PHARMACOTHERAPY CASES IN DIABETES

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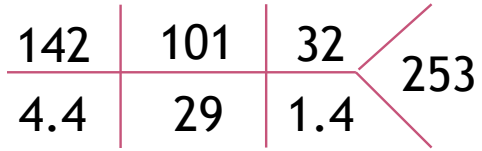
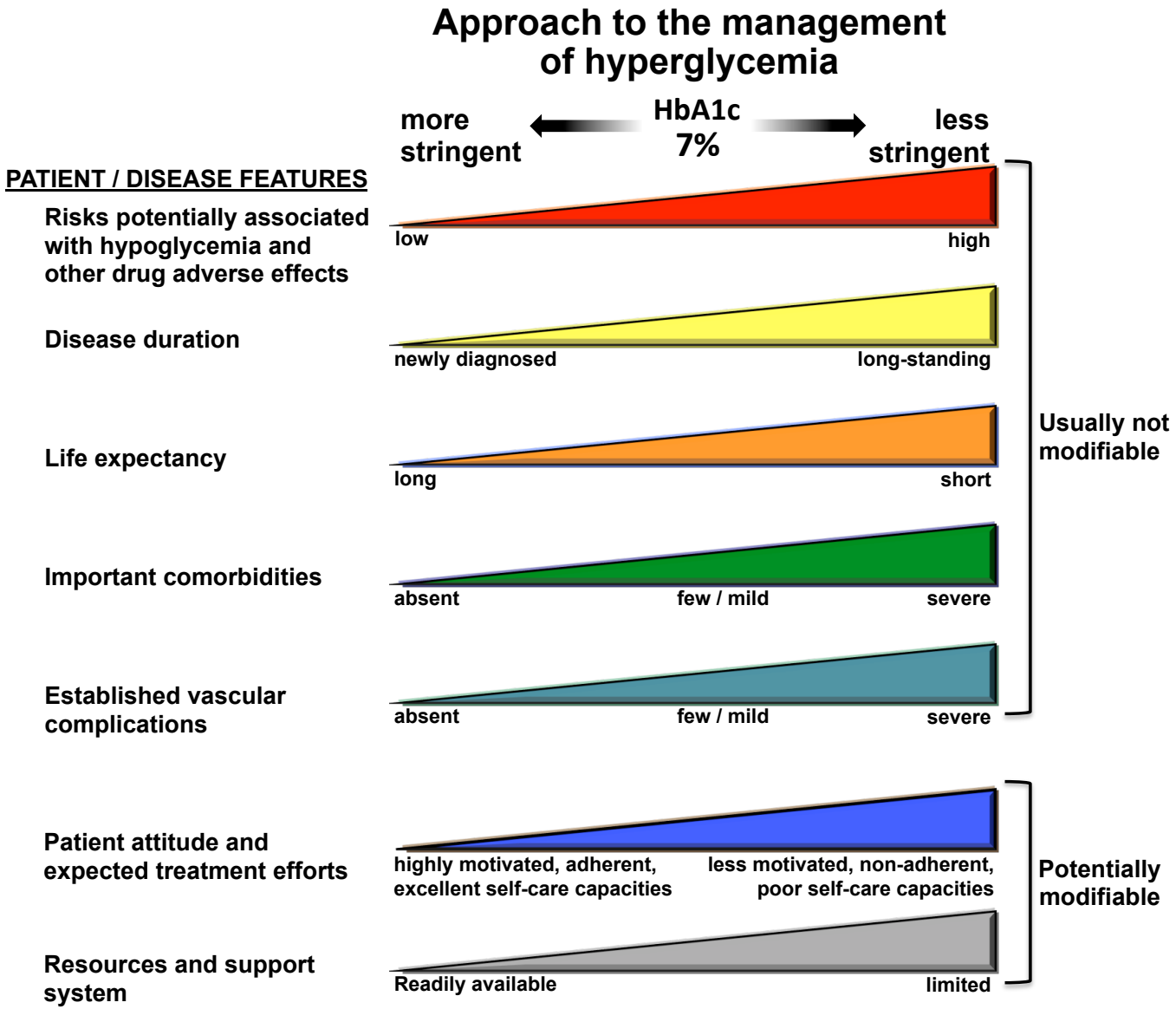
CASE #1

- 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


Approach to the management of hyperglycemia
more stringent
HbA1c 7%
less stringent
PATIENT / DISEASE FEATURES
Risks potentially associated with hypoglycemia and other drug adverse effects
low
high
Disease duration
newly diagnosed
long-standing
Life expectancy
long
short
Important comorbidities
absent
few / mild
severe
Established vascular complications
absent
few / mild
severe
Usually not modifiable
Patient attitude and expected treatment efforts
highly motivated, adherent, excellent self-care capacities
less motivated, non-adherent, poor self-care capacities
Resources and support system
Readily available
limited
Potentially modifiable

CASE #1

Either metformin or a DPP4 antagonist would be an appropriate selection.

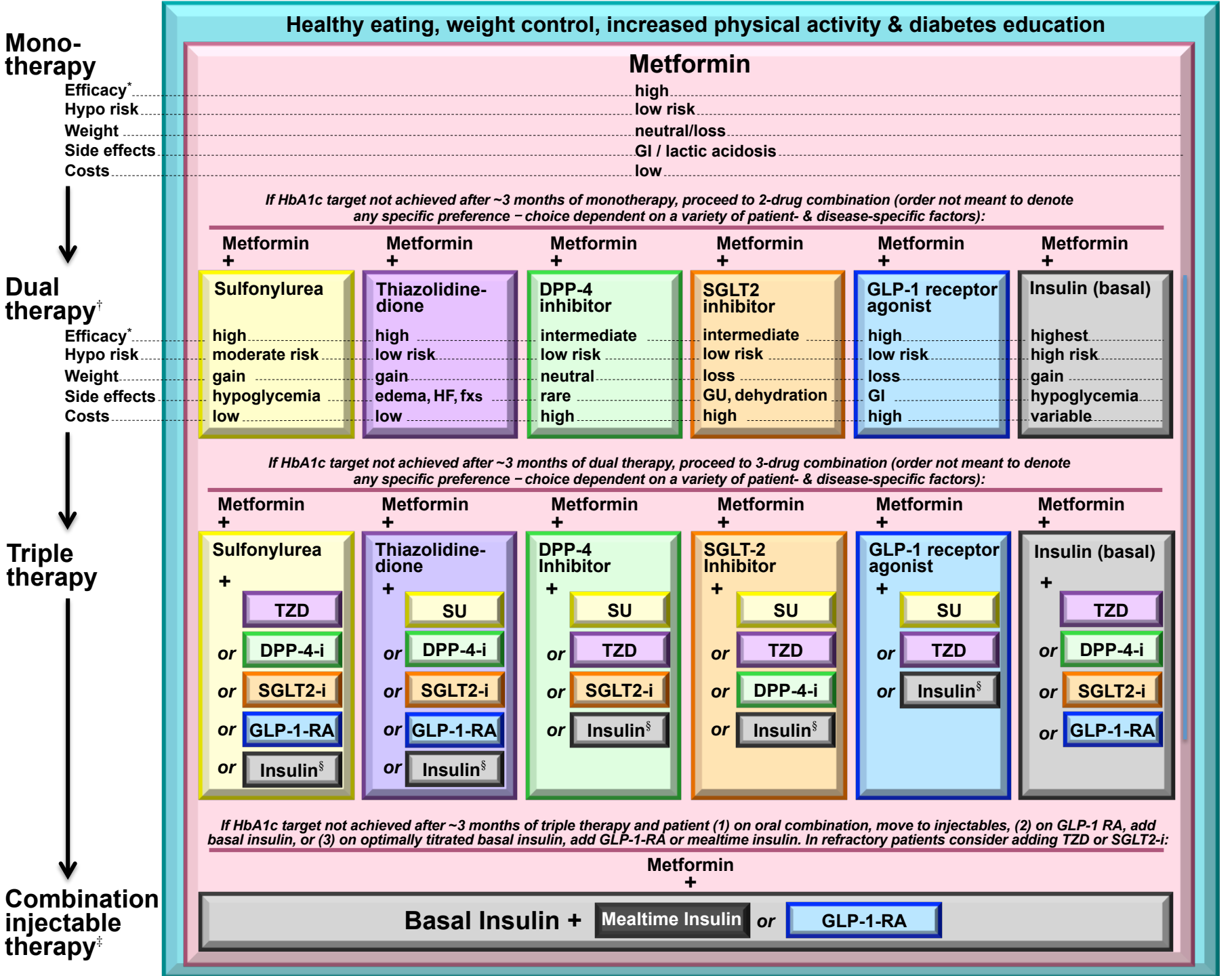
- Metformin (Glucophage®) PO
  - SFX – nausea/vomiting/diarrhea
  - Take twice daily with meals (to help GI upset)
  - PROS – help with weight loss, cholesterol; lower HbA1c 1-2%, reduction in microvascular complications (peripheral neuropathy)
- Linagliptin (Tradjenta®) PO
  - SFX – well tolerated; 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)

CASE #2

- A.N. is a 44 year old female diagnosed with T2DM last year. She presents to clinic over weight, 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
Metformin
Efficacy*
high
Hypo risk
low risk
Weight
neutral/loss
Side effects
GI / lactic acidosis
Costs
low
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):
Dual therapy†
Metformin + Sulfonylurea
high
moderate risk
gain
hypoglycemia
low
Metformin + Thiazolidine-dione
high
low risk
gain
edema, HF, fxs
low
Metformin + DPP-4 inhibitor
intermediate
low risk
neutral
rare
high
Metformin + SGLT2 inhibitor
intermediate
low risk
loss
GU, dehydration
high
Metformin + GLP-1 receptor agonist
high
low risk
loss
GI
high
Metformin + Insulin (basal)
highest
high risk
gain
hypoglycemia
variable
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):
Triple therapy
Metformin + Sulfonylurea + TZD or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin§
Metformin + Thiazolidine-dione + SU or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin§
Metformin + DPP-4 Inhibitor + SU or TZD or SGLT2-i or Insulin§
Metformin + SGLT-2 Inhibitor + SU or TZD or DPP-4-i or Insulin§
Metformin + GLP-1 receptor agonist + SU or TZD or Insulin§
Metformin + Insulin (basal) + TZD or DPP-4-i or SGLT2-i or GLP-1-RA
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‡
Metformin +
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

CASE #3

- 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

135	99	28	190
3.5	17	1.5	

CASE #3

- 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

CASE #3

- 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

CASE #3

- 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.