2022년 대한임상건강증진학회

추계학술대회

당뇨병 치료의 새로운 패러다임1 (SGLT2 억제제 중심)

김도훈(고려의대)

대한임상건강증진학회
Korean Society for Health Promotion and Disease Prevention

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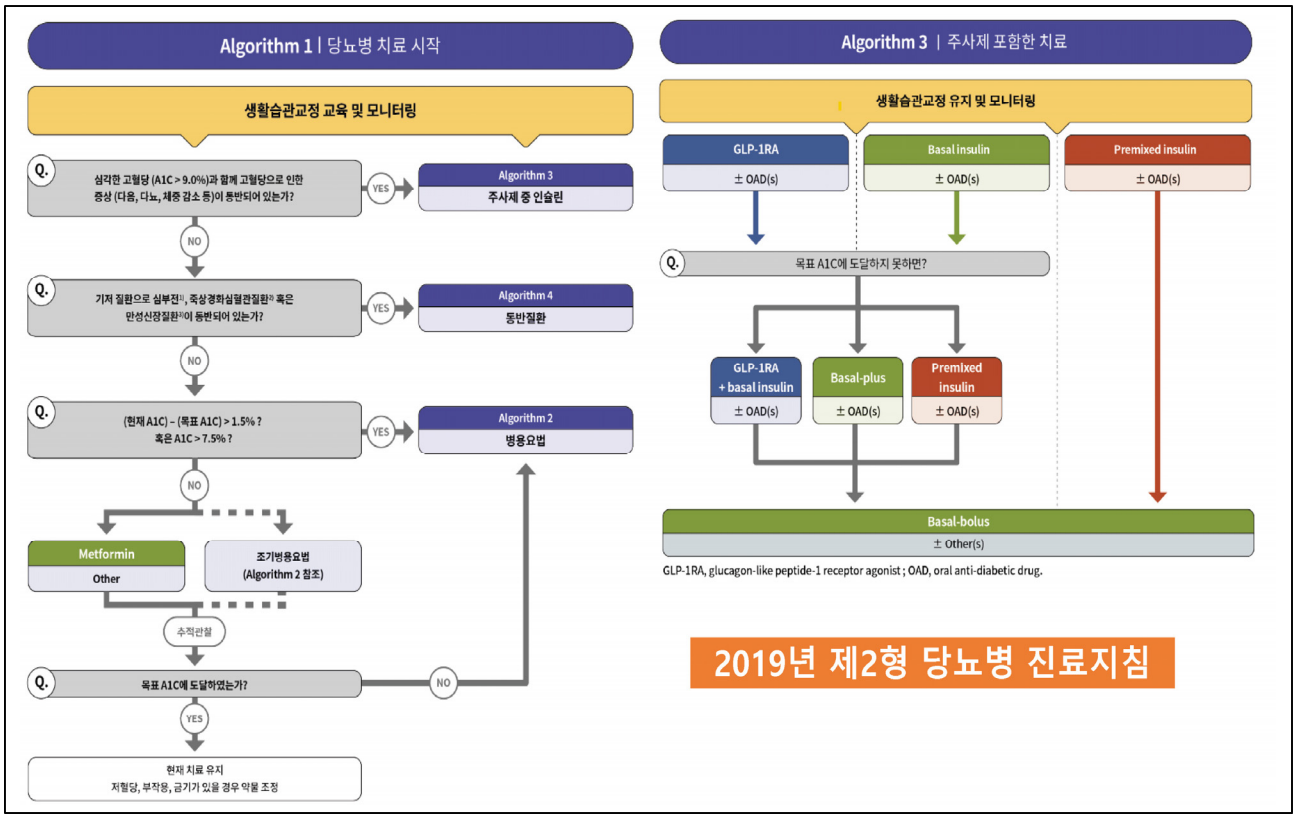
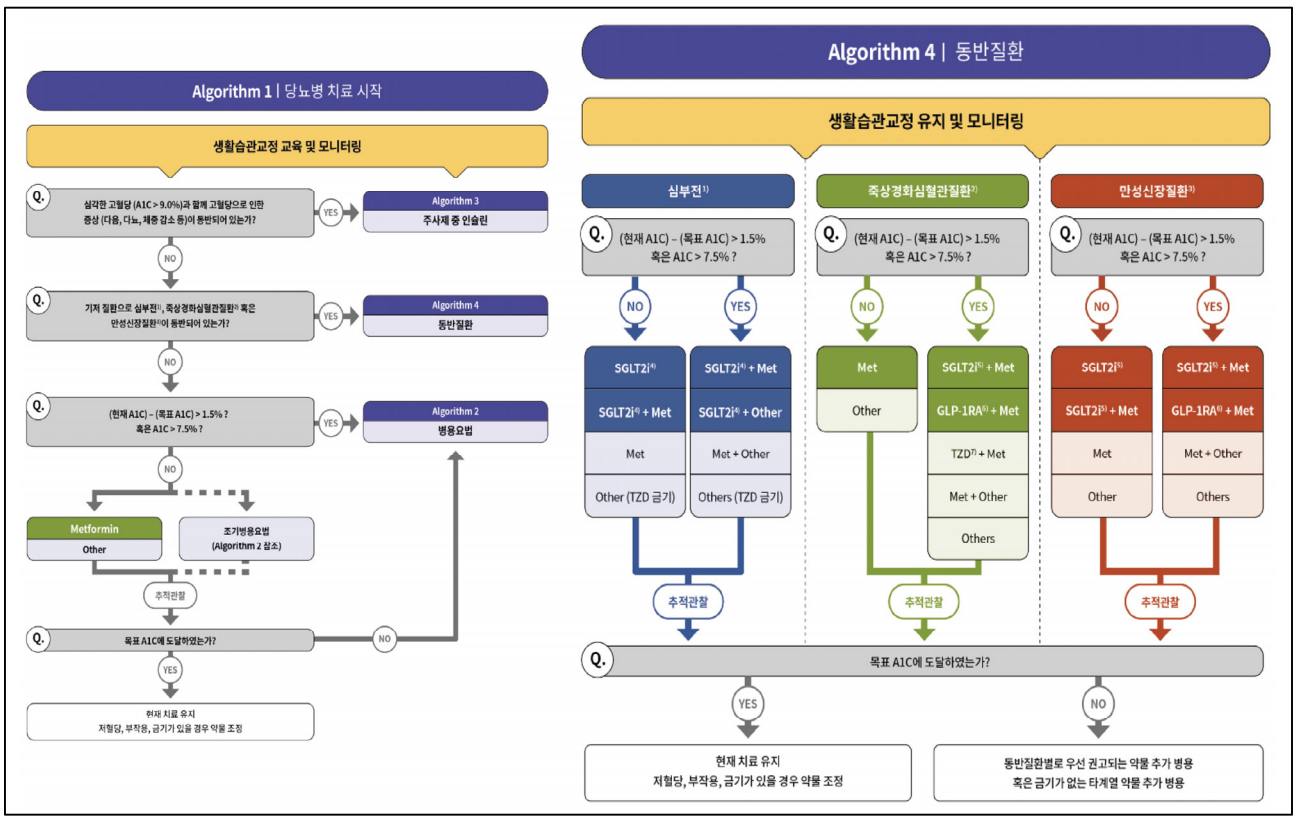

Algorithm 1 | 당뇨병 치료 시작
생활습관교정 교육 및 모니터링
Q. 심각한 고혈당 (A1C > 9.0%)과 함께 고혈당으로 인한 증상 (다음, 다뇨, 체중 감소 등)이 동반되어 있는가?
YES
Algorithm 3
주사제 중 인슐린
NO
Q. 기저 질환으로 심부전[1], 죽상경화심혈관질환[2] 혹은 만성신장질환[3]이 동반되어 있는가?
YES
Algorithm 4
동반질환
NO
Q. (현재 A1C) – (목표 A1C) > 1.5% ? 혹은 A1C > 7.5% ?
YES
Algorithm 2
병용요법
NO
Metformin
Other
조기병용요법
(Algorithm 2 참조)
추적관찰
Q. 목표 A1C에 도달하였는가?
NO
YES
현재 치료 유지
저혈당, 부작용, 금기가 있을 경우 약물 조정
Algorithm 3 | 주사제 포함한 치료
생활습관교정 유지 및 모니터링
GLP-1RA
± OAD(s)
Basal insulin
± OAD(s)
Premixed insulin
± OAD(s)
Q. 목표 A1C에 도달하지 못하면?
GLP-1RA + basal insulin
± OAD(s)
Basal-plus
± OAD(s)
Premixed insulin
± OAD(s)
Basal-bolus
± Other(s)
GLP-1RA, glucagon-like peptide-1 receptor agonist ; OAD, oral anti-diabetic drug.
2019년 제2형 당뇨병 진료지침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Algorithm 3
주사제 중 인슐린
NO
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동반질환
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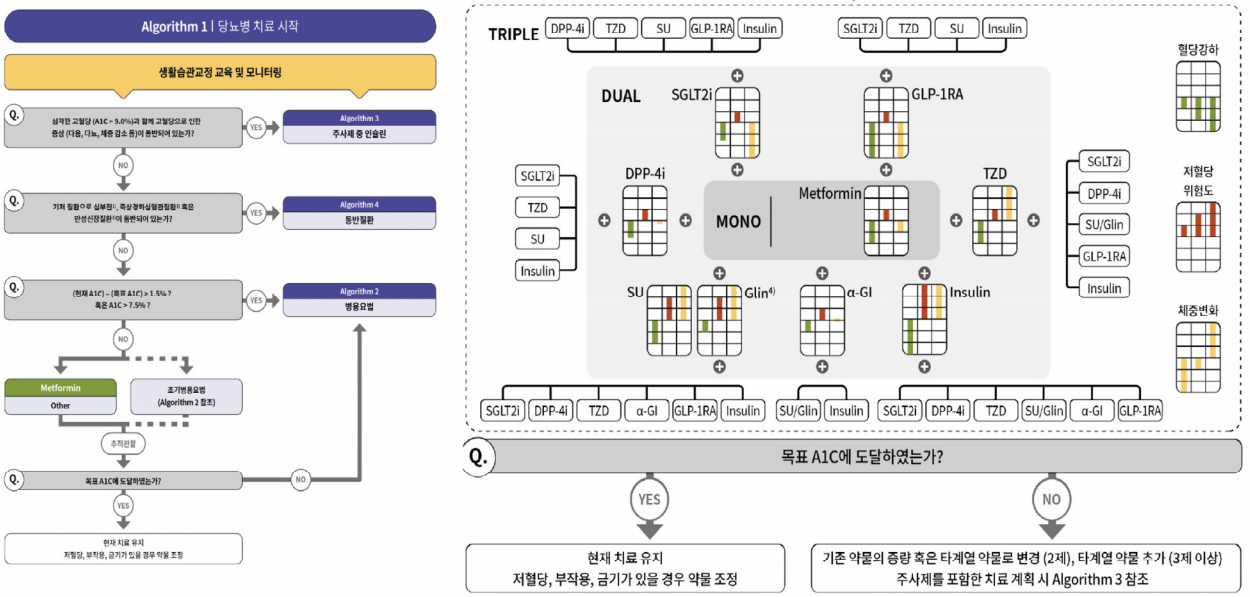
Algorithm 2
병용요법
NO
Metformin
Other
조기병용요법
(Algorithm 2 참조)
추적관찰
Q. 목표 A1C에 도달하였는가?
NO
YES
현재 치료 유지
저혈당, 부작용, 금기가 있을 경우 약물 조정
Algorithm 4 | 동반질환
생활습관교정 유지 및 모니터링
심부전[1]
죽상경화심혈관질환[2]
만성신장질환[3]
Q. (현재 A1C) – (목표 A1C) > 1.5% 혹은 A1C > 7.5% ?
NO
YES
SGLT2i[4]
SGLT2i[4] + Met
SGLT2i[4] + Met
SGLT2i[4] + Other
Met
Met + Other
Other (TZD 금기)
Others (TZD 금기)
Met
Other
SGLT2i[5] + Met
GLP-1RA[6] + Met
TZD[7] + Met
Met + Other
Others
SGLT2i[5]
SGLT2i[5] + Met
GLP-1RA[8] + Met
Met
Met + Other
Other
Others
추적관찰
Q. 목표 A1C에 도달하였는가?
YES
NO
현재 치료 유지
저혈당, 부작용, 금기가 있을 경우 약물 조정
동반질환별로 우선 권고되는 약물 추가 병용
혹은 금기가 없는 타계열 약물 추가 병용


Algorithm 1 | 당뇨병 치료 시작
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Algorithm 3
주사제 중 인슐린
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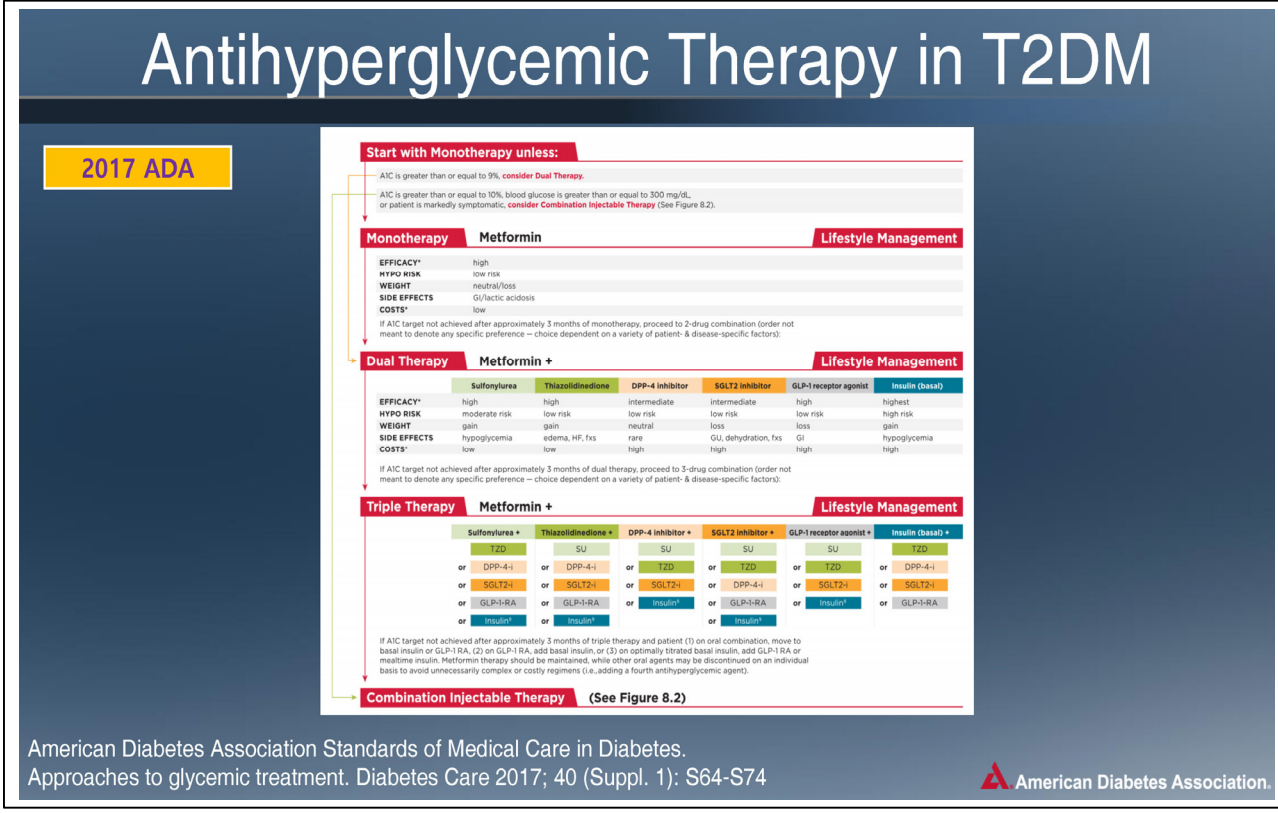
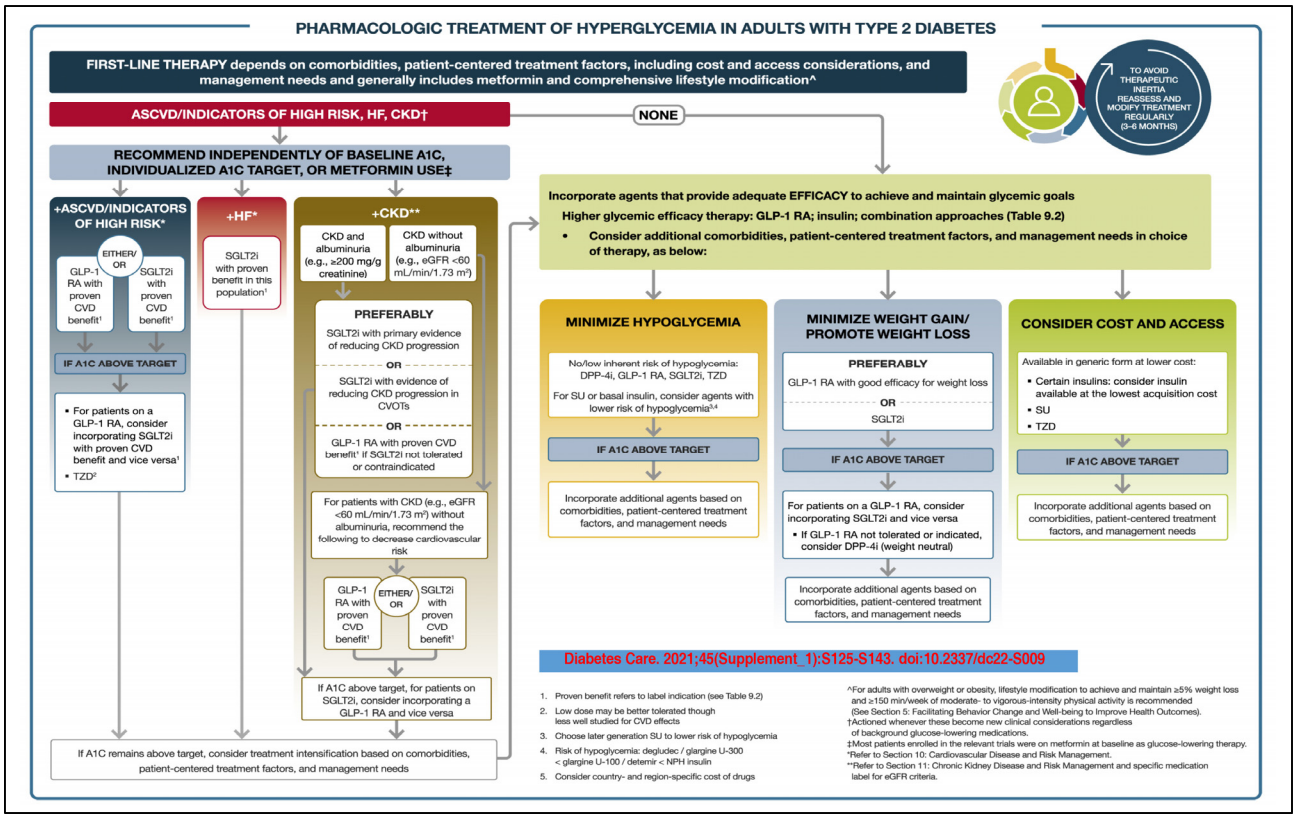
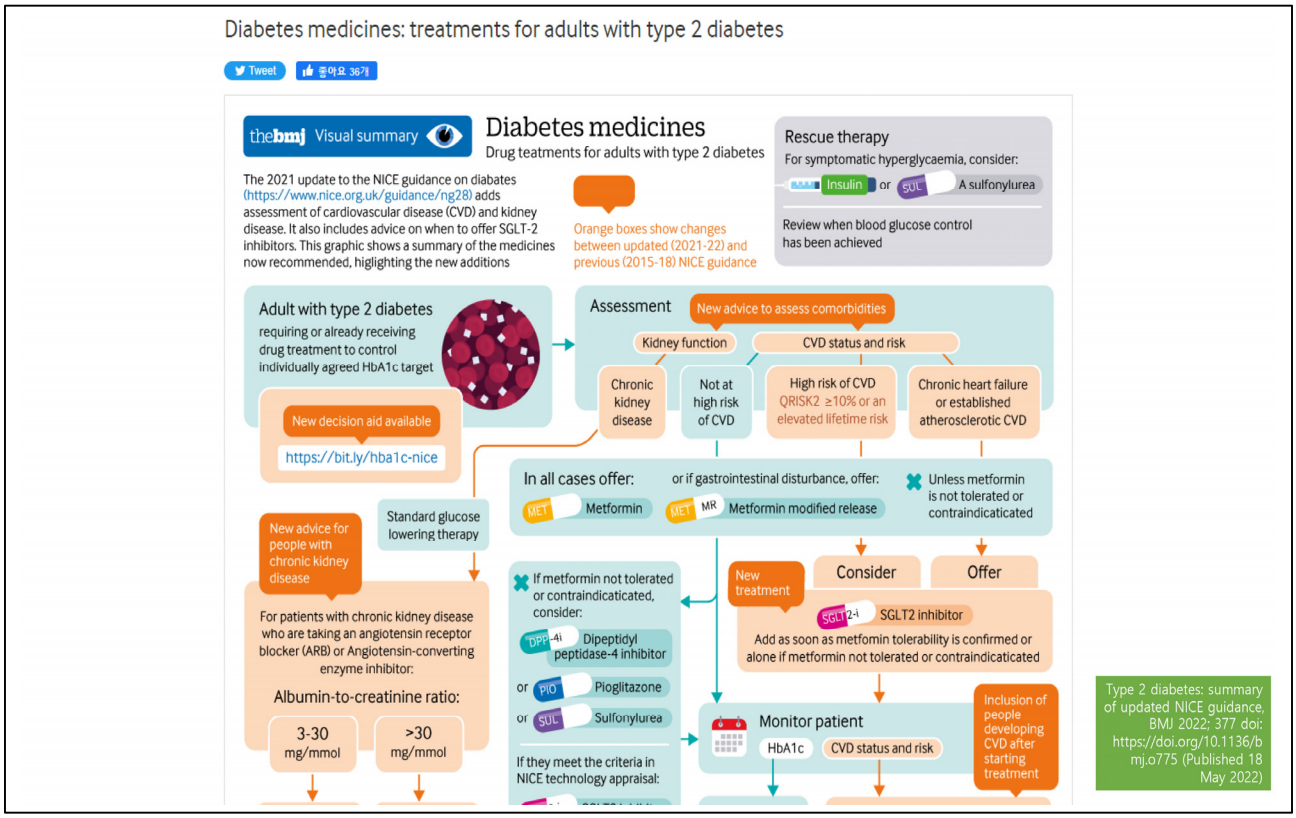
Metformin
Other
조기병용요법
(Algorithm 2 참조)
추적관찰
현재 치료 유지
저혈당, 부작용, 금기가 있을 경우 약물 조정
TRIPLE
DPP-4i
TZD
SU
GLP-1RA
Insulin
SGLT2i
DUAL
MONO
Metformin
Glin4)
α-GI
혈당강하
저혈당
위험도
체중변화
Q.
목표 A1C에 도달하였는가?
YES
NO
현재 치료 유지
저혈당, 부작용, 금기가 있을 경우 약물 조정
기존 약물의 증량 혹은 타계열 약물로 변경 (2제), 타계열 약물 추가 (3제 이상)
주사제를 포함한 치료 계획 시 Algorithm 3 참조


Antihyperglycemic Therapy in T2DM
2017 ADA
Start with Monotherapy unless:
A1C is greater than or equal to 9%, consider Dual Therapy.
A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, consider Combination Injectable Therapy (See Figure 8.2).
Monotherapy
Metformin
Lifestyle Management
EFFICACY*
HYPO RISK
WEIGHT
SIDE EFFECTS
COSTS*
high
low risk
neutral/loss
GI/lactic acidosis
low
If A1C target not achieved after approximately 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 +
Lifestyle Management
Sulfonylurea
Thiazolidinedione
DPP-4 inhibitor
SGLT2 inhibitor
GLP-1 receptor agonist
Insulin (basal)
EFFICACY*
HYPO RISK
WEIGHT
SIDE EFFECTS
COSTS*
high
moderate risk
gain
hypoglycemia
low
high
low risk
gain
edema, HF, fxs
low
intermediate
low risk
neutral
rare
high
intermediate
low risk
loss
GU, dehydration, fxs
high
high
low risk
loss
GI
high
highest
high risk
gain
hypoglycemia
high
If A1C target not achieved after approximately 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 +
Lifestyle Management
Sulfonylurea +
Thiazolidinedione +
DPP-4 inhibitor +
SGLT2 inhibitor +
GLP-1 receptor agonist +
Insulin (basal) +
TZD
SU
or DPP-4-i
or SGLT2-i
or GLP-1-RA
or Insulin5
If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e.,adding a fourth antihyperglycemic agent).
Combination Injectable Therapy
(See Figure 8.2)
American Diabetes Association Standards of Medical Care in Diabetes.
Approaches to glycemic treatment. Diabetes Care 2017; 40 (Suppl. 1): S64-S74
American Diabetes Association.


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 INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
ASCVD/INDICATORS OF HIGH RISK, HF, CKD†
NONE
RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡
+ASCVD/INDICATORS OF HIGH RISK*
EITHER/ OR
GLP-1 RA with proven CVD benefit¹
SGLT2i with proven CVD benefit¹
IF A1C ABOVE TARGET
▪ For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa¹
▪ TZD²
+HF*
SGLT2i with proven benefit in this population¹
+CKD**
CKD and albuminuria (e.g., ≥200 mg/g creatinine)
CKD without albuminuria (e.g., eGFR <60 mL/min/1.73 m²)
PREFERABLY
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 benefit¹ if SGLT2i not tolerated or contraindicated
For patients with CKD (e.g., eGFR <60 mL/min/1.73 m²) without albuminuria, recommend the following to decrease cardiovascular risk
GLP-1 RA with proven CVD benefit¹
EITHER/ OR
SGLT2i with proven CVD benefit¹
If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA and vice versa
If A1C 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 (Table 9.2)
• 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 hypoglycemia³,⁴
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
Diabetes Care. 2021;45(Supplement_1):S125-S143. doi:10.2337/dc22-S009
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-specific cost of drugs
^For adults with overweight or obesity, lifestyle modification 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 metformin 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.


Diabetes medicines: treatments for adults with type 2 diabetes
Tweet
좋아요 367
thebmj Visual summary
Diabetes medicines
Drug teatments for adults with type 2 diabetes
The 2021 update to the NICE guidance on diabetes (https://www.nice.org.uk/guidance/ng28) adds assessment of cardiovascular disease (CVD) and kidney disease. It also includes advice on when to offer SGLT-2 inhibitors. This graphic shows a summary of the medicines now recommended, higlighting the new additions
Orange boxes show changes between updated (2021-22) and previous (2015-18) NICE guidance
Rescue therapy
For symptomatic hyperglycaemia, consider:
Insulin or SUL A sulfonylurea
Review when blood glucose control has been achieved
Adult with type 2 diabetes
requiring or already receiving drug treatment to control individually agreed HbA1c target
New decision aid available
https://bit.ly/hba1c-nice
Assessment
New advice to assess comorbidities
Kidney function
CVD status and risk
Chronic kidney disease
Not at high risk of CVD
High risk of CVD QRISK2 ≥10% or an elevated lifetime risk
Chronic heart failure or established atherosclerotic CVD
In all cases offer:
MET Metformin
or if gastrointestinal disturbance, offer:
MET MR Metformin modified release
Unless metformin is not tolerated or contraindicated
New advice for people with chronic kidney disease
Standard glucose lowering therapy
For patients with chronic kidney disease who are taking an angiotensin receptor blocker (ARB) or Angiotensin-converting enzyme inhibitor:
Albumin-to-creatinine ratio:
3-30 mg/mmol
>30 mg/mmol
If metformin not tolerated or contraindicataced, consider:
DPP-4i Dipeptidyl peptidase-4 inhibitor
or PIO Pioglitazone
or SUL Sulfonylurea
If they meet the criteria in NICE technology appraisal:
New treatment
Consider
Offer
SGLT2-i SGLT2 inhibitor
Add as soon as metfomin tolerability is confirmed or alone if metformin not tolerated or contraindicataced
Monitor patient
HbA1c
CVD status and risk
Inclusion of people developing CVD after starting treatment
Type 2 diabetes: summary of updated NICE guidance, BMJ 2022; 377 doi: https://doi.org/10.1136/bmj.o775 (Published 18 May 2022)

UKPDS33

Background: Improved blood-glucose control decreases the progression of diabetic microvascular disease, but the effect on macrovascular complications is unknown. There is concern that sulphonylureas may increase cardiovascular mortality in patients with type 2 diabetes and that high insulin concentrations may enhance atheroma formation. We compared the effects of intensive blood-glucose control with either sulphonylurea or insulin and conventional treatment on the risk of microvascular and macrovascular complications in patients with type 2 diabetes in a randomised controlled trial.

Methods: 3867 newly diagnosed patients with type 2 diabetes, median age 54 years (IQR 48-60 years), who after 3 months' diet treatment had a mean of two fasting plasma glucose (FPG) concentrations of 6.1-15.0 mmol/L were randomly assigned intensive policy with a sulphonylurea (chlorpropamide, glibenclamide, or glipizide) or with insulin, or conventional policy with diet. The aim in the intensive group was FPG less than 6 mmol/L. In the conventional group, the aim was the best achievable FPG with diet alone; drugs were added only if there were hyperglycaemic symptoms or FPG greater than 15 mmol/L. Three aggregate endpoints were used to assess differences between conventional and intensive treatment: any diabetes-related endpoint (sudden death, death from hyperglycaemia or hypoglycaemia, fatal or non-fatal myocardial infarction, angina, heart failure, stroke, renal failure, amputation [of at least one digit], vitreous haemorrhage, retinopathy requiring photocoagulation, blindness in one eye, or cataract extraction); diabetes-related death (death from myocardial infarction, stroke, peripheral vascular disease, renal disease, hyperglycaemia or hypoglycaemia, and sudden death); all-cause mortality. Single clinical endpoints and surrogate subclinical endpoints were also assessed. All analyses were by intention to treat and frequency of hypoglycaemia was also analysed by actual therapy.

Findings: Over 10 years, haemoglobin A1c (HbA1c) was 7.0% (6.2-8.2) in the intensive group compared with 7.9% (6.9-8.8) in the conventional group--an 11% reduction. There was no difference in HbA1c among agents in the intensive group. Compared with the conventional group, the risk in the intensive group was 12% lower (95% CI 1-21, p=0.029) for any diabetes-related endpoint; 10% lower (-11 to 27, p=0.34) for any diabetes-related death; and 6% lower (-10 to 20, p=0.44) for all-cause mortality. Most of the risk reduction in the any diabetes-related aggregate endpoint was due to a 25% risk reduction (7-40, p=0.0099) in microvascular endpoints, including the need for retinal photocoagulation. There was no difference for any of the three aggregate endpoints between the three intensive agents (chlorpropamide, glibenclamide, or insulin). Patients in the intensive group had more hypoglycaemic episodes than those in the conventional group on both types of analysis (both p<0.0001). The rates of major hypoglycaemic episodes per year were 0.7% with conventional treatment, 1.0% with chlorpropamide, 1.4% with glibenclamide, and 1.8% with insulin. Weight gain was significantly higher in the intensive group (mean 2.9 kg) than in the conventional group (p<0.001), and patients assigned insulin had a greater gain in weight (4.0 kg) than those assigned chlorpropamide (2.6 kg) or glibenclamide (1.7 kg).

Interpretation: Intensive blood-glucose control by either sulphonylureas or insulin substantially decreases the risk of microvascular complications, but not macrovascular disease, in patients with type 2 diabetes.

Lancet . 1998 Sep 12;352(9131):837-53. UKPDS33

UKPDS34

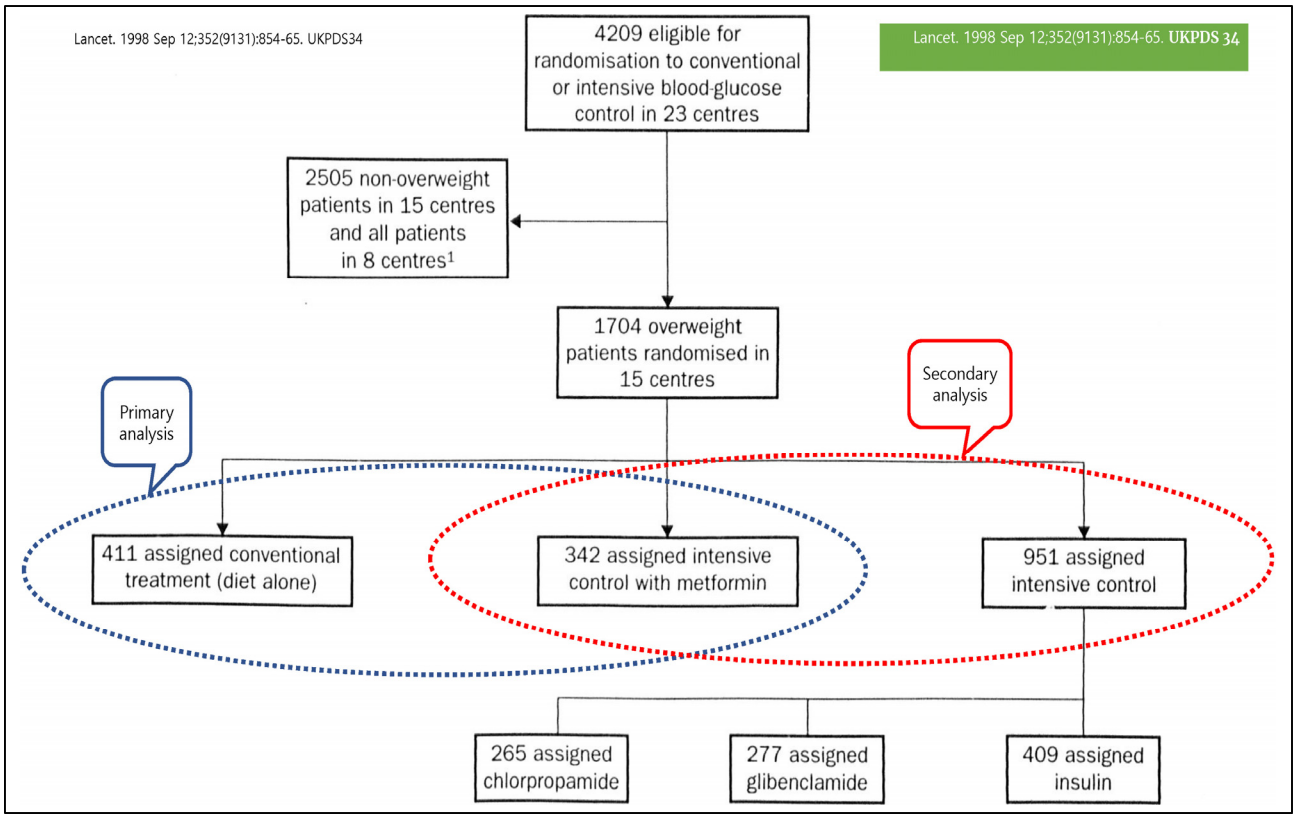
Background
In patients with type 2 diabetes, intensive blood-glucose control with insulin or sulphonylurea therapy decreases progression of microvascular disease and may also reduce the risk of heart attacks. This study investigated whether intensive glucose control with metformin has any specific advantage or disadvantage.

Methods
Of 4075 patients recruited to UKPDS in 15centres, 1704 overweight (>120% ideal bodyweight) patients with newly diagnosed type 2 diabetes, mean age 53 years, had raised fasting plasma glucose (FPG;6·1–15·0 mmol/L) without hyperglycaemic symptoms after 3 months' initial diet. 753 were included in a randomised controlled trial, median duration 10·7 years, of conventional policy, primarily with diet alone (n=411) versus intensive blood-glucose control policy with metformin, aiming for FPG below 6 mmol/L (n=342). A secondary analysis compared the 342 patients allocated metformin with 951 overweight patients allocated intensive blood-glucose control with chlorpropamide (n=265), glibenclamide (n=277), or insulin (n=409). The primary outcome measures were aggregates of any diabetes-related clinical endpoint, diabetes-related death, and all-cause mortality. In a supplementary randomised controlled trial, 537 non-overweight and overweight patients, mean age 59 years, who were already on maximum sulphonylurea therapy but had raised FPG (6·1–15·0 mmol/L) were allocated continuing sulphonylurea therapy alone (n=269) or addition of metformin (n=268).

Findings
Median glycated haemoglobin (HbA1c) was 7·4%in the metformin group compared with 8·0% in the conventional group. Patients allocated metformin, compared with the conventional group, had **risk reductions of 32% (95% CI 13–47, p=0·002) for any diabetes-related endpoint, 42% for diabetes-related death (9–63, p=0·017), and 36% for all-cause mortality (9–55, p=0·011).** Among patients allocated intensive blood glucose control, metformin showed **a greater effect than chlorpropamide, glibenclamide, or insulin** for any diabetes-related endpoint (p=0·0034), all-cause mortality (p=0·021), and stroke (p=0·032). Early addition of metformin in sulphonylurea-treated patients was associated with an increased risk of diabetes-related death (96% increased risk [95% CI 2–275], p=0·039) compared with continued sulphonylurea alone. A combined analysis of the main and supplementary studies showed fewer metformin-allocated patients having diabetes-related endpoints (risk reduction 19% [2–33], p=0·033). Epidemiological assessment of the possible association of death from diabetes-related causes with the concurrent therapy of diabetes in 4416 patients did not show an increased risk in diabetes-related death in patients treated with a combination of sulphonylurea and metformin (risk reduction 5% [−33 to 32], p=0·78).

Interpretation
Since intensive glucose control with metformin appears to decrease the risk of diabetes related endpoints in overweight diabetic patients, and is associated with less weight gain and fewer hypoglycaemic attacks than are insulin and sulphonylureas, it may be the first-line pharmacological therapy of choice in these patients.

Lancet. 1998 Sep 12;352(9131):854-65. **UKPDS 34**



Lancet. 1998 Sep 12;352(9131):854-65. UKPDS34

AGGREGATE ENDPOINT	p for metformin *vs* other intensive	Patients with aggregate endpoints: Metformin or intensive	Patients with aggregate endpoints: Conventional	Absolute risk (events per 1000 patient-years): Metformin or intensive	Absolute risk (events per 1000 patient-years): Conventional	Log-rank 2p	RR (95% CI) *vs* conventional
Any diabetes-related endpoint	p=0·0034						
Metformin		98	160	29·8	43·3	0·0023	0·68 (0·53–0·87)
Intensive		350	160	40·1	43·3	0·46	0·93 (0·77–1·12)
Diabetes-related death	p=0·11						
Metformin		28	55	7·5	12·7	0·017	0·58 (0·37–0·91)
Intensive		103	55	10·3	12·7	0·19	0·80 (0·58–1·11)
All-cause mortality	p=0·021						
Metformin		50	89	13·5	20·6	0·011	0·64 (0·45–0·91)
Intensive		190	89	18·9	20·6	0·49	0·92 (0·71–1·18)
Myocardial infarction	p=0·12						
Metformin		39	73	11·0	18·0	0·01	0·61 (0·41–0·89)
Intensive		139	73	14·4	18·0	0·11	0·79 (0·60–1·05)
Stroke	p=0·032						
Metformin		12	23	3·3	5·5	0·13	0·59 (0·29–1·18)
Intensive		60	23	6·2	5·5	0·60	1·14 (0·70–1·84)
Peripheral vascular disease	p=0·62						
Metformin		6	9	1·6	2·1	0·57	0·74 (0·26–2·09)
Intensive		12	9	1·2	2·1	0·18	0·56 (0·24–1·33)
Microvascular	p=0·39						
Metformin		24	38	6·7	9·2	0·19	0·71 (0·43–1·19)
Intensive		74	38	7·7	9·2	0·38	0·84 (0·57–1·24)

Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. N Engl J Med. 2007 Jun 14;356(24):2457-71.

- Rosiglitazone was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from cardiovascular causes that had borderline significance. Our study was limited by a lack of access to original source data, which would have enabled time-to-event analysis. Despite these limitations, patients and providers should consider the potential for serious adverse cardiovascular effects of treatment with rosiglitazone for type 2 diabetes.

Table 5. Risk of Myocardial Infarction and Death from Cardiovascular Cau for Patients Receiving Rosiglitazone versus Several Comparator Drugs.

Comparator Drug	Odds Ratio (95% CI)	P Value
Myocardial infarction		
Metformin	1.14 (0.70–1.86)	0.59
Sulfonylurea	1.24 (0.78–1.98)	0.36
Insulin	2.78 (0.58–13.3)	0.20
Placebo	1.80 (0.95–3.39)	0.07
Combined comparator drugs	1.43 (1.03–1.98)	0.03
Death from cardiovascular causes		
Metformin	1.13 (0.34–3.71)	0.84
Sulfonylurea	1.42 (0.60–3.33)	0.43
Insulin	5.37 (0.51–56.52)	0.16
Placebo	1.22 (0.64–2.34)	0.55
Combined comparator drugs	1.64 (0.98–2.74)	0.06

아반디아 스토리로부터 무엇을 배울 것인가?

- 대리표지자와 임상결과
- 메타분석과 무작위배정연구
- 이해상충(Conflicts of Interest)
- 증거와 가치(Evidence vs Value)
- 과학과 정치(Science vs Politics)

Surrogate Marker vs Outcome

글리타존은 혈당을 좋게 한다.

혈압도 좋게 하고 이상지혈증도 호전시킨다.

죽상경화증의 병인에 중요한 염증도 호전시킨다.

심혈관질환의 위험요인인 미세단백뇨도 좋게한다.

그렇다면 심혈관질환에 예상되는 결과는?

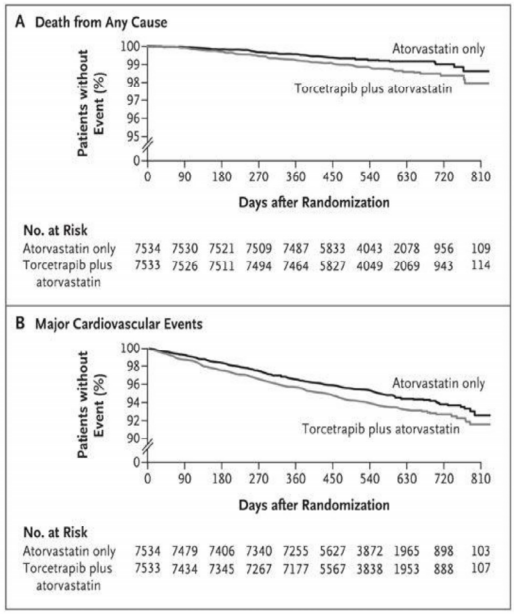
Diabetes Care 2008;31:1007-14.

Effects of ramipril and rosiglitazone on cardiovascular and renal outcomes in people with impaired glucose tolerance or impaired fasting glucose: results of the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) trial

CONCLUSIONS: Ramipril did not alter the cardiorenal outcome or its components. Rosiglitazone, which reduced diabetes, also reduced the development of renal disease but not the cardiorenal outcome and increased the risk of heart failure.

Effects of Torcetrapib in Patients at High Risk for Coronary Events. N Engl J Med 2007;357:2109-22.

- Cholesteryl ester transfer protein (CETP) 억제제인 torsetrapib은 HDL 콜레스테롤을 무려 70%나 올림
- 그러나 임상결과는 사망률의 증가로 나타남



당뇨병약의 반전의 역사

01

미국 FDA 2008년 이후 허가를 신청한 당뇨병 신약에 대해 혈당을 낮추는 효능 외에 심장병에 대해 무해함을 증명해야 허가하기로 결정

02

그 후에 나온 많은 당뇨병약들은 모두 심장병 사망에 대한 임상실험을 의무적으로 시행(cardiovascular outcome trial non-inferiority)

03

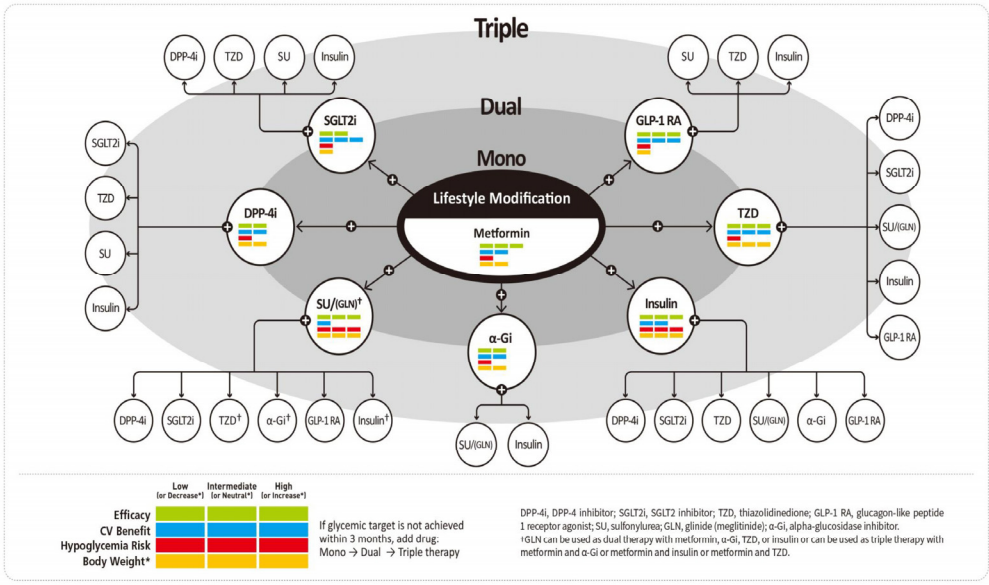
새롭게 DPP4억제제, PPAR agonist, SGLT억제제, GLP-1 수용체자극제 모두 심장병을 증가시키지 않음

04

SGLT 억제제, GLP-1 수용체자극제는 오히려 심장병 감소효과

10. 제2형 당뇨병환자의 경구약제 (5)

그림 10-1. 제2형 당뇨병 약물치료 알고리즘



2019 당뇨병 진료지침

10. 제2형 당뇨병환자의 경구약제 (6)

그림 10-1. 설명

- 제2형 당뇨병의 치료는 생활습관개선이 기본이 되어야 하며 일반적인 혈당조절 목표는 당화혈색소 6.5% 미만으로 하되 환자에 따라 개별화하여 적용하는 것이 중요함.
- 첫 진단 시 당화혈색소가 7.5% 미만인 경우, 생활습관조절과 함께 메트포르민 단독요법을 시작할 수 있음.
- 메트포르민의 금기증이나 부작용이 있을 경우, 환자 상태에 따라 다른 계열 약제로 단독요법을 사용할 수 있음.
- 초기 당화혈색소가 7.5% 이상이거나 단독요법으로 3개월 이내 목표에 도달하지 못한 경우 2제 병합요법을 고려함. 이 경우 대개 메트포르민에 두번째 약제를 병합하는 것이 일반적이나, 환자 상태에 따라 다른 기전을 가진 약제의 병합도 사용할 수 있음.
- 2제 병합요법으로도 3개월 이내 목표에 도달하지 못한 경우 3제 병합요법을 시행함.
- 약제 선택 시 혈당강하 효능, 저혈당 위험, 체중증가, 심혈관질환 발생 및 국내 임상자료 결과 여부를 우선적으로 고려함.
- 4가지 항목에 대한 각 약제별 특징을 막대 그래프로 표시하였음.
- 2019년 4월 기준, 식품의약품안전처의 허가사항에 준하여 작성되었음.

2019 당뇨병 진료지침

10. 제2형 당뇨병환자의 경구약제 (7)

표 10-2. 신기능에 따른 약제 조절

e-GFR	CKD1-2	CKD3a	CKD3b	CKD4	ESRD
	≥ 60	45-59	30-44	15-29	< 15
Metformin		최대용량 1000 mg/일 이하	금지	금지	금지
Meglitinides					
Repaglinide					주의
Mitiglinide					주의
Nateglinide					금지
DPP-4 inhibitors					
Sitagliptin	100 mg	100 mg	50 mg	25 mg	25 mg
Vildagliptin	100 mg	50 mg*	50 mg	50 mg	50 mg
Saxagliptin	5 mg	2.5 mg*	2.5 mg	2.5 mg	2.5 mg
Linagliptin	5 mg	5 mg	5 mg	5 mg	5 mg
Gemigliptin	50 mg	50 mg	50 mg	50 mg	50 mg
Teneligliptin	20 mg	20 mg	20 mg	20 mg	20 mg
Alogliptin	25 mg	12.5 mg*	12.5 mg	6.25 mg	6.25 mg
Evogliptin	5 mg	5 mg	5 mg	5 mg	자료 없음
Anagliptin	200 mg	200 mg	200 mg	100 mg	100 mg

*e-GFR ≥ 50 용량 조절 불필요, ¶ e-GFR < 60 시작 금지, **e-GFR < 25 금지
용량 조절 불필요. CKD, chronic kidney disease
2019년 4월 기준, 식품의약품안전처의 허가사항에 준하여 작성되었음.

2019 당뇨병 진료지침

10. 제2형 당뇨병환자의 경구약제 (8)

표 10-2. 신기능에 따른 약제 조절 (계속)

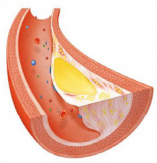
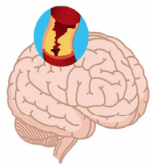
e-GFR	CKD1-2	CKD3a	CKD3b	CKD4	ESRD
	≥ 60	45-59	30-44	15-29	< 15
SGLT2 inhibitors					
Dapagliflozin	10 mg	주의¶	금지	금지	금지
Empagliflozin	10 mg/25 mg	주의¶	금지	금지	금지
Ertugliflozin	5 mg	주의¶	금지	금지	금지
Ipragliflozin	50 mg	금지	금지	금지	금지
Sulfonylureas					
Gliclazide			주의	주의	주의
Glimepiride			주의	주의	주의
Glipizide			주의	주의	주의
Alpha-glucosidase inhibitors					
Acarbose				금지**	금지
Voglibose				자료 없음	자료 없음
Thiazolidinediones					
Pioglitazone	15/30 mg	15/30 mg	15/30 mg	15/30 mg	15/30 mg
Lobeglitazone	0.5 mg	0.5 mg	0.5 mg	0.5 mg	0.5 mg
GLP-1 receptor agonists					
Lixisenatide				자료 없음	자료 없음
Liraglutide					자료 없음
Dulaglutide					

*e-GFR ≥ 50 용량 조절 불필요, ¶ e-GFR < 60 시작 금지, **e-GFR < 25 금지
용량 조절 불필요. CKD, chronic kidney disease
2019년 4월 기준, 식품의약품안전처의 허가사항에 준하여 작성되었음.

2019 당뇨병 진료지침

10. 제2형 당뇨병환자의 경구약제 (9)

표 10-3. 당뇨병 약제의 심뇌혈관질환에 대한 효과

죽상경화성 심혈관질환 (ASCVD)	심부전 (HF)	죽상경화성 뇌혈관질환 (Stroke)
		
Metformin	Metformin	Metformin
TZD	TZD	**TZD***
DPP-4i	DPP-4i	DPP-4i
SGLT2i*	**SGLT2i***	SGLT2i
GLP-1 RA*	GLP-1 RA	GLP-1 RA
SU	SU	SU
Insulin	Insulin	Insulin
α-Gi	α-Gi	α-Gi
GLN	GLN	GLN

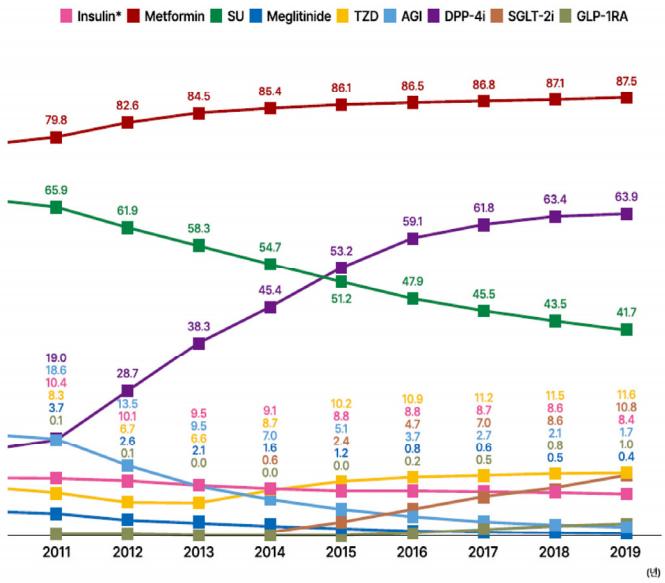
붉은색: 금기 혹은 주의 **녹색:** 예방효과 **검은색:** neutral

*임상효과가 입증된 경우

ASCVD, atherosclerotic cardiovascular disease; HF, heart failure; TZD, thiazolidinedione; DPP-4i, DPP-4 inhibitor; SGLT2i, SGLT2 inhibitor; GLP-1 RA, glucagon-like peptide 1 receptor agonist; SU, sulfonylurea; α-Gi, alpha-glucosidase inhibitor; GLN, glinide (meglitinide)

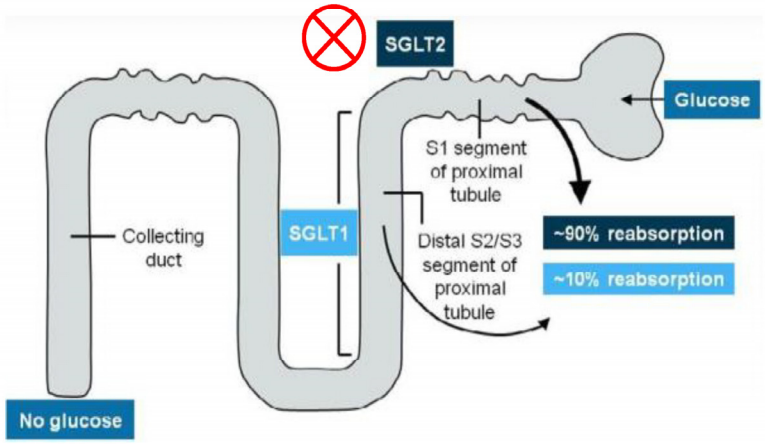
2019 당뇨병 진료지침

우리나라 성인 당뇨병 환자의 당뇨병 약물 사용 경향 (2002-2019 국민건강 보험자료)



SU: sulfonylurea, TZD: thiazolidinedione, AGI: alpha-glucosidase inhibitor, DPP-4i: dipeptidyl peptidase-4 inhibitor, SGLT-2i: sodium-glucose cotransporter 2 inhibitor, GLP-1 RA: glucagon-like peptide-1 receptor agonist

SGLT 2 Inhibitor



List of current SGLT2 inhibitors.

Generic Name	Brand Name	Available Doses (mg)	Administration
canagliflozin[a]	Invokana®	100, 300	qam before 1st meal
dapagliflozin[a]	Farxiga™	5, 10	qam
empagliflozin[a]	Jardiance®	10, 25	qam
canagliflozin/metformin[a]	Invokamet®	50/500, 50/1000, 150/500, 150/1000	BID with meals, max dose 300mg/2000mg
dapagliflozin/metformin[a]	Xigduo™ XR	5/500, 5/1000, 10/500, 10/1000	qam with food, max dose 10mg/2000mg
empagliflozin/metformin[a]	Synjardy®	5/500, 5/1000, 12.5/500, 12.5/1000	BID with meals, max dose 25mg/2000mg
empagliflozin/linagliptin[a]	Glyxambi®	10/5, 25/5	qam
Ipragliflozin[b]	Suglat®	25, 50	qam, max dose 100mg
tofogliflozin[bc]	Apleway®, Deberza®	20	qam
luseogliflozin[c]			
remogliflozin etabonate[c]			
ertugliflozin[c]			
sotagliflozin[c]			

[a]FDA and EMA approved,
[b]Ministry of Health, Labour and Welfare approved in Japan,
[c]currently in clinical trials or seeking market approval; qam taken once daily in the morning, BID twice daily

Curr Opin Endocrinol Diabetes Obes. 2017 Feb; 24(1): 73–79.

Prospective cardiovascular safety trials for SGLT2 inhibitors

Name of Trial	Intervention	Primary Endpoint	No. of Patients	Duration of Trial (y)	Projected Year of Completion
Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME)	Empagliflozin 10 or 25 mg daily	Time to the first occurrence of any of the following adjudicated components of the primary composite endpoint: CV death (including fatal stroke and fatal MI), nonfatal MI, and nonfatal stroke	7000	5	2015
Canagliflozin cardiovascular Assessment Study (CANVAS)	Canagliflozin 100 or 300 mg daily	Major adverse cardiovascular events, including CV death, nonfatal MI, and nonfatal stroke	4330	≥ 4	2017
Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants With Diabetic Nephropathy (CREDENCE)	Canagliflozin 100 mg daily	Time to the first occurrence of an event in the primary composite endpoint: ESRD, doubling of serum creatinine, renal or CV death	3627	5.5	2019
Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events (DECLARE-TIMI58)	Dapagliflozin 10 mg daily	Time to first event included in the composite end point of CV death, MI or ischemic stroke	17150	6	2019
Cardiovascular Outcomes Following Treatment With Ertugliflozin in Participants With Type 2 Diabetes Mellitus and Established Vascular Disease (NCT01986881)	Ertugliflozin 5 or 15 mg daily	Time to first occurrence of any component of the composite endpoint of CV death, nonfatal MI, or nonfatal stroke	3900	6.3	2020

Curr Opin Endocrinol Diabetes Obes. 2017 Feb; 24(1): 73–79.

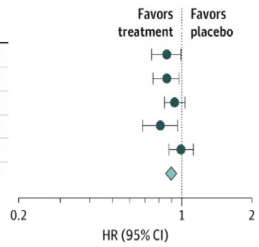
Summary of CV and renal outcome trials with SGLT2 inhibitor in type 2 diabetes

	EMPA-REG OUTCOME	DECLARE-TIMI 58	DAPA-HF[1)]	VERTIS-CV	DAPA-CKD	EMPEROR-R
Patients enrolled, n	7,020	17,160	4,744	8,246	4,304	3,730
Drug	empagliflozin	dapagliflozin	dapagliflozin	ertugliflozin	dapagliflozin	empagliflozin
Median duration of follow up (years)	3.1	4.2	1.5	3.0	2.4	1.3
Mean baseline A1C (%)	8.1	8.3	*	8.2	*	*
Mean duration of diabetes (years)	NA	11.0	*	13.0	*	*
Baseline statin (%)	77.0	75.0	NA	82.3	65.0	NA
Baseline prevalence of CVD/HF (%)	99/10	41/10	NA/100	100/23.7	37/10.8	NA/100
MACE outcome[2)]	0.86 (0.74–0.99)	0.93 (0.84–1.03)	Not reported	0.97 (0.85–1.11)	Not reported	Not reported
Hospitalization for HF or CV death	0.66 (0.55–0.79)	0.83 (0.73–0.95)	0.75 (0.65–0.85)	0.88 (0.75–1.03)	0.71 (0.55–0.92)	0.75 (0.65–0.86)
CV death	0.62 (0.49–0.77)	0.98 (0.82–1.17)	0.82 (0.69–0.98)	0.92 (0.77–1.11)	0.58-1.12	0.92 (0.75–1.12)
Fatal or nonfatal MI	0.87 (0.70–1.09)	0.89 (0.77–1.01)	Not reported	1.04 (0.86–1.26)	Not reported	Not reported
Fatal or nonfatal stroke	1.18 (0.89–1.56)	1.01 (0.84–1.21)	Not reported	1.06 (0.82–1.37)	Not reported	Not reported
All-cause mortality	0.68 (0.57–0.82)	0.93 (0.82–1.04)	0.83 (0.71–0.97)	0.93 (0.80–1.08)	0.69 (0.53–0.88)	0.92 (0.77–1.10)
HF hospitalization	0.65 (0.50–0.85)	0.73 (0.61–0.88)	0.70 (0.59–0.83)	0.70 (0.54–0.90)	Not reported	0.69 (0.59–0.81)
Renal composite outcome	0.54 (0.40–0.75)	0.53 (0.43–0.66)	0.71 (0.44–1.16)	0.81 (0.63–1.04)	0.61 (0.51–0.72)	0.50 (0.32–0.77)
ESKD	0.45 (0.21–0.97)	0.31 (0.13–0.79)	1.00 (0.50–1.99)	0.81 (0.63–1.04)	0.64 (0.50–0.82)	Not reported
Renal death	Not reported	0.60 (0.22–1.65)	NA	NA	NA	Not reported

2021 당뇨병 진료지침 제7판, Clinical Practice Guidelines for Diabetes

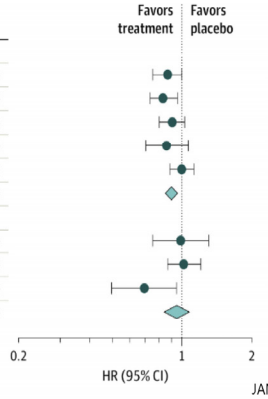
A Overall MACEs

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
EMPA-REG OUTCOME	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)		15.72
CANVAS program	NA/5795	26.9	NA/4347	31.5	0.86 (0.75-0.97)		20.12
DECLARE-TIMI 58	756/8582	22.6	803/8578	24.2	0.93 (0.84-1.03)		32.02
CREDENCE	217/2202	38.7	269/2199	48.7	0.80 (0.67-0.95)		10.92
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)		21.23
Fixed-effects model (Q=5.22; *df*=4; *P*=.27; I^2=23.4%)					0.90 (0.85-0.95)		



B MACEs by ASCVD status

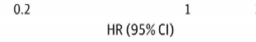
	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
Patients with ASCVD							
EMPA-REG OUTCOME	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)		19.19
CANVAS program	NA/3756	34.1	NA/2900	41.3	0.82 (0.72-0.95)		21.16
DECLARE-TIMI 58	483/3474	36.8	537/3500	41.0	0.90 (0.79-1.02)		24.90
CREDENCE	155/1113	55.6	178/1107	65.0	0.85 (0.69-1.06)		8.82
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)		25.93
Fixed-effects model (Q=4.53; *df*=4; *P*=.34; I^2=11.8%)					0.89 (0.84-0.95)		
Patients without ASCVD							
CANVAS program	NA/2039	15.8	NA/1447	15.5	0.98 (0.74-1.30)		21.70
DECLARE-TIMI 58	273/5108	13.4	266/5078	13.3	1.01 (0.86-1.20)		62.07
CREDENCE	62/1089	22.0	91/1092	32.7	0.68 (0.49-0.94)		16.23
Fixed-effects model (Q=4.59; *df*=2; *P*=.10; I^2=56.5%)					0.94 (0.83-1.07)		



JAMA Cardiol. 2021 Feb; 6(2): 1–11.

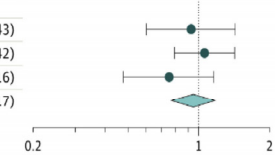
A Overall CV death

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
EMPA-REG OUTCOME	172/4687	12.4	137/2333	20.2	0.62 (0.49-0.77)		15.61
CANVAS program	NA/5795	11.6	NA/4347	12.8	0.87 (0.72-1.06)		21.32
DECLARE-TIMI 58	245/8582	7.0	249/8578	7.1	0.98 (0.82-1.17)		25.24
CREDENCE	110/2202	19.0	140/2199	24.4	0.78 (0.61-1.00)		13.05
VERTIS CV	341/5499	17.6	184/2747	19.0	0.92 (0.77-1.10)		24.77
Fixed-effects model (Q=11.22; *df*=4; *P*=.02; I^2=64.3%)					0.85 (0.78-0.93)		



B CV death by ASCVD status

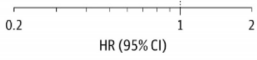
	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
Patients with ASCVD							
EMPA-REG OUTCOME	172/4687	12.4	137/2333	20.2	0.62 (0.49-0.77)		18.61
CANVAS program	NA/3756	14.8	NA/2900	16.8	0.86 (0.70-1.06)		22.08
DECLARE-TIMI 58	153/3474	10.9	163/3500	11.6	0.94 (0.76-1.18)		19.64
CREDENCE	75/1113	25.7	93/1107	32.4	0.79 (0.58-1.07)		10.14
VERTIS CV	341/5499	17.6	184/2747	19.0	0.92 (0.77-1.10)		29.52
Fixed-effects model (Q=9.10; *df*=4; *P*=.06; I^2=56.1%)					0.83 (0.76-0.92)		
Patients without ASCVD							
CANVAS program	NA/2039	6.5	NA/1447	6.2	0.93 (0.60-1.43)		24.02
DECLARE-TIMI 58	92/5108	4.4	86/5078	4.1	1.06 (0.79-1.42)		52.70
CREDENCE	35/1089	12.2	47/1092	16.4	0.75 (0.48-1.16)		23.27
Fixed-effects model (Q=1.65; *df*=2; *P*=.44; I^2=0.0%)					0.95 (0.77-1.17)		



JAMA Cardiol. 2021 Feb; 6(2): 1–11.

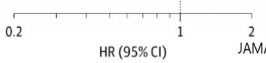
A Overall HHF

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)		16.09
CANVAS program	NA/5795	5.5	NA/4347	8.7	0.67 (0.52-0.87)		17.10
DECLARE-TIMI 58	212/8582	6.2	286/8578	8.5	0.73 (0.61-0.88)		33.72
CREDENCE	89/2202	15.7	141/2199	25.3	0.61 (0.47-0.80)		16.01
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)		17.08
Fixed-effects model (Q = 1.39; *df* = 4; *P* = .85; I^2 = 0.0%)					0.68 (0.61-0.76)		



B HHF by ASCVD status

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
Patients with ASCVD							
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)		19.62
CANVAS program	NA/3756	7.3	NA/2900	11.3	0.68 (0.51-0.90)		17.13
DECLARE-TIMI 58	151/3474	11.1	192/3500	14.1	0.78 (0.63-0.97)		29.66
CREDENCE	59/1113	20.6	92/1107	33.2	0.61 (0.44-0.85)		12.74
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)		20.84
Fixed-effects model (Q = 1.97; *df* = 4; *P* = .74; I^2 = 0.0%)					0.70 (0.62-0.78)		
Patients without ASCVD							
CANVAS program	NA/2039	2.6	NA/1447	4.2	0.64 (0.35-1.15)		16.38
DECLARE-TIMI 58	61/5108	3.0	94/5078	4.6	0.64 (0.46-0.88)		55.07
CREDENCE	30/1089	10.6	49/1092	17.5	0.61 (0.39-0.96)		28.56
Fixed-effects model (Q = 0.03; *df* = 2; *P* = .99; I^2 = 0.0%)					0.63 (0.50-0.80)		



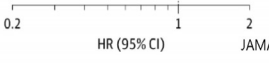
JAMA Cardiol. 2021 Feb; 6(2): 1–11.

A Overall kidney outcomes

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)		11.51
CANVAS program	NA/5795	5.5	NA/4347	9.0	0.60 (0.47-0.77)		18.66
DECLARE-TIMI 58	127/8582	3.7	238/8578	7.0	0.53 (0.43-0.66)		24.77
CREDENCE	153/2202	27.0	224/2199	40.4	0.66 (0.53-0.81)		25.28
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)		19.79
Fixed-effects model (Q = 7.96; *df* = 4; *P* = .09; I^2 = 49.7%)					0.62 (0.56-0.70)		

B Kidney outcomes by ASCVD status

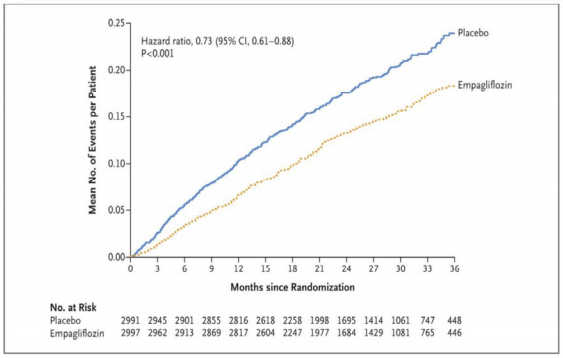
	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
Patients with ASCVD							
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)		16.67
CANVAS program	NA/3756	6.4	NA/2900	10.5	0.59 (0.44-0.79)		19.23
DECLARE-TIMI 58	65/3474	4.7	118/3500	8.6	0.55 (0.41-0.75)		18.06
CREDENCE	69/1113	24.1	102/1107	36.5	0.64 (0.47-0.87)		17.37
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)		28.66
Fixed-effects model (Q = 6.09; *df* = 4; *P* = .19; I^2 = 34.4%)					0.64 (0.56-0.72)		
Patients without ASCVD							
CANVAS program	NA/2039	4.1	NA/1447	6.6	0.63 (0.39-1.02)		15.72
DECLARE-TIMI 58	62/5108	3.0	120/5078	5.9	0.51 (0.37-0.69)		37.41
CREDENCE	84/1089	29.9	122/1092	44.3	0.68 (0.51-0.89)		46.87
Fixed-effects model (Q = 1.86; *df* = 2; *P* = .40; I^2 = 0.0%)					0.60 (0.50-0.73)		



JAMA Cardiol. 2021 Feb; 6(2): 1–11.

심혈관 이익이 입증된 SGLT 2 Inhibitor

CV effect		Renal effect
ASCVD	HF	Progression of DKD
Empagliflozin Canagliflozin	Emagliflozin Canagliflozin Dapagliflozin Ertugliflozin	Emagliflozin Canagliflozin Dapagliflozin

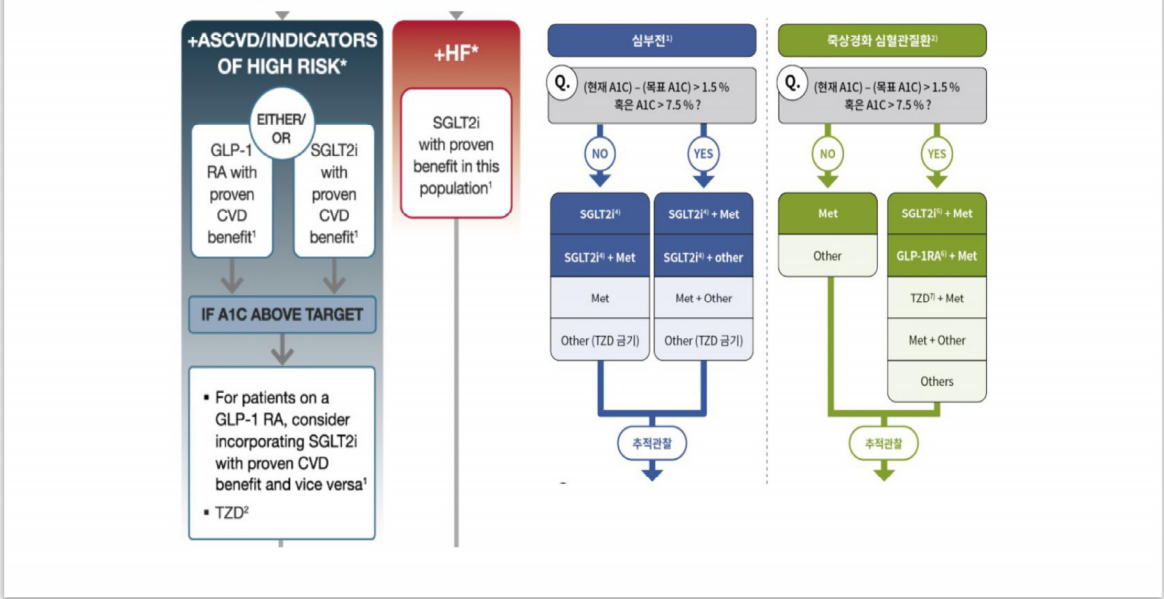


Effect of Empagliflozin on Hospitalization of HF

In HFpEF patient

- NT proBNP ≥ 300 mL
- NYHA class II-III dyspnea
- EF ≥ 40%

N Engl J Med 2021; 385:1451-1461



당뇨병 약물 보험 인정기준

구분		Metformin	Sulfonylurea	Meglitinide	α-glucosidase inhibitor	Thiazoli-dinedione	DPP-4 inhibitor	SGLT2 inhibitor			
								Dapagliflozin	Ipragliflozin	Empagliflozin	Ertugliflozin
Metformin			인정	인정	인정	인정	인정	인정	인정	인정	인정
Sulfonylurea		인정		×	인정	인정	인정	인정	×	×	×
Meglitinide		인정	×		인정	인정	×	×	×	×	×
α-glucosidase inhibitor		인정	인정	인정		×	×	×	×	×	×
Thiazolidinedione		인정	인정	인정	×		인정	×	×	×	×
DPP-4 inhibitor		인정	인정	×	×	인정		×	×	×	×
SGLT2 inhibitor	Dapagliflozin[1)]	인정	인정	×	×	×	×				
	Ipragliflozin	인정	×	×	×	×	×				
	Empagliflozin	인정	×	×	×	×	×				
	Ertugliflozin	인정	×	×	×	×	×				

Dapagliflozin[1)]: 허가사항 범위 내에서 만성 심부전에 투여 시 약값 전액을 환자가 부담토록 함 (2021-01-16) – 고시 제 2021-11호.

SGLT 2 Inhibitor 보험기준

Empagliflozin

- Empagliflozin + Linagliptin + Metformin 가능 metformin 포함한 3 제만 가능)
  * DPP4억제제와 SGLT2 억제제 중 약가가 상대적으로 저렴한 것을 본인 부담 100% 로 처방

Dapagliflozin

- Dapagliflozin + Sitagliptin + Metformin 가능 metformin 없이 2 제도 가능
- Dapagliflozin + Saxagliptin + Metformin 가능 (3제만 가능)
- Dapagliflozin + Gemigliptin + Metformin 가능 (3제만 가능)
  * DPP4 억제제와 SGLT2 억제제 중 약가가 상대적으로 저렴한 것을 본인 부담 100% 로 처방

1) 자디앙 25 mg 852원 자디앙 10mg 660원 + 트라젠타 750원

2) 포시가 10 mg 760원 + 자누비아 100mg 855원 / 온글라이자 5mg 826원 / 제미글로 50mg 772원

SGLT 2 Inhibitor 보험기준

Empagliflozin

- Empagliflozin + Pioglitazone + Metformin 가능 (metformin 포함한 3 제만 가능)

  * TZD와 SGLT2 억제제 중 약가가 상대적으로 저렴한 것을 본인 부담 100% 로 처방

1) 자디앙10mg 660원/자디앙25mg 852원+ 액토스15mg 625원/ 30mg 937원

SGLT 2 Inhibitor 허가기준

Empagliflozin

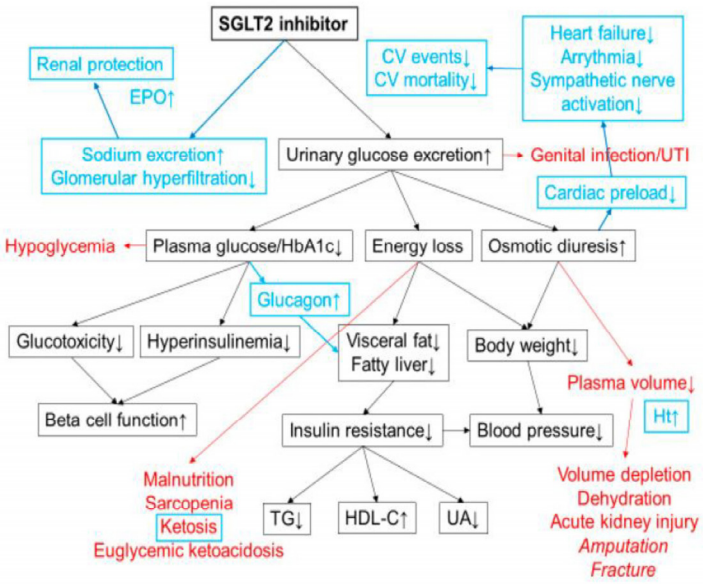
* 2형 당뇨병에서 Emplagliflozin 10mg/day and 25mg/day (2022.5.24)

투약 시작	기존 허가 사항	변경 허가 사항
eGFR 60 미만(mL/min/1.73m²)	투약 시작해서는 안된다	가능
eGFR 45 미만(mL/min/1.73m²)		권장되지 않는다

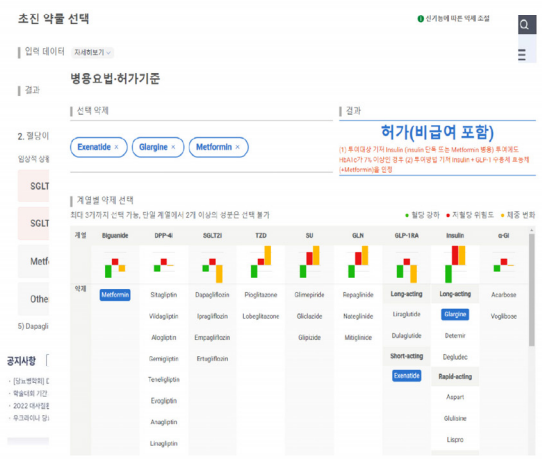
투약 유지	기존 허가 사항	변경 허가 사항
eGFR 60 미만(mL/min/1.73m²)	25mg → 10mg 감량	용량 조절 필요 없음
eGFR 45 미만(mL/min/1.73m²)	중단	ESRD 또는 투석 중인 환자는 사용하지 않는다.

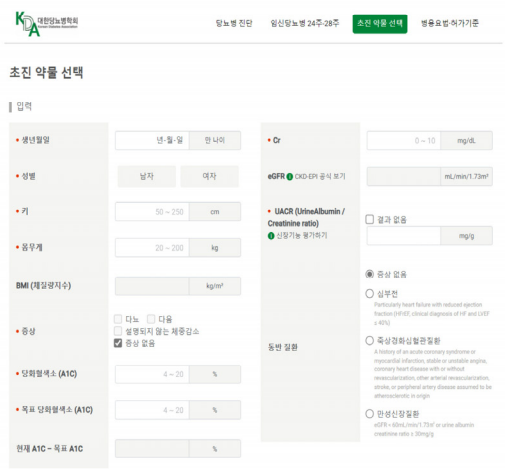
SGLT 2 Inhibitor 부작용

- Diseases. 2020 Jun; 8(2): 14.



초진약물선택 가이드


초진 약물 선택
병용요법·허가기준
선택 약제
Exenatide
Glargine
Metformin
결과
허가(비급여 포함)
계열별 약제 선택
Biguanide
DPP-4i
SGLT2i
TZD
SU
GLN
GLP-1RA
Insulin
α-GI
Metformin
Sitagliptin
Vildagliptin
Alogliptin
Gemigliptin
Teneligliptin
Evogliptin
Anagliptin
Linagliptin
Dapagliflozin
Ipragliflozin
Empagliflozin
Ertugliflozin
Pioglitazone
Lobeglitazone
Glimepiride
Gliclazide
Glipizide
Repaglinide
Nateglinide
Mitiglinide
Long-acting
Liraglutide
Dulaglutide
Short-acting
Exenatide
Long-acting
Glargine
Determir
Degludec
Rapid-acting
Aspart
Glulisine
Lispro
Acarbose
Voglibose


당뇨병 진단
임신당뇨병 24주-28주
초진 약물 선택
병용요법·허가기준
초진 약물 선택
입력
생년월일
성별
남자
여자
키
몸무게
BMI (체질량지수)
증상
다뇨
다음
설명되지 않는 체중감소
증상 없음
당화혈색소 (A1C)
목표 당화혈색소 (A1C)
현재 A1C ~ 목표 A1C
Cr
eGFR
CKD-EPI 공식 보기
UACR (UrineAlbumin / Creatinine ratio)
신장기능 평가하기
결과 없음
동반 질환
증상 없음
심부전
죽상경화심혈관질환
만성신장질환