Detection of Antibodies to Natalizumab Biosimilar Drugs

Helen LOCK, Diane MACDONALD and Elizabeth WALKER
Department of Immunology, Royal London Hospital, East and South East London Pathology Partnership, Barts Health NHS Trust

Introduction

- Natalizumab is a humanised monoclonal
  - Developed to target α4-integrin to inhibit the migration of leukocytes across the blood-brain barrier in the
  - Treatment of relapsing-remitting Multiple Sclerosis (RRMS)[1]
  - Patented as Tysabri
- Patients may develop antibodies to non-humanised regions
  - Detection of immunogenicity important for effective patient management
- Biosimilar Tyruko developed following Tysabri patent expiration[2]
  - Development of lower-cost biosimilar biologic therapies has made these treatments more accessible
- Tyruko has been available since January 2024
  - Approved for use by MHRA[3]
  - Neurologists being encouraged to switch treatment with Tysabri to Tyruko
  - Similar immunogenicity[4]
- Department of Immunology, ESEL NHS Pathology Partnership is the national reference centre for the detection and confirmation of antibodies to Natalizumab
- Treatment of RRMS with Tyruko is increasing
- The aim of this study is to determine if our assay is suitable for the detection of antibodies to Tyruko

Materials & Methods

- Natalizumab antibodies detected by a bridging ELISA
  - Patient serum samples stored at -80^{0}C
  - Screening and competition assays run in parallel
- Positive results were categorised by treatment
  - Tysabri or Tyruko
- Positivity rate calculated and plotted for 2018-2024
  - Number of positive results as a percentage of total samples tested

Results

- 278 samples tested between January 2024 and March 2025, since the introduction of Tyruko (Figure 1)
  - 25 positive results

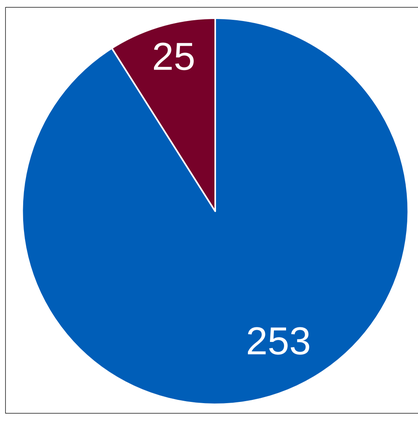

Figure 1: 25/278 samples tested between January 2024 and March 2024, since the introduction of Tyruko, were positive for Natalizumab antibodies

- 3 patients with positive Natalizumab antibody test results were on Tyruko (Figure 2)

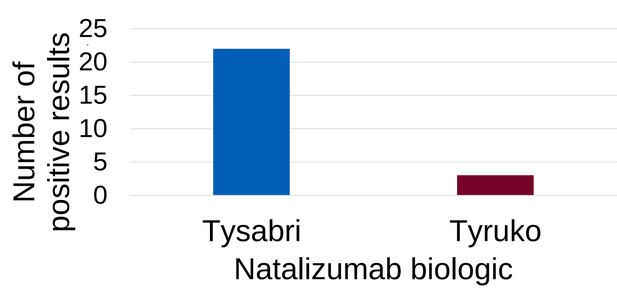

Figure 2: 3/25 positive Natalizumab results between January 2024 and March 2025 were from patients taking Tyruko

- The positivity rate of the Natalizumab antibody test has not been impacted by the introduction of Tyruko (Figure 3)
  - Positivity rate in 2024 (8.5%) within mean ± 2SD range (4.9-10.1%) for 2018-2023

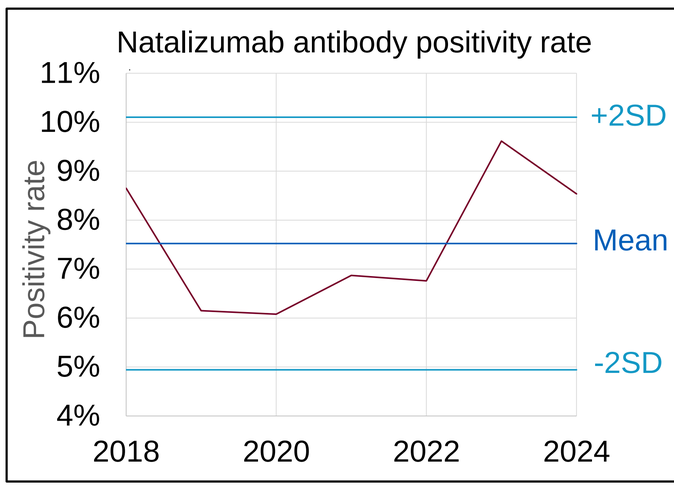

Figure 3: Natalizumab antibody positivity rate between 2018 and 2024. The positivity rate in 2024 was within the mean positivity ±2SD range

Discussion & Conclusion

- Our assay was able to detect Natalizumab antibodies in patients taking Tyruko
  - Antibodies detected in 3 patients taking Tyruko
- Results to date suggest Tyruko has not affected the positivity rate of our Natalizumab assay
  - Limited interpretation of impact of Tyruko on positivity rate
  - Only 14% of positive results were from patients taking Tyruko
  - Impact of Tyruko on positivity rates will continue to be assessed as the use of Tyruko to treat RRMS becomes more widespread in the UK
- Not always clear from requests if patients on Tysabri or Tyruko
  - Requestors were contacted, 4/16 did not respond
  - Request form updated to include tick boxes for Natalizumab antibody treatment
- Our Natalizumab antibody assay is suitable for the detection of antibodies to the biosimilar Tyruko

References

1. Rudick RA, Panzara MA. Natalizumab for the treatment of relapsing multiple sclerosis. *Biologics* 2008; **2**: 189–199.
2. Shirley M. PB006: A Natalizumab Biosimilar. *Clin Drug Investig* 2024; **44**: 367–370.
3. McCartney F. September Industry News Update. *Ther Deliv* 2023; **14**: 669–673.
4. Chamberlain P, Hemmer B, Höfler J, Wessels H, von Richter O, Hornuss C *et al.* Comparative immunogenicity assessment of biosimilar natalizumab to its reference medicine: a matching immunogenicity profile. *Front Immunol* 2024; **15**. doi:10.3389/fimmu.2024.1414304.