PHARMACOTHERAPY CASES IN DIABETES

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A Duke Lifepoint Hospital
Case #1

- B.K. is an 80 year old male with a 10 year history of T2DM, previously controlled with lifestyle modifications only. At clinic, he complains of pain/burning in his legs, and more frequent urination & thirst than usual.
  - HbA1c: 9.2%

- How aggressive would you be with his HbA1c goal?
- Suggest a first line adjuvant medication.
  - What are some side effects to tell the patient?
  - How should the patient take the medication?
## CASE #1

### PATIENT / DISEASE FEATURES

<table>
<thead>
<tr>
<th>Feature</th>
<th>More Stringent</th>
<th>Less Stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks potentially associated with hypoglycemia and other drug adverse effects</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>Disease duration</td>
<td>newly diagnosed</td>
<td>long-standing</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>long</td>
<td>short</td>
</tr>
<tr>
<td>Important comorbidities</td>
<td>absent</td>
<td>severe</td>
</tr>
<tr>
<td>Established vascular complications</td>
<td>absent</td>
<td>few / mild</td>
</tr>
<tr>
<td>Patient attitude and expected treatment efforts</td>
<td>highly motivated, adherent, excellent self-care capacities</td>
<td>less motivated, non-adherent, poor self-care capacities</td>
</tr>
<tr>
<td>Resources and support system</td>
<td>Readily available</td>
<td>limited</td>
</tr>
</tbody>
</table>

### Approach to the management of hyperglycemia

- **HbA1c 7%**
- **Potentially modifiable**
- **Usually not modifiable**
Metformin (Glucophage®) PO
- SFX - nausea/vomiting/diarrhea
- Take twice daily with meals (to help GI upset)
- PROS - help with weight loss, cholesterol; lower HbA1c 1-2%, reduction in microvascular complications (peripheral neuropathy)

Linagliptin (Tradjenta®) PO
- SFX - well tolerated; small risk for pancreatitis
- Take once daily without regard to meals
- PROS - may help with weight loss, lower HbA1c 0.5-0.75%, no dose adjustment for renal dysfunction

GLP-1 RAs would be effective, but require injections, slow titration due to GI SFX and are very costly $$$
Insulin, SFUs pose high risk for hypoglycemia
TZDs may have detrimental FX in this patient
SGLT2 inhibitors would increase his urination/thirst (which he is complaining about)
A.N. is a 44 year old female diagnosed with T2DM last year. She presents to clinic overweight, admitting to non-compliance with her diet & exercise regimen due to increasing pressures from and time spent at work. She is well-educated, motivated, and smokes 1PPD.

- **Current Med List**
  - Metformin 1000mg PO twice daily for DM
  - Lisinopril 20mg PO once daily for HTN
  - Lasix 20mg PO once daily prn edema
  - Rosuvastatin 10mg PO once daily for Hyperlipidemia

- HbA1c 9.2% (from 11% at diagnosis), FBG 200mg/dL, Scr 1mg/dL
- LDL-c 69mg/dL, HDL-c 50mg/dL, BP 135/85
CASE #2

- How aggressive would you be with her HbA1c goal?
  - Is she meeting other goals for cardiovascular risk reduction?

- Do you have any other suggestions or counseling points for A.N.?
  - Smoking cessation?

- What are some adjuvant medication therapies that you would consider initiating?
Healthy eating, weight control, increased physical activity & diabetes education

### Mono-therapy

<table>
<thead>
<tr>
<th>Efficacy*</th>
<th>Hypo risk</th>
<th>Weight</th>
<th>Side effects</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>high</td>
<td>low</td>
<td>neutral/loss</td>
<td>GI/lactic acidosis</td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

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#### Dual therapy

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</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>high</td>
<td>moderate risk</td>
<td>gain</td>
<td>hypoglycemia</td>
</tr>
<tr>
<td>Thiazolidinedione</td>
<td>high</td>
<td>low risk</td>
<td>gain</td>
<td>edema, HF, fx</td>
</tr>
<tr>
<td>DPP-4 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>neutral</td>
<td>rare</td>
</tr>
<tr>
<td>SGLT2 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>loss</td>
<td>GU, dehydration</td>
</tr>
<tr>
<td>GLP-1 receptor agonist</td>
<td>high</td>
<td>high</td>
<td>low risk</td>
<td>loss</td>
</tr>
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If HbA1c target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

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#### Triple therapy

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If HbA1c target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i.

### Combination injectable therapy

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**Basal Insulin +**

**Mealtime Insulin or GLP-1-RA**
**CASE #2**

Better Options

- **Insulin**
  - Basal – Glargine or detemir
  - Bolus – Aspart, Lispro or Glulisine

- **GLP-1RAs**
  - Byetta® or Victoza® daily
  - Bydureon®, Tanzeum®, Trulicity® once weekly

Options

- **SFUs**
  - Glyburide, glimepiride or glipizide

- **DPP4 Inhibitors**
  - Saxagliptin or sitagliptin

- **SGLT2 Inhibitors**
  - Invokana®, Jardiance® or Farxiga®

**Contraindicated medications:**

- TZDs - fluid retention/heart failure and bone fracture risk in patient with hx of edema
- Afreeza® INH insulin - pt is smoker; BBW for acute bronchospasm

BBW - black box warning
J.C. is a 53 year old male well known to your service who returns to clinic for a 6 month follow-up after starting Byetta® (exenatide) twice daily injections. He complains of abdominal pain.

- **Labs**
  - HbA1c 10%
  - Amylase, Lipase
  - and Alk Phos elevated

- **Current Meds**
  - Metformin 850mg PO twice daily for DM
  - Exenatide 5mcg Sub-Q twice daily before meals for DM
  - Lasix 40mg PO once daily for edema/HF symptoms
  - Metoprolol XL 100mg PO once daily for prior MI
  - Rosuvastatin 20mg PO once daily for CVD
  - Glulisine (Apidra®) insulin Sub-Q on a sliding scale
Based on a high suspicion for acute pancreatitis, which medication would you recommend he stops taking?

Are any other DM medications contraindicated in J.C.?

In light of your decision to stop the one drug, you and J.C. decide to change his sliding scale insulin to a basal-bolus regimen with Detemir and Glulisine. What would an appropriate starting dose of each of these be?

- His average total daily dose of sliding scale insulin is 200 units
In light of your decision to stop the one drug, you and J.C. decide to change his sliding scale insulin to a basal-bolus regimen with Detemir and Glulisine. What would an appropriate starting dose of each of these be?

- His average total daily dose of sliding scale insulin is 200 units
  - TDD = 200 units x 0.4 (40% basal) = 80 units detemir
  - TDD = 200 units x 0.6 (60% bolus) = 120 units glulisine
    - Glulisine pre-prandial = 120 units ÷ 3 = 40 units

- Detemir 80 units sub-q once daily (or 40 units BID)
- Glulisine 40 units sub-q 15 minutes before meals 3 x daily
J.C. asks if he can utilize inhaled insulin Afrezza® for one or both of his injectable insulin products. What do you think?

- Cannot use for basal insulin (detemir). Remember... Afrezza® is regular insulin (short-acting).
- Could potentially use for meal-time insulin (glulisine)
  - J.C. requires 40 units. The current max dose of Afrezza is 24 units, so this would not be effective enough for J.C.