Comparative Effects of Semaglutide vs Tirzepatide on Weight Change and Cardiovascular Risk in Breast Cancer Survivors

Hundal J[1], Parekh D[2], Harisingani A[3], Abushamma A[4], Ashruf O[5], Sukumar J[6]

[1]Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, [2]SUNY Upstate Medical University, Syracuse, NY, [3]Loyola Medicine MacNeal Hospital, Berwyn, IL, [4]Akron General Medical Ctr, Akron, OH, [5]University of Texas MD Anderson Cancer Center, Houston, TX

Introduction

• Obesity and cardiometabolic dysfunction are prevalent among breast cancer survivors and associated with treatment-related toxicity and increased mortality
• Semaglutide (GLP1-Receptor Agonist, S) and tirzepatide (GLP1/GIP Receptor Agonist, T) are approved for weight management and glycemic control in type 2 diabetes (DM2)
•However, their impact on weight loss and CV outcomes in breast cancer survivors are not well elucidated

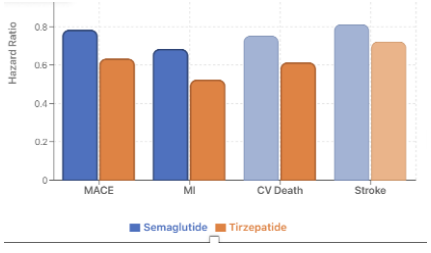
Study Objective:
• Evaluate the effects of S versus metformin and T versus metformin on weight change and CV outcomes in breast cancer survivors from a real-world national database

Methods

• Retrospective cohort study utilizing the TriNetX national platform
Key Inclusion Criteria: Female breast cancer patients (Stage I–III) with BMI > 27 kg/m² and/or DM2, prescribed S or T from 2018-2025 after breast cancer diagnosis
Key Exclusion Criteria: Stage IV disease, type 1 DM, thyroid malignancy, pancreatitis/gastroparesis, ECOG ≥ 3, Major Adverse Cardiovascular Events (MACE, defined as composite MI, CV death, and stroke) within 3 months of breast surgery
- S and T users each propensity matched 1:1 to metformin users
- 22 Matching covariates : age, sex, race, metabolic comorbidities, medications, tobacco use, and laboratory values
• Weight change (12 and 24 months) and MACE between S/T and metformin groups compared
• Statistical analysis: Cox proportional hazards models; Hazard ratios (HRs) and 95% confidence intervals (CIs)

Results

Group	Baseline Weight (lbs) mean +/-SD	12-Month Weight (lbs) mean +/-SD	24-Month Weight (lbs) mean +/-SD	Weight Loss at 12 Months mean +/-SD	Weight Loss at 24 Months mean +/-SD
Semaglutide (n=3,009)	204 ± 45.4	195.2 ± 45.0	193.3 ± 45.2	8.8 ± 9.6 lbs (4.3 ± 4.5%)	10.7 ± 10.8 lbs (5.2 ± 5.1%)
Matched Metformin (Semaglutide)	198 ± 45.7	193.4 ± 44.8	192.2 ± 44.6	4.6 ±7.8 lbs (2.3 ± 3.7%)	5.8 ± 8.1lbs (2.9 ± 3.9%)
Tirzepatide (n=1,652)	211 ± 44.4	200.3 ± 45.1	198.8 ± 45.6	10.7 ± 10.2 lbs (5.1 ± 4.8%)	12.2 ± 11.1lbs (5.8 ± 5.2%)
Matched Metformin (Tirzepatide)	203 ± 46.1	199.4 ± 45.2	197.9 ± 44.9	3.6 ± 7.2 lbs (1.8 ± 3.6%)	5.1 ± 7.5lbs (2.5 ± 3.7%)



S vs Metformin:
•MACE: HR 0.78 (**p=0.03**)
•MI: HR 0.68 **(p=0.05)**
•CV death: HR 0.75 (p=0.07)
•Stroke: HR 0.81 (p=0.18)

T vs Metformin:
•MACE: HR 0.63 (**p=0.001**)
•MI: HR 0.52 (**p=0.004**)
•CV death: HR 0.61 (**p=0.03**)
•Stroke: HR 0.72 (p=0.09)

Results

• There were 3,009 S users and 1,652 T users
  • Median follow up time: 2 years
  • Median duration of S and T use: 1.5 (range 0.03-7.35) and 0.8 (range 0.03-5.77) years, respectively
• Key baseline characteristics included:
  • S group: mean age 63 +/- 10 years, 68% white race and 17% Black race, 63% with DM2, 67% with overweight/obesity
  • T group: mean age 62 +/- 10 years, 73% white race and 14% Black race, 59% with DM2, 77% with overweight/obesity
• Both S and T resulted in modest weight loss at 12 and 24 months compared with metformin
  • At 12 months, T ~18% greater relative weight reduction compared to S
  • At 24 months, T ~12% greater relative weight reduction compared to S
• Both S and T significantly reduced MACE compared to metformin
  • T vs metformin resulted in greater CV risk reduction compared with S vs metformin

Conclusions

• GLP-1 and GLP1/GIP receptor agonists show promise for the reduction in weight and cardiovascular risk, two key modifiable risk factors, in breast cancer survivors
  • Weight loss efficacy was modest
  • T may offer superior cardiometabolic benefits over S due to its dual GLP1/GIP agonism
• Prospective studies should investigate mechanisms of these cardiometabolic effects and evaluate the impact of differing GLP1 drug types, dosing, and schedules in cancer survivors