



La terapia del diabete Meglio *stepwise approach*

Edoardo Mannucci

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Endocrinologia, Università di Firenze*

Conflitti di interesse

Negli ultimi due anni, E. Mannucci ha ricevuto compensi per relazioni e/o consulenze da

Boehringer Ingelheim, Dexcom, Eli Lilly, Novo Nordisk, Sanofi

La struttura di appartenenza di E. Mannucci ha ricevuto :

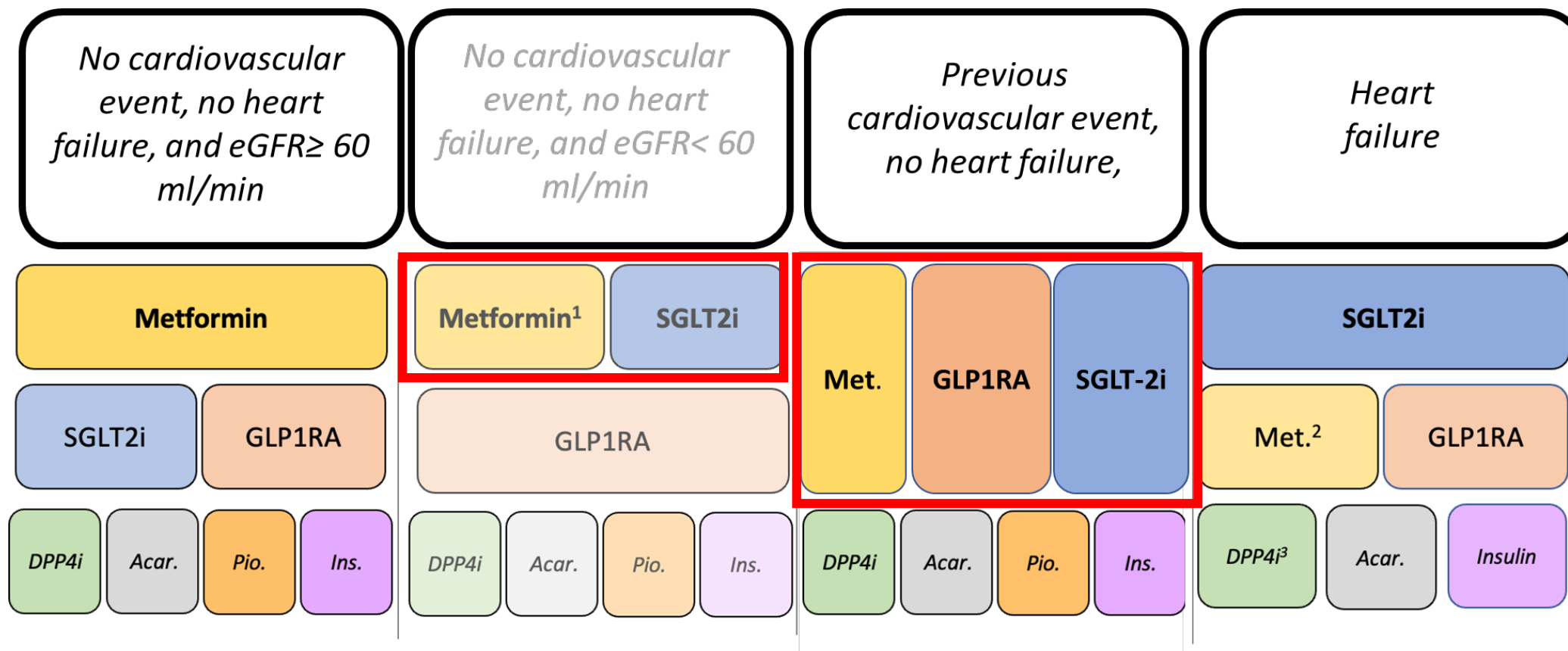
- Finanziamenti per ricerca indipendente non condizionata da ***Abbott***
- Compensi per studi clinici sponsorizzati da ***Amgen, AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo, Eli Lilly, Genentech, Molteni, Novo Nordisk***



Se tutti i pazienti con diabete di tipo 2 dovessero assumere un GLP1RA, la spesa per GLP1RA sarebbe di oltre 3 miliardi l'anno (oltre il doppio della spesa farmaceutica complessiva attuale per il diabete, circa il 12% della spesa farmaceutica totale)

Italian guidelines for the treatment of T2DM, 2023

Drug therapy



^{1,2} If metformin is not contraindicated.

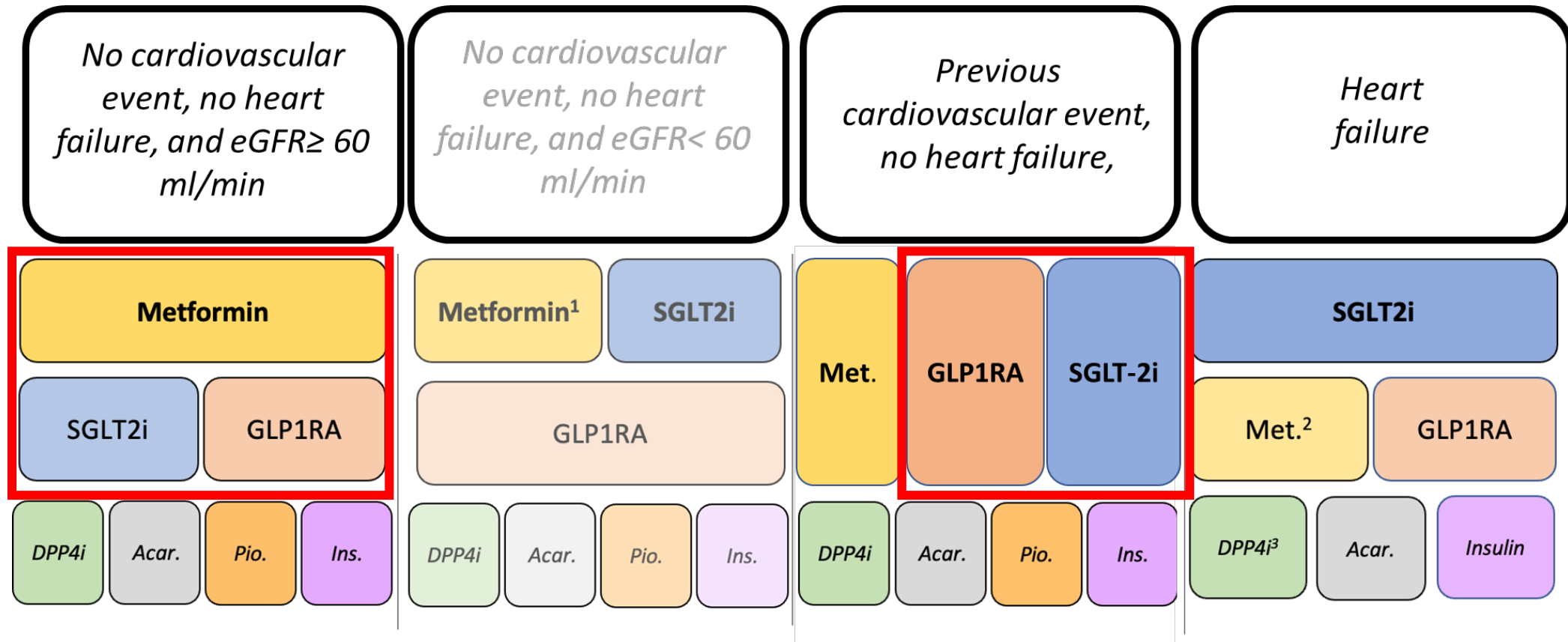
³ With the exception of saxagliptin which is not indicated for patients with heart failure.

The recommendation for patients with $eGFR < 60$ ml/min is weak (few studies on this population) and therefore is written with a lighter type

We recommend to deprescribe sulfonylureas and glinides.

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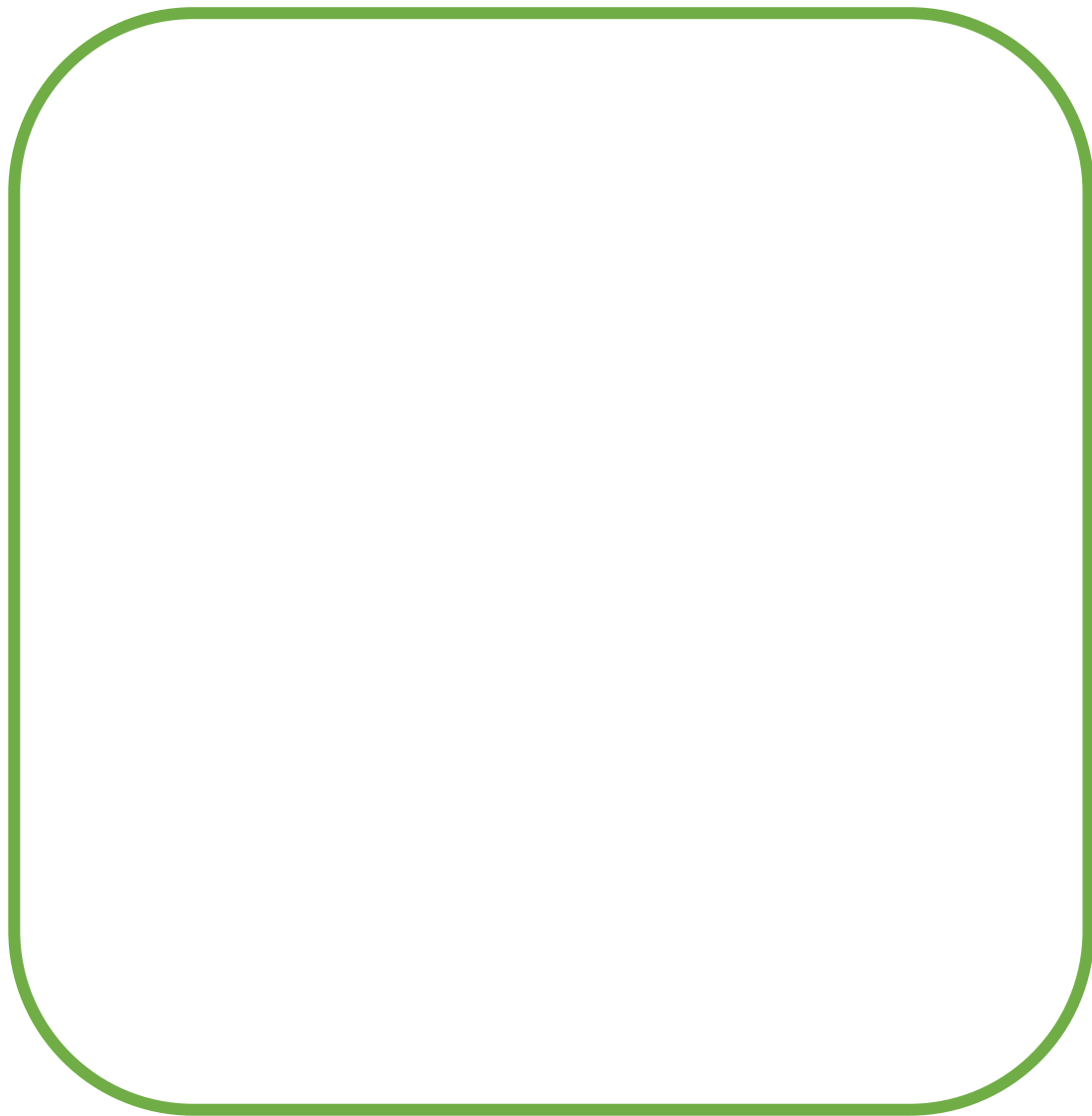
HbA1c targets

1.1. A target HbA1c between 49 mmol/mol (6.6%) and 58 mmol/mol (7.5%) is recommended for patients with type 2 diabetes treated with drugs capable of inducing hypoglycemia.

1.2.1. A target HbA1c below 53 mmol/mol (7%) is recommended for patients with type 2 diabetes treated with drugs which are not capable of inducing hypoglycemia.

Subgroup considerations. There are no available data from randomized trials on the safety and efficacy of intensification of glucose control in patients aged >75 years; in addition, benefits of long-term glucose control are evident only after 2 years of treatment. This could motivate higher HbA1c targets in patients aged >75 years or with reduced life expectancy because of comorbidities.

1.2.2. A target HbA1c of 48 mmol/mol (6.5%) or lower is suggested for patients with type 2 diabetes treated with drugs which are not capable of inducing hypoglycemia.



Articles

Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial



David R Matthews, Páivi M Paldanius, Pieter Proot, YannTong Chiang, Michael Stumvoll, Stefano Del Prato, for the VERIFY study group

VERIFY RCT

Treatment: metformin+vildagliptin

Comparator: metformin (vildagliptin stepwise)

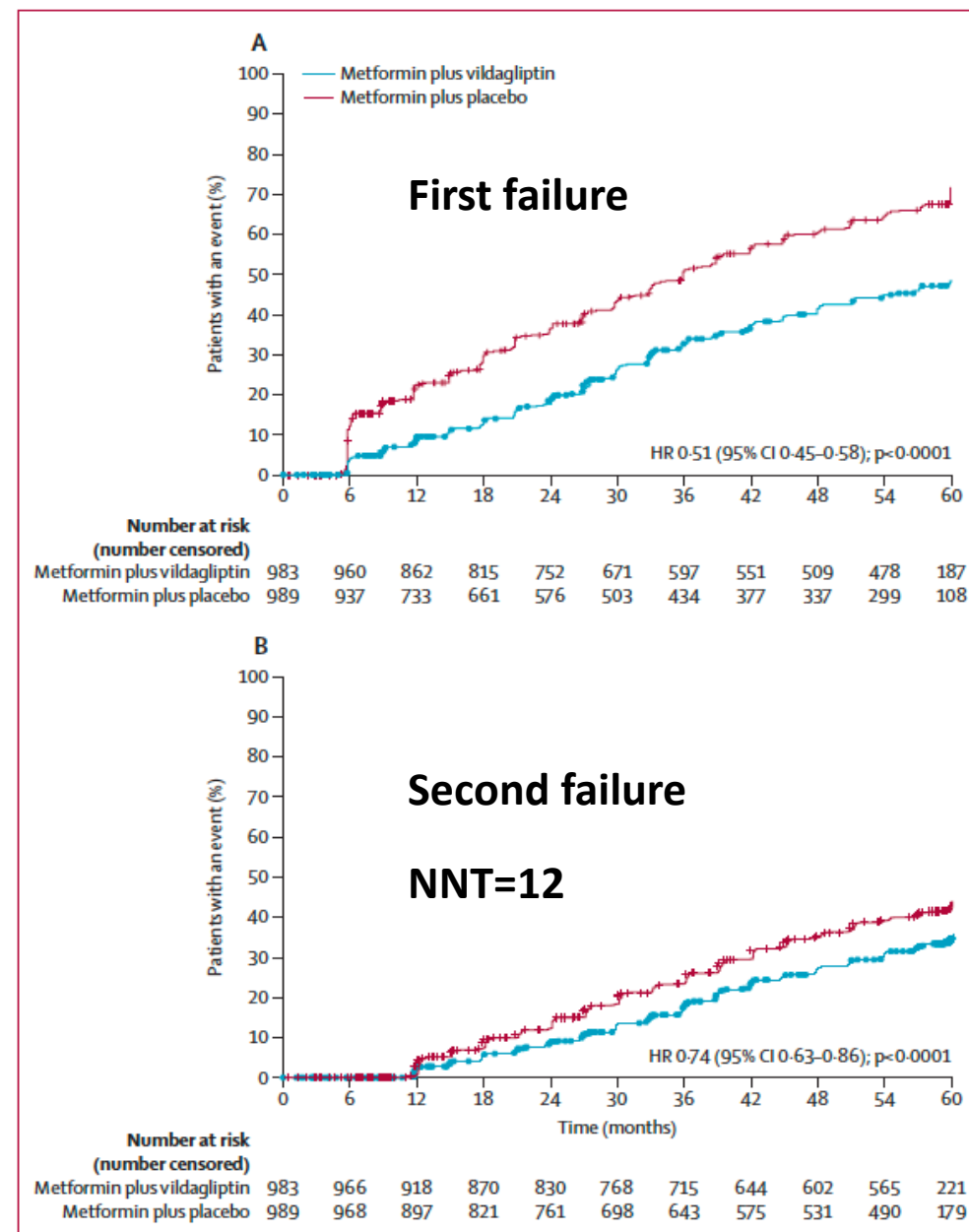
Patients: 2001 T2DM with A1c 48-58 mmol/mol

Principal endpoint: Time to first failure

Secondary endpoint: time to second failure
(initiation of insulin)

Follow-up: 5 years

Matthews DR et al. *Lancet*, 394:1519-29, 2019



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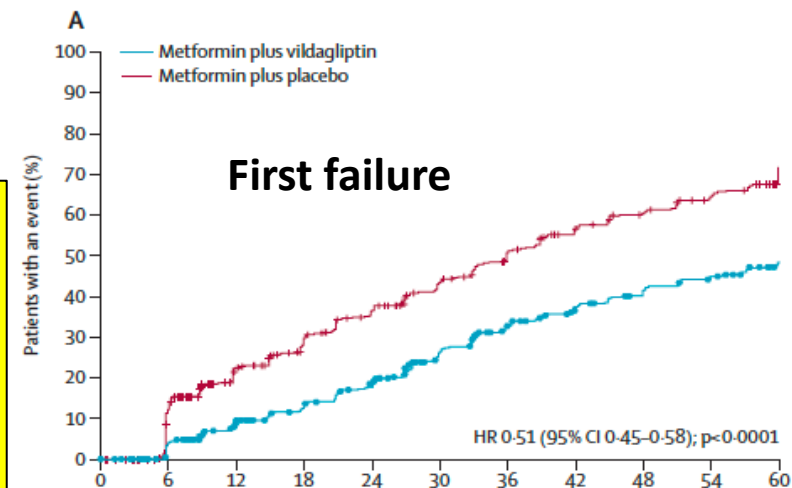
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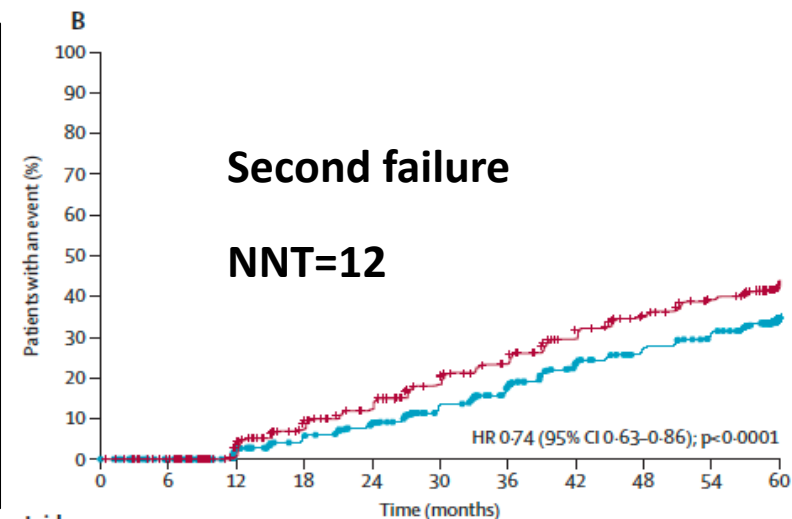
Follow-up: 5 years

5 out of 6 patients do not need the 2nd drug after 6 months

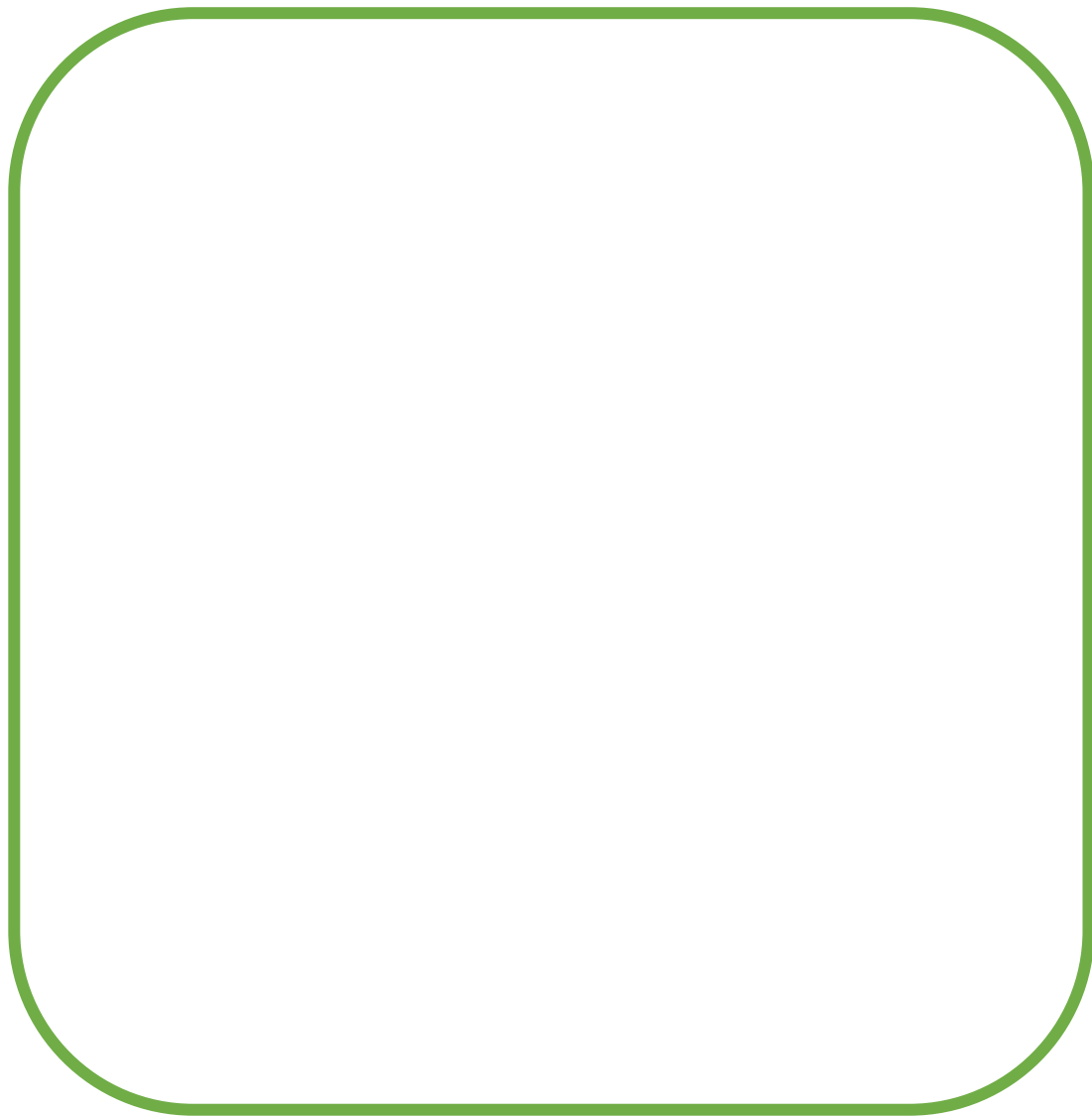
Treating all patients with two drugs from the start avoids a third drug in 5 years in one out of 12 patients



	0	6	12	18	24	30	36	42	48	54	60
Metformin plus vildagliptin	983	960	862	815	752	671	597	551	509	478	187
Metformin plus placebo	989	937	733	661	576	503	434	377	337	299	108



	0	6	12	18	24	30	36	42	48	54	60
Metformin plus vildagliptin	983	966	918	870	830	768	715	644	602	565	221
Metformin plus placebo	989	968	897	821	761	698	643	575	531	490	179



Received: 21 May 2023 | Revised: 11 July 2023 | Accepted: 11 July 2023

DOI: 10.1111/dom.15226

REVIEW ARTICLE

WILEY

Cardiovascular prevention with glucose-lowering drugs in type 2 diabetes: An evidence-based approach to the categories of primary and secondary prevention

Edoardo Mannucci MD | Giovanni Antonio Silverii MD

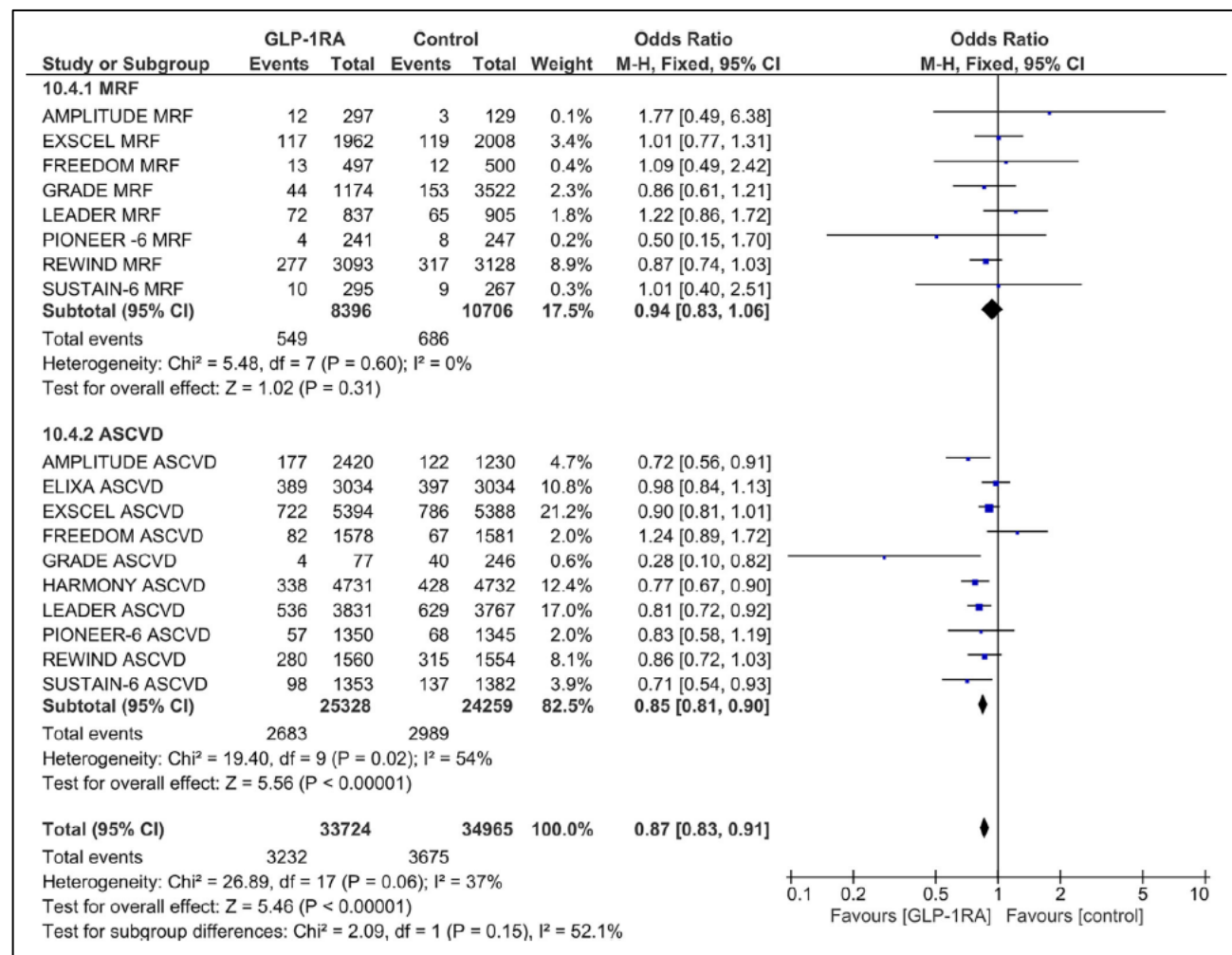
Meta-analysis of RCTs>52 wk

Treatment: GLP1RA

Comparator: placebo

Principal outcome: MACE (adjudicated)

Patients: adults with T2DM



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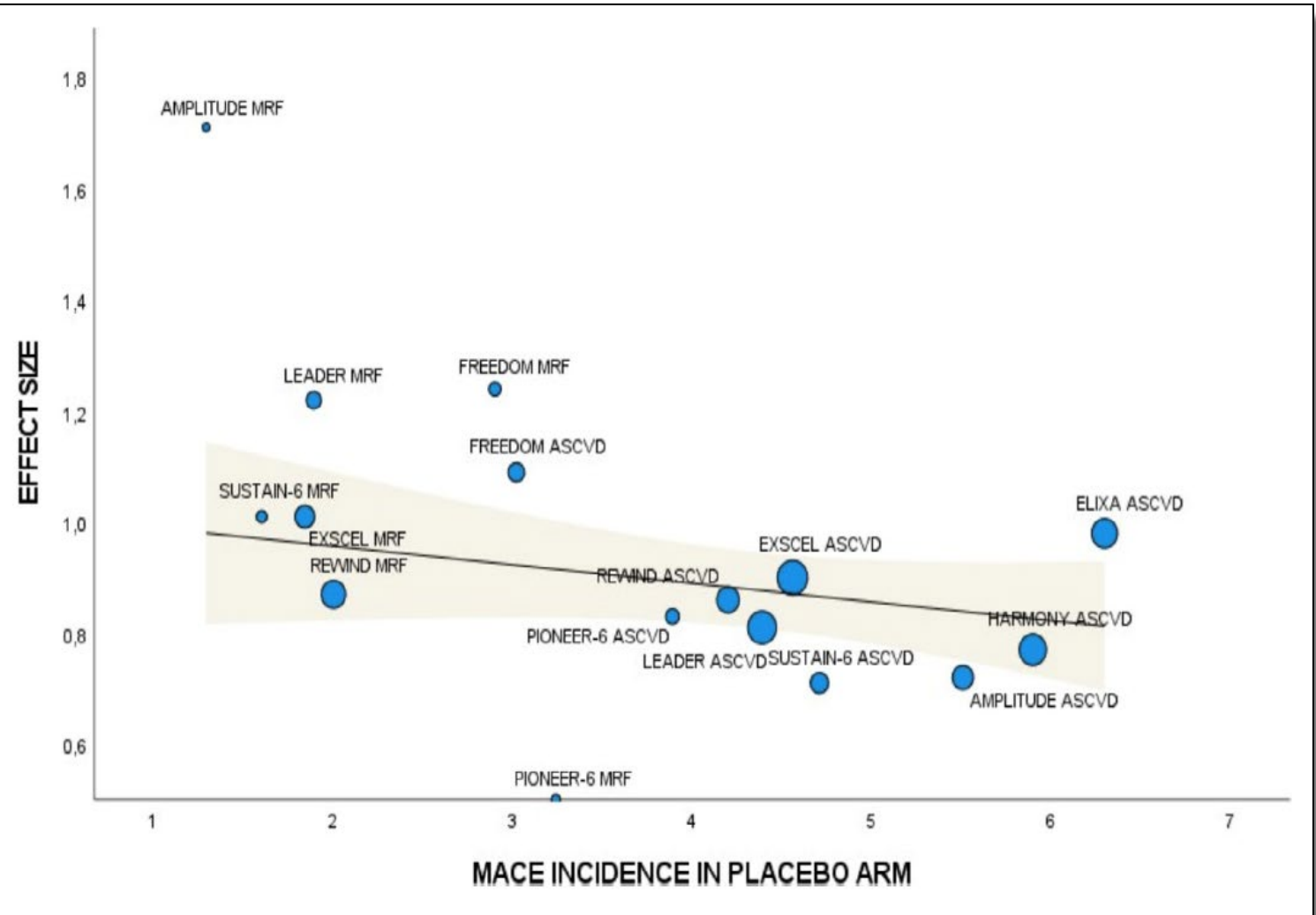
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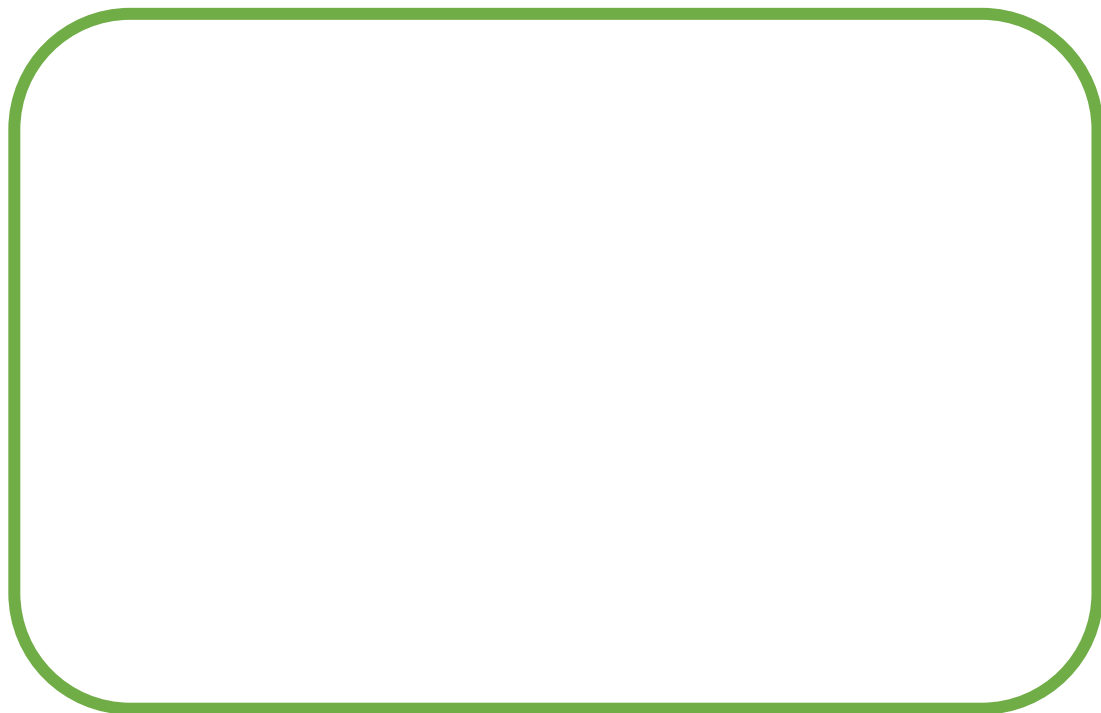
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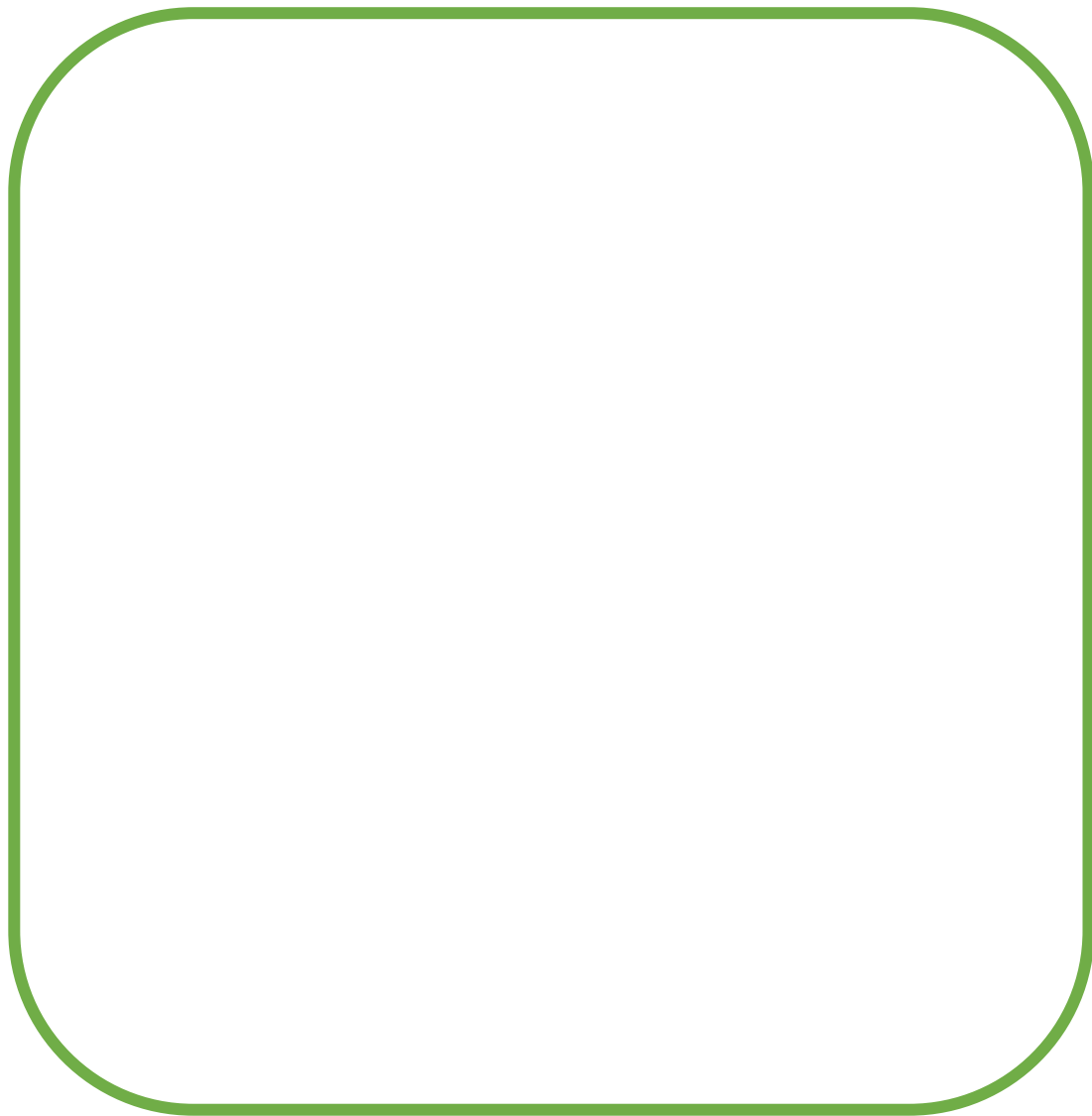
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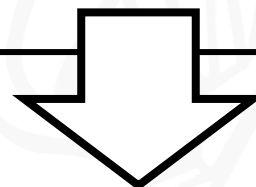
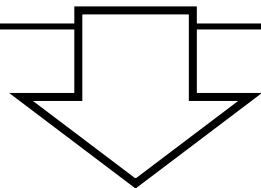
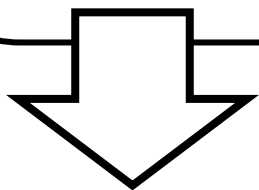
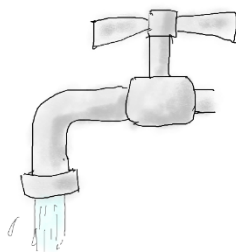
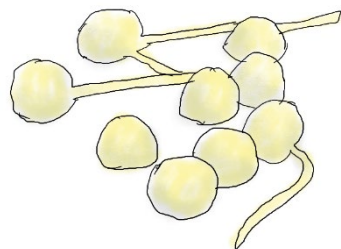
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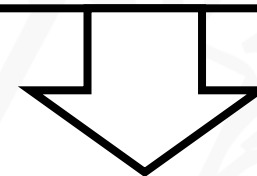
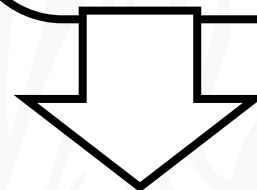
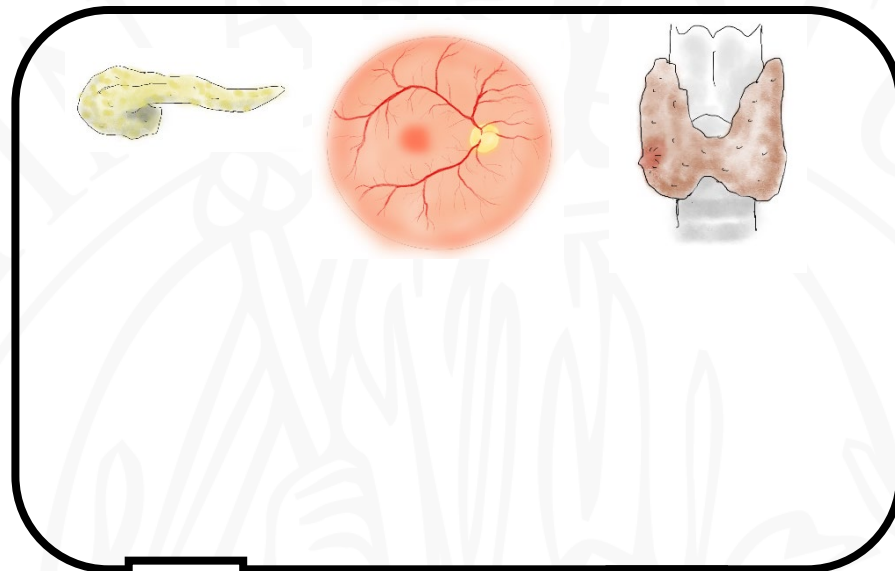
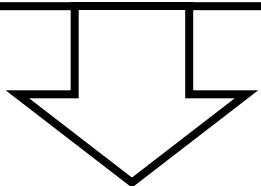
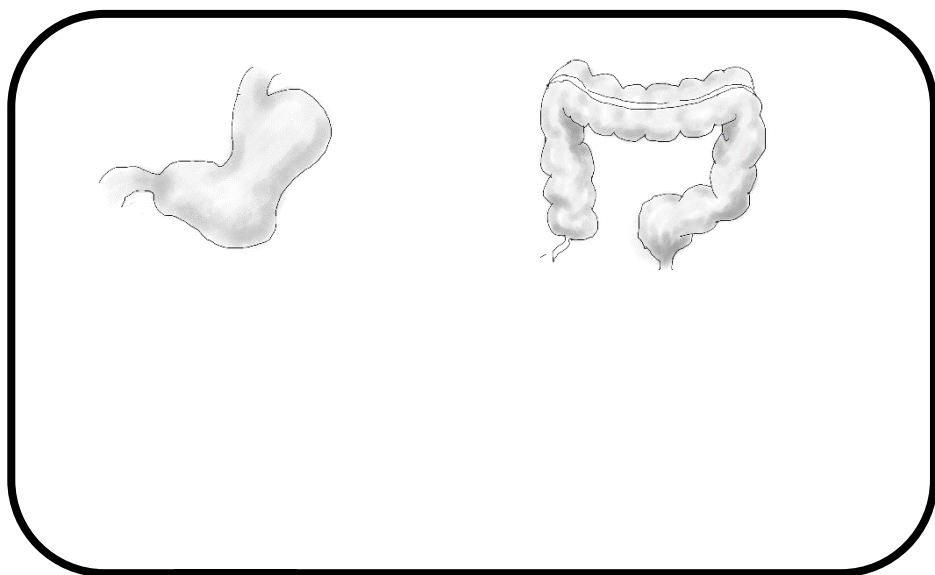
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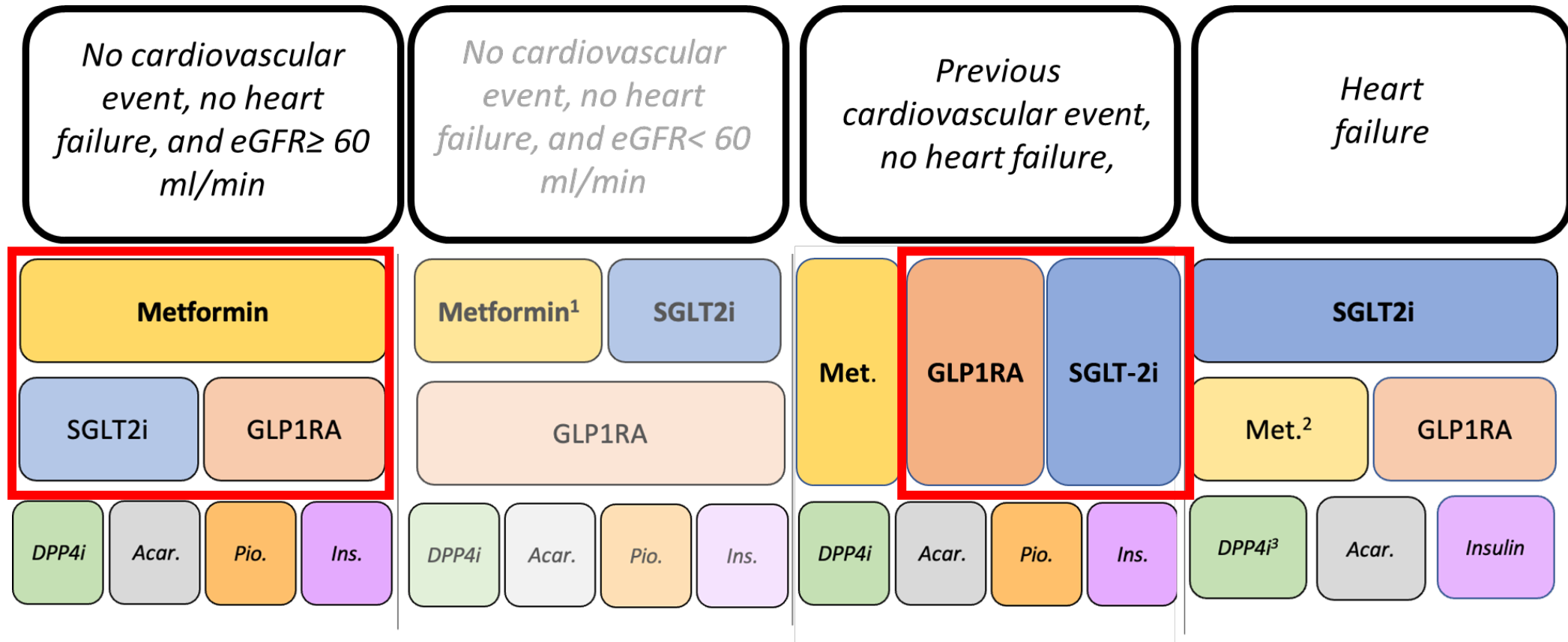






Italian guidelines for the treatment of T2DM, 2023

Drug therapy

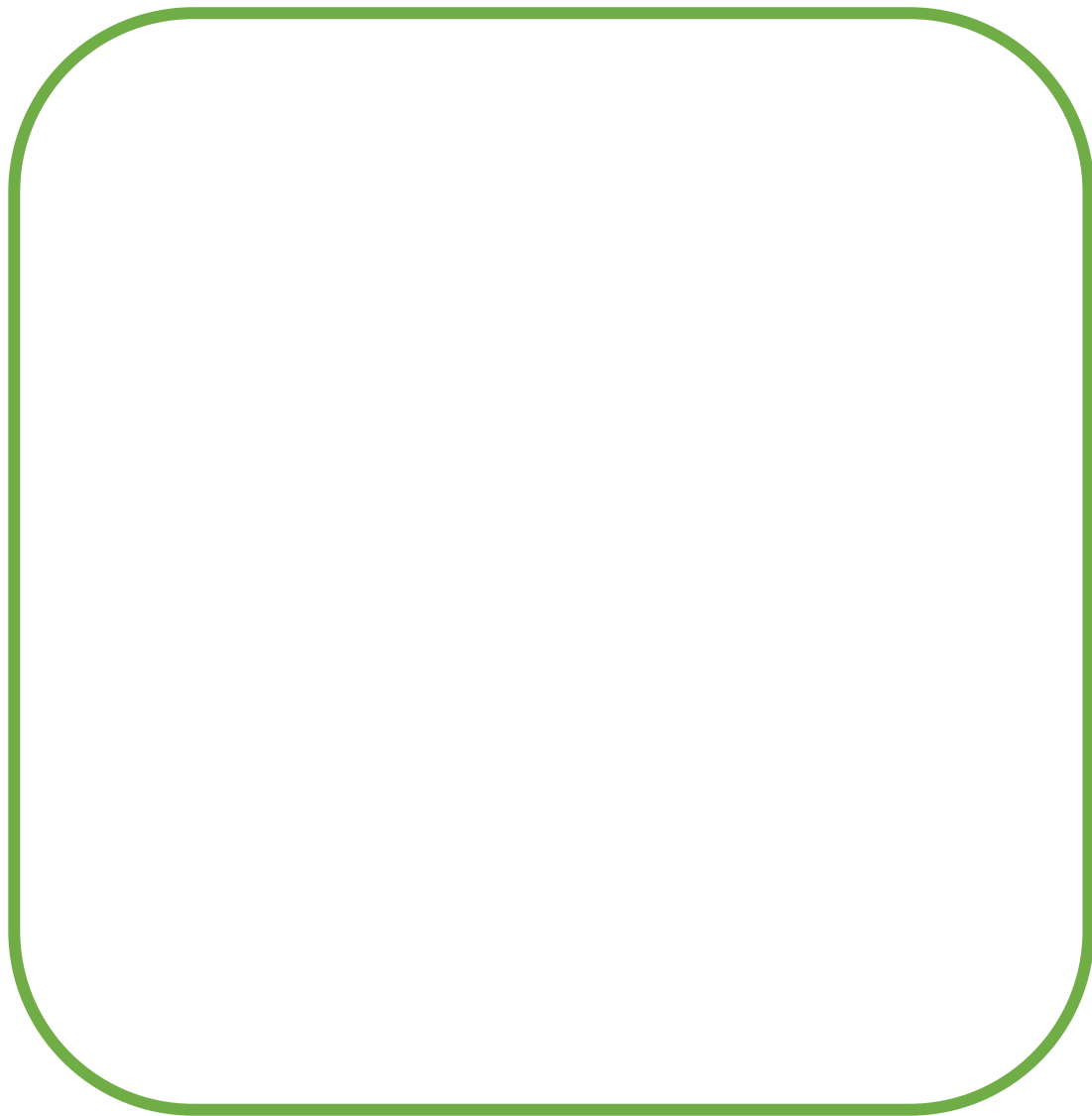


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nature medicine



Article

<https://doi.org/10.1038/s41591-024-03133-0>

Effects of semaglutide with and without concomitant SGLT2 inhibitor use in participants with type 2 diabetes and chronic kidney disease in the FLOW trial

FLOW RCT

Treatment: semaglutide

Comparator: placebo

Principal outcome: composite renal outcome

Patients: 3533 with T2DM and CKD

		HR (95% CI)	P interaction	Number of events/analyzed participants (semaglutide 1.0 mg; placebo)
Composite renal event (primary endpoint)				
Composite renal event (primary endpoint)		0.76 (0.66, 0.88)		331/1,767; 410/1,766
SGLT2i: No		0.73 (0.63, 0.85)		290/1,490; 372/1,493
SGLT2i: Yes		1.07 (0.69, 1.67)	0.109	41/277; 38/273
eGFR < 15				
eGFR < 15		0.80 (0.61, 1.06)		92/1,767; 110/1,766
SGLT2i: No		0.72 (0.53, 0.98)		72/1,490; 95/1,493
SGLT2i: Yes		1.29 (0.67, 2.57)	0.120	20/277; 15/273
50% reduction in eGFR				
50% reduction in eGFR		0.73 (0.59, 0.89)		165/1,766; 231/1,766
SGLT2i: No		0.66 (0.53, 0.83)		135/1,489; 190/1,493
SGLT2i: Yes		1.30 (0.76, 2.26)	0.023	30/277; 23/273



Acta Diabetologica
<https://doi.org/10.1007/s00592-026-02666-9>

REVIEW ARTICLE



The combination of glucagon-like peptide-1 receptor agonists and sodium–glucose cotransporter-2 inhibitors: a narrative review of existing meta-analysis

Angelo Avogaro¹ · Matteo Neccia² · Marina Delfini³ · Aldo Franculli⁴ · Giulia Enea⁵ · Anna Magli⁶ · Joshua Bemporad⁷ · Gian Paolo Fadini¹

