Diabetes Update

Elys M. Perez, MD
Department of Endocrinology, Diabetes, and Metabolism
Broward Health Medical Center

Conflict of Interest

- I have no conflict of interest to report

Overview

- Clinical practice in the patient population with diabetes
- Classification and diagnosis
- Prevention or delay of type 2 diabetes
- Assessment of comorbidities and management
- Glycemic targets
- Pharmacologic approaches to glycemic treatment

Diabetes and Population Health

- Treatment recommendations should follow current evidence-based guidelines
- Tailored to every individual patient based on patient preference, prognosis and comorbidities
- According to a 2013 report, 33-49% of patients still did not meet general targets for glycemic, blood pressure, or cholesterol control
- Only 14% met targets for all three measures and smoking cessation
- Economic costs of diabetes have increased by 26% from 2012-2017

Chronic Care Model

- Proactive care delivery system with a team based approach
- Self-management support
- Basing care on evidence based guidelines
- Using registries that provide patient-specific and population-based support to the care team
- Identifying or developing resources to support healthy lifestyles

Classification and Diagnosis

- Type 1 diabetes
- Type 2 diabetes
- Gestational diabetes
- Other (monogenic diabetes syndromes, diabetes secondary to diseases of the exocrine pancreas, drug induced)

Screening

- Test adults with a BMI ≥ 25 or ≥ 23 in Asian Americans who have any of the following risk factors
  - 1° relative with diabetes
  - High risk race/ethnicity
  - History of CVD
  - HTN
  - HDL ≤ 35 or triglycerides ≥ 250
  - PCOS
  - Physical inactivity
  - Severe obesity or acanthosis nigricans
- For all people testing should begin at age 45

Diagnosis

FPG ≥ 126 mg/dl

OGTT ≥ 200 mg/dl at 2 hours (after the administration of 75g of glucose)

A1c ≥ 6.5%

RPG ≥ 200 mg/dl in patients with classic symptoms of hyperglycemia

Prevention and Delay

- Annual monitoring is suggested for those with prediabetes
- All patient should be referred to an intensive lifestyle intervention program at diagnosis of prediabetes or diabetes
  - Aim to achieve and maintain 7% loss of initial body weight
  - Increase moderate-intensity physical activity to 150min/week
  - In the DPP, diabetes incidence was reduced by 58% over 3 years
  - The diabetes prevention program outcomes study has shown sustained reduction in the rate of conversion to type 2 diabetes of 34% at 10 years and 27% at 15 years
- Pharmacologic therapy with metformin should be considered for those with prediabetes and:
  - BMI ≥ 35
  - Age < 60 years
  - Women with prior GDM

Assessment of Comorbidities

- Consider screening patients with type 1 diabetes for autoimmune disorders
- In patients with cognitive impairment treatment goals should aim at avoiding hypoglycemia
- Evaluate the need for diabetes self management education and support (DSMES) at diagnosis, annually, when complications arise, and during transition of care
- Refer all patients for medical nutrition therapy (MNT)
- Assess patients for symptoms of diabetes distress, depression, anxiety, disordered eating and cognitive capacities

Blood Pressure

- Aim to maintain blood pressure < 140/90 mmHg for patients with diabetes
- For those patients with ASCVD > 15%, aim for a target blood pressure of < 130/80 mmHg
- ACE-I or ARBs are the recommended first line therapy

Lipids

- For patients with diabetes and ASCVD, if LDL cholesterol is ≥ 70 mg/dl on maximally tolerated statin therapy consider adding additional LDL-lowering drugs such as ezetimibe or a PCSK9 inhibitor

Cardiovascular Disease

- In patients with ASCVD consider use ACE-I or ARBs to reduce risk
- Those with type 2 diabetes and established ASCVD using SGLT2 inhibitors or GLP-1 receptor agonists with proven benefit is recommended
  - In those with heart failure or high risk of heart failure SGLT2 inhibitors are preferred

Microvascular Complications

- Chronic kidney disease
  - Check urine albumin to creatinine ratio (UACR)
    - In patients with type 1 diabetes 5 years after diagnosis and then yearly thereafter
    - In all patients with type 2 diabetes
    - In all patients with hypertension
  - ACE-I or ARBs are recommended in patients with hypertension and UACR between 30-299 mg/g creatinine
  - For patients with type 2 diabetes and CKD use a SGLT2 inhibitor or a GLP-1 receptor agonist

Microvascular Complications

- Diabetic retinopathy
  - Patients with type 1 diabetes should have a dilated eye exam 5 years after diagnosis
  - Patients with type 2 diabetes should have a dilated eye exam at the time of diagnosis
  - Women planning to become pregnant should be warned about worsening retinopathy during pregnancy

Microvascular Complications

- Neuropathy
  - All patients with type 1 should be assessed 5 years after the diagnosis
  - All patients with type 2 diabetes should be assessed starting at diagnosis
  - Pharmacologic treatment is aimed at neuropathic pain
  - There is no specific treatment for the underlying nerve damage other than glycemic control

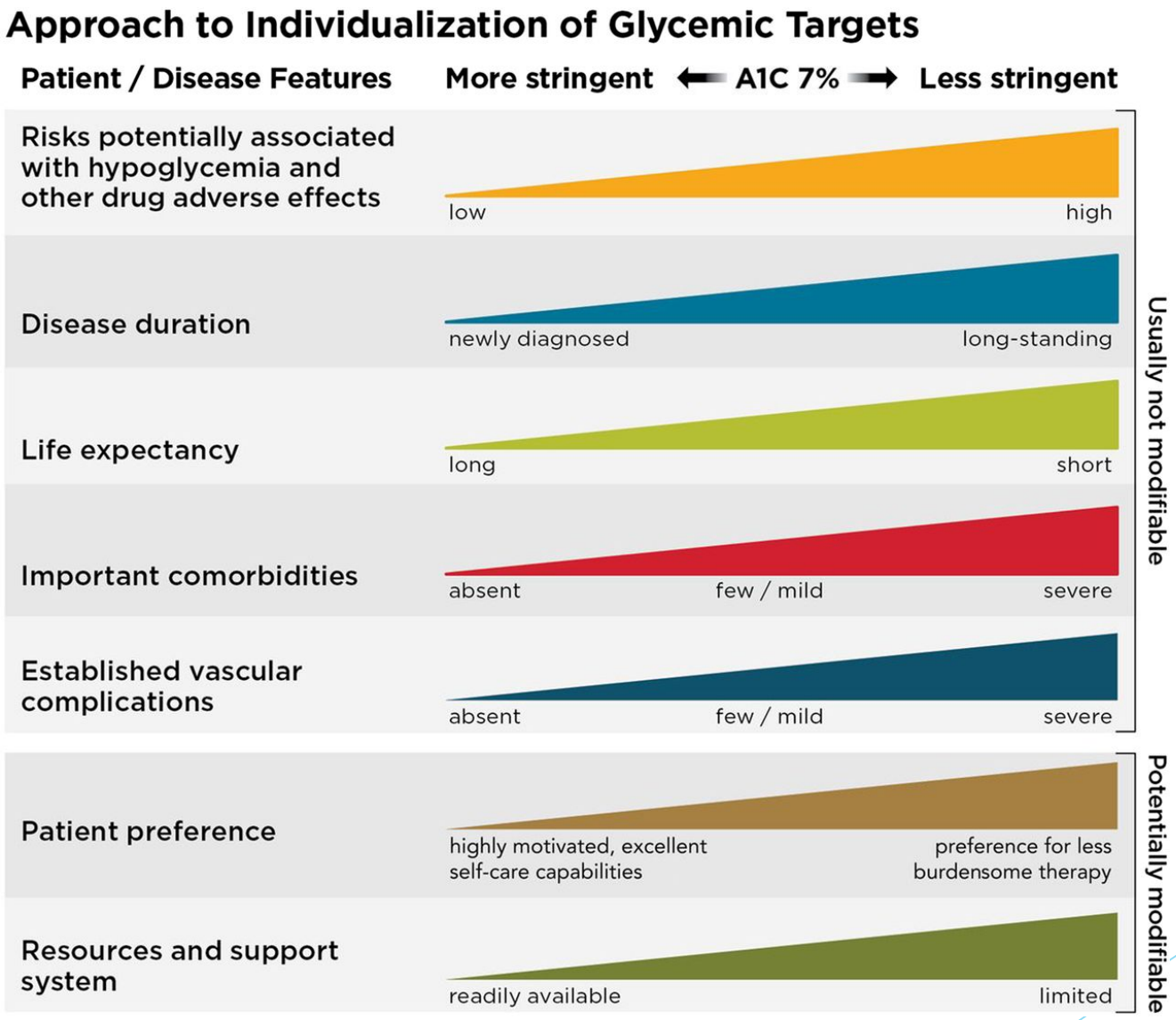
Glycemic Targets

- In all patients, test A1c twice a year if they are meeting targets and quarterly if they are not on target or are starting a new therapy
- Nonpregnant adults
  - A1c < 7% is recommended
  - A1c < 6.5% is recommended for those in which it can be achieved without significant hypoglycemia or polypharmacy
  - A1c < 8% should be considered for adults with multiple microvascular and macrovascular complications and limited life expectancy

Glycemic Targets

- Older adults
  - A1c < 7.5% is recommended for adults age 65 or older who are otherwise healthy with few coexisting chronic illnesses and intact cognition
  - A1c < 8.0 – 8.5% is recommended for those with multiple coexisting chronic illnesses, cognitive impairment, or functional dependence
  - Simplification of complex regimens is recommended

Depicted are patient and disease factors used to determine optimal A1C targets



American Diabetes Association Dia Care 2020;43:S66-S76

American Diabetes Association.

Pharmacologic Approaches

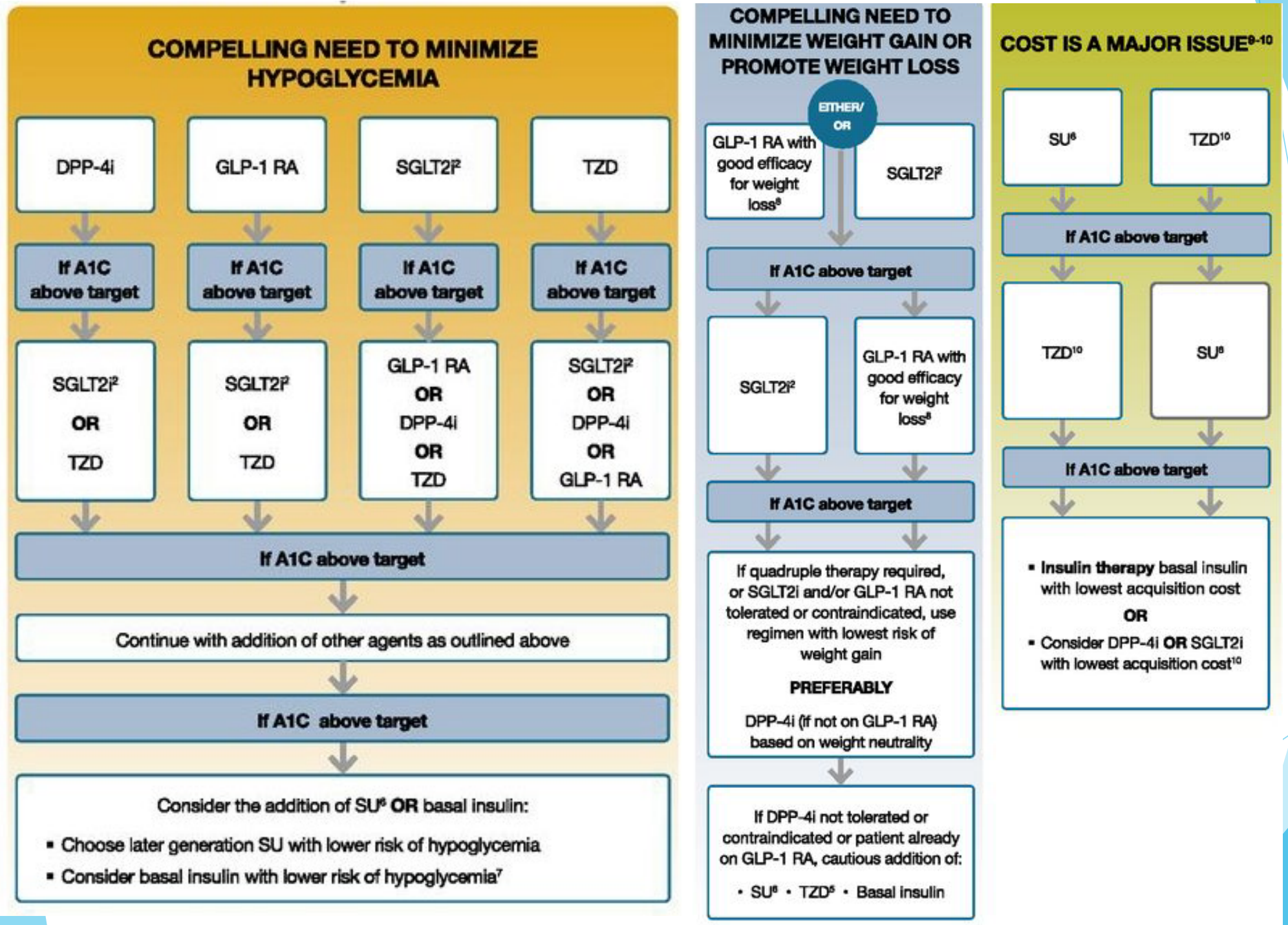
- Therapy for patients with type 1 diabetes is insulin
  - 0.4 to 1.0 units/kg/day is usually the requirement
    - Half is given as basal and half as premeal insulin
  - Higher doses are needed during puberty, pregnancy, and medical illness
  - Pump therapy can help reduce A1c slightly
  - Patients on pump therapy should be continued on it regardless of age
  - Continuous glucose sensor can help reduce the rate of nocturnal hypoglycemia
  - Noninsulin treatments include pramlintide

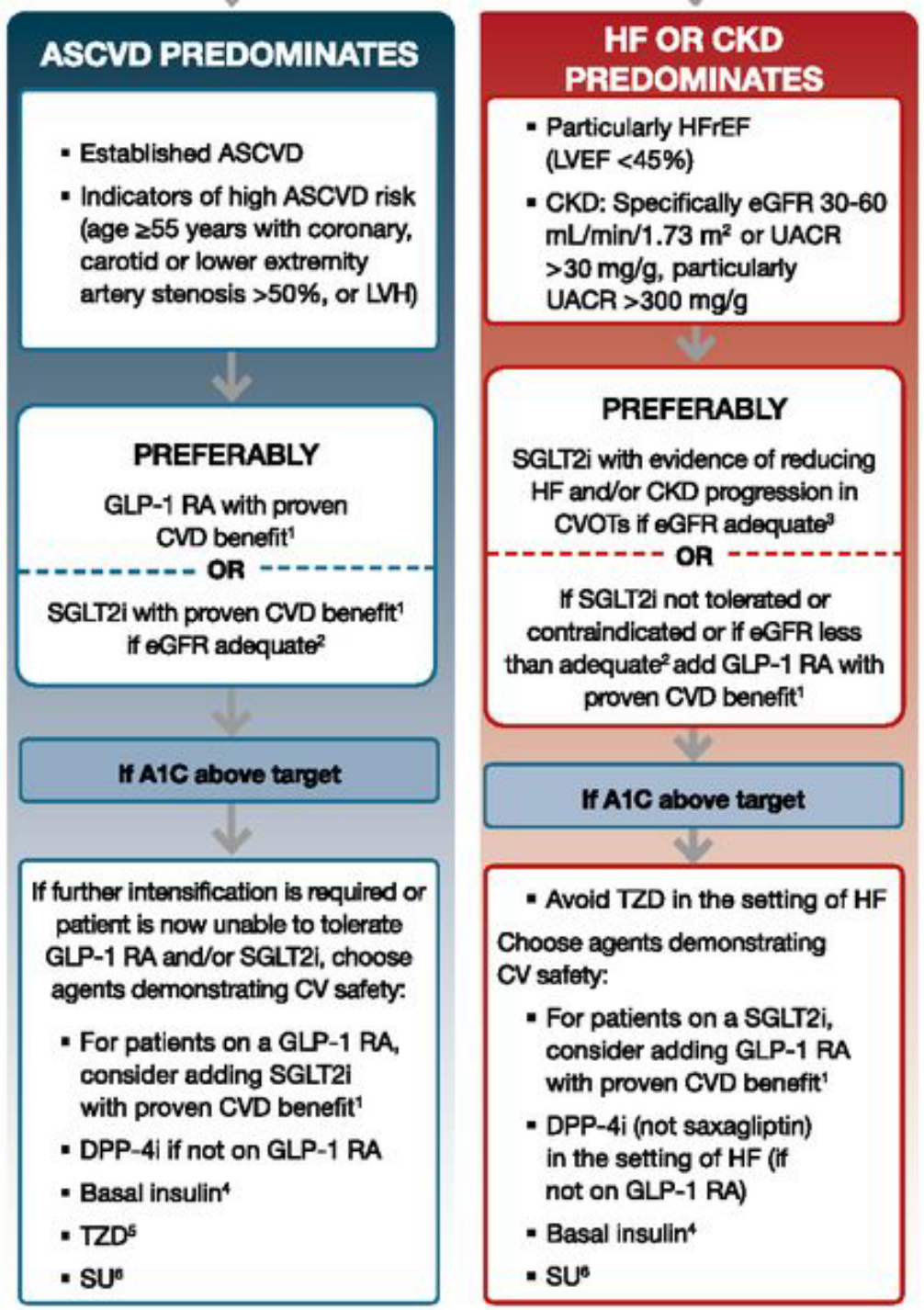
Pharmacologic Approaches for Patients with Type 2 Diabetes

- Metformin is the preferred initial treatment
  - Should be continued for as along as tolerated
  - Recommend periodic measurement of B12 as long term treatment may be associated with B12 deficiency
- Consider introducing insulin early if there is evidence of catabolism or when hyperglycemia is severe (A1c ≥ 10%)
  - Simplify treatment once glucose toxicity resolves
- When A1c is ≥ 1.5% above glycemic target dual combination therapy is often required

Pharmacologic Approaches for Patients with Type 2 Diabetes

- If the A1c target is not achieved at 3 months in a patient without ASCVD or CKD, consider adding a second agent
  - Choice of agent is based on drug specific effect and patient factors
    - Cost
    - Side effects
    - Avoidance of hypoglycemia
    - Promote weight loss


COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA
DPP-4i
GLP-1 RA
SGLT2i[2]
TZD
If A1C above target
SGLT2i[2] OR TZD
SGLT2i[2] OR TZD
GLP-1 RA OR DPP-4i OR TZD
SGLT2i[2] OR DPP-4i OR GLP-1 RA
If A1C above target
Continue with addition of other agents as outlined above
If A1C above target
Consider the addition of SU[6] OR basal insulin:
Choose later generation SU with lower risk of hypoglycemia
Consider basal insulin with lower risk of hypoglycemia[7]
COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS
EITHER/ OR
GLP-1 RA with good efficacy for weight loss[8]
SGLT2i[2]
If A1C above target
SGLT2i[2]
GLP-1 RA with good efficacy for weight loss[8]
If A1C above target
If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain
PREFERABLY
DPP-4i (if not on GLP-1 RA) based on weight neutrality
If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:
• SU[6] • TZD[5] • Basal insulin
COST IS A MAJOR ISSUE[9-10]
SU[6]
TZD[10]
If A1C above target
TZD[10]
SU[6]
If A1C above target
Insulin therapy basal insulin with lowest acquisition cost
OR
Consider DPP-4i OR SGLT2i with lowest acquisition cost[10]



Escalating Therapy in Patients with High Risk for or Established ASCVD, CKD, or HF

- GLP-1 receptor agonists with proven benefit: liraglutide > semaglutide > exenatide
- SGLT2 inhibitor agents with evidence of reducing HF or CKD in cardiovascular outcome trials: empagliflozin, canagliflozin, and dapagliflozin

Initiating Injectable Therapy

- Trials which compared adding insulin versus adding a GLP-1 receptor agonist showed that the efficacy in lowering A1c was similar
- GLP-1 receptor agonists had lower risk of hypoglycemia and promoted weight loss
- GLP-1 receptor agonists are the preferred option for patients requiring injectable therapy

Insulin

- The utility and importance of insulin as disease progresses should be explained to patients
- Self-titration based on self-monitoring should be encouraged and it usually leads to better compliance and thus outcomes
- Basal insulin can be started at 0.1-0.2 units/kg/day or at 10 units per day and titrated every 3 days or so as needed
  - NPH as well as U-100 glargine or detemir can be used to achieve fasting targets
  - Longer acting insulins such as Tresiba (Degludec) or Toujeo (U-300 glargine) have lower risk of hypoglycemia

Insulin

- Keep in mind that newer and longer acting insulins are more expensive
- Prandial insulin should be given before meals, starting dose can be 4 units or 10% of basal dose at each meal time
- Combination therapy with human Regular insulin, NPH insulin, and 70/30 NPH/Regular insulin products is more cost effective
  - Trials comparing human Regular insulin with rapid-acting analogs have not found significant differences in A1c or hypoglycemia

Acknowledgments

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Questions?

Elys M. Perez, MD

1625 SE 3rd Ave Suite 700, Fort Lauderdale, Fl 33316

Email: e5perez@browardhealth.org

Phone: 954-831-2760

Fax: 954-831-2765

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