A Real-World Retrospective Analysis of Outcomes in Multiple Sclerosis Patients Who Transitioned to Alemtuzumab After Rituximab or Ocrelizumab

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Disclosures

- **Marie Coste, Miriam C Fenton, Zia Choudhry, Mark Ozog, Elizabeth Poole, and Bill Aschenbach:** Employees of Sanofi.
- **Lobat Hashemi and Benjamin Guikema:** Employee of Sanofi during the course of the work.
- **Michael Behling and Kathleen Mortimer:** Received compensation as employees of OM1.
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Alemtuzumab is approved in >70 countries for treatment of adults with relapsing forms of multiple sclerosis (MS). In the US, the indication provides that, because of its safety profile, the use of alemtuzumab should be reserved for patients who generally have had an inadequate response to 2 or more therapies indicated for the treatment of MS. In the EU, alemtuzumab is indicated as a single disease-modifying therapy in adults with highly active relapsing-remitting MS; for patients with highly active disease despite a full and adequate course of treatment with at least 1 disease-modifying therapy or patients with rapidly evolving severe relapsing-remitting MS defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium-enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI. This material may contain information that is outside of the approved labeling in some countries.

Introduction

- Despite reduction in relapse rates and MRI activity, some relapsing-remitting MS patients on anti-CD20 antibody therapies (rituximab and ocrelizumab) have discontinued treatment due to lack of efficacy and AEs
- Transition to another higher-efficacy therapy may be needed to control disease activity
- In CARE-MS I (NCT00530348) and II (NCT00548405), 2 courses of alemtuzumab demonstrated significantly greater improvements in clinical and MRI outcomes versus subcutaneous interferon beta-1a over 2 years[1,2]
- AEs associated with alemtuzumab treatment in clinical trials and postmarketing experience include[1-8]
  - Infusion-associated reactions
  - Increased frequency of infection and the potential for opportunistic infections
  - Secondary autoimmunity (thyroid disorders, immune thrombocytopenia, nephropathies, autoimmune cytopenias, autoimmune hepatitis, and other less common autoimmune events)
  - Acute acalculous cholecystitis
  - Cardiovascular and pulmonary events possibly related to infusion problems
- Data are limited on outcomes in patients who transition from anti-CD20 therapies to alemtuzumab
  - A recent retrospective case series of 3 patients who transitioned from ocrelizumab or rituximab to alemtuzumab within 5 months showed no immediate serious AEs or impact on expected efficacy of alemtuzumab[9]

AE=adverse event. 1. Cohen JA, et al. *Lancet* 2012;380:1819-28. 2. Coles AJ, et al. *Lancet* 2012;380:1829-39. 3. Havrdova E, et al. *Neurology* 2017;89:1107-16. 4. Coles AJ, et al. *Neurology* 2017;89:1117-26. 5. Montalban X, et al. *Mult Scler* 2019;25:P974. 6. Comi G, et al. *Mult Scler* 2019;25:P645. 7. LEMTRADA (alemtuzumab) [Prescribing Information]. Genzyme Corporation, USA. 8. LEMTRADA [Summary of Product Characteristics] January 2020. Diegem, Belgium: Sanofi Belgium. 9. Hunt DJ, Traboulsee A. ACTRIMS 2020, Poster P116.

Methods and Objective

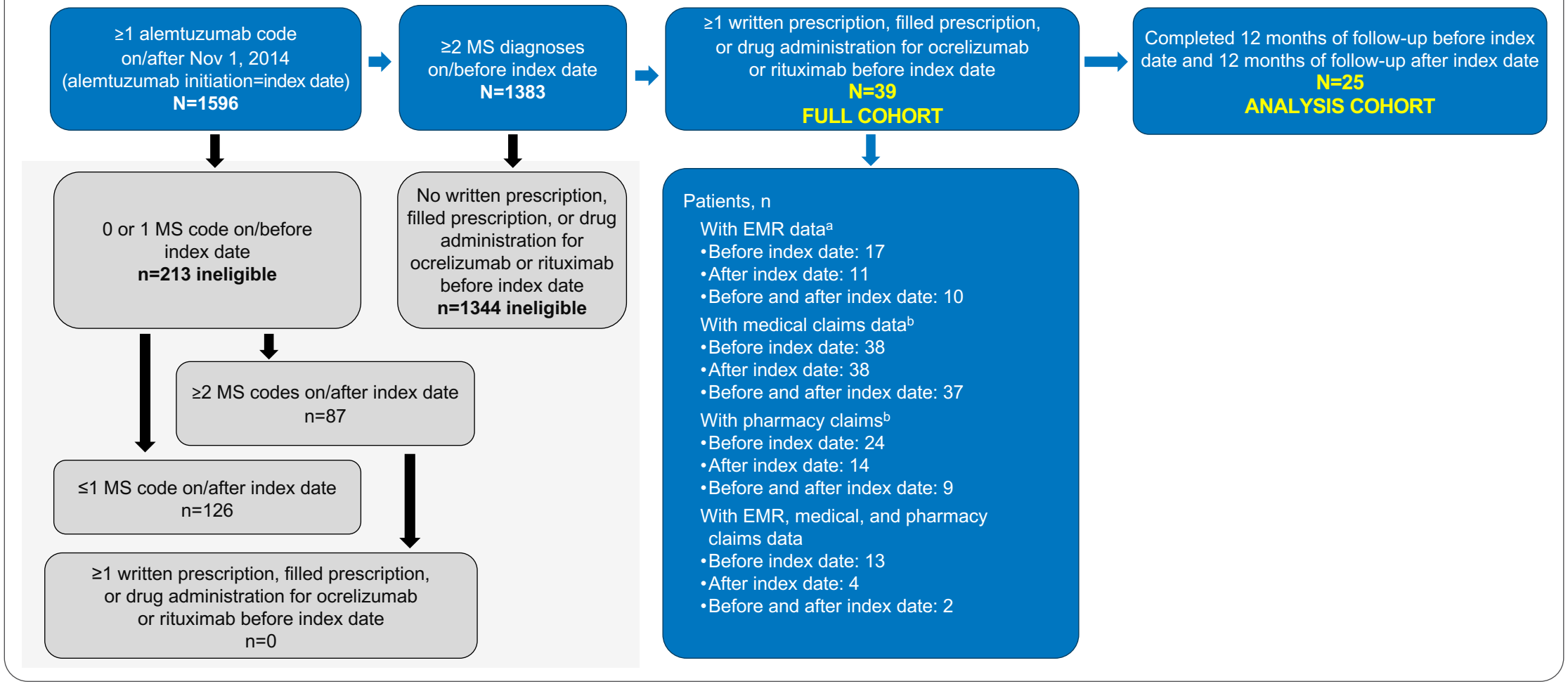
Objective:
To report demographics, treatment exposure, and outcomes in MS patients who transitioned from anti-CD20 therapies to alemtuzumab in real-world clinical settings

- **Study Design**
  - Retrospective, EMR and claims-based exploratory study of commercially insured and Medicaid/Medicare enrollees with an alemtuzumab prescription or claim who had prior treatment with an anti-CD20 therapy
- **Inclusion Criteria**
  - ≥2 ICD codes for MS (340 in ICD-9; G35 in ICD-10)
  - Treatment with ≥1 alemtuzumab course
  - Prior treatment with rituximab or ocrelizumab
- **Analysis**
  - Patients who received or were prescribed alemtuzumab from November 1, 2014, to September 30, 2019, were identified from the OM1® Real-World Data Cloud
  - The start of alemtuzumab treatment was considered the index date
  - Prespecified symptoms and comorbidities were analyzed in patients with a full 12 months of follow-up before the index date and 12 months after the index date

EMR=electronic medical record; ICD=International Classification of Diseases.

Patient Cohort Selection

Figure 1. Patient Cohort Selection



- After database screening, 39 (3%) alemtuzumab-treated MS patients met inclusion criteria, of which 25 (2%) had 12 months of follow-up before and after the index date (**Figure 1**)

[a]≥1 encounter; [b]≥1 claim

Cohort Characteristics, Anti-CD20 Therapies, and Follow-up Duration

- Mean age was 41.7 years, mean total follow-up was 64 months, and mean follow-up after index date was 18.5 months (**Table 1**)
- Prior to alemtuzumab, 28 patients were on rituximab, 10 were on ocrelizumab, and 1 was on both

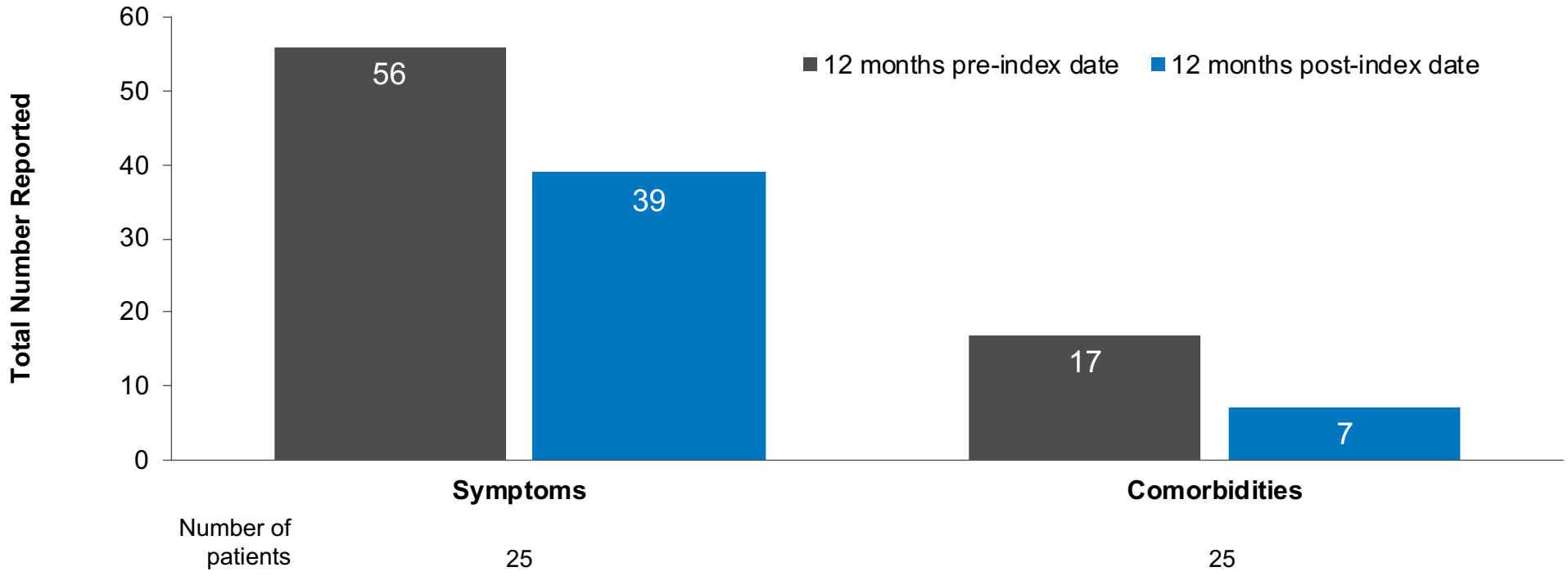
Table 1. Cohort Characteristics, Anti-CD20 Therapies, and Follow-up Duration

Parameter	Full Cohort (N=39)
Age, years	41.7 (11.1)
Age >40 years, n (%)	23 (59.0)
Female sex, n (%)	25 (64.1)
Total follow-up, months	64.0 (13.5)
Follow-up duration post-index, months	18.5 (14.6)
Prior anti-CD20 therapy, n (%)	
Rituximab	28 (71.8)
Ocrelizumab	10 (25.6)
Both	1 (2.6)
Rituximab exposure duration, months	13.2 (8.2)
Ocrelizumab exposure duration, months	8.7 (3.1)
Time between rituximab and alemtuzumab, months	12.7 (10.3)
Time between ocrelizumab and alemtuzumab, months	6.4 (1.6)

Values are mean (SD) unless indicated otherwise

Total Numbers of Reported Symptoms and Comorbidities in the Analysis Cohort

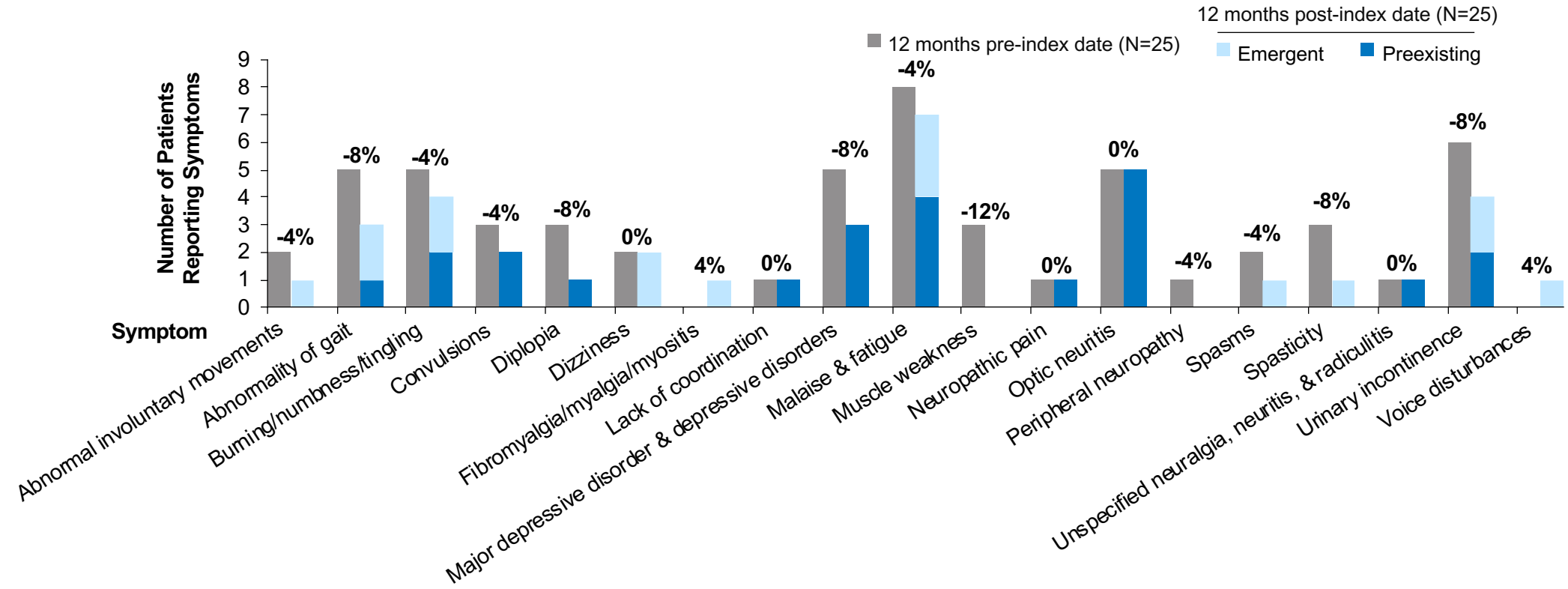
Figure 2. Total Numbers of Reported Symptoms and Comorbidities in the Analysis Cohort



- The total numbers of reported symptoms and comorbidities were lower post-index versus pre-index (**Figure 2**)

Patients Reporting Symptoms Pre- and Post-Index (Analysis Cohort)

Figure 3. Patients Reporting Symptoms Pre- and Post-Index (Analysis Cohort)

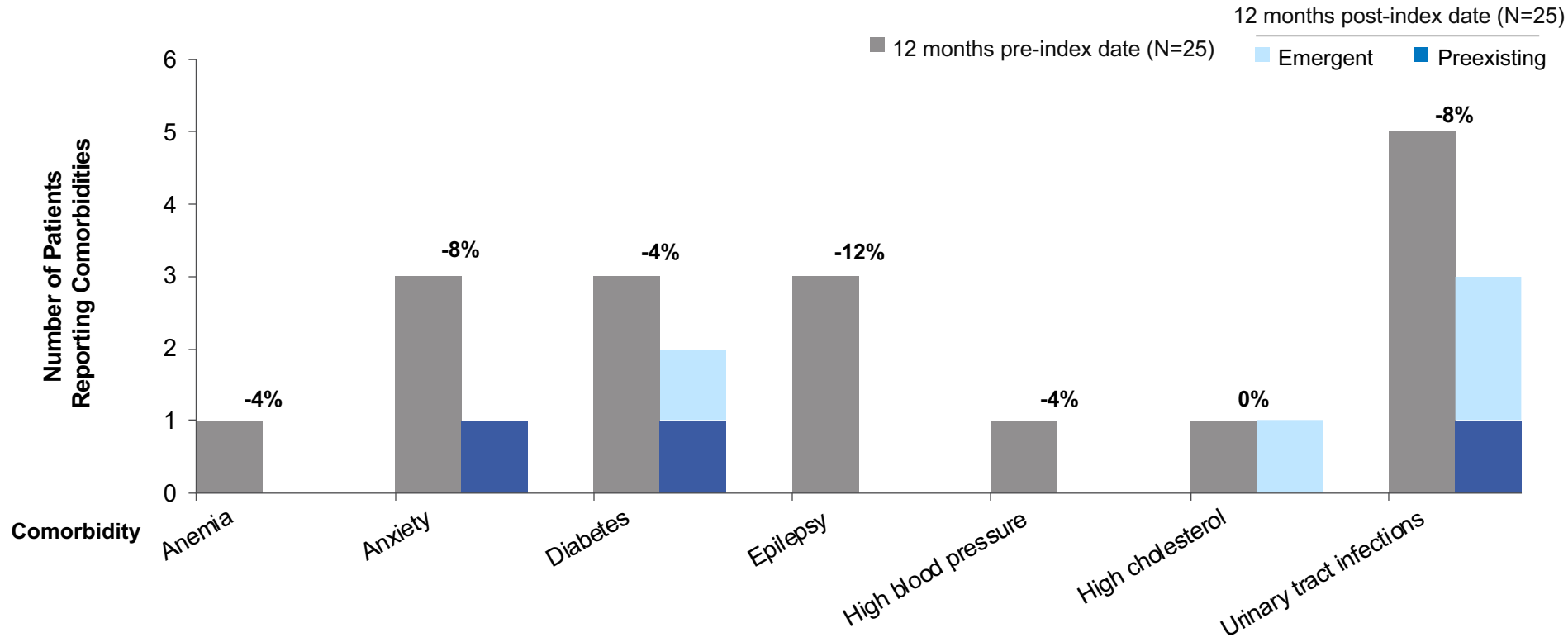


- The number of patients reporting symptoms was lower post-index versus pre-index for most symptom types (**Figure 3**)
  - The number of patients reporting fibromyalgia/myalgia/myositis and voice disturbances was higher post-index, and the number reporting dizziness, lack of coordination, neuropathic pain, optic neuritis, or unspecified neuralgia, neuritis, and radiculitis did not change post-index versus pre-index

Percentage values indicate change in the proportion of patients reporting symptoms pre- versus post-index date

Patients Reporting Comorbidities Pre- and Post-Index (Analysis Cohort)

Figure 4. Patients Reporting Comorbidities Pre- and Post-Index (Analysis Cohort)



- With the exception of high cholesterol, the number of patients reporting comorbidities was lower post-index versus pre-index (**Figure 4**)

Percentage values indicate change in the proportion of patients reporting comorbidities pre- versus post-index date

Conclusions

- In this exploratory study of a small real-world cohort of MS patients who transitioned from anti-CD20 therapies to alemtuzumab, the total numbers of reported prespecified symptoms and comorbidities were lower after initiating alemtuzumab
- Further characterization of outcomes will inform the benefit versus risk of transitioning to alemtuzumab after discontinuing anti-CD20 therapies