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Guillain–Barré Syndrome and Related Neurologic Outcomes Following Abrysvo versus Arexvy in Older Adults: A Propensity Score–Matched Real-World Cohort Study

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Research Article

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Abstract

Background

Post-licensure surveillance has raised concerns regarding Guillain–Barré syndrome (GBS) following respiratory syncytial virus (RSV) vaccination, but product-specific findings for Abrysvo and Arexvy have been inconsistent. We aimed to directly compare GBS and related neurologic outcomes between older adults receiving Abrysvo and those receiving Arexvy in a large real-world population.

Methods

We conducted a retrospective, active-comparator cohort study using the TriNetX Global Collaborative Network. Adults aged ≥ 60 years vaccinated with Abrysvo or Arexvy during 2023–2025 were propensity score–matched 1:1. The prespecified GBS risk window was days 1–42; because events were too rare for comparative estimation, exploratory analyses extended follow-up to 1 year. Secondary outcomes included inflammatory polyneuropathy, plasmapheresis, intravenous immunoglobulin use, and electrodiagnostic testing.

Results

After matching, each group included 132,892 recipients. At 1 year, GBS occurred in 26 Abrysvo and 19 Arexvy recipients (RR, 1.369; 95% CI, 0.757–2.473). Inflammatory polyneuropathy was more frequent after Abrysvo (RR, 1.500; 95% CI, 1.015–2.217), although this association was not statistically significant in sensitivity analysis. Other outcomes showed no consistent differences.

Conclusion

GBS risk did not differ significantly between Abrysvo and Arexvy recipients. Rare events and limited precision preclude conclusions of equivalent neurologic safety, supporting continued surveillance in larger populations.

Background

Respiratory syncytial virus (RSV) is an important cause of acute respiratory illness, hospitalization, and death, with the greatest burden occurring among older adults and individuals with underlying cardiopulmonary or other chronic medical conditions [1–3]. The introduction of RSV vaccines for older adults in 2023 represented an important advance in the prevention of RSV-associated lower respiratory tract disease. Two protein-based RSV vaccines, Abrysvo (RSVpreF; Pfizer) and Arexvy (RSVPreF3-AS01; GSK), were initially licensed for adults aged 60 years and older [4, 5]. In a national retrospective study of adults aged over 65 years old, the estimated vaccine effectiveness was 81.8% (95% CI, 80.0%-83.4%)

against RSV-related hospitalization, and 85.0% (95% CI, 75.1%-90.9%) against RSV-related death [6]. Other real-world studies have similarly demonstrated substantial protection against RSV-associated hospitalization among adults aged ≥ 60 years [7]. Although both vaccines target the prefusion F protein of RSV, they differ in their vaccine composition and immune-stimulatory formulation: Abrysvo is a bivalent, nonadjuvanted RSV prefusion F vaccine, whereas Arexvy contains RSVPreF3 antigen formulated with the AS01E adjuvant system [8, 9]. These differences provide a rationale for comparing their postmarketing safety profiles in real-world populations.

Guillain-Barré syndrome (GBS) is a rare but potentially severe immune-mediated peripheral neuropathy characterized by rapidly progressive weakness and, in severe cases, respiratory failure and autonomic dysfunction [10]. GBS is most commonly preceded by infection. *Campylobacter jejuni* is the best-established antecedent, although influenza virus, cytomegalovirus, varicella-zoster virus, SARS-CoV-2 and RSV have also been implicated [3, 11, 12]. Molecular mimicry is considered a key pathogenic mechanism, whereby microbial antigens induce cross-reactive antibodies or T-cell responses against peripheral nerve components, including gangliosides such as GM1 and GD1a [10]. Similar immune mechanisms have been proposed for vaccine-associated GBS, although direct mechanistic evidence remains limited. Because both infection and vaccination can precede GBS, distinguishing vaccine-related events from background or infection-associated disease is particularly challenging in older adults.

Post-licensure surveillance of the RSV vaccine has raised concerns regarding a potential safety signal for GBS. Early U.S. surveillance using the Vaccine Adverse Event Reporting System (VAERS) found GBS reporting rates of approximately 4.4 reports per million administered doses of Abrysvo and 1.8 per million doses of Arexvy, both higher than expected background reporting rates. However, VAERS is a passive surveillance system subject to underreporting, stimulated reporting, incomplete information, and differences in reporting behavior, and therefore cannot establish causal associations or directly quantify comparative risk between products [5]. Subsequent population-based studies have provided additional but not entirely consistent findings. In a self-controlled case series analysis of Medicare beneficiaries aged ≥ 65 years, GBS incidence during days 1–42 after vaccination was significantly increased following Arexvy (IRR, 2.46; 95% CI, 1.19–5.08), whereas the corresponding estimate following Abrysvo was elevated but did not reach statistical significance (IRR, 2.02; 95% CI, 0.93–4.40). Nevertheless, the estimated attributable risk was numerically higher for Abrysvo than for Arexvy, at approximately 9.0 versus 6.5 excess cases per million doses [13]. In contrast, an electronic health record–based study using the Epic Cosmos database found a statistically significant increase in GBS during the 1–42-day risk period following Abrysvo but not Arexvy, with estimated excess risks of 18.2 and 5.2 cases per million recipients, respectively [4]. The inconsistent findings across previous studies highlight the need for a direct head-to-head comparison of the two vaccines to help determine whether the observed GBS signal represents a broadly shared safety concern associated with protein-based RSV vaccination or whether clinically meaningful differences exist between vaccine products.

GBS encompasses several electrophysiologic subtypes, including acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy, and acute motor and sensory axonal neuropathy.

AIDP represents the predominant electrophysiologic subtype in North America and Europe [10]. However, administrative and electronic health record data may incompletely distinguish GBS from specific electrophysiologic subtypes, and diagnostic misclassification is an important consideration when evaluating such a rare outcome. Therefore, complementary outcome definitions, including inflammatory polyneuropathy, hospitalization, electrodiagnostic evaluation, and disease-specific treatment, may provide a more robust assessment of the potential neurologic safety signal.

Despite increasing post-licensure evidence regarding GBS following RSV vaccination, an important knowledge gap remains. Most existing safety assessments have evaluated RSV vaccination against background or self-controlled comparison periods, whereas direct comparative evidence between Abrysvo and Arexvy in a real-world population remains limited. Accordingly, we conducted a retrospective, propensity score–matched, active-comparator cohort study using real-world healthcare data to compare the risk of GBS and broader inflammatory polyneuropathy-related neurologic outcomes among adults aged 60 years and older receiving Abrysvo versus Arexvy. Extensive baseline covariates, including demographic characteristics, comorbidities, infectious antecedents, prior vaccinations, medications, and laboratory parameters, were incorporated into propensity score matching. Our study was designed to provide direct real-world comparative evidence regarding whether clinically meaningful differences in neurologic outcomes exist between the two widely used protein-based RSV vaccines.

MATERIALS and METHODS

Data source and study population

We conducted a retrospective, propensity score–matched, active-comparator cohort study using the TriNetX Global Collaborative Network, a federated research platform containing de-identified electronic health record data from 181 healthcare organizations. The study was designed to compare neurologic safety outcomes following administration of the two protein-based RSV vaccines, Abrysvo (RSVpreF; Pfizer) and Arexvy (RSVPreF3-AS01; GSK). This retrospective study was approved by the Institutional Review Board of Taichung Veterans General Hospital (approval number CE24589B-1). All procedures were performed in accordance with the ethical standards of the Helsinki Declaration. The requirement for informed consent was waived because only de-identified data were analyzed.

Adults aged ≥ 60 years who received either Abrysvo or Arexvy between January 1, 2023 and December 1, 2025 were eligible for inclusion. Receipt of Abrysvo and Arexvy was identified using vaccine-specific CPT and RxNorm records as specified in Fig. 1. The date of RSV vaccination was defined as the index date.

In both cohorts, patients were excluded if the EHR contained a record of the prespecified alternative RSV vaccine codes, including the mRNA RSV vaccine code used in the TriNetX query, or inflammatory polyneuropathy during the preceding 12 months. After application of these eligibility criteria, 152,335 Abrysvo recipients and 160,497 Arexvy recipients were available before propensity score matching. (Fig. 1, Fig. 2A-2B)

Baseline characteristics were determined from information recorded during the 12 months before the index date, using the most recent available measurement when multiple values were present.

Covariates and Propensity Score Matching

To minimize confounding, we performed 1:1 propensity score matching (PSM) to balance baseline characteristics assessed in the 12 months preceding the index date. Covariates included demographics (age, sex, race), comorbidities (e.g., hypertension, diabetes mellitus (DM), chronic kidney disease [CKD], cardiovascular disease, neurological disease), medication use and prior vaccinations (e.g., covid-19 vaccine, varicella zoster virus vaccine, tetanus vaccine, immunosuppressants) during the 1-year preceding RSV vaccination, and laboratory values (e.g., blood pressure, estimated glomerular filtration rate [eGFR]). Specific diagnosis, procedure, and medication codes are listed in the Supplement.

Outcomes

The primary outcome was incident GBS following RSV vaccination. Participants were followed from day 1 after vaccination until the first occurrence of the outcome, death, loss of observable records, 365 days after vaccination, or the database cutoff date, whichever occurred first. After propensity score matching, the mean follow-up duration was 351 days in the Abrysvo cohort and 355 days in the Arexvy cohort. GBS was assessed during the early 1–42-day postvaccination risk window. Because GBS events were extremely uncommon during this early period, an additional exploratory analysis examined outcomes at the first 3 months and up to 1 year after vaccination. Complementary outcomes included inflammatory polyneuropathy, electrodiagnostic evaluation, and disease-specific treatments, including plasmapheresis and intravenous immunoglobulin (IVIG). For each outcome analysis, patients with a documented history of the corresponding outcome before the analytic time window were excluded, consistent with the TriNetX outcome-analysis procedure. Because follow-up duration varied across participants, time-to-event analyses were additionally performed using the Kaplan–Meier method.

Subgroup Analyses

Exploratory subgroup analyses were performed for 1-year outcomes according to sex and age. Sex-stratified analyses were conducted separately for men and women, and age-stratified analyses compared adults aged 60–75 years with those aged > 75 years. Risk estimates were generated separately within each subgroup using the same outcome definitions as in the primary cohort analyses.

Sensitivity Analysis

A sensitivity analysis was performed to evaluate whether concomitant vaccination in the year preceding the index date influenced the observed associations. Patients with concomitant influenza, typhoid, or

hepatitis A vaccination were excluded, and clinical outcomes were re-evaluated in the restricted cohorts. The sensitivity analysis examined GBS-related outcomes, IVIG administration and nerve conduction/electromyographic testing.

Statistical Analysis

We performed 1:1 PSM using a greedy nearest-neighbor algorithm with a caliper of 0.1 pooled standard deviations. Covariate balance was assessed using standardized mean differences (SMD), with values < 0.1 indicating negligible imbalance. Between-group comparisons were expressed as risk ratios (RRs) with 95% confidence intervals (CIs), as generated by the TriNetX analytics platform. For 1-year time-to-event analyses, Kaplan–Meier methods were used to estimate event-free survival, and curves were compared using the log-rank test. Hazard ratios (HRs) with 95% CIs were obtained from the TriNetX time-to-event analysis.

RESULTS

Study Population and Baseline Characteristics

Among adults aged ≥ 60 years who met the eligibility criteria, 152,335 Abrysvo recipients and 160,497 Arexvy recipients were included before propensity score matching. Following 1:1 PSM, 132,892 patients remained in each cohort. All 47 baseline covariates, including demographics, comorbidities, medications, and laboratory values, were well-balanced between the cohorts, with standardized mean differences < 0.1 for all variables (Table 1).

Neurologic Outcomes During Early 3-Month Follow-up

No incident GBS event was captured within the prespecified 1–42-day post-vaccination window, precluding comparative risk estimation for the primary outcome during this interval.

We therefore examined outcomes over an extended 3-month follow-up period. The broader inflammatory polyneuropathy outcome occurred in 17 of 132,667 Abrysvo recipients (0.0128%) and 14 of 132,717 Arexvy recipients (0.0105%), with no significant between-group difference (RR, 1.215; 95% CI, 0.599–2.464; P = 0.589). IVIG use was similarly uncommon and did not differ significantly between the two groups (31/132,515 [0.0234%] vs 30/132,611 [0.0226%]; RR, 1.034; 95% CI, 0.626–1.708; P = 0.896). Comparative estimates for GBS and plasmapheresis were not available in the 3-month analysis. In contrast, nerve conduction/electrodiagnostic testing was more frequent in the Abrysvo cohort (328/123,627 [0.265%] vs 279/124,198 [0.225%]; RR, 1.181; 95% CI, 1.007–1.385; P = 0.041). (Table 2)

Table 1

Baseline characteristics before and after propensity score matching Values are presented as mean ± standard deviation or number (percentage), as appropriate. P values are shown for comparisons before propensity score matching, whereas standardized mean differences (SMDs) are shown after propensity score matching. An SMD < 0.1 was considered indicative of adequate covariate balance. **Total 47 covariates were listed in Supplementary Table 1**

Variable	Abrysvo Before PSM (N = 152,335)	Arexvy Before PSM (N = 160,497)	P value	Abrysvo After PSM (N = 132,892)	Arexvy After PSM (N = 132,892)	SMD
Demographics						
Age at index, years	72.8 ± 7.8	73.2 ± 7.6	< 0.001	73.0 ± 7.8	73.0 ± 7.6	0.006
White	128,499 (84.4%)	137,864 (85.9%)	< 0.001	113,620 (85.5%)	114,168 (85.9%)	0.012
Black or African American	13,885 (9.1%)	10,771 (6.7%)	< 0.001	10,117 (7.6%)	10,025 (7.5%)	0.003
Male	66,408 (43.6%)	68,120 (42.4%)	< 0.001	57,242 (43.1%)	56,908 (42.8%)	0.005
Asian	3,826 (2.5%)	5,131 (3.2%)	< 0.001	3,697 (2.8%)	3,589 (2.7%)	0.005
Diagnosis						
Hypertensive diseases	88,157 (57.9%)	98,179 (61.2%)	< 0.001	78,620 (59.2%)	78,262 (58.9%)	0.005
Diabetes mellitus	38,240 (25.1%)	39,727 (24.8%)	0.024	33,048 (24.9%)	32,517 (24.5%)	0.009
Ischemic heart diseases	28,942 (19.0%)	32,395 (20.2%)	< 0.001	25,860 (19.5%)	25,490 (19.2%)	0.007
Cerebrovascular diseases	11,333 (7.4%)	12,799 (8.0%)	< 0.001	10,205 (7.7%)	9,983 (7.5%)	0.006
Other chronic obstructive pulmonary disease	15,226 (10.0%)	16,814 (10.5%)	< 0.001	13,439 (10.1%)	13,215 (9.9%)	0.006
Chronic kidney disease (CKD)	23,150 (15.2%)	25,637 (16.0%)	< 0.001	20,432 (15.4%)	20,112 (15.1%)	0.007
Epilepsy and recurrent seizures	1,857 (1.2%)	1,940 (1.2%)	0.793	1,599 (1.2%)	1,567 (1.2%)	0.002
Polyneuropathies and other disorders of the peripheral nervous system	8,860 (5.8%)	9,243 (5.8%)	0.494	7,559 (5.7%)	7,425 (5.6%)	0.004

Variable	Abrysvo Before PSM (N = 152,335)	Arexvy Before PSM (N = 160,497)	P value	Abrysvo After PSM (N = 132,892)	Arexvy After PSM (N = 132,892)	SMD
Demographics						
COVID-19	9,757 (6.4%)	11,183 (7.0%)	< 0.001	8,765 (6.6%)	8,640 (6.5%)	0.004
Influenza and pneumonia	7,241 (4.8%)	7,773 (4.8%)	0.241	6,363 (4.8%)	6,132 (4.6%)	0.008
Campylobacter enteritis	36 (0.0%)	26 (0.0%)	0.140	23 (0.0%)	25 (0.0%)	0.001
Cytomegaloviral disease	220 (0.1%)	135 (0.1%)	< 0.001	127 (0.1%)	132 (0.1%)	0.001
Zoster [herpes zoster]	1,380 (0.9%)	1,591 (1.0%)	0.014	1,229 (0.9%)	1,176 (0.9%)	0.004
Encounter for immunization	50,617 (33.2%)	47,202 (29.4%)	< 0.001	41,244 (31.0%)	40,882 (30.8%)	0.006
Procedure						
Pneumococcal polysaccharide vaccine, 23-valent (PPSV23)	775 (0.5%)	1,011 (0.6%)	< 0.001	717 (0.5%)	709 (0.5%)	0.001
Pneumococcal conjugate vaccine, 13-valent (PCV13)	139 (0.1%)	165 (0.1%)	0.300	125 (0.1%)	122 (0.1%)	0.001
Chemotherapy	9,914 (6.5%)	8,818 (5.5%)	< 0.001	7,658 (5.8%)	7,576 (5.7%)	0.003
Medication						
COVID-19 vaccines	49,502 (32.5%)	37,158 (23.2%)	< 0.001	34,365 (25.9%)	35,164 (26.5%)	0.014
Varicella zoster virus glycoprotein E	15,258 (10.0%)	16,065 (10.0%)	0.951	13,210 (9.9%)	13,039 (9.8%)	0.004
Tetanus vaccines	8,694 (5.7%)	6,858 (4.3%)	< 0.001	6,129 (4.6%)	6,159 (4.6%)	0.001
Glucocorticoids	53,283 (35.0%)	56,711 (35.3%)	0.037	46,564 (35.0%)	45,978 (34.6%)	0.009
Immunosuppressants	5,795 (3.8%)	4,867 (3.0%)	< 0.001	4,391 (3.3%)	4,301 (3.2%)	0.004
Laboratory						

Variable	Abrysvo Before PSM (N = 152,335)	Arexvy Before PSM (N = 160,497)	P value	Abrysvo After PSM (N = 132,892)	Arexvy After PSM (N = 132,892)	SMD
Demographics						
Systolic blood pressure, mmHg	129.0 ± 16.8	128.8 ± 16.3	< 0.001	128.9 ± 16.8	128.7 ± 16.3	0.015
HbA1c, %	6.3 ± 1.1	6.2 ± 1.0	< 0.001	6.3 ± 1.1	6.2 ± 1.0	0.024
eGFR, mL/min/1.73 m²	73.0 ± 19.8	73.7 ± 19.0	< 0.001	73.1 ± 19.7	73.9 ± 19.0	0.039
LDL cholesterol, mg/dL	87.5 ± 34.0	88.2 ± 33.5	< 0.001	87.6 ± 34.0	88.3 ± 33.5	0.021
BMI, kg/m²	29.3 ± 6.6	29.0 ± 6.4	< 0.001	29.2 ± 6.5	29.1 ± 6.4	0.026

Table 2
3-month outcomes after RSV vaccination

Outcome	Pfizer/Abrysvo Patients	Events (%)	GSK/Arexvy Patients	Events (%)	Risk Ratio (95% CI)	P
Guillain–Barré syndrome	—	—	—	—	—	—
Inflammatory polyneuropathy	132,667	17 (0.0128%)	132,717	14 (0.0105%)	1.215 (0.599–2.464)	0.589
Plasmapheresis	—	—	—	—	—	—
IVIG	132,515	31 (0.0234%)	132,611	30 (0.0226%)	1.034 (0.626–1.708)	0.896
NEV/EMG	123,627	328 (0.265%)	124,198	279 (0.225%)	1.181 (1.007–1.385)	0.041

Neurologic Outcomes During 1-Year follow up

During the 1-year follow-up, clinically diagnosed GBS remained rare. After exclusion of patients with pre-existing GBS, 26 events occurred among 132,818 Abrysvo recipients and 19 among 132,828 Arexvy recipients. The difference was not statistically significant (RR, 1.369; 95% CI, 0.757–2.473). (Table 3) Kaplan–Meier analysis likewise showed no significant difference between groups (HR, 1.378; 95% CI, 0.763–2.489; log-rank P = 0.286). (Fig. 3A)

The broader inflammatory polyneuropathy phenotype occurred in 63 of 132,590 Abrysvo recipients and 42 of 132,614 Arexvy recipients, corresponding to a significantly higher risk in the Abrysvo group (RR, 1.500; 95% CI, 1.015–2.217; P = 0.040). **(**Table 3**)** Kaplan-Meier analysis yielded a similar result (HR, 1.515; 95% CI, 1.025–2.238; log-rank P = 0.036). **(**Fig. 3B**)** Nerve conduction/electrodiagnostic testing occurred more frequently in the Abrysvo cohort during 1-year follow-up. Among patients without prior testing, 1,272 of 123,549 Abrysvo recipients and 1,138 of 124,129 Arexvy recipients underwent nerve conduction evaluation (RR, 1.123; 95% CI, 1.037–1.216; P = 0.004). Kaplan–Meier analysis also showed significant difference between groups (HR, 1.136; 95% CI, 1.049–1.231; log-rank P = 0.002). **(**Table 3 **and** Fig. 3C**)**

Treatment-related outcomes remained comparable between cohorts. Specifically, plasmapheresis occurred in 17 Abrysvo recipients and 20 Arexvy recipients (relative risk [RR], 0.850; 95% confidence interval [CI], 0.445–1.623). Intravenous immunoglobulin (IVIG) administration was observed in 116 of 132,421 Abrysvo recipients and 96 of 132,527 Arexvy recipients (RR, 1.209; 95% CI, 0.923–1.585), with corresponding time-to-event comparisons yielding no statistically significant differences. **(**Table 3, Fig. 3D and 3E**)**

Table 3
One-year outcomes after RSV vaccination

Outcome	Pfizer (Abrysvo), n/N (%)	GSK (Arexvy), n/N (%)	Risk Ratio (95% CI)	P value
Guillain–Barré syndrome	26/132,818 (0.0196%)	19/132,828 (0.0143%)	1.369 (0.757–2.473)	0.297
Inflammatory polyneuropathy	63/132,590 (0.0475%)	42/132,614 (0.0317%)	**1.500 (1.015–2.217)**	**0.040**
Plasmapheresis	17/132,892 (0.0128%)	20/132,892 (0.0150%)	0.850 (0.445–1.623)	0.622
IVIG	116/132,421 (0.0876%)	96/132,527 (0.0724%)	1.209 (0.923–1.585)	0.168
NEV/EMG	1,272/123,549 (1.030%)	1,138/124,129 (0.917%)	**1.123 (1.037–1.216)**	**0.004**

Data are presented as number of patients and events (%).

Risk ratios were calculated from the TriNetX risk analysis. Hazard ratios were obtained from Kaplan–Meier survival analysis.

The outcome window was day 1 through day 365 after the index RSV vaccination. For outcomes with pre-index events, patients with the outcome before the time window were excluded from the corresponding analysis.

IVIG, intravenous immunoglobulin; NEV/EMG, nerve conduction/electromyography; CI, confidence interval.

Because the TriNetX report used slightly different analysis populations after exclusion of pre-existing outcomes, denominators vary by outcome.

Subgroup analyses conducted based on sex and age

Subgroup analyses for outcomes of follow-up up to 1 year were performed separately according to sex and age. In exploratory subgroup analyses, the frequency of nerve conduction/electrodiagnostic testing was significantly higher among male Abrysvo recipients than among male Arexvy recipients (RR, 1.174; 95% CI, 1.035–1.333). No statistically significant between-vaccine differences were observed among women or within the prespecified age strata. Risk estimates for GBS could not be reliably calculated because of the small number of events. No consistent between-vaccine differences were observed for inflammatory polyneuropathy, plasmapheresis, or IVIG use across the examined subgroups. Because formal interaction testing was not performed, these subgroup findings should be considered exploratory. **(**Fig. 4**)**

Sensitivity analysis

In the sensitivity analysis excluding patients with concomitant influenza, typhoid, or hepatitis A vaccination, inflammatory polyneuropathy remained numerically more frequent among Abrysvo recipients, although the association did not reach conventional statistical significance (43/84,910 [0.051%] vs 27/84,931 [0.032%]; RR, 1.593; 95% CI, 0.985–2.577; P = 0.056). IVIG use was significantly more frequent among Abrysvo recipients (62/84,853 [0.073%] vs 40/84,921 [0.047%]; RR, 1.551; 95% CI, 1.043–2.308; P = 0.029). In contrast to the primary analysis, the difference in nerve conduction/electrodiagnostic testing was absent in the restricted cohorts (700/79,898 [0.876%] vs 701/79,943 [0.877%]; RR, 0.999; 95% CI, 0.901–1.109; P = 0.987). **(**Table 4**)**

Table 4
Clinical outcomes after RSV vaccination among adults aged ≥ 60 years after exclusion of concomitant influenza, typhoid, and hepatitis A vaccination

Outcome	Pfizer/Abrysvo Patients	Events (%)	GSK/Arexvy Patients	Events (%)	Risk Ratio (95% CI)	P
Inflammatory polyneuropathy	84,910	43 (0.051%)	84,931	27 (0.032%)	**1.593 (0.985–2.577)**	0.0556
IVIG	84,853	62 (0.073%)	84,921	40 (0.047%)	**1.551 (1.043–2.308)**	0.0290
NEV/EMG	79,898	700 (0.876%)	79,943	701 (0.877%)	**0.999 (0.901–1.109)**	0.9870

DISCUSSION

In this large propensity score–matched active-comparator cohort study, we found no statistically significant difference in clinically diagnosed GBS between older adults receiving Abrysvo and those receiving Arexvy during follow-up of up to 1 year. Although clinically diagnosed GBS did not differ significantly between vaccine groups, the broader inflammatory polyneuropathy outcome was more frequent among Abrysvo recipients at 1 year. This finding should be interpreted cautiously because the association was not evident during the earlier 3-month window and did not meet conventional statistical significance in the sensitivity analysis after exclusion of selected concomitant vaccinations. Moreover, administrative coding for inflammatory polyneuropathy is less specific than a clinically adjudicated diagnosis of GBS. In the primary analysis, IVIG and plasmapheresis use did not differ significantly between vaccine groups. In contrast, IVIG use was significantly more frequent among Abrysvo recipients in the sensitivity analysis, despite the absence of a significant difference in clinically diagnosed GBS. Because this was a secondary exploratory comparison and was not supported by the primary IVIG analysis, the finding should be regarded as hypothesis-generating. Although electrodiagnostic testing was more frequently recorded among Abrysvo recipients in the main analysis, this association was not reproduced after exclusion of concomitant vaccinations in the sensitivity analysis. Importantly, only 26 GBS events occurred in the Abrysvo group and 19 in the Arexvy group. The resulting wide confidence interval indicates limited statistical precision; therefore, the absence of a statistically significant difference should not be interpreted as evidence of equivalent risk, and clinically meaningful between-product differences cannot be excluded.

Rare neurologic events observed during the pivotal clinical development programs contributed to the need for continued post-licensure surveillance of both vaccines [8, 9] Early VAERS surveillance reported a higher crude reporting rate of GBS after Abrysvo than after Arexvy, whereas subsequent population-based studies produced heterogeneous product-specific findings [5]. A self-controlled analysis among

Medicare beneficiaries aged ≥ 65 years identified a statistically significant increase during the 1–42-day risk window after Arexvy but not Abrysvo [13, 14], whereas an Epic Cosmos electronic health record analysis reported a significant signal after Abrysvo but not Arexvy [4]. In contrast, Vaccine Safety Datalink surveillance did not identify a statistically significant signal for either product [15]. Differences in study design, source populations, comparator periods, outcome ascertainment, risk-window specification, and analytic approaches may contribute to these apparently discrepant findings, as different observational vaccine-safety designs estimate related but not necessarily identical causal contrasts [16]. Importantly, most previous studies evaluated individual RSV vaccines relative to background or self-controlled periods, whereas our active-comparator design directly compared Abrysvo with Arexvy. Thus, our findings provide complementary evidence regarding comparative product safety but cannot determine whether either vaccine increases GBS risk relative to an unvaccinated background population. Recent systematic synthesis of real-world RSV vaccination studies similarly highlights the evolving nature of the safety evidence and the challenges associated with estimating very rare outcomes such as GBS [17]. Ongoing postauthorization studies using prespecified adverse events of special interest and large routinely collected healthcare datasets further illustrate that characterization of rare neurologic outcomes remains an active area of surveillance [18].

The higher frequency of electrodiagnostic testing observed after Abrysvo vaccination warrants cautious interpretation. Previous claims-based validation work has suggested that combining a GBS diagnosis code with nerve conduction testing and GBS-directed treatment can improve the positive predictive value of administrative case identification [19]. More broadly, contemporary approaches to electronic safety surveillance increasingly combine diagnosis codes with procedures, treatments, laboratory findings, or other clinical information to improve the specificity of computable adverse-event phenotypes [20]. However, electrodiagnostic testing is not specific to GBS and may be performed for a wide range of peripheral neurologic symptoms and disorders. Although both NEV/EMG utilization and inflammatory polyneuropathy diagnoses were more frequent among Abrysvo recipients during 1-year follow-up, these patterns were not consistently observed in the earlier analysis or in the sensitivity analysis. Accordingly, the findings may reflect differences in diagnostic intensity, referral patterns, healthcare utilization, residual confounding, or chance rather than a product-specific increase in GBS risk. Similarly, nominal differences observed in selected age- and sex-stratified analyses should be considered exploratory because formal interaction testing was not performed.

This study has several methodological strengths. First, the active-comparator design enabled a direct head-to-head comparison between Abrysvo and Arexvy and may reduce some confounding related to vaccine eligibility, healthcare-seeking behavior, and access to vaccination that can complicate comparisons with unvaccinated populations. Second, propensity score matching achieved good balance across a broad range of measured demographic, clinical, infectious, medication, and vaccination-related characteristics, including several recognized antecedents of GBS. Third, because clinically diagnosed GBS is rare and may be incompletely captured in electronic health records, we evaluated inflammatory polyneuropathy diagnoses, electrodiagnostic testing, and GBS-directed therapies as complementary outcomes rather than relying on a single diagnosis code. Finally, the large multi-institutional real-world

cohort provided substantially greater numbers than are typically available in pre-licensure trials for evaluating rare neurologic events. Nevertheless, only 45 GBS events occurred across the matched cohorts, underscoring the difficulty of obtaining precise comparative estimates even in very large observational databases. Accordingly, the principal contribution of this study is to provide a large active-comparator perspective that complements passive surveillance, self-controlled, and near-real-time safety studies rather than to establish equivalence between the two vaccines.

Several limitations should be considered. First, previous studies suggest that the risk of postvaccination GBS is greatest approximately 8–21 days after vaccination and approaches baseline after day 42 [21]. Although the 1–42-day period after vaccination is commonly used to assess vaccine-associated GBS, no evaluable GBS events were available for comparative estimation during this interval in our matched cohorts. We therefore evaluated outcomes over longer follow-up periods of 3 months and up to 1 year to increase event capture. These extended windows inevitably include events that are less temporally related to vaccination and therefore should not be interpreted as direct estimates of vaccine-attributable risk. Second, this active-comparator study did not include an unvaccinated reference group and therefore cannot determine whether either vaccine increases GBS risk above the background rate. Third, diagnoses, vaccination records, procedures, and treatments were derived from electronic health record coding rather than direct clinical adjudication. Misclassification, incomplete capture of care delivered outside participating healthcare systems, and differences in coding, referral, and testing practices across institutions may therefore have affected outcome ascertainment. Standardized clinical case definitions, such as the Brighton Collaboration criteria, incorporate clinical, cerebrospinal fluid, and electrophysiological findings and may improve diagnostic specificity in vaccine-safety studies [22]. Fourth, despite extensive propensity score matching, residual confounding may remain. Vaccine product selection may vary according to healthcare organization, geographic region, product availability, local prescribing practices, and unmeasured patient characteristics. Such factors may also influence the duration and intensity of follow-up. Fifth, statistical precision remained limited because GBS was extremely rare at the population level, with incidence varying according to age, comorbidity, and antecedent infection[23]. The comparison of 26 versus 19 events yielded an RR of 1.369 with a wide 95% CI of 0.757–2.473; thus, the study cannot exclude either a clinically meaningful decrease or increase in comparative risk. Finally, secondary, subgroup, and sensitivity analyses involved multiple comparisons and should be interpreted as exploratory. The absence of an electrodiagnostic association in the sensitivity analysis indicates that this finding was not robust across analytic specifications; however, this observation does not by itself establish concomitant vaccination as a confounder.

Although direct evidence that RSV vaccination reduces RSV-associated GBS is currently lacking, rare neurologic adverse events should be interpreted within a broader benefit–risk framework that considers both vaccine-associated risks and the clinically important outcomes prevented by vaccination. Such assessments are particularly relevant for rare adverse events that may not be adequately characterized in pre-licensure trials and therefore require continued evaluation using real-world and postmarketing data [24]. Evidence from other respiratory vaccines further provides context for weighing uncommon neurologic events against infection-related morbidity [25–27]. Accordingly, the present findings should

be interpreted within the broader benefit–risk framework of RSV vaccination and should not, in isolation, be used to alter current vaccination decisions or recommendations. Future studies should incorporate larger linked populations, prespecified interaction analyses, validated or chart-adjudicated GBS diagnoses, detailed neurologic symptoms, electrodiagnostic findings, cerebrospinal fluid data, and treatment information. Such studies may help distinguish true inflammatory neuropathy from differences in diagnostic surveillance or healthcare utilization.

CONCLUSION

In this large propensity score–matched active-comparator cohort of adults aged ≥ 60 years, clinically diagnosed GBS did not differ significantly between Abrysvo and Arexvy recipients. Inflammatory polyneuropathy was more frequent among Abrysvo recipients in the 1-year primary analysis, although this association did not reach conventional statistical significance in the sensitivity analysis. Electrodiagnostic testing was also more frequent among Abrysvo in the primary analysis but was not reproduced in the sensitivity analysis. Given the rarity of GBS, the wide confidence intervals, and the inability to estimate comparative risk during the prespecified 1–42-day window, these findings should not be interpreted as establishing equivalent safety between the two vaccines. Larger studies using validated neurologic outcomes are needed to clarify these product-specific safety signals.

Abbreviations

AIDP: acute inflammatory demyelinating polyneuropathy; CI: Confidence interval; CKD: chronic kidney disease; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; GBS: Guillain–Barré syndrome; HR: Hazard ratio; PSM: propensity score matching; RR: risk ratio; RSV: respiratory syncytial virus; SMD: standardized mean differences; VAERS: Vaccine Adverse Event Reporting System

Declarations

Ethics approval:

our study was approved by the Institutional Review Board of the Taichung Veterans General Hospital (approval number CE24589B-1).

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Data availability statement: The data that support the findings of this study are available from TriNetX, LLC, but restrictions apply to the availability of these data, which were used under license for the current study. Researchers may apply for access to the data by contacting TriNetX

Competing interests: The authors declare no competing interests.

Author Contribution

C.Y. Wang wrote the main manuscript text, and S.F. Tsai contributed to study concept and design, acquisition of data, analysis and interpretation of data, statistical analysis, obtained funding and study supervision. All authors reviewed the manuscript.

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None

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Figures

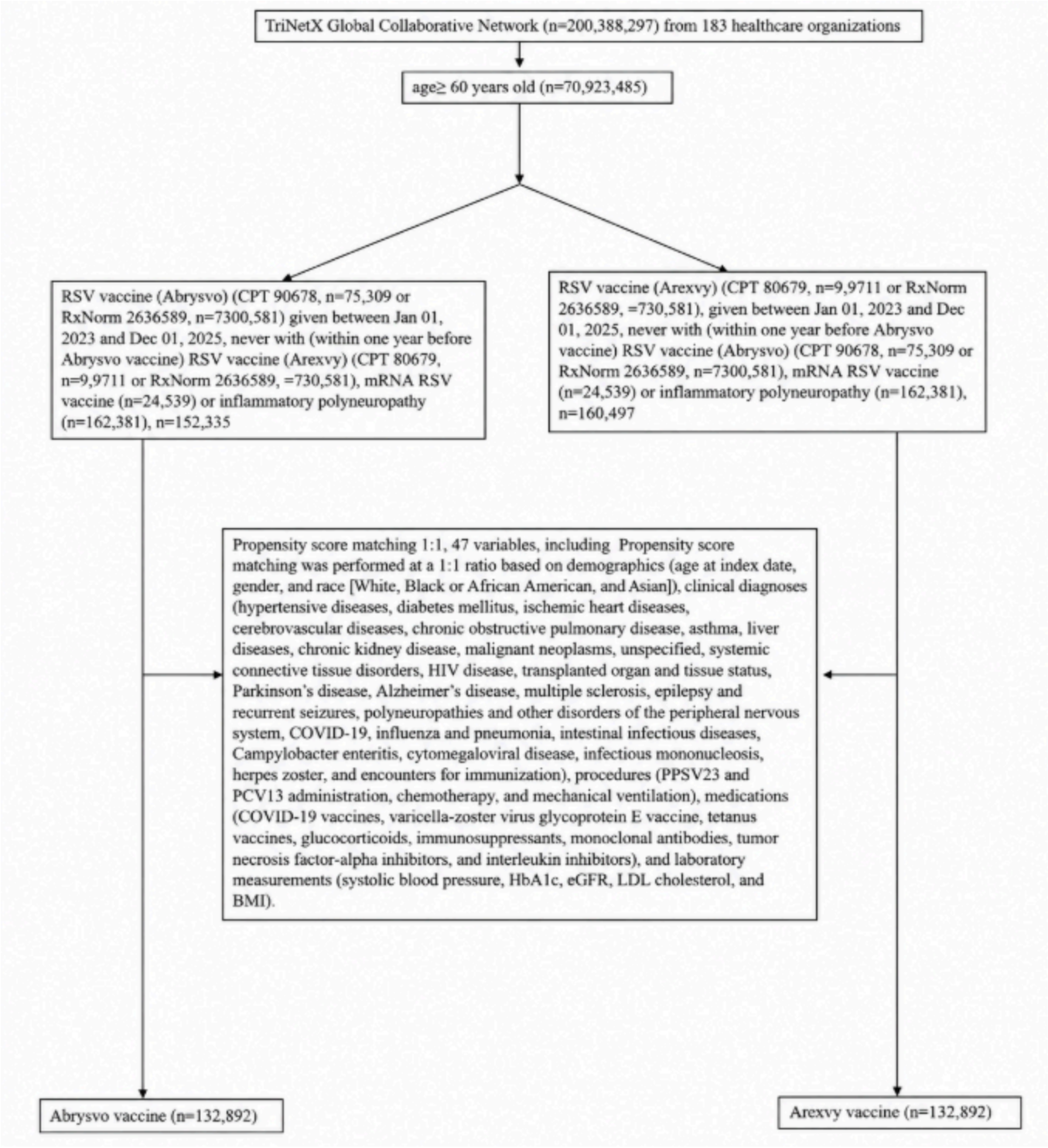

Figure 1

Patient selection algorithm

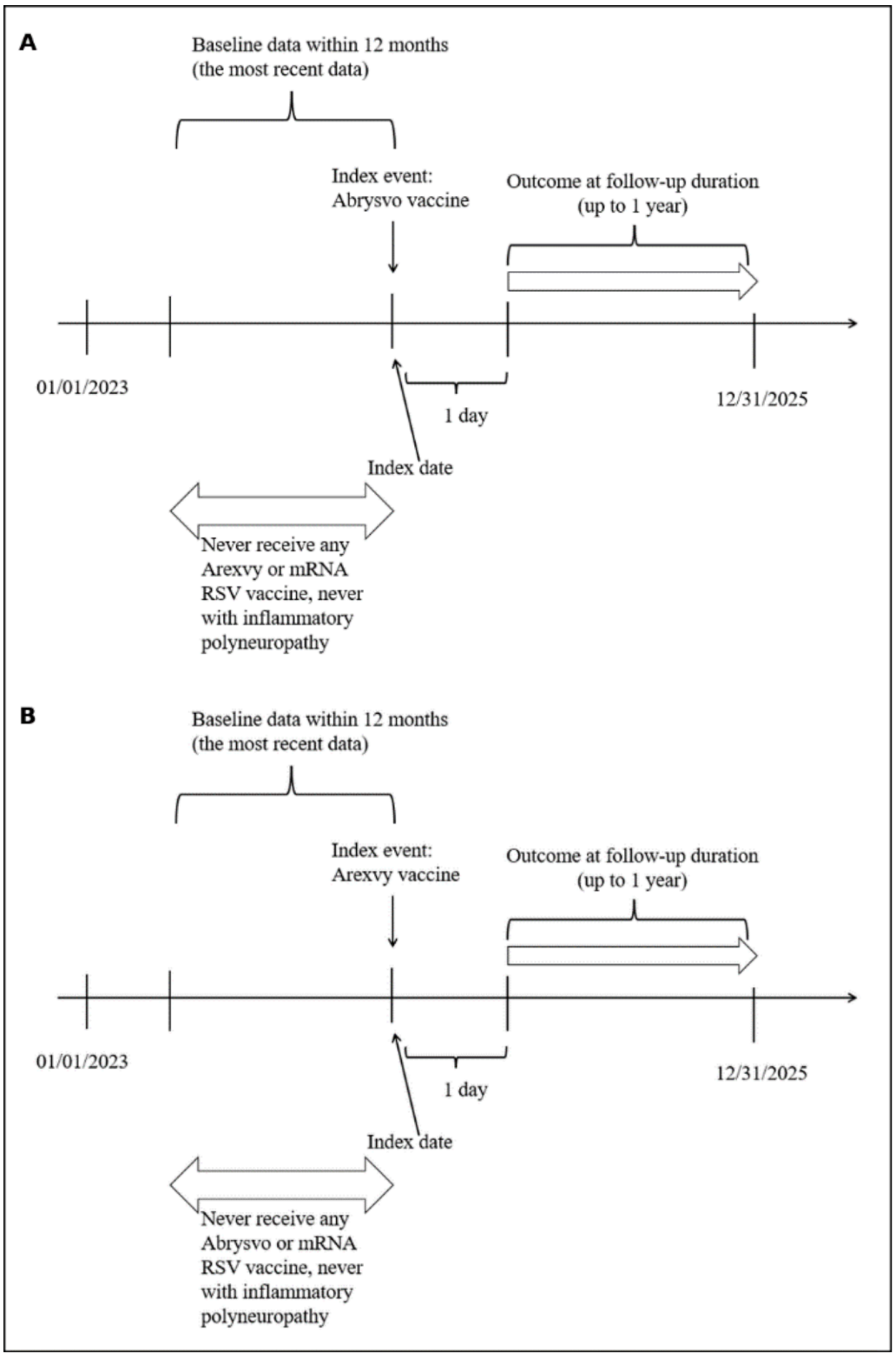

Figure 2

Definition of Abrysvo/Arexvy vaccine group

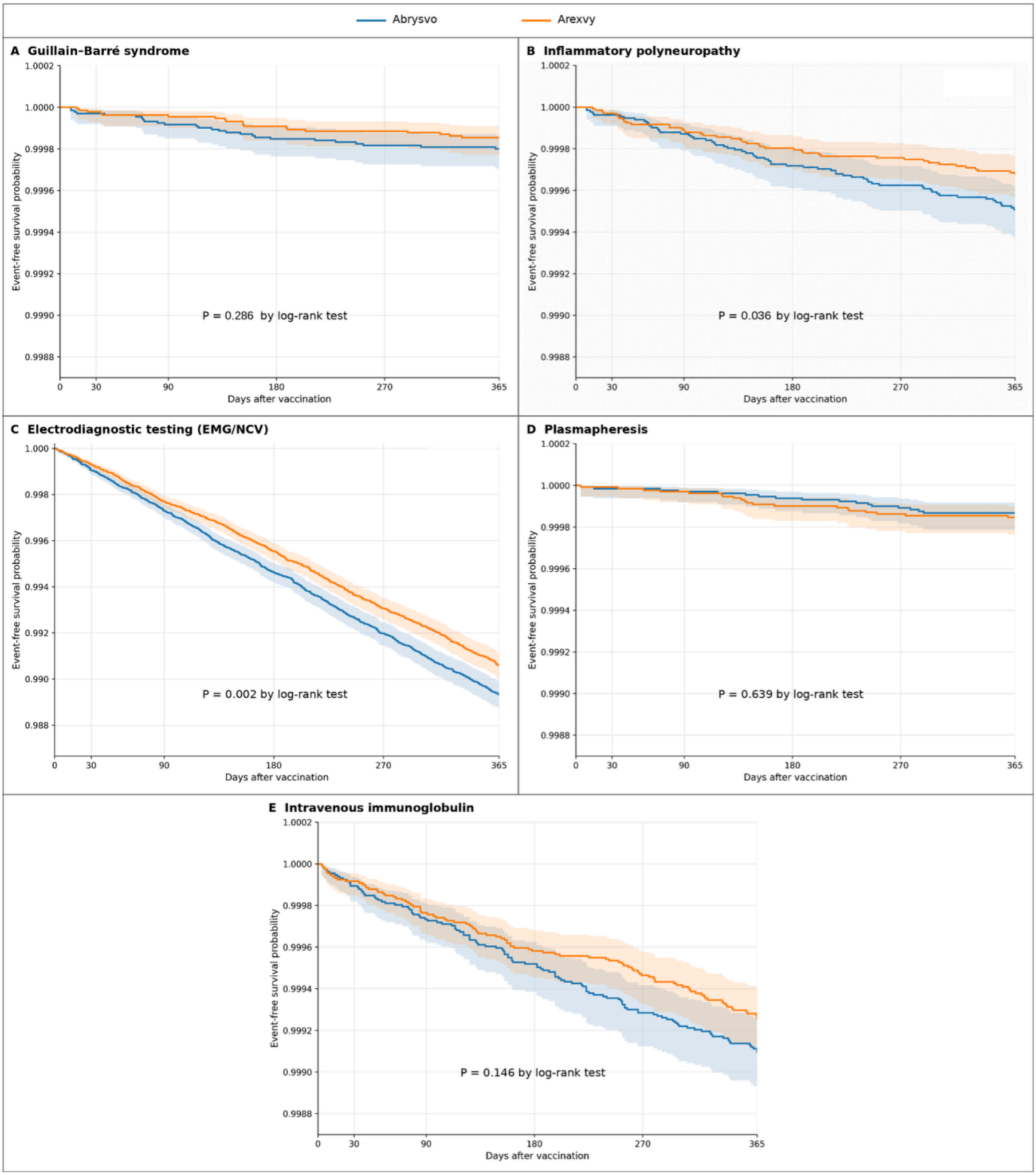

Figure 3

KM survival curve of outcomes

Outcome	Subgroup	Abrysvo (events / N, %)	Arexvy (events / N, %)	Risk Ratio (95% CI)	P value
Inflammatory polyneuropathy (G61.x)	Male	29 / 49,323 (0.059%)	19 / 49,356 (0.038%)	1.527 (0.857–2.723)	0.148
	Female	31 / 75,197 (0.041%)	29 / 75,227 (0.039%)	1.069 (0.645–1.774)	0.795
	Age 60–75	36 / 56,547 (0.064%)	22 / 56,578 (0.039%)	1.637 (0.963–2.782)	0.066
	Age ≥75	32 / 55,706 (0.057%)	23 / 55,747 (0.041%)	1.392 (0.815–2.379)	0.224
Plasmapheresis	Male	—	—	Not estimable	—
	Female	—	—	Not estimable	—
	Age 60–75	—	—	Not estimable	—
	Age ≥75	11 / 55,826 (0.020%)	14 / 55,826 (0.025%)	0.786 (0.357–1.731)	0.549
IVIG	Male	57 / 49,262 (0.116%)	41 / 49,314 (0.083%)	1.392 (0.932–2.079)	0.105
	Female	47 / 75,116 (0.063%)	53 / 75,152 (0.071%)	0.887 (0.599–1.314)	0.550
	Age 60–75	69 / 56,420 (0.122%)	63 / 56,501 (0.112%)	1.097 (0.780–1.543)	0.596
	Age ≥75	62 / 55,555 (0.112%)	64 / 55,653 (0.115%)	0.970 (0.685–1.376)	0.866
NEV/EMG	Male	515 / 46,265 (1.113%)	441 / 46,521 (0.948%)	1.174 (1.035–1.333)	**0.013**
	Female	673 / 69,950 (0.962%)	654 / 70,369 (0.929%)	1.035 (0.930–1.152)	0.527
	Age 60–75	574 / 52,678 (1.090%)	561 / 53,000 (1.058%)	1.029 (0.917–1.156)	0.623
	Age ≥75	553 / 51,892 (1.066%)	510 / 52,455 (0.972%)	1.096 (0.972–1.235)	0.133

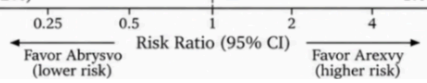

Figure 4

Subgroup analysis of one-year outcomes after RSV vaccination

Supplementary Files

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- supplementarytable.docx