A Retrospective Evaluation of Glycemic Effects in Veterans With Type 2 Diabetes After Addition of SGLT2 Inhibitors or GLP-1 Receptor Agonists to Basal-Bolus Insulin Regimens

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Conflict of Interest

- The speaker has no actual or potential conflicts of interest in relation to this presentation

Learning Objective

- Evaluate the effects on glycemic control, in addition to pleiotropic effects and insulin dose requirements, when either an SGLT2 Inhibitor or GLP-1 Receptor Agonist is added to basal-bolus insulin regimens in a Veteran population with Type 2 Diabetes

Abbreviations

- ADA – American Diabetes Association
- ASCVD – atherosclerotic cardiovascular disease
- DM – Diabetes Mellitus
- eGFR – estimated glomerular function
- GLP-1 – glucagon like peptide 1
- IRB – Institutional Review Board
- SGLT2 – sodium glucose co-transporter 2
- TDD – total daily dose
- VISN – Veterans Integrated Service Networks

Background[1]

- An estimated 30.3 million people were affected or diagnosed with Type 2 DM in the United States in 2015
  - More than half are adults aged 45 to 65 years of age

- With an increased prevalence of DM, pharmacological therapies have continued to expand
  - SGLT2 Inhibitors
  - GLP-1 Receptor Agonists

SGLT2 Inhibitors[2,3]

- Mechanism: excretion of glucose through urine
  - Minimal to no risk of beta-cell burnout and overstimulation
- Place in therapy:
  - Second, third, and fourth-line agents
  - Consider sooner in therapy with established ASCVD or if heart failure or chronic kidney disease predominates
  - Consider to minimize hypoglycemia or weight gain

GLP-1 Receptor Agonist[2,4]

- Mechanism: mimics natural hormone GLP-1:
  - Increased insulin secretion
  - Decreased glucagon release
  - Decreased hepatic glucose output
- Place in therapy:
  - Second, third, and fourth-line agents
  - Consider sooner in therapy with established ASCVD or if heart failure or chronic kidney disease predominates and unable to utilize SGLT2 inhibitor
  - Consider to minimize hypoglycemia or weight gain

VA Population and DM Management

- SGLT2 inhibitors and GLP-1 receptor agonists relatively restricted
  - Due to cost of therapy

- Use of either agent requires prior approval

Utility of Novel Agents with Insulin[3,4]

- Studies have shown improvement in A1c and reduction in insulin doses with combination of either SGLT2 inhibitors or GLP-1 agonists to basal insulin therapy
- Limited evidence evaluating glycemic outcomes when either agent is added to basal-bolus insulin regimens

Research Outcomes

Primary Outcome

- Change in A1c from baseline to 12 months after the addition of either an SGLT2 inhibitor or GLP-1 receptor agonist to basal-bolus insulin regimens

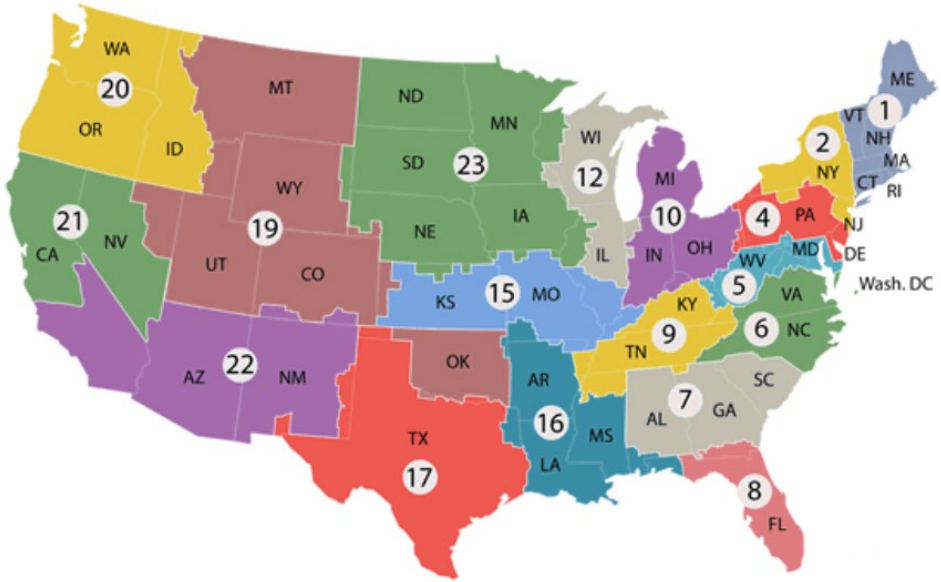
Research Outcomes

Secondary Outcomes

- After the addition of either a SGLT2 inhibitor or GLP-1 receptor agonist to basal-bolus insulin:
  - The mean change from baseline to 6, 18, and 24 months in A1c
  - The mean change from baseline to 6, 12, 18, and 24 months in:
    - Weight
    - TDD of basal insulin
    - TDD of bolus insulin
    - Blood Pressure
    - Renal Function
- Safety Outcomes

Methods: Study Design

- Retrospective, multi-center cohort study
- Flipped PGY2 Research Project
- Data collected from VA VISN 15
- Approved through Kansas City Veteran's Affairs IRB
  - Submitted November 2018
    Approved January 2019



https://www.va.gov/directory/guide/map.asp?dnum=1

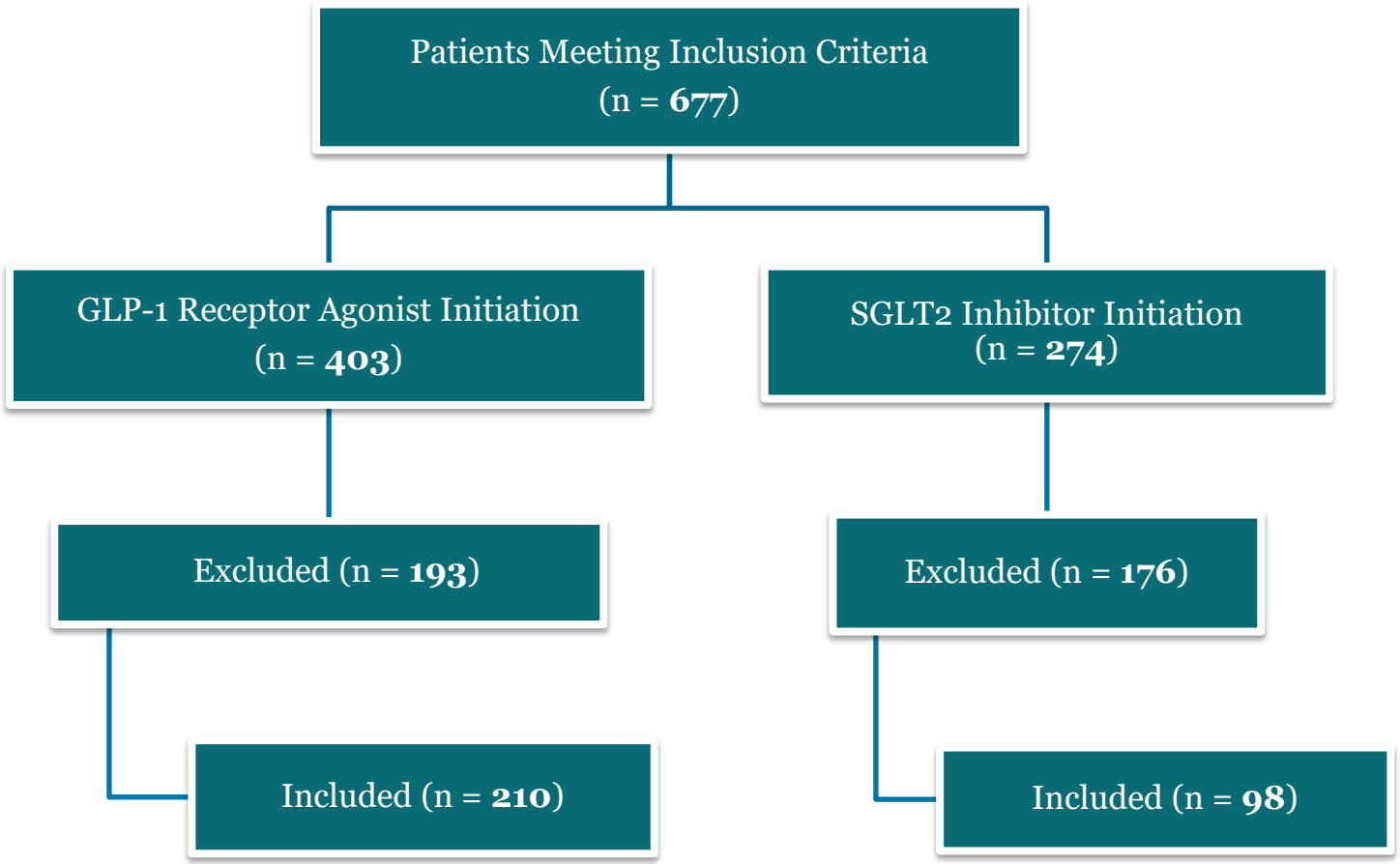
Methods: Criteria

- **<u>Inclusion Criteria</u>**
  - US adult Veterans with Type 2 Diabetes
  - Initiation of either an SGLT2 inhibitor or GLP-1 receptor agonist in addition to a basal-bolus insulin regimen within the defined study period
    - January 1st, 2015 to January 1st, 2019

Methods: Criteria

- **<u>Exclusion Criteria</u>**
  - Type 1 Diabetes
  - Acute Metabolic Complications present at the time of study drug initiation
  - Initiation of an SGLT2 inhibitor within 12 months of GLP-1 receptor initiation, or vice versa
  - If A1c was missing at 6 and 12 months following study drug initiation
  - If the study agent was discontinued within 12 months of initiation
  - If there was no active prescription for the study agent at 6, 12, and 18 months
  - eGFR less than 45 ml/min/1.73m^2 at study drug initiation

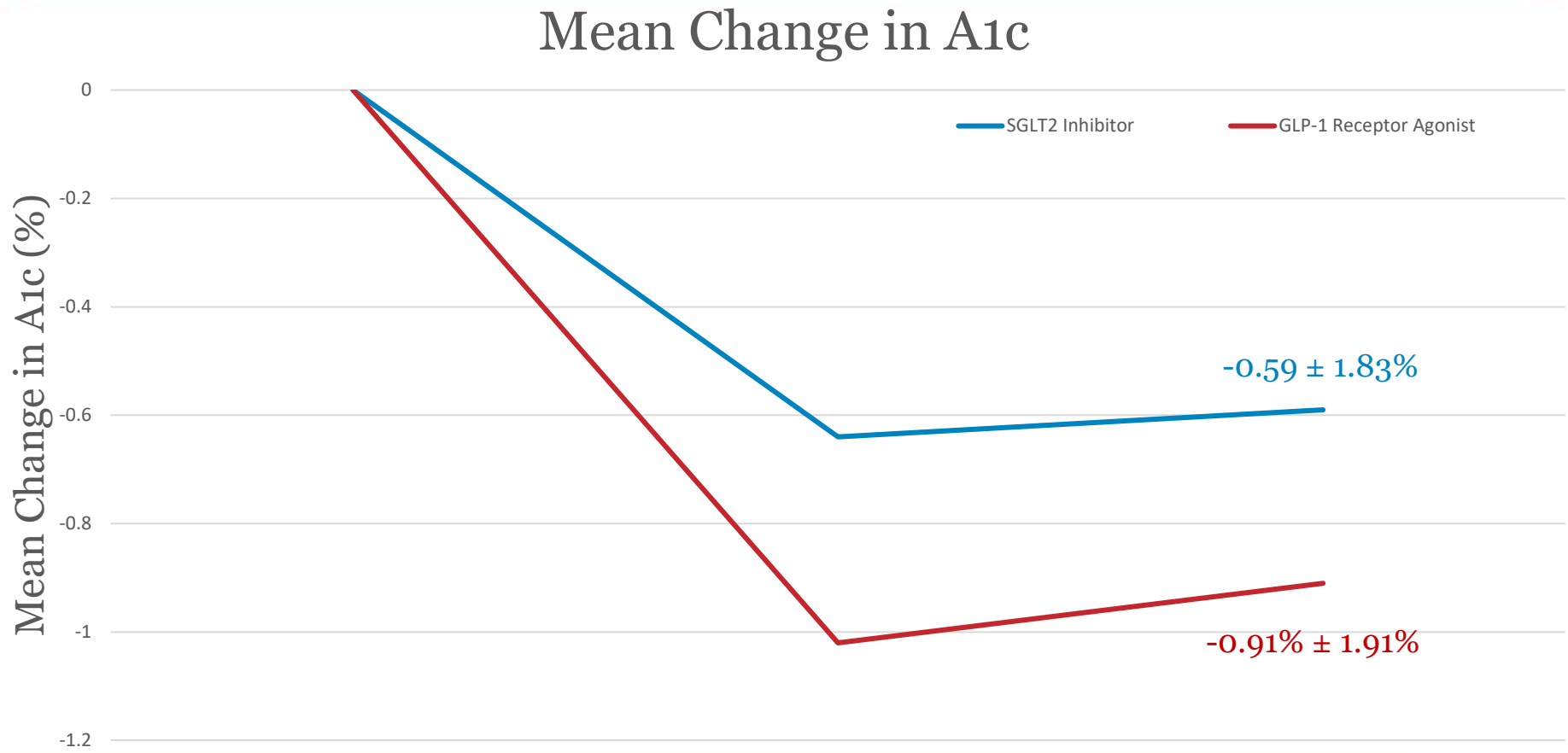
Results: Patient Population



Results: Patient Demographics

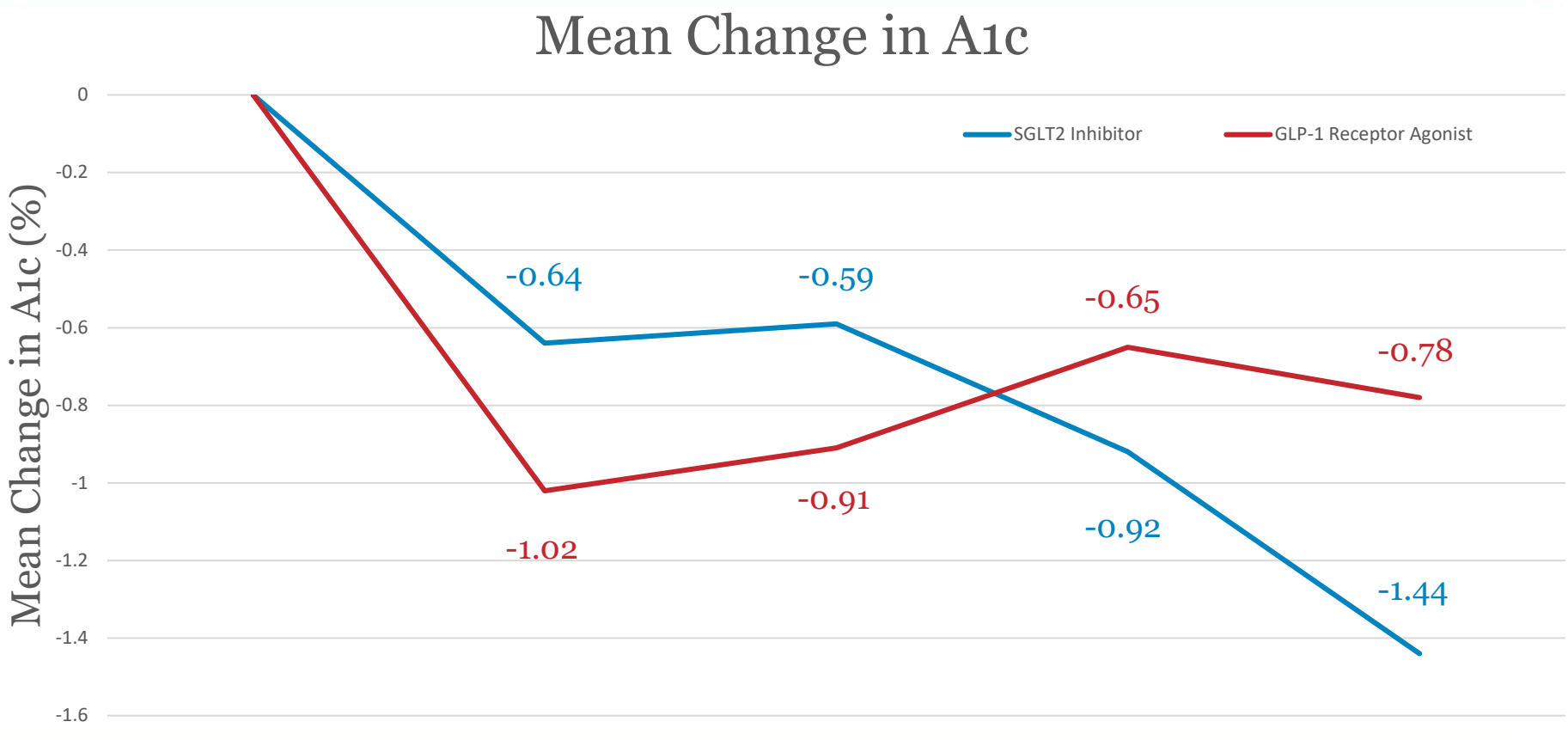
	SGLT2 Inhibitor (N = 98)	GLP-1 Receptor Agonist (N = 210)
Age, years, mean	64.8	62.3
Male Sex, no. (%)	95 (96.9)	199 (94.8)
A1c, %, mean	8.73	8.94
Weight, pounds, mean	263.3	268.5
ASCVD History, No. (%)	34 (35)	59 (28)
TDD of Basal Insulin, units, mean	82	85
TDD of Bolus Insulin, units, mean	85	78
Blood Pressure, mmHg, mean	133/72	132/74
eGFR, ml/min/1.73m^2, mean	73	66
Primary Study Agent (%)	empagliflozin (98)	liraglutide (88)

Results: Primary Outcome



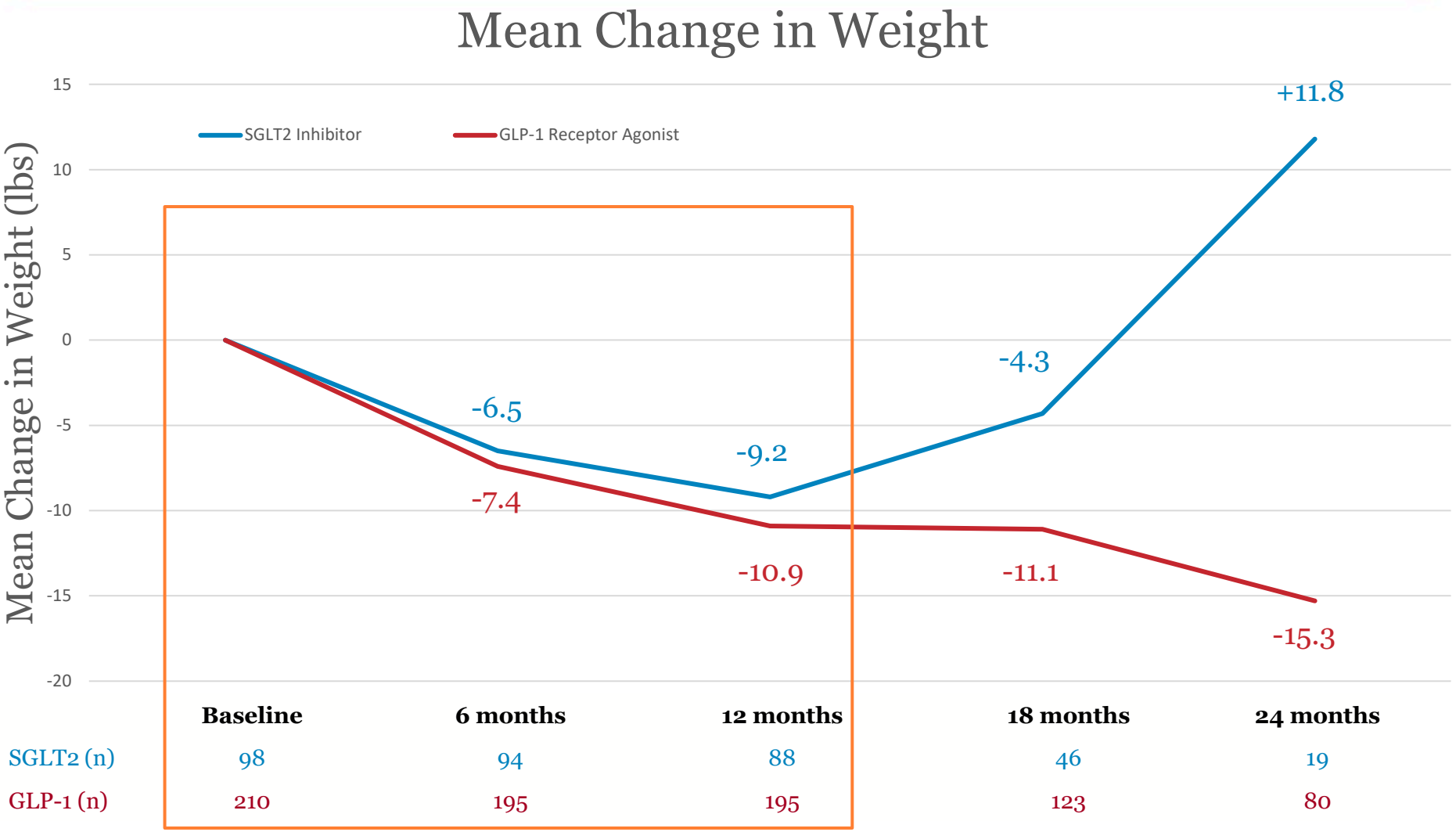
	Baseline	6 months	12 months
SGLT2 Inhibitor (n)	98	88	98
GLP-1 Receptor Agonist (n)	210	203	210

Results: Secondary Outcomes



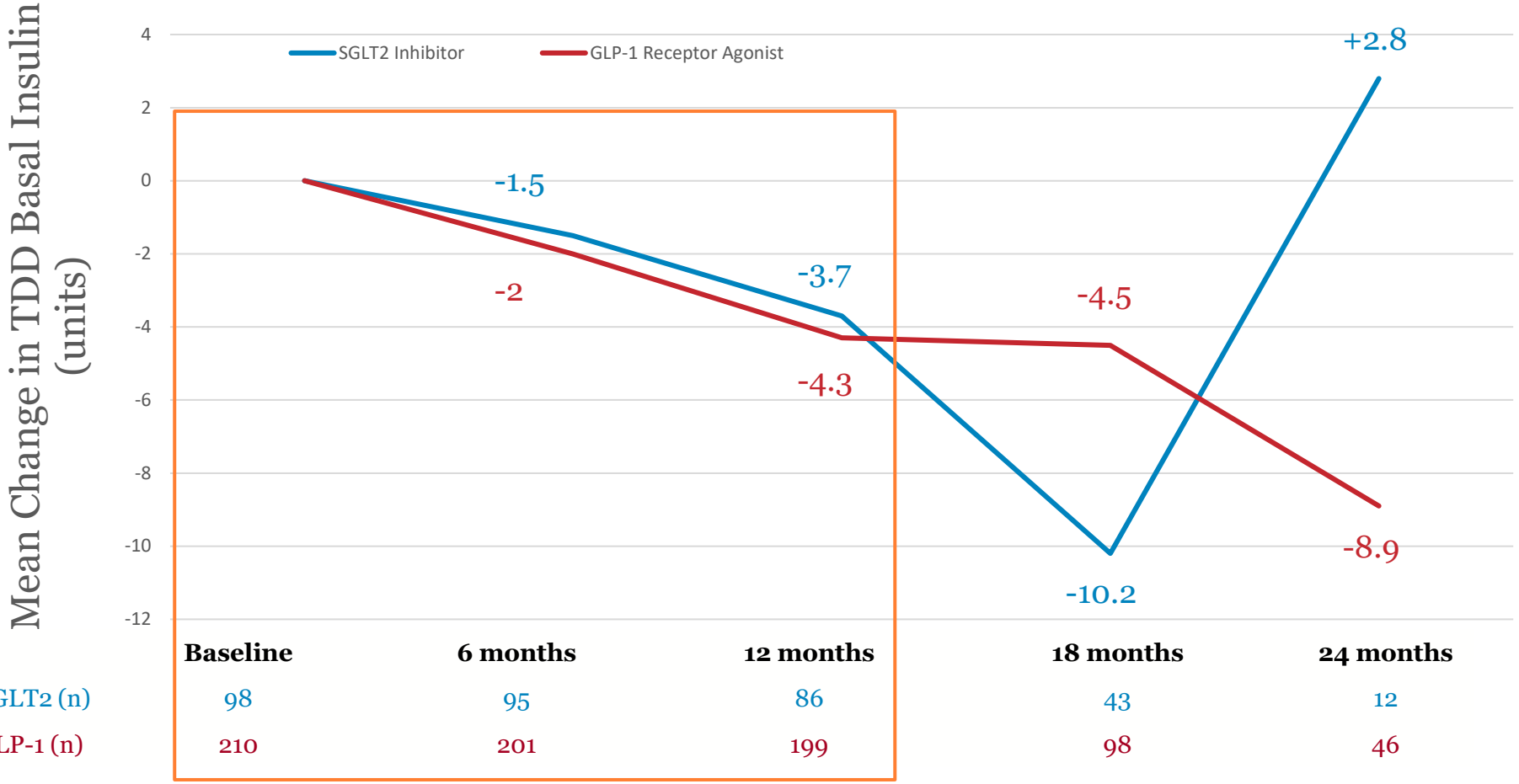
	Baseline	6 months	12 months	18 months	24 months
SGLT2 (n)	98	88	98	40	17
GLP-1 (n)	210	203	210	133	79

Results: Secondary Outcomes



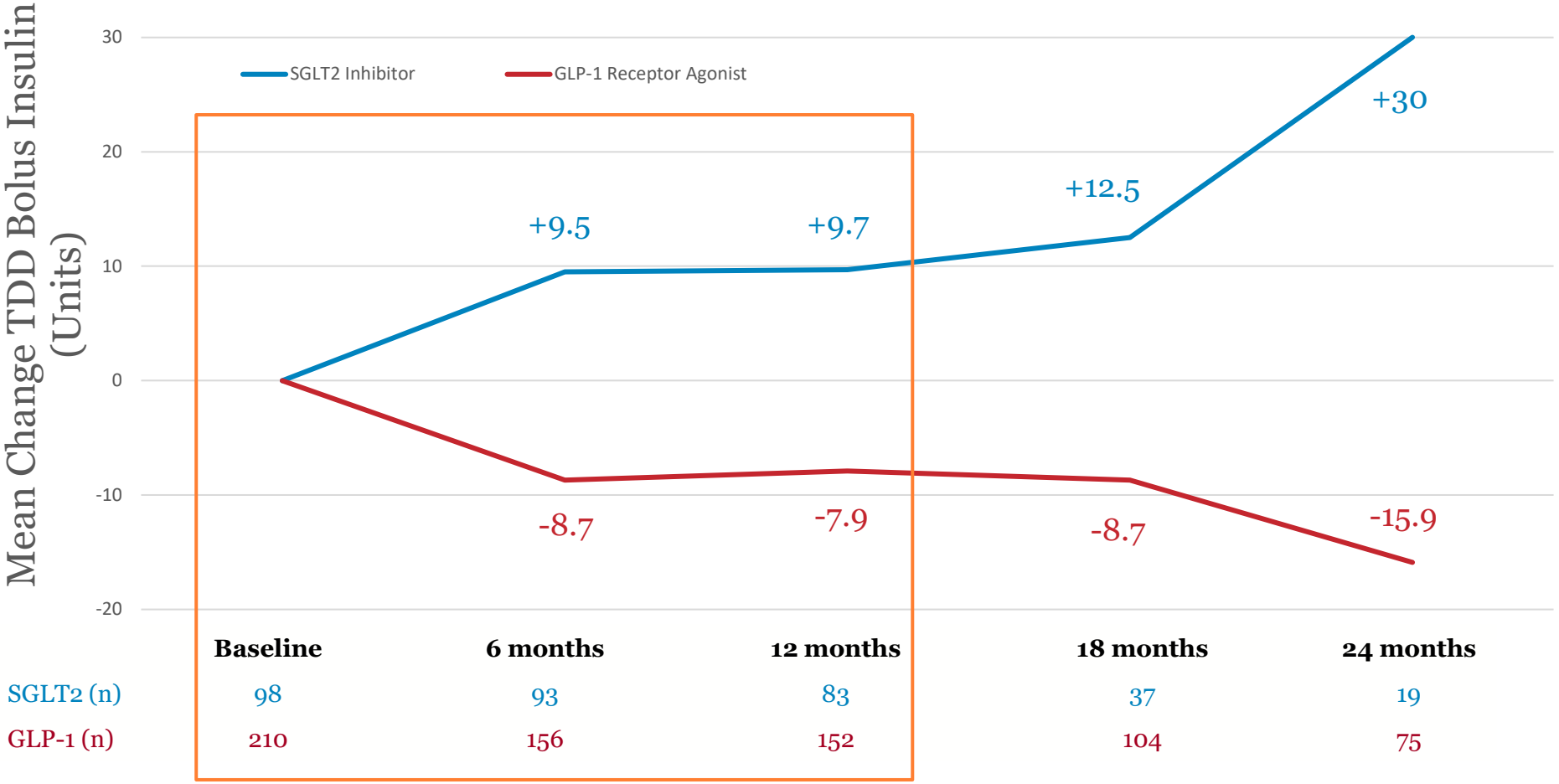
Results: Secondary Outcomes

Mean Change in Basal Insulin



Results: Secondary Outcomes

Mean Change in Bolus Insulin



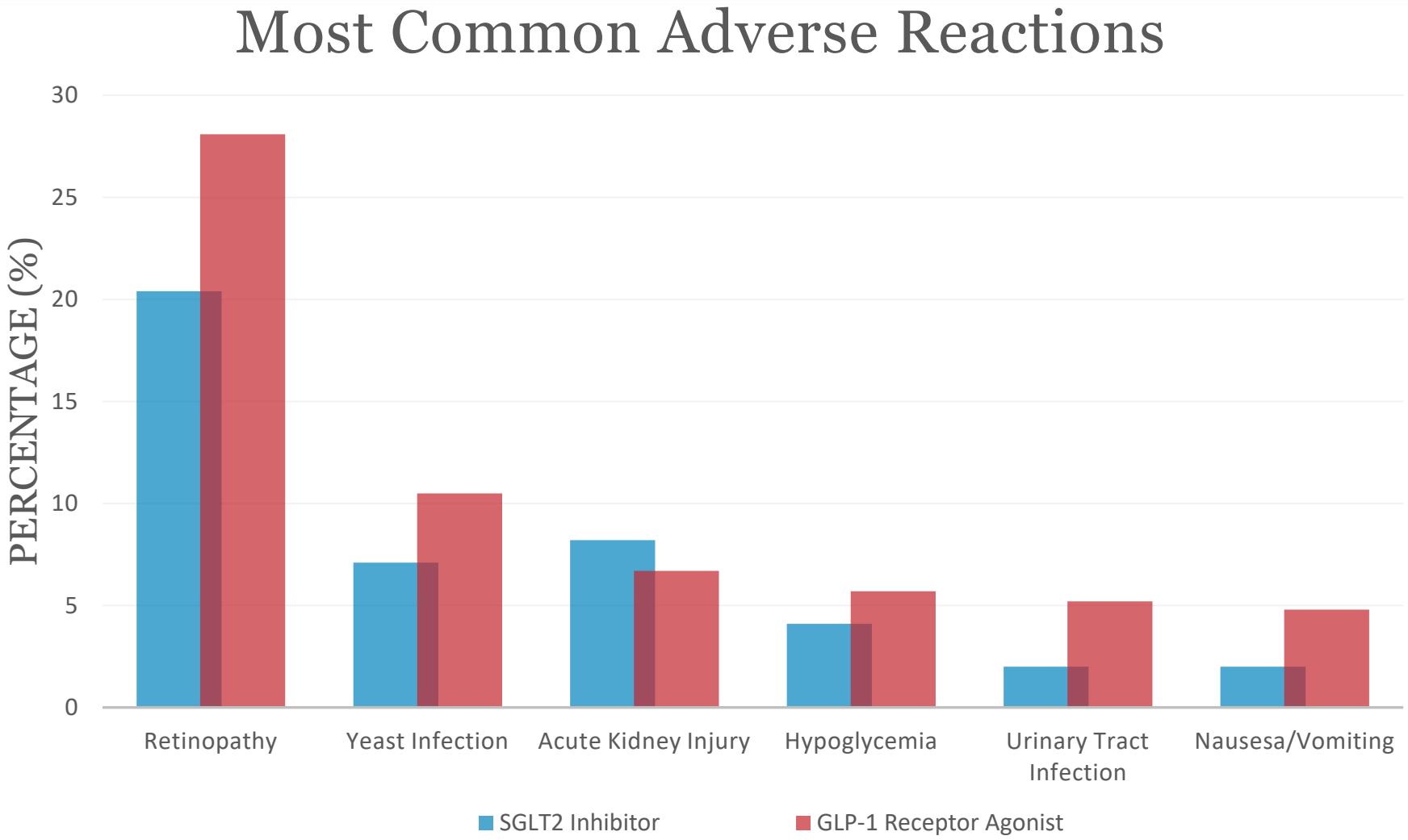
	Baseline	6 months	12 months	18 months	24 months
SGLT2 (n)	98	93	83	37	19
GLP-1 (n)	210	156	152	104	75

Results: Secondary Outcomes

Change in Blood Pressure, mmHg					
	Baseline	6 months	12 months	18 months	24 months
SGLT2i	133/72	130/72	132/73	130/74	136/75
GLP-1 RA	132/74	131/74	131/74	129/72	131/73

Change in eGFR, mL/min/1.73m²					
	Baseline	6 months	12 months	18 months	24 months
SGLT2i	73	67	68	65	68
GLP-1 RA	66	67	66	67	61

Results: Safety



Conclusions

- The addition of SGLT2 Inhibitors and GLP-1 Receptor Agonists to basal-bolus insulin therapy improved glycemic control
- When evaluating data from baseline to twelve months, GLP-1 Receptor Agonists had a greater impact on:
  - Mean A1c reduction
  - Mean Weight loss
  - Mean reduction in basal and bolus insulin total daily doses
- Blood pressure and renal outcomes were minimally changed with either study drug
- Both study drugs were overall well tolerated
- Cost should be taken into consideration with both drug classes

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QUESTIONS?

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