Transformative Impact of SGLT2 Inhibitors on Survival and Complication Rates Following Autologous Stem Cell Transplant in Multiple Myeloma: A Global Comparative study

Asfand Yar Cheema[1,2], Mishaal Munir[3], Aashary Mandala[2], Faiz Anwer[4], Sandra Mazzoni[4]

[1]Cleveland Clinic Foundation-Fairview Hospital, OH [2]Translational Hematology and Oncology Research, Cleveland Clinic, OH [3]Lahore Medical and Dental College, LHR, [4]Taussig Cancer Center, Cleveland Clinic, OH

Cleveland Clinic

Introduction

- Multiple myeloma (MM) remains incurable despite advances in treatment, with autologous stem cell transplantation (AHSCT) being a key therapeutic approach.
- Post transplant complications significantly impact morbidity and survival. Sodium-glucose cotransporter 2 inhibitors (SGLT2i), originally used for glycemic control, exhibit antineoplastic and anti-inflammatory properties by modulating glutamine metabolism, activating AMPK, decreasing CRRY expression, and inhibiting PI3K/AKT/mTOR signaling.
- These metabolic effects can improve transplant-related outcomes.
- Our study aims to evaluate the impact of SGLT2i on clinical outcomes in MM patients in a large global database who underwent AHSCT.

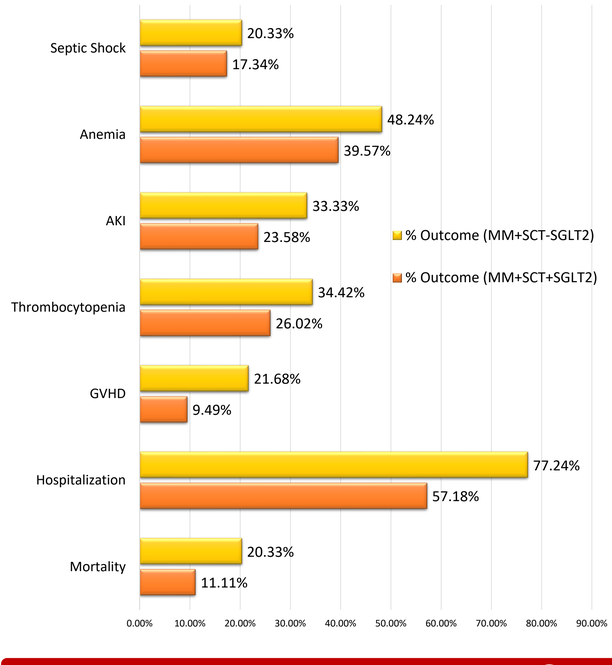
Methods and Materials

- We conducted a retrospective, propensity score-matched (PSM) cohort study using the TriNetX database, including MM patients aged ≥18 years who had AHSCT treated with SGLT2i (n=400) and matched controls without SGLT2i (n=7,435) from 2015 to 2021. PSM (1:1) was applied using a greedy nearest-neighbor method with a caliper of 0.1 pooled standard deviations, adjusting for demographics, MM-directed therapy, comorbidities, laboratory values, and cardiovascular medications.
- **Primary outcomes** were all-cause mortality, hospitalization rate, and graft-versus-host disease (GVHD). **Secondary outcomes** included anemia, thrombocytopenia, acute kidney injury (AKI), and septic shock.
- Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated over a **3-year follow-up**.

Results

- After PSM, 366 matched pairs were analyzed in both cohorts.
- Mean time for patients on SGLT2i therapy was 297.60 ± 162.42 days

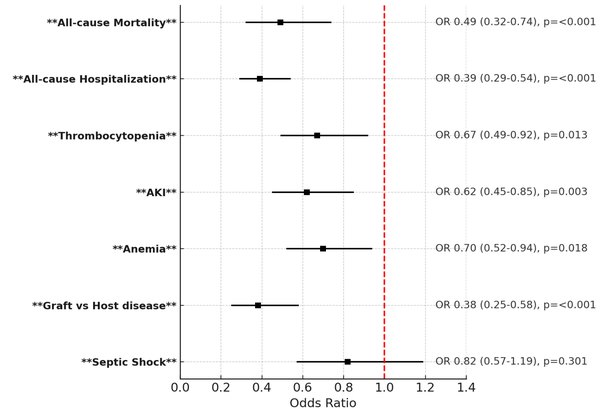
Number of Events %



Patient Characteristics

Characteristic	SGLT2i Users, n=366	SGLT2i Non-Users n=366	Standardized Difference
Demographics			
Age at Index,	61.8 ± 8.8	62.1 ± 9.9	0.033
White	162 (43.9)	165 (44.7)	0.016
African American	68 (18.4)	71 (19.2)	0.021
Asian	10 (2.7)	10 (2.7)	<0.001
Hispanic or Latino	33 (8.9)	33 (8.9)	<0.001
Female	162 (43.9)	153 (41.5)	0.049
Male	207 (56.1)	216 (58.5)	0.049
Unknown Race	96 (26.0)	94 (25.5)	0.012
AIAN	10 (2.7)	0 (0.0)	0.236
Diagnosis			
Hypertension	313 (84.8)	321 (87.0)	0.062
Cardiomyopathy	77 (20.9)	81 (22.0)	0.026
Lipid disorders	274 (74.3)	284 (77.0)	0.063
CAD	138 (37.4)	130 (35.2)	0.045
Obesity	159 (43.1)	164 (44.4)	0.027
Heart failure	129 (35.0)	132 (35.8)	0.017
CKD stage 3	84 (22.8)	86 (23.3)	0.013
COPD	41 (11.1)	34 (9.2)	0.063
Cerebral infarction	25 (6.8)	22 (6.0)	0.033
Hepatic fibrosis	10 (2.7)	10 (2.7)	<0.001
PAD	29 (7.9)	26 (7.0)	0.031
ESRD	15 (4.1)	15 (4.1)	<0.001
OSA	89 (24.1)	86 (23.3)	0.019
Afib/flutter	75 (20.3)	69 (18.7)	0.041
Nicotine disorder	61 (16.5)	68 (18.4)	0.050
Alcohol disorders	11 (3.0)	10 (2.7)	0.016
Diabetes mellitus	258 (69.9)	264 (71.5)	0.036
Medications			
Antilipemic agents	244 (66.1)	246 (66.7)	0.011
Insulin	163 (44.2)	166 (45.0)	0.016
Aspirin	150 (40.7)	143 (38.8)	0.039
Bortezomib	124 (33.6)	129 (35.0)	0.029
Daratumumab	106 (28.7)	109 (29.5)	0.018
Carfilzomib	35 (9.5)	37 (10.0)	0.018
Rituximab	10 (2.7)	10 (2.7)	<0.001
Venetoclax	10 (2.7)	10 (2.7)	<0.001
Ixazomib	18 (4.9)	14 (3.8)	0.053
Elotuzumab	10 (2.7)	10 (2.7)	<0.001
Selinexor	10 (2.7)	10 (2.7)	<0.001
Isatuximab	10 (2.7)	10 (2.7)	<0.001
Teclistamab	10 (2.7)	10 (2.7)	<0.001
Cyclophosphamide	55 (14.9)	58 (15.7)	0.023
Doxorubicin	11 (3.0)	11 (3.0)	<0.001
Abecma	10 (2.7)	10 (2.7)	<0.001
Laboratory			
LDL cholesterol	87.4 ± 43.7	85.0 ± 44.9	0.053
Hemoglobin A1c	7.0 ± 1.8	6.7 ± 1.7	0.152

Forest Plot



Outcomes

Outcome	OR	95% CI	P-Value
All-cause Mortality	0.49	0.32 – 0.74	<0.001
All-cause Hospitalization	0.39	0.29 – 0.54	<0.001
Thrombocytopenia	0.67	0.49 – 0.92	0.013
AKI	0.62	0.45 – 0.85	0.003
Anemia	0.70	0.52 – 0.94	0.018
Graft vs Host disease	0.38	0.25 – 0.58	<0.001
Septic Shock	0.82	0.57 – 1.19	0.301

Conclusion

- This large PSM cohort study demonstrates that SGLT2i are associated with significantly reduced risks of mortality, hospitalization, and several major complications in MM patients undergoing AHSCT.
- Notwithstanding the limitation of registery database, and lack of clinical granularity, these findings underscore the potential of SGLT2i as a transformative adjunctive therapy in the posttransplant setting, warranting further investigation in prospective trials.

Asfand Yar Cheema, MD
Cleveland Clinic Foundation/Fairview
Cheemaa@ccf.org

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