Complimentary CME/CE

Adjusting Insulin in Patients With Dosing Concerns: Using Evolving Basal Insulins to Enhance Adherence

Provided by

Med-IQ

Activity Overview

In this case-based webcast, meet Jackie, a 62-year-old woman with type 2 diabetes. Her glycated hemoglobin (HbA1C) is 9.2%, and she is taking 2 oral agents and basal insulin; however, she does not want to take any additional injections and has a history of medication adherence issues. Faculty experts Vivian Fonseca, MD, and Timothy Reid, MD, discuss how they would approach this patient case scenario, including identifying an insulin treatment plan for Jackie that takes into account her concerns regarding dosing frequency and treatment adherence.

Target Audience

This activity is intended for family practice physicians, general practice physicians, internal medicine physicians, primary care physicians, nurse practitioners, physician assistants, and nurses.

Instructions to Receive Credit

To receive credit, read the introductory CME/CE material, watch the webcast, and complete the evaluation, attestation, and post-test, answering at least 70% of the post-test questions correctly.

Faculty

Vivian Fonseca, MD (*Co-Chair, Presenter*)
Professor of Medicine and Pharmacology
Assistant Dean for Clinical Research
Tullis Tulane Alumni Chair in Diabetes
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Tulane University Health Sciences Center
New Orleans, LA

Timothy S. Reid, MD (*Co-Chair, Presenter*)
Medical Director
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Disclosure Statement

The content of this activity has been peer reviewed and has been approved for compliance. The faculty and contributors have indicated the following financial relationships, which have been resolved through an established COI resolution process, and have stated that these reported relationships will not have any impact on their ability to give an unbiased presentation.

Faculty Disclosure Statements

Vivian Fonseca, MD
Consulting fees/advisory boards: Bayer HealthCare Pharmaceuticals, Boehringer-Ingelheim Pharmaceuticals, Inc.
Contracted research: Asahi Kasei Pharma Corporation, AstraZeneca, Eli Lilly and Company, Intarcia Therapeutics, Inc., Novo Nordisk, Sanofi Genzyme, Takeda Pharmaceuticals North America, Inc.

Timothy S. Reid, MD
Consulting fees/advisory boards: AstraZeneca, Intarcia Therapeutics, Inc., Janssen Pharmaceuticals, Inc., Novo Nordisk, Sanofi Genzyme
Fees received for promotional/non-CME activities: Janssen Pharmaceuticals, Inc., Novo Nordisk, Sanofi Genzyme

The peer reviewers and activity planners have no financial relationships to disclose.

Learning Objective

Upon completion, participants should be able to:

- Evaluate the potential benefits and limitations of long-acting basal insulin for patients with adherence-related challenges

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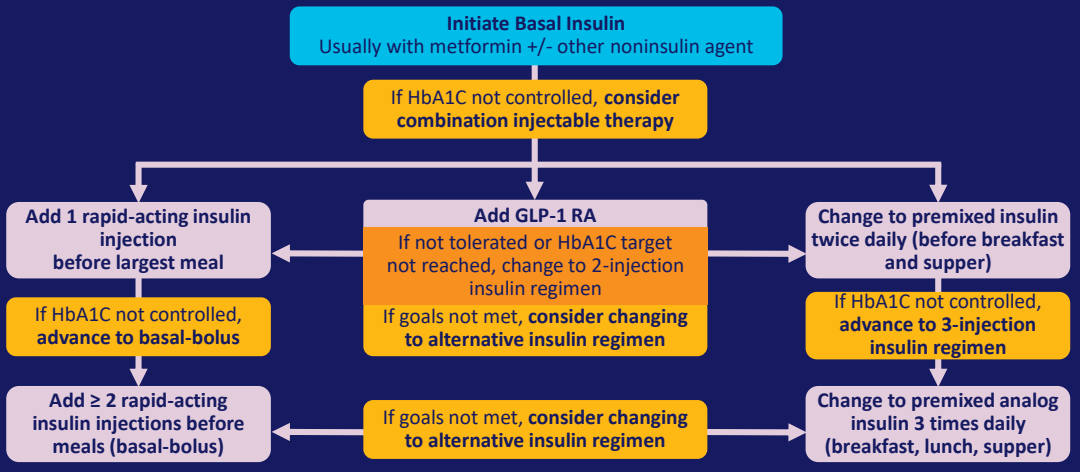
Meet Jackie

- 62-year-old woman with a 19-year history of T2D
- HbA1C = 9.2%
- Currently treated with metformin 1 g BID, sitagliptin 100 mg daily, and glargine U-100 65 units daily
- History of medication adherence challenges and refusal of additional injections
- At today's visit: states that she has been injecting the glargine only 4-5 times per week in either the morning or late afternoon

Therapeutic Options in Patients Not Achieving Glycemic Goals With Basal Insulin



ADA. *Diabetes Care*. 2018;41:S73-85.

Things to Consider

- Jackie does not want to take any additional injections
  - Is an ultra-long-acting basal insulin an option for her?
  - Is a basal insulin/GLP-1 RA FRC agent an option for her?
  - Are there behavioral considerations in her adherence patterns?
  - Are there opportunities to simplify her treatment regimen and improve control?

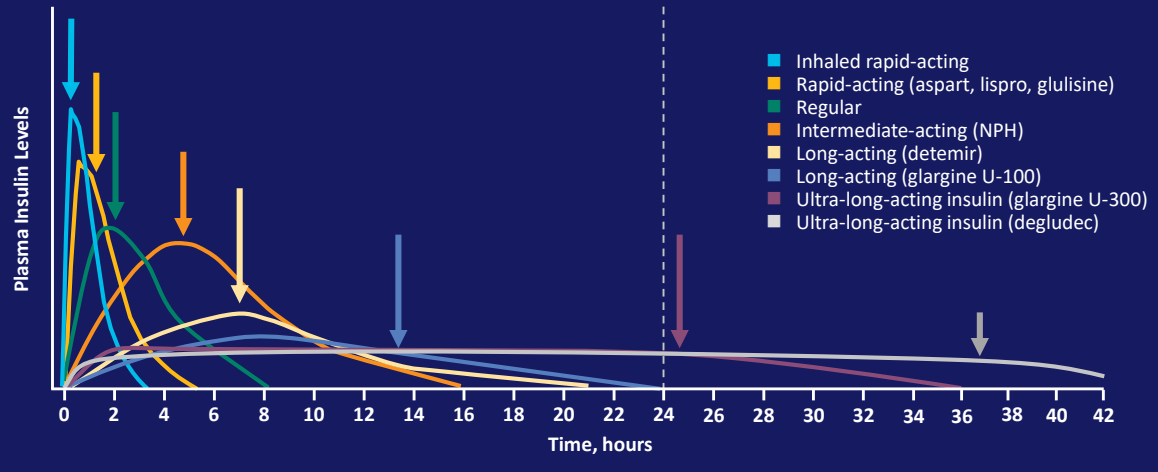
Provider- and Patient-Related Barriers to Insulin Intensification

- Physician:
  - Limited time
  - Lack of resources to assist patient
  - Concerns about hypoglycemia
  - Concerns about weight gain
  - Fear of alienating patient
  - Inadequate knowledge
- Patient:
  - Lack of preparation
  - **Impact on daily life**
  - Fear of hypoglycemia
  - Fear of weight gain
  - Sense of failure
  - Marker of disease worsening

Do Not Ever Threaten a Patient With Insulin Therapy
They will hear the threat but not the benefit

Koerbel G, et al. *Practical Diabetology.* 2003;22:36-40.
Kruger DF, et al. *Diabetes Metab Syndr Obes*. 2015;8:49-56.
Russell-Jones D, et al. *Diabetes Obes Metab*. 2018;20:488-96.

PK Profile of Currently Available Insulins



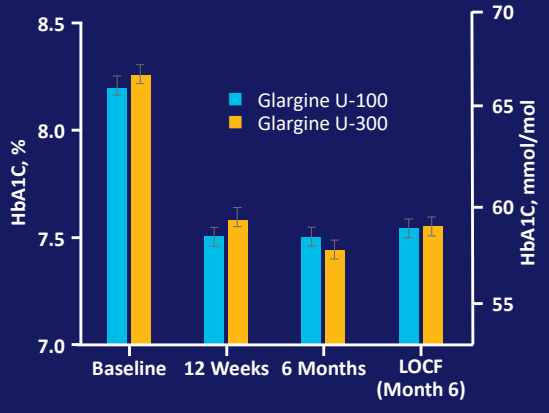
Adapted from Hirsch IB. *N Engl J Med*. 2005;352:174-83. Flood TM. *J Fam Pract.* 2007;56:S1-12. Becker RH, et al. *Diabetes Care*. 2015;38:637-43.
Prescribing information. Lamos EM, et al. *Ther Clin Risk Management*. 2016;12:389-400.

FDA-Approved Ultra-Long-Acting Basal Insulins

- Two are currently available
  - Degludec U-100 and U-200
  - Glargine U-300
- Benefits
  - Once-daily dosing
  - Reduced nocturnal hypoglycemia
- Limitations
  - Titration is limited to every 3-5 days
  - Cost

Lamos EM, et al. *Ther Clin Risk Manag*. 2016;12:389-400.
Ritzel R, et al. *Diabetes Obes Metab*. 2018;20:541-54.
Russell-Jones D, et al. *Nutr Metab Cardiovasc Dis*. 2015;25:898-905.
Prescribing information.

EDITION 2: Glargine U-300 vs Glargine U-100 in Patients With T2D Using Oral Agents and Basal Insulin



Hypoglycemia:

- Lower rates of nocturnal confirmed hypoglycemia (≤ 3.9 mmol/L [≤ 70 mg/dL]) or severe hypoglycemia were observed with glargine U-300 from week 9 to month 6 (RR, 0.77 [95% CI, 0.61-0.99]; *P* = .038)

Yki-Jarvinen H, et al. *Diabetes Care*. 2014;37:3235-43.

BEGIN FLEX: Degludec Given in Variable Once-Daily Dosing Intervals

26-week, open-label, treat-to-target study of adults with T2D who were either insulin naïve and taking OADs or previously on basal insulin

	Injection Time	Improvement in HbA1C
Degludec OD flex (100 units)	Dosing schedule with 8-40 hours between injections	1.28%[a]
Degludec OD (100 units)	Once daily at evening meal	1.07%[a]
Glargine OD (100 units)	Once daily at same time every day	1.26%[a]

No statistically significant differences in overall or nocturnal hypoglycemia observed between the degludec OD flex and glargine OD groups

[a]Degludec OD flex was noninferior to glargine OD in lowering HbA1C. No statistically significant difference in HbA1C was found between degludec OD flex and degludec OD.

Meneghini L, et al. *Diabetes Care*. 2013;36:858-64.

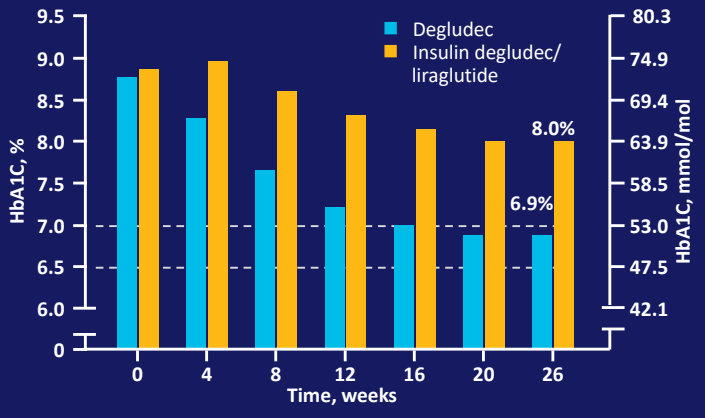
FDA-Approved Basal Insulin/GLP-1 RA FRC

- Two FRCs currently available
  - Insulin degludec/liraglutide
  - Insulin glargine/lixisenatide
- Benefits
  - Better efficacy than either component given alone
  - Improved FPG and PPG levels
  - Lower rates of hypoglycemia and weight gain vs insulin monotherapy
  - Reduced GI effects due to slow uptitration vs GLP-1 RA alone
  - Potential for increased patient adherence due to simplified regimen
- Limitations
  - Potential for GI adverse effects
  - Insulin titration is limited by GLP-1 component
  - Cost

Prescribing information.
Rosenstock J, et al. *Diabetes Care*. 2016;39:2026-35. Aroda VR, et al. *Diabetes Care*. 2016;39:1972-80.
Gough S, et al. *Lancet Diabetes Endocrinol*. 2014;2:885-9. Buse JB, et al. *Diabetes Care*. 2014;37:2926-33.

DUAL-II: Insulin Degludec/Liraglutide vs Degludec in Patients Inadequately Controlled on Basal Insulin and Metformin With or Without Sulfonylureas/Glinides

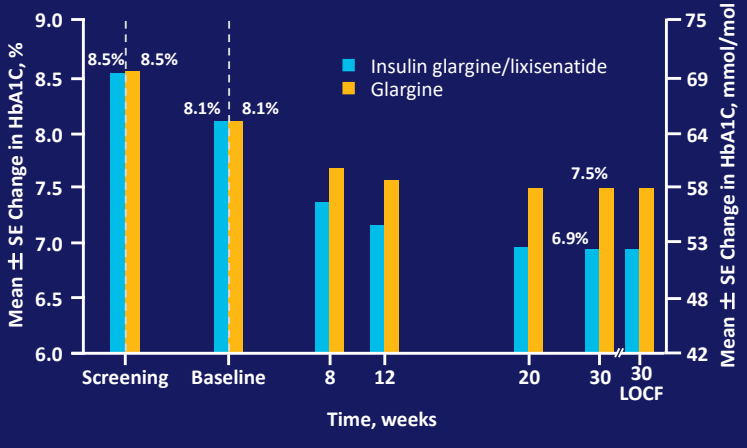
- Insulin degludec/liraglutide FRC significantly reduces HbA1C and body weight vs degludec alone (both $P < .0001$)
- Rates of hypoglycemia were comparable with insulin degludec/liraglutide FRC vs degludec alone



Buse JB, et al. *Diabetes Care.* 2014;37:2926-33.

LixiLan-L: Insulin Glargine/Lixisenatide vs Glargine in Patients Inadequately Controlled With Basal Insulin and Metformin With or Without ≤ 2 Oral Agents

- Insulin glargine/ lixisenatide FRC significantly reduces HbA1C and body weight vs glargine U-100 alone (both $P < .0001$)
- Rates of hypoglycemia were comparable with insulin glargine/lixisenatide FRC vs glargine alone



Aroda VR, et al. *Diabetes Care*. 2016;39:1972-80.

Things to Consider

- If Jackie were open to taking additional injections:
  - Would adding a GLP-1 RA as a separate injection be an option for her?
    - Also associated with improved glycemic control
    - Advantages compared with FRCs: lower risk of dosing errors, dose of individual component can be adjusted
    - Once weekly versus once daily
  - Would changing to a premixed insulin be an option for her?
    - Advantages: effective, convenient
    - Disadvantages: dose of individual insulins cannot be adjusted, hypoglycemia risk

ADA. *Diabetes Care*. 2018;41:S73-85.
Nuffer W, et al. *Ther Adv Endocrinol*. 2018;9:69-79.
Rizvi AA. *Eur Med J Diabetes*. 2016;4:74-83.

Conclusion

- Many patients struggle with diabetes management and busy lifestyles
- Injection therapy can be challenging, resulting in poor goal achievement
- Simplifying therapy to options with fewer dosing events may improve goal attainment and adherence for patients

Acknowledgment of Commercial Support

This activity is supported by an educational grant from Sanofi US.

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Contact Information

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Abbreviations and Acronyms

FRC = fixed-ratio combination
FPG = fasting plasma glucose
GI = gastrointestinal
GLP-1 = glucagon-like peptide-1
HbA1C = glycated hemoglobin
LOCF = last observation carried forward
NPH = neutral protamine hagedorn
OAD = oral anti-diabetic drug
OD = once daily
PK = pharmacokinetic
PPG = postprandial plasma glucose
RA = receptor agonist
T2D = type 2 diabetes