IN PATIENTS WITH HIGHLY ACTIVE RELAPSING-REMITTING MULTIPLE SCLEROSIS (RRMS)[1,2]

TREAT WITH THE POWER AND EXPERIENCE OF TYSABRI

NOW WITH 10-YEAR TYSABRI OBSERVATIONAL PROGRAM (TOP) DATA

EVERY 4 WEEKS 300mg IV

TYSABRI® (natalizumab)

TOP: TYSABRI Observational Program.

A DECADE OF WELL-ESTABLISHED EFFICACY AND SAFETY OBSERVED IN REAL-WORLD PATIENTS TAKING TYSABRI[3]

TOP began over 10 years ago, and is the largest ongoing, real-world study of TYSABRI-treated patients with RRMS.

92.5%

relative
ARR REDUCTION
at **year 10** vs. baseline

Mean ARR decreased from 1.99 (n=6148; 95% CI 1.97 to 2.02) in the 12 months prior to baseline to 0.15 (n=375; 95% CI 0.14 to 0.15) at year 10 on TYSABRI treatment

ANNUALISED RELAPSE RATE (ARR) AT 10 YEARS

In line with the results from the TOP 5-year interim analysis, patients on TYSABRI experienced **significant reductions in ARR over 10 years.**[3]

- Greater reductions were observed in TYSABRI patients with:[3]
  - lower baseline EDSS scores (≤3.0 vs >3.0)
  - fewer prior DMTs (0 vs 1; 0 vs ≥2; 1 vs ≥2) or
  - fewer relapses in the year prior to treatment (≤1 vs >1)

The cumulative probability of remaining relapse-free at 10 years was **45.8%** in the overall population[3]

DISABILITY AT 10 YEARS

33.1%

cumulative probability of 24-week
CONFIRMED DISABILITY IMPROVEMENT*[3]
(n=5179 at baseline; n=28 at year 10)

27.8%

cumulative probability of 24-week
CONFIRMED DISABILITY WORSENING†[3]
(n=6148 at baseline; n=32 at year 10)

*Disability improvement defined as a decrease of ≥1.0 point from baseline score, confirmed 24 weeks later, among patients with baseline EDSS scores ≥2.0.
† Disability worsening defined as an increase, confirmed 24 weeks later, of ≥0.5 points from a baseline EDSS score of ≥6.0, ≥1.0 point from a baseline EDSS score of ≥1.0 to <6.0, or ≥1.5 points from a baseline EDSS score of 0.0.
ARR: Annualised Relapse Rate; **EDSS:** Expanded Disability Status Scale; **RRMS:** Relapsing-Remitting Multiple Sclerosis; **TOP:** TYSABRI Observational Program.

10-YEAR TOP INTERIM ANALYSIS CONFIRMS WELL-ESTABLISHED TYSABRI SAFETY PROFILE IN REAL LIFE[3]

>85%
of patients had no SAEs

Safety findings were **consistent with the current safety profile** of TYSABRI, and **no new safety concerns** were identified.[3]

4.7% experienced ≥1 SAE considered related or possibly related to treatment[1]

- The most common SAEs were infections and infestations, with an incidence of 4.1%
- PML, pneumonia, urinary tract infection and herpes zoster were the most commonly reported infections

INCIDENCE RATES FOR OPPORTUNISTIC INFECTIONS, MALIGNANCY, AND PML REMAIN LOW[3]

Incidence of opportunistic infection, malignancy, and PML

Event	Overall (26,060.25 patient-years;* N=6148)		≤3 years (15,773.19 patient-years;* n=6148)		>3 years (10,233.77 patient-years;* n=3719)	
	Patients with an event, n (%)	Incidence rate per 1000 patient-years (95% CI)†	Patients with an event, n (%)	Incidence rate per 1000 patient-years (95% CI)†	Patients with an event, n (%)	Incidence rate per 1000 patient-years (95% CI)†
Opportunistic infection	**11** (0.18)	**0.422** (0.234–0.762)	**10** (0.16)	**0.634** (0.341–1.178)	**1** (0.03)	**0.098** (0.014–0.694)
PML	**53** (0.86)	**2.034** (1.554–2.662)	**17** (0.28)	**1.078** (0.67–1.734)	**36**‡ (0.97)	**3.518** (2.537–4.877)
Malignancy	**63** (1.02)	**2.417** (1.889–3.095)	**35** (0.57)	**2.219** (1.593–3.090)	**28** (0.75)	**2.736** (1.889–3.963)

Adapted from Butzkueven H, et al. 2019.[3]

TOP is an ongoing multinational, open-label, prospective study designed to study the long-term safety of TYSABRI monotherapy in patients with relapsing-remitting multiple sclerosis under routine clinical practice conditions. At the time of this (10-year analysis), 6148 patients from 17 different countries had been enrolled. Patients enrolled in TOP were required to have a diagnosis of RRMS and to be natalizumab naïve or have received ≤3 doses of natalizumab in their lifetime at the time of enrolment. Patients in TOP were treated according to the approved dosing of 300 mg intravenous TYSABRI every 4 weeks.

The primary endpoint was long-term safety (the incidence and pattern of SAEs) in patients receiving TYSABRI. Secondary endpoints evaluated multiple sclerosis (MS) disease activity as measured by relapses and changes in disability.

* Based on the time from the first dose of natalizumab until the last natalizumab dosing date + 6 months.

† Calculated as (1000 × number of patients with an event)/(total patient-years of follow-up). Exact CIs are calculated based on the Poisson distribution.

‡ Of the 36 cases with reported anti-JCV antibody serostatus 6 months prior to PML development, 35 were positive. 14 (26.4%) of the 36 cases occurred in patients reporting prior immunosuppressant use.

CI: Confidence Interval; **PML:** Progressive Multifocal Leukoencephalopathy; **SAE:** Serious Adverse Event.

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TOP PROVIDES 10 YEARS OF DATA DEMONSTRATING EXCELLENT LONG-TERM SAFETY AND SUBSTANTIAL DISEASE CONTROL[3]

TOP: TYSABRI Observational Program.

References

1. TYSABRI (natalizumab) Summary of Product Characteristics. Please refer to the approved SmPC in your country. **2.** Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. New Engl J Med. 2006;354(9):899-910. **3.** Butzkueven H, Kappos L, Wiendl H, et al. Long-term safety and effectiveness of natalizumab treatment in clinical practice: 10 years of real-world data from the Tysabri Observational Program (TOP). J Neurol Neurosurg Psychiatry. 2019; epub March 2020; doi: 10.1136/jnnp-2019-322326.

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