the formerly Stratify® negative patients according to JCV IgG by ImmunoWELL® test and to JCV Stratify® retest (negative as red bars and positive as yellow bars).

Increase in positive results and higher index values have implications for treatment, as natalizumab may be discontinued when a patient tests positive for JCV antibodies or when the index increases.

When immunopositivity was detected in both tests, all patients were switched to antiCD20 mAbs. Among cases presenting discrepancy between the two tests (ImmunoWELL® positivity and Stratify® retest negativity), 5 patients were switched to antiCD20 mAbs, 15 patients continued natalizumab at standard dosing interval (all with low index positivity at ImmunoWELL®), and 15 patients were administered natalizumab at extended dosing interval. Patients continuing Natalizumab both at extended and standard dosing were followed with intensive MRI screening at MS center. Choosing to switch to antiCD20 mAbs in this subgroup of patients mostly occurred during the very beginning of ImmunoWELL® test use

Fig. 4 Treatment choices in patients who tested positive to both tests and in patients presenting discrepancy between the two tests



CONCLUSIONS

Our study confirms that a high rate of **discrepancy** between the Stratify® JCV and ImmunoWELL® JCV test results exists, particularly in patients with low positive index values, as previously observed [1, 2, 3]. In fact, despite ImmunoWELL reliability in detecting patients at risk of PML, the high rate of discrepancy between the two tests is challenging in clinical practice [3]. This discrepancy has a significant impact on clinical decision-making by both physicians and patients regarding natalizumab treatment in multiple sclerosis [2]. Such unfortunate situation requires shared decision making, balancing risks and benefits [6]: in our cohort this process led most patients to decide to continue Natalizumab, although in a protected setting. Further investigations are warranted to assess the clinical relevance of the differences in the two currently available JCV assays. Moreover, it would be advisable to develop a publicly standardised JCV assay, which would guarantee uniform results independently from biosimilar preparations [1].

References: 1. Dobson R, et al Approach to JCV testing with natalizumab biosimilar: a UK consensus statement. *Mult Scler Relat Disord.* 2025 Aug; 2. Vukusic S, et al, Beyond the switch to the biosimilar of natalizumab: What is the impact of changing the JCV test? *Mult Scler.* 2025 Jun; 3. Guerrieri S, et al, Stratify and ImmunoWELL JCV tests performances in a real-world multiple sclerosis cohort: possible clinical implications of biosimilar Natalizumab use. *J Neurol.* 2025 Aug