Diabetes Updates: A Comprehensive Update of New Developments in the Treatment of T1DM and T2DM

- Disclosures: I have no relevant relationships with ineligible companies to disclose within the past 24 months.

- Objectives:
  Discuss new pharmacotherapy treatment options in T2DM.

  Review advancements in diabetes technology.

  Discuss the key updates from the ADA Standards of Care 2023.

  (briefly) Explore new diabetes trends on the horizon.

- Tirzepatide

FDA approval May 2022 as add on or monotherapy for patients with T2DM
Once weekly injection available in six doses: 2.5mg, 5mg, 7.5mg 10mg, 12.5mg, and 15mg
Start 2.5mg SC weekly x 4 weeks, then increase by 2.5mg/wk no more frequently than q 4 weeks
Renal impairment: no adjustment
Hepatic dosing: no adjustment
Black box warning: contraindicated in patients with medullary thyroid cancer (MTC) hx or family hx, or in patients with multiple endocrine neoplasia type 2 (MEN 2)
Side effects – similar to those seen in GLP1-RA, typically mild to moderate GI (N/V, diarrhea)

- SURPASS 1: evaluated efficacy and safety of 3 doses (5mg, 10,mg and 15mg) of tirzepatide as monotherapy against placebo amongst people with T2DM

Primary endpoint: change in Hba1c from baseline at 40 weeks
At 40 weeks, all tirzepatide doses were superior to placebo for changes in baseline Hba1c, fasting serum glucose, body weight, and Hba1c target < 7.0%
31%-52% of patients on tirzepatide versus 1% on placebo reached an A1c of <5.7%
Tirzepatide induced a dose dependent body weight loss ranging from 7.0kg to 9.5kg

- SURPASS 4: evaluated efficacy and safety of 3 doses (5mg, 10mg, and 15mg) of tirzepatide versus insulin glargine in T2DM and increased cardiovascular risk

Primary endpoint: noninferiority or tirzepatide 10mg or 15mg (or both) vs glargine in Hba1c changes rom baseline to 52 weeks
Tx continued for max of 104 weeks or study completion to collect and adjudicate major adverse cardiovascular events
52 weeks, Hba1c reduction:
-2.43% 10mg
-2.58% 15mg
-1.44% glargine
In patients with T2DM and increased CV risk, tirzepatide compared with glargine, demonstrated greater and clinically meaningful Hba1c reduction with lower incidence of hypoglycemia. Tirzepatide had no association with increased CV risk.

- SURPASS 3: evaluated efficacy and safety of 3 doses (5mg, 10mg, and 15mg) of tirzepatide versus once-daily insulin degludec as add-on to metformin with or without SGLT-2i in patients with type 2 diabetes

Baseline Hba1c 7%-10.5%

Primary endpoint: non-inferiority in Hba1c change at 52 weeks

Superiority of ALL doses of tirzepatide vs degludec in mean change Hba1c and body weight

Hba1c < 7 – 82% to 93%***

Body weight change -7.5kg to -12.9kg vs increase 2.3kg degludec

- SURPASS 5: evaluated the efficacy and safety of 3 doses (5mg, 10mg, and 15mg) of tirzepatide as an add-on to insulin glargine compared to placebo

Primary endpoint: mean change in baseline Hba1c at week 40
Key secondary: mean change in body weight; % of patients achieving Hba1c level

-2.1% 5mg tirzepatide, -2.4% 10mg tirzepatide, -2.3% tirzepatide 15mg, -0.86% placebo
Mean body weight Δ:
-5.4kg – 5mg
-7.5kg - 10mg
-8.8kg – 15mg
+1.6kg – placebo

- SURPASS CVOT

A Study of Tirzepatide Compared With Dulaglutide on Major Cardiovascular Events in Participants With Type 2 Diabetes (SURPASS-CVOT)

Phase 3 trial
13,299 participants
Randomized to dulaglutide once weekly or tirzepatide once weekly (? doses)
Primary outcome: time to first occurrence of component event of MACE – 3
Secondary outcomes: numerous

Estimated completion date Oct 17, 2024

- SURPASS 2: evaluated efficacy and safety of 3 doses (5mg, 10mg, and 15mg) of tirzepatide versus semaglutide once weekly in patients with T2DM in patients inadequately controlled with metformin monotherapy

40 week
1:1:1:1 – tirzepatide 5mg, 10mg, or 15mg vs semaglutide 1mg
Baseline Hba1c 8.28%
Mean weight 93.7kg
Primary endpoint: change in Hba1c level from baseline to 40 wks
Key secondary: change body weight from baseline, Hba1c targets < 7% and <5.7%

- SUSTAIN FORTE- Efficacy and safety of once-weekly semaglutide 2·0 mg versus 1·0 mg in patients with type 2 diabetes

- GLP1-RA AND DKD
  ELIXA 2015
  LEADER 2016
  SUSTAIN-6 2016
  EXSCEL 2017
  HARMONY 2018
  AWARD-7 2018
  REWIND 2019
  PIONEER 6 2019
  AMPLITUDE-O 2021

    - GLP-1 RA- suggested nephroprotective mechanisms

Indirect effects
Lowering of hyperglycemia
Reduction in body weight, blood pressure, and dyslipidemia

Potential direct mechanisms
Inhibition of oxidative stress and inflammation
Induction of natriuresis
Reduction of intraglomerular pressure

Kidney Disease: Improving Global Outcomes (KDIGO) 2020 clinical practice guidelines recommend GLP-1 RA as an option for patients with DKD who have not achieved their glycemic target or as an alternative for patients unable to tolerate metformin or an SGLT-2i

    - FLOW trial – evaluate the effect of once-weekly semaglutide on progression of renal impairment

Will be the first study to investigate effects of GLP-1 RA on primary kidney outcomes
Estimated completion date 2024
3000 patients with T2DM and moderate/advanced CKD and albuminuria
Primary renal outcome:
Persistent ≥ 50% reduction in eGFR or a persistent eGFR ≤ 15 mL/min/1.73m2, initiation of RRT, or death from kidney disease or CVD

    - SOUL trial – CVOT to evaluate the hypothesis that oral semaglutide lowers the risk of CV events in T2DM patients at high risk for CVD

Composite renal endpoint is a secondary outcome: persistent ≥50% reduction in eGFR or a persistent eGFR < 15mL/min/1.73m2, initiation of RRT, and renal death.

- SGLT-2i Updates

Not much has changed from a diabetes aspect – ADA SOC continues to indicate use in patients with CKD/CHF/CAD, however we have seen changes in level of acceptable eGFR use.

We continue to see evolution in use for patients with CHF (with or without T2DM) and CKD (with or without T2DM), and acute hospitalization for heart failure.

The glycemic efficacy of SGLT-2i is dependent on glomerular filtration and is attenuated in patients with more advanced CKD.
The glucose-lowering effect of SGLT2 inhibitors is attenuated in patients with eGFR <60 ml/min per 1.73 m2 and minimal when eGFR is <30 ml/min per 1.73 m2
Keep in mind, we know SLGT-2i are safe and efficacious for management and prevention of CKD, however we do not anticipate to see similar glycemic efficacy from the SGLT-2i class in patients with lower eGFR levels.

- Indications:

Glycemic control/metabolic risk , Reduction is ASCVD, Heart failure, DKD with albuminuria, and Nondiabetic CKD with albuminuria

- Glycemic control

T2DM
Can be indicated first line for glycemic control

eGFR ≥ 60 mL/min/1.73m2
Hba1c reduction 0.6% to 1%

eGFR; 45-59 mL/min/1.73m2
Hba1c reduction 0.3% to 0.5%

eGFR
Hba1c reduction is minimal

- CHF

NYHA class II-IV
Elevated NT proBNP
All ejection fractions

eGFR > 20 mL/min/1.73m2

Reduction in ASCVD
T2DM
Established ASCVD or high risk for ASCVD

eGFR ≥ 30 mL/min/1.73m2

- DKD/T2DM

eGFR ≥ 25 mL/min/1.73m2
UACR 200-5000 mg/gb

- Non-DM CKD

Etiology of CKD:
Ischemic nephropathy
IgA nephropathy
FSGS
Chronic pyelonephritis
Chronic interstitial nephritis

eGFR ≥ 25 mL/min/1.73m2
UACR 200-5000 mg/gb

- Potential MOAs of SGLT-2i in cardio-renal risk reduction

Weight loss
Anti-hypertensive effect
Glycosuria accompanied osmotic diuresis decreased intravascular volume
SGLT-2 inhibitors decrease sodium re-absorption in the proximal tubal

⇩ oxidative stress
⇩ fibrosis induction
⇩ local inflammation
⇩ tubular senescence
⇩ glomerular damage

- SGLT-2i – Effect of Hyperketonemia on Cardiac Efficacy in Patients with Heart Failure and Type 2 Diabetes

Two groups of T2DM and HFrEF (LVEF < 45%) were studied (12 per group)

Group 1
6h beta-hydroxybutyrate infusion (BOHB)
vs
6h HCO3 infusion (control)
Group 2
3h BOHB infusion at a higher rate

Results: in both groups, BHOB infusion significantly increased CO, stroke volume, and ejection fraction; NaHCO3 infusion had no effect on CO, SV, or EF. Myocardial glucose uptake was not altered by BOHB.

- ADA Standards of Care 2023 - Section 9. Pharmacologic Approaches to Glycemic Treatment: Pharmacologic Approaches to Glycemic Treatment

Recommendation 9.4b was added to indicate that in adults with type 2 diabetes and established/high risk of atherosclerotic cardiovascular disease, heart failure, and/or chronic kidney disease, the treatment plan should include agents that reduce cardiorenal risk.

Recommendation 9.4c was added to address the consideration of pharmacologic approaches that provide the efficacy to achieve treatment goals.

Recommendation 9.4d was added to address weight management as an impactful component of glucose-lowering management in type 2 diabetes

- Finerenone – nonsteroidal, selective mineralocorticoid receptor antagonist
- FIDELO-DKD

Examine long-term effects on kidney and cardiovascular outcomes
Patients with T2DM and CKD
Eligible patients:
Urinary albumin-to-creatinine ratio of 30 to less than 300, an estimated eGFR of 25 to less than 60ml/min/1.73m2, and diabetic retinopathy
Urinary albumin-to-creatinine ratio of 300 to 5000 and an eGFR of 5 to less than 75ml/min/1.73m2
All patients treated with renin-angiotensin system blockade
Primary composite outcome: assessed in a time-to-event analysis, was kidney failure, a sustained decrease of at least 40% in the eGFR from baseline, or death from renal causes.
Key secondary composite outcome: assessed in a time-to-event analysis, was death from cardiovascular causes, nonfatal MI, nonfatal stroke, or hospitalization from heart failure

- FIGARO-DKD trial – Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease

Examined whether treatment with finerenone would lead to lower risks of cardiovascular events and death from cardiovascular causes among patients with either stage 2 to 4 CKD and moderately elevated albuminuria or stage 1 or 2 CKD with severe increased albuminuria
Eligible patients:
Urinary albumtin-to-creatinine ratio of 30 to less than 300 and an eGFR of 25 to 90 ml/min/1.73m2 (stage 2 or 4 CKD)
Urinary albumin-to-creatinine ratio of 300 to 5000 and an eGFR of at lest 60 ml/min/1.73m2 (stage 1 or 2 CKD)
Primary outcome:
Assessed in a time-to-event analysis – composite of death from cardiovascular causes, nonfatal MI, nonfatal stroke, or hospitalization from heart failure
Secondary outcome: composite of kidney failure, a sustained decrease from baseline of at least 40% in the eGFR, or death from renal causes.

- FIDELITY – Cardiovascular and Kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis

Conclusion: finerenone reduced the risk of clinically important cardiovascular and kidney outcomes vs placebo across the spectrum of CKD in patients with T2DM
Screening for albuminuria to identify at-risk patients among patients with T2DM facilitates reduction of both cardiovascular and kidney disease.

- ADA Standards of Care 2023 – CKD

10.43 was added to recommend the addition of finerenone in the treatment of individuals with type 2 diabetes and chronic kidney disease with albuminuria treated with maximum tolerated doses of ACE inhibitor or angiotensin receptor blocker

11.5a For people with type 2 diabetes and diabetic kidney disease, use of a sodium–glucose cotransporter 2 inhibitor is recommended to reduce chronic kidney disease progression and

cardiovascular events in patients with an estimated glomerular filtration rate ≥20 mL/min/1.73 m2 and urinary albumin ≥200 mg/g creatinine. A

11.5b For people with type 2 diabetes and diabetic kidney disease, use of a sodium–glucose cotransporter 2 inhibitor is recommended to reduce chronic kidney disease progression and cardiovascular events in patients with an estimated glomerular filtration rate ≥20 mL/min/1.73 m2 and urinary albumin ranging from normal to 200 mg/g creatinine. B

11.5c In people with type 2 diabetes and diabetic kidney disease, consider use of sodium–glucose cotransporter 2 inhibitors (if estimated glomerular filtration rate is ≥20 mL/min/1.73 m2), a glucagon-like peptide 1 agonist, or a nonsteroidal mineralocorticoid receptor antagonist (if estimated glomerular filtration rate is ≥25 mL/min/1.73 m2) additionally for cardiovascular risk reduction. A

11.5d In people with chronic kidney disease and albuminuria who are at increased risk for cardiovascular events or chronic kidney disease progression, a nonsteroidal mineralocorticoid receptor antagonist shown to be effective in clinical trials is recommended to reduce chronic kidney disease progression and cardiovascular events. A

- ADA Standards of Care 2023- pioglitazone

3.10 In people with a history of stroke and evidence of insulin resistance and prediabetes, pioglitazone may be considered to lower the risk of stroke or myocardial infarction. However, this benefit needs to be balanced with the increased risk of weight gain, edema, and fracture. A Lower doses may mitigate the risk of adverse effects. C

New recommendation based off of an old(er) study: Pioglitazone after Ischemic Stroke or Transient Ischemic Attack – (IRIS trial – "Insulin Resistance Intervention After Stroke"

3876 patients – recent ischemic stroke or TIA – (+)insulin resistance (HOMA >3.0)
Randomized to pioglitazone or placebo
Exclusion criteria: HF, DM
Primary outcome: fatal or nonfatal stroke or MI– pioglitazone 24% RRR
Secondary outcome: progression to DM – 52% RRR

- EMPRISE study – Effectiveness and Safety of empagliflozin in routine care patients: results from the EMPagliflozin comparative effectiveness and SafEty study

Study looking to evaluate the beneficial effects of empagliflozin in routine clinical care in head-to-head comparisons with alternative glucose-lowering medications, particularly in patients without established CVD.

Included nearly 40,000 routine-care patients with T2DM
Provides nearly ten times larger than the population enrolled in the EMPA-REG OUTCOME trial – provides clinically relevant findings that complement available evidence from RCTs

Empagliflozin associated with 37-52% decreased risk of HHF compared with DPP-4i
Similar risk of MI or CVA (independent of the presence or established CVD at baseline)
Empagliflozin vs DDP-4i associated with reduction in the risk of all-cause mortality

Empagliflozin vs DPP-4i was associated with a similar risk of LLA and fractures, a 71% increased risk of DKA, and a 38-40% decreased risk of AKI
Findings were consistent in sensitivity and analyses and subgroup analyses of patients with and without history of established cardiovascular disease.

- Teplizumab – anti-CD3 monoclonal antibody

FDA approval November 17, 2022 as the first disease-modifying therapy for impeding progression of T1DM
Approved to delay the onset of stage 3 T1DM in adults and pediatric patients 8 yrs of age and older who currently have stage 2 T1DM

Administered by IV infusion once daily for 14 days
Expected to cost in the region of $200,000 for the course of treatment
COMPASS program -- helps navigate insurance reimbursement +/- financial assistance

Various modalities for screening under investigation – labs, who, etc.

Phase 2 trial, published in the NEJM in August 2019: An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes
involving relatives of patients with type 1 diabetes who did not have diabetes but were at high risk for development of clinical disease
14 day course of teplizumab vs placebo
follow-up for progression to clinical type 1 diabetes was performed with the use of oral glucose-tolerance tests at 6-month intervals
Median time to diagnosis: 48.4 months teplizumab group, 24.4 months placebo
Annualized rates of diabetes were 14.9% per year teplizumab 35.9% per year placebo

Currently evaluating teplizumab in patients with newly diagnosed insulin-dependent T1D in the global PROTECT (PROvention T1D trial Evaluating C-peptide with Teplizumab) Phase 3 study (NCT03875729). This randomized, double-blind, placebo-controlled, multicenter trial will enroll 300 patients with recent onset T1D who will be randomized 2:1 to either two 12-day cycles of teplizumab (IV) or placebo. The primary efficacy endpoint is C-peptide change. Secondary endpoints include insulin use, HbA1c, hypoglycemic episodes, and safety.

- Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

- American Diabetes Association (ADA) Standards of Care in Diabetes

Available December 2022; published January 2023
Updated annually

Focus on screening, diagnostic, and therapeutic actions

The annual Standards of Care supplement to Diabetes Care contains the official ADA position, is authored by the ADA, and provides all of the ADA's current clinical practice recommendations.

- Diabetes Technology

The American Diabetes Association (ADA) defines diabetes technology as a term used to describe the hardware, devices, and software that people with diabetes use to assist with self-management; this ranges from lifestyle modifications to glucose monitoring and therapy adjustments.
Insulin administration
Syringe/pen/pump/smart pen/insulin delivery device
Glucose monitoring
SMBG with accuchecks vs continuous glucose monitoring (CGM)
Automated insulin delivery systems (AID)
where CGM-informed algorithms modulate insulin delivery

7.1 – type(s) and selection of devices should be individualized based on a person's specific needs, preferences, and skill level

7.8 – be aware of differences in accuracy among blood glucose meters; only FDA approved glucometers with proven accuracy should be used, with unexpired strips purchased from a pharmacy or licensed distributor

7.10 – Health care professionals should be aware of medications and other factors, such as high-dose vitamin C and hypoxemia, that can interfere with glucose meter accuracy and provide clinical management as indicated.

7.12 – Real-time continuous glucose monitoring (A) or intermittently scanned continuous glucose monitoring (C) should be offered for diabetes management in adults with diabetes on basal insulin who are capable of using the devices safely (either by themselves or with a caregiver).
7-.19 – CGM users should be educated on potential interfering substances and other factors that may affect accuracy.

Continuous glucose monitoring devices interfering substances (inserted table)

- DEXCOM G7

Cleared by the FDA for approval 12/2022
Approved for all persons with diabetes age 2 years or older
Currently not cleared by FDA for integrated use with pump technology for AID systems

What's new??
60% smaller (less waste)
30 minute sensor warm-up (fastest, vs 1h or longer)
12h grade period to replace finished sensors (more seamless transitions)
Redesigned and simplified mobile app (with Dexcom Clarity integration)
Improved alert settings (enhanced discretion)
Optional receiver (smaller, but more vibrant and easier to read display)
Wear
Back of arm: ages 2 years and older
Upper buttocks: ages 2-17 years old

- FREESTYLE LIBRE 3

Realtime glucose readings sent every minute to your smart phone (no reader device, no scanning needed) (see compatibility guide for compatible smart phone technology)
Freestyle libre 3 app

Freestyle libre 3 app – voice accessibility for the visually impaired

Most accurate

Smallest/thinnest/most discrete
 smaller than 2 stacked pennies
Optional, real time glucose alarms
33 ft unobstructed reading device

- OMNIPOD 5

Automated insulin delivery system
Integrates with Dexcom G6
Approved for T1DM age 2 yrs and older
Uses compatible smartphone
Up to 3d (72h) continuous insulin delivery

Omnipod 5 app
Or free controller (can use if smart phone not compatible)
Build in SmartAdjust technology
Dexcom G6 CGM sold separately
Dexcom G6 mobile app
Dexcom G6 receiver not compatible

Smart Adjust technology, Omnipod 5, and the Dexcom G6 CGM are in constant communication, enabling automatic insulin adjustments to help improve time in range (TIR).

What's new?

SmartAdjust technology – q 5 mins, the system automatically increases, decreases, or pauses insulin delivery based on your customized target glucose.

Activity feature – reduces insulin deliver when glucose typically go slow, like when exercising

SmartBolus Calculator – only AID system with a built-in bolus calculator that automatically incorporates your CGM data and trend

- MEDTRONIC MINIMED 780G SYSTEM

Self-adjusting basal insulin pump system with new autocorrection dosing.

Three components:
Insulin pump
Receives data from CGM every 5 minutes
Makes automatic adjustments and correction to insulin delivery

MiniMed Mio Advance Infusion set
Designed with a preloaded inserter
Quicker, easier set changes with fewer steps
Can be inserted with one hand

Continuous glucose monitor – Guardian Sensor 3
Measures glucose values 288 times per day, every 5 minutes
Sends values automatically to your insulin pump

What's new?

SmartGuard technology
system continuously anticipates insulin needs, adjusts insulin delivery and corrects highs automatically*, while helping to protect you from lows

MiniMed Mobile app
Data can be viewed on smartphone
Most IOS and Android devices

CareLink Connect app
Can choose to share data with care partners

Accu-chek Guide Link blood glucometer
Sent wirelessly to pump for sensor calibrations

- Wearable insulin patches

- CeQur Simplicity Device

?FDA approval 2021
3 day wearable insulin patch
For T1DM or T2DM on MDI
Removes mealtime insulin dosing barriers
Convenient/discreet/injection free way to deliver mealtime and correction boluses

Up to 200 units rapid acting insulin
One click administers 2 units of insulin

Thin: < 4 stacked quarters
Compact: 65 x 36mm
Lightweight: 10gm

- Compared to: V-Go wearable insulin delivery device….

Provides basal insulin (20u/30u/40u) and on-demand blousing in 2 unit increments
(only has 36 units of insulin available for bolus)

- What's to come? -- Effect Of Once-Weekly Semaglutide on Weight Change and Metabolic Control in People with Type 1 Diabetes—Six-Months Results from the Real-World STEMT Trial

Real-world exploratory study looking at the effect and safety of semaglutide in patients with T1DM.
Semaglutide 1mg once-weekly was started in adults with T1DM and overweight/obesity

Body weight evolution
-8.5 +/- 7.8kg
Range +1.5 and-24.7kg
Hba1c reduction -0.3 +/- 0.7%
30% - had no Hba1c reduction
35% of cases had >0.5% reduction

Adding semaglutide 1.0 mg once-weekly in people with T1D was safe, well-tolerated and resulted in promising effects on weight, insulin requirement and glycemic control.

- What's to come? – SGLT-2i for T1DM?

May 2018 - The Potential Role of SGLT2 Inhibitors in the Treatment of Type 1 Diabetes Mellitus
Henry and colleagues (2015)
Canagliflozin
Dandora (2017) (DEPICT 1)
dapagliflozin
Garg (September 2017) (inTandem 3)
Sotagliflozin

October 2018 - Empagliflozin as Adjunctive to Insulin Therapy in Type 1 Diabetes: The EASE Trials

February 2021 (online) -Efficacy and safety of the SGLT2 inhibitor dapagliflozin in type 1 diabetes: A meta-analysis of randomized controlled trials

June 2022 - Automated Insulin Delivery with SGLT2i Combination Therapy in Type 1 Diabetes
Empagliflozin 5mg, etc

- What's to come? - Clinical and Safety Outcomes With GLP-1 Receptor Agonists and SGLT2 Inhibitors in Type 1 Diabetes: A Real-World Study

Published in The Journal of Clinical Endocrinology and Metabolism – October 2022

Aimed to determine the efficacy and safety of GLP-1RAs and sodium-glucose SGLT2is in the management of T1DM in real-world practice.

After 1 year.
GLP1-RA: statistically significant decrease in weight, Hba1c, and TDD insulin
SGLT-2i: statistically significant decrease in Hba1c and basal insulin dose

GLP1-RA > SGLT-2i with weight reduction
Hba1c decrease – comparable between the two
Discontinuation due to adverse events: 26.9% GLP-1 RA and 27.7% SGLT-2i

- What's to come? – once weekly basal insulin – literature and timeline – where are we?

July 2021 - Switching to Once-Weekly Insulin Icodec Versus Once-Daily Insulin Glargine U100 in Type 2 Diabetes Inadequately Controlled on Daily Basal Insulin: A Phase 2 Randomized Controlled Trial

October 2022 – once weekly basal insulin submitted to FDA following successful phase 3 trials

Six-part ONWARDS phase 3 trial
ONWARDS 5 - reached its primary endpoint with Icodec demonstrating non-inferiority in reducing hemoglobin A1C (HbA1c) in patients with type 2 diabetes (T2D) at week 52 in comparison to once-daily basal insulin analogs
May 2021 - Once Weekly Basal Insulin Fc (BIF) is Safe and Efficacious in Patients with Type 2 Diabetes Mellitus (T2DM) Previously Treated With Basal Insulin

Estimated completion May 2024 -- A Phase 3, Multicenter, Randomized, Parallel-Design, Open-Label Trial to Evaluate the Efficacy and Safety of LY3209590 Compared With Insulin Degludec in Participants With Type 2 Diabetes Currently Treated With Basal Insulin (QWINT-3)
What's to come? - A Research Study to See How Well the New Weekly Medicine IcoSema, Which is a Combination of Insulin Icodec and Semaglutide, Controls Blood Sugar Level in People With Type 2 Diabetes Compared to Insulin Glargine Taken Daily With Insulin Aspart (COMBINE 3)
680 participants
Once weekly IcoSema vs once daily insulin glargine with insulin aspart 2-4 times daily
Primary outcome: change in Hba1c at 52 weeks
Numerous secondary outcomes
Estimated completion date – primary September 2023, secondary November 2023

- What's to come? - Stem Cell–Derived, Fully Differentiated Islet Cells for Type 1 Diabetes

First patient-administered VX-880, an investigational allogeneic stem cell–derived, fully differentiated, pancreatic islet cell replacement therapy

64 y/o male, h/o T1DM x 40 years
c/b hypoglycemic unawareness
Baseline: Hba1c 8.6%, undetectable fasting and stimulated Cpeptide

Single VX-880 infusion at ½ target dose
Fasting Cpeptide was detected by Day 29 and increased rapidly
In parallel, Hba1c and daily insulin decreased
Day 90 – robust increases in fasting and stimulated Cpeptide, improved glycemic control, and a substantial reduction in exogenous insulin administration
Most adverse events were mild to moderate and consistent with immunosuppression