EPH145

# Association Between Metformin Use and Major Adverse Cardiac Events in Multiple Myeloma Patients With Type 2 Diabetes Mellitus Receiving Carfilzomib: A Population-Based Cohort Study

**Jiyeon Lee[1, 2], Miryoung Kim[1,2], Hyun Jin Han[1,2], Hae Sun Suh[1, 2, 3] ***

*1 Department of Regulatory Science, Graduate School, Kyung Hee University, Seoul, Republic of Korea*
*2 Institute of Regulatory Innovation through Science, Kyung Hee University, Seoul, Republic of Korea*
*3 College of Pharmacy, Kyung Hee University, Seoul, Republic of Korea.*

**Corresponding author*

Pharmaceutical Economics
Big Data Analysis and Policy Lab

## INTRODUCTION

- Although carfilzomib is an effective treatment for multiple myeloma (MM), its cardiotoxicity has been a concern.
- There have been promising laboratory findings on the protective potential of metformin against carfilzomib-induced cardiotoxicity.

## OBJECTIVE

To evaluates the real-world effectiveness of metformin in reducing MACE in MM patients with type 2 diabetes mellitus (T2DM) receiving carfilzomib treatment.

## METHOD

**Study design**
**Data source**
Population-based retrospective cohort study
Health Insurance Review and Assessment Service database

**Population**
Adult **MM** (ICD-10 C90) patients with **T2DM** (ICD-10 E11) who initiated **carfilzomib** including regimens

**Exclusion Criteria**
Patients with advanced chronic kidney disease (stage 4, 5)
Patients with recent history of major cardiac adverse event (MACE)

**Comparison**

| Metformin User | Metformin Non-user |
|---|---|
| At least 1 prescription both within 6 months prior to and during carfilzomib treatment | No prescription within 6 months prior to and throughout carfilzomib treatment |

**Outcome**
**Time to first MACE** and its individual components (AMI, IS, HF and CV death) during carfilzomib treatment period

**Statistical Analysis**
- **Inverse probability treatment weighting** to adjust for baseline difference
- **Fine-Gray model** to account for competing mortality risks

## RESULTS

**Table 1. Baseline characteristics**

| Characteristics | Metformin Non-user N=145 | Metformin User N=294 | P-value |
|---|---|---|---|
| **Age, mean (sd)** | 69.1 (7.3) | 67.6 (8.1) | 0.0545 |
| **Female, n (%)** | 57 (39.3) | 126 (42.8) | 0.4784 |
| **Medial aid, n (%)** | 10 (6.9) | 12 (4.1) | 0.2036 |
| **LOT, mean (sd)** | 2.9 (1.2) | 2.8 (1.2) | 0.5673 |
| **CCI, mean (sd)** | 4.8 (3.2) | 4.6 (3.0) | 0.3921 |
| **Regimen, n (%)** | | | |
| KRd | 71 (49.0) | 165 (56.1) | 0.1572 |
| Kd | 74 (51.0) | 129 (43.9) | |
| **Previous treatment, n(%)** | | | |
| Stem cell transplant | 53 (36.6) | 121 (41.2) | 0.3536 |
| Proteasome inhibitors | 99 (68.3) | 191 (65.0) | 0.4909 |
| Immunomodulatory drugs | 76 (52.4) | 138 (46.9) | 0.2804 |
| CD38 antibody | 8 (5.5) | 6 (2.0) | 0.0512 |

*LOT, Line of therapy; CCI, Charlson comorbidity index*

- A total of 439 MM patients with T2DM treated with carfilzomib were categorized based on metformin use. The incidence of MACE per 100 person-year was 22.8 in metformin users and 26.3 in non-users.
- Using IPTW and Fine-Gray model analysis, metformin use was not associated with a significant reduction in the incidence of MACE (HR 0.861; 95% CI 0.628–1.180). Although no significant differences were observed in the individual components of MACE either, it is noteworthy that there was a borderline significant reduction in heart failure risk (HR 0.694, p=0.057).

**Table 2. Incidence rate per 100 person-years**

| Outcome | Metformin Non-user | Metformin User |
|---|---|---|
| MACE | 26.3 | 22.8 |
| Acute Myocardial Infarction | 0.0 | 1.2 |
| Stroke | 3.8 | 6.1 |
| Heart Failure | 20.8 | 14.1 |
| Cardiovascular death | 3.7 | 2.8 |

*ICD-10 codes for outcome – Acute Myocardial Infarction I21, I22; Stroke I63, I64; Heart Failure I50; Cardiovascular death I461, I469*

## CONCLUSIONS

Our findings do not support a significant cardioprotective effect of metformin in reducing overall MACE incidence in MM patients with T2DM on carfilzomib but suggest a potential for reducing heart failure risk.

## REFERENCES

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## ACKNOWLEDGMENT

This research was supported by grants from the Ministry of Food and Drug Safety in 2024 (21153MFDS601, RS-2024-00331719) and by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (RS-2024-00345981).