PASS INFORMATION

Title	Risk factors for cardiac events in carfilzomib-treated patients in the Marketscan database
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Active Substance	Carfilzomib
Medicinal Product	Carfilzomib
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Marketing Authorization Holder(s)	Amgen Inc.
Joint PASS	Is this PASS conducted with another MAH? No
Research Question and Objectives	Aim 1 was to identify and estimate the incidence rates of any cardiac events in carfilzomib-treated MM patients during the treatment period, which includes the 30-day period after termination of treatment, and to identify and estimate the incidence rates of cardiac events during the post-treatment period. Aim 2 was to compare the demographic and clinical characteristics of carfilzomib-treated patients with and without the occurrence of any cardiac events.
Country(ies) of Study	United States
Author	Winifred Werther Director, Center for Observational Research Amgen Inc., South San Francisco 650.244.3710

Marketing Authorization Holder(s)

Marketing Authorization Holder(s)	Amgen Inc. One Amgen Center Drive Thousand Oaks, CA 91320-1799 United States 18054473505
MAH Contact Person	Amgen Inc. One Amgen Center Drive Thousand Oaks, CA 91320-1799 United States 18054473505

1. ABSTRACT

- **Title**

Risk factors for cardiac events in carfilzomib-treated patients in the Marketscan database

- **Keywords**

Multiple myeloma, cardiac events, carfilzomib, administrative claims data, non-interventional study

- **Rationale and Background**

During the ASPIRE and ENDEAVOR clinical trials more cardiac events were observed in carfilzomib arms relative to the control arms (Stewart et al. 2015) (Dimopoulos et al. 2016). The purpose of this study was to investigate the incidence of cardiac events in the carfilzomib treated population in a real world data source.

- **Research Question and Objectives**

Primary objectives:

Aim 1 was to identify and estimate the incidence rates of any cardiac events in carfilzomib-treated MM patients during the treatment period, which includes the 30-day period after termination of treatment, and to identify and estimate the incidence rates of cardiac events during the post-treatment period.

Aim 2 was to compare the demographic and clinical characteristics of carfilzomib-treated patients with and without the occurrence of any cardiac events.

- **Study Design**

This was a retrospective non-interventional cohort study of multiple myeloma patients treated with carfilzomib.

- **Setting**

The study population was assembled from the Marketscan claims database in the United States.

- **Subjects and Study Size, Including Dropouts**

Newly diagnosed multiple myeloma patients identified from the Marketscan Claims Database from January 1, 2005- June 30, 2015 were eligible for inclusion.

Table A. Eligibility criteria for inclusion

Eligibility Criteria	N
Multiple myeloma diagnosis 1 January 2005- 30 June 2015 And administration anti-myeloma therapy And administration carfilzomib	24,048 18,683 498

- **Variables and Data Sources**

Outcome:

The primary outcomes of interest were the incidence of cardiac events from inpatient and outpatient claims associated with International Classification of Diseases-9 Diagnosis Codes during the follow-up period. The following events were analyzed separately:

- Hypertension including malignant hypertension,
- Heart failure,

- Ischemic heart disease including acute myocardial infarction,
- Cardiac arrhythmias and conduction disorders,
- Cardiomyopathy,
- Any cardiac event (defined by all above outcomes combined)

Additionally, the above cardiac events were recorded based on two time periods depending on timing of event relative to carfilzomib treatment

- Treatment period defined as during treatment period though ≤ 30 days after last carfilzomib injection
- Post-treatment period defined as > 30 days after carfilzomib injection

Exposure:

Carfilzomib exposure was characterized by regimen and line of therapy.

Covariates:

Comorbidities were defined by the presence of a claim (1 inpatient or 1 outpatient) on the patient record during the baseline period. The baseline period started at 12 months prior to diagnosis of multiple myeloma and ended at the initiation of carfilzomib (index date).

- **Results**

The results of primary objective-aim 1 showed that among carfilzomib-treated patients in a United States claims database (Marketscan), the occurrence of primary hospitalization for a cardiac event during carfilzomib treatment was low (2.2%). Eleven patients (2.2%) were hospitalized with the cardiac event as the primary diagnosis during carfilzomib treatment; 8 events were incident events and 3 were recurrent events as indicated by a prior history of the same cardiac event. In addition, 6 patients were hospitalized for cardiac events during the post-treatment period. The incidence rate per 1000 patient-years (95% Confidence Interval) for primary hospitalization during the treatment period was 73.2 (31.60–144.24) (Table B). Incidence rates for individual cardiac events can be seen in the Figure below.

Figure. Incidence rate and 95% Confidence Intervals per 1000 patient-years for incident primary hospitalizations for cardiac events during the treatment period in carfilzomib-treated multiple myeloma patients (n=8).

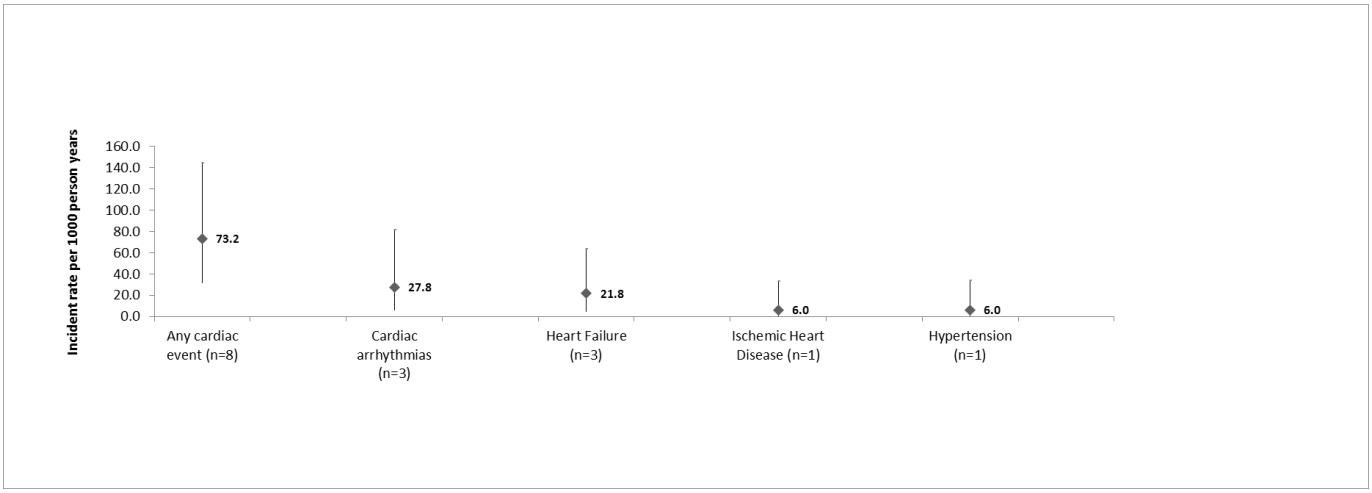

Table B. Incident hospitalization rate for cardiac events by treatment period

	At Risk N	Events N	Time at risk Patient Years	Incidence Rate/1000 Patient Years	95% Confidence Interval
Incident primary hospitalization	345	14			
Treatment period	345	8	109.3	73.2	31.60, 144.24
Post-treatment	243	6	117.0	51.3	18.82, 111.61

When comparing clinical characteristics between patients experiencing a cardiac event and those who did not, baseline comorbidities that were significantly different in the primary hospitalization cohort compared to patients with no cardiac events were chronic kidney disease (73% vs. 31%), hypertension (91% vs. 60%), and heart failure (36% vs. 10%), respectively.

Discussion

The results of this observational study show that among carfilzomib-treated patients in US claims database, the occurrence of primary hospitalization for a cardiac event during carfilzomib treatment was low (2.2%). Patients who were hospitalized for a primary cardiac event were more likely to have a medical history of chronic kidney disease, hypertension, and heart failure. The results of this study suggest that the occurrence of cardiac events during carfilzomib-treatment was low. Overall, given the common cardiac medical history for multiple myeloma patients and the low rate of hospitalizations due to cardiac events (e.g. primary diagnosis) in the study population, the benefit risk profile of carfilzomib remains unchanged for the approved indications.

- **Marketing Authorization Holder(s)**

Amgen Inc.

- **Names and Affiliations of Principal Investigators**

Winifred Werther, PhD
Director, Center for Observational Research, Amgen Inc.