# **Tirzepatide for Type 2 Diabetes: Effectiveness and Value**

Public Meeting — January 20, 2022



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### **Clinical and Patient Experts**

- Sarah Kim, MD, Associate Clinical Professor, University of California San Francisco
  - No conflicts of interest to disclose.
- Joanna Mitri, MD, MS, Medical Director, Global Education and Care Division Joslin Diabetes Center, Assistant Professor, Harvard Medical School
  - Dr. Mitri has received manufacturer support of research in the clinical area of this meeting, and her institution conducts clinical trials and educational programs that may be supported by health care companies. A household member of Dr. Mitri's has received consulting fees from health care companies including AbbVie, Roche, Janssen Pharmaceuticals, Pharmacyclics, and BeiGene.
- Lizzette Cambron, PhD Type 2 Diabetes Patient and Advocate
  - No conflicts of interest to disclose.
- Liz Leff, Senior Corporate Relations Director, National Kidney Foundation
  - The National Kidney Foundation receives less than 25% of its funding from pharmaceutical manufacturers, including from Novo Nordisk and the BI-Lilly Diabetes Alliance.



#### Why are we here today?

""[My biggest fear about having diabetes] is complications...I'm so concerned about kidney issues, heart disease. My fear is not necessarily living with diabetes forever, it's making sure I manage it well enough to keep complications as manageable as possible, and losing mobility is my absolute biggest fear. I worry about it all the time."

Patient with Type 2 Diabetes

# Why Are We Here Today?

- What happens the day these treatments are approved by the FDA?
- Patients can have difficulty accessing drugs
  - Coverage eligibility
  - Costs (out-of-pocket and insurance premiums)
- What happens others in the health care "system"?

#### **The Impact of Rising Health Care Costs**

#### Leonard Edloe Richmond, Virginia

The Whitman family Bird City, Alaska

#### The Maccoux family Brooklyn Park, Minnesota





# **Organizational Overview**

- New England Comparative Effectiveness Public Advisory Council
- The Institute for Clinical and Economic Review (ICER)





ICER Policy Summit and non-report activities only



# How was the ICER report developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Washington cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - Todd Boudreaux, Director of Publishing, Beyond Type 1
    - Beyond Type 1 receives 3.5% of it's funding from Eli Lilly and 1% from Novo Nordisk
  - Joanna Mitri, MD, MS, Medical Director, Global Education and Care Division Joslin Diabetes Center, Assistant Professor, Harvard Medical School
    - Dr. Mitri has received manufacturer support of research in the clinical area of this meeting, and her institution conducts clinical trials and educational programs that may be supported by health care companies. A household member of Dr. Mitri's has received consulting fees from health care companies including AbbVie, Roche, Janssen Pharmaceuticals, Pharmacyclics, and BeiGene.
  - Hui Shao, MD, PhD, Assistant Professor, Pharmaceutical Outcomes and Policy Department, University of Florida
    - Dr. Shao holds a position with BRAVO4Health LLC which receives more than 25% of its funding from health care companies, including Sanofi and AstraZeneca.
- How is the evidence report structured to support NE CEPAC voting and policy discussion?

#### Value Assessment Framework: Long-Term Value for Money

**Special Social/Ethical Priorities** 

**Benefits Beyond "Health"** 

**Total Cost Overall** Including Cost Offsets

Health Benefits: Return of Function, Fewer Side Effects

> Health Benefits: Longer Life



# Agenda

Time (ET)	Activity
10:00 AM	Meeting Convened and Opening Remarks
10:20 AM	Presentation of the Evidence
11:00 AM	Presentation of the Economic Model
11:40 AM	Public Comments and Discussion
12:05 PM	Lunch
12:50 PM	New England CEPAC Panel Deliberation and Vote
1:50 PM	Break
2:00 PM	Policy Roundtable Discussion
3:30 PM	Reflections from New England CEPAC Panel
4:00 PM	Meeting Adjourned

# **Presentation of the Clinical Evidence**

Grace A. Lin, MD

Medical Director, Health Technology Assessment, ICER

Associate Professor of Medicine and Health Policy, University of California, San Francisco



### **Key Collaborators**

- Dmitriy Nikitin, Research Lead, Evidence Synthesis, ICER
- Serina Herron-Smith, Research Assistant III, Evidence Synthesis, ICER
- Foluso Agboola, Vice President of Research, ICER

Disclosures:

Grace Lin received funding from ICER for this report



#### **Prevalence and Economic Impact of Type 2 Diabetes (T2DM)**



Adapted from: https://www.cdc.gov/diabetes/library/socialmedia/infographics/diabetes.html

#### **Standard of Care and Management of T2DM**



ASCVD: atherosclerotic cardiovascular disease, CKD: chronic kidney disease, CV: cardiovascular, CVD: cardiovascular disease, GLP-1 RA: glucagon-like 1 receptor agonist, HF: heart failure, SGLT-2i: sodium glucose transport protein 2 inhibitor, DPP-4i: dipeptidyl-peptidase 4 inhibitor, TZD: thiazolidinedione, SU: sulfonylurea



American Diabetes Association; 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2021. Diabetes Care 1 January 2021; 44 (Supplement\_1): S111–S124. https://doi.org/10.2337/dc21-S009

# **Scope of Review**

- Scope: Clinical and cost effectiveness of adding tirzepatide to background therapy
- Patient population: Adult patients with T2DM with inadequate glycemic control despite current treatment with antihyperglycemic agent(s)

#### Comparators:

- Background therapy (metformin +/- sulfonylureas or thiazolidinediones) alone
- Injectable semaglutide (Ozempic<sup>®</sup>) + background therapy
- Empagliflozin (Jardiance<sup>®</sup>) + background therapy

#### **Tirzepatide: Mechanism of Action**

- Novel dual GIP and GLP-1 receptor agonist
- Once weekly injectable (5, 10, or 15 mg)
- FDA decision expected in mid-2022



Baggio, L. L., & Drucker, D. J. (2021). Glucagon-like peptide-1 receptor coagonists for treating metabolic disease. Molecular metabolism, 46, 101090.



GLP-1: Glucagon-Like Peptide 1, GIP: Glucose-dependent insulinotropic polypeptide

# **Insights from Discussions with Patients**

- T2DM has substantial impact on daily life
  - Challenges with managing diet, blood glucose, and T2DM comorbidities
  - Stigma surrounding diagnosis
- Unmet need for comprehensive and culturally tailored education
- Affordability
  - Testing supplies, especially continuous glucose monitoring
  - Medication costs are substantial, even with insurance



# **Clinical Evidence**

### **Tirzepatide Key Trials (Intermediate Outcomes)**

Trial	Key Trial Characteristics	Baseline Population Characteristics	Key Outcomes	
Tirzepatide vs Background Therapy (Frias 2018)	Phase 2b trial, N=316 26 weeks	Mean age 57 years 47% female, 80% white HbA1c 8.1% BMI 32.6 kg/m <sup>2</sup>	Change from baseline	
Tirzepatide vs Background Therapy (Frias 2020)	Phase 2 trial, N=111 12 weeks	Mean age 57.4 years 40.5% female HbA1c 8.4% BMI 31.9 kg/m <sup>2</sup>	Change in body weight (kg) Change in LDL (mg/dL) Change in SBP (mmHg)	
Tirzepatide vs Injectable Semaglutide (SURPASS-2)	Phase 3 trial, N=1878 40 weeks	Mean age 56.6 years 53% female, 82.6% white HbA1c 8.3% BMI 34.2 kg/m <sup>2</sup>	Quality of life Harms	

BMI: Body Mass Index, HbA1c: Hemoglobin A1c/glycosylated hemoglobin, kg: kilogram, LDL: low density lipoprotein, m: meter, mg/dL: milligram per deciliter, SBP: systolic blood pressure



#### **Network Meta-Analysis**



### **Cardiovascular Outcomes Trials**

Trial	Key Trial Characteristics	Baseline Population Characteristics	Key Outcomes
Tirzepatide vs Insulin glargine (SURPASS-4)	Cardiovascular safety trial N=1995 Median follow-up 85 weeks	Mean age 64 years 38% female 82% white HbA1c 8.5%	MACE-4 (CV death, MI, stroke, CV hospitalization)
Injectable Semaglutide vs Placebo (SUSTAIN-6)	Cardiovascular outcomes trial N=3297 Median follow-up 2.1 years	Mean age 64.6 years 39.3% female 83% white HbA1c 8.7%	MACE-3 (CV death, nonfatal MI or stroke)
Empagliflozin vs Placebo (EMPA-REG-OUTCOME)	Cardiovascular outcomes trial N=7020 Median follow-up 3.1 years	Mean age 63.1 years 28% female 72% white HbA1c 8.1%	MACE-3 (CV death, nonfatal MI or stroke)

HbA1c: Hemoglobin A1c/glycosylated hemoglobin, MACE-3: 3-point major adverse cardiovascular event, MACE-4: 4-point major adverse cardiovascular event, mg/dL: milligram per deciliter, MI: myocardial infarction

# **Tirzepatide versus Background Therapy (BT)**

• Tirzepatide showed decreases in intermediate outcomes in both the Phase 2 trial and Network Meta-Analysis (NMA)

#### **Estimated Treatment Difference Tirzepatide versus Background Therapy**

Tirzepatide 15 mg	Frias 2018 (26 weeks)	NMA results (40 weeks)
HbA1c	-2.5%*	-1.7%*
Weight	-10.9 kg*	-9.5 kg*
LDL	-11.6 mg/dL	-4.3 mg/dL*
SBP	-2.7 mmHg	-7.5 mmHg*

HbA1c: Hemoglobin A1c/glycosylated hemoglobin, kg: kilogram, LDL: Low density lipoprotein cholesterol, mg/dL: milligram per deciliter, mmHg: millimeter mercury, SBP: Systolic blood pressure \*Statistically significant change



#### **Tirzepatide versus Semaglutide (SURPASS-2) Outcomes**



- Majority of participants on tirzepatide 15 mg (86%) and semaglutide 1 mg (79%) achieved HbA1c ≤ 7.0%
- Almost half of participants on tirzepatide 15 mg achieved HbA1c
  < 5.7% (46% vs 19% semaglutide)</li>

#### **Tirzepatide versus Semaglutide (SURPASS-2) Outcomes**

Estimated treatment difference at 40 weeks		
Weight	- 5.5 kg*	
LDL	+ 1.2 mg/dL	
SBP	- 2.9 mmHg*	

kg: kilograms, LDL: low density lipoprotein, mg/dL: milligram per deciliter, mmHg: millimeter mercury, SBP: systolic blood pressure \*Statistically significant change

- Majority of participants lost at least 5% of body weight on tirzepatide 15 mg (80% vs 54% semaglutide)
  - More participants lost ≥15% of body weight vs semaglutide (36% vs 8%)

#### **Patient-Reported Outcomes**

- Treatment with 15 mg of tirzepatide resulted in better overall quality of life\* than semaglutide across several quality-of-life measures, including:
  - Diabetes Treatment Satisfaction Questionnaire change version (DTSQc)
  - EQ-5D-5L (index score)
  - EQ-5D-5L visual analogue scale (VAS)
  - Impact of Weight on Quality of Life-Lite Clinical Trials Version (IWQOL-Lite-CT)

\*Data provided by manufacturer as academic-in-confidence



## **Tirzepatide versus Empagliflozin**

 Network meta-analysis of tirzepatide 15 mg versus empagliflozin 25 mg using five Phase 3 trials

Estimated Treatment Difference at 40 weeks		
HbA1c	- 1.1%*	
Weight	- 7.2 kg*	
LDL	- 7.5 mg/dL*	
SBP	- 2.6 mmHg*	

HbA1c: Hemoglobin A1c/glycosylated hemoglobin, kg: kilogram, LDL: Low density lipoprotein cholesterol, mg/dL: milligram per deciliter, mmHg: millimeter mercury, SBP: Systolic blood pressure

\*Statistically significant change using 95% credible interval from NMA

#### **Cardiovascular and Renal Outcomes**

Trial	Comparator	MACE-3 or -4 HR (95% CI)	All-Cause Mortality	New or Worsening Nephropathy HR (95% CI)
Tirzepatide (SURPASS-4)	Insulin glargine	0.74 (0.51-1.08)	0.70 (0.42-1.17)	NR
Semaglutide (SUSTAIN-6)	Placebo	0.74* (0.58-0.95)	1.05 (0.74-1.50)	0.64* (0.46-0.88)
Empagliflozin (EMPA-REG- OUTCOME)	Placebo	0.86* (0.74-0.99)	0.68* (0.57-0.82)	0.61* (0.53-0.70)

\*Statistically significant change

CI: confidence interval, HR: hazard ratio, MACE-3 or 4: 3 or 4-point major adverse cardiovascular event NR: not reported



#### Harms

Adverse Event	Tirzepatide 15 mg, % (N=470)	Semaglutide 1 mg, % (N=469)
Nausea	22.1	17.9
Diarrhea	13.8	11.5
Vomiting	9.8	8.3
Hypoglycemia (glucose ≤ 54 mg/dL)	1.7	0.4
Severe hypoglycemia	0.2	0
Injection-site reaction	4.5	0.2
Diabetic retinopathy	0	0
Death	0.9	0.2

mg: milligram, mg/dL: milligram per deciliter



### **Controversies and Uncertainties**

- Outcomes beyond glycemic control increasingly important
  - No definitive data yet for tirzepatide on CV or renal outcomes (CVOT ongoing)
- Long-term safety with new mechanism of action (dual GLP-1/GIP receptor agonism) unknown
- Lack of head-to-head trials for tirzepatide versus empagliflozin
- Minority populations underrepresented in clinical trials



#### **ICER Health Improvement Distribution Index Overview**

- T2DM disproportionately affects minority populations
  - Health Improvement Distribution Index (HIDI): quantifies an opportunity for effective and accessible treatments to achieve proportionately greater health gains within identified subpopulations.
  - For example, Hispanic Americans who have access to effective T2DM therapy may gain 20% more health compared to a representative sample of Americans.

Subgroup	HIDI
American Indian/Alaska Native	1.4
Asian Indian	1.2
Hispanic	1.2
Black	1.1



#### **Potential Other Benefits and Contextual Considerations**

- Prevention or delay of microvascular and macrovascular complications
  - May allow for greater work or educational productivity
  - May lessen caregiving burden over the lifetime
- Delivery device may be preferred by some patients compared with the delivery device of other GLP-1 RAs



# **Public Comments Received**

- "Limited indirect comparative data [tirzepatide versus empagliflozin] increases the uncertainty of NMA based treatment effects"
  - Role in therapy for SGLT-2i and GLP-1 RA overlap
- "Evaluating empagliflozin solely on its merits of a glucose lowering T2DM agent without accounting for its established CV benefits underestimates the value of empagliflozin"
  - Evaluation of CV and renal benefits of empagliflozin in patients with T2DM is accounted for in report & evidence rating
- "Evaluating the effect of T2DM treatment must consider the impact on comorbid conditions, such as CVD and renal disease"
  - Report evaluated data available at the time, which was more limited for tirzepatide than comparators



# Summary

- Tirzepatide has superior HbA1c and weight reduction versus comparators, changes in LDL and SBP are more modest
- No serious safety concerns from tirzepatide
- Without CVOT results, there is uncertainty around tirzepatide's impact on cardiovascular outcomes, though signals are promising



### **ICER Evidence Ratings**

Treatment	Comparator	Evidence Rating
	Background therapy	B+
Tirzepatide	Injectable semaglutide	C+
	Empagliflozin	C++




## **Tirzepatide for Type 2 Diabetes: Effectiveness and Value**

**Elizabeth D. Brouwer, PhD MPH** 

**Research Scientist** 

CHOICE Institute, University of Washington



#### **Key Review Team Members**

- Elizabeth D. Brouwer, PhD, MPH, Research Scientist, University of Washington
- Ryan Hansen, PharmD, PhD, Associate Professor, University of Washington
- Yilin Chen, PhD student, University of Washington

Disclosures:

Financial support was provided to the University of Washington from the Institute for Clinical and Economic Review.

University of Washington researchers have no conflicts to disclose defined as more than \$10,000 in health care company stock or more than \$5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.





Estimate the cost-effectiveness of tirzepatide as an add-on treatment to background therapy in people living with T2DM.



# **Methods in Brief**

#### **Methods Overview**

- **Model**: Patient-level microsimulation
- Setting: United States
- Perspective: Health Care Sector Perspective
- Time Horizon: Lifetime
- Discount Rate: 3% per year (costs and outcomes)
- Cycle Length: 1-year
- **Primary Outcome**: Cost per quality-adjusted life year (QALY) gained; cost per life year (LY) gained; cost per equal-value life-year (evLY) gained



### **Treatments Considered**

- Active therapies added to background therapy:
  - Tirzepatide
  - Injectable semaglutide
  - Empagliflozin
- Background therapy alone



#### **Patient Population**

- Patient cohort derived from the CDC's National Health and Nutrition Examination Survey (NHANES)
  - Three survey years included: 2013-14, 2015-16, 2017-18
- Cohort inclusion defined by:
  - Self-reported T2DM
  - T2DM Medications
- 387 unique patients with baseline clinical and demographic data





#### **ICER**

## **Model Characteristics**

- Microsimulation
  - Applied UKPDS-OM2 risk equations to a US population and adjusted risk equation outputs using hazard ratios from available long-term data
- Quality of life
  - Modeled using projected patient survival weighted by regression-based disutilities for each diabetes-related complication in each model cycle
- Costs
  - Included treatment costs (drug regimens, downstream treatment, supportive care) and costs associated with diabetes-related complications/events in each model cycle



## **Key Model Inputs: Efficacy Outcomes**

- Initial treatment efficacy measured as change after one year on treatment in following biomarkers:
  - HbA1c (%)
  - Weight (kg)
  - SBP (mmHg)
  - LDL (mmol/L)
- Change in biomarkers (point estimates and uncertainty estimates) for each active treatment versus background therapy alone derived from NMA described earlier in presentation
- After the first year, patients' HbA1c and weight (BMI) values progress over their simulated lifetime following published progression equations<sup>1</sup>



46

## **Key Model Assumptions**

- Patients discontinued add-on treatment at 9.1% in second model cycle<sup>1</sup>, contingent on successful treatment in first cycle
  - Those remaining on treatment after second cycle assumed to stay on therapy for life
- Ongoing background therapy (metformin and/or sulfonylureas) assumed the same for all comparators
- Insulin added to modeled active therapies if HbA1c exceeded 8.5%



## **Key Model Assumptions (continued)**

- Event risks were adjusted with trial-based CVO HRs for active therapy comparators in each model cycle (1-year)
  - Long-term outcome data informed MACE, heart failure, and nephropathy HRs for semaglutide and empagliflozin
  - Tirzepatide MACE outcomes were adjusted to reflect SURPASS-4, heart failure and nephropathy HRs were left unadjusted (HR=1) due to lack of long-term or in-class proxy data



## **Key Model Inputs: Drug Costs**

Drug	WAC per 30-Pill Bottle/Pen	Net Price Per 30-Pill Bottle/Pen	Discount From WAC	Annualized Treatment Cost
Tirzepatide*	(4 weekly doses)	(4 weekly doses)	-	-
<b>Semaglutide (Ozempic®)</b> 4 mg/3 mL pen (1 mg qw)	\$851.60 (4 weekly doses)	\$355.97 (4 weekly doses)	58.20%	\$4,644
Empagliflozin (Jardiance <sup>®</sup> ) 30-tablet bottle (25 mg qd)	\$548.54	\$107.51	80.40%	\$1,402
<b>Metformin</b> (1,000 mg qd)	\$0.83	-	-	\$10

mg: milligram, qd: daily, qw: weekly, WAC: wholesale acquisition cost

\*As a placeholder, we used the net price of Ozempic<sup>®</sup> (semaglutide), which is a once weekly injectable GLP-1; WAC pricing and discounts reflect the number of pen doses and quantity of pens necessary for Ozempic<sup>®</sup> use.

## **Key Model Inputs: Costs**

- Consistent health state cost values across treatments evaluated in model
- Costs applied for the year in which a complication occurred or for which there was a history of an event
  - Costs for multiple concurrent events or histories were applied additively
- Estimates based on published literature



## **Key Model Inputs: Utilities**

- Consistent health state utility estimates used across treatments evaluated in model
- A common baseline utility was assumed, and utility decrements were applied for the year in which a complication occurred and for patient history of each complication
- Regression-based estimates for T2DM complications
  - Regressions based on events as well as clinical and demographic characteristics
  - Multiple complications led to additive utility decrements



## Results

#### **Base-Case Results**

	Add-On Drug Cost		Total Cost (including background therapy and insulin)		QALYs		Life-years	
Treatment	Mean	95% CR	Mean	95% CR	Mean	95% CR	Mean	95% CR
Tirzepatide*	\$40,500	(\$38,200 - \$42,900)	\$306,200	(\$275,100 - \$338,600)	4.90	(4.68 – 5.12)	9.36	(8.91 – 9.83)
Injectable Semaglutide	\$41,200	(\$38,800 - \$43,500)	\$309,200	(\$280,000 - \$339,400)	4.85	(4.64 – 5.05)	9.53	(9.08 – 9.97)
Empagliflozin	\$12,000	(\$11,300 - \$12,700)	\$275,700	(\$247,600 - \$304,600)	4.60	(4.40 – 4.79)	9.17	(8.73 – 9.61)
Background Therapy	\$0	NA	\$261,800	(\$234,500 - \$290,800)	4.13	(3.95 – 4.33)	8.34	(7.93 – 8.77)

CR: credible range, NA: not applicable, QALY: quality-adjusted life-year

\* Using a placeholder price equal to the net price of semaglutide

#### **Base-Case Incremental Results**

Treatment	Comparator	Cost	per QALY Gained	Cost per Life Year Gained	
		Mean	95% Credible Range	Mean	95% Credible Range
Tirzepatide*	Injectable Semaglutide	Less Costly, More Effective	(-\$1,546,000 to \$1,384,000)	\$17,000	(-\$709,100 to \$633,700)
Tirzepatide*	Empagliflozin	\$101,000	(-\$54,800 to \$331,100)	\$160,000	(-\$950,700 to \$1,265,100)
Tirzepatide*	Background Therapy Alone	\$58,000	(\$10,900 to \$99,100)	\$44,000	(\$10,400 to \$82,500)

QALY: quality-adjusted life-year

\*Using a placeholder price equal to the net price of semaglutide

## **One Way Sensitivity Analyses**

- We performed OWSA to understand the impact of individual parameters on outcomes
- For tirzepatide vs injectable semaglutide, the parameters with the largest impact on total cost outcomes were treatment cost and hazard ratios
- For tirzepatide vs injectable semaglutide, the parameters with the largest impact on total QALYs were hazard ratios and insulin addition threshold



## **Scenario Analyses**

- We performed scenario analyses to understand the impact of certain model assumptions on incremental results, including:
  - Societal perspective, shortened time horizon, hazard ratio adjustment, insulin initiation point, and risk factor progression
- Key findings:
  - No analyzed scenario changed our core conclusions
  - Credible ranges for the incremental results in the base case and in each scenario ranged from approximately \$0 to \$100,000
  - Societal perspective, compared to the base-case health care perspective, led to lower ICER estimates for both QALYs and LYG (i.e. higher value)

#### Health Benefit Price Benchmarks (HBPB) for Tirzepatide

Annual HBPBs for Tirzepatide plus Background Therapy as Compared to Semaglutide plus Background Therapy

	Net Price per Unit	Annual Price to Achieve \$100,000 per Outcome	Annual Price to Achieve \$150,000 per Outcome	
Mean QALYs Gained	To be determined	\$5,500	\$5,700	

QALY: quality-adjusted life-year

\*Net price and wholesale acquisition cost for tirzepatide have not been publicly stated at the time of this report; equal value of life years gained were not reported given tirzepatide average life years were not greater than injectable semaglutide average life years.



#### Limitations

- Price and long-term outcome data for tirzepatide were unavailable at the time of this report; outcomes are based on a placeholder price.
- UKPDS-OM2 risk equations were developed for a different patient population and may not fully capture the impact of weight loss on CV and renal outcomes.



#### **Comments Received**

- UKPDS-OM2 not well-suited to assess newer therapies
  - Response: Applied trial-based HRs to outcomes where available; 2- and 3-year scenarios run to compare model outcomes to available cardiovascular outcome trials for external validity.
- Original assumptions regarding treatment discontinuation were not reflective of clinical practice
  - Response: Updated the model to life-long therapy, with insulin added when HbA1c >8.5%.
- Microsimulation model needed more transparency, via scenario analysis and more comprehensive outcomes
  - Response: Added scenarios with no risk factor progression for BMI and HbA1c, as well as disaggregated and undiscounted outcomes in the supplement. Also added more comprehensive OWSA outcomes.



### **Conclusions**

- Tirzepatide had the highest average lifetime QALYs of all considered therapies, however the 95% CRs for active comparators overlapped.
- No average increased survival when comparing tirzepatide with injectable semaglutide.
- Tirzepatide estimates are based on assumptions about long-term cardiovascular benefits that have not yet been demonstrated in clinical trials.
- When compared to injectable semaglutide, the estimated annualized Health Benefit Price Benchmark range for tirzepatide is \$5,500 to \$5,700.





# Manufacturer Public Comment and Discussion

#### Christian Nguyen, PharmD, MBA, MS Vice President Eli Lilly Value Evidence and Outcomes

#### Conflicts of Interest:

• Dr. Christian Nguyen is a full-time employee of Eli Lilly





#### Leo Seman, MD, PhD Medical Expert, Boehringer Ingelheim

#### Conflicts of interest:

• Dr. Leo Seman is a full-time employee of Boehringer Ingelheim Pharmaceuticals, Inc



#### Michael Radin, MD Executive Director, Diabetes Medical Affairs, Novo Nordisk, Inc.

Conflicts of Interest:

• Dr. Michael Radin is a full-time employee at Novo Nordisk





## Lunch

Meeting will resume at 12:50 PM



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# **Voting Questions**

1. Is the currently available evidence adequate to demonstrate that the net health benefit of <u>tirzepatide added</u> to background therapy is superior to that provided by background therapy alone?

A. Yes

B. No



2. Is the currently available evidence adequate to demonstrate that the net health benefit of <u>tirzepatide added</u> to background therapy is superior to that of adding injectable semaglutide (Ozempic<sup>®</sup>) to background therapy?

A. Yes

B. No



3. Is the currently available evidence adequate to demonstrate that the net health benefit of <u>tirzepatide added</u> to background therapy is superior to that of adding empagliflozin (Jardiance<sup>®</sup>) to background therapy?

A. Yes

B. No



Contextual Considerations and Potential Other Benefits or Disadvantages Please vote on the following contextual considerations:

When making judgments of overall long-term value for money, what is the relative priority that should be given to *any* effective treatment for type 2 diabetes on the basis of the following contextual considerations:

4. Acuity of need for treatment of individual patients based on shortterm risk of death or progression to permanent disability

- A. Very low priority
- B. Low priority
- C. Average priority
- D. High priority
- E. Very high priority

0	0	0	0	0	
Α.	В.	С.	D.	Ε.	2
Please vote on the following contextual considerations:

When making judgments of overall long-term value for money, what is the relative priority that should be given to *any* effective treatment for type 2 diabetes on the basis of the following contextual considerations:

## **5. Magnitude of the lifetime impact on individual patients of the condition being treated**

- A. Very low priority
- B. Low priority
- C. Average priority
- D. High priority
- E. Very high priority



Please vote on the following potential other benefits or disadvantages: What are the relative effects of tirzepatide added to background therapy versus injectable semaglutide (Ozempic®) added to background therapy on the following outcomes that inform judgment of the overall long-term value for money of tirzepatide?

6. Patients' ability to achieve major life goals related to education, work, or family life

- A. Major negative effect
- B. Minor negative effect
- C. No difference
- D. Minor positive effect
- E. Major positive effect



Please vote on the following potential other benefits or disadvantages: What are the relative effects of tirzepatide added to background therapy versus injectable semaglutide (Ozempic®) added to background therapy on the following outcomes that inform judgment of the overall long-term value for money of tirzepatide?

7. Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life

- A. Major negative effect
- B. Minor negative effect
- C. No difference
- D. Minor positive effect
- E. Major positive effect



Please vote on the following potential other benefits or disadvantages: What are the relative effects of tirzepatide added to background therapy versus injectable semaglutide (Ozempic®) added to background therapy on the following outcomes that inform judgment of the overall long-term value for money of tirzepatide?

- 8. Society's goal of reducing health inequities
- A. Major negative effect
- B. Minor negative effect
- C. No difference
- D. Minor positive effect
- E. Major positive effect



### Break

Meeting will resume at 2:00 PM



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## **Policy Roundtable**

#### **Policy Roundtable**

Participant	Conflict of Interest
Lizzette Cambron, PhD, Type 2 Diabetes Patient and Advocate	No conflicts of interest to disclose.
Mohammad Dar (MoDar), MD, Senior Medical Director, MassHealth	Mohammad Dar practices as an Internist in the VA Boston Healthcare system
Bonnie Donato, PhD, Executive Director, HEOR VDT CV-MET & Respiratory, Boehringer Ingelheim	Bonnie Donato is a full-time employee at Boehringer-Ingleheim
Sarah Kim, MD, Associate Clinical Professor, University of California San Francisco	No conflicts of interest to disclose.
Lizz Leff, Senior Corporate Relations Director, National Kidney Foundation	The National Kidney Foundation receives less than 25% of its funding from pharmaceutical manufacturers, including from Novo Nordisk and the BI-Lilly Diabetes Alliance.
<b>Joanna Mitri, MD, MS,</b> Medical Director, Global Education and Care Division Joslin Diabetes Center, Assistant Professor, Harvard Medical School	Joanna Mitri has received manufacturer support of research in the clinical area of this meeting, and her institution conducts clinical trials and educational programs that may be supported by health care companies. A household member of Dr. Mitri's has received consulting fees from health care companies including AbbVie, Roche, Janssen Pharmaceuticals, Pharmacyclics, and BeiGene.
William Riesner, Director	William Riesner is a full-time employee at Eli Lilly.
Katie Thompson, PharmD, Sr. Director, Formulary Solutions	A household member of Katie Thompson's works for Janssen.

# New England CEPAC Council Reflections

#### **Next Steps**

- Meeting recording posted to ICER website next week
- Final Report published on or around February 15, 2022
  - Includes description of New England CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: <u>https://icer.org/assessment/diabetes-type-2-</u> 2022/#timeline







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