2022 ADA Standards of Care

Pharmacologic Treatment of Hyperglycemia in Adults with Type 2 Diabetes

FIRST-LINE THERAPY depends on comorbidities, patient-centered treatment factors, including cost and access considerations, and management needs and generally includes metformin and comprehensive lifestyle modification^

To avoid therapeutic insertia reassess and modify treatment regularly (3-6 Monts)

ASCVD/INDICATORS OF HIGH RISK, HF, CKD†

NONE

RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡

+ASCVD/INDICATORS OF HIGH RISK*

GLP-1 RA with proven CVD benefit[1] — Either/or — SGLT2I with proven CVD benefit[1]

IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]

+HF*

SGLT2I with proven benefit in the population[1]

+CKD**

CKD and albuminuria (e.g.,≥200 mg/g creatine)

CKD without albuminuria (e.g., eGFR <60 mL/min/1.73 m^2)

PREFERABLE

SGLT2i with primary evidence of reducing CKD progression

--------OR--------

SGLT2i with evidence of reducing CKD progression in CVOTs

--------OR--------

GLP-1 RA with proven CVD benefit[1] if SGLT2i not tolerated or contraindicated

For patients with CKD (e.g., eGFR <60 mUmin/1.73 m') without albuminuria, recommend the following to decrease cardiovascular risk

GLP-1 RA with proven CVD benefit[1] — Either/or — SGLY2I with proven CVD Benefit[1]

If A1C above target, for patients on SGLT2I, consider incorporating a GLP-1 RA and vice versa

If A 1 C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

Incorporate agents that provide adequate EFFICACY to achieve and maintain glycemic goals
Higher glycemic efficacy therapy: GLP-1 RA; insulin; combination approaches

- Consider additional comorbidities, patient-centered treatment factors, and management needs in choice of therapy, as below:

MINIMIZE HYPOGLYCEMIA

No/low inherent risk of hypoglycemia: DPP-4i, GLP-1 RA, SGLT2i, TZD

For SU or basal insulin, consider agents with lower risk of hypoglycemia[3,4]

IF A1C ABOVE TARGET

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

MINIMIZE WEIGHT GAIN/ PROMOTE WEIGHT LOSS

PREFERABLY

GLP-1 RA with good efficacy for weight loss

----------OR----------

SGLT2i

IF A1C ABOVE TARGET

For patients on a GLP-1 RA, consider incorporating SGLT2i and vice versa

•If GLP-1 RA not tolerated or indicated, consider DPP-4i (weight neutral)

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

CONSIDER COST AND ACCESS

Available in generic form at lower cost:

- Certain insulins: consider insulin available at the lowest acquisition cost
- SU
- TZD

IF A1C ABOVE TARGET

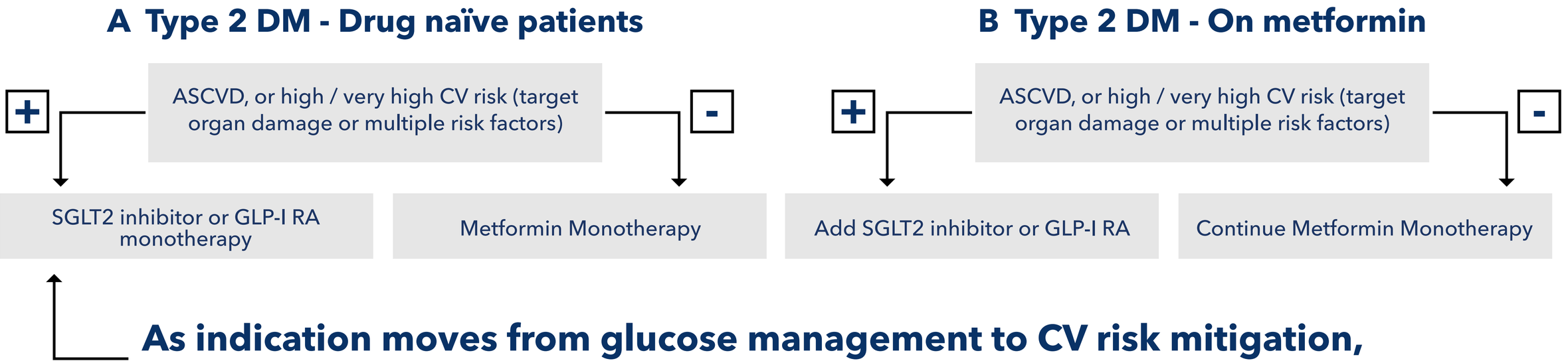
Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

1. Proven benefit refers to label indication (see Table 9.2)
2. Low dose may be better tolerated though less well studied for CVD effects
3. Choose later generation SU to lower risk of hypoglycemia
4. Risk of hypoglycemia: degludec / glargine U-300 <glargine U-100 / detemir < NPH insulin
5. Consider country- and region-specrtic cost of drugs

^For adults with overweight or obesity, lifestyle modrtication to achieve and maintain ≥5% weight loss and ≥150 min/week of moderate- to vigorous-intensity physical activity is recommended (See Section 5: Facilitating Behavior Change and Well-being to Improve Health Outcomes).
†Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.
‡ Most patients enrolled in the relevant trials were on metfoonin at baseline as glucose-lowering therapy.
*Refer to Section 10: Cardiovascular Disease and Risk Management .
**Refer to Section 11: Chronic Kidney Disease and Risk Management and specific medication label for eGFR criteria.

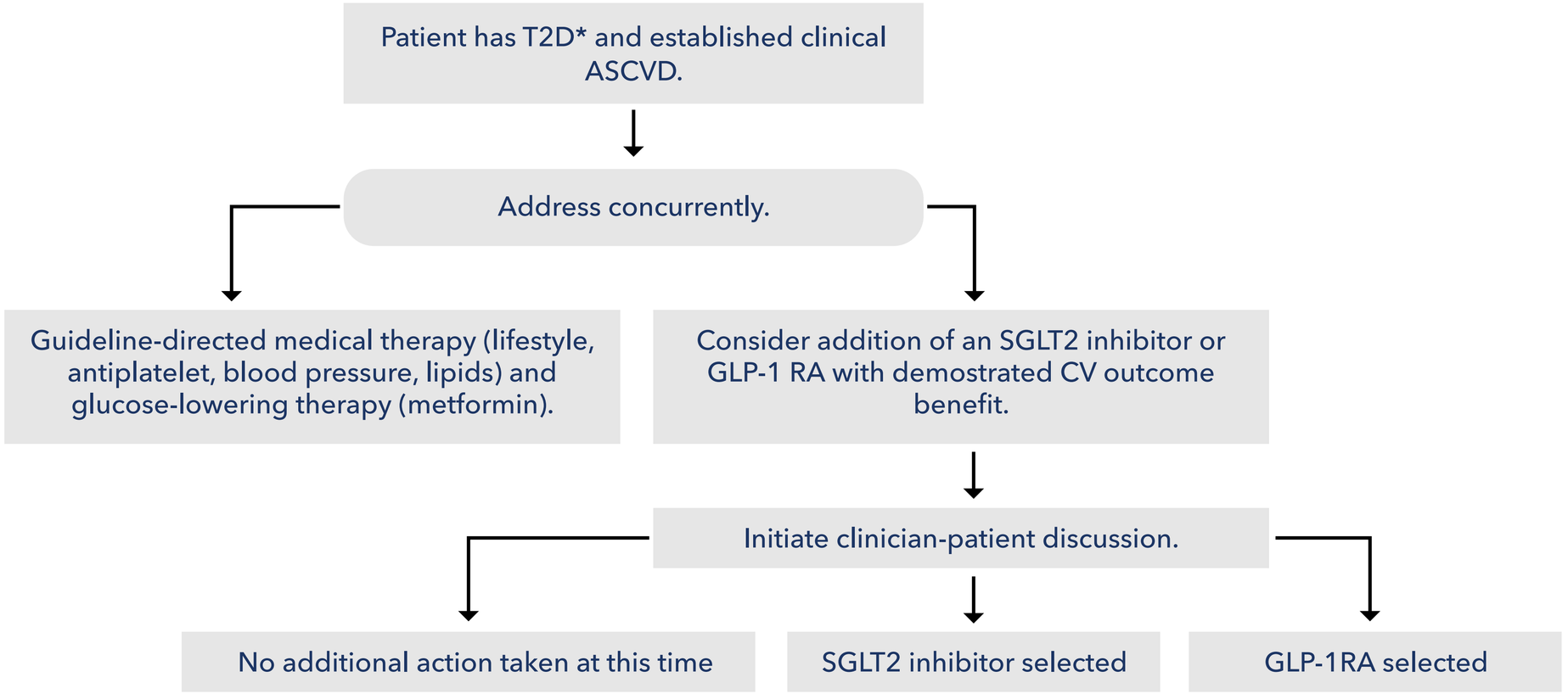
For more information: Draznin, Boris, et al. "9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2022." Diabetes Care 45.Supplement_1 (2022): S125-S143.

2019 ESC Guidelines for Type 2 Diabetes Treatment



As indication moves from glucose management to CV risk mitigation, challenges the "metformin first" recommendation of ADA/EASD

From Glucocentricity to CV Risk Mitigation: ACC Decision Pathway



*Most trials of SGLT2i and GLP-1RA required baseline A1C≥7% (Example: EXCEL Trial required HbA1c ≥ 6.5%), and most patients were already on metformin as first-line therapy if tolerated and not contraindicated

Abbreviations: ASCVD = atherosclerotic cardiovascular disease;
CV = cardivascular;
GLP-1RA = glucagon-like peptide-1 receptor agonist;
SGLT2 = sodium-glucose cotransporter-2;
T2D = type 2 diabetes.

For more information: Das SR et al. J Am Coll Cardiol 2020; 76: 1117-1145.

ACC Decision Pathway: Deciding Between an SGLT2 Inhibitor or a GLP-1 RA

Consider Using an SGLT2 Inhibitor First When Patient and Clinician Priorities Include:
MACE prevention (+++)
HF prevention (+++)
Weight loss (+)
Renal disease progression and prevention{+++)
Mode of administration: oral

Consider alternative agents if:

- Significant CKD
- History of prior amputation, severe peripheral arterial disease, neuropathy, or diabetic foot ulcers (avoid canagliflozin)
- History of recurrent genital candidiasis
- History of diabetic ketoacidosis
- History of osteoporosis (avoid canagliflozin)
- The patient is considering pregnancy
- The patient is breastfeeding

Consider Using a GLP-1 RA First When Patient and Clinician Priorities Include:
MACE prevention (+++)
HF prevention
Weight loss (+++)
Renal disease progression and prevention (+)
Mode of administration: subcutaneous and oral

Consider alternative agents if:

- Persistent nausea, even at low doses
- History of gastroparesis
- History of gallbladder disease
- History of MEN2 or medullary thyroid cancer
- History of proliferative retinopathy (caution with semaglutide or dulaglutide)
- The patient is considering pregnancy
- The patient is breastfeeding

For more information: Das SR et al. J Am Coll Cardiol 2020; 76: 1117-1145.