

Treatment Outcomes in People With Multiple Sclerosis Who Switched From Teriflunomide to Fumarates Versus Initiating Fumarates as a First-Line Therapy

OBJECTIVE

- To compare the annualized relapse rate (ARR) and healthcare resource utilization (HCRU) in people with multiple sclerosis (pwMS) who were initiated on teriflunomide (TERI) then switched to fumarates (FUM) versus those who initiated FUM first-line (FUM-1L).

CONCLUSIONS

- PwMS who initiated FUM-1L had significantly lower ARR and multiple sclerosis (MS)-related HCRU versus pwMS receiving second-line FUM after switching from TERI.
- Relapse rates declined by 29% in pwMS who switched to FUM after initial TERI treatment.
- In parallel, there was a reduction in MS-related HCRU and healthcare cost (HCC) in pwMS who switched to FUM after treatment with TERI.
- FUM-1L pwMS had consistently lower relapse rates throughout FUM treatment (compared with TERI to FUM switchers).
- The declining trend in HCRU of pwMS with early and sustained treatment with FUM suggests long-term benefits of FUM.
- Patients demonstrated improved outcomes after they switched from TERI to FUM, but optimal clinical and economic outcomes were achieved when FUM was initiated first-line.

Conway D,¹ Mahatoo A,² Shah S,^{3,4} Travis L,⁵ Akinsanya J,⁶ Szewczyk A,⁷ Lewin JB,⁷ Belviso N,⁷ Shankar SL⁷

¹Mellen Center for Multiple Sclerosis Treatment and Research, Cleveland Clinic, Cleveland, OH, USA; ²Trinity Health of New England, Hartford, CT, USA; ³Department of Neurology, Northwestern University, Chicago, IL, USA;

⁴Department of Neurology, Vanderbilt University Medical Center, Nashville, TN, USA; ⁵Banner-University Medical Center, Phoenix, AZ, USA; ⁶MedStar Southern Maryland Hospital Center, Clinton, MD, USA; ⁷Biogen, Cambridge, MA, USA

Introduction

- More than 25 disease-modifying therapies (DMTs) have been approved for the treatment of relapsing-remitting multiple sclerosis (RRMS).¹
- TERI (Aubagio® or generic),² dimethyl fumarate (Tecfidera® or generic),³ and diroximel fumarate (Vumerity®)⁴ are U.S. Food and Drug Administration-approved oral DMTs for treating RRMS in adults.
- DMT switches are common over the disease course of pwMS.^{5,6}
 - These therapy switches may be implemented due to lack of efficacy (including worsening of disease activity or a higher relapse rate), intolerance, patient preference, or cost.^{7,8}
- Optimization of long-term outcomes of MS requires early intervention using effective DMTs, increased DMT adherence, and reduced medication switching.^{9,10}
- We have previously shown that pwMS who switched from TERI to FUM showed a statistically significant reduction in MS-related HCRU and HCCs.
- However, there is limited understanding of real-world clinical outcomes among pwMS who start with TERI first-line then switch to FUM (TERI-FUM switchers) when compared with pwMS treated with FUM-1L.

Results

Baseline Characteristics and Follow-Up Periods

- Overall, this analysis included 8973 pwMS (FUM-1L cohort, n = 8801; TERI-FUM switchers cohort, n = 172) (Figure 2).
- After 1:2 PS matching: TERI-FUM, n = 172; FUM-1L, n = 344 (Table 1).
 - The demographic baseline characteristics were balanced for both treatment groups.
 - The mean (SD) age was 46.4 (9.7) years for FUM-1L and 46.1 (10.0) years for TERI-FUM switchers, where 78.8% (FUM-1L) and 79.1% (TERI-FUM switchers) of patients were female.

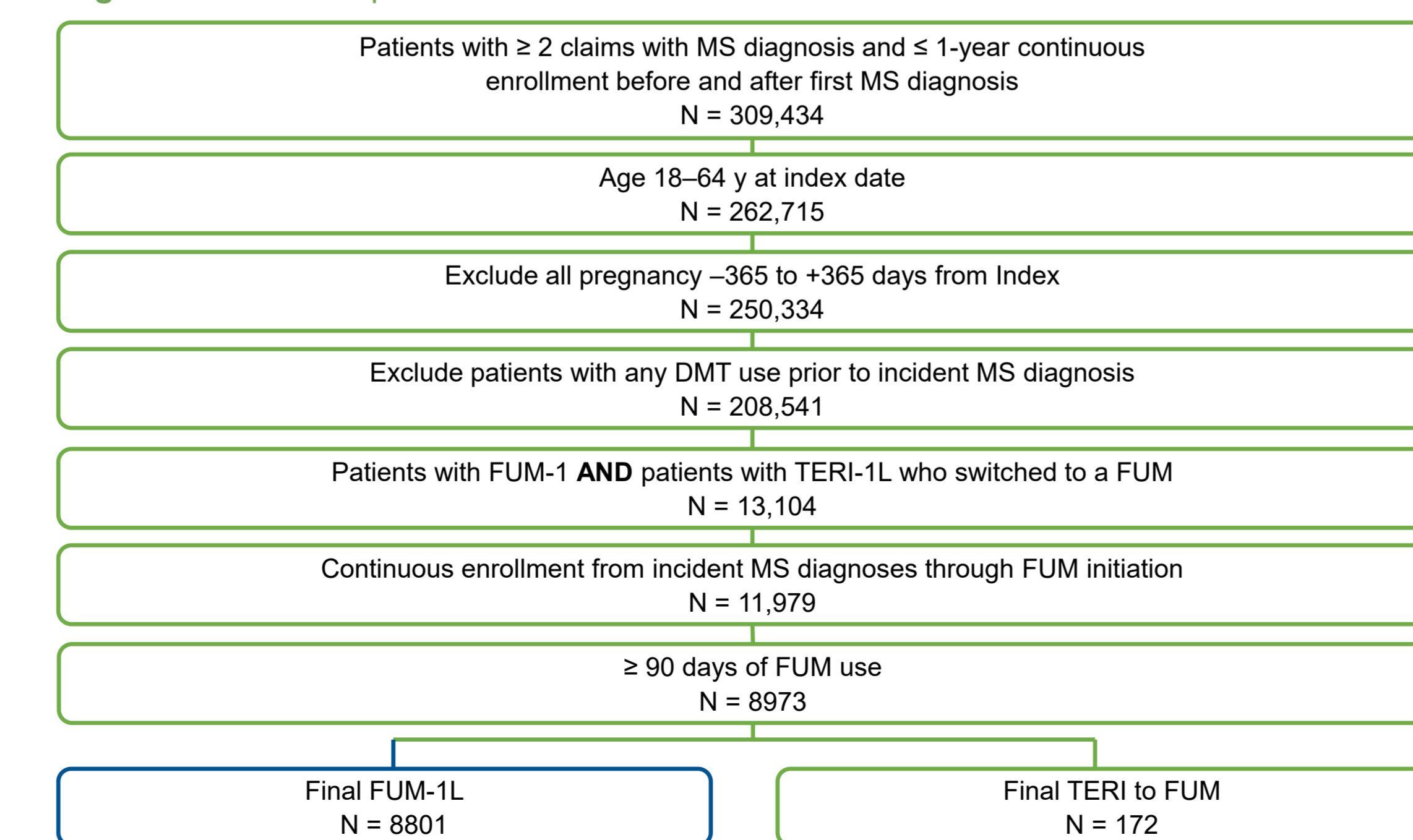
Relapse Outcomes

- The mean number of years on treatment for both FUM-1L cohort and TERI-FUM switchers cohort was 2.9 years.
- Patients switching from TERI to FUM experienced a 29% lower risk in ARR after initiation of FUM (rate ratio [95% CI]: 0.71 [0.54–0.94]; p = 0.02) (Figure 3).
- Among patients who initiated FUM-1L, there was no statistically significant difference in ARR from Follow-Up Period 1 versus Follow-Up Period 2 (p = 0.20). This indicates that FUM-1L patients had a consistent effect with FUM throughout the treatment.
- The mean (95% CI) ARR for FUM-1L was 0.18 (0.14–0.23), and 0.42 (0.33–0.53) for TERI-FUM switchers (Figure 4), where the rate ratio was 0.43 (0.30–0.61), representing a 57% lower ARR for the FUM-1L group (p < 0.0001).

MS-Related HCRU and HCC

- The mean (95% CI) overall MS-related HCRU and HCC were significantly lower in FUM-1L cohort versus the TERI-FUM switchers cohort.
 - The mean (95% CI) full follow-up MS-related HCRU for the FUM-1L cohort was 9.28 (7.48–11.53) compared with the TERI-FUM switchers cohort rate of 14.39 (11.80–17.55), representing a 35% lower ARR of HCRU for the FUM-1L group (p = 0.003) (Figure 5).
 - The mean (95% CI) overall MS-related HCC for the FUM-1L cohort was \$14,545 (\$11,997–\$17,635) compared with the TERI-FUM switchers cohort cost of \$29,949 (\$22,446–\$39,961), representing a 51% lower HCC for the FUM-1L group (p < 0.0001) (Figure 6).
- The HCRU and HCC of the TERI-FUM cohort were higher during Follow-Up Period 1 while pwMS were receiving TERI-1L and decreased during Follow-Up Period 2 after the switch to FUM.
- The mean MS-related HCRU and HCC of the FUM-1L cohort were lower during Follow-Up Period 2, after longer exposure to FUM.

Figure 2. Patient Disposition



DMT = disease-modifying therapy; FUM = fumarates; FUM-1L = FUM first-line; TERI = teriflunomide; TERI-1L = TERI first-line

Methods

Study Design

- The Komodo Health Claims database integrates disparate sources of patient-level information to map de-identified, patient-level claims data from multiple payer sources in the US.
- This retrospective analysis of the Komodo Health claims database included patients newly diagnosed with MS who initiated either TERI or FUM as first-line therapy for ≥ 90-days between 01 January 2017 and 31 July 2023.
 - The full follow-up period was composed of Period 1 and Period 2 (Figure 1).
- TERI-FUM switchers were propensity-score (PS) matched 1:2 with FUM-1L patients.
- For each TERI-FUM switcher, a cohort of FUM-1L patients was evaluated as potential matches by having at least as many days between (1) initial MS diagnosis and DMT initiation, and (2) initiation of first-line DMT and end of follow-up in the study.
- TERI-FUM switchers were then matched without replacement to the FUM-1L controls on baseline demographics and comorbidities measured during the 12-months prior to first-line DMT initiation.
- ARRs and HCRU in both treatment cohorts were computed using generalized linear models, adjusting for matched-pair correlation.

Table 1. Patient Demographics and Characteristics

Demographics and Characteristics	Unadjusted Population		PS-Matched Population	
	FUM-1L n = 8801	TERI-FUM n = 172	FUM-1L n = 344	TERI-FUM n = 172
Age, y, mean (SD)	44.3 (10.9)	46.1 (10.0)	46.4 (9.7)	46.1 (10.0)
Female, n (%)	6348 (72.1)	136 (79.1)	271 (78.8)	136 (79.1)
Race/ethnicity ^a , n (%)				
White	4479 (65.2)	96 (64.9)	206 (67.8)	96 (64.9)
Black	1233 (17.9)	22 (14.9)	45 (14.8)	22 (14.9)
Other	1165 (16.9)	30 (20.2)	53 (17.4)	30 (20.2)
State with high level of poverty, n (%)	2304 (26.2)	49 (28.5)	87 (25.3)	49 (28.5)
Time since MS diagnosis to first DMT, y, mean (SD)	0.38 (0.74)	0.40 (0.65)	0.88 (1.01)	0.40 (0.65)
MS severity score, mean (SD)	3.47 (3.38)	4.22 (3.87)	4.71 (4.05)	4.22 (3.87)
Charlson comorbidity index, mean (SD)	0.54 (1.21)	0.92 (1.56)	0.92 (1.64)	0.92 (1.56)
Insurance type, n (%)				
Commercial	5896 (67.0)	104 (60.5)	204 (59.3)	104 (60.5)
Medicaid	1946 (22.1)	47 (27.3)	82 (23.8)	47 (27.3)
Medicare	482 (5.5)	10 (5.8)	23 (6.7)	10 (5.8)
Combination insurance ^b /unknown	477 (5.4)	11 (6.4)	35 (10.2)	11 (6.4)
ARR 1 y prior to first DMT date, regardless of MS diagnosis date, mean (SD)	0.25 (0.50)	0.39 (0.77)	0.44 (0.67)	0.39 (0.77)
All-cause HCRU in prior 1 y, mean (SD)	10,969 (19,830)	15,950 (23,968)	15,899 (20,404)	15,950 (23,968)
All-cause HCC in prior 1 y, \$, mean (SD)	16.18 (23.32)	25.34 (37.78)	26.56 (38.71)	25.34 (37.78)

ARR = annualized relapse rate; DMT = disease-modifying therapy; FUM-1L = fumarate first-line; MS = multiple sclerosis; PS = propensity score; TERI-FUM = teriflunomide to fumarate switcher.
^aUnknown race for 1924 FUM-1L and 24 TERI-FUM in the unadjusted population; and 40 FUM-1L and 24 TERI-FUM in the PS-matched population.
^bUnknown race for 1924 FUM-1L and 24 TERI-FUM in the unadjusted population; and 40 FUM-1L and 24 TERI-FUM in the PS-matched population.
^cMedicaid, Medicare, Commercial, Medicaid, Medicare, Commercial, Medicare, Supplemental, or Medicare, Supplemental.

Figure 3. ARR on Prior TERI vs. ARR After Switching to FUM

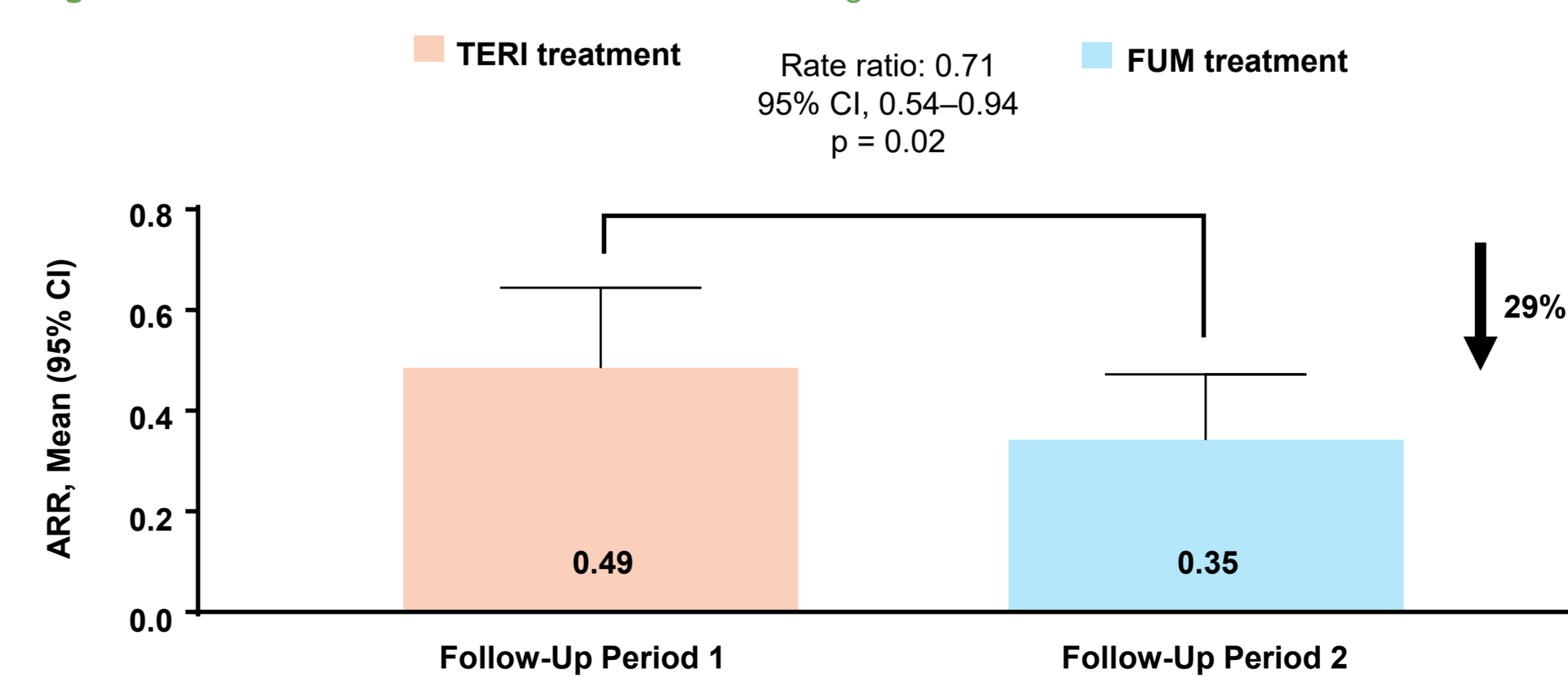


Figure 1. Study Design

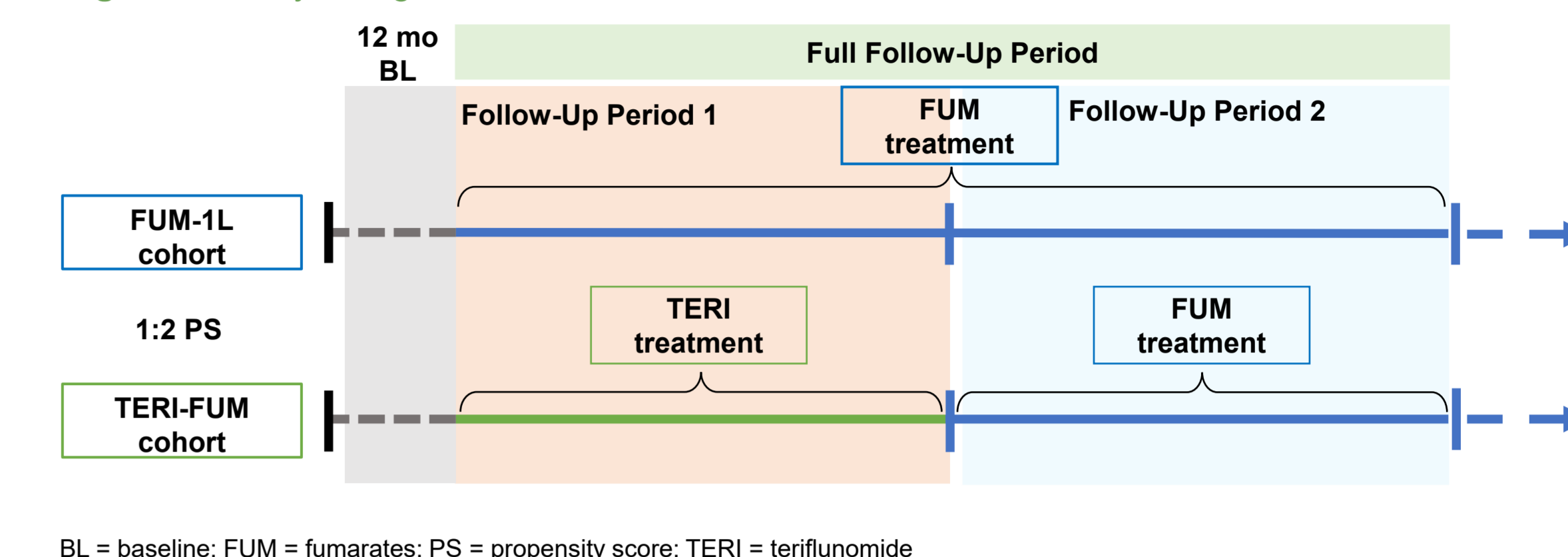


Figure 4. ARR in the FUM-1L Cohort and TERI to FUM Switch Cohort

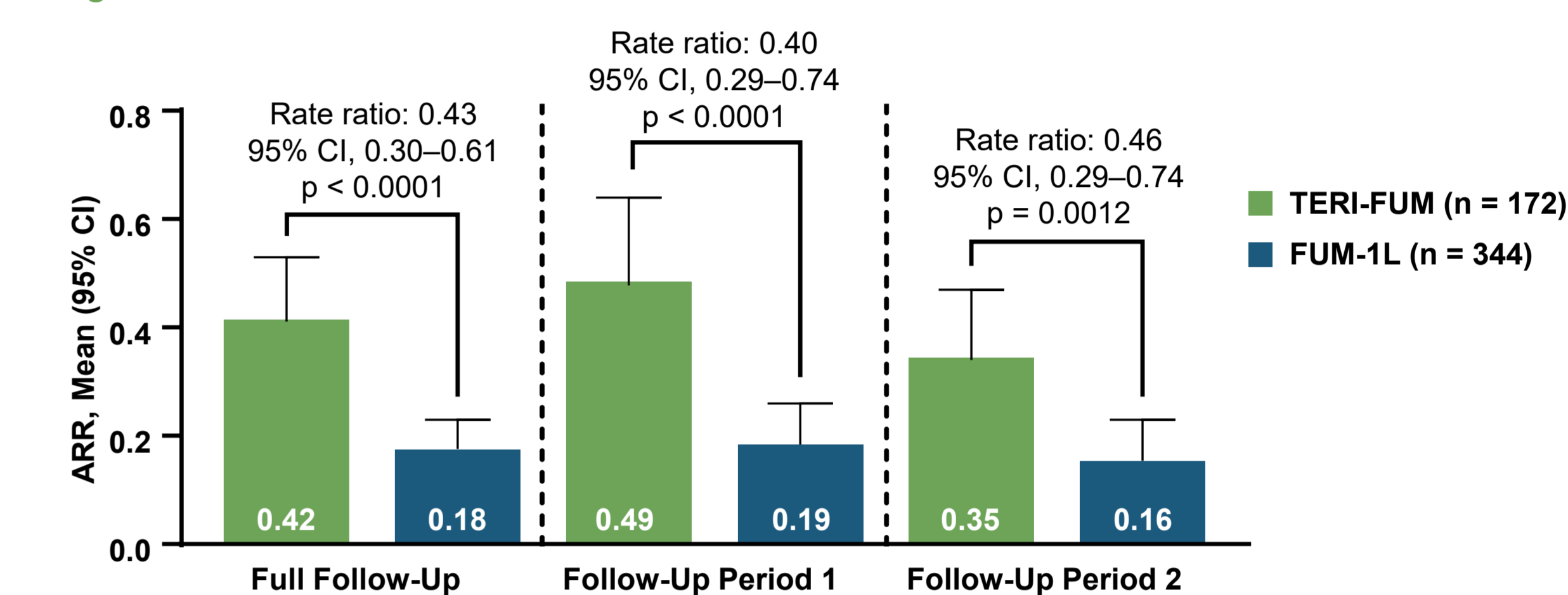


Figure 5. MS-Related HCRU

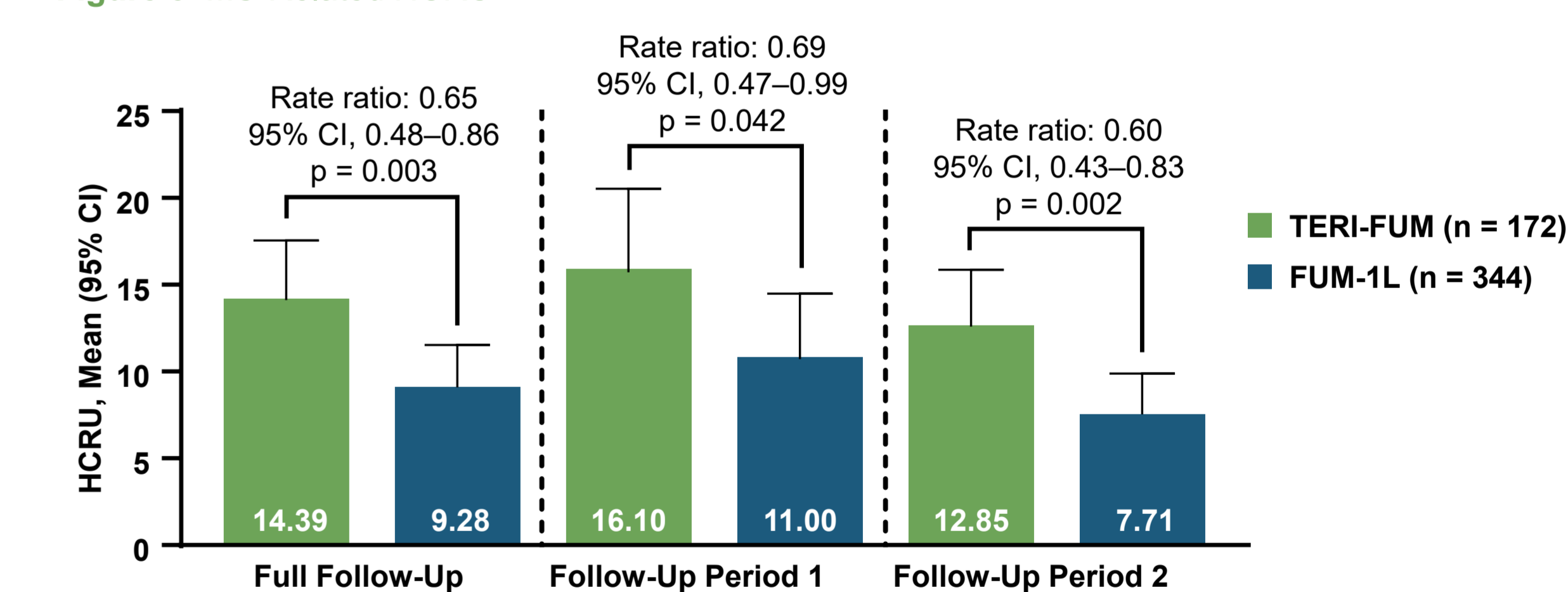


Figure 6. MS-Related HCC

