INDIVIDUALIZING DIABETES MANAGEMENT WITH INJECTABLE THERAPIES
Moving Beyond Oral Agents to Achieve Glycemic Control

June 4, 2014
Long Beach, California
Session 2: Individualized Diabetes Management with Injectable Therapies: Moving Beyond Oral Agents to Achieve Glycemic Control

Learning Objectives

1. Implement strategies to mitigate patient-perceived barriers to injectable therapies and explore pathways physicians can employ to overcome clinical inertia associated with type 2 diabetes mellitus (T2DM) management.
2. Evaluate the latest clinical evidence for GLP-1 receptor agonists (GLP-1 RAs) with respect to differences among agents and potential role in combination therapy with basal insulin.
4. Develop a patient-centered, guidelines-based approach for intensifying T2DM therapy with injectable agents to achieve glycemic control.

Faculty

Yehuda Handelsman MD, FACP, FACE, FNLA
Medical Director & Principal Investigator
Metabolic Institute of America
President Elect, American College of Endocrinology
Past President, American Association of Clinical Endocrinologists
Tarzana, California

Dr Handelsman is an endocrinologist in private practice, and Medical Director & Principal Investigator of the Metabolic Institute of America. He is a nationally and internationally-recognized authority on obesity, insulin resistance, pre-diabetes, and the comprehensive approach to treating diabetes, controlling all cardiovascular risks. He is a pioneer and leader in the understanding of the body’s metabolic and energy systems, fat, and the gut-brain connection. A clinician, researcher and educator, he publishes and lectures extensively. He is president elect of the American College of Endocrinology; past president of the American Association of Clinical Endocrinologists; and a board member the Pacific Lipid Association. He is chair, founder and program director of the acclaimed annual World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease; associate editor of the Journal of Diabetes; a frequent guest editor for publications such as the Journal of Clinical Hypertension; chair of the AACE 2011 Comprehensive Diabetes Guidelines and its 2014 update committee, member of the AACE 2013 Comprehensive Diabetes Algorithm and the 2012 AACE lipid guideline; he also co-chaired consensuses on diabetes & cancer, insulin resistance and pre-diabetes. Dr Handelsman has been listed repeatedly in “Top Doctors of Los Angeles,” “Southern California Super Doctors,” and “Best Doctors of America.”

Etie Moghissi, MD, FACE
Board Certified Endocrinologist
Marina del Rey, California

Dr Moghissi is an associate professor of clinical medicine, University of California in Los Angeles and a consultant in diabetes, endocrinology and metabolism in Marina del Rey California.

A native of Shiraz, Iran, she moved to the United States in 1979 to complete her internal medicine training at St. Luke’s/Roosevelt Hospital affiliated with Columbia University in New York City and subsequently a fellowship in endocrinology, diabetes & metabolism at the University of California, Los Angeles.

Dr Moghissi’s primary interests lie in improving the metabolic control of patients with diabetes and other endocrine disorders through the application of cutting edge knowledge and technologies, and the implementation of these management strategies through patient and professional education activities.
Dr Moghissi, has been engaged in leadership positions locally and nationally over the past twenty years and has served as the secretary, treasurer, vice president and the president elect of the American Association of Clinical Endocrinology and President of the California Chapter of AACE. She has served on multiple hospital governing boards in her community.

Faculty Financial Disclosure Statements
The presenting faculty reported the following:

Dr Handelsman receives research/grant support from Amgen, Boehringer Ingelheim, Gilead, Intarcia, GlaxoSmithKline, Lexicon, Merck, Novo Nordisk, sanofi-aventis, and Takeda; He is a consultant for Amarin, Amgen, AstraZeneca-Bristol-Meyers Squibb (Amylin), Boehringer Ingelheim, diaDeux, Daiichi Sankyo, Eisai, Gilead, GlaxoSmithKline, Halozyme, Janssen, LipoScience, Merck, Novo Nordisk, sanofi-aventis, Santarus, and Vivus; He is on the speakers’ bureau for Amarin, AstraZeneca-Bristol-Meyers Squibb (Amylin), Bi-Lilly, Daiichi Sankyo, GlaxoSmithKline, Janssen, Novo Nordisk, Santarus, and Vivus.

Dr Moghissi has disclosed that she has received speaker honorarium from Boehringer Ingelheim, Lilly, Merck, and Novo Nordisk.

Education Partner Financial Disclosure Statement
The content collaborators at Creative Educational Concepts, Inc. have reported the following:

Dr Susan Gitzinger has no financial relationships to disclose in relation to the content of this activity.

Suggested Reading List


SESSION 2
8:45–10am

Individualizing Diabetes Management with Injectable Therapies: Moving Beyond Oral Agents to Achieve Glycemic Control

SPEAKERS
Etie Moghissi, MD, FACE
Yehuda Handelsman, MD, FACP, FACE, FNLA

Presenter Disclosure Information
The following relationships exist related to this presentation:
► Etie Moghissi, MD, FACE, has received speaker honorarium from Boehringer Ingelheim, Lilly, Merck, and Novo Nordisk.
► Yehuda Handelsman, MD, FACP, FACE, FNLA, research grants from Amgen, Boehringer Ingelheim, Gilead, Intarcia GlaxoSmithKline, Lexicon, Merck, Novo Nordisk, Sanofi, and Takeda. He is a consultant for Amarin, Amgen, (Amaryl) Bristol-Myers Squibb, Boehringer Ingelheim, Eisai, Gilead, GlaxoSmithKline, Halozyme, Janssen, Liposcience, Merck, Novo Nordisk, Sanofi, Santarus, and Vivus. He is on the speakers’ bureau for Amarin, AstraZeneca-Bristol-Myers-Squibb (Amaryl), BI/Lilly, OSI, GlaxoSmithKline, Janssen, Novo Nordisk, Santarus, and Vivus. He is the president-elect of the American College of Endocrinology and the associate editor of the Journal of Diabetes.

Drug List (Generic: Brand)
• Metformin: Glucophage
• Glimepiride: Amaryl
• Canagliflozin: Invokana
• Lisproglutide: Victoza
• Insulin detemir: Levemir
• Insulin glargine: Lantus
• Insulin lispro: Humalog Mix 75/25
• Ramipril: Altace
• Linagliptin: Tradjenta
• Pioglitazone: Actos
• Pramlintide: Symlin
• Sitagliptin: Januvia
• Saxagliptin: Onglyza
• Alogliptin: Nesina
• Exenatide BID: Byetta
• Exenatide Weekly: Bydureon
• Topiramate/Phentermine Combination: Qsymia
• Insulin lispro: Humalog
• Insulin aspart: Novolog
• Insulin glulisine: Apidra

Learning Objectives
• Implement strategies to mitigate patient-perceived barriers to injectable therapies and explore pathways physicians can employ to overcome clinical inertia associated with type 2 diabetes mellitus (T2DM) management.
• Evaluate the latest clinical evidence for GLP-1 receptor agonists (GLP-1 RAs) with respect to differences among agents and potential role in combination therapy with basal insulin.
• Compare and contrast available insulin products and develop strategies for timely initiation, selection, intensification, and self-management of insulin therapy for T2DM based on patient specific factors.
• Develop a patient-centered, guidelines-based approach for intensifying T2DM therapy with injectable agents to achieve glycemic control.

Presenter Disclosure Information
Off-Label/Investigational Discussion
► In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

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Clinical Case Scenario

- A 68-year-old school bus driver with a four year history of diabetes presents for follow-up.
- Ht 68 in; Wt 255 lbs; BMI = 38.8
- Blood pressure = 144/80
- eGFR = 65 mL/min/1.73 m²
- LDL = 110 mg/dL
- Initial A1C = 8%
  - Initiated metformin and titrated it to 1,000 mg twice daily
  - Started ramipril 10 mg daily

AACE 2011/2013 and ADA 2014 Goals for Glycemic Control

<table>
<thead>
<tr>
<th>Target Treatment Goals</th>
<th>AACE 2011/2013²,⁶</th>
<th>ADA 2014⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>&lt;6.5%</td>
<td>&lt;7.0%</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>Fasting and premeal plasma glucose: &lt;100 mg/dL</td>
<td>Preprandial capillary plasma glucose: 70-130 mg/dL⁷</td>
</tr>
<tr>
<td>Postprandial glucose</td>
<td>2-hour postprandial glucose: &lt;140 mg/dL</td>
<td>Peak postprandial capillary plasma glucose: &lt;180 mg/dL⁴</td>
</tr>
</tbody>
</table>

AACE=American Association of Clinical Endocrinologists
ADA=American Diabetes Association

*Goals should be individualized based on duration of diabetes, age, life expectancy, comorbid conditions (known CVD or advanced microvascular complications), hypoglycemia awareness, and individual patient considerations.
*More or less stringent glycemic goals may be appropriate for individual patients.
*Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals.
*Postprandial glucose measurements should be made 1-2 hours after the beginning of the meal; generally peak levels in patients with diabetes.


The Incretin Effect of GLP-1 and GIP

CLIN: promotes satiety and reduction of appetite
Liver: glucagon reduces hepatic glucose output
Stomach: inhibits gastric emptying
Beta cell: enhances glucose-dependent insulin secretion and beta cell functional mass

¹Improvements in beta cell mass have only been shown in animals.
GIP=Gastric Inhibitory Polypeptide

ADA/EASD: Approach to the Management of Hyperglycemia

<table>
<thead>
<tr>
<th>More stringent</th>
<th>Less stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient attitude and expected treatment efforts:</td>
<td></td>
</tr>
<tr>
<td>Very motivated, adherent, excellent self-care capacities</td>
<td>Less motivated, less adherent, poor self-care capacities</td>
</tr>
<tr>
<td>Risks potentially associated with hyperglycemia, other adverse events:</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Long-standing</td>
</tr>
<tr>
<td>Disease duration</td>
<td></td>
</tr>
<tr>
<td>Short</td>
<td>Long</td>
</tr>
<tr>
<td>Life expectancy</td>
<td></td>
</tr>
<tr>
<td>Very</td>
<td>Short</td>
</tr>
<tr>
<td>Important comorbidities</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>Present</td>
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<tr>
<td>Established vascular complications</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Resources, support system</td>
<td></td>
</tr>
<tr>
<td>Readily available</td>
<td>Limited</td>
</tr>
</tbody>
</table>

EASD=European Association for the Study of Diabetes

Glucose-Dependent Actions of GLP-1 in T2DM Patients

Insulin (pmol/L)
Glucagon (pmol/L)
Glucose (mmol/L)

Data are mean ± SE
*P<0.05

SGLT2 Inhibitors

- SGLT2 responsible for 90% of glucose reabsorption in proximal tubule of kidney; inhibition causes glycosuria
- HbA1C reductions of 0.8% to 1.0% as monotherapy or in combination with other agents, including insulin
- Consistently observed weight loss and blood pressure reduction
- Reduced efficacy in patients with renal insufficiency
- Overall AE rates generally similar to placebo
  - Low risk of hypoglycemia
  - Higher risk of genital infections, but most readily resolved
  - Higher risk of renal and volume related adverse reactions in elderly, patients with renal impairment or low SBP, patients on ACE inhibitor, ARB or diuretics
  - Patients need to have renal function and volume status assessed before initiation
  - Canagliflozin should not be started or continued if eGFR is < 45 ml/min and dose limited to 100 mg if eGFR is between 45 & <60 ml/min
  - Dapagliflozin should not be started or continued if eGFR is < 60 mg/min

Effects of Antihyperglycemic Therapies on Blood Pressure: Meta-Analyses

<table>
<thead>
<tr>
<th>Agent Class</th>
<th>ΔSBP (mm Hg) (95% CI)</th>
<th>ΔDBP (mm Hg) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2Dsa</td>
<td>-4.70 (-6.13 to -3.27)</td>
<td>-3.79 (-5.91 to -1.67)</td>
</tr>
<tr>
<td>GLP-1 RAs*</td>
<td>-3.57 (-5.49 to -1.66)</td>
<td>-1.88 (-2.02 to -0.73)</td>
</tr>
<tr>
<td>Metformin*</td>
<td>-1.09 (-3.01 to 0.82)</td>
<td>-0.97 (-2.15 to 0.21)</td>
</tr>
<tr>
<td>DPP-4 inhibitors*</td>
<td>-0.97 (-1.2 to 0.11)</td>
<td>--</td>
</tr>
<tr>
<td>SGLT2 inhibitors*</td>
<td>-3.77 (-4.65 to -2.90)</td>
<td>-1.75 (-2.27 to -1.23)</td>
</tr>
</tbody>
</table>

*individual GLP-1 RAs yield similar BP changes, based on head-to-head trial results 5,7


Hypoglycemia With GLP-1 Receptor Agonists

Hypoglycemia with DPP-4 inhibitors

- Risk of hypoglycemia is low with DPP-4 inhibitor treatment (RR 0.92 [0.74, 1.15] vs. placebo)
- RR 0.20 [0.17, 0.24] compared to sulfonylurea) in absence of sulfonylurea or insulin co-therapy
- Significantly elevated for combination therapy of sulfonylurea or insulin with sitagliptin or linagliptin (RR 1.86 [1.46, 2.37] vs. placebo).

Hypoglycemia with SGLT2 Inhibitors

- Risk of hypoglycemia in low with SGLT2 inhibitors because of their mechanism of action
- When combined with metformin, risk of symptomatic hypoglycemia was similar between canagliflozin 50 mg/day to 300 mg twice/day (0-6%) and sitagliptin 100 mg/day (5%)
Clinical Case Scenario

• A 48-year-old female with a history of gestational diabetes during her second pregnancy presents for evaluation.
• She is a single mother and a shift worker at a toll booth.
• Currently taking metformin 1,000 mg twice daily and glimepiride 4 mg daily (initiated three years ago);
  atorvastatin 10 mg
• Blood pressure = 136/80  BMI 30.5
• A1C = 9.6%; eGFR = 70 mL/min/1.73 m²
• LDL = 80 mg/dL

Clinical Case Scenario, cont.

• Recent weight gain of 8 lbs, despite exercising and watching her diet.
• She has experienced 3 documented minor hypoglycemic events over the past year.

When to Initiate Insulin Therapy in Type 2 Diabetes

• ADA/BASD Writing Group¹:
  • As initial therapy in patients with significant symptoms associated with hypoglycemia
  • In a patient with dramatically elevated glucose concentrations (>300-350 mg/dL) or A1C >10.0%.
  • Failure of non-insulin therapies
  • Unintentional weight loss

• AACE/ACE Writing Group²:
  • As dual therapy in patients an A1C value of >7.5% (use with caution) or in asymptomatic patients with an A1C value of >9.0%
  • As triple therapy in asymptomatic patients with an A1C value of >9.0%
  • As initial therapy in symptomatic patients with an A1C value of >9.0%

• Other considerations:
  • Acute onset of diabetes
  • In hospitalized patients with diabetes


Currently Available Insulin Products

<table>
<thead>
<tr>
<th>Insulin³</th>
<th>Onset</th>
<th>Peak</th>
<th>Effective Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-Acting</td>
<td></td>
<td></td>
<td>&lt;5 hours</td>
</tr>
<tr>
<td>Aspart, lispro,</td>
<td>5-15 minutes</td>
<td>30-90 minutes</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-Acting</td>
<td>30-60 minutes</td>
<td>2-3 hours</td>
<td>Regular: 5-8 hours</td>
</tr>
<tr>
<td>Regular</td>
<td>U-500</td>
<td>U-100: 12 hours</td>
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<td></td>
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<tr>
<td>Intermediate (Biphasic)</td>
<td>2-4 hours</td>
<td>4-10 hours</td>
<td>10-16 hours</td>
</tr>
<tr>
<td>NPH</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Long-Acting (Biphasic)</td>
<td>2-4 hours²</td>
<td>No peak</td>
<td>20-24 hours</td>
</tr>
<tr>
<td>Glargine, detemir</td>
<td></td>
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</tr>
</tbody>
</table>

³NPH=Neutralized Protamine Lispro; NPL=Neutralized Protamine Hagedorn

References

Clinical Inertia to Initiation and Intensification of Injectable Therapies

- Self-blame
- Less with history of better adherence, less DM "stress"
- Avoidance of injections
- Concerns of risk
- Hypoglycemic effects
- Complexity of regimens
- Misconceptions about complications
- Weight gain
- Skepticism of efficacy
- Negative impact on social life


Initiation and Titration of Basal Insulin

Bedtime intermediate-acting insulin or bedtime/morning long-acting insulin (10 units or 0.2 units/kg)

Check fasting glucose daily and increase dose by 2 units Q3 days until fasting consistently 70-130 mg/dL; can increase by 4 units Q3 days if fasting >180 mg/dL.

If hypoglycemia or fasting <70 mg/dL – reduce bedtime dose by 4 units or 10% (whichever is greater)


Treat-to-Target Trial: Glargine or NPH Added to Regimen

Favors Detemir/Glargine Favors NPH

In both groups, FPG decreased from 194 or 198 mg/dL to 120 or 117 mg/dL, respectively, by study end, and A1C decreased from 8.6% to 6.9% by 18 weeks.

N=756
NPH=Neutral Protamine Hagedorn

Hypoglycemic Potential of Glargine and Detemir vs. NPH (Meta-Analysis)


*P<.05 (between treatment)
PG=plasma-referenced glucose

**Favors Detemir/Glargine
Favors NPH

Patients Can Safely and Effectively Self-Titrate Basal Insulin

- Frequent contacts with patients (12 in 24 weeks)
- Mixed specialty and general medicine clinics
- Audit to ensure investigator compliance of protocol algorithms

GLP-1 RAs Added to Multiple Oral Agents: Comparisons With Basal Insulin

<table>
<thead>
<tr>
<th>Group</th>
<th>Δ A1C (%)</th>
<th>Δ Weight*</th>
<th>Δ FPG†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonbasal vs. insulin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P&lt;NS vs. insulin</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>P&lt;0.05 vs. insulin</td>
<td></td>
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<tr>
<td>P&gt;0.05 vs. insulin</td>
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<tr>
<td>P&gt;0.01 vs. insulin</td>
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<tr>
<td>GLAR 0.5</td>
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<tr>
<td>EXN BID 1.5</td>
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<td></td>
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<tr>
<td>LIRA 1.5</td>
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<tr>
<td>EXN QW 1.5</td>
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<tr>
<td>IDET</td>
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<th>Δ A1C (%)</th>
<th>Δ Weight*</th>
<th>Δ FPG†</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET + SU1 (N=535)</td>
<td>-1.1-1.1</td>
<td>-0.8-0.6</td>
<td>-0.6-0.7</td>
</tr>
<tr>
<td>2–3 OADs2 (N=235)</td>
<td>-1.3-1.3</td>
<td>-0.6-0.6</td>
<td>-0.7-0.8</td>
</tr>
<tr>
<td>MET + GLIM3 (N=576)</td>
<td>-1.1-1.1</td>
<td>-0.8-0.6</td>
<td>-0.6-0.7</td>
</tr>
<tr>
<td>MET + SUL4 (N=456)</td>
<td>-1.3-1.3</td>
<td>-0.6-0.6</td>
<td>-0.7-0.8</td>
</tr>
<tr>
<td>MET + SU55 (N=216)</td>
<td>-1.3-1.3</td>
<td>-0.6-0.6</td>
<td>-0.7-0.8</td>
</tr>
</tbody>
</table>

But what about using a GLP-1 receptor agonist instead of basal insulin?

GLP-1 RAs Added to Multiple Oral Agents: Comparisons With Basal Insulin

Insulin Detemir Added to Liraglutide: Results From Randomization to Week 52

Clinical Case Scenario

- A 64-year-old man with T2DM for eight years presents for follow-up.
  - He is active, walking for 20 to 30 min daily and plays golf at least once each week
  - History of BPH, with on average 2 episodes of nocturia
  - Widower — his children live close by
  - He is currently using insulin glargine and metformin
Clinical Case Scenario, cont.

- A1C is 7.4% and FPG averages ~ 115 mg/dL.
- At his clinician’s request he performed a glucose profile which showed modestly increased pre-bedtime glucose values.
- He is concerned about hypoglycemia, especially since he lives alone, and weight gain, which has also steadily worsened over time.

Pharmacokinetics of Available Prandial Insulins: Rapid-Acting Analogues vs. Regular Human Insulin

Rapid-acting analogues have more rapid onset and shorter time to peak than regular human insulin.

Better Mean PPG Levels after Meals with Aspart vs. Regular Human Insulin

Fewer Nocturnal Hypoglycemic Events in Patients Treated with Aspart vs. Regular Human Insulin

Insulin + DPP-4 Inhibitor A1C at 24 Weeks
**Investigational Agents**

- **Lixisenatide**
  - Basal Insulin + Lixisenatide** vs. Basal Insulin**
  - **A1C** change at 28 days: -1.7 vs. -1.0 (P < 0.001)

**Glycemic Control With Investigational vs. Available GLP-1 RAs**

- **GetGoal** X³
  - N=166
  - 24 weeks

- **Outcome**
  - **EXN BID**
  - **LIXI**

- **A1C (%)**
  - 1.0
  - 0.8

- **ΔFPG (mg/dL)**
  - 26
  - 22

- **Noninferiority**
  - LIXI noninferior vs. EXN BID


**Dulaglutide**

- Long-acting GLP-1 analog with amino acid substitution
- Less susceptible to hydrolysis by DPP-4
- A recombinant GLP-1 Fc fusion protein linking a human GLP-1 peptide analog and a variant of a human IgG4 Fc fragment
- Reduced immunogenicity and limited renal clearance
- Half-life=4 days
- AWARD-1, AWARD-3, AND AWARD-5
- Dulaglutide 1.5 mg and 0.75 mg vs. comparators
- Superior glycemic control
- Sustained weight loss

New Insulin Formulation GLAR-300® vs. GLAR-100 In Patients on Basal Plus Mealtime Insulin

- Noninferior A1C change for GLAR-300 vs. GLAR-100 (both groups, 0.83%)
- No between-group differences in adverse events
- Significantly fewer with nocturnal hypoglycemia (≥3 severe or confirmed) with GLAR-300 (graph)

GLAR=Glargine
GLAR-300® is not FDA approved for clinical use.
*Confirmed hypoglycemia, ≤70 mg/dL

PEGylated Lispro® vs. Glargine in Adults With T2DM at 12 Weeks

- Patients with T2DM, 12 weeks
- After adjusting for baseline rates, nocturnal hypoglycemia was 48% lower in the pegylated lispro group (P<.021)

PEGylated lispro is not FDA approved for clinical use.
Hypoglycemia, plasma glucose ≤70 mg/dL or severe per ADA definition.

Degludec QD® vs. Glargine QD in Insulin-Naïve Patients With T2DM at 1 Year

- Similar A1C and weight changes
  - 0.1% vs. 0.2% (P=.40)
  - 0.4% vs. -0.1% (P=.28)
- Similar overall hypoglycemia
  - 1.5 vs. 1.9 events/y (NS)
- Lower nocturnal hypoglycemia® with degludec QD (graph)

IDegLira: A Fixed Ratio Combination of Insulin Degludec® and Liraglutide

- 1663 T2DM patients on MET or PIO; 26 week open-label trial
- Patients achieving A1C <7%
  - IDegLira: 81%
  - DEG: 65%
  - LIRA: 60%
  - IDegLira vs. DEG
    - Weight change: -2.22 kg; P<.001
    - Hypoglycemia: RR 0.89, P<.002
    - IDegLira vs. LIRA
      - Weight change: -2.44 kg; P<.001
      - Hypoglycemia: RR 7.65, P<.001

IDeg=Liraglutide; LRA=Liraglutide; MET=Metformin; PIO=Pioglitazone; RR=Risk Ratio
*IDegLira and insulin degludec are not FDA approved for clinical use.
Summary

• Type 2 diabetes patients need therapeutic interventions to control glycemic levels.
• Lifestyle interventions remain the cornerstone of therapy.
• Most patients will require combination pharmacotherapy in addition to lifestyle changes.
• Incretin-related agents have good glycemic lowering efficacy, a low risk for hypoglycemia, and weight neutrality or weight loss.
• Incretin optimization of endogenous insulin secretion before adding exogenous insulin may reduce insulin requirements, hypoglycemia and weight gain.
• When insulin is needed, basal and prandial analog insulins have a number of advantages compared to human insulin.

Questions

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