Role Of New Insulins In Current Diabetics

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Dr. Andukuri has no conflict of interest disclosures.
Objectives

- Learn about when to choose insulin over oral agents
- Different kinds of insulin, how newer ones are different from existing ones
- New insulins in market as well as in development
- When to choose new insulin over older ones
- Advantages and disadvantages of new insulins
The Diabetes Epidemic: Global Projections for 2030

World
2011 = 366 million
2030 = 552 million
Increase = 51%

37.7
51.2
36%

52.8
64.2
22%

71.4
120.9
69%

32.6
59.7
83%

14.7
28.0
90%

131.9
187.9
42%

25.1
39.9
59%

IDF. Diabetes Atlas 5th Ed. 2011
1 of 3 U.S. adults is at high risk of developing type 2 diabetes.

Get the facts about diabetes

DM 29 million
9.3% of US population

Pre-diabetes 86 million
~33% of US population

FBS = 100-125
A1c = 5.7-6.4%

Unaffected ~200 million
Pathophysiologic Progression of T2DM and Vascular Complications

IFG = impaired fasting glucose; IGT = impaired glucose tolerance; T2DM = type 2 diabetes mellitus.

9 FDA Approved Classes of Oral Medications for Type 2 Diabetes

1. **Biguanide**: metformin, metformin ER, Glucophage, glumetza (first line of therapy unless contraindicated)
2. **Sulfonylureas**: glyburide, glimepiride (amaryl), glipizide
3. **Meglitinides**: repaglinide (prandin), nateglinide (starlix)
4. **Glitazones (TZDS)**: Pioglitazone (actos)
5. **DPP-4 Inhibitors**: sitagliptin (Januvia), saxagliptin (onglyza), linagliptin (tradjenta), alogliptin (nesina)
6. **SGLT-2 inhibitors**: canagliflozin (invokana), dapagliflozin (farxiga), empagliflozin (jardiance)
7. **Alpha-glucosidase inhibitors**: acarbose (precose), miglitol (glyset)
8. **Bile acid sequestrant**: colesevelam (welchol)
9. **Dopamine receptor agonist**: bromocriptine (parlodel)
Injectables for Diabetes

1. GLP-1 Receptor Agonists: exenatide (byetta), exenatide ER (bydureon), liraglutide (victoza), dulaglutide (trulicity), albiglutide (tanzeum).

2. Amylinomimetic: pramlintide (symlin)

Insulins

1. Intermediate acting: NPH, Humulin R U-500

2. Basal or Long acting Insulin: glargine 100 units/ml (lantus), glargine 300 units/ml (toujeo), detemir (levemir), degludec (tresiba), basaglar

3. Bolus or Rapid acting Insulin: aspart (novolog), lispro (humalog), glulisine (apidra)

4. Short acting insulin: regular insulin

5. Pre-Mix Insulin: Humulin 70/30, Novolin 70/30, Novolog 70/30, Humalog 75/25, Humalog 50/50, ryzodek 70/30

6. Inhaled Insulin: Technosphere Inhaled insulin (afrezza)
Why and When to start insulin

- When combination oral/injectable agents become inadequate
- Unacceptable side effects of other agents
- Patient with advanced hepatic or renal disease
- Special circumstances (i.e. steroids, infection, pregnancy)
- Patient with hyperglycemia in the hospital

“Severely” uncontrolled diabetes*

*Defined as fasting glucose > 250 mg/dl, random glucose > 300 mg/dl, A1C >10%, ketonuria, or symptomatic (polyuria, polydipsia, and weight loss) After glucose controlled, oral agents can be added and insulin withdrawn if preferred.

Why is insulin so important in diabetes….

Efficacy: Comparison of A1c Reduction between Selected Anti-Diabetic Agents (Monotherapy)

%A1c ↓ from baseline

- DPP4-I
- SGLT2
- GLP-1
- Pioglitazone (A1c < 9.0)
- Glimepiride
- Metformin (A1c > 9.0)
- Pioglitazone (A1c > 9.0)
- Insulin

1.2
1.5
1.9
2.0
2.2
≥ 2.5
Benefits of Insulin Therapy for Type 2 Diabetes

- Biologic replacement of deficient hormone
- High safety profile
- Easy to titrate
- No contraindications
- No dose limits
- Therapy will ↓ A1c to < 7% in most cases
- Facilitates “β-cell rest”

- Corrects hyperglycemia and reduces glucotoxicity
- Increases glycolysis and reduces production of oxidative stressors
- Inhibits FFA production
- Improves endothelial dysfunction (antioxidant)
- Increases vasodilatation and slightly lowers BP
- Reduces CRP and cytokines (anti-inflammatory)

History of Insulin

Discovered in 1921 by Canadian scientists Banting and Best along with colleagues JB Collip and J Macleod
Timeline of Insulin Advancements

- **1920**: Frederick Banting, Charles Best, James Collip, and J.J.R. Macleod treat first patient with insulin.
- **1930**: Eli Lilly produces commercial quantities of bovine insulin.
- **1940**: Nordisk (later Novo Nordisk) scientist discovers that insulin action is extended with protamine. Nordisk markets Neutral Protamine Hagedorn insulin (aka NPH), derived from pig insulin in 1950.
- **1950**: Novo Nordisk markets human insulin (Novolin).
- **1960**: Eli Lilly markets human insulin (Humulin).
- **1970**: A biotech company called Genentech produces human insulin in bacteria. Sells recombinant DNA technology to Eli Lilly.
- **1980**: Eli Lilly markets Humalog in US.
- **1990**: Novo Nordisk markets Novolog in US.
- **2000**: Sanofi’s Lantus and Apidra insulin analogues approved in the US.
- **2010**: Pfizer discontinues inhaled insulin (Exubera).
- **2020**: Novo Nordisk introduces insulin detemir (Levemir).
We have long had these insulins

• Basal Insulins
  • Glargine - Lantus
  • Detemir - Levemir
  • NPH - Humulin N & Novolin N

• Bolus Insulins
  • Aspart - Novolog
  • Lispro - Humalog
  • Glulisine - Apidra
  • Regular - HumulinR and Novolin R
We have all sorts of combinations of basal and bolus insulins

- Novolog 70/30
- Humalog 70/30
- Humalog 50/50
Why do we need new insulins???

• Because existing insulins have shortcomings.....

• What would an ideal insulin ???
One which mimics normal insulin secretion

Basal: Continuous insulin to compensate for liver glucose
Bolus: Surge for food
  1st phase: Rapid rise in serum insulin inhibits glucagon release and glycogenolysis
  2nd phase: To maintain postprandial hyperglycemia
24 Hour Glucose Profiles for Different A1c Levels in T2DM

Uncontrolled A1C = 9.0%

“Controlled” A1C < 7.0%

A1C = 6.0%

Normal A1C 5.0% - 6.0%

PG (mg/dL)

Time of Day

0800 1200 1800 0800

Cefalu and Lahey Insulin Therapy 2002
Shortcomings of existing basal insulins

- Insufficient glycemic control
- Insufficient duration of action sometimes requiring twice daily injections
- Frequent dosing/injections
- Fear of hypoglycemia
  - Under dosing
  - Insufficient glycemic control
- Weight gain
Shortcomings of existing bolus insulins

- Not rapid enough
  - Need to take up to ½ hr prior to meal
- Lasts too long leading to delayed hypoglycemia
Properties an ideal basal insulin should have

- Long duration allowing for less frequent dosing
  - Once daily?
  - Once every other day?
  - Once weekly?
- Flexible timing of doses
- No peaking and allow for safe and easy titration
- Minimal or no risk of hypoglycemia
- No weight gain
Properties of an ideal bolus insulin

• Instant action so it can be taken immediately pre-prandially
• Short duration of action with no hypoglycemia
• No weight gain
Can newer insulins help address these challenges

2014
- Glargine-U300 (Toujeo)
- Affreza (inhalational)

2015
- Degludec U-100
- Degludec U-200
- Ryzodek 70/30
- Humalog U-200

2016
- “Biosimilar” insulins: Basaglar
- FDA approved in Dec 2016
Toujeo

- Generic name: Glargine U-300, concentrated form of traditional glargine
- Initial approval in Feb 2015, manufactured by sanofi
- 1.5ml pens (300/ml), total of 450 units (50% more than solostar)
- Duration of action: 36 hours, onset of action: 6 hours and no peak
- Maximum single injection: 80 units
Toujeo® Provides More Constant Absorption of Glargine after Subcutaneous Injection

- Three-fold more concentrated formulation of glargine
- Reduced volume (1/3) and reduced surface area (1/2) of subcutaneous depot
- Slower and more constant rate of absorption
More insulin in every mL vs. Lantus®

Each unit of Toujeo® has 1/3 the fluid volume of Lantus®. The smaller injection volume of Toujeo® results in a slow release of insulin.
Toujeo® Has a Flatter and More Prolonged PK/PD Profile than Lantus®
Offering Greater Consistency Over the Course of the Day

Type 1 Diabetes - Continuous Glucose Monitoring Study(1)

Average 24-hour glucose profiles showed a more constant glucose level with Toujeo® vs Lantus®

(1) Bergenstal RM et al. Poster presentation at EASD 2014: data combining morning and evening injections
Edition trials with glargine U-300
Is toujeo better than glargine???
Pooled Analysis of EDITION Phase III Trials in Type 2 Diabetes (T2D)\(^\text{1}\)

**Baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Toujeo(^\text{(\circ)})</th>
<th>Lantus(^\text{(\circ)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.7</td>
<td>58.5</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>34.7</td>
<td>34.8</td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>12.7</td>
<td>12.6</td>
</tr>
<tr>
<td>A1c (%)</td>
<td>8.31</td>
<td>8.32</td>
</tr>
</tbody>
</table>

**Concomitant glucose-lowering therapy**

<table>
<thead>
<tr>
<th>EDITION</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+ Mealtime insulin + Met</td>
</tr>
<tr>
<td>2</td>
<td>+ Met + OADs(^\text{(3)})</td>
</tr>
<tr>
<td>3</td>
<td>+ Met + OADs(^\text{(4)})</td>
</tr>
</tbody>
</table>

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1. Ritzel R et al, 2014 ADA, abstract 90-LB
2. Total daily dose Lantus\(\text{L}\) \(\leq 22 U\) or equivalent dose of NPH
3. Use of sulfonylureas were prohibited within 2 months prior to screening and during the study
4. Except sulfonylureas, glinides and other OADs not approved for use with insulin

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SANOFI
A1C reductions in EDITION 1 study

Toujeo®
(n=404)

Lantus®
(n=400)
With Toujeo® -- Lower Rates of Confirmed\(^{(1)}\) or Severe Hypoglycemic Events\(^{(2)}\)

**Cumulative Mean Number of Events Per Patient**

- **Any Time (24 h)**
  - Lantus®
  - Toujeo®

- **Nocturnal (00:00-05:59)**
  - Lantus®
  - Toujeo®

**Event Rate Per Patient-Year Across The 6-Month Study Period**

- **RR: 0.86 (0.77 to 0.97)**
  - p=0.0116
  - Lantus®: 17.73
  - Toujeo®: 15.22
  - -14%

- **RR: 0.69 (0.57 to 0.84)**
  - p=0.0002
  - Lantus®: 3.06
  - Toujeo®: 2.10
  - -31%

\(^{(1)}\) Confirmed: ≤70 mg/dL (≤3.9 mmol/L)

\(^{(2)}\) Pooled analysis of EDITION 1, 2 & 3 - Ritzel R et al, 2014 ADA, abstract 90-UB
Small but consistent weight differences between lantus and toujeo.
Toujeo summary

- Flatter PD and PD profile with lower risk of hypoglycemia and weight gain
- Titrate to achieve goal fasting blood sugars like any other basal insulin
- Target BG based on patient needs
- Titrate no more frequently than every 3 days
- Not for treatment of DKA
Insulin Glargine U100 vs U300

HbA1c Reduction

- Glargine U300
- Glargine U100

- Weight gain
  - Glargine U100, +0.79 kg
  - Glargine U300, +0.51 kg
  - LSM Difference, -0.28 kg

N=1247 patients treated with glargine U300 and 1249 treated with glargine U100 in 3 phase 3 EDITION studies.

Insulin Degludec - Tresiba

- Ultra long-acting insulin approved by FDA in September 2015
- Manufactured by Novo Nordisk
- Initially submitted to FDA in 2013
- Completed additional cardiac safety studies requested by FDA in Feb 2013
- Insulin degludec has an onset of action of 30–90 minutes (similar to insulin glargine and insulin detemir)
- There is no peak activity (due to slow systemic release)
- Duration of action >24 hours, lasts up to 42 hours (compared to 18 to 26 hours provided by other marketed long-acting insulins such as Insulin glargine and insulin detemir) making it a once daily basal insulin
Degludec molecule

Modified insulin with one amino acid deleted compared to human insulin and replaced by a fatty acid.
- Addition of fatty acid to lysine allows the formation of multi-hexamers in subcutaneous tissues.
- As phenol diffuses, this allows for slow insulin release into systemic circulation.
Pharmacodynamics of Degludec

- Available only as pens
- Available in 2 doses 100 units/ml and 200 units/ml
- 20-30% less dose dose required compared to other basal insulins
Degludec vs Glargine U-100 - BEGIN trials

- Total 6 trials in type 2 diabetics
- One year randomized treat to target trial by Zinman et al
- Comparing degludec with glargine in insulin naive type 2 diabetes inadequately controlled on oral agents

Conclusions

- Similar long-term glycemic control with lower rates of nocturnal hypoglycemia with degludec
- BEGIN trial
  - Similar A1c reductions
  - Similar reductions in glucose excursions

Zinman B et al. Diabetes Care 2012 Dec; 35(12): 2464-2471 similar
BEGIN TRIAL
- 18% lower overall hypoglycemia
- 36% lower nocturnal hypoglycemia

Zinman B et al. Diabetes Care 2012 Dec; 35(12): 2464-2471
BEGIN Basal-Bolus Type 1: 2 Year RCT

- Patients with Type 1 diabetes who continued insulin degludec therapy
  - Similar HbA1c reductions
  - Similar fasting plasma reductions
  - Lower nocturnal hypoglycemia by 25%
  - Lower insulin requirements by the end of study
    - 9% less daily insulin
  - 12% less basal
  - 6% less bolus insulin

SWITCH-1 & SWITCH-2 Trials

- Designed to demonstrate
- 64 week randomized double blind cross over trial
- SWITCH-1: Type 1 DM on basal insulin
- SWITCH-2: Type 2 DM, on basal insulin with or without OHA (excluding SU and Meglitinides)
- Patients assigned to Degludec U-100 or Glargine U-100 1:1 for 32 weeks and crossed over to other group
- Primary endpoint is superiority of confirmed severe hypoglycemia in maintenance phase
Switch 1 Crossover Trial Design

N = 501
Patients with Type 1 DM
Conclusion of SWITCH-1 Trial

• Similar reduction in A1c at 32 weeks

• Non-inferiority and superiority for primary endpoint of reduction in overall hypoglycemia (11% reduction in maintenance phase)

• Non-inferiority and superiority for secondary endpoint of reduction in nocturnal hypoglycemia (36% reduction in maintenance phase)
SWITCH - 2 Crossover Trial Design

N = 721
Patients with Type 2 DM

16 week titration
16 week maintenance
16 week titration
16 week maintenance
Conclusions of SWITCH-2 Trial

- Similar reduction in A1c at 32 weeks
- Superiority for primary endpoint of reduction in overall hypoglycemia (30% reduction in maintenance phase)
- Non-inferiority and superiority for secondary endpoint of reduction in nocturnal hypoglycemia (42% reduction in maintenance phase)
Tresiba's SWITCH 1 & SWITCH 2 Trials' Outcome

**SWITCH 1 – type 1 diabetes**

- **Hypoglycaemic events per 100 PYE**
  - Severe or BG confirmed symptomatic events: 2,463 vs. 2,201 (11%*)
  - Severe or BG confirmed symptomatic nocturnal events: 429 vs. 277 (-36%*)
  - Severe events: 92 vs. 69 (-35%*)

**SWITCH 2 – type 2 diabetes**

- **Hypoglycaemic events per 100 PYE**
  - Severe or BG confirmed symptomatic events: 265 vs. 186 (-30%*)
  - Severe or BG confirmed symptomatic nocturnal events: 94 vs. 55 (-42%*)
  - Severe events: 9 vs. 5 (-46%*)

*Note: The prevalence of hypoglycaemia is measured during the maintenance period. Blood glucose confirmed hypoglycaemia is defined as ≤56 mg/dL (≤3.1 mmol/L). The confirmatory secondary endpoint of proportions of subjects experiencing severe hypoglycaemia during the maintenance period did not reach statistical significance in the SWITCH 2 trial. * Statistically significant; BG: Blood glucose; PYE: Patient years exposed.

Source: Novo Nordisk, 3Q16 Investor Presentation
Biosimilar insulins are here…

**Basaglar**

**Definition**

Biosimilars are a type of biological product that are licensed (approved) by FDA because they are highly similar to an already FDA-approved biological product, known as the biological reference product (reference product), and have been shown to have no clinically meaningful differences from the reference product. In terms of safety, purity and potency of the product.
Insulin Basaglar

A - chain
Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Gly
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

B - chain
Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Leu Val Cys Gly
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

Insulin Lantus

A - chain
Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Gly
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

B - chain
Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Leu Val Cys Gly
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

Glu
21
Is Biosimilar Insulin the same as Generic Insulin???

Biosimilar insulin and generic insulin are not synonymous.
Generic vs Biosimilar

Generic drugs are copies of brand-name drugs, have the same active ingredient, and are the same as those brand name drugs in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. So, generic and brand name are bioequivalent.
Biological products

- Biological products are made from living organisms. The material they are made from can come from many sources, including humans, animals and microorganisms such as bacteria or yeast.
Biological products - biosimilar vs interchangeable

- Biosimilars are highly similar to have no clinically meaningful differences in terms of safety and effectiveness.
- Prescribed by health care provider.

- An interchangeable biological product, in addition to meeting the biosimilarity standard, is expected to produce the same clinical result as the reference product in any given patient.
- May be substituted for the reference product by a pharmacist without the intervention of the health care provider who prescribed the reference product.

Once a biosimilar or interchangeable has been approved by FDA, patients and health care providers will be able to rely upon the safety and effectiveness of an FDA approved biosimilar just as they would for the reference product that the biosimilar was compared to.
Why make Biosimilar insulins

- Compete with other insulin producing companies
- Reduce the cost and increase availability of certain insulins
- Not as inexpensive as generics
Lantus vs basaglar kwik Pen
U-500

- Concentrated Regular insulin, 5 times more concentrated
- Injection volume down by 80% compared to U-100
- Profile closely mimics to NPH
- Injection can be done twice daily
  - Comparable to three times daily
- Humulin R U-500 exhibits both basal and prandial insulin properties allowing it to be used as insulin monotherapy
- This effect is attributed to high concentration of the preparation
- FDA approved first U-500 insulin pen device in January 2016
- Each pen holds 1500 units
- Vial holds 20ml
- Better fit for patients requiring high insulin doses per day
- Better patient satisfaction and quality of life
Meta-Analysis of Studies using U-500R MDI

(A) Changes in HbA1c with an overall significant reduction of 1.59% (95% CI, 1.26–1.92);
(B) Changes in weight with an overall significant increase of 4.38 kg (95% CI, 2.35–6.41);
(C) Changes in TDD with an overall significant increase of 51.9 units (95% CI, 19.6–84.1)

Why change from your present basal to concentrated basal insulin?

• Reduce variability of glucose levels
• Reduce risk of hypoglycemia, severe and nocturnal
• Give higher doses of insulin with pens
• Improved adherence with no split in basal dosing
# Switching between insulins

<table>
<thead>
<tr>
<th>Current therapy</th>
<th>Switch to U-100 Glargine</th>
<th>Switch to U-300 Glargine</th>
<th>Switch to degludec</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-100 Glargine</td>
<td>----</td>
<td>1:1 Initial. Likely uptitrate by 10%</td>
<td></td>
</tr>
<tr>
<td>U-300 Glargine</td>
<td>Consider ↓ dose by 10%</td>
<td>----</td>
<td>Consider ↓ dose by 10%</td>
</tr>
<tr>
<td>Degludec</td>
<td>1:1 Initial Likely need to uptitrate</td>
<td>1:1 Initial Likely need to uptitrate</td>
<td>----</td>
</tr>
</tbody>
</table>
## Comparison of pens

<table>
<thead>
<tr>
<th></th>
<th>U-100 Glargine</th>
<th>U-300 Glargine</th>
<th>U-100 Degludec</th>
<th>U-200 Degludec</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Units per pen</strong></td>
<td>300</td>
<td>450</td>
<td>300</td>
<td>600</td>
</tr>
<tr>
<td><strong>Max units per pen</strong></td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>160</td>
</tr>
<tr>
<td>Stability once opened at room temp</td>
<td>28</td>
<td>42</td>
<td>56</td>
<td>56</td>
</tr>
</tbody>
</table>
What’s new in bolus insulins??

A decade ago, there was exubera....

Pfizer stopped production in 2007
Inhaled human Insulin – Affreza

- Approved by FDA in 2014
- Manufactured by Mannkind corp
- This is a very fast analogue that can be given with meals and snacks.
Pharmacokinetics

Peaks faster and offsets faster compared to available rapid acting insulin

Less delayed hypoglycemia
Adverse effects

• Hypoglycemia
• Throat discomfort
• Requires extra doses to cover a meal considering short duration of action
• Weight gain (like other insulins)
• Cough
  • Dry intermittent (upto 30%)
  • Leads to discontinuation by 2.8%
Pulmonary side-effects

• Mild decline in pulmonary function
  • Forced Expiratory Volume (FEV1) by 40ml
• Occurred in first 3 months
• Returned to baseline after discontinuation
Precautions/Recommendations

- Perform spirometry
  - At baseline
  - After 6 months and then annually
  - More frequent monitoring with pulmonary symptoms
- If FEV1 declines by >20%, consider stopping
- Not recommended in patients with asthma/COPD
- Black box warning of causing acute bronchospasm in
Humalog U-200

- For patients requiring high meal time insulins
- First concentrated mealtime insulin
- Pharmacokinetic and dynamic profiles similar to U-100
- Can hold up to 600 units (than traditional pen holding 300 units)
- Single dose can only deliver up to 60 units like U-100
Ryzodeg 70/30 (Insulin Degludec and Insulin Aspart)

- FDA approved September 2015
- 3 ml flex touch disposable pre-filled pen
- Recommended to start once daily with biggest meal and titrate to twice daily
26 week randomized, open label, Treat-to-Target trial involving ryzodeg vs BiAsp (70% protamine aspart and 30% aspart)

Clinical end points
A: Mean HbA1c over time
B: Mean FPG over time
C: Cumulative rate of confirmed hypoglycemic episodes
D: Cumulative rate of nocturnal conformed hypoglycemic episodes

G Fulcher. Et al Diabetes Care 2014 Aug; 37(8): 2084-2090
Ultra rapid acting insulin aspart in pipeline

• Rapid acting insulin aspart with nicotinamide and hyalurodinase
• Being developed by Novo Nordisk
• Studies started in 2013, promising so far
• Hopefully coming soon.......
Timely initiation of insulin therapy to achieve glycemic goals

No one insulin is right for every patient

Insulin therapy customise based on patients needs, goals, barriers and cost

Never forget non-glycemic therapies (e.g. statins, ACE-I or ARB, ASA, and smoking cessation) to reduce CVD risk
Thank you all…
Special thank you to Dr. Wahl and Dr. Sundaram for letting me use some of their slides
Questions ???