2. SYNOPSIS/ABSTRACT

TITLE

Long-term surveillance study of rituximab (MabThera)-treated patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA).

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KEYWORDS

ANCA associated vasculitis, rituximab, safety, infection, long-term surveillance

RATIONALE AND BACKGROUND

Rituximab (MabThera) is an approved therapy for the treatment of adult patients with severe, active granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). There is a paucity of data on the long term safety of rituximab (MabThera) for this indication.

RESEARCH QUESTION AND OBJECTIVES

How does the time to first serious adverse event (SAE) compare between first treatment with rituximab and a cohort treated with non-rituximab standard of care medication? The objectives were to estimate and compare the incidence and to compare the time to first SAE and the time to first SAE in specific categories of safety events between the rituximab cohort and the cohort treated with other available therapies.

AMENDMENT AND UPDATES TO PROTOCOL

The protocol was initially conceived as a prospective observational study and was changed to a retrospective observational cohort study.

STUDY DESIGN

All GPA/MPA patients for whom there was at least six months data who had received rituximab (MabThera) since 2003 were studied from time of first rituximab to common close out in 2018.They were compared to GPA/MPA patients receiving induction therapy for new or relapsing disease using non-rituximab regimens during the same observational period. Serious adverse events (SAE) and non-serious adverse events of special interest (AESI) were documented.

SETTING

A tertiary referral vasculitis clinic in a University Medical Centre in the UK.

SUBJECT AND STUDY SIZE (INCLUDING DROPOUTS)

418 GPA/MPA patients were enrolled, 26 were excluded and 392 followed, 247 in the rituximab and 145 in the control (standard of care) treatment groups.

VARIABLES AND DATA SOURCES

Baseline demographic, disease and treatment histories and subsequent events were captured from the electronic patient record system of Addenbrooke's Hospital, Cambridge.

RESULTS

The primary endpoint analysis demonstrated a shorter time to first SAE in the rituximab group than in the control group.

Among the pre-defined categories of serious infection, cardiovascular disorders, haematological events, malignant events, renal insufficiency or additional safety

events, secondary endpoint analysis showed a shorter time to first serious infection in the rituximab group than in the control treatment group. Predictors of SAEs were Vasculitis Damage Index (VDI) and co-morbidities known to be previously associated with increased safety risks. An exploratory analysis observed a shorter time to recurrent SAEs in the rituximab treatment group. There was a high number of SAEs in both treatment groups, but it was higher in the rituximab group, mainly driven by a higher number of infections.

DISCUSSION

Treatment groups were not well matched for baseline variables and reflected the predominant use of rituximab (MabThera) for relapsing or refractory disease, in line with NHS guidelines. Patients with GPA/MPA receiving rituximab treatment were at high risk of a broad range of safety events, but particularly of infections. The time to first SAE was shorter in the rituximab than in the control treatment group, however, this difference may be due to the imbalance in baseline characteristics and does not add important safety concerns to the current use of rituximab for GPA/MPA. The observed safety risks for the rituximab and control groups reflect the high inherent risks in this patient population and the need for improved treatment strategies.

CONCLUSION

In this study, over 40% of patients with GPA/MPA experienced an SAE during the course of the observational period. No new safety risks of rituximab were observed.

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