扭轉糖尿病治療趨勢—

口服腸泌素臨床實務經驗分享

瑞倍適®

林正日 醫師

安家診所

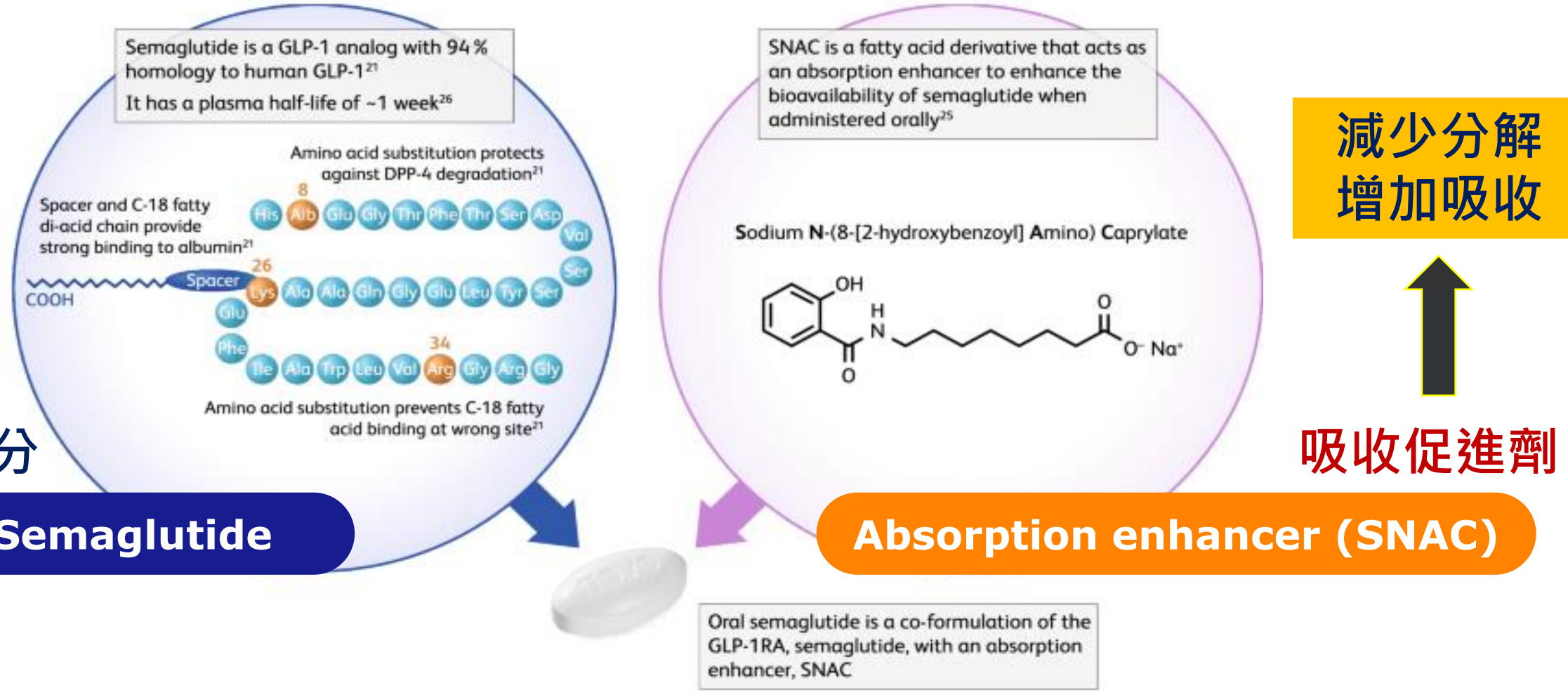
- 全球唯一口服 GLP1-RA 藥物: Rybelsus
  - ✓效果
  - ✓安全性 & 副作用
- Rybelsus 起手式
- 常見問題 & 經驗分享

Outline

世界第一且唯一的口服蛋白質降血糖藥物

Rybelsus®含有 Semaglutide 與 吸收促進劑SNAC

Co-formulation structure of Rybelsus®



Drugs (2021) 81:1003–1030

A series of 10 RCTs was designed to test Rybelsus® across the spectrum of T2D

PIONEER programme

Common key inclusion criteria

收入族群

Age	Diagnosis
≥18 years	**T2D ≥3** months prior to screening
Baseline HbA_{1c}	**Stable background therapies**
7–9.5%	From diet and exercise, through daily insulin were **allowed**

劑量選擇 Selected doses

3 mg **7 mg** **14 mg**

劑量調整 Dosing adjustment

To mitigate potential GI AEs…

3 mg → **7 mg** / **14 mg**

Starting dose — Escalate **every 4 weeks** — until randomized dose

GI, gastrointestinal; PIONEER, the phase 3 Peptide InnOvatioN for the Early diabEtes tReatment; RCT, randomized controlled trial; T2D, type 2 diabetes.

Thethi TK, et al. Diabetes Obes Metab. 2020 Aug;22(8):1263-1277.

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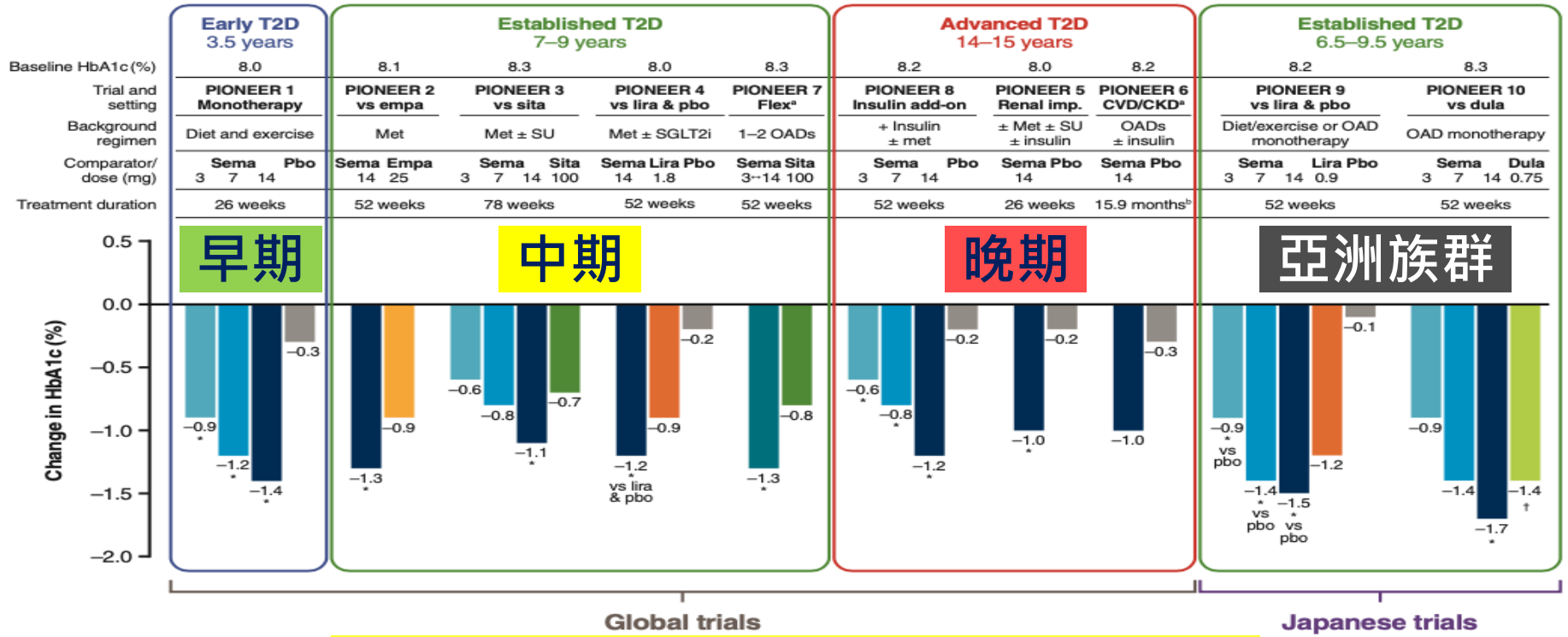
RYBELSUS® semaglutide tablets

Rybelsus® was effective in reducing HbA_{1C} in all types of T2D patients

PIONEER programme

降糖效果

Change in HbA_{1C} – End of treatment in the PIONEER trials, by the treatment policy estimand



[a]HbA_{1C} reduction was not the primary endpoint in PIONEER 6 or 7. [b]event-driven trial: efficacy outcomes were not analyzed statistically. *$p<0.05$ for the estimated treatment difference with oral semaglutide vs. placebo and/or active comparator; †$p<0.05$ for the estimated treatment difference with oral semaglutide 7 mg.

HbA1C 降幅達 1.0~1.7% 高劑量(14mg)

CKD, chronic kidney disease; CVD, cardiovascular disease; dula, dulaglutide; empa, empagliflozin; HbA_{1c}, glycated hemoglobin; imp, impairment; lira, liraglutide; met, metformin; OAD, oral antidiabetic drug; pbo, placebo; sema, semaglutide; SGLT2i, sodium-glucose co-transporter-2 inhibitor; sita, sitagliptin; SU, sulfonylurea; T2D, type 2 diabetes.

Thethi TK, et al. Diabetes Obes Metab. 2020 Aug;22(8):1427-1431.

HbA1C 降幅達 0.8~1.4% 中劑量(7mg)

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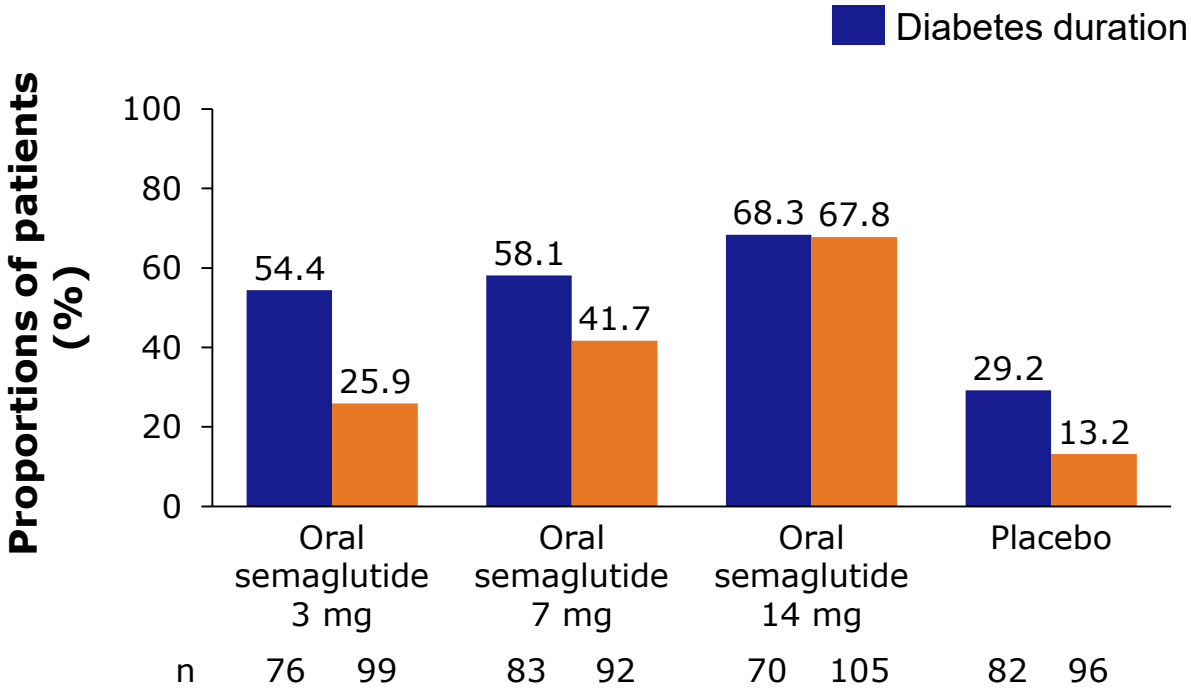
Earlier initiation of Rybelsus® results in more people reaching glycemic targets

PIONEER 1
Post-hoc analysis

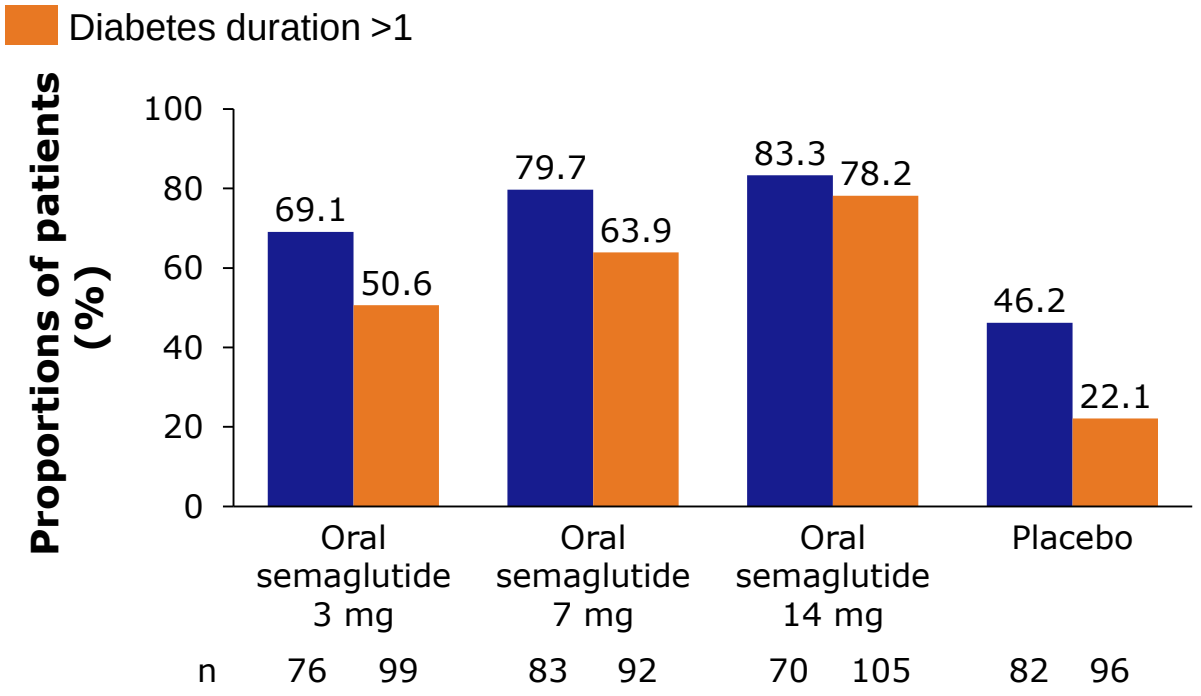
血糖達標 & 罹病年

A post-hoc analysis of the PIONEER 1 study to assess the efficacy of oral semaglutide vs placebo in people with T2D duration ≤1 year and >1 year for comparison

Proportions of patients (HbA_{1C} ≤6.5%)



Proportions of participants (HbA_{1C} <7%)



早期使用oral Semaglutide
血糖達標率越高

HbA_{1C}, glycated hemoglobin; T2D, type 2 diabetes.

Goldenberg R, et al. Can J Diabetes. 2021 Nov;45(7_Supplement):S28-S29.

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RYBELSUS® semaglutide tablets

Asian patients in some PIONEER trials achieved greater HbA_{1C} reduction with Rybelsus®

PIONEER
Sub-analysis by race

降糖效果 & 種族

An exploratory subgroup analysis evaluated the effect of race on HbA_{1C} and body weight reductions at the end of treatment in PIONEER trials

Change in HbA_{1C} from baseline to end of treatment, by race

Trial (comparator) Background medication Total duration	Race	Number of patients	Baseline HbA_{1c} (%)†	Baseline body weight (kg)†	Estimated mean change from baseline in HbA_{1c} (%)		Estimated treatment difference vs comparator [95% CI]	
					Oral semaglutide 14 mg or flex	Comparator (active or placebo)		
PIONEER 1 (vs placebo) NCT02906930								
Diet & exercise only Week 26	White	262	8.0	92.4	−1.5	−0.2	−1.3 [−1.6; −1.0]	
	Black/AA	20	7.8	92.0	−1.3	−0.3	−1.0 [−2.0; 0.1]	*
	Asian	60	8.0	68.2	−1.6	0.6	−2.2 [−2.8; −1.6]	
PIONEER 4 (vs placebo and vs liraglutide 1.8 mg) NCT02863419								
vs placebo Met ± SGLT2i Week 52	White	307	8.0	96.9	−1.0	0.2	−1.2 [−1.4; −0.9]	
	Black/AA	20	8.1	90.3	−1.4	0.4	−1.8 [−2.7; −0.8]	*
	Asian	58	8.0	80.9	−1.7	0.4	−2.1 [−2.7; −1.6]	
vs liraglutide Met ± SGLT2i Week 52	White	420	8.0	96.9	−1.0	−0.9	−0.1 [−0.3; 0.1]	
	Black/AA	21	8.1	90.3	−1.4	−0.8	−0.5 [−1.5; 0.4]	*
	Asian	75	8.0	80.9	−1.7	−1.0	−0.7 [−1.1; −0.3]	
PIONEER 8 (vs placebo) NCT03021187								
INS ± Met Week 52	White	192	8.1	90.8	−1.1	−0.1	−0.9 [−1.3; −0.6]	
	Black/AA	24	7.9	100.2	−0.6	0.0	−0.6 [−1.7; 0.4]	*
	Asian	131	8.3	71.6	−1.5	0.3	−1.9 [−2.2; −1.5]	

亞洲人
使用Rybelsus
降糖效果更佳

*p<0.05 unadjusted two-side test of treatment by subgroup interaction. †Baseline data are for the oral semaglutide 14 mg arm, and were generally similar to the comparator arm.

AA, African American; flex, flexible dose; HbA_{1C}, glycated hemoglobin; Ins, insulin; Met, metformin; OAD, oral antidiabetic drug; SGLT2i, sodium-glucose co- transporter-2 inhibitor; SU, sulfonylurea; T2D, type 2 diabetes.

Desouza C, et al. Diabetes 2020;69(Supplement_1):930-P.

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Efficacy and safety of Rybelsus® in T2D Chinese patients

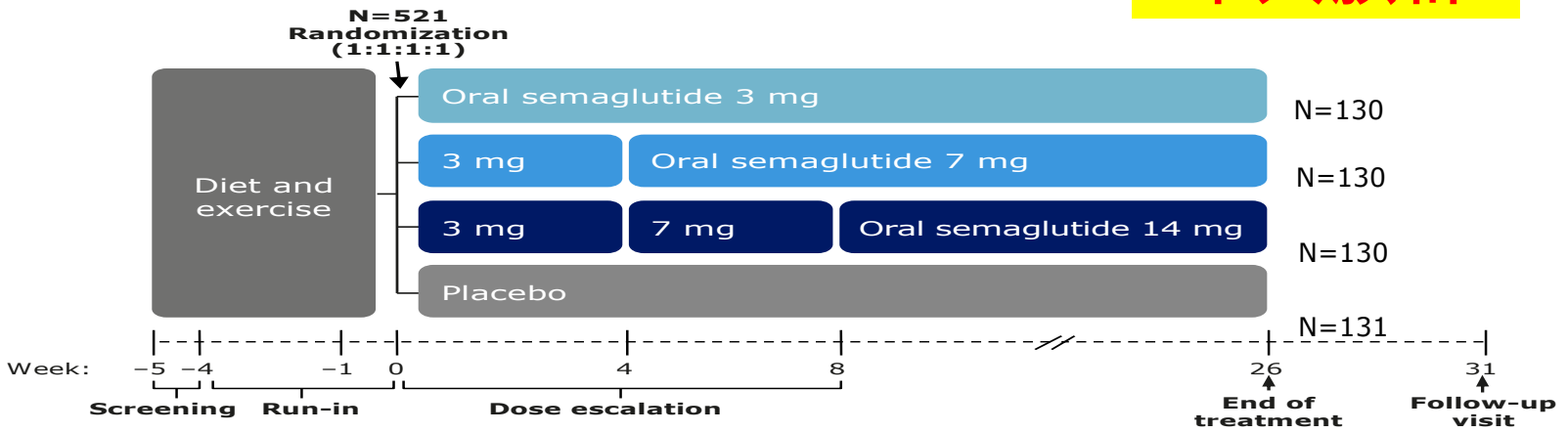
PIONEER 11 & 12

降糖效果
華人族群

PIONEER 11[1]

Key inclusion criteria:

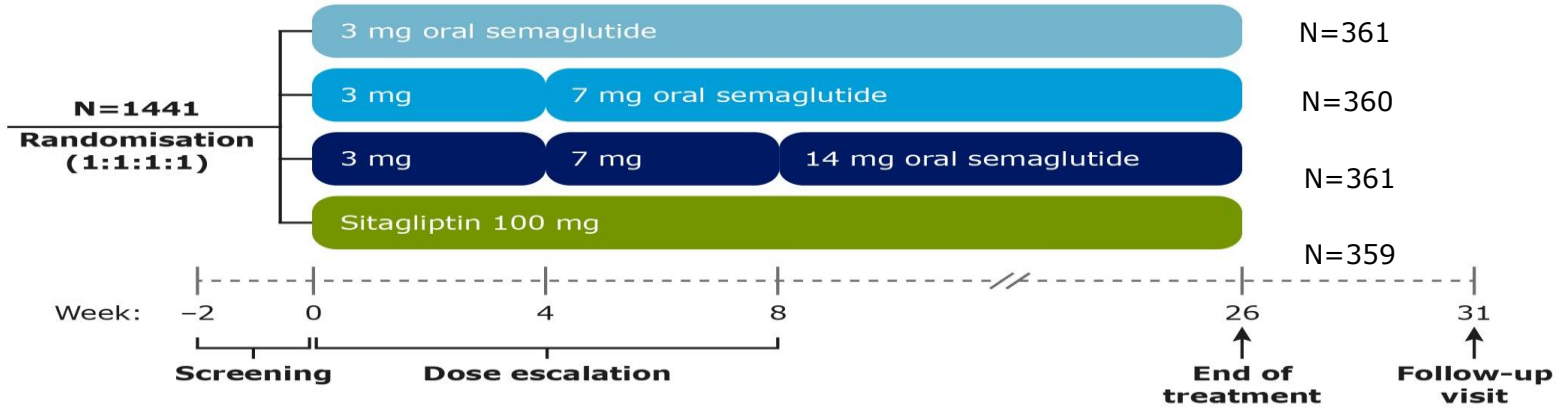
- Adults aged ≥18 years (≥20 years if in Taiwan)
- Diagnosed with T2D with HbA_{1c} 7.0–10.0% and not receiving any anti-diabetic drugs
- After the 4-week run-in period, participants with HbA_{1c} 7.0–9.5% were randomized



PIONEER 12[2]

Key inclusion criteria:

- Adults aged ≥18 years (≥20 years if in Taiwan)
- Diagnosed with T2D for ≥60 days prior to screening
- On a stable dose of metformin for ≥60 days prior to screening
- HbA_{1C} 7.0–10.5%



HbA_{1C}, glycated hemoglobin; T2D, type 2 diabetes.

1. Wang W, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0613.
2. Ji L, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0780.

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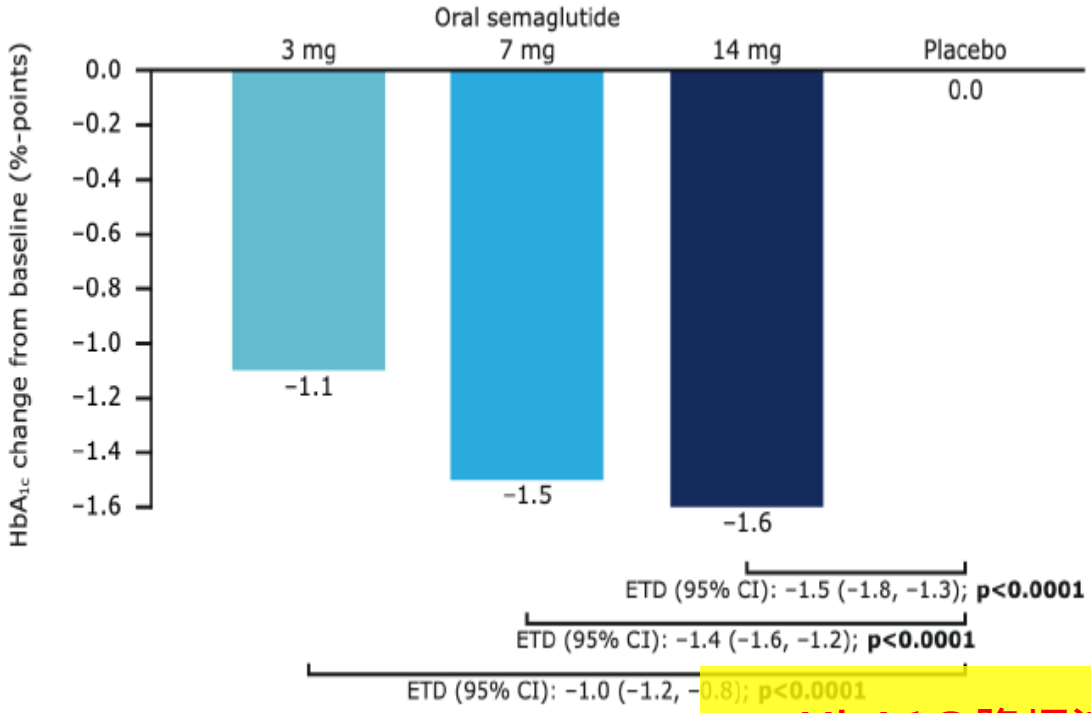
RYBELSUS® semaglutide tablets

Rybelsus® significantly reduced HbA_{1C} in T2D Chinese patients

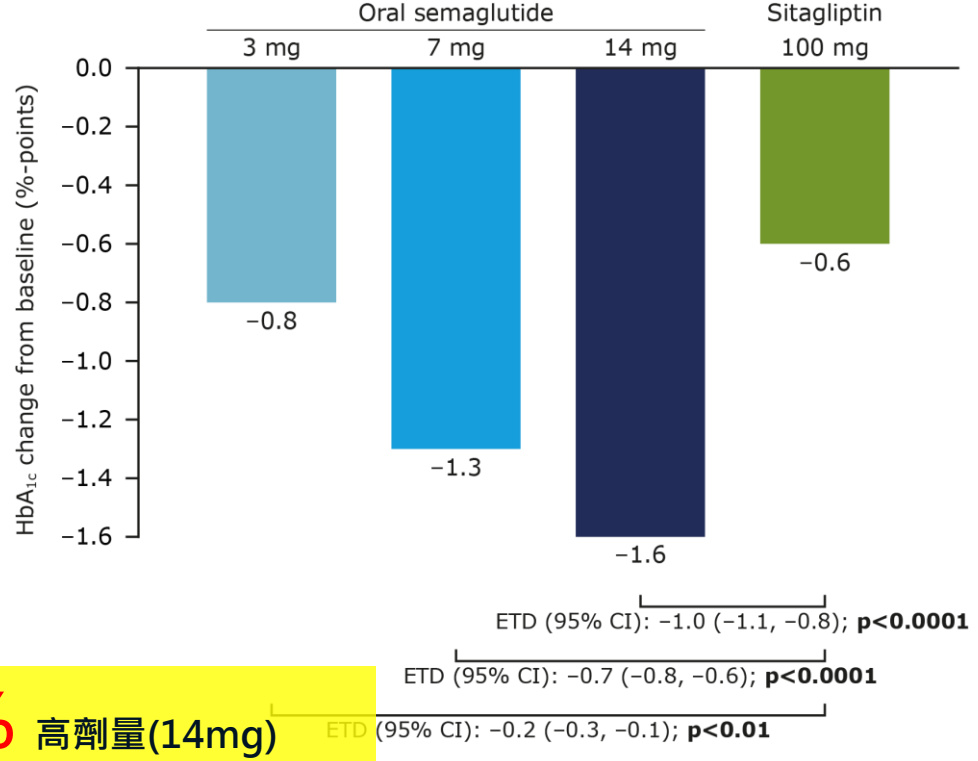
PIONEER 11 & 12

降糖效果
華人族群

Estimated mean change in HbA_{1C} at week 26 of treatment-naïve patients[1]



Estimated mean change in HbA_{1C} at week 26 of patients uncontrolled with metformin[2]



HbA1C 降幅達 1.6% 高劑量(14mg)

HbA1C 降幅達 1.3~1.5% 中劑量(7mg)

CI, confidence interval; ETD, estimated treatment difference; HbA_{1C}, glycated hemoglobin; T2D, type 2 diabetes.

1. Wang W, et al. Presented at the International Diabetes Federation Congress; 5-9 December 2022. Abstract number: I-2022-000612.
2. Ji L, et al. Presented at the International Diabetes Federation Congress; 5-9 December 2022. Abstract number: I-2022-000601.

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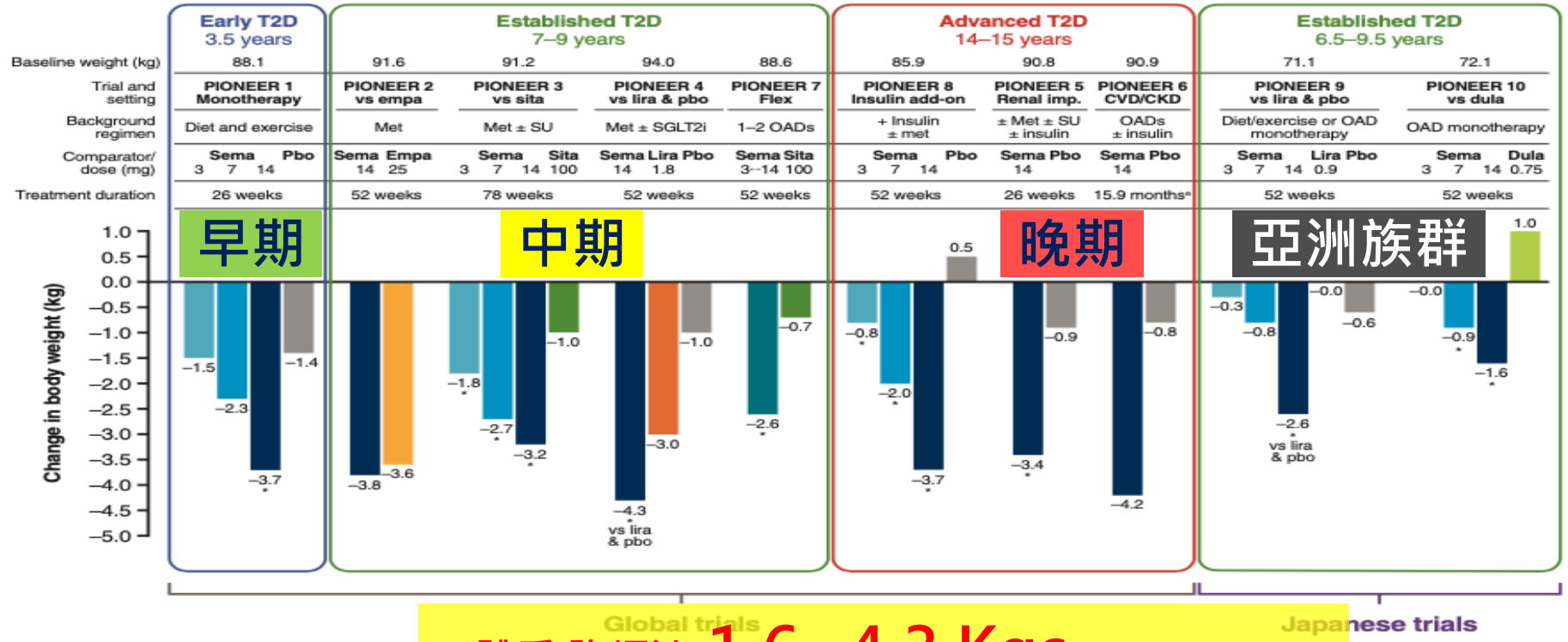
Rybelsus® was effective in reducing body weight in all types of T2D patients

PIONEER programme

體重控制

Change in body weight – End of treatment in the PIONEER trials, by the treatment policy estimand



體重 降幅達 1.6~4.3 Kgs 高劑量(14mg)

體重 降幅達 0.8~2.7 Kgs 中劑量(7mg)

[a]Event-driven trial: efficacy outcomes were not analyzed statistically. *$p<0.05$ for the estimated treatment difference with oral semaglutide vs. placebo and/or active comparator.

CKD, chronic kidney disease; CVD, cardiovascular disease; dula, dulaglutide; empa, empagliflozin; imp, impairment; lira, liraglutide; met, metformin; OAD, oral antidiabetic drug; pbo, placebo; sema, semaglutide; SGLT2i, sodium-glucose co- transporter-2 inhibitor; sita, sitagliptin; for T2D, type 2 diabetes.

Thethi TK, et al. Diabetes Obes Metab. 2020 Aug;22(8):1263-1277.

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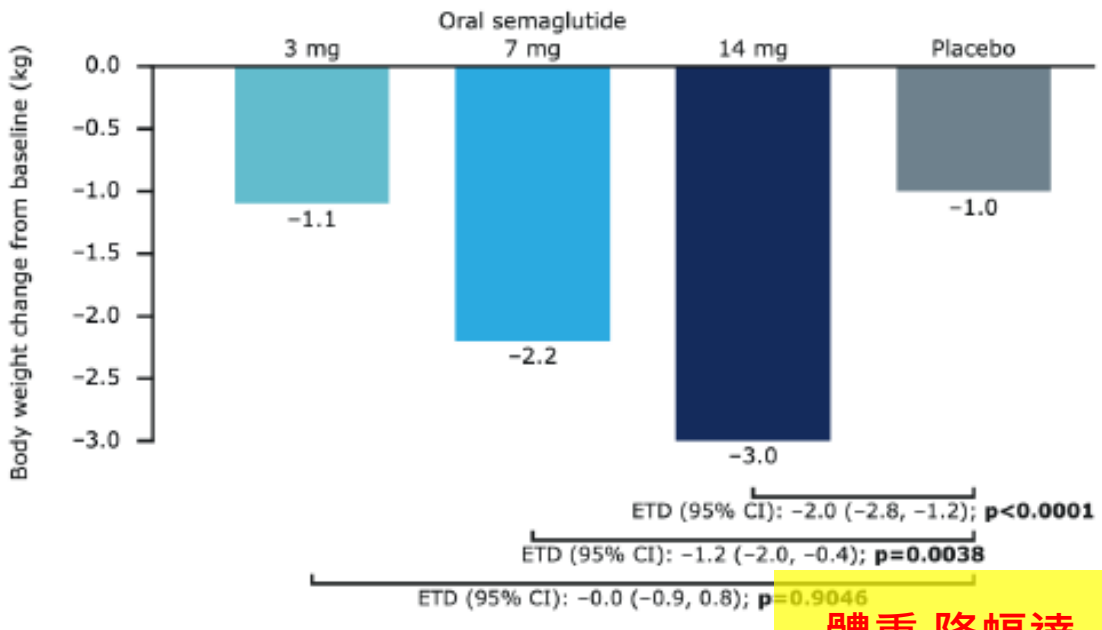
Rybelsus® significantly reduced body weight in T2D Chinese patients

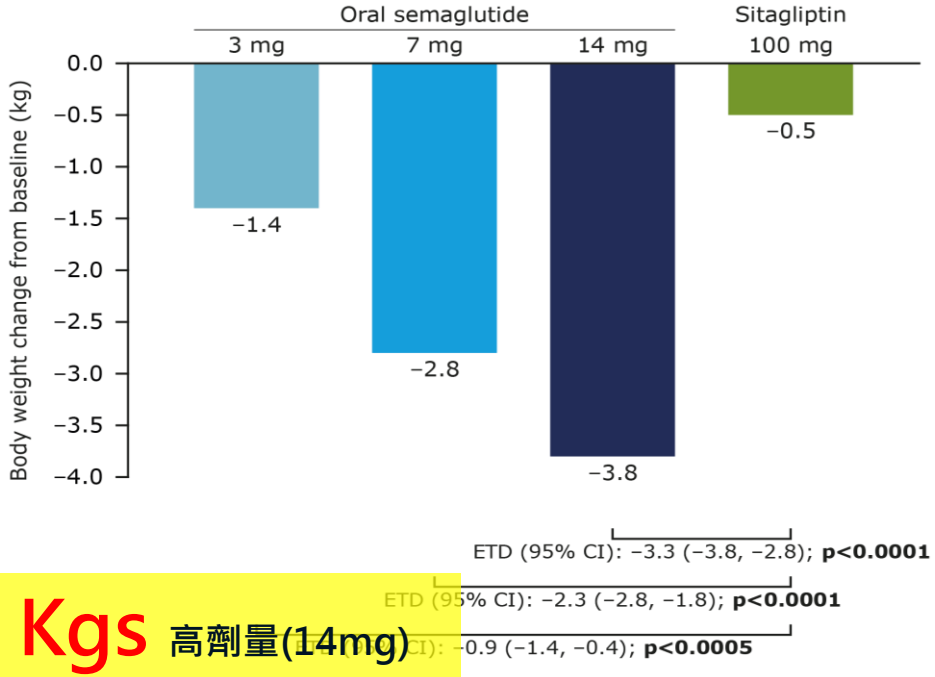
PIONEER 11 & 12

體重控制
華人族群

Estimated mean change in body weight at week 26 of treatment-naïve patients[1]



Estimated mean change in body weight at week 26 of patients uncontrolled with metformin[2]



體重 降幅達 3.0~3.8 Kgs 高劑量(14mg)

體重 降幅達 2.2~2.8 Kgs 中劑量(7mg)

CI, confidence interval; ETD, estimated treatment difference; HbA1c, glycated haemoglobin; T2D, type 2 diabetes.

1. Wang W, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0613.
2. Ji L, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0780.

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CVOTs have been conducted with semaglutide in T2D patients: SUSTAIN 6 and PIONEER 6

高CV風險DM族群

Similarities[1,2]

Inclusion criteria:

- Age ≥50 years and established CV disease or CKD ***or***
- Age ≥60 years and CV risk factors

Endpoint:

- Time to first occurrence of MACE, defined as CV death, non-fatal MI, or non-fatal stroke

Differences[1,2]

PINOEER 6:

- A shorter trial duration
- Smaller number of events

SUSTAIN 6 *vs.* PIONEER 6

針劑 — SUSTAIN 6[1]

Time and event-driven

n=3,297

R

- 0.5 or 1.0 mg semaglutide + SoC
- Placebo + SoC

Treatment duration 104 weeks

Risk reduction of MACE:[1] 26%

Confirms CV safety and superiority of semaglutide vs. placebo

Median follow-up: **2.1 years**
Number of MACE recorded: **254**

口服 — PIONEER 6[2]

Event-driven

n=3,183

R

- 14 mg oral semaglutide + SoC
- Placebo + SoC

Continuation until accrual of at least 122 events (first occurrence of MACE)

Risk reduction of MACE:[2] 21%

Confirms CV safety and non-inferiority of semaglutide vs. placebo

Median follow-up: **1.3 years**
Number of MACE recorded: **137**

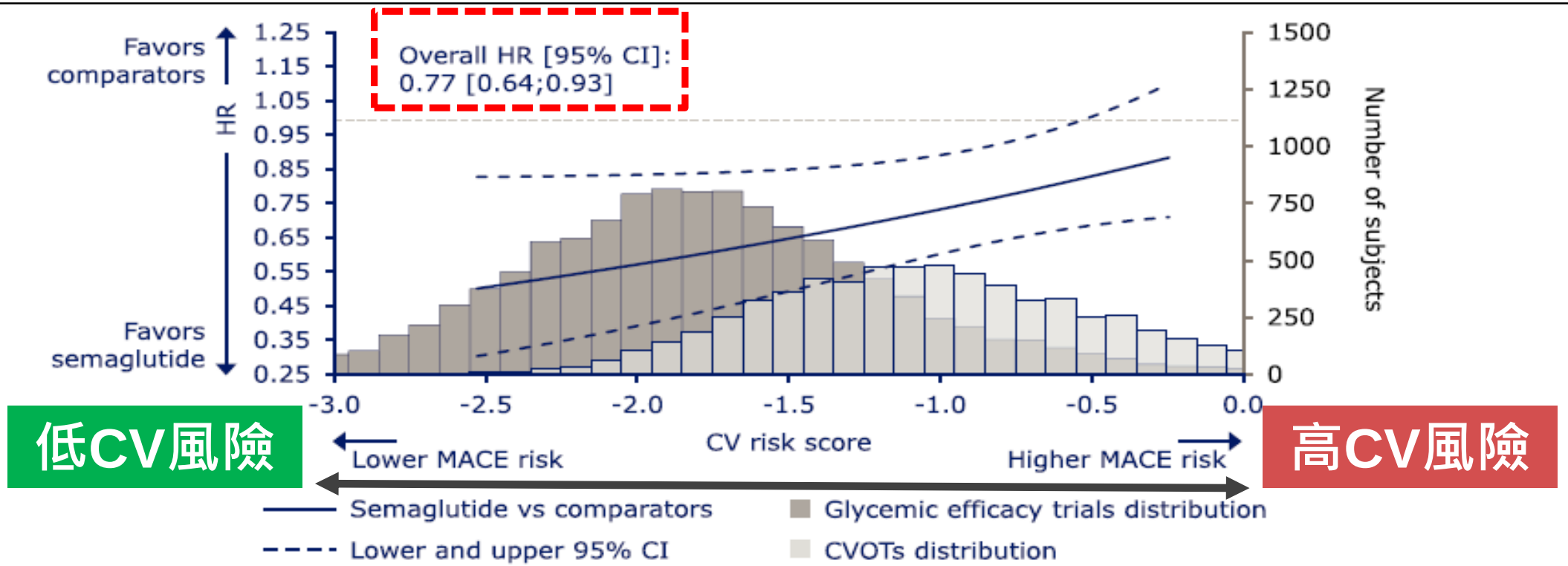
CKD, chronic kidney disease; CV, cardiovascular; CVOT, cardiovascular outcome trial; MACE, major adverse cardiovascular events; MI, myocardial infarction; R, randomization; SoC, standard of care; T2D, type 2 diabetes.

1. Marso SP, et al. N Engl J Med. 2016 Nov 10;375(19):1834-1844. **2.** Husain M, et al. N Engl J Med. 2019 Aug 29;381(9):841-851.

Semaglutide significantly reduces MACE risk in a broad range of T2D population

SUSTAIN and PIONEER
Pooled analysis

Relative risk of MACE as a function of baseline CV risk



HR for treatment effect (semaglutide vs comparator) and 95% CI estimated using a stratified Cox proportional hazards model including effects of treatment, CV risk score and interaction between both. The x-axis shows the CV risk score derived from subjects' baseline characteristics in the semaglutide trials. Data on graph cut off at the 5th and 95th percentile of the whole dataset. Hazard ratio value of 1.00 is indicated by a horizontal dashed line. Underlying histograms: distribution of subjects in the glycemic efficacy trials or CVOTs across baseline CV risk scores (histogram data for 439 subjects not shown, as these subjects had a CV risk score of <−3.0 or >0.0).

CI, confidence interval; CV, cardiovascular; CVOT, cardiovascular outcomes trial; HR, hazard ratio; MACE, major adverse cardiovascular events; T2D, type 2 diabetes.

Husain M, et al. Cardiovasc Diabetol. 2020 Sep 30;19(1):156.

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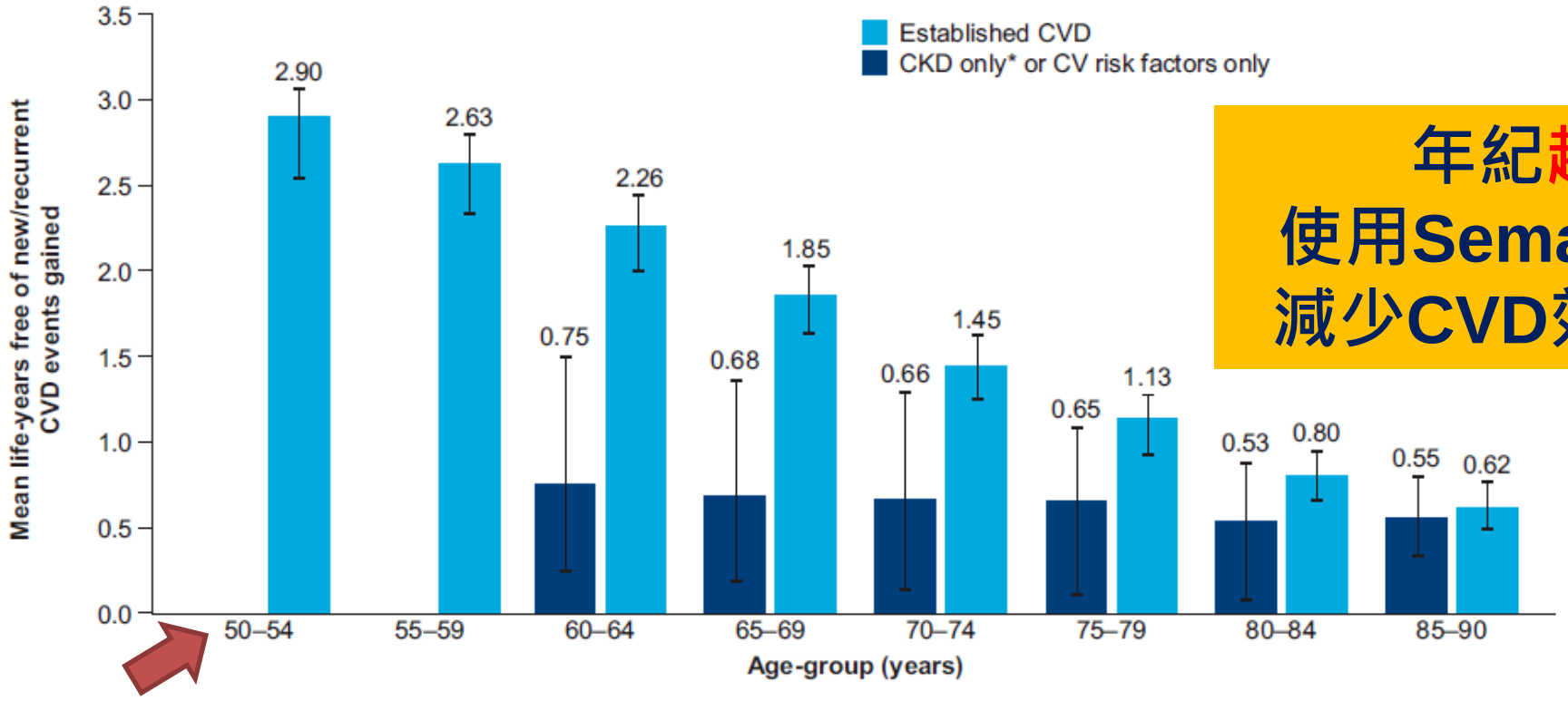
Adding semaglutide to T2D therapy increased life-years free of CVD, especially those with high risk and young age

SUSTAIN and PIONEER
Pooled analysis

Life-years free of new/recurrent CVD events gained by adding semaglutide to SoC



年紀越輕
使用Semaglutide
減少CVD效果越佳

*Estimated glomerular filtration rate <60 mL/min/1.73 m^2 (estimated using the CKD-EPI creatinine equation) and no established CVD. Error bars show interquartile range.

CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; SoC, standard of care; T2D, type 2 diabetes.

Westerink J, et al. Diabetes Care. 2022 May 1;45(5):1211-1218.

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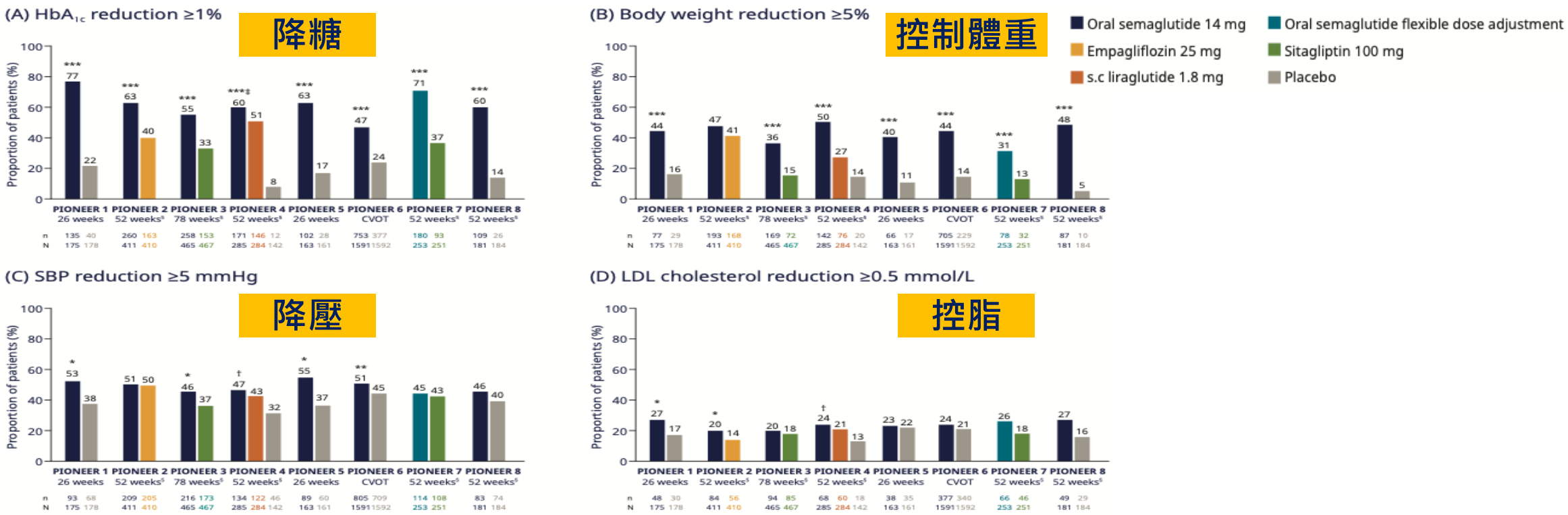
Rybelsus® demonstrated the significant effects of improving cardiometabolic risk factors

PIONEER 1-8
Post-hoc analysis

Proportion of patients achieving improvements in cardiometabolic risk factors



*p<0.05 for estimated odds ratio vs comparator. **p<0.001 for estimated odds ratio vs comparator; ***p≤0.0001 for estimated odds ratio vs comparator. †p<0.05 for estimated odds ratio vs placebo only in PIONEER 4. ‡p<0.05 for estimated odds ratio vs liraglutide only in PIONEER 4. §Time to primary endpoint: 26 weeks for PIONEER 1–5 and 8.

CVOT, cardiovascular outcomes trial; HbA_{1C}, glycated hemoglobin; LDL, low-density lipoprotein; SBP, systolic blood pressure; s.c., subcutaneous.

Aroda VR, et al. Presented at the Hybrid 58th EASD Annual Meeting on 21 December 2022.

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Potential multiple mechanisms of CV risk reduction in T2D by Rybelsus®

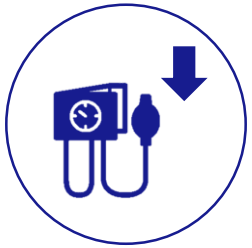
Rybelsus®

▼ **Inflammation**[1,2]

減少發炎

▼ **Body weight**[3,4]

降低體重

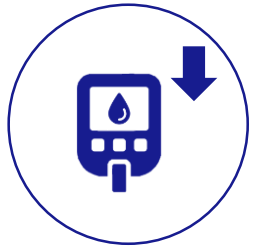


▼ **Blood pressure**[3,4]

降低血壓

▲ **Lipid homeostasis**[3,4]

控制血脂



▼ **HbA_{1c}**[3,4]

血糖達標

▼ **Atherosclerosis**

CV risk reduction

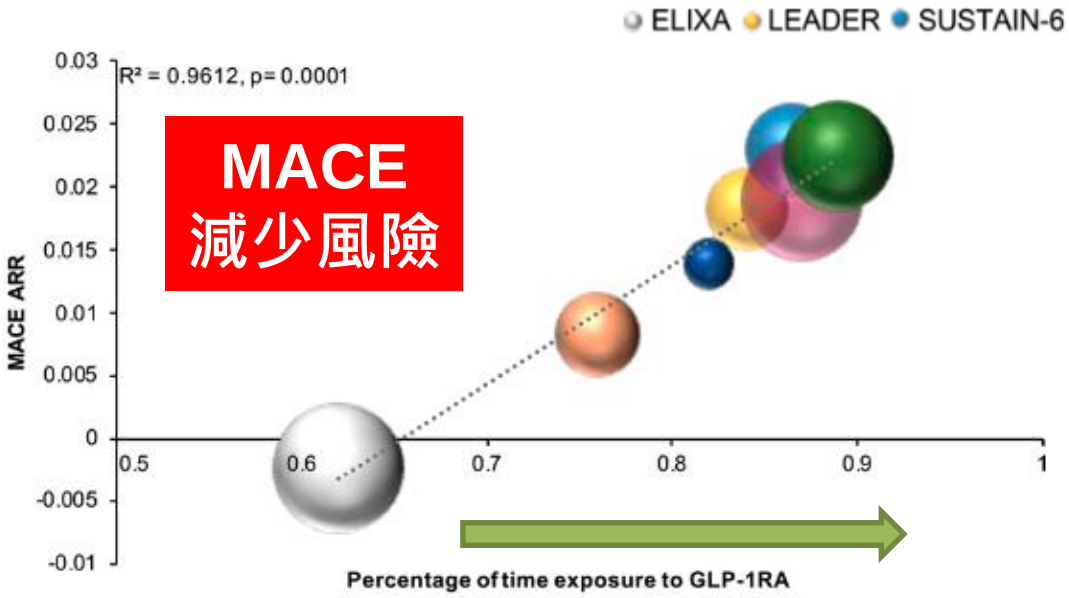
CV, cardiovascular; HbA_{1C}, glycated hemoglobin; T2D, type 2 diabetes.

1. Aroda V, et al. Diabetes Care. 2019 Sep;42(9):1724-1732. **2.** Rodbard HW, et al. Diabetes Care. 2019 Dec;42(12):2272-2281. **3.** Marso SP, et al. N Engl J Med. 2016 Nov 10;375(19):1834-1844. **4.** Husain M, et al. N Engl J Med. 2019 Aug 29;381(9):841-851.

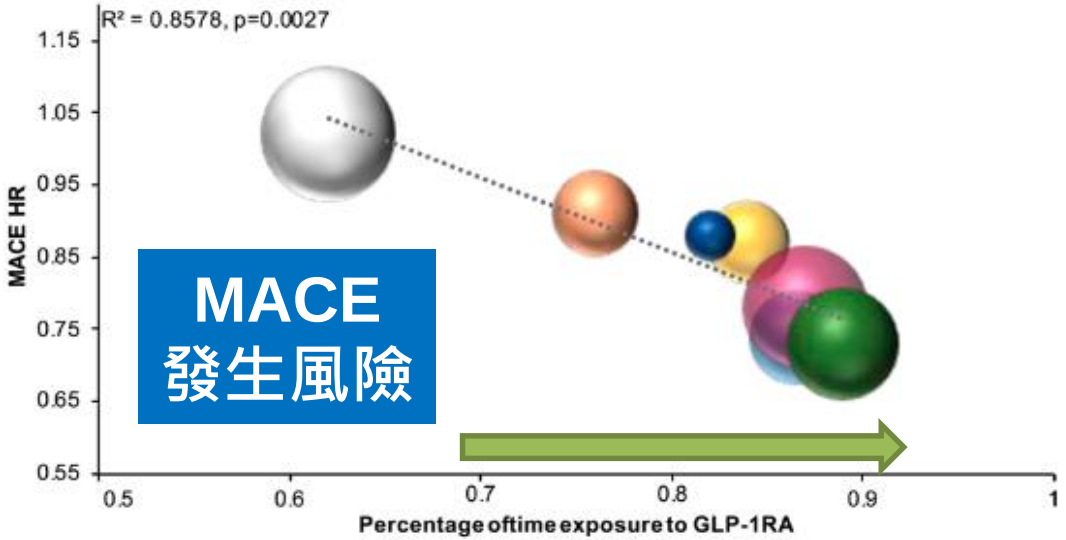
GLP-1 RAs shown to have a time-dependent cardiovascular protective effect

Correlation between percentage of time of exposure to GLP-1RA and the risk of MACE in CVOTs

"Positive" correlation between MACE ARR and time of exposure to GLP-1 RAs



"Negative" correlation between MACE HR and time of exposure to GLP-1 RAs



AMPLITUDE-O, Effect of Efpeglenatide on Cardiovascular Outcomes; ARR, absolute risk reduction; CVOT, cardiovascular outcomes trial; ELIXA, the Evaluation of Lixisenatide in Acute Coronary Syndrome; EXSCEL, Exenatide Study of Cardiovascular Event Lowering; GLP-1 RA; Glucagon-like peptide-1 receptor agonists; HR, hazard ratio; LEADER, Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results; MACE, major adverse cardiovascular events; SUSTAIN-6, Trial to Evaluate Cardiovascular and Other Long-term Outcomes With Semaglutide in Subjects With Type 2 Diabetes; HARMONY, Harmony Outcomes trial; REWIND, Dulaglutide and Cardiovascular Outcomes in Type 2 Diabetes.

Caruso I, et al. Diabetes Care. 2022 Feb 1;45(2):e30-e31.

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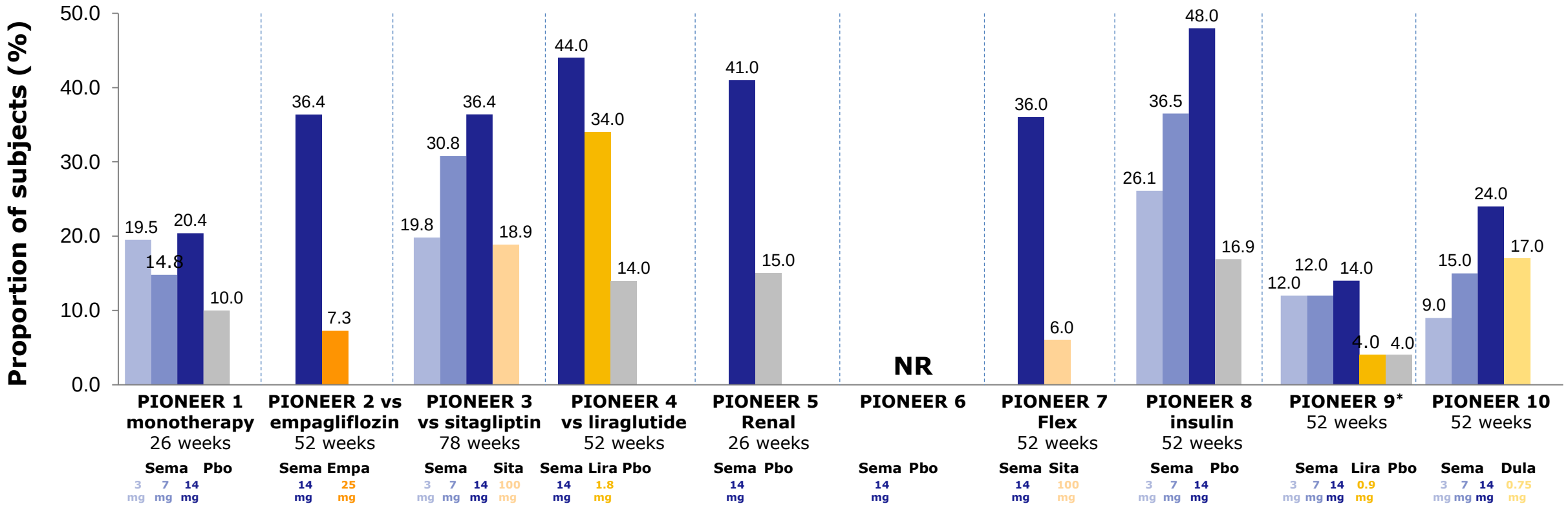
The most frequent AEs were mild-to-moderate and transient gastrointestinal disturbances

PIONEER programme

不良反應
腸胃道

Proportion of patients with gastrointestinal AEs (nausea, vomiting & diarrhea)



副作用主要為腸胃道相關,且多半為輕度至中度

AE, adverse event; Dula, dulaglutide; Empa, empagliflozin; Lira, liraglutide; NR, not recorded; Sema, semaglutide; Sita, sitagliptin; Pbo, placebo.

Smits MM, et al. Front Endocrinol (Lausanne). 2021 Jul 7;12:645563.

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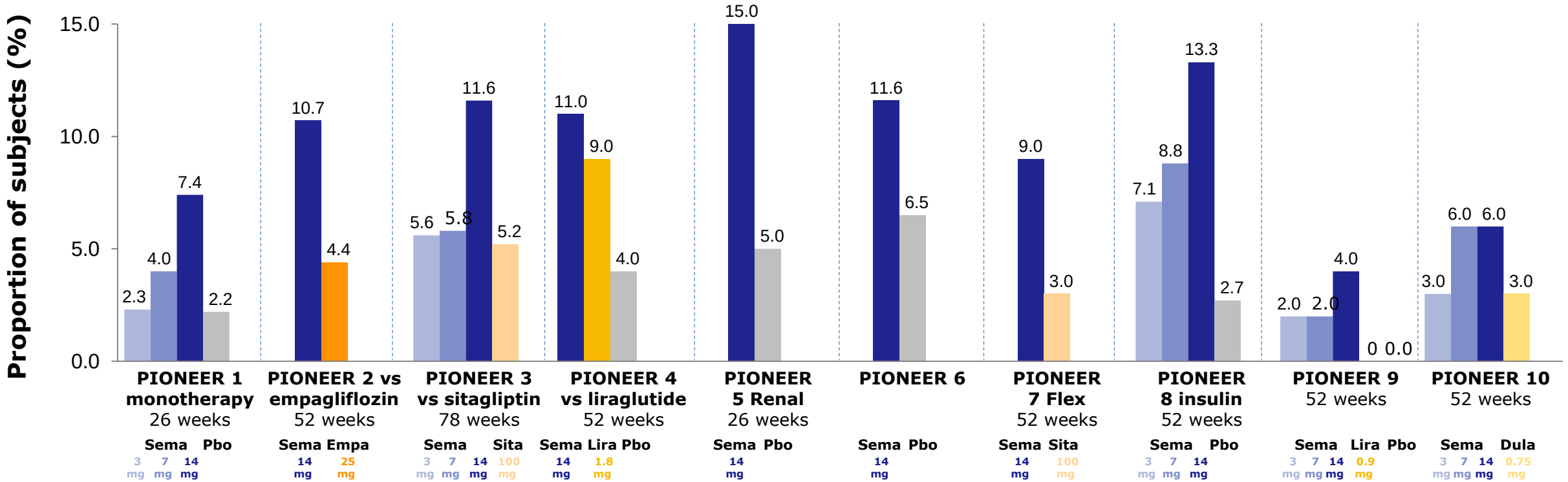
RYBELSUS® semaglutide tablets

Rybelsus® was well tolerated and discontinuation due to GI disturbances was approximately 10%

PIONEER programme

不良反應
腸胃道

Proportion of patients with AEs leading to discontinuation



因腸胃道副作用，導致停藥比例: ~10%

AE, adverse event; Dula, dulaglutide; Empa, empagliflozin; Lira, liraglutide; NR, not recorded; Sema, semaglutide; Sita, sitagliptin; SU, sulfonylurea; Pbo, placebo.

Smits MM, et al. Front Endocrinol (Lausanne). 2021 Jul 7;12:645563.

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RYBELSUS® semaglutide tablets

GI disturbances remained the most common AEs in Rybelsus®-treated T2D Chinese patients

PIONEER 11 & 12

不良反應
華人族群

	PIONEER 11 safety results[1] (Overall population)				PIONEER 12 safety results[2] (Overall population)			
	Oral semaglutide 3 mg (N=130)	Oral semaglutide 7 mg (N=130)	Oral semaglutide 14 mg (N=130)	Placebo (N=130)	Oral semaglutide 3 mg (N=361)	Oral semaglutide 7 mg (N=358)	Oral semaglutide 14 mg (N=361)	Sitagliptin 100 mg (N=358)
Total AEs	85 (65.4)	94 (72.3)	87 (67.4)	75 (57.3)	234 (64.8)	257 (71.8)	263 (72.9)	237 (66.2)
AEs by severity								
Mild	77 (59.2)	89 (68.5)	84 (65.1)	73 (55.7)	221 (61.2)	240 (67.0)	238 (65.9)	219 (61.2)
Total SAEs	6 (4.6)	10 (7.7)	5 (3.9)	2 (1.5)	16 (4.4)	11 (3.1)	11 (3.0)	15 (4.2)
AEs leading to trial product discontinuation	3 (2.3)	2 (1.5)	3 (2.3)	3 (2.3)	17 (4.7)	16 (4.5)	35 (9.7)	6 (1.7)
Gastrointestinal AEs	21 (16.2)	42 (32.3)	41 (31.8)	12 (9.2)	97 (26.9)	122 (34.1)	142 (39.3)	78 (21.8)
Diarrhoea	4 (3.1)	12 (9.2)	12 (9.3)	2 (1.5)	30 (8.3)	32 (8.9)	48 (13.3)	16 (4.5)
Nausea	6 (4.6)	4 (3.1)	8 (6.2)	2 (1.5)	36 (10.0)	39 (10.9)	44 (12.2)	14 (3.9)
Vomiting	2 (1.5)	2 (1.5)	4 (3.1)	1 (0.8)	16 (4.4)	18 (5.0)	29 (8.0)	1 (0.3)
Severe hypoglycaemic episodes (ADA 2018)	0	0	0	0	0	0	0	0
Deaths	0	0	0	0	2 (0.6)	2 (0.6)	1 (0.3)	0

Data are n (%). Data are from the on-treatment period. AEs are shown for the safety analysis set.
Adapted from Wang W, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0613. table 4 and Ji L, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0780. table 4.

ADA, American Diabetes Association; AE, adverse event; SAE, serious adverse event; T2D, type 2 diabetes.

1. Wang W, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0613.
2. Ji L, et al. Presented at the International Diabetes Federation conference, 5-8 December 2022. Abstract number: LI2022-0780.

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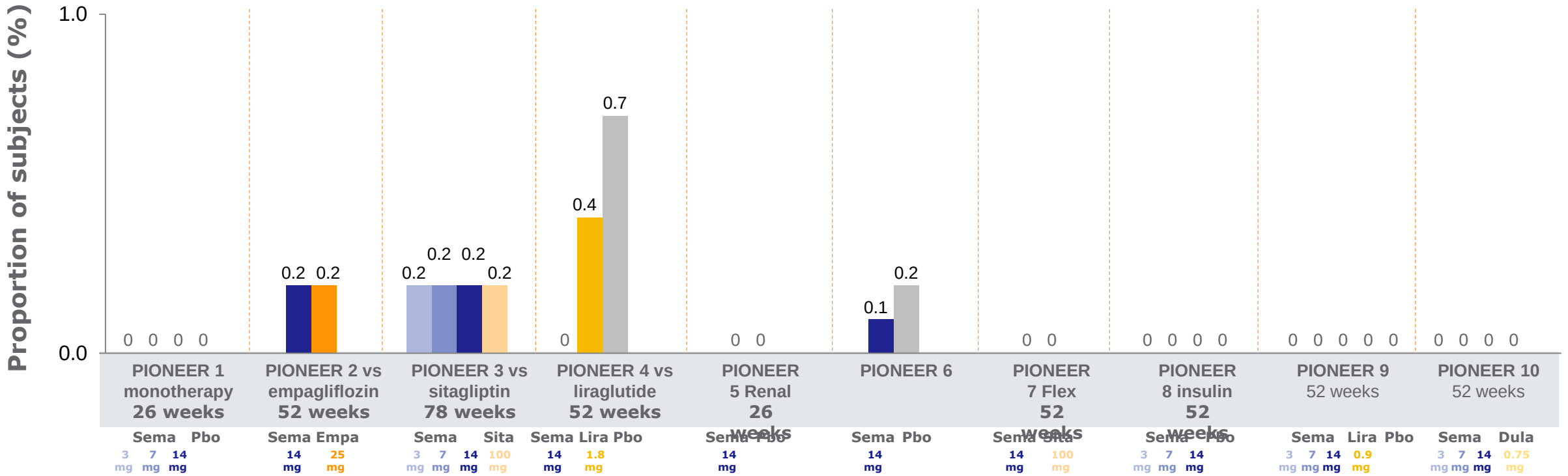
Acute pancreatitis was relative rare and the occurrence was similar between oral semaglutide and placebo/active comparator

PIONEER programme

不良反應
胰臟炎

Proportion of patients with pancreatitis



When combining all phase 3a data, pancreatitis occurred in five semaglutide-treated patients in PIONEER (six in the comparator group)

急性胰臟炎與對照組相當，且發生率很低

BG, blood glucose; Dula, dulaglutide; Empa, empagliflozin; Lira, liraglutide; Pbo, placebo; PIONEER, Peptide Innovation for Early Diabetes Treatment; Sema, semaglutide; Sita, sitagliptin.

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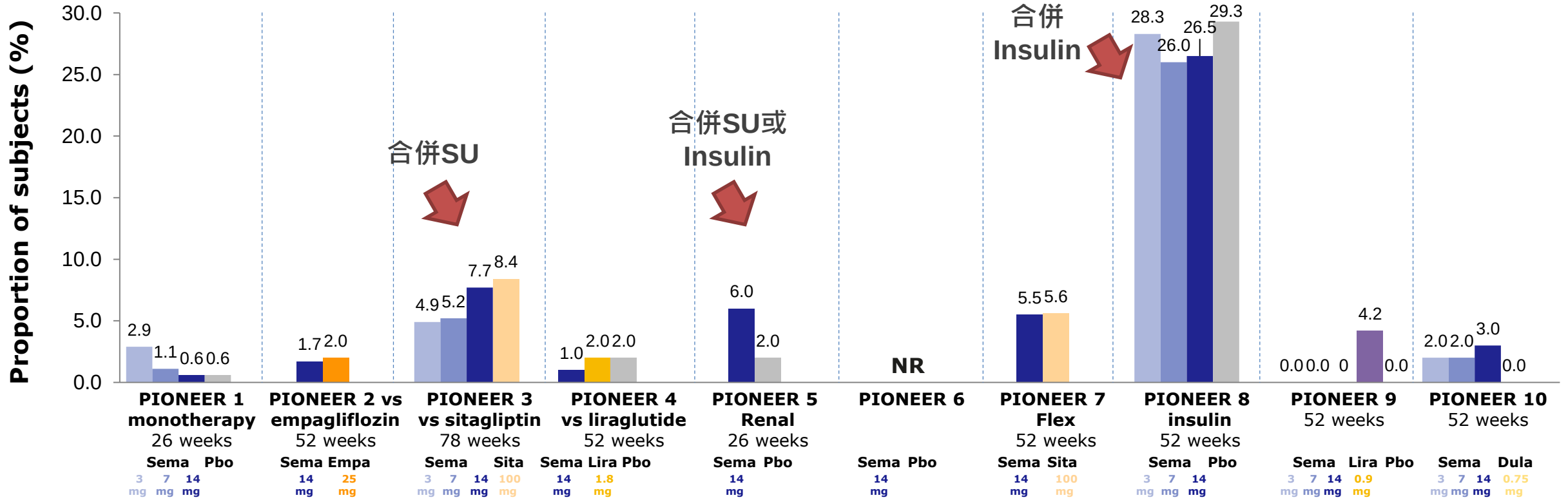
The risk of hypoglycemia was low and increased when combined with SU and/or insulin

PIONEER programme

不良反應
低血糖

Proportion of patients with sever or confirmed symptomatic hypoglycemic episode*



*An episode that was severe according to the ADA classification (requires assistance of another person to actively administer carbohydrate, glucagon, or other corrective action) or an episode with confirmed blood glucose value < 56 mg/dL and symptoms consistent with hypoglycemia.

Dula, dulaglutide; Empa, empagliflozin; Lira, liraglutide; NR, not recorded; Sema, semaglutide; Sita, sitagliptin; SU, sulfonylurea; Pbo, placebo.

Smits MM, et al. Front Endocrinol (Lausanne). 2021 Jul 7;12:645563.

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Metabolic risk factors assessment of Rybelsus® in a real-world Japanese study

REAL Japan

真實世界研究
日本

- A retrospective study using an electronic medical record to obtain information about patients
- T2D patients who have not been treated with injectable glucose-lowering drugs previously
- Initiated treatment with oral semaglutide from March 2021 to June 2022
- Metabolic parameters were compared at baseline with data at 3 and 6 months after starting of Rybelsus®

Baseline characteristics (N=47)

Age (mean)	58.2 years old
Male sex	25 (53.2%)
Treatment for T2D at baseline	
DPP-4 inhibitors	30 (63.8%)
Metformin	35 (74.5%)
SGLT2 inhibitors	39 (83.0%)
Sulfonylurea	8 (17.0%)
α-glucosidase inhibitors	7 (15.0%)
Pioglitazone	17 (36.2%)
Insulin	3 (6.4%)
GLP-1 analogues Subcutaneous semaglutide Dulaglutide	11 (23.4%) 8 (17.0%) 3 (6.4%)

Adapted from table 1.

DPP-4, Dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT2, Sodium-glucose cotransporter 2; T2D, type 2 diabetes.

Yanai H, et al. Cardiol Res. 2022 Oct;13(5):303-308.

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RYBELSUS® semaglutide tablets

Rybelsus® demonstrated significant improvements in HbA_{1C}, body weight, SBP, LDL-C and UACR

Changes in metabolic parameters from baseline in all patients

		N	Baseline	After 3 months	N	Baseline	After 6 months
體重	Body weight (kg)	40	78.9 ± 17.7	77.5 ± 17.9**	25	79.7 ± 19.3	77.3 ± 19.5**
血壓	Systolic blood pressure (mm Hg)	41	133.1 ± 14.1	130.1 ± 15.8	25	134.0 ± 14.7	127.8 ± 14.3**
	Diastolic blood pressure (mm Hg)	41	77.9 ± 10.6	76.7 ± 11.7	25	77.9 ± 10.6	77.0 ± 12.6
	Plasma glucose (mg/dL)	40	179.2 ± 96.1	170.6 ± 57.8	26	183.5 ± 116.2	162.3 ± 63.1
血糖	HbA1c (%)	41	8.1 ± 1.5	7.9 ± 1.5*	26	8.4 ± 1.5	7.8 ± 1.5**
	AST (IU/L)	41	30.3 ± 17.3	29.0 ± 14.3	28	32.1 ± 19.3	31.0 ± 20.0
	ALT (IU/L)	41	43.2 ± 32.5	40.4 ± 27.6	28	45.0 ± 35.0	41.0 ± 35.0
	GGT (IU/L)	36	49.5 ± 43.8	45.5 ± 37.1	24	56.3 ± 51.2	53.0 ± 51.0
	TG (mg/dL)	39	205.5 ± 129.2	199.0 ± 168.9	26	210.9 ± 137.5	190.2 ± 123.9
	HDL-C (mg/dL)	39	52.2 ± 13.5	51.0 ± 11.5	26	50.8 ± 14,1	49.2 ± 13.1
血脂	LDL-C (mg/dL)	37	96.8 ± 28.5	92.5 ± 25.6	26	101.0 ± 31.0	91.3 ± 25.5**
	Non-HDL-C (mg/dL)	36	128.3 ± 36.6	125.0 ± 36.1	24	132.0 ± 39.6	122.2 ± 31.7*
	UA (mg/dL)	39	5.1 ± 1.2	4.9 ± 1.3	27	5.1 ± 1.5	5.1 ± 1.2
	eGFR (mL/min/1.73 m^2)	41	80.5 ± 25.3	82.5 ± 25.3	28	80.6 ± 26.8	78.7 ± 26.8
尿蛋白	UACR	25	107.9 ± 224.9	62.5 ± 117.4*	14	123.1 ± 255.8	93.9 ± 211.8*

*p<0.1. **p<0.05 vs. baseline.

ALT, alanine aminotransferase; AST, aspartate ami- notransferase; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyl transferase; HbA_{1C}, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non-high-density lipoprotein cholesterol; SBP, systolic blood pressure; TG, triglyceride; UA, uric acid; UACR, urinary albumin to creatinine ratio.

Yanai H, et al. Cardiol Res. 2022 Oct;13(5):303-308.

使用 Rybelsus 的好處

ABCBA 改善

The earlier the better

From Early To Eternity

The longer the better

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口服腸泌素起手式

瑞倍適起手式

- ✓ 起始族群：起始原因、挑選病人、主動出擊
- ✓ 如何起始：起始劑量、劑量調整、使用多久
- ✓ 起始前 注意事項
- ✓ 起始後 注意事項

瑞倍適起手式

✓ 起始族群：起始原因、挑選病人、主動出擊

- 病患
- 醫護本身


偏頭痛、憂鬱、
打鼾、假性腦瘤
心血管疾病
高血壓
阻塞性肺疾病
氣喘
脂肪肝
胃食道逆流
多囊性卵巢
下肢靜脈曲張
糖尿病
代謝症候群
高膽固醇血症
血脂異常
癌症 (多種)
尿失禁(壓力性)
退化性關節炎
痛風
肥胖可能導致的疾病

過去的我

99公斤

糖(前)胖症

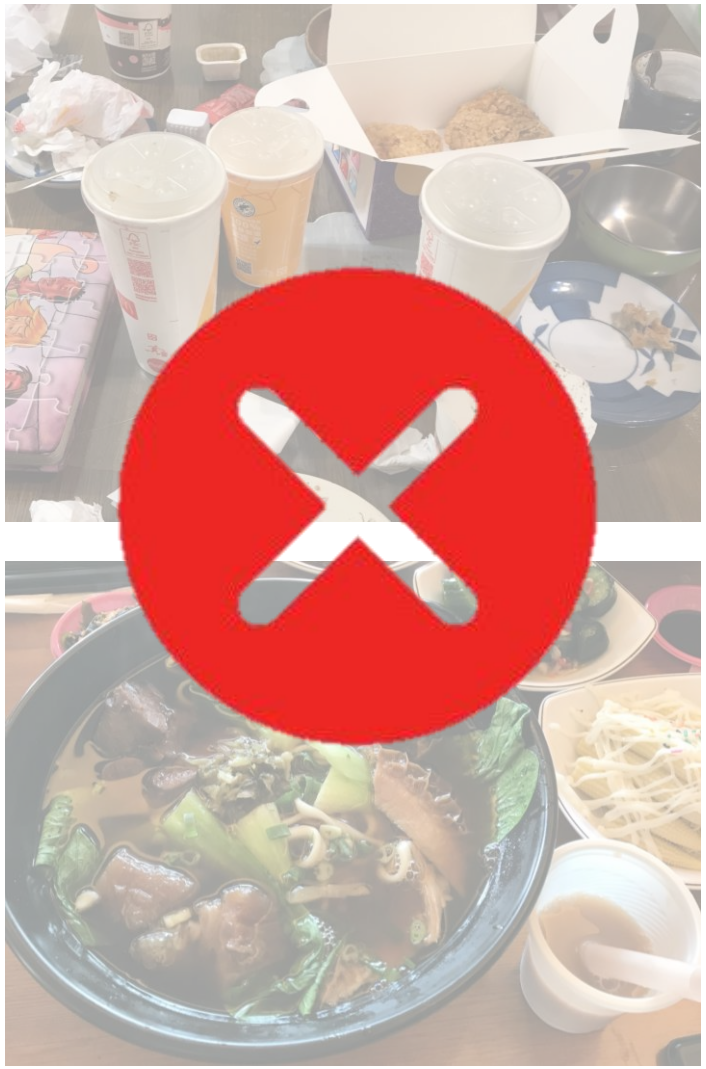
抽血報告

就診日	檢驗簡稱	結果值	結果值判讀
112/02/18	檢HbA1C 糖化血色素	5.8	Ⅱ 過高
112/02/18	檢glucos PC 飯後血糖	115	

阿金: 老川，我來跟你說說怎麼瘦肚子

老川: 我聽你在...，你先顧好你自己吧 .....

為了避免肥胖相關併發症



飲食
習慣
改變

加上 持續運動

阻力運動

+

有氧運動

改變後的我

78公斤

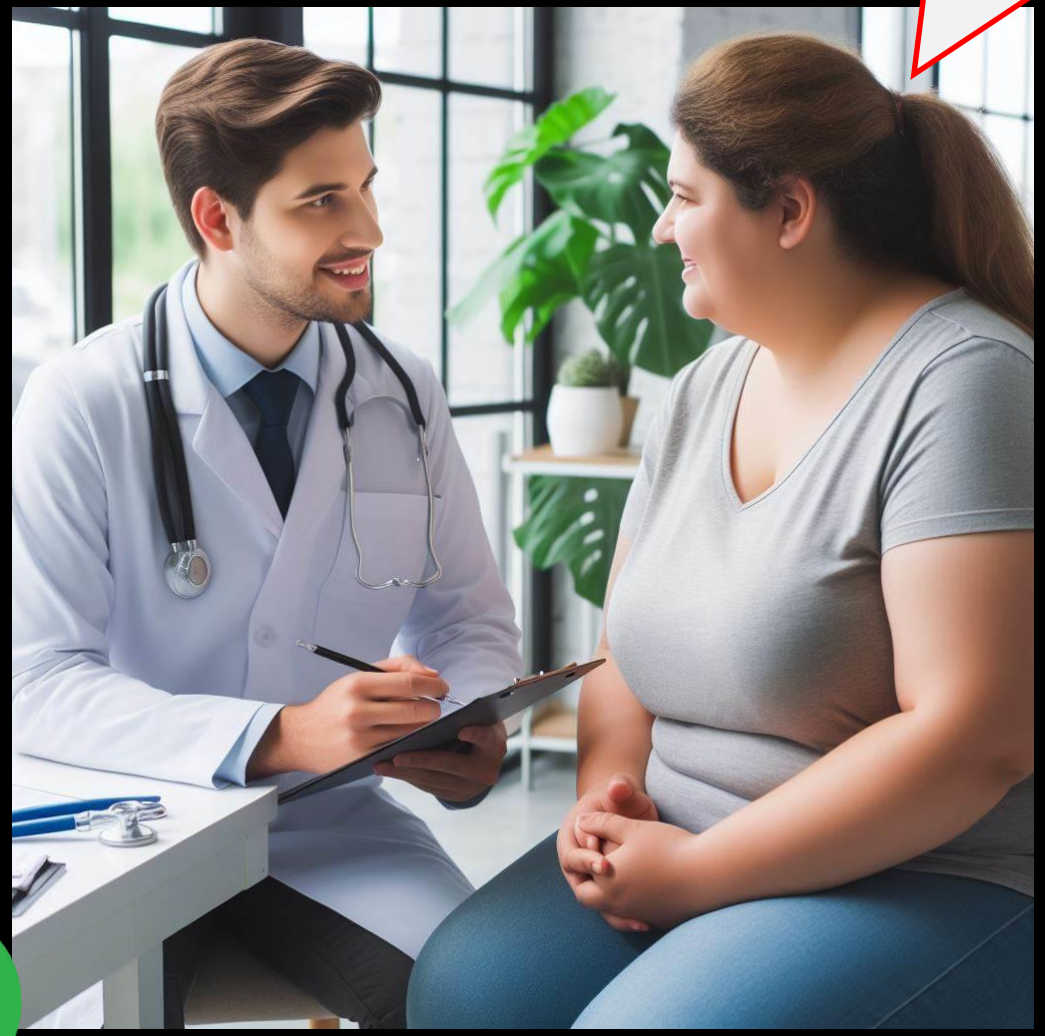
抽血報告

就診日	檢驗簡稱	結果值	結果值判讀
112/05/16	檢glucos PC	106	正常
112/05/16	檢HbA1C	5.6	

非常滿意

當病患看到我們的改變時.....

- 怎麼瘦的？
- 控制不了吃耶?
- 沒時間運動捏
- 怎辦? 可以吃藥嗎？



瑞倍適起手式

✓ 起始族群：起始原因、挑選病人、主動出擊

- 病患
- 醫護本身

使用瑞倍適(Rybelsus) 的好處

ABCBA 改善

血糖

A1C

體重

BW

血脂

LDL-**C**

血壓

BP

尿蛋白

U**A**CR

使用瑞倍適(Rybelsus) 的好處

ABCBA 改善

血糖

A1C

- 糖尿病患者，尤 **糖胖症** 者
- 不論DM罹病年、不論是否合併其他藥物，**降糖效果佳**
- 糖尿病**越早期**使用血糖**達標率越高**
- 血糖控制不佳，**食慾佳**，**無法控制飲食**，三餐**外食族**

使用瑞倍適(Rybelsus) 的好處

ABCBA 改善

體重

BW

- 肥胖患者，尤 **糖胖症** 者
- 不論DM罹病年、是否合併其他藥物，**降體重**效果佳
- 自我要求-**短期減重**需求:如結婚、拍婚紗、同學會等
- Pure obesity - 減少**肥胖併發症**
- 看別人打瘦瘦針，自己**不敢施打**者

Weight loss leads to clinically significant improvements in multiple obesity-related diseases

- Hypertension[1]
- Hyperglycemia[1]
- Dyslipidemia[1]
- GERD (females)[1]

- Prevention of T2D[1]
- PCOS[1]
- NAFLD[1]
- NASH[1]
- GERD (males)[1]
- OSA[1]
- Knee OA[1]
- Urinary stress incontinence[2]
- Heart failure[4]

- CV outcome*[3]
- T2D remission[5,6]

- Advanced T2D remission[6]

1-5% | **5-10%** | **10-15%** | **>20%**

Magnitude of weight loss (%)

Guideline recommendations[7,8]

American Diabetes Association. | ESC European Society of Cardiology

3-7%

- Glycemia/ CV risk factors[7]

>5%

- ▼ Lipid level[8]
- Glycemia control[8]
- Hypertension[8]

>10%

- T2D remission[7]
- CV outcomes and mortality[7]

*CV outcomes include non-fatal acute myocardial infarction or stroke, hospitalized angina, CV death, coronary-artery bypass grafting, carotid endartectomy, percutaneous coronary intervention, hospitalization for congestive heart failure, peripheral vascular disease, or total mortality.

CV, cardiovascular; GERD, gastroesophageal reflux disease; MASH, metabolic dysfunction-associated steatohepatitis; NAFLD; non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; OA, osteoarthritis; OSA, obstructive sleep apnea; PCOS, polycystic ovary syndrome; T2D, type 2 diabetes.

1. Horn D, et al. Postgrad Med. 2022 May;134(4):359-375. **2.** Garvey WT, et al. Endocr Pract 2016;22(Suppl. 3):1–203. **3.** Look AHEAD Research Group. Lancet Diabetes Endocrinol 2016;4:913–21. **4.** Sundström J, et al. Circulation 2017;135:1577–85. **5.** Lean ME, et al. Lancet 2018;391:541–51. **6.** Meerasa A, et al. Diabetes Care 2022;45:28–30. **7.** American Diabetes Association Professional Practice Committee. Diabetes Care. 2024 Jan 1;47(Suppl 1):S145-S157. **8.** Marx N, et al. Eur Heart J. 2023 Oct 14;44(39):4043-4140.

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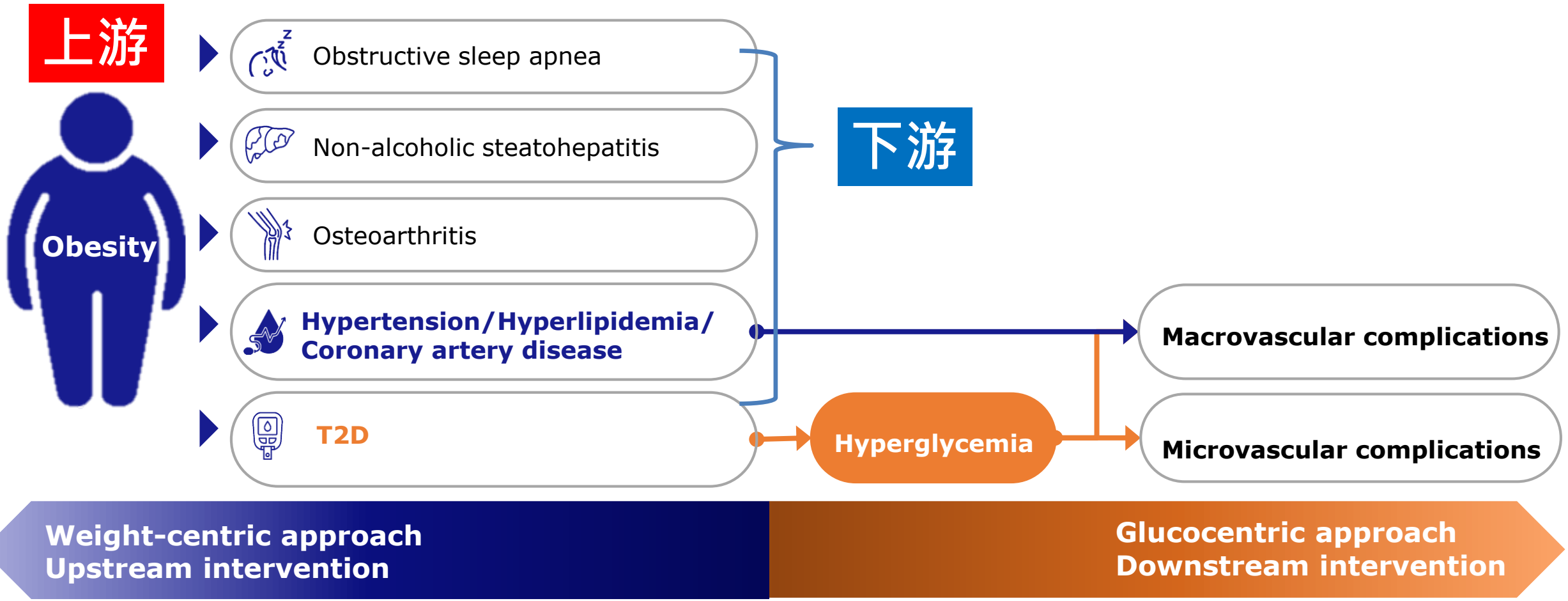
The wide range of benefits of upstream weight-centric approach *vs.* downstream glucocentric management approach



T2D, type 2 diabetes.

Lingvay I, et al. Lancet. 2022 Jan 22;399(10322):394-405.

Effects of Semaglutide on Body Composition in Obese and Diabetic Patients Attended in Internal Medicine Wards

Clinical, analytics and anthropometric variables at baseline and change during follow up

- **體脂肪減最多 (約6成5)**
- **肌肉稍減少 (不到1成)**

	F			
	Uric acid (mg/dl)	5.6 (1.9)	-0.3 (0.00002-0.9)	0.044
	UACR (mg/g)	11.4 (49.8)	-65 (0.93-32.9)	0.008
	Weight (kg)	114.1 (33.3)	-9.5 (7.2-11.9)	0.00
	BMI (%)	42.8 (9.8)	-3.5 (2.7-4.3)	0.000
脂肪	**Fat mass (kg)**	53.6 (18.5)	-6 (4.1-8.5)	0.00
瘦體組織	**Lean mass (kg)**	59.4 (19)	-2.6 (1.3-4.1)	0.0004
肌肉	**Muscle mass (kg)**	30.1 (11.7)	-0.8 (0.0004-1.6)	0.04

Lean Mass (LM)
= BW – Fat Mass

Observational, prospective study. Body composition was studied by bioimpedance (BIO) .
Changes were evaluated over a median of 26 wk.

Diabetes. 2022;71(Supplement_1). doi:10.2337/db22-1493-PUB

Oral semaglutide improves body composition and preserves lean mass in patients with type 2 diabetes: a 26-week prospective real-life study

Estimated means of [illegible] over the study period.

- **體脂肪顯著減少**
- **肌肉無明顯變化**

	Param			T6
	Body we			71.6 ± 1.9**
	Body mass index (kg/m2)	28.2 ± 0.6	27.1 ± 0.5**	26.8 ± 0.6**
脂肪	**Fat Mass (Kg)**	29.5 ± 1.2	24.9 ± 1.2**	24.3 ± 1.2**
	Fat Mass %	39.3 ± 1.3	34.7 ± 1.5**	34.2 ± 1.5**
去脂肪重	**Fat-Free Mass (Kg)**	45.4 ± 1.4	47.1 ± 1.7**	46.9 ± 1.6**
	Fat-Free Mass %	60.5 ± 1.3	65.2 ± 1.6**	65.7 ± 1.5**
骨骼肌	**Skeletal Muscle Mass (SMM; Kg)**	20.0 ± 0.8	20.6 ± 1.0	20.3 ± 0.9
內臟脂肪	**Visceral Adipose Tissue (VAT; L)**	3 ± 0.2	2.7 ± 0.2	2.8 ± 0.2
總水分	**Total Body Water (TBW; L)**	34.1 ± 1.0	35.2 ± 1.2*	35.0 ± 1.1*

Parameters are expressed as mean ± S.E. Estimated changes were analyzed at different times.
Change versus T0: *p<0.05; : ** p<0.01

https://doi.org/10.3389/fendo.2023.1240263 Front. Endocrinol., 13 September 2023

Transforming body composition with semaglutide in adults with obesity and type 2 diabetes mellitus

Variation in body composition parameters from baseline to end of follow-up (6 months) using bioelectrical impedance analysis.

	SUBCUTANEOUS SEMAGLUTIDE (n=55)				ORAL SEMAGLUTIDE (n = 33)			
	BASELINE mean (SD)	6 MONTHS mean (SD)	DIFFERENCE [CI 95%]	P-value	BASELINE mean (SD)	6 MONTHS mean (SD)	DIFFERENCE [CI 95%]	P-value
Weight (kg)*	109.2 (24.6)	98.5 (21.6)	-10 [-11.9; -8.2]	<0.001	94.8 (15.6)	86.2 (16.3)	-8.6 [-10.3; -6.8]	<0.001
BMI (kg/m2)*	40.1 (11)	36.1 (9.3)	-3.7 [-4.4; -3]	<0.001	34.2 (3.9)	31 (4.2)	-3.1 [-3.7; -2.5]	<0.001
Body Fat Mass (kg)*	50.5 (17.6)	41.3 (15)	-8.5 [-10.2; -6.9]	<0.001	39.9 (8)	31.9 (8.7)	-8 [-9.7; -6.2]	<0.001
Fat mass (%)	45.7 (9.3)	41.4 (9.1)	-4 [-4.9; -3.1]	<0.001	42.2 (5.6)	36.8 (6.1)	-5.2 [-6.7; -3.6]	<0.001
Fat Free Mass (kg)*	59.3 (13.5)	57.1 (12.7)	-1.7 [-2.5; -0.9]	<0.001	54.9 (10.9)	54.3 (10.8)	-0.6 [-1.5; 0.3]	0.162
Fat free mass (%)	54.9 (9.2)	58.6 (9.1)	3.6 [2.8; 4.6]	<0.001	57.8 (5.6)	63.2 (6.1)	5.2 [3.6; 6.7]	<0.001
Visceral Fat Area (cm2)*	227.1 (62.2)	196.5 (54.4)	-30.2 [-37.5; -23.2]	<0.001	203.6 (37.1)	161.3 (47.3)	-42.3 [-52.9; -31.8]	<0.001
Skeletal Muscle Mass (kg)	33.1 (8.5)	31.7 (7.7)	-1.1 [-1.5; -0.6]	<0.001	30.3 (6.5)	29.9 (6.4)	-0.5 [-1; 0.1]	0.081
Total body water (L)	44 (10.6)	42.2 (9.5)	-1.3 [-1.9; -0.8]	<0.001	40.5 (8)	40 (8)	-0.5 [-1.2; 0.1]	0.117
Basal Metabolic Rate (Kcal)	1651.3(292.1)	1604.3(274.5)	-36.3 [-53; -19.5]	<0.001	1555.7 (234.8)	1542.2(232.9)	-13.5 [-33; 5.9]	0.166

脂肪

去脂肪重

內臟脂肪

骨骼肌

總水分

基礎代謝

- **體脂肪 & 內臟脂肪顯著減少**

*Parameters in which we fou ss Index.

https://doi.org/10.3389/fendo.2024.1386542 Front. Endocrinol., 04 June 2024

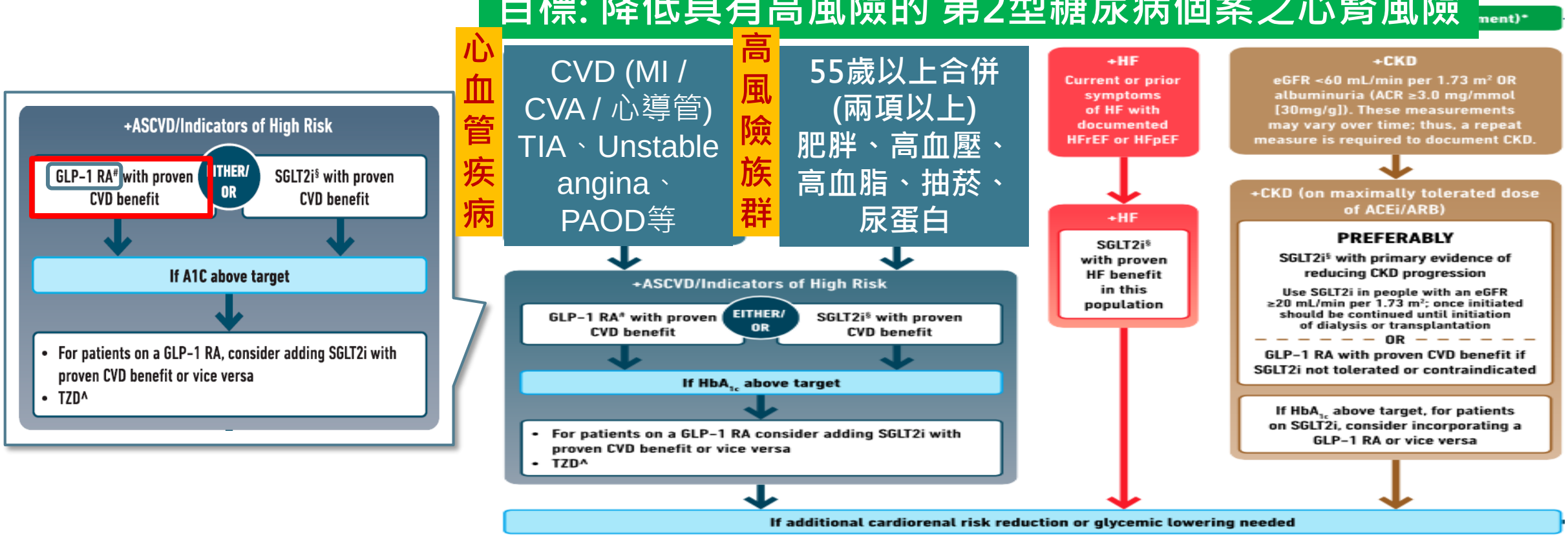
使用瑞倍適(Rybelsus) 的好處

ABCBA 改善

GLP-1 RAs are recommended as appropriate initial therapy for T2D with or at high risk for ASCVD or CKD

2024 ADA/2022 ESAD guidelines

目標: 降低具有高風險的 第2型糖尿病個案之心腎風險



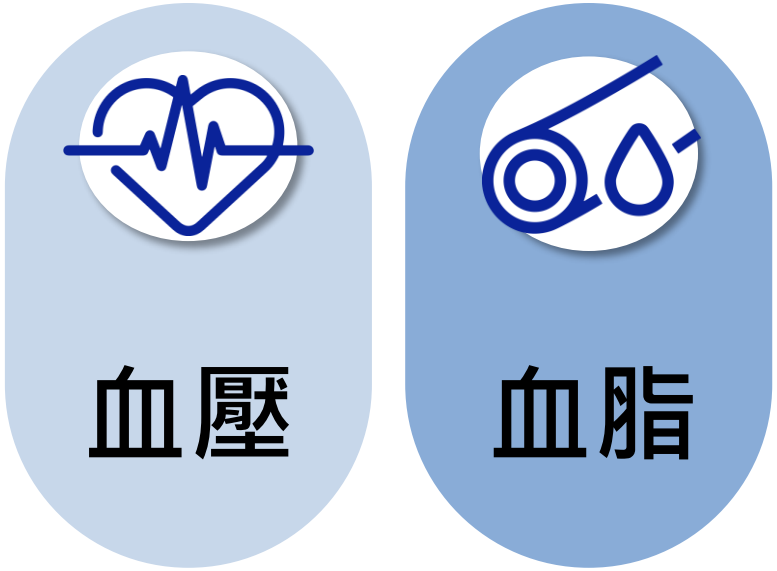
*In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin. †A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. ^Low-dose TZD may be better tolerated and similarly effective. §For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD. #For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

Adapted from American Diabetes Association Professional Practice Committee. Diabetes Care. 2024 Jan 1;47(Suppl 1):S158-S178 figure 9.3 and Davies MJ, et al. Diabetes Care. 2022 Nov 1;45(11):2753-2786 figure 3.

1. American Diabetes Association Professional Practice Committee. Diabetes Care. 2024 Jan 1;47(Suppl 1):S158-S178. **2.** Davies MJ, et al. Diabetes Care. 2022 Nov 1;45(11):2753-2786.

使用瑞倍適(Rybelsus) 的好處

ABCBA 改善

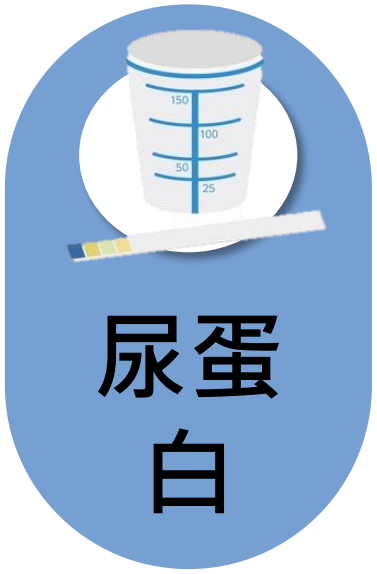


- 糖尿病併**心血管共病**或**高風險**族群者
- **不論CV**風險**高低，一致下降MACE**效果
- **越早期**(年紀越輕)，降低CVD風險**越多**
- **用得越久**CV**保護越好**(MACE下降越多)

(Time-dependent)

使用瑞倍適(Rybelsus) 的好處

ABCBA 改善



- DM合併**CKD**患者，若使用SGLT2i**耐受不良**，或有**禁忌症**，建議用上也具**腎臟保護的Semaglutide**
- DKD患者，使用SGLT2i後，**白蛋白尿還是高**，建議**合併使用 Semaglutide**

The cornerstone treatments of diabetic kidney disease

Adv Chronic Kidney Dis. 2021;28(4):347-360

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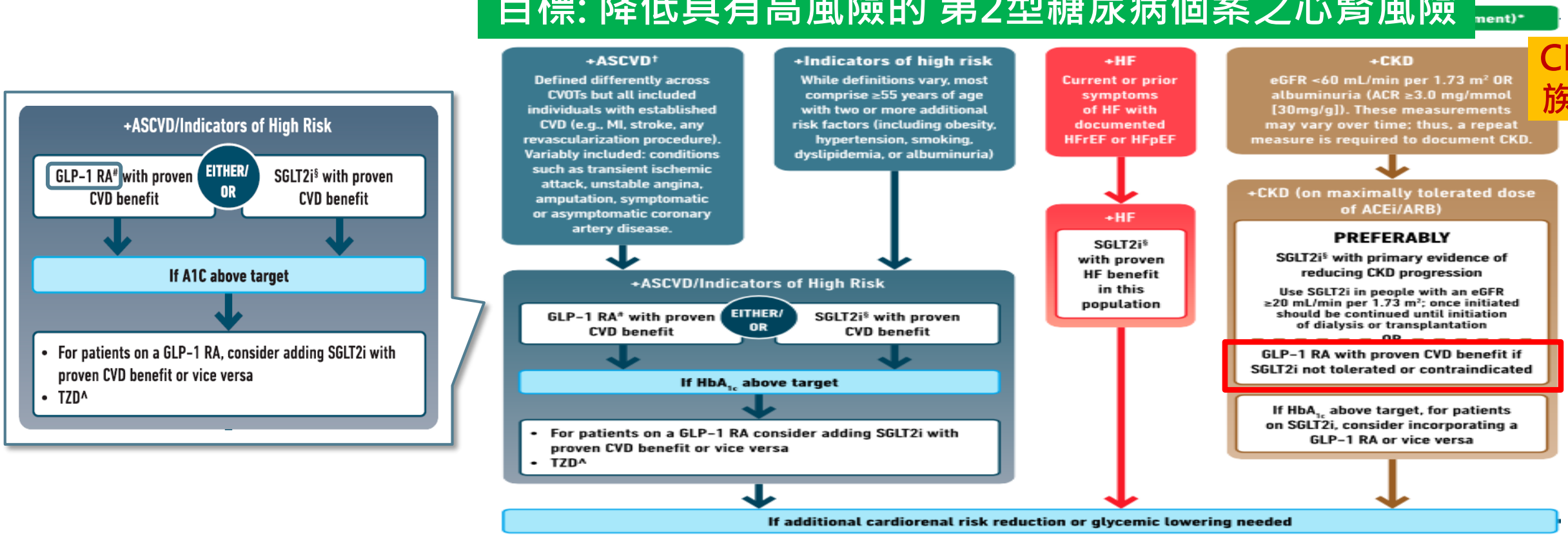
GLP-1 RAs are recommended as appropriate initial therapy for T2D with or at high risk for ASCVD or CKD

2024 ADA/2022 ESAD guidelines

目標: 降低具有高風險的 第2型糖尿病個案之心腎風險

CKD 族群



*In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin. †A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. ^Low-dose TZD may be better tolerated and similarly effective. §For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD. #For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

Adapted from American Diabetes Association Professional Practice Committee. Diabetes Care. 2024 Jan 1;47(Suppl 1):S158-S178 figure 9.3 and Davies MJ, et al. Diabetes Care. 2022 Nov 1;45(11):2753-2786 figure 3.

1. American Diabetes Association Professional Practice Committee. Diabetes Care. 2024 Jan 1;47(Suppl 1):S158-S178. **2.** Davies MJ, et al. Diabetes Care. 2022 Nov 1;45(11):2753-2786.

瑞倍適起手式

✓ 起始族群：起始原因、挑選病人、**主動出擊**

- 病患
- 醫護本身

- Words that Change Lives -

Say more, Save more

多說幾句話 多救一個人

瑞倍適起手式

✓ 如何起始：起始劑量、劑量調整、使用多久

標準

起始劑量

3 mg

持續一個月

7 mg

持續一個月

14 mg

The longer the better

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瑞倍適起手式

✓ 起始前 注意事項

(正確服藥)

瑞倍適起手式

✓ 起始前 注意事項 (正確服藥)

應空腹服用，
可在一天中任何時間服藥

應搭配少量的水
(約半杯，相當於120毫升)

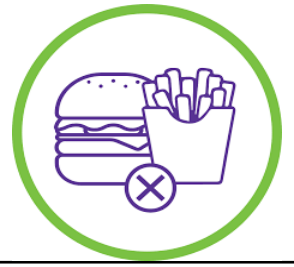
應等待至少30分鐘後，
再進行飲食或服用其他口服藥物

不可剝半、不可咀嚼、不可磨粉、使用時再打開(不要事先打開放置於藥盒)

瑞倍適起手式

✓ 起始前 注意事項 (事先提醒、事先預防)

Adverse effect	
低血糖	併用SU、Insulin 要小心
GI 副作用	Nausea (15-20%) Diarrhea (10%) Vomiting (7%)

避免方式		
	少吃油膩、甜食、刺激性食物	
	細　嚼　慢　嚥	
	飽　了　就　停	

瑞倍適起手式

✓ 起始後 注意事項

- 副作用是否可以忍受，是否開立症狀控制藥物
- 檢視相關指數改善程度- 體重、腰圍 、血糖 、慢性病用藥、抽血指數
- 減重以每週下降 **0.5-1.0 kg** 的速度，持續到建議的目標體重
- 假如效果不彰，至少要保持體重不再增加

Rybelsus
常見問題 & 經驗分享

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semaglutide tablets

瑞倍適 Q1 副作用與效果關係？

副作用主要為腸胃道相關,且多半為輕度至中度

- **腸胃道副作用**跟**A1C降幅**無直接相關
- **腸胃道副作用**跟**BW降幅**無直接相關
- **BW降幅**與**A1C降幅**無直接相關

副作用與效果無線性關係

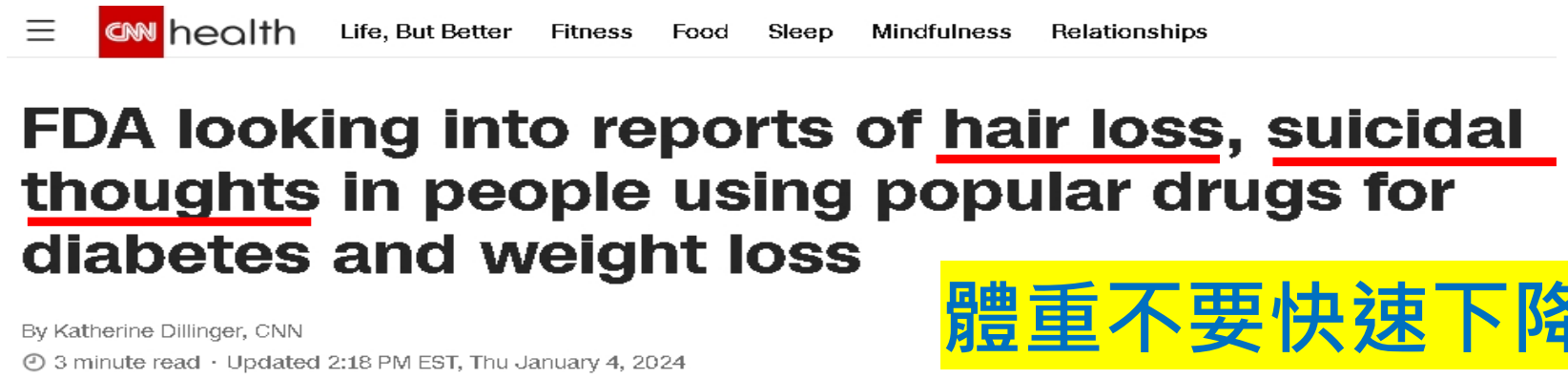
瑞倍適 Q2 效果不彰，該怎辦？

假如效果不彰，至少要保持體重不再增加

- ✓便祕 (衛教、藥物)
- ✓時間 (至少3-6個月)
- ✓運動 (150mins/wk)
- ✓水量 (BW*30 /day)
- ✓飲食 (少油、少甜等)
- ✓規則回診

瑞倍適 Q3 除GI副作用，其他副作用怎辦？

- 落髮
- 憂鬱
- 頭痛
- 疲倦



CNN health Life, But Better Fitness Food Sleep Mindfulness Relationships

FDA looking into reports of hair loss, suicidal thoughts in people using popular drugs for diabetes and weight loss

By Katherine Dillinger, CNN

3 minute read · Updated 2:18 PM EST, Thu January 4, 2024

體重不要快速下降

與腦部receptor 或 脫水相關，可使用普拿疼治療

降低卡洛里攝取，即會感到疲倦。隨時間而緩解

1. https://edition.cnn.com/2024/01/03/health/glp1-agonist-side-effects-fda/index.html 2. https://www.goodrx.com/ozempic/semaglutide-side-effects

瑞倍適 Q4 仿單取得適應症，健保有給付？

衛部菌疫輸字 第 001171 號
版本日期 2024-07-05

Rybelsus 取得糖尿病用藥第一線之適應症

- 原適應症：搭配飲食及運動療法，用於治療血糖控制不良的第二型糖尿病成人病人，以改善血糖控制
  - 若病人因耐受不良或有禁忌症而不適合使用 metformin，可做為單一療法
  - 與其他糖尿病藥物合併使用。

- **新適應症：單一療法或與其他糖尿病治療藥物併用，治療控制不佳的第二型糖尿病成人病人，作為飲食及運動之外的輔助治療。**

- Approval date: 2-Jan-2024

有適應症 ≠ 健保給付

糖尿病患者可使用Rybelsus作為起始治療

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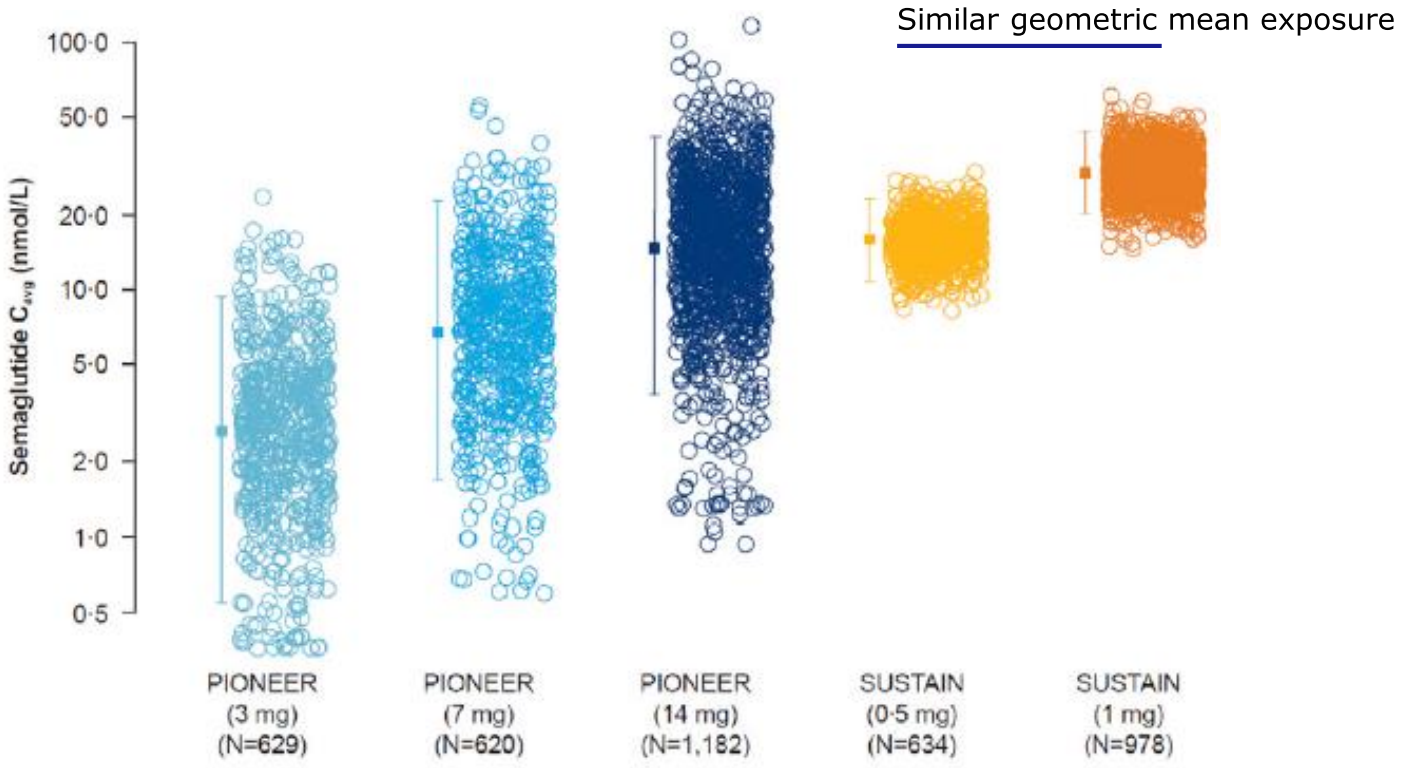
瑞倍適 Q5 針劑要怎麼改口服？

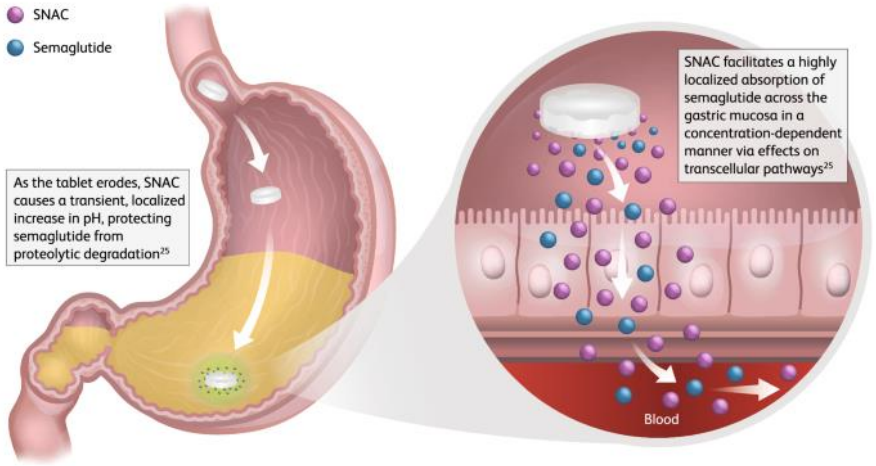
Semaglutide exposure via different routes of administration[2]



Overgaard RV, et al. Cell Rep Med. 2021 Sep 3;2(9):100387.

Semaglutide 轉換 (針劑 轉 口服)

劑量轉換



Approximately **1%** of semaglutide is absorbed, the rest is degraded in the GI tract

以每周劑量轉換

	原劑量		
針劑	0.25 mg/wk	0.5 mg/wk	1 mg/wk
口服	3 mg	7 mg	14 mg

轉換劑量

轉換日 ➡ 針劑打完一周後，直接轉換口服劑型

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瑞倍適 Q6 如何推薦病患使用？

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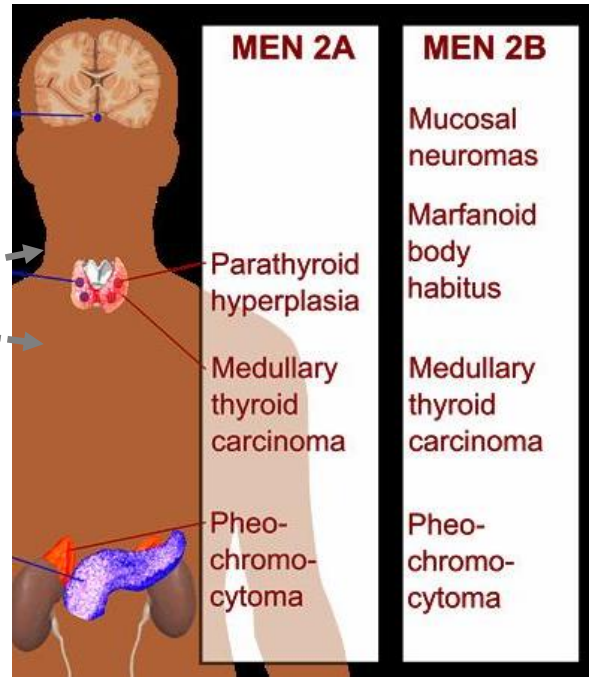
semaglutide tablets

瑞倍適 Q7 哪些病患禁忌使用？

衛部菌疫輸字 第 001171 號
版本日期 2024-07-05

成分過敏	對於 semaglutide 或 RYBELSUS®的其他成分**過敏**。
髓質甲狀腺癌 (MTC) 病史	本身或家族有髓質甲狀腺癌 **(MTC) 病史**，或罹患第二型多發性內分泌腫瘤症候群 **(MEN 2)**。
懷孕	動物試驗證實具生殖毒性，懷孕女性使用 semaglutide 的資料有限，因此懷孕期間不可使用 semaglutide。計畫懷孕前至少**兩個月**應停用
哺乳	哺乳大鼠會將 semaglutide、salcaprozate sodium 及/或其代謝物透過乳汁排出。由於無法排除哺乳嬰幼兒的風險，哺乳期間**不應**使用瑞倍適®。



https://step1.medbullets.com/endocrine/109035/multiple-endocrine-neoplasias

瑞倍適 Q8 需要常規甲超檢查嗎？

衛部菌疫輸字 第 001171 號
版本日期 2024-07-05

特殊警語：甲狀腺C細胞腫瘤的風險

在小鼠和大鼠中，具臨床意義的semaglutide暴露量會提高甲狀腺C細胞腫瘤(腺瘤及惡性腫瘤)發生率，且腫瘤發生率與劑量和治療持續時間相關。由於尚未確立semaglutide誘發嚙齒類的甲狀腺C細胞腫瘤，與人類的相關性，因此目前並不清楚瑞倍適®是否會在人體內造成甲狀腺C細胞腫瘤，包括甲狀腺髓質癌(MTC)。

瑞倍適®禁止用於本身或家族有甲狀腺髓質癌病史，或罹患第二型多發性內分泌腫瘤症候群(Multiple Endocrine Neoplasia syndrome type 2, MEN 2)的病人。應提醒病人，瑞倍適®治療有可能引發甲狀腺髓質癌，並提醒病人注意甲狀腺腫瘤的症狀(例如頸部腫塊、吞嚥困難、呼吸困難、聲音持續沙啞)。接受瑞倍適®治療的病人，定期監測血清降鈣素或甲狀腺超音波檢查，是否有助於早期發現MTC，目前尚無定論。

不建議 & 沒證據需要常規檢查超音波

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瑞倍適 Q9 開刀前要停多久?

GLP-1受體促效劑類藥品安全資訊風險溝通表

製表日期：113/8

藥品成分	GLP-1 受體促效劑(glucagon-like peptide-1 receptor agonists)，包含dulaglutide、liraglutide、lixisenatide、semaglutide、tirzepatide 等。
藥品名稱及許可證字號	衛生福利部核准 GLP-1 受體促效劑類藥品許可證共 28 張。 查詢網址：https://lmspiq.fda.gov.tw/web/DRPIQ/DRPIQLicSearch
適應症	第二型糖尿病、體重控制，詳見附件。
藥理作用機轉	Glucagon-like peptide-1(GLP-1)為一種腸泌素(incretin)，具有促進胰島素分泌、抑制升糖素分泌、延遲胃排空、促使下視丘產生飽足感而抑制食慾等作用。GLP-1受體促效劑具有類似於GLP-1之作用，而可用於血糖控制。
訊息緣由	2024/7/12 歐洲醫藥管理局(EMA)之藥品安全監視風險評估委員會(PRAC)針對使用 GLP-1 受體促效劑可能於手術接受全身麻醉或深度鎮靜時增加誤嚥(aspiration)和吸入性肺炎(aspiration pneumonia)風險，建議採取新的風險管控措施。 網址：https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-8-11-july-2024

食品藥物管理署風險溝通說明	◎ **醫療人員應注意事項：** 1. GLP-1 受體促效劑類藥品具有延遲性胃排空作用，使用該類藥品之病人若需接受全身麻醉或深度鎮靜的手術，應考量延遲性胃排空導致胃部內容物殘留，既而可能增加誤嚥和吸入性肺炎的風險。 2. 處方 GLP-1 受體促效劑類藥品時，應告知病人相關風險。 ◎ **病人應注意事項：** 1. GLP-1 受體促效劑類藥品會延遲胃排空，而可能增加手術時全身麻醉或深度鎮靜相關的誤嚥和吸入性肺炎風險。若您正在使用 GLP-1 受體促效劑類藥品，並計畫進行需接受全身麻醉或深度鎮靜的手術，應告知醫療人員。 2. 如果您對於使用 GLP-1 受體促效劑類藥品治療有任何疑問或疑慮，請諮詢醫療人員。

使用GLP-1受體促效劑可能於手術接受全身麻醉或深度鎮靜時增加誤嚥(aspiration)和吸入性肺炎(aspiration pneumonia)風險，建議採取新的風險管控措施。

瑞倍適 Q9 開刀前要停多久?

American Society of Anesthesiologists

ASA Consensus-Based Guidance on Preoperative Management of Patients (Adults and Children) on GLP-1RA

□ Day(s) Prior to the Procedure:

• For patients on daily dosing consider holding GLP-1 agonists on the day of the procedure/surgery. For patients on weekly dosing consider **holding** GLP-1 agonists **a week** prior to the procedure/surgery.

至少停用一周

• This suggestion is irrespective of the indication (type 2 diabetes mellitus or weight loss), dose, or the type of procedure/surgery.

無論何種手術或處置

https://www.asahq.org/about-asa/newsroom/news-releases/2023/06/american-society-of-anesthesiologists-consensus-based-guidance-on-preoperative

瑞倍適 Q10 最小使用年紀？

瑞倍適®錠 Rybelsus® Tablets

衛部菌疫輸字 第 001171 號
版本日期 2024-07-05

小兒族群：

瑞倍適®用於 18 歲以下兒童和青少年的安全性及療效尚未確立，目前沒有相關資料。

胰妥讚 注射劑 Ozempic solution for injection

衛部菌疫輸字 第 001107 號
版本日期 2023-09-06

兒童族群：

針對 18 歲以下的兒童和青少年，尚未確立 semaglutide 的安全性及療效，目前沒有相關資料。

瑞倍適 Q10 最小使用年紀？

ORIGINAL ARTICLE

Once-Weekly Semaglutide in Adolescents with Obesity

12-18歲

Daniel Weghuber, M.D., Timothy Barrett, Ph.D., Margarita Barrientos-Pérez, M.D., Inge Gies, Ph.D., Dan Hesse, Ph.D., Ole K. Jeppesen, M.Sc., Aaron S. Kelly, Ph.D., Lucy D. Mastrandrea, M.D., Rasmus Sørrig, Ph.D., and Silva Arslanian, M.D., for the STEP TEENS Investigators*

ABSTRACT

BACKGROUND

A once-weekly, 2.4-mg dose of subcutaneous semaglutide, a glucagon-like peptide-1 receptor agonist, is used to treat obesity in adults, but assessment of the drug in adolescents has been lacking.

CONCLUSIONS

Among adolescents with obesity, once-weekly treatment with a 2.4-mg dose of semaglutide plus lifestyle intervention resulted in a greater reduction in BMI than lifestyle intervention alone. (Funded by Novo Nordisk; STEP TEENS ClinicalTrials.gov number, NCT04102189.)

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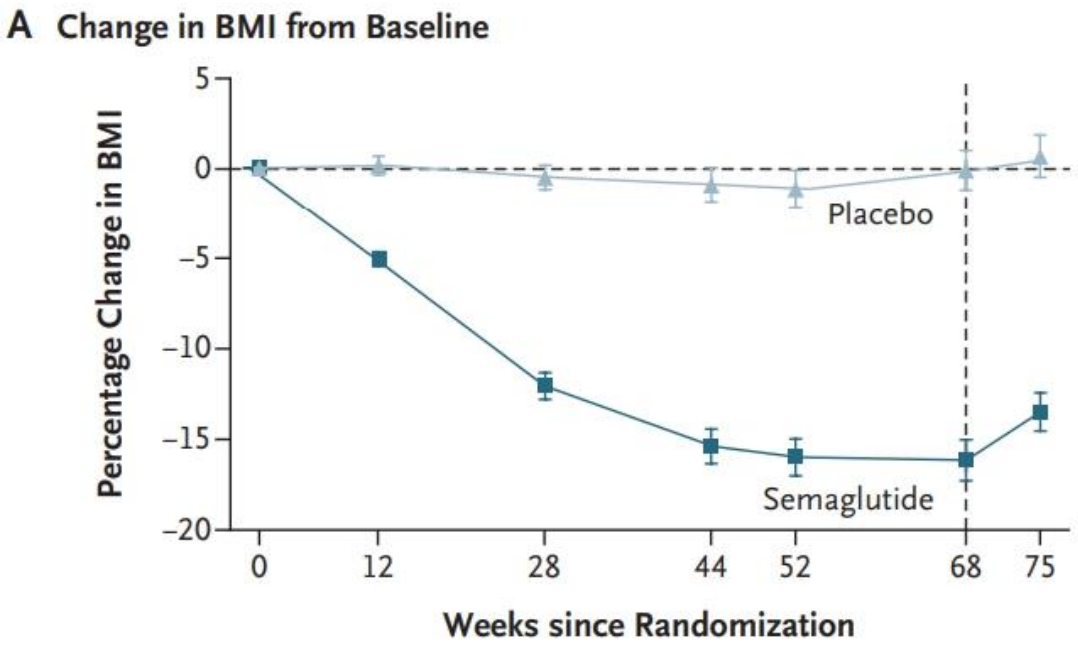

No. of Participants							
Placebo	67	56	63	61	62	62	61
Semaglutide	134	119	131	130	131	131	128

Wegovy- FDA 通過 for Obesity

RYBELSUS® semaglutide tablets

N Engl J Med 387;24 nejm.org december 15, 2022

Conclusions

- GLP-1 RAs are recommended as an appropriate initial therapy for T2D by multiple current international guidelines[1-4], early and consistent use would reduce risk for MACE[5]
  多個學會建議T2DM患者，GLP1RA適合起始治療
- Rybelsus® is the only oral form of GLP-1 RA approved for treatment of T2D[6] and was as effective as subcutaneous semaglutide in glycemic control[7]
  瑞貝適全球唯一口服GLP-1RA，控糖效果針劑相當
- PIONEER studies proved that Rybelsus® was effective in reducing HbA_{1C} in T2D patients with different duration of disease and in combination with all kinds of other antidiabetic medications.[8] Asian patients in some PIONEER trials even achieved greater HbA_{1C} reduction than other racial groups[9]
  不論DM病齡、是否合併其他降糖藥，降糖效果維持。亞洲族群更佳
- Rybelsus® showed its significant effects on improving multiple cardiometabolic risk factors,[10] leading to significantly reduction in MACE risk in a broad T2D population[11]
  不僅控糖，在心血管、腎臟風險的parameter，也有顯著改善
- The better glycemic control, weight control and reduction of CV risks of Rybelsus® were not only demonstrated in PIONEER studies but also in various real-world data,[12-14] proven its benefits in early initiation in treating T2D patients[15]
  眾多好處在真實世界證實。及早使用益處多

CV, cardiovascular; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1C}, glycated hemoglobin; MACE, major adverse cardiovascular events; T2D, type 2 diabetes.

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