Diabetes Treatment Options in 2017

Christopher Corsi MD
The number of medications for treating diabetes has increased exponentially over the last several years.

How do we choose the best agents for our patients?
- Insulins
- Non-insulin hypoglycemic agents
Diabetes Drug Classes Increasing Rapidly

Number of Medication Classes

12 11 10 9 8 7 6 5 4 3 2 1

- Sulfonylureas
- Biguanides
- Glinides
- TZDs
- GLP-1 Receptor Agonists
- DPP-4 inhibitors
- Amylinomimetics
- Bile acid sequestrants
- Dopamine agonists
- SGLT-2 inhibitors

Insulin (1922)

Insulin

- Coming up on the 100th anniversary of discovery of insulin.

- Regular, NPH were mainstays of treatment until Analogs became available in mid-90s.

- Since results of DCCT (1990s), tight control is advocated, making a stronger case for use of insulins/devices that more closely mimic normal islet cell function.
Basal–Bolus Insulin

**Bolus:**
- Rapid Analogs: Lispro (Humalog), Aspart (Novolog), Glulisine (Apidra)
- Inhaled (Afrezza)

**Basal Analogs:**
- Detemir (Levemir)
- Glargine (Lantus, Toujeo)
- Degludec (Tresiba)
DEVOTE (Degludec)

- 7600 patients with T2DM and a hypoglycemic event in last 90 days.

- Degludec vs Glargine

- No difference A1c or CV outcome

- 53% less nocturnal hypoglycemia w/degludec

- 40% less severe hypoglycemia w/degludec
Insulin

- Cost has been the big story this year

- Biosimilars (Lispro, Glargine) now hitting market may have impact.
- Insurance/ prior auth woes
Type 2 Diabetes Treatments

- All have pros/cons
- Cost/ prior auth issues
- Weight
- Hypoglycemic risk
- Potential other side effects
- Interactions with other diseases/medications
- Prevention of complications
Metformin

- OK down to eGFR 35
- Remains best first pharmacologic treatment in T2DM

- After that…. Complicated!!
# Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>GLP-1 RA</th>
<th>SGLT-2i</th>
<th>DPP-4i</th>
<th>AGi</th>
<th>TZD (moderate dose)</th>
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<tbody>
<tr>
<td><strong>HYPO</strong></td>
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<td>Moderate/Severe</td>
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<td><strong>WEIGHT</strong></td>
<td>Slight Loss</td>
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<tr>
<td><strong>RENO / GU</strong></td>
<td>Contraindicated if eGFR &lt; 30 mL/min/1.73 m²</td>
<td>Possible Benefit of Liraglutide</td>
<td>Possible Benefit of Empagliflozin</td>
<td>Genital Mycotic Infections</td>
<td>Dose Adjustment Necessary (Except Linagliptin)</td>
<td>Effective in Reducing Albuminuria</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
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- **Few adverse events or possible benefits**
- **Use with caution**
- **Likelihood of adverse effects**
- **Uncertain effect**
- **FDA indication to prevent CVD death in diabetes plus prior CVD events**

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GLYCEMIC CONTROL ALGORITHM

LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

Entry A1C < 7.5%

MONOTHERAPY*
- Metformin
- GLP-1 RA
- SGLT-2i
- DPP-4i
- TZD
- AGI
- SU/GLN

If not at goal in 3 months proceed to Dual Therapy

Entry A1C ≥ 7.5%

DUAL THERAPY*
- GLP-1 RA
- SGLT-2i
- DPP-4i
- TZD
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGI
- SU/GLN

If not at goal in 3 months proceed to Triple Therapy

Entry A1C > 9.0%

TRIPLE THERAPY*
- GLP-1 RA
- SGLT-2i
- DPP-4i
- TZD
- Basal insulin
- Colesevelam
- Bromocriptine QR
- AGI
- SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

SYMPTOMS

NO
- DUAL Therapy

OR

YES
- INSULIN ± Other Agents

- ADD OR INTENSIFY INSULIN
  Refer to Insulin Algorithm

LEGEND
- Few adverse events and/or possible benefits
- Use with caution

PROGRESSION OF DISEASE

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* Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation.
SGLT2–I’s and GLP-ra’s (–flozins and –tides)

- Have moved higher in algorithm due to favorable outcome studies.
- Differences between products?
EMP A–REG (Empagliflozin)

- Just over 7000 pts with T2DM and h/o CVD x 3 years.
- 14% decrease in primary composite endpoint (CV death, nonfatal MI, nonfatal stroke)
- 38% decrease in CV death
- 32% decrease all cause mortality
- 40% decrease in renal disease (incident or worsening nephropathy)

- CANVAS (canagliflozin)
LEADER (Liraglutide)

- 9340 patients with T2DM x 3.5 years
- Pts >50 with CV disease or >60 with risk factor
- 13% reduction in primary outcome (CV death, nonfatal MI, nonfatal stroke)
- 22% reduction in CV death and 15% drop in all cause mortality
- 22% reduction in nephropathy

- Exscel (Exena), Elixa (lixi), Sustain–6 (sema)
Pioglitazone and SU’s added to metformin in carefully selected T2DM patients (11% prior CV).

Safe over 4 years
- Low MACE scores
- Low hypoglycemia
- Low CHF
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<td>Possible CV Benefit</td>
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<td>Neutral</td>
<td>May Reduce Stroke Risk</td>
<td>?</td>
<td>Benefit</td>
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<td>Canagliflozin Warning</td>
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How to go forward?

- Diet/Exercise
- Metformin
- If affordable/appropriate, SGLT2i or GLPra
- If affordable/appropriate, SGLT2i or GLPra
- Can consider SU and/or pio still, in carefully selected patients.
- DPP-4 a good option when minimal side effects of utmost importance (hospital).
- Basal insulin
- Intensive insulin (u–500)
Statins and Glucose

- Jupiter study– rosuvastatin
- Meta–analyses
- Pravastatin different? (not P–450)
- Pitavastatin

- Usual risks
- 0.1% increase in A1c
- Reduce CV outcomes, mortality, amputation