

- Start Recording

# Welcome to UVM ECHO: Treatment of Diabetes Mellitus Type II

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The University of Vermont  
LARNER COLLEGE OF MEDICINE



# “Introduction” to ZOOM

- Please mute microphone when not speaking
- Please use camera as much as possible
- Test both audio & video before joining
- Communicate clearly during clinic:
  - Can use “raise hand” feature to comment
  - Speak clearly
  - Use chat function for technical issues
- We are recording the didactic section



# CME disclosures

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## **Interest Disclosures:**

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# Disclosures: None or have been resolved

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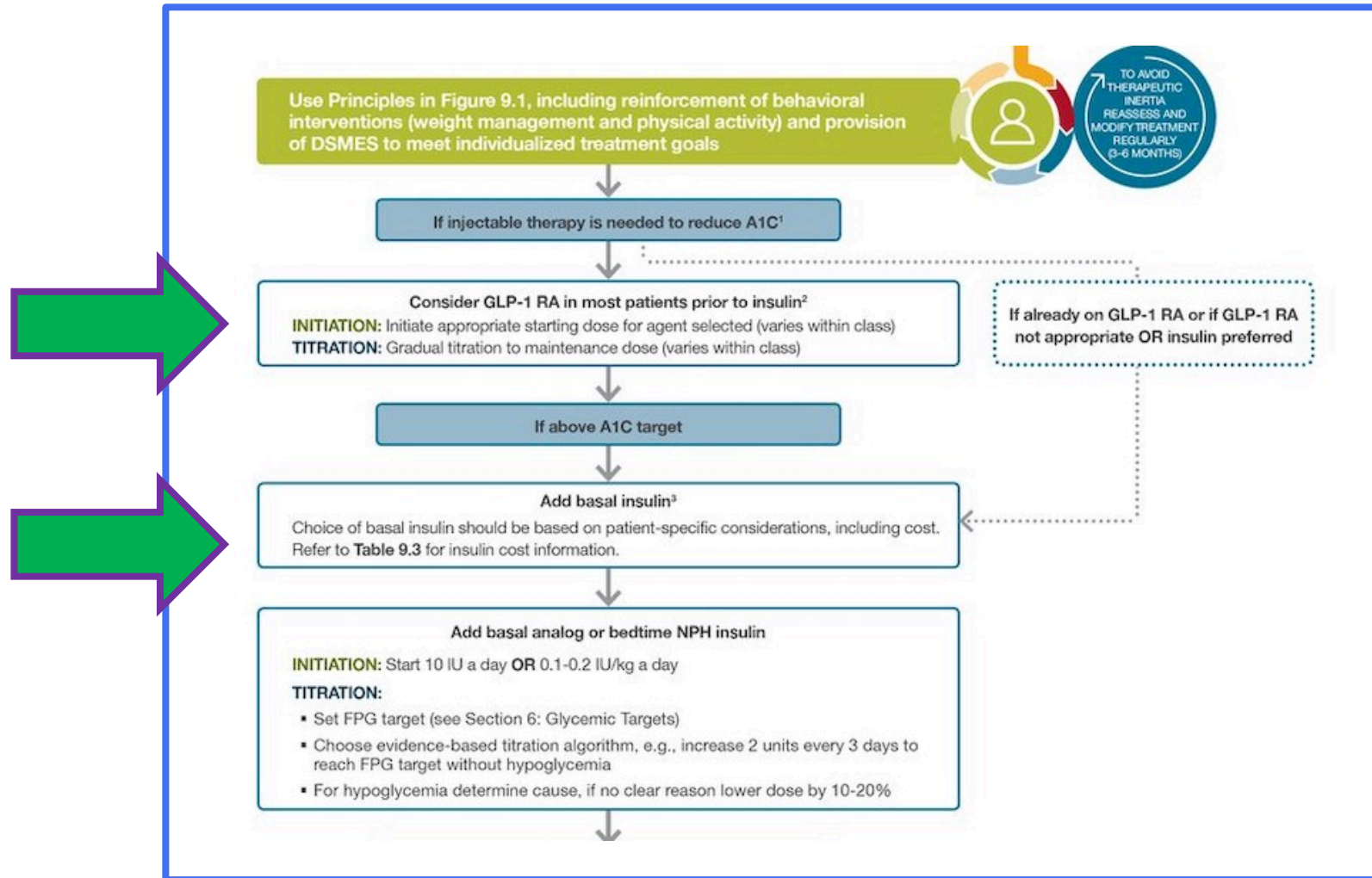
**Diabetes Echo 11/12/2020**  
**Beyond Basal Insulin Therapy**

Jack L. Leahy, M.D.

Endocrinology, Diabetes and Metabolism

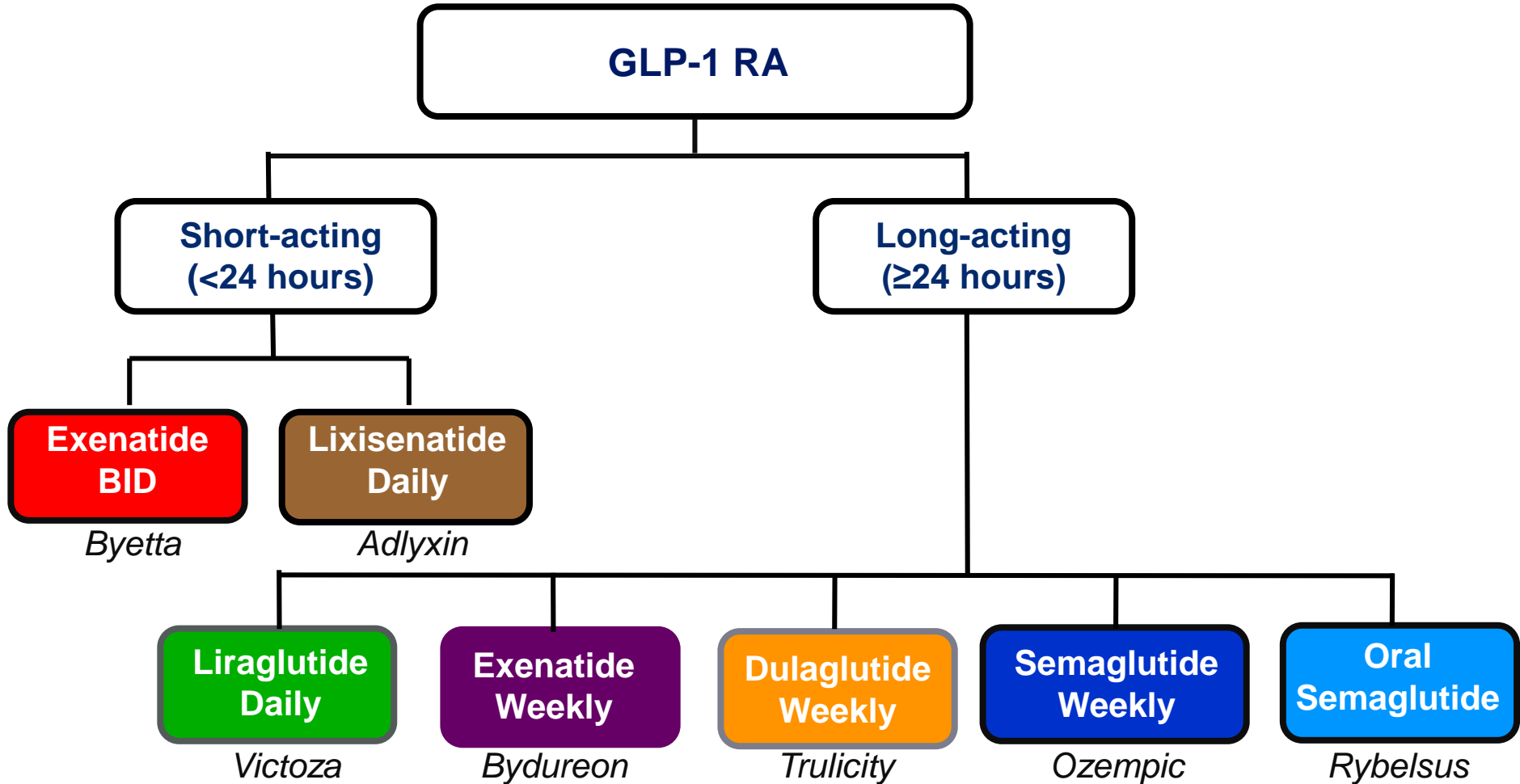
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# ADA/EASD Guidelines for Starting Insulin Therapy in Type 2 DM



**Why GLP-1 RA vs Basal Insulin?**

# Available GLP-1 RA Agents in the US





# Comparison GLP-1 RA Agents and Insulin

	GLP-1 RA	Insulin
Actions	Multi-organ	Glucose-centric
Weight	↓	↑
Hypoglycemia	--	++
Injections	Daily/weekly	Daily
Require titration	±	Yes
GI side effects	++	--
CV protection	+++	--
Renal protection	+	--

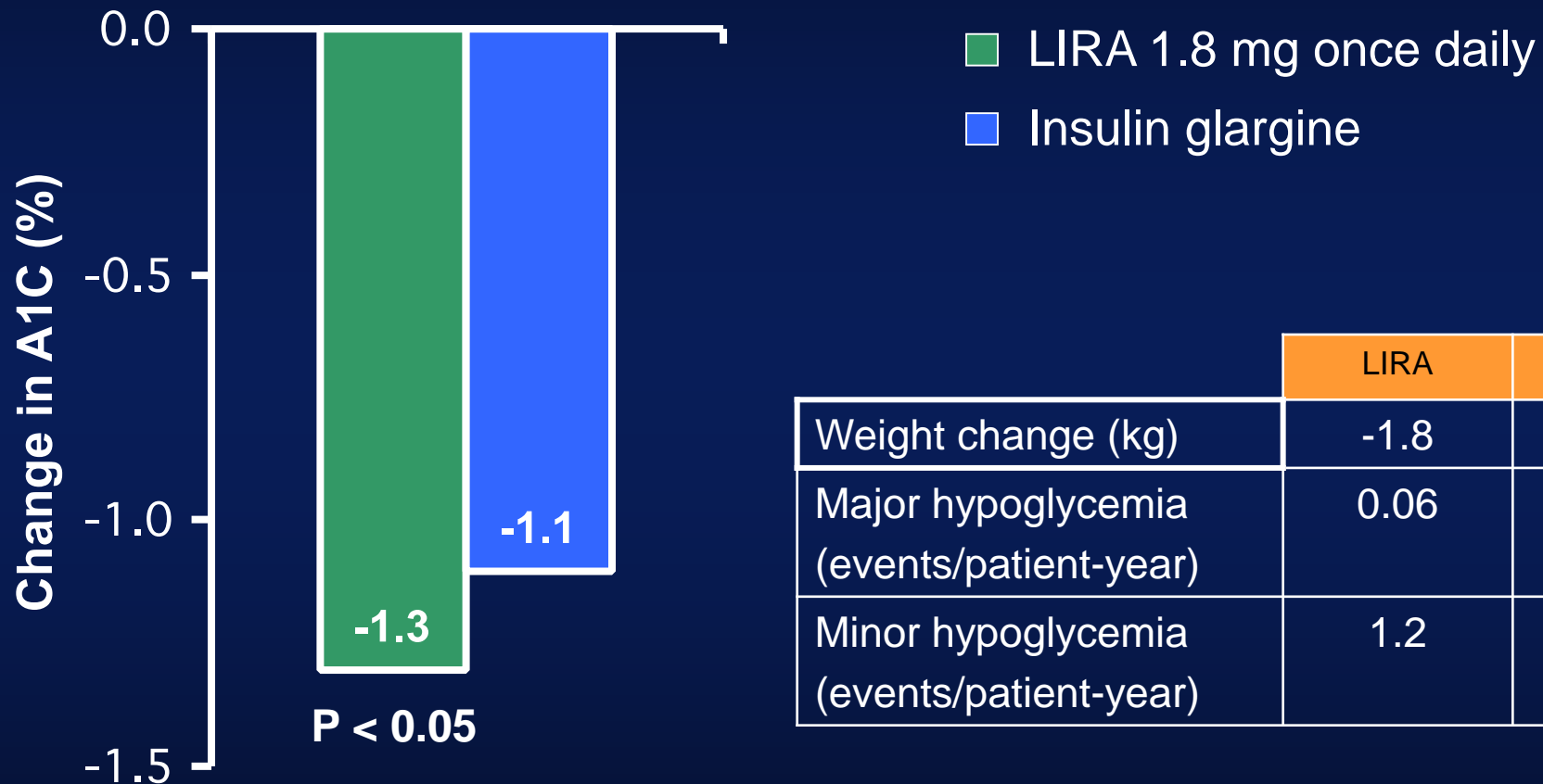


**SET IT**

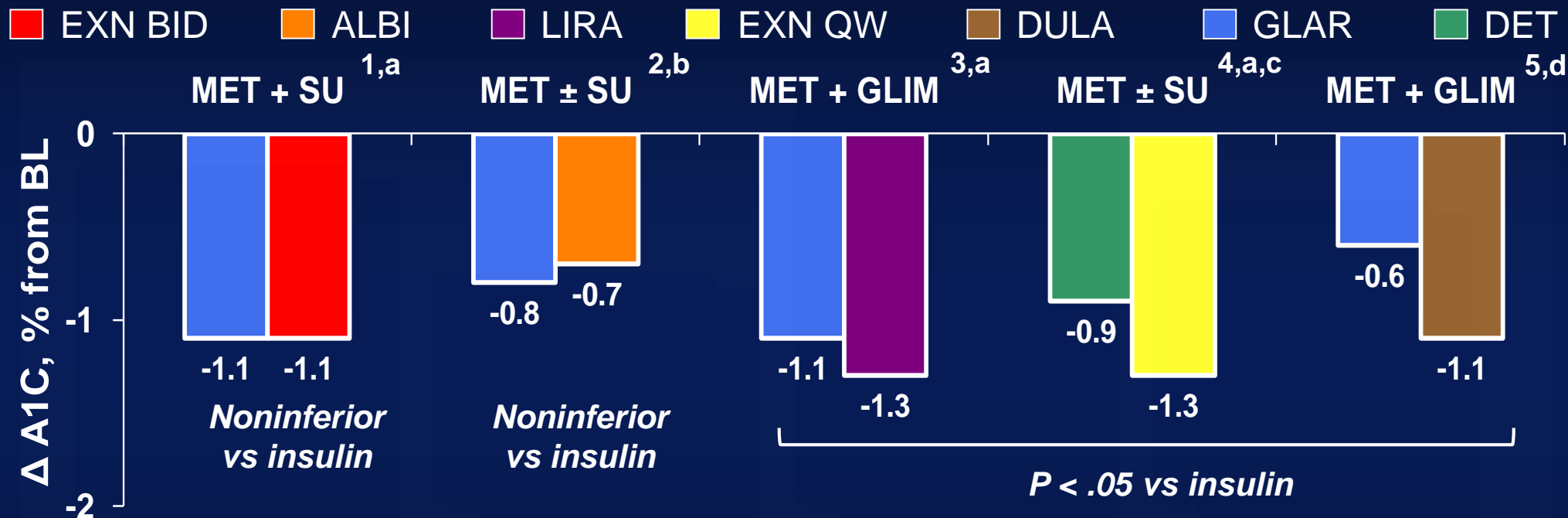
**AND FORGET IT**

# Liraglutide vs. Once-Daily Insulin Glargine

## 26-weeks. Baseline A1c 8.2%. N = 549



# Failing Oral Therapy: Efficacy of GLP-1 RAs Compared to Basal Insulin



Average weight change: GLP-1 RA -1.8 to -2.7 kg versus insulin +1.4 to +3.0 kg

<sup>a</sup> 26 weeks, BL A1C 8.2% to 8.7%.

<sup>b</sup> 52 weeks, BL A1C 8.3%, 82% on MET + SU background.

<sup>c</sup> ≈ 70% on MET + SU background.

<sup>d</sup> 52 weeks, BL A1C 8.1%.

1. Heine R, et al. *Ann Intern Med.* 2005;143:559-569.

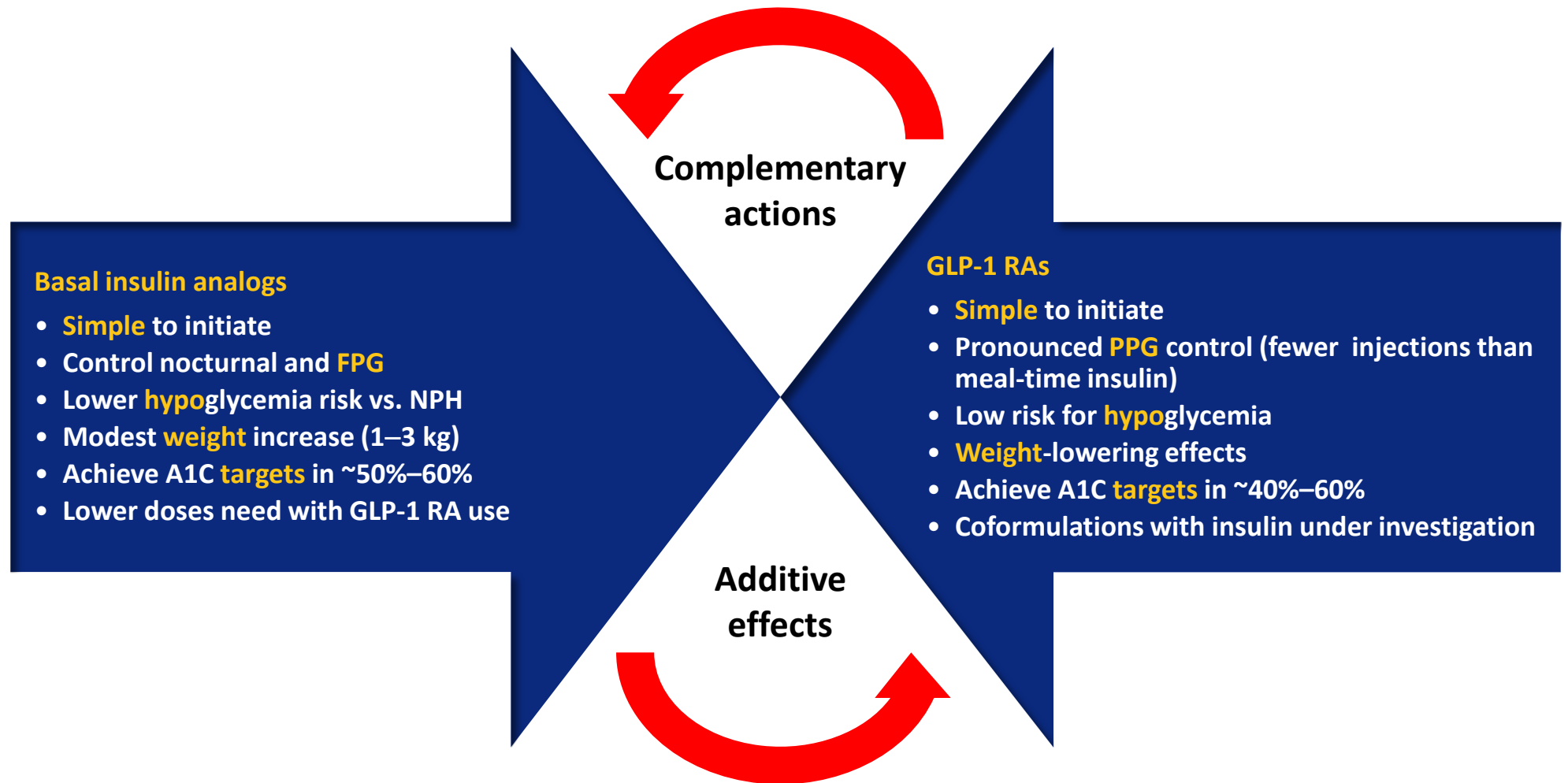
2. Pratley R, et al. ADA 73rd Scientific Sessions. 2013 [abstract 54-LB].

3. Russell-Jones D, et al. *Diabetologia.* 2009;52:2046-2055.

4. Davies M, et al. *Diabetes Care.* 2013;36:1368-1378.

5. Giorgino F, et al. *Diabetes.* 2014;63(suppl 1):A8

# Combination of Basal Insulin With a GLP-1 Receptor Agonists Has Scientific Logic



# DUAL I – Comparison IDegLira Versus the Individual Agents in Insulin Näive

- 26 week open label comparison of fixed dose insulin degludec + liraglutide (n=834) to insulin degludec (414) or liraglutide (415).
- Patients: on metformin  $\pm$  pioglitazone, A1c 8.3%

	IDegLira	Degludec	Liraglutide
Final A1c	6.4% Noninferior Degludec Superior to Liraglutide	6.9%	7.0%
Nausea	8.8%	3.6%	19.7%
Weight	-0.5 kg	1.6 kg	-3.0 kg

# LixiLan-O – Comparison LixiLan Versus the Individual Agents in OHA Failures

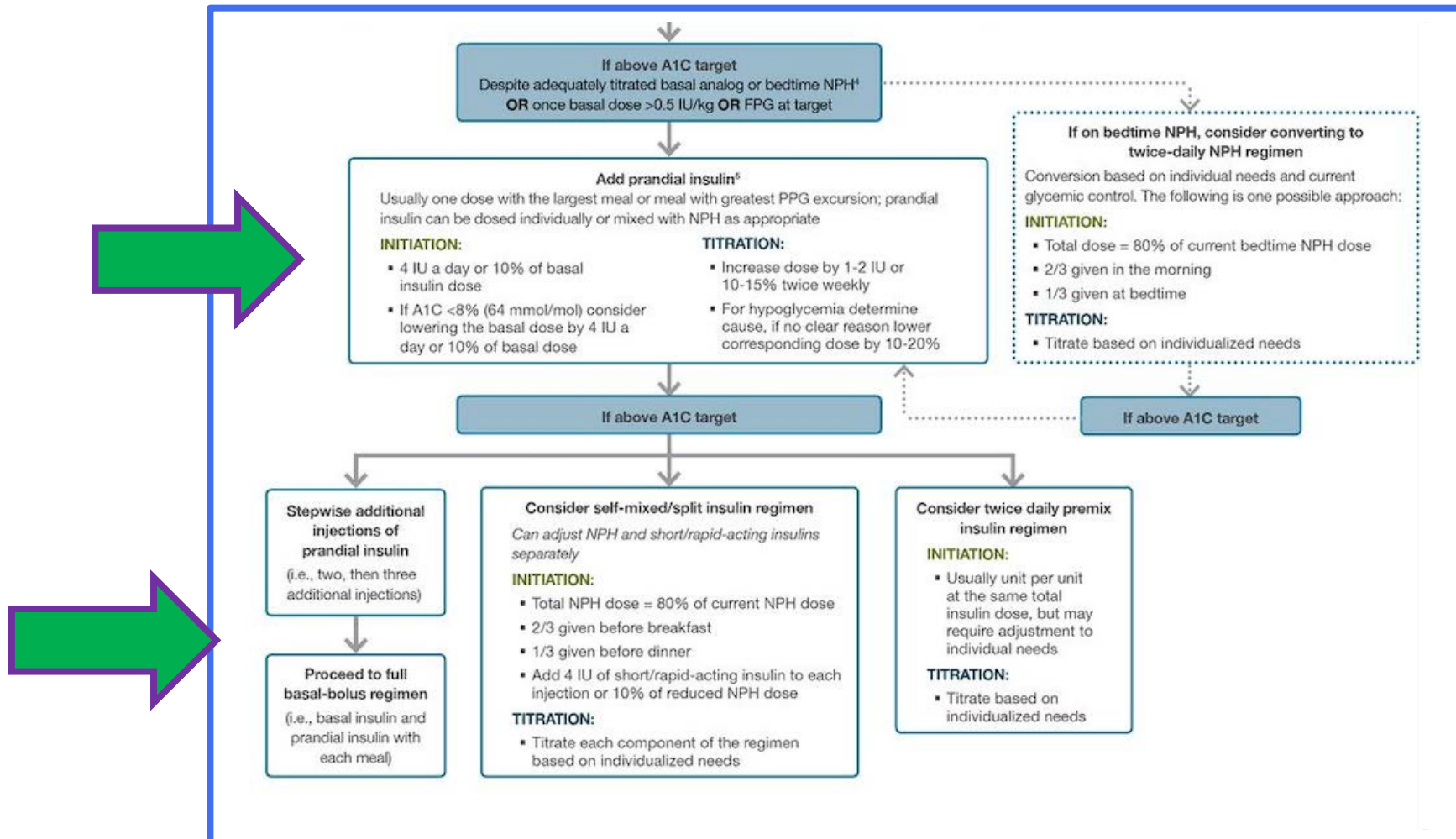
- 26 week open label comparison of fixed dose insulin glargine + lixisenatide to insulin degludec or liraglutide (total 1,170).
- Patients: on metformin  $\pm$  second OHA, A1c 8.1%

	LixiLan	Glargine	Lixisenatide
Final A1c	6.5% Superior both Glargine and Lixisenatide	6.8%	7.3%
BG <70 mg/dL	1.4/pt-year	1.2/pt-year	0.3/pt-year
Weight	-0.3 kg	1.1 kg	-2.3 kg

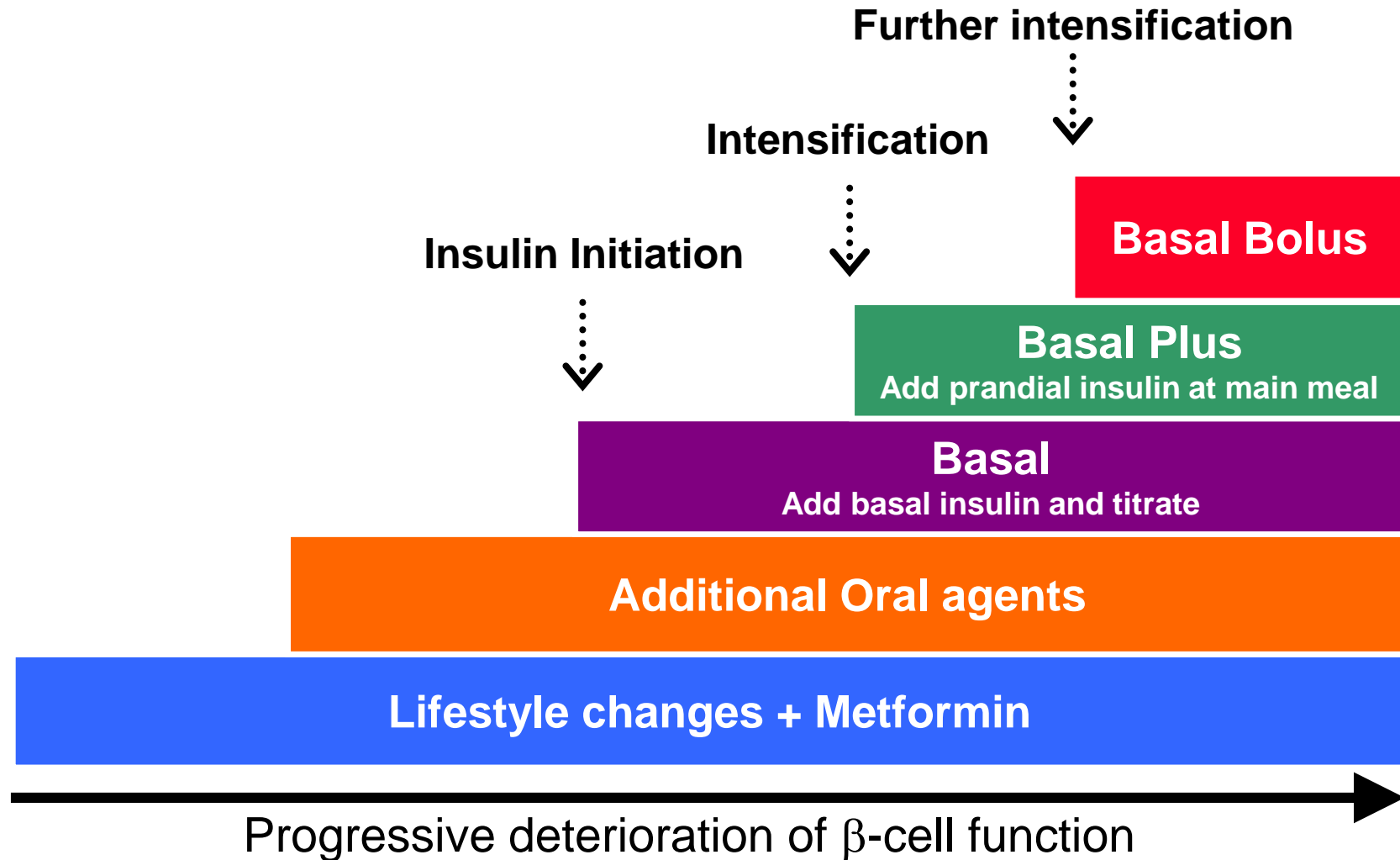
**What if Basal Insulin is Not Enough?**



# After First Injection ADA/EASD Guidelines in Type 2 DM

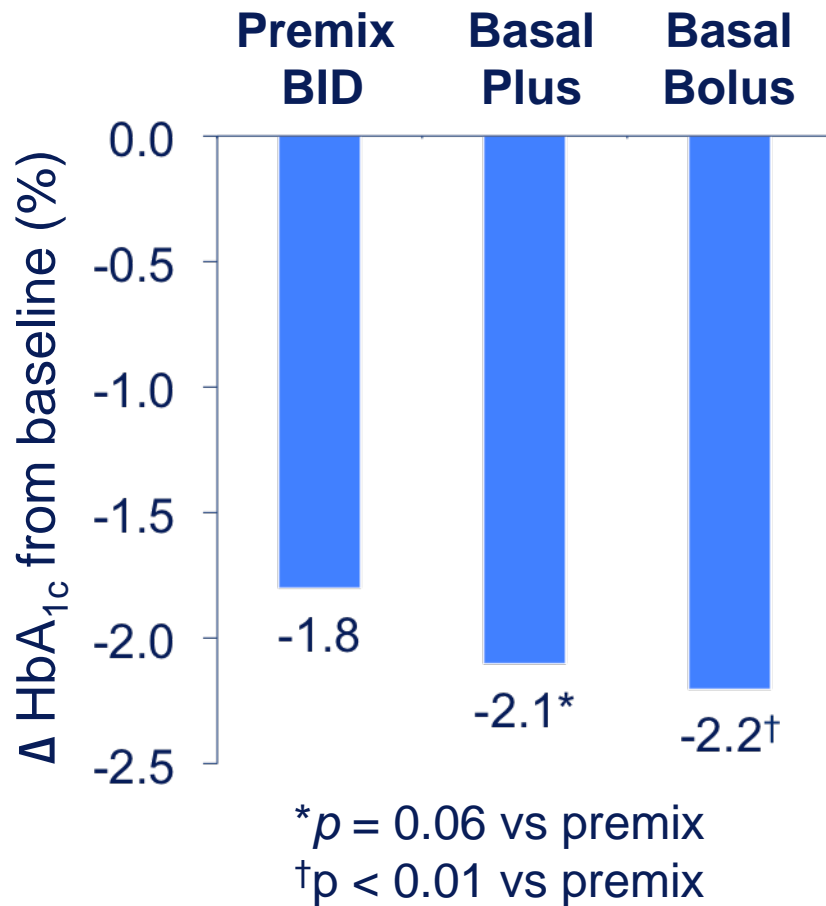


# Stepwise Treatment of Type 2 Diabetes





# All-to-Target: Stepwise Intensification With Glargine and Glulisine vs Aspart Premix



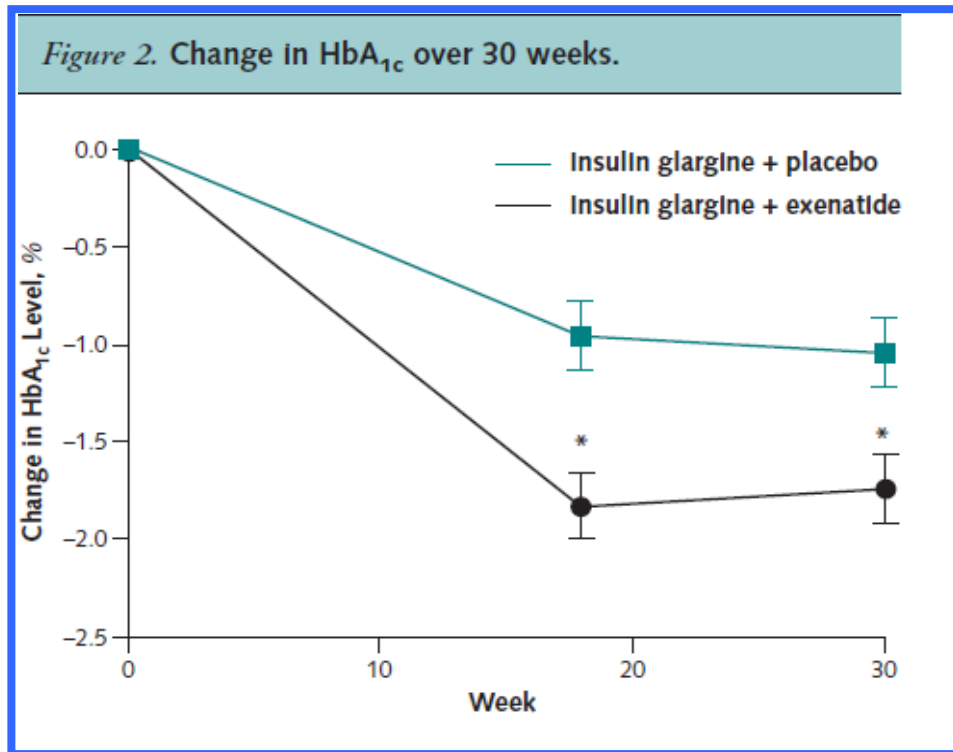
- 60-week study of 3 treatment strategies in 572 patients on orals with average A1c 9.4%.
  - Optimize glargine followed adding 1 injection glulisine (*Basal plus*)
  - Optimize glargine followed by stepped addition to 3 injections glulisine (*Basal bolus*)
  - Twice daily aspart 70/30 (*Premix*).
- 49% reached A1c <7% with basal plus versus 39% with premix ( $p < 0.05$ )
- 40-60% reduction in hypoglycemia with basal plus versus premix ( $P < 0.01$ )

# Mealtime Insulin

- Use rapid-acting analogues, not regular insulin
  - Less postprandial hypoglycemia
  - Can be taken up to 20 minutes after start eating
  - Best about 15 minutes premeal.
- Start with 1 shot, at largest meal:
  - 4 units, and titrate, OR
  - By weight - 0.1 U/kg
- Titrate to:
  - <160 mg/dL 2 hours post-prandial OR
  - <130 mg/dL next meal or bedtime
- Carb counting in type 2 DM – unproven.

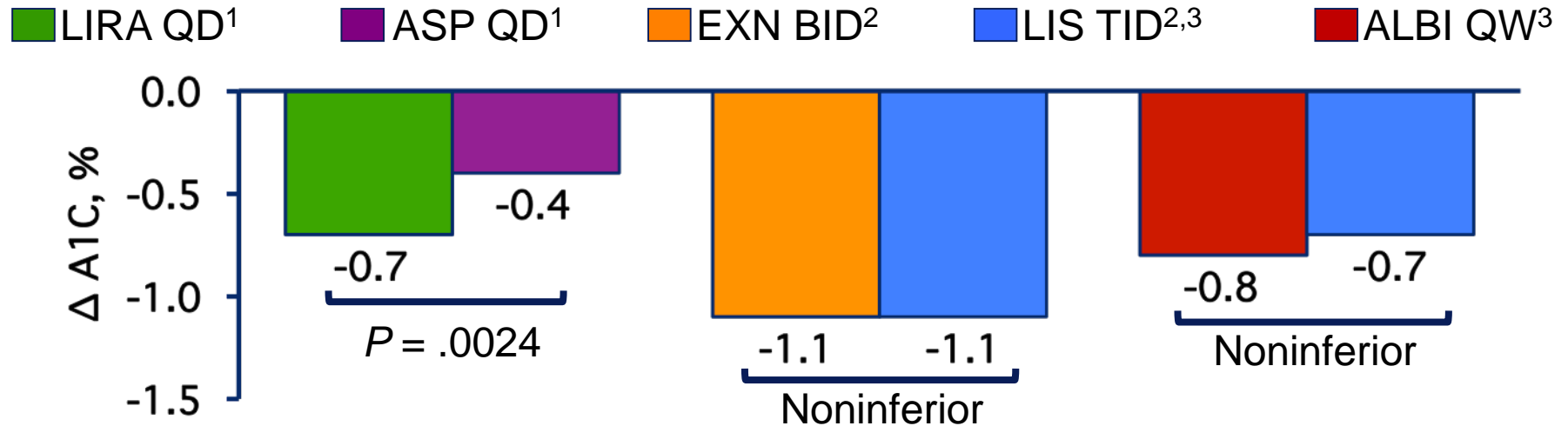
# **What About Agents Other Than Prandial Insulin?**

# Addition of Twice-daily Exenatide to Glargine Insulin-treated Type 2 DM



- N=259. Baseline A1c 8.5% (placebo) and 8.32% (exenatide)
- Better improvement A1c: -1.7% exenatide versus -1.0% placebo.
- Weight loss: -1.8 kg with exenatide versus +1.0 kg placebo.
- Smaller increase glargine dose: 13 units exenatide versus 20 placebo.
- Similar hypoglycemia.
- More study dropouts: 13 exenatide versus 1 placebo

# GLP-1 RA vs Prandial insulin Added to Basal Insulin

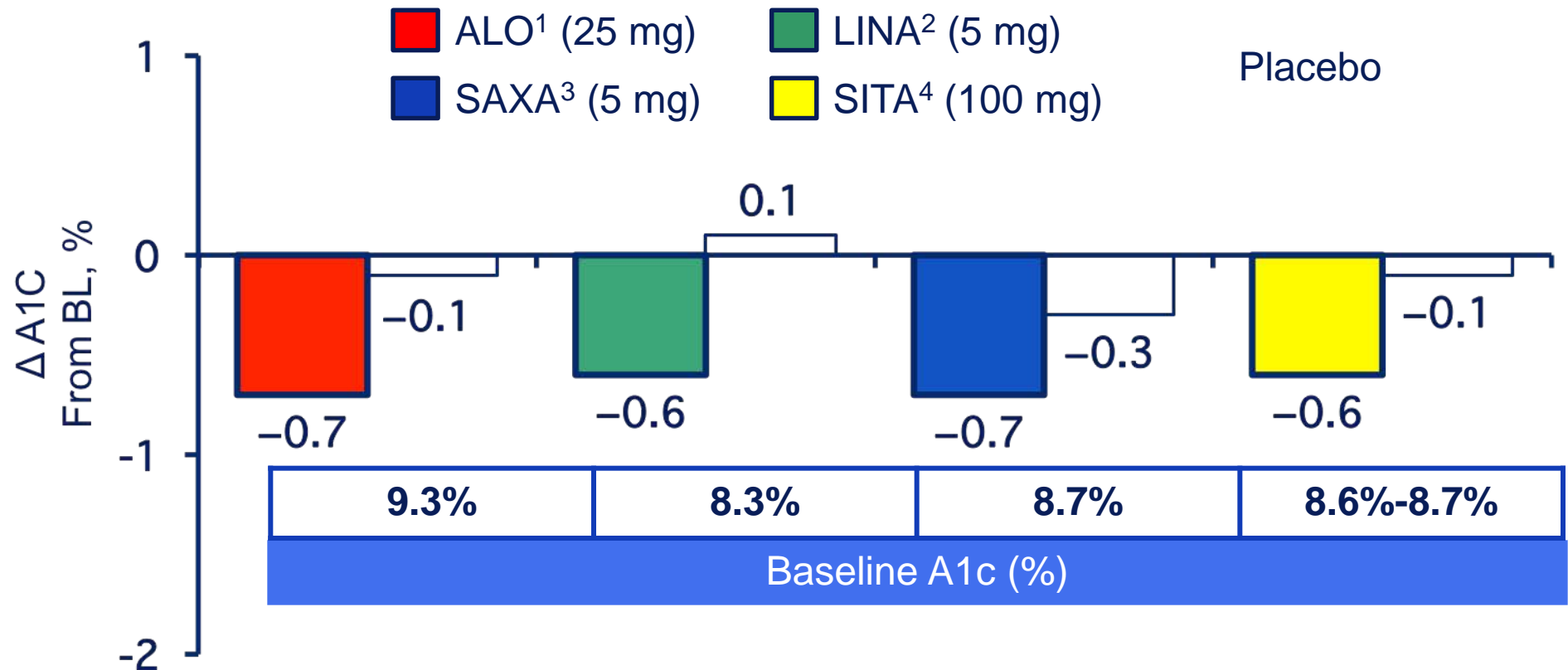


Outcome	LIRA vs ASP <sup>1</sup>		EXN BID vs LIS <sup>2</sup>		ALBI vs LIS <sup>3</sup>	
Δ Weight, kg	<b>-2.8</b>	<b>0.9</b>	<b>-2.5</b>	<b>2.1</b>	<b>-0.7</b>	<b>0.8</b>
Hypo, EPY <sup>e</sup>	<b>1.0</b>	<b>8.2</b>	<b>2.1</b>	<b>5.0</b>	<b>0.9</b>	<b>2.3</b>
Nausea, %	LIRA > ASP, first 2 wk		<b>2.9</b>	<b>0</b>	<b>11</b>	<b>1</b>

1. Mathieu C, et al. *Diabetes Obes Metab.* 2014;16:636-644. 2. Diamant M, et al. *Diabetes Care.* 2014;37:2763-2773. 3. Rosenstock J, et al. *Diabetes Care.* 2014;37:2317-2325.

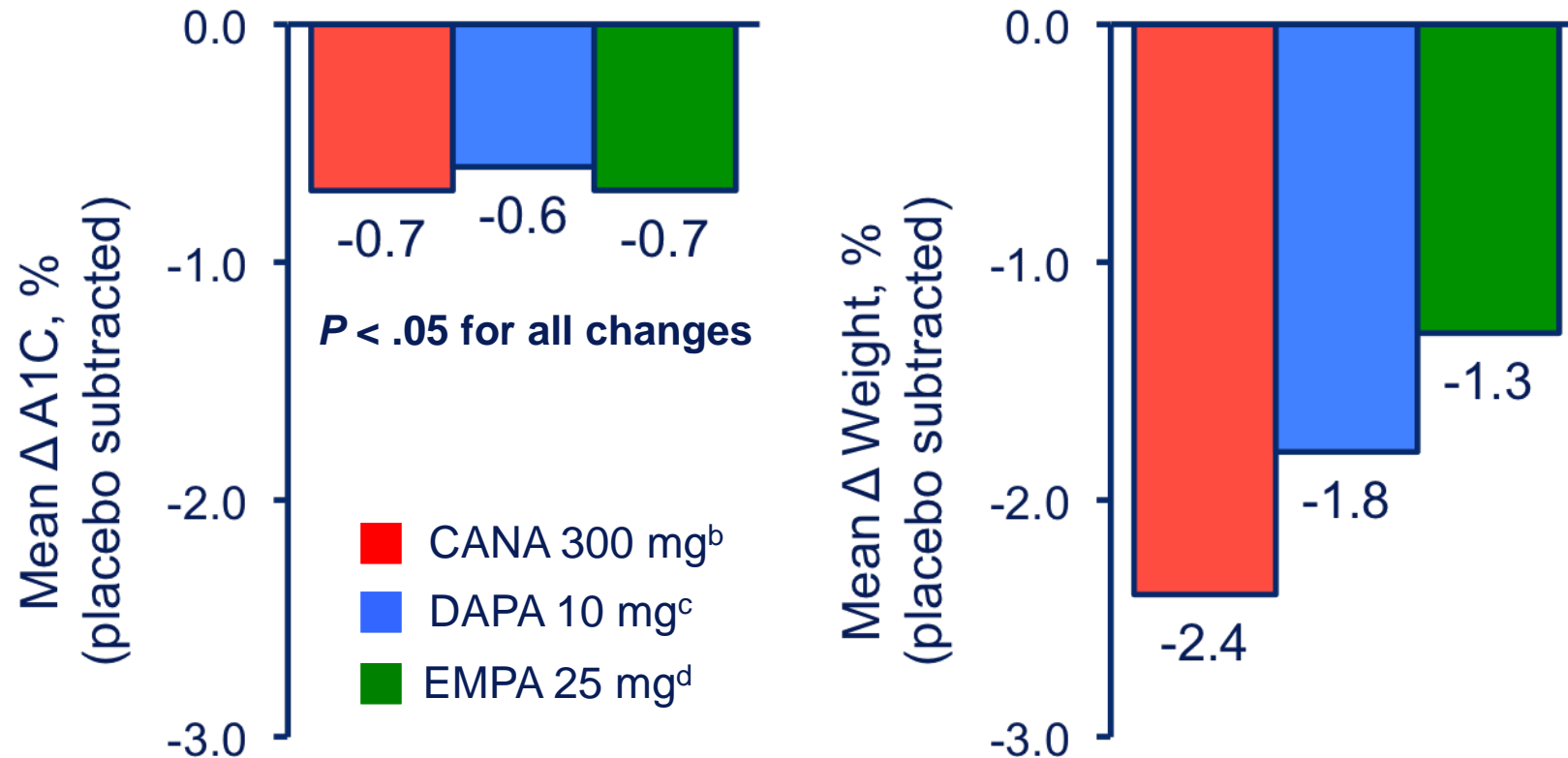


# DPP-4 Inhibitors Added to Regimens That Include Insulin



1. Rosenstock J et al. *Diabetes Obes Res* 2009;11:1145-1152. 2. Yki-Jarvinen H et al. *Diabetes Care* 2013;36:3875-3881. 3. Barnett AH et al. *Clin Drug Investig* 2013;33:707-717. 4. Visbøll T et al. *Diabetes Obes Res* 2010;12:167-177.

# SGLT2 Inhibitors Added to Regimens That Include Insulin



<sup>a</sup> SGLT2is are not approved for weight loss; data are from individual trials and do not represent head-to-head comparisons: 18-24 weeks; BL A1C, 8.3%-8.6%; BL weight, 95-97 kg.

<sup>b</sup> CANA added to basal, bolus, or basal/bolus insulin;  $\geq 30$  U/d with or without other AHAs.

<sup>c</sup> DAPA added to unspecified stable insulin regimen;  $\geq 30$  U/d and  $\leq 2$  other AHAs.

<sup>d</sup> EMPA added to basal insulin (45-48 U/d) with or without MET and/or SU.

# Conclusions

- Injection therapy (GLP-1 RA or basal insulin) has higher potency than oral pharmaceuticals in type 2 DM.
- Can start with either although very different clinical profiles.
- Diabetes specialty world recommends GLP-1 RA agents as first agent if affordable and tolerated – high potency, weekly, easy titration, weight loss, low rate of hypoglycemia, CVD/renal benefits.
- Next steps after basal insulin:
  - Prandial insulin – often start with single injection largest meal.
  - GLP-1 RA therapy.
  - Other agents (A1c < mid 7s).

- RECORDING TO BE STOPPED FOR CASE PRESENTATION

# Cases/HIPAA

- Names
- Address
- DOB
- Phone/Fax #
- Email address
- Social Security #
- Medical Record #



The discussion and materials included in this conference are confidential and privileged pursuant to 26VSA Section 1441-1443. This material is intended for use in improving patient care. It is privileged and strictly confidential and is to be used only for the evaluation and improvement of patient care.

# ECHO Reminders

- Volunteers to present cases (this is key to the Project ECHO model)
- Please complete evaluation survey for each session
  - CME code will be emailed once session evaluation form is received at UVM
- UVM Project ECHO materials available at [www.vtahec.org](http://www.vtahec.org)
- Please contact us with any questions/suggestions
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