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Personally identifiable information (PII) within this document is either removed or redacted (i.e., specific content is masked irreversibly from view with a black bar) to protect personal privacy. Personally identifiable information includes:

- All named persons associated with the study
- Patient identifiers within text, tables, or figures
- By-patient data listings

Anonymized patient data may be made available subject to an approved research proposal submitted. Information which is considered intellectual property or company confidential was also redacted.

1.0 ABSTRACT

Title

Evaluating the Safety of GAMMAGARD LIQUID for the Treatment of Patients With Chronic Inflammatory Demyelinating Polyradiculoneuropathy

Keywords

Drug-related side effects and adverse reactions; immunoglobulins, intravenous; pharmacoepidemiology; pharmacovigilance; polyradiculoneuropathy, chronic inflammatory demyelinating.

Rationale and Background

GAMMAGARD LIQUID (GGL) is an intravenous immunoglobulin (IGIV). Other IGIV products are indicated in the United States (US) for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). This study evaluated the safety of GGL when used in patients with CIDP compared with other comparator IGIV products that are indicated for the treatment of patients with CIDP in real-world healthcare delivery databases in the US.

Research Question and Objectives

The primary objectives of the study were to determine whether rates of adverse events of special interest (eg, composite measure of thrombotic events, acute kidney injury [AKI], hemolytic events) among patients initiating GGL differ from rates of adverse events of special interest among patients initiating comparator IGIV products in patients with CIDP who have not previously been treated with any immunoglobulin (Ig) product (Ig-naive cohort) and in patients with CIDP who have previously used another Ig product (Ig-experienced cohort)

Study Design

This study was a nonrandomized, active-comparator, new-user, retrospective cohort study of patients with CIDP initiating treatment with an IGIV product. The treatment group was patients initiating GGL, and the comparator group was a combined group of patients initiating an IGIV specifically indicated for the treatment of CIDP (GAMMAKED, GAMUNEX-C, PRIVIGEN). Analyses were performed separately in cohorts of Ig-naive and Ig-experienced participants and in a combined cohort where applicable.

Setting

This study was conducted in US–based administrative claims databases, including the Merative (formerly IBM) MarketScan Research Databases and the Optum Clinformatics Data Mart. The cohort entry period began on 1 January 2008 and ended on 31 December 2019.

Participants and Study Size, Including Dropouts

The source population for this study was adult patients (aged ≥18 years) in the US with CIDP who initiated 1 of the study IGIV products. Patients were identified at the first observed use of 1 of the study IGIV products during the cohort entry period. All patients who met the inclusion/exclusion criteria were included in the study and no prespecified sample size was calculated.

Participants initiating an IGIV product were categorized as either naive to Ig products (Ig-naive) or having prior experience with Ig products (Ig-experienced) based on Ig use before the index date. Patients were excluded if they had a diagnosis of another condition typically treated with IGIV. Participants were followed from the date of IGIV initiation until occurrence of an outcome or censoring at 31 December 2019, disenrollment from the data source, end of continuous use of the IGIV, or switching to/adding another Ig product.

[redacted], this study identified 1,021 participants in the Ig-naive cohort and 916 in the Ig-experienced cohort. [redacted], this study identified 2,452 participants in the Ig-naive cohort and 1,697 in the Ig-experienced cohort.

Variables and Data Sources

The administrative claims data sources contain insurance enrollment information and billing claims for healthcare services. IGIV use was identified in claims for in-office IGIV administration or pharmacy claims for IGIV dispensing. Safety outcomes during follow-up were identified with diagnosis and procedure codes. The outcome rates among participants receiving GGL were compared with rates among participants receiving comparator IGIV products within propensity score–weighted samples by estimating hazard ratios (HRs) and time period–specific risk ratios (RRs) and risk differences (RDs) with 95% confidence intervals (CIs). Sensitivity analyses and quantitative bias analyses evaluated the robustness of the study design.

Results

Identified cases of the primary and secondary study outcomes were rare for almost all outcomes among all cohorts. Results for the composite thrombotic events outcome were inconsistent across data sources and over time; [redacted], more cases of thrombotic events occurred early after treatment initiation among the GGL group than among the comparator group but had a lower overall risk after 1 year; [redacted], the 2 groups were similar throughout follow-up. The HR, 1-year RR, and 1-year RD estimates in the combined cohort pooled across data sources for composite thrombotic events were consistent with no overall difference between groups (HR = 1.35, 95% CI 0.84-2.15; RR = 0.86, 95% CI 0.47-1.57; RD = −0.0008, 95% CI −0.0138 to 0.0122). Pooled combined cohort results across data sources for AKI were also consistent with no difference across groups (HR not estimated due to violation of proportional hazards assumption; RR = 1.03, 95% CI, 0.58-1.85; RD = −0.0001, 95% CI −0.0142 to 0.0139). Analyses of hemolytic events were limited by small case counts, but the Ig-naive and Ig-experienced cohort 1-year RD estimates pooled across the data sources were also consistent with no difference in risk between groups (Ig-naive cohort RD = −0.0032, 95% CI −0.0098 to 0.0035; Ig-experienced cohort RD = 0.0085, 95% CI −0.0019 to 0.0189; pooled analyses of the combined cohort not performed). Analyses of secondary outcomes (ie, anaphylaxis and transfusion-associated circulatory overload) were limited by very small case counts. No cases of transfusion-related acute lung injury were identified during follow-up in either data source.

Discussion

This study evaluated the comparative risks of thrombosis, AKI, hemolytic events, and other, rarer secondary outcomes among participants with CIDP initiating treatment with GGL or other IGIVs. Many of the outcomes were very rare, despite the use of multiple data sources, long study periods, and separate cohorts of Ig-naive and Ig-experienced participants. Overall, this study did

not suggest consistently different risks of the outcomes among GGL users compared with those among users of other IGIVs currently authorized in the US for use in patients with CIDP.

[redacted]

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