Études principales en maladie cardiovasculaire en 2022

VINCENT BERGERON MD FRCPC

SSVQ - 18 NOVEMBRE 2022

CONFLITS D'INTÉRÊT

- Honoraires de conférencier 2020 et 2021
  + BMS-Pfizer
  + Bayer
  + LEO Pharma

OBJECTIFS

- Citer les résultats d’études pertinentes en médecine vasculaire en 2021-2022
- Intégrer dans sa pratique de nouvelles approches thérapeutiques fondées sur des données récemment publiées
- Critiquer les études récentes en médecine vasculaire

Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

DELIVER

N Engl J Med 2022; 387:1089-1098

- 6263 patients avec insuffisance cardiaque stabilisée et avec FeVG > 40%
  + Avec ou sans diabète
  + Élévation du peptide natriurétique
  + **ATCD** de FeVG < 40% **non exclus**
- Dapagliflozine **10 mg** ou placebo
- Conduite de l'étude et analyses en collaboration avec le **commanditaire**
- Critère d'évaluation primaire: **composite**
  + Détérioration de **l'insuffisance cardiaque** ou **mortalité cardiovasculaire**

DOI:10.1056/NEJMoa2206286
nejm août 2022

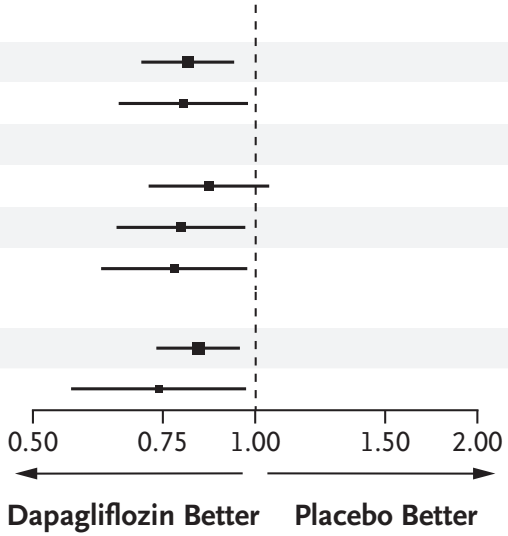
DELIVER - résultats

Variable	Dapagliflozin (N=3131)		Placebo (N=3132)	
	values	*events/ 100 patient-yr*	*values*	*events/ 100 patient-yr*
Efficacy outcomes		* EMPEROR-PRESERVED		
Primary composite outcome — no. (%)	512 (16.4) (13.8)	7.8	610 (19.5) (17.1)	9.6
Hospitalization for heart failure or an urgent visit for heart failure	368 (11.8)	5.6	455 (14.5)	7.2
Hospitalization for heart failure	329 (10.5) (8.6)	5.0	418 (13.3) (11.8)	6.5
Urgent visit for heart failure	60 (1.9)	0.9	78 (2.5)	1.1
Cardiovascular death†	231 (7.4) (7.3)	3.3	261 (8.3) (8.2)	3.8
Secondary outcomes				
Total no. of worsening heart failure events and cardiovascular deaths‡	815	11.8	1057	15.3
Change in KCCQ total symptom score at mo 8§	—	—	—	—
Mean change in KCCQ total symptom score at mo 8 among survivors	—	—	—	—
Death from any cause — no. (%)	497 (15.9) (14.1)	7.2 6.6	526 (16.8) (14.1)	7.6 6.7

nejm août 2022

DELIVER – sous-groupes

NYHA class at enrollment			
II	331/2314	411/2399	0.81 (0.70–0.94)
III or IV	181/817	198/732	0.80 (0.65–0.98)
LVEF at enrollment			
≤49%	207/1067	229/1049	0.87 (0.72–1.04)
50–59%	174/1133	211/1123	0.79 (0.65–0.97)
≥60%	131/931	170/960	0.78 (0.62–0.98)
Previous LVEF ≤40%			
No	420/2559	491/2553	0.84 (0.73–0.95)
Yes	92/572	119/579	0.74 (0.56–0.97)



Gliflozines et insuffisance cardiaque

- Bénéfices pour la réduction des **hospitalisations pour insuffisance cardiaque** dans une population avec une insuffisance cardiaque stabilisée

Recommendations for HF With Preserved Ejection Fraction*
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	RECOMMENDATIONS
1	C-LD	1. Patients with HFpEF and hypertension should have medication titrated to attain blood pressure targets in accordance with published clinical practice guidelines to prevent morbidity (1-3).
2a	B-R	2. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality (4).

JACC VOL. 79, NO. 17, 2022

doi.org/10.1016/j.jacc.2021.12.012
ACC/AHA mai 2022

Canadian Journal of Cardiology 38 (2022) 1153–1167

Society Guidelines

2022 Canadian Cardiovascular Society Guideline for Use of GLP-1 Receptor Agonists and SGLT2 Inhibitors for Cardiorenal Risk Reduction in Adults

RECOMMENDATION

1. In adults with HF and LVEF $\leq$ 40%, we recommend use of SGLT2i to reduce all-cause and CV mortality, hospitalization for HF, and the composite end point of significant decline in eGFR, progression to end-stage kidney disease, or death due to kidney disease (Strong Recommendation; Moderate-Quality Evidence).

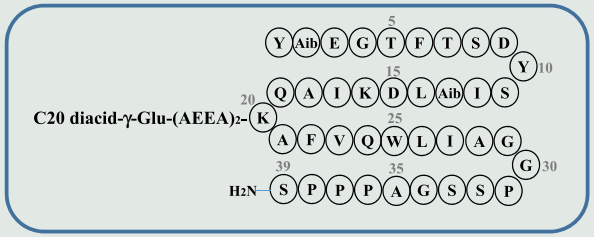
RECOMMENDATION

2. In adults with HF and LVEF $>$ 40%, we recommend use of SGLT2i to reduce hospitalization for HF (Strong Recommendation; Moderate-Quality Evidence).

doi.org/10.1016/j.cjca.2022.04.029

Tirzepatide Once Weekly for the Treatment of Obesity

SURMOUNT-1



- 2539 adultes avec IMC > 30 kg/m² ou IMC > 27 kg/m² avec complication de l'obésité
  + Non diabétiques
- Tirzepatide 5, 10 ou 15 mg une fois par semaine contre placebo (1:1:1:1) durant 72 mois
- Critère d'évaluation primaire double:
  + Pourcentage de diminution du poids
  + Réduction du poids de 5% et plus

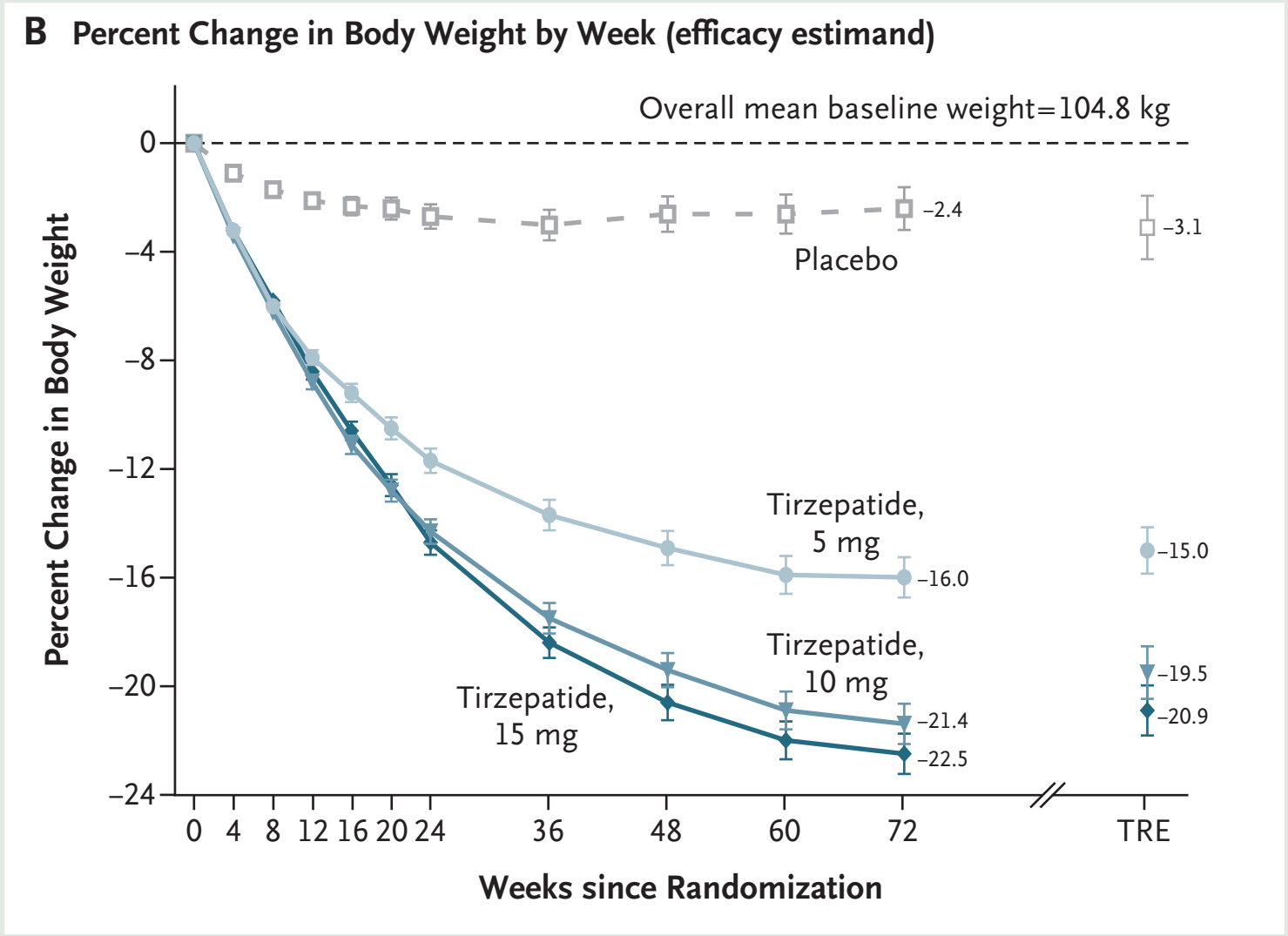
N Engl J Med 2022;387:205-16.

DOI:10.1056/NEJMoa2206038
nejm juillet 2022

GIP – polypeptide insulinotropique dépendant du glucose

- **cellules K intestin grêle**
  + Niveaux post-prandiaux 4x les niveaux de GLP-1.
  + Principale hormone insulinotropique
- **Tissus adipeux:**
  + Régulation des apports glucides
  + Lipolyse et lipoprotéine lipase
  + Perfusion du tissus adipeux
- **SNC**
  + Sites **complémentaires** à l'action du **GLP-1**

Molecular metabolism 2018

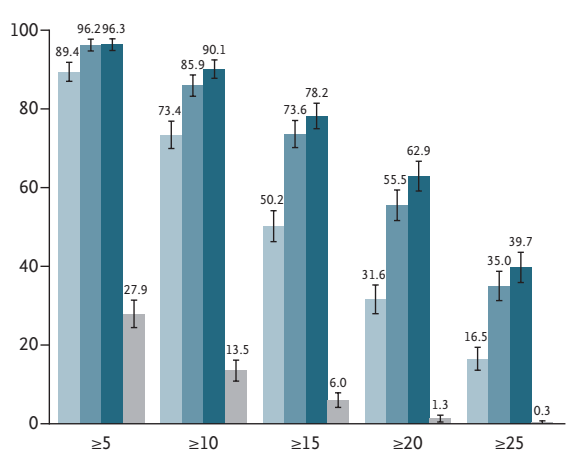

B Percent Change in Body Weight by Week (efficacy estimand)
Overall mean baseline weight=104.8 kg
Percent Change in Body Weight
0
−4
−8
−12
−16
−20
−24
Placebo
−2.4
−3.1
Tirzepatide, 5 mg
−16.0
−15.0
Tirzepatide, 10 mg
−21.4
−19.5
Tirzepatide, 15 mg
−22.5
−20.9
0 4 8 12 16 20 24 36 48 60 72 TRE
Weeks since Randomization

Tirzepatide – effets secondaires

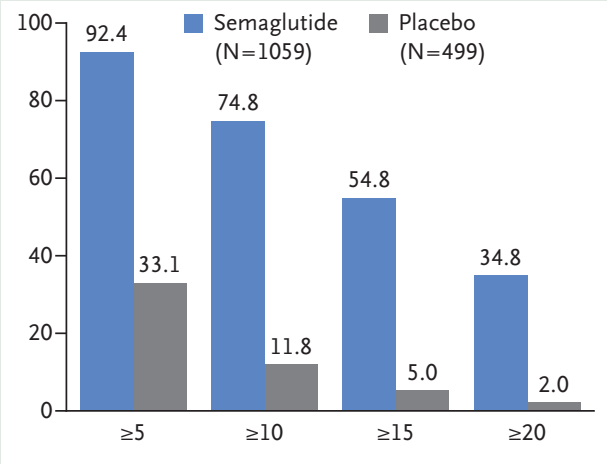
Variable	Tirzepatide, 5 mg (N=630)	Tirzepatide, 10 mg (N=636)	Tirzepatide, 15 mg (N=630)	Placebo (N=643)
		number (percent)		
Adverse events leading to discontinuation of trial drug or placebo†	27 (4.3)	45 (7.1)	39 (6.2)	17 (2.6)
Nausea	6 (1.0)	7 (1.1)	12 (1.9)	2 (0.3)
Diarrhea	2 (0.3)	5 (0.8)	3 (0.5)	0
Abdominal pain	0	2 (0.3)	3 (0.5)	0
Vomiting	0	4 (0.6)	0	0
Adverse events occurring in at least 5% of participants in any treatment group†				
Nausea	155 (24.6)	212 (33.3)	195 (31.0)	61 (9.5)
Diarrhea	118 (18.7)	135 (21.2)	145 (23.0)	47 (7.3)
Covid-19	94 (14.9)	98 (15.4)	82 (13.0)	90 (14.0)
Constipation	106 (16.8)	109 (17.1)	74 (11.7)	37 (5.8)
Dyspepsia	56 (8.9)	62 (9.7)	71 (11.3)	27 (4.2)
Vomiting	52 (8.3)	68 (10.7)	77 (12.2)	11 (1.7)
Decreased appetite	59 (9.4)	73 (11.5)	54 (8.6)	21 (3.3)
Headache	41 (6.5)	43 (6.8)	41 (6.5)	42 (6.5)
Abdominal pain	31 (4.9)	34 (5.3)	31 (4.9)	21 (3.3)

nejm juillet 2022

ARGLP-1 – catégories de perte pondérale

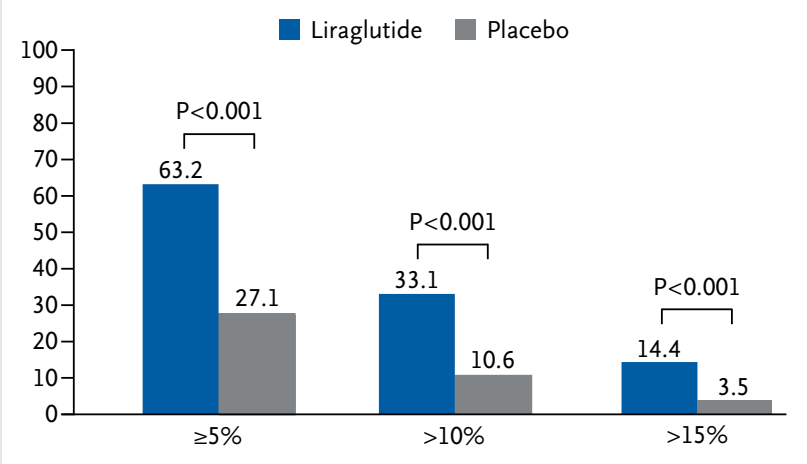


Tirzepatide
5,10,15 mg par semaine
SURMOUNT-1



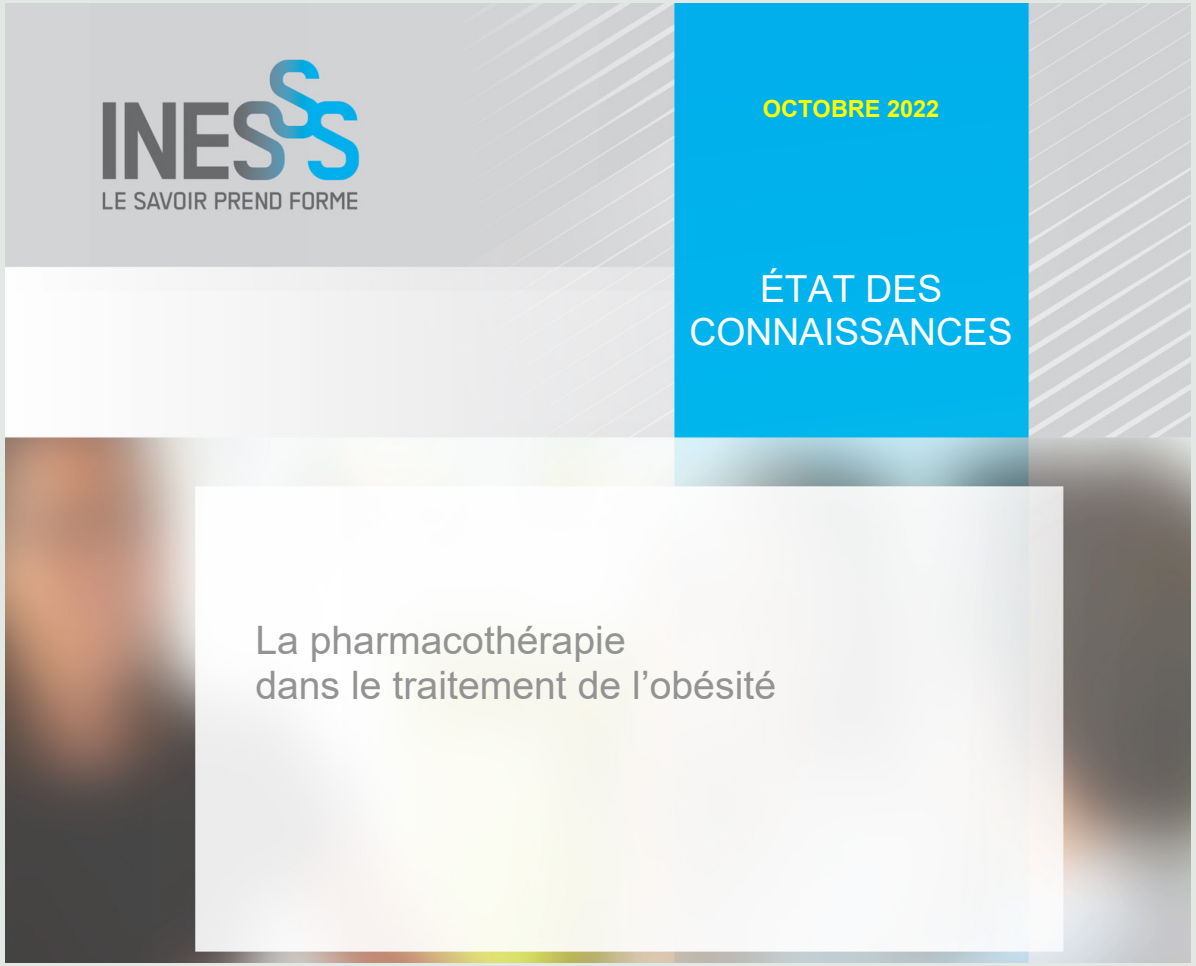
Semaglutide
2,4 mg par semaine
STEP-1

N Engl J Med 2021;384:989-1002.



Liraglutide
3 mg par jour
SCALE

N Engl J Med 2015;373:11-22.



https://www.inesss.qc.ca/publications/repertoire-des-publications/publication/la-pharmacotherapie-dans-le-traitement-de-lobesite.html

SURMOUNT-1 – conclusion

- Impressionnante perte pondérale dans un contexte de recherche clinique
- Bénéfices et effets secondaires reproductibles dans notre pratique clinique?
- **SURPASS-CVOT**: Étude de protection cardiovasculaire
- **SURMOUNT-4**: maintien de la perte de poids à l'arrêt du médicament

nejm juillet 2022

Surgery or Endovascular Therapy for Chronic Limb-Threatening Ischemia

BEST-CLI

DOI: 10.1056/NEJMoa2207899

- 1830 patients avec maladie artérielle périphérique **infra-inguinale** et **douleur de repos** ou **lésions tissulaires**
  + Cohorte **AVEC** segment unique **saphène interne** : 1434 patients
  + Cohorte **SANS** segment unique **saphène interne** : 396 patients
- Répartition aléatoire ouverte entre traitements chirurgical et endovasculaire
- Cible de recrutement: 2100 patients
  + Problème de financement

nejm novembre 2022

BEST-CLI – résultats cohorte AVEC saphène

Outcome	Surgery	Endovascular Therapy	Hazard Ratio (95% CI)†	P Value
Efficacy				
Primary outcome: major adverse limb event or death from any cause — no./total no. (%)‡	302/709 (42.6)	408/711 (57.4)	0.68 (0.59–0.79)	<0.001
Secondary outcomes — no./total no. (%)				
Death from any cause	234/709 (33.0)	267/711 (37.6)	0.98 (0.82–1.17)	
Above-ankle amputation of the index limb	74/709 (10.4)	106/711 (14.9)	0.73 (0.54–0.98)	
Intervention in index limb				
Major	65/709 (9.2)	167/711 (23.5)	0.35 (0.27–0.47)	
Minor	205/718 (28.6)	237/716 (33.1)	0.85 (0.70–1.02)	
Perioperative death§	12/687 (1.7)	9/708 (1.3)	1.54 (0.64–3.68)	
Major adverse limb event or perioperative death	139/687 (20.2)	246/708 (34.7)	0.53 (0.43–0.65)	
Myocardial infarction	75/718 (10.4)	85/716 (11.9)	0.97 (0.71–1.33)	
Stroke	39/718 (5.4)	44/716 (6.1)	0.93 (0.60–1.43)	

nejm novembre 2022

BEST-CLI – sécurité

	Surgery	Endovascular Therapy	Hazard Ratio (95% CI)†	P Value
Safety				
Major adverse cardiovascular event — no. of patients with ≥1 event/total no. of patients (%)				
Event ≤30 days after procedure¶	33/718 (4.6)	23/716 (3.2)	1.46 (0.86–2.50)	0.16
Event during follow-up	269/718 (37.5)	309/716 (43.2)	0.94 (0.80–1.11)	0.48
Serious adverse event				
Event occurred ≤30 days after index procedure — no. of patients with ≥1 event/total no. of patients (%)‖	244/718 (34.0)	226/716 (31.6)		0.34
No. of events ≤30 days after index procedure	427	379		0.10
No. of patients with ≥1 event/total no. of patients (%)	590/718 (82.2)	614/716 (85.8)		0.07
No. of events during follow-up	3141	3468		<0.001
Technical success of index procedure — no./total no. (%)**	651/662 (98.3)	596/704 (84.7)		
Length of hospital stay after index procedure††				
No. of days	7.5±6.2	5.9±7.3		
Median no. of days (IQR)	6 (4–9)	3 (1–8)		

nejm novembre 2022

BEST-CLI – conclusion

- Individualisation des choix thérapeutiques
- L’approche **chirurgicale** pour la **maladie infra-poplitée** est **sécuritaire** comparée au traitement endovasculaire
- 50% de l’augmentation des réinterventions et événements indésirables majeurs sur les membres est documentée dans les **6 premiers mois.**

nejm novembre 2022

Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis

European Heart Journal (2022) **43**, 474–484

Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes — FIDELIO-DKD

Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes — FIGARO-DKD

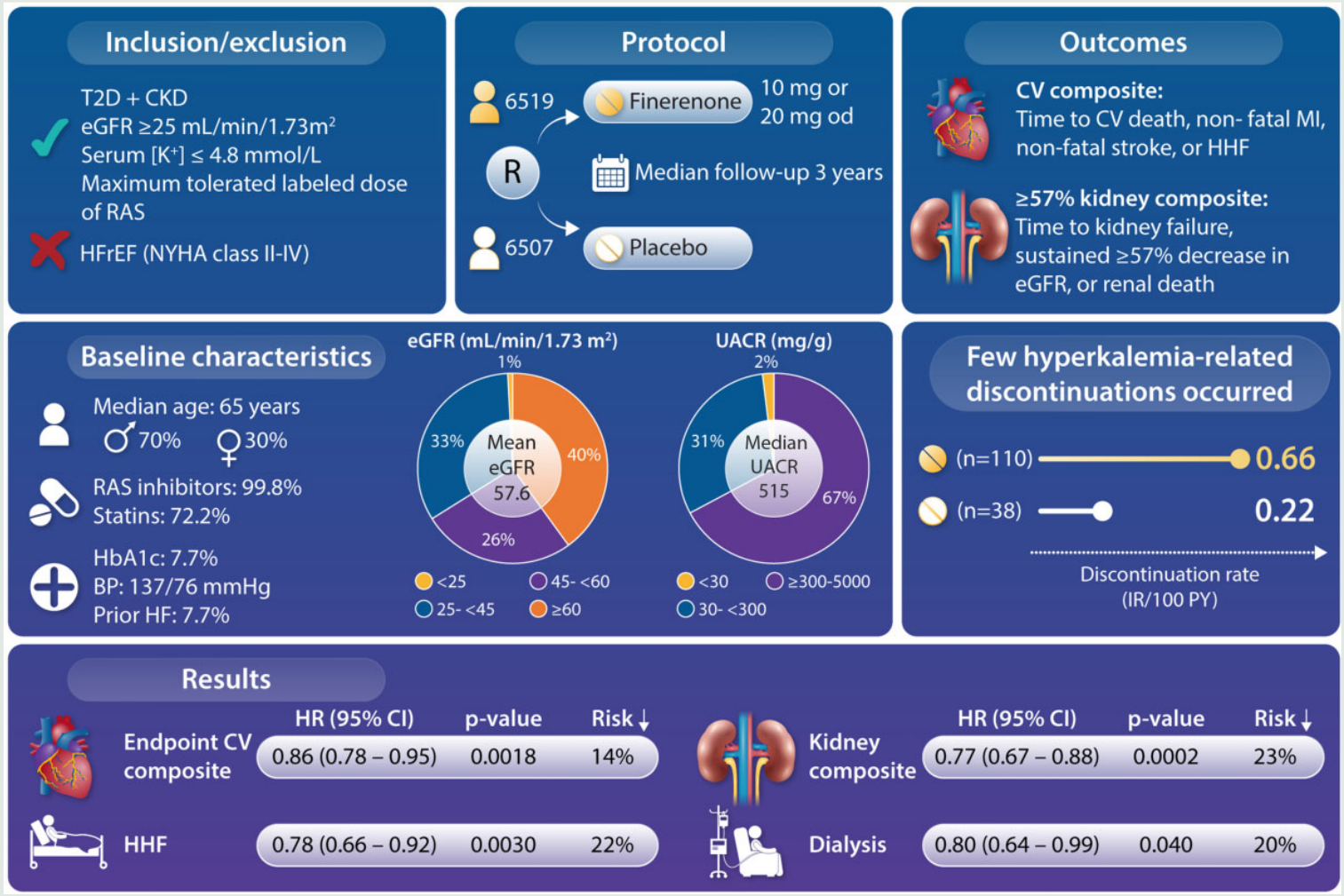
doi.org/10.1093/eurheartj/ehab777
EHJ février 2022

FIDELITY

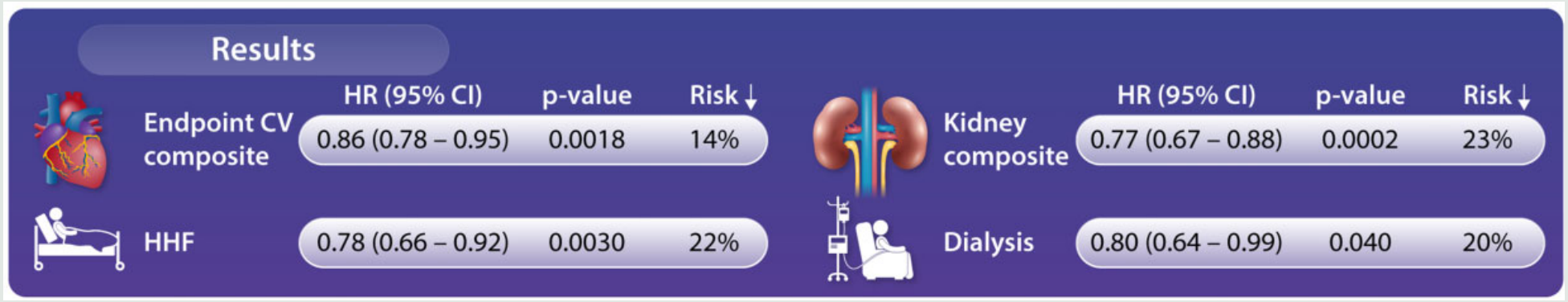
- 13026 adultes avec **néphropathie diabétique** traités par **iSRA** (IECA, ARA)
- **Finerenone 10 à 20 mg** versus placebo

FIDELIO-DKD	FIGARO-DKD
30-300 mg/g (3.4-34 mg/mmol)	
25-60 mL/min et rétinopathie	25-90 mL/min
300-5000 mg/g (34-565 mg/mmol)	
25-75 mL/min	> 60 mL/min
Kaliémie < 4.9 mmol/L	

EHJ février 2022


Inclusion/exclusion
T2D + CKD
eGFR ≥25 mL/min/1.73m²
Serum [K⁺] ≤ 4.8 mmol/L
Maximum tolerated labeled dose of RAS
HFrEF (NYHA class II-IV)
Protocol
6519
Finerenone
10 mg or 20 mg od
R
Median follow-up 3 years
6507
Placebo
Outcomes
CV composite:
Time to CV death, non- fatal MI, non-fatal stroke, or HHF
≥57% kidney composite:
Time to kidney failure, sustained ≥57% decrease in eGFR, or renal death
Baseline characteristics
Median age: 65 years
70%
30%
RAS inhibitors: 99.8%
Statins: 72.2%
HbA1c: 7.7%
BP: 137/76 mmHg
Prior HF: 7.7%
eGFR (mL/min/1.73 m²)
1%
33%
Mean eGFR 57.6
40%
26%
<25
45- <60
25- <45
≥60
UACR (mg/g)
2%
31%
Median UACR 515
67%
<30
≥300-5000
30- <300
Few hyperkalemia-related discontinuations occurred
(n=110)
0.66
(n=38)
0.22
Discontinuation rate (IR/100 PY)
Results
HR (95% CI)
p-value
Risk ↓
Endpoint CV composite
0.86 (0.78 – 0.95)
0.0018
14%
HHF
0.78 (0.66 – 0.92)
0.0030
22%
Kidney composite
0.77 (0.67 – 0.88)
0.0002
23%
Dialysis
0.80 (0.64 – 0.99)
0.040
20%

FIDELITY – résultats



EHJ février 2022

FIDELITY – effets indésirables

Treatment-emergent AEs[a]	Number of patients with event (%)	
	Finerenone (*n* = 6510)	Placebo (*n* = 6489)
Any AE	5602 (86.1)	5607 (86.4)
AE related to study drug	1206 (18.5)	862 (13.3)
AE leading to treatment discontinuation	414 (6.4)	351 (5.4)
Any serious AE[b]	2060 (31.6)	2186 (33.7)
Serious AE[b] related to study drug	83 (1.3)	61 (0.9)
Serious AE[b] leading to treatment discontinuation	145 (2.2)	154 (2.4)
Investigator-reported hyperkalaemia[c]	912 (14.0)	448 (6.9)
Hyperkalaemia related to study drug	573 (8.8)	249 (3.8)
Permanent discontinuation due to hyperkalaemia	110 (1.7)	38 (0.6)
Serious hyperkalaemia[b]	69 (1.1)	16 (0.2)
Hospitalization due to serious hyperkalaemia	61 (0.9)	10 (0.2)
Fatal hyperkalaemia	0 (0.0)	0 (0.0)
Investigator-reported renal-related AEs		
Acute kidney injury[d]	220 (3.4)	234 (3.6)
Hospitalization due to acute kidney injury[d]	85 (1.3)	86 (1.3)
Treatment discontinuation due to acute kidney injury[d]	14 (0.2)	10 (0.2)

EHJ février 2022

Réduction du risque absolue: composite de maladie rénale terminale

	DFGe (mL/min/1.73 m^2)	Albuminurie (mg/mmol)	RRA
RENAAL	168 umol/L	141	5.9%
IDNT	148 umol/L	1,9 g/d	3.6%
DAPA-CKD	43.1	107	2.4%
CREDENCE	56.2	105	2.2%
FIDELIO	44.3	96	3.3%
EMPA-KIDNEY	37.5	47	3.6%

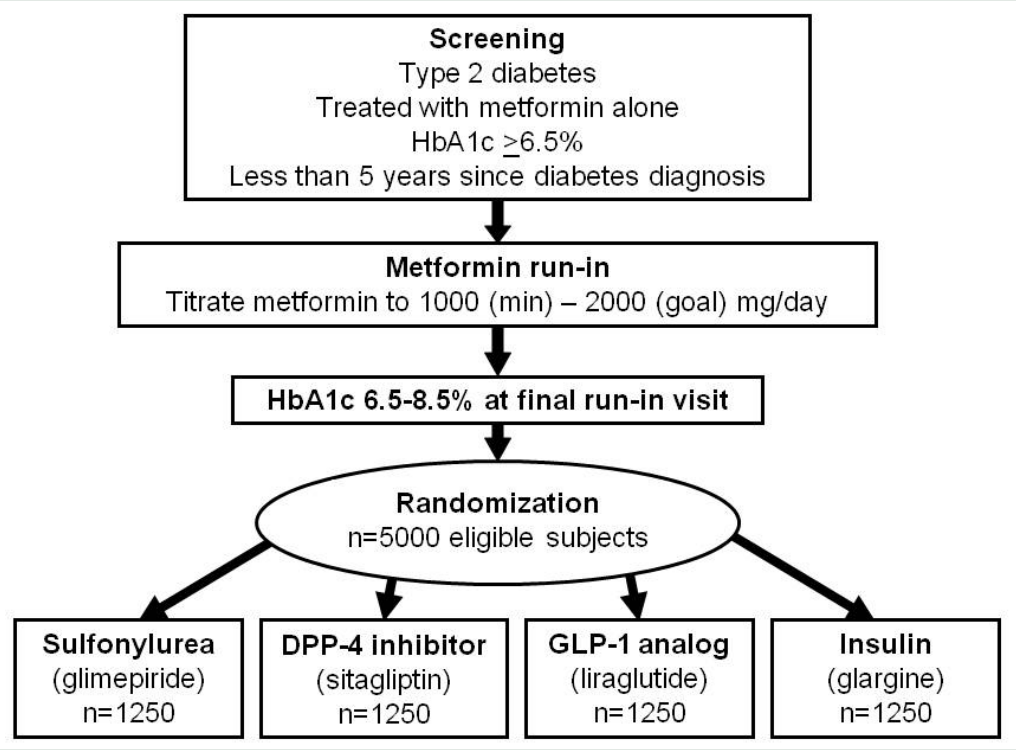
FIDELITY - conclusion

- Réduction des hospitalisations pour **insuffisance cardiaque** et de la survenue d'**insuffisance rénale sévère** chez une population **déjà traitée** avec agents **iSRA**
  + Bénéfice similaire à **iSRA** et **gliflozines**
- *Surveillance et gestion de la **kaliémie**
- Pas les **effets sexuels** documentés avec spironolactone
- Monographie canadienne publiée octobre 2022

EHJ février 2022

Glycemia Reduction in Type 2 Diabetes — Glycemic Outcomes

Glycemia Reduction in Type 2 Diabetes — Microvascular and Cardiovascular Outcomes



N Engl J Med 2022;387:1063-74.
DOI:10.1056/NEJMoa2200433
nejm septembre 2022

GRADE – critère d'évaluation primaire (contrôle glycémique)

Outcome	Glargine (N = 1263)	Glimepiride (N = 1254)	Liraglutide (N = 1262)	Sitagliptin (N = 1268)
Primary metabolic outcome†				
Participants — no. (%)	852 (67.4)	908 (72.4)	860 (68.2)	981 (77.4)
Hazard ratio in the treatment group as compared with all other treatments combined (95% CI)	0.87 (0.80–0.94)§	1.01 (0.93–1.09)	0.84 (0.78–0.91)§	1.37 (1.27–1.48)§

nejm septembre 2022

Outcome	Glargine (N = 1263)	Glimepiride (N = 1254)	Liraglutide (N = 1262)	Sitagliptin (N = 1268)	Total (N = 5047)
Hospitalization for heart failure					
No. of participants/no. at risk (%)	26/1257 (2.1)	30/1247 (2.4)	14/1251 (1.1)	30/1264 (2.4)	100/5019 (2.0)
Rate (95% CI)	0.42 (0.27–0.61)	0.48 (0.33–0.69)	0.22 (0.12–0.38)	0.48 (0.32–0.68)	0.40 (0.33–0.49)
Pairwise hazard ratio (95% CI)					
Glargine		0.86 (0.51–1.45)	1.85 (0.96–3.55)	0.87 (0.51–1.47)	
Glimepiride			2.16 (1.14–4.06)	1.01 (0.61–1.67)	
Liraglutide				0.47 (0.25–0.88)	
Sitagliptin					
Hazard ratio (95% CI) in one agent as compared with the others combined	1.11 (0.70–1.76)	1.36 (0.88–2.11)	0.49 (0.28–0.86)	1.35 (0.87–2.08)	
Death from cardiovascular causes					
No. of participants/no. at risk (%)	21/1257 (1.7)	16/1247 (1.3)	9/1251 (0.7)	21/1264 (1.7)	67/5019 (1.3)
Rate (95% CI)	0.33 (0.21–0.51)	0.26 (0.15–0.42)	0.14 (0.07–0.27)	0.33 (0.21–0.51)	0.27 (0.21–0.34)
Pairwise hazard ratio (95% CI)					
Glargine		1.29 (0.67–2.47)	2.30 (1.05–5.01)	1.00 (0.55–1.82)	
Glimepiride			1.78 (0.79–4.04)	0.77 (0.40–1.48)	
Liraglutide				0.43 (0.20–0.95)	
Sitagliptin					
Hazard ratio (95% CI) in one agent as compared with the others combined	1.43 (0.85–2.43)	1.02 (0.58–1.82)	0.47 (0.23–0.95)	1.44 (0.85–2.44)	

événements cardiovasculaires - perspective

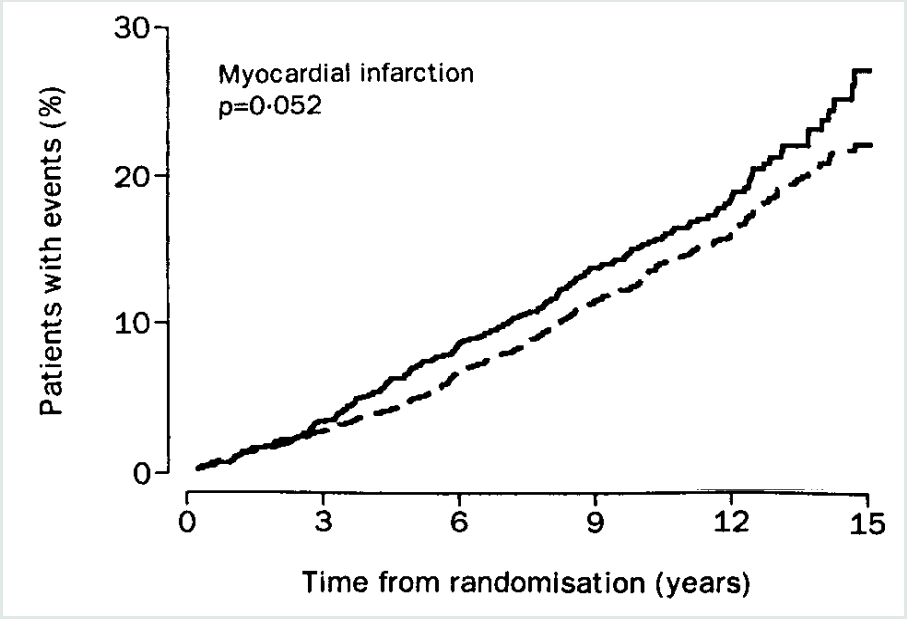
	Prévention primaire	Prévention secondaire	Mortalité CV	hIC
EMPAREG-OUTCOME	0%	100%	5.9%	4.1%
CANVAS	34%	66%	12.8%	8.7%
DECLARE-TIMI 58	60%	40%	2.9%	3.3%
REWIND	69%	31%	7%	4.6%
LEADER	20%	80%	6%	5.3%
SUSTAIN-6	?	60% MCAS	2.8%	3.3%
DAPA HF		100%	11.5%	13.4%
EMPEROR REDUCED		100%	10.8%	18.3%
EMPEROR PRESERVED		100%	8.2%	11.8%
DELIVER		100%	8.3%	13.3%
GRADE	93%	7%	1.3%	2%

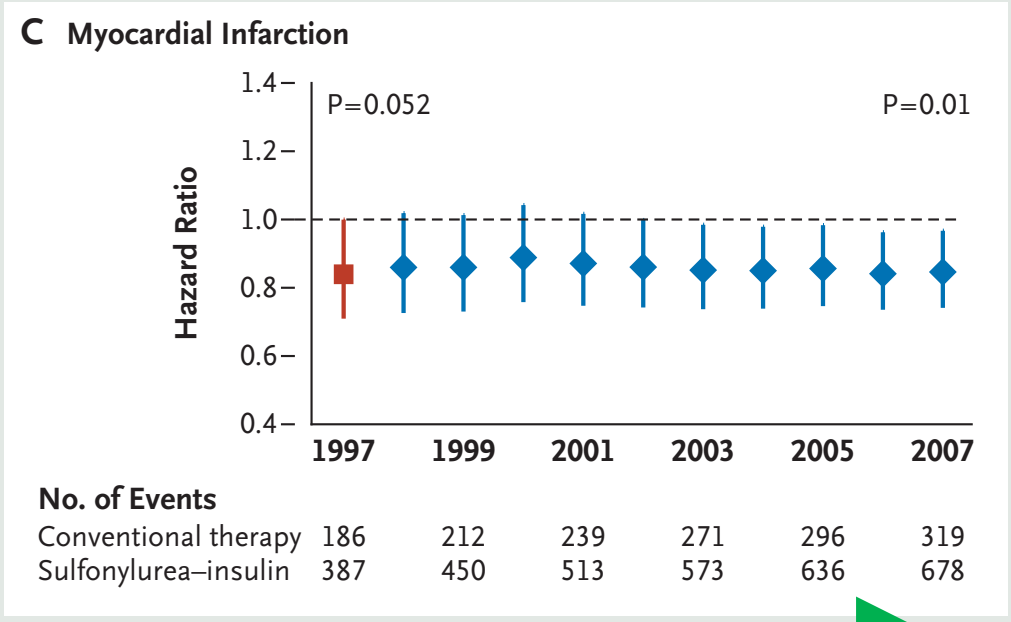
GRADE – conclusion

- **contrôle glycémique** était particulièrement **mauvais**:
  70% échec métabolique
  + Ce qui explique **l'absence de bénéfice** sur les critères **microvasculaires**
- **Réduction** significative du **risque relatif cardiovasculaire** de **50%** avec **Liraglutide**
  + dans une population à faible risque (1-2% d'événements)
  + après **5 ans** de suivi

nejm septembre 2022

UKPDS – événements macrovasculaires





20 ans

UKPDS-33

Hypertriglycéridémie

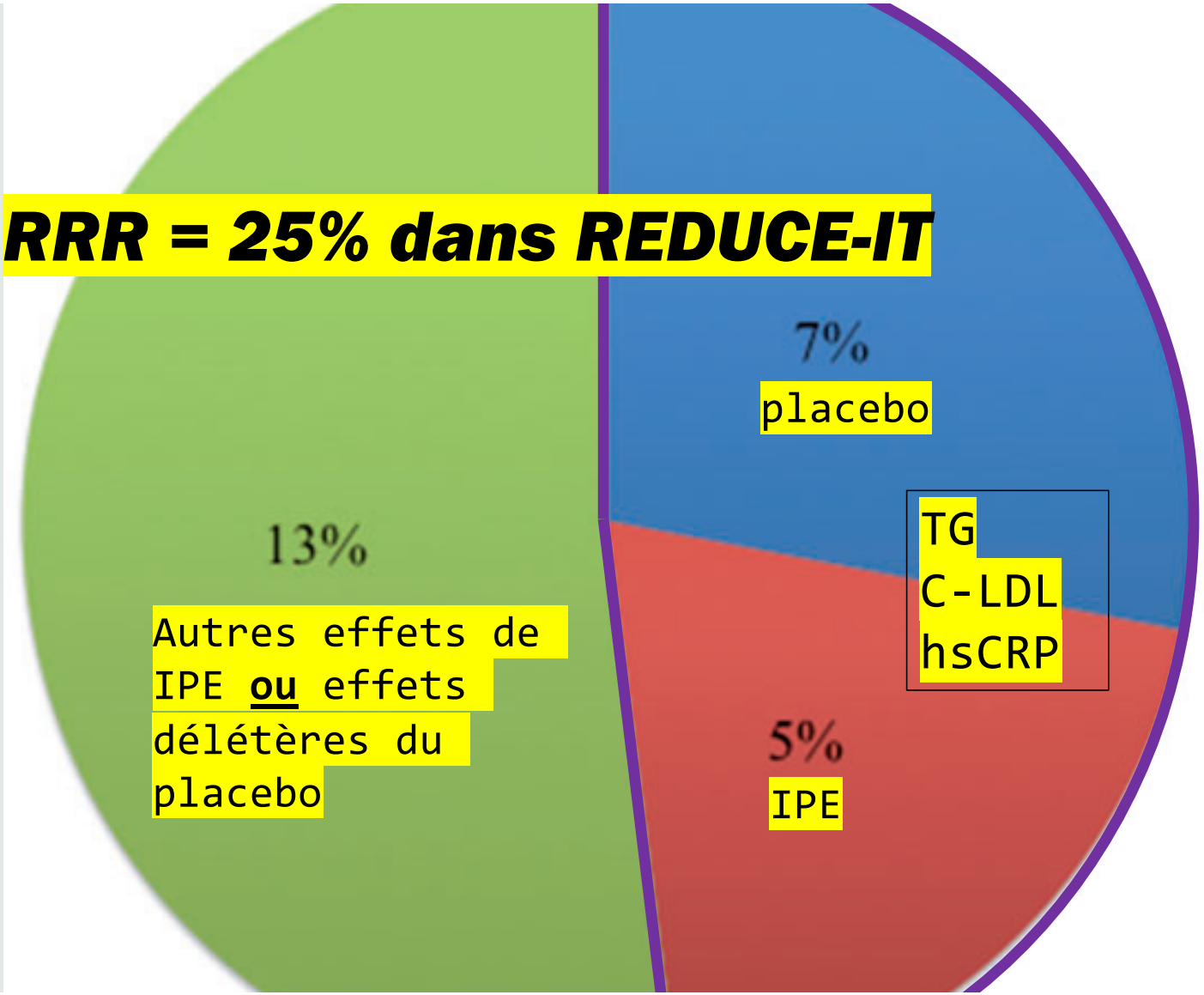
ORIGINAL RESEARCH ARTICLE

Effects of Randomized Treatment With Icosapent Ethyl and a Mineral Oil Comparator on Interleukin-1β, Interleukin-6, C-Reactive Protein, Oxidized Low-Density Lipoprotein Cholesterol, Homocysteine, Lipoprotein(a), and Lipoprotein-Associated Phospholipase A2: A REDUCE-IT Biomarker Substudy

Paul M Ridker, MD, MPH; Nader Rifai, MD; Jean MacFadyen, BA; Robert J. Glynn, ScD; Lixia Jiao, PhD; Ph. Gabriel Steg, MD; Michael Miller, MD; Eliot A. Brinton, MD; Terry A. Jacobson, MD; Jean-Claude Tardif, MD; Christie M. Ballantyne, MD; R. Preston Mason, MD; Deepak L. Bhatt, MD, MPH

DOI:10.1161/CIRCULATIONAHA.122.059410
Circulation août 2022

RRR = 25% dans REDUCE-IT



EHJ octobre 2021

	Minérale				IPE			
hsCRP, mg/L								
Baseline (n=4089:4086)	2.15 (1.07–4.50)				2.18 (1.07–4.49)			
	.3–5.2)	0	21.95	<0.0001	1.90 (0.9–3.9)	–0 8	–12.41	0.003
	.3–5.8)	0.4	32.26	<0.0001	1.79 (0.86–4.01)	–	–13.86	0.04
Last visit‖ (3113:3198)	2.79 (1.33–5.49)	0.42	30.12	<0.0001	1.69 (0.81–3.99)	–0.19	–13.25	0.58
Interleukin-6, pg/mL								
Baseline (n=3133:3203)	3.27 (2.16–5.17)				3.23 (2.14–5.02)			
	.42–6.09)	0	16.22	<0.0001	3.09 (2.05–5.06)	–0.08	–2.60	0.005
	.53–6.04)	0.5	18.21	<0.0001	3.08 (2.04–4.98)	–0.05	–1.98	0.0004
Last visit‖ (2491:2654)	3.97 (2.56–6.49)	0.73	26.25	<0.0001	3.24 (2.05–5.16)	0.09	3.01	<0.0001
Interleukin-1β, pg/mL								
Baseline (n=3134:3204)	0.06 (0.03–0.10)				0.06 (0.03–0.10)			
	04–0.13)	0	28.89	<0.0001	0.06 (0.03–0.10)	0.00	0.00	<0.0001
	04–0.13)	0.0	30.68	<0.0001	0.05 (0.03–0.09)	0.00	0.00	<0.0001
Last visit‖ (2492:2655)	0.09 (0.05–0.15)	0.03	48.28	<0.0001	0.05 (0.03–0.09)	0.00	0.00	<0.0001
OxLDL, mU/L								
Baseline (n=3134:3204)	45 879 (37 523–54 088)				44 641 (36 863–53 483)			
12 months (2875:2908)	50 457	4877.57	10.94	<0.0001	45 594 (37 888–56 627)	1293.21	2.94	<0.0001
		34 .54	7.81	<0.0001	45 410 (36 819–55 576)	400.70	0.81	<0.0001
Last visit‖ (2492:2655)	47 838 (38 710–58 877)	2301.78	5.06	<0.0001	45 251 (36 669–55 529)	59.68	0.15	<0.0001

hsCRP

IL-6

IL-1B

LDL oxydés

Circulation août 2022

Triglycerides, mg/dL	Minérale				IPE			
Baseline (n=4089:4086)	216.0 (175.5–274.0)				216.5 (176.5–272.0)			
12 months (3633:3689)	221.0 (164.0–298.0)	4.50	2.24	<0.0001	175.0 (132.0–238.0)	–3.00	–18.32	<0.0001
TG	220.0 (164.0–294.0)	4.25	2.09	<0.0001	173.0 (129.0–238.0)	–3.50	–18.86	<0.0001
Last visit‖ (3152:3243)	200.5 (148.5–275.0)	–15.0	–7.57	<0.0001	169.0 (124.0–234.0)	–4.00	–22.22	<0.0001
Lp-PLA2, nmol/min/mL								
Baseline (n=3485:3480)	134.00 (113.00–159.00)				134.00 (113.00–157.00)			
12 months (3032:3057)	157.90 (131.40–185.60)	24.0	18.46	<0.0001	129.8 (107.50–153.30)	–4.50	–3.50	<0.0001
Lp-PLA2	159.65 (132.50–191.00)	26.6	20.18	<0.0001	128.2 (106.80–152.10)	–5.90	–4.42	<0.0001
Last visit‖ (2543:2705)	166.90 (136.90–202.60)	33.4	25.81	<0.0001	133.2 (111.60–159.30)	–1.70	–1.30	0.72

Omega-3 et hyperTG – conclusions

- Courage/humilité des investigateurs
- **1/5 bénéfice** est attribuable à effets de **IPE** sur **lipides/hs-CRP**
- L'importance de **confirmer** les données dans plusieurs études

Triglyceride Lowering with Pemafibrate to Reduce Cardiovascular Risk

PROMINENT

DOI: 10.1056/NEJMoa2210645

End Point	Pemafibrate (N = 5240)		Placebo (N = 5257)		Hazard Ratio (95% CI)*	P Value
	No. of Patients with Event	Incidence/ 100 Person-yr	No. of Patients with Event	Incidence/ 100 Person-yr		
Primary composite end point	572	3.60	560	3.51	1.03 (0.91–1.15)	0.67

Variable	Pemafibrate (N = 5240)	Placebo (N = 5257)	Treatment Effect†
	Median Value (IQR)		Mean % Change (95% CI)
Apolipoprotein B level, measured			
Baseline — mg/dl	90 (75 to 108)	89 (74 to 107)	
4 Mo — mg/dl	93 (77 to 111)	87 (73 to 105)	
Median change from baseline — %	3.2 (–12.0 to 19.7)	–1.6 (–13.4 to 11.8)	4.8 (3.8 to 5.8)

Hypertriglycéridémie et risque cardiovasculaire résiduel

- **Bénéfices de IPE** documentés dans REDUCE-IT et JELIS
- **Pas de rôle** pour les **fibrates** dans la réduction des **événements CV** chez des patients avec statine (FIELD, ACCORD, PROMINENT)

  + Progression de la **rétinopathie** diabétique (ACCORD, FIELD)

  + Prévention des pancréatites aiguës
- Le **contenu en triglycéride** des particules de cholestérol ne détermine **pas le risque cardiovasculaire**

Intermediate-dose versus low-dose low-molecular-weight heparin in pregnant and post-partum women with a history of venous thromboembolism (Highlow study): an open-label, multicentre, randomised, controlled trial

doi.org/10.1016/ S0140-6736(22)02128-6

- 1,110 Femmes enceintes de 14 semaines ou moins avec ATCD de TEV

  + TEV **non provoquée** ou facteur de risque **hormonal**

- Dose **intermédiaire** (environ demi-dose thérapeutique) vs dose **prophylactique**

  + Jusqu'à **6 semaines post partum**

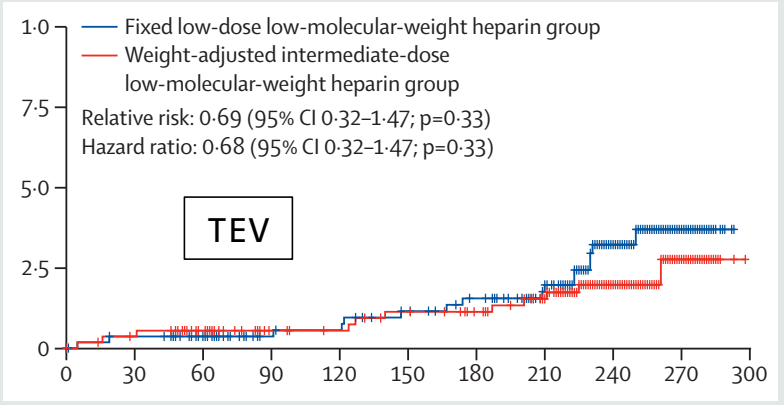
	Nadroparin dose, IU	Enoxaparin dose, IU	Dalteparin dose, IU	Tinzaparin dose, IU
Weight-adjusted intermediate dose group				
<50 kg bodyweight	3800	6000	7500	4500
50 to <70 kg bodyweight	5700	8000	10 000	7000
70 to <100 kg bodyweight	7600	10 000	12 500	10 000
≥100 kg bodyweight	9500	12 000	15 000	12 000

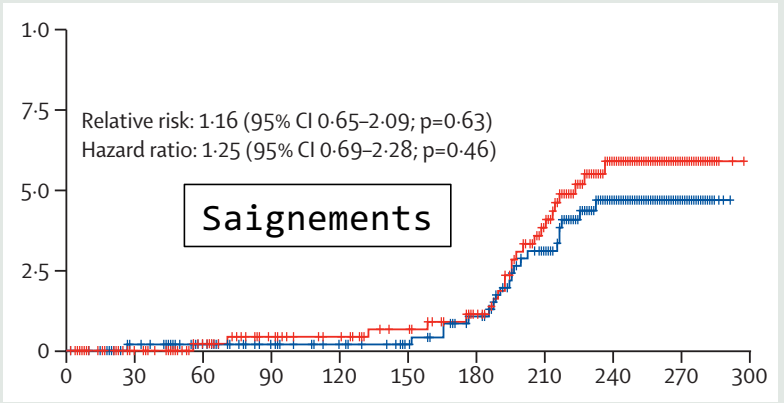
	Nadroparin dose, IU	Enoxaparin dose, IU	Dalteparin dose, IU	Tinzaparin dose, IU
Fixed low-dose group				
<100 kg bodyweight	2850	4000	5000	3500
≥100 kg bodyweight	3800	6000	7500	4500

lancet octobre 2022

Highlow - résultats

	Intermediate-dose low-molecular-weight heparin group (n=555)	Low-dose low-molecular-weight heparin group (n=555)	Relative risk (95% CI)	Hazard ratio (95% CI)
From randomisation until 6 weeks post partum				
Venous thromboembolism (primary outcome)	11 (2%)	16 (3%)	0·69 (0·32–1·47)	0·68 (0·32–1·47)
Antepartum	5 (1%)	5 (1%)	..	..
Post partum	6 (1%)	11 (2%)	..	..
Pulmonary embolism	1 (<1%)	9 (2%)	0·11 (0·01–0·87)	..*
Antepartum	0	2 (<1%)	..	..
Post partum	1 (<1%)	7 (1%)	..	..
Superficial thrombophlebitis‡	3 (1%)	13 (2%)	0·23 (0·07–0·81)	0·22 (0·06–0·79)
Antepartum	3 (1%)	2 (<1%)	..	..
Post partum	0	11 (2%)	..	..





lancet octobre 2022

Highlow - conclusion

- Pas de bénéfice à la dose intermédiaire
- Risque TEV élevé (**2-3 %**) chez des patientes **traitées**
- Le risque relatif semble sensible à la période **ANTE versus POST** partum
  + Embolies pulmonaires
  + Thromboses veineuses superficielles
- Générer des **hypothèses**:
  + Dose **prophylactique ante partum** et dose **intermédiaire post partum**?
  + Dose **thérapeutique**?

lancet octobre 2022

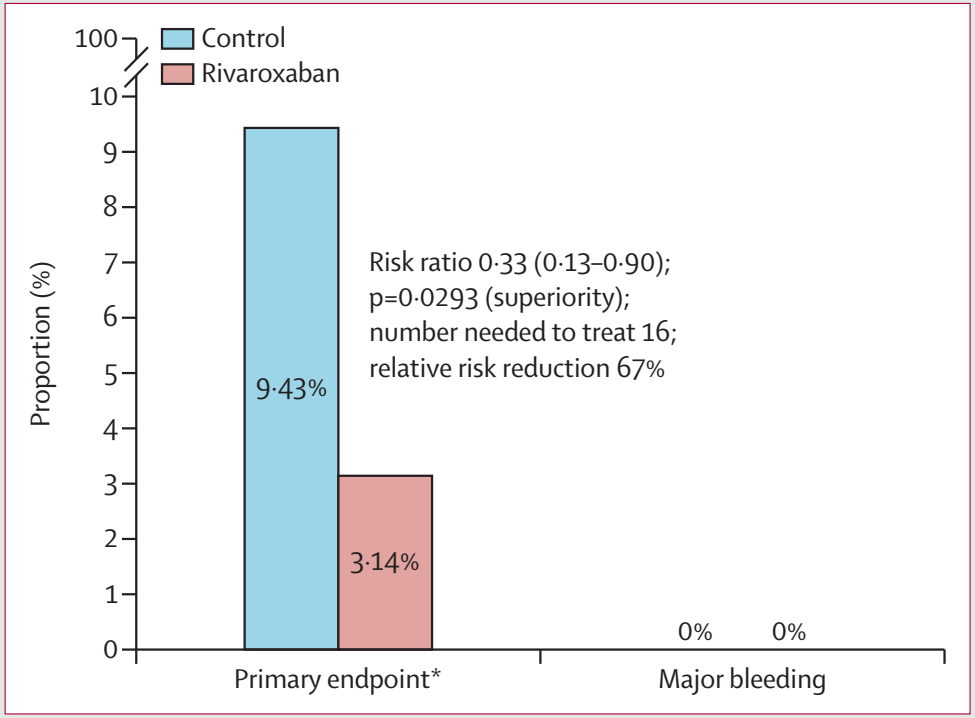
COVID-19

TRAITEMENTS ANTI-THROMBOTIQUES

Rivaroxaban versus no anticoagulation for post-discharge thromboprophylaxis after hospitalisation for COVID-19 (MICHELLE): an open-label, multicentre, randomised, controlled trial

Lancet 2022; 399: 50–59

- Rivaroxaban 10 mg vs placebo
- Durée 35 jours
- Après hospitalisation COVID-19
- Score IMPROVE-VTE > 3 **ou** 2-3 avec D-dimères > 500 ng/L



doi.org/10.1016/S0140-6736(21)02392-8
lancet janvier 2022

MICHELLE - résultats

	Rivaroxaban (n=159)	Control (n=159)	Relative risk (95% CI)	p values (two-sided)
Primary efficacy outcome	5/159 (3·14%)	15/159 (9·43%)	0·33 (0·13–0·90)	0·0293
Secondary efficacy outcomes				
Symptomatic and fatal VTE	1/159 (0·63%)	8/159 (5·03%)	0·13 (0·02–0·99)	0·0487
Symptomatic VTE and all-cause mortality	4/159 (2·52%)	9/159 (5·66%)	0·44 (0·14–1·41)	0·1696
Composite of symptomatic VTE, myocardial infarction, stroke, and cardiovascular death	1/159 (0·63%)	9/159 (5·66%)	0·11 (0·01–0·87)	0·0360

lancet janvier 2022

MICHELLE - conclusion

- Indice de **fragilité très bas**: 1

COR	LOE	
2b	B-R	12. In select patients who have been hospitalized for COVID-19, post-discharge treatment with prophylactic dose rivaroxaban for approximately 30 days may be considered to reduce risk of VTE.[55,56]

jth juillet 2022

lancet janvier 2022

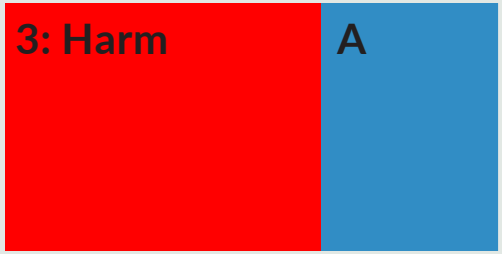
Effect of P2Y12 Inhibitors on Survival Free of Organ Support Among Non-Critically Ill Hospitalized Patients With COVID-19

A Randomized Clinical Trial

JAMA. 2022;327(3):227-236.

	Therapeutic dose of heparin plus P2Y12 inhibitor (n = 293)	Therapeutic dose of heparin only (usual care) (n = 269)
Composite primary outcome[b]		
Organ support-free days, median (IQR)	21 (20-21)	21 (21-21)
Components of the primary outcome		
Alive and free of organ support	218 (74.4)	211 (78.4)
Alive with organ support	57 (19.5)	47 (17.5)
Death	18 (6.1)	11 (4.1)
Survival to hospital discharge	275 (93.9)	258 (95.9)

Outcome	No. (%) Therapeutic dose of heparin plus P2Y12 inhibitor (n = 293)	Therapeutic dose of heparin only (usual care) (n = 269)
Secondary outcomes		
Major thrombotic event[c] or in-hospital death	18 (6.1)	12 (4.5)
Any thrombotic event[d] or in-hospital death	20 (6.8)	12 (4.5)
Major bleeding event[e] or in-hospital death	18 (6.1)	10 (3.7)
Components of the secondary outcomes		
In-hospital death	13 (4.4)	8 (3.0)
Major thrombotic event[c]	7 (2.4)	5 (1.9)
Any thrombotic event[d]	9 (3.1)	5 (1.9)
Major bleeding event[e]	6 (2.0)	2 (0.7)



7. In non-critically ill patients hospitalized for COVID-19, add-on treatment with an antiplatelet agent is potentially harmful and should not be used.[35,36]

ACTIV-4a

jth juillet 2022
jama janvier 2022

Effect of Antiplatelet Therapy on Survival and Organ Support–Free Days in Critically Ill Patients With COVID-19

A Randomized Clinical Trial

REMAP-CAP Writing Committee for the REMAP-CAP Investigators

JAMA. 2022;327(13):1247-1259

- Patients hospitalisés aux **soins intensifs** avec la COVID-19
  + **Anticoagulants non protocolisés** à différentes posologies
- Répartition aléatoire entre trois traitements: **AAS**, inhibiteur **P2Y12** ou **pas d'antiplaquettaire**
- Durée de l'hospitalisation ou maximum 14 jours
- Critère d'évaluation primaire:
  + Journées sans traitement de support au jour 21

REMAP-CAP – antiplaquettaires aux SI

Outcomes	Pooled antiplatelets (n = 1020)	Aspirin (n = 565)[a]	P2Y12 inhibitors (n = 455)[a]	Control (n = 529)
Organ support-free days to day 21[b]				
No. of patients with known outcome	1011	563	448	521
Median (IQR), d	7 (-1 to 16)	8 (-1 to 16)	7 (-1 to 16)	7 (-1 to 16)
Adjusted proportional odds ratio (95% CrI)	1.02 (0.86-1.23)	1.05 (0.85-1.30)	1.00 (0.80-1.27)	1 [Reference]
Probability of futility, %	95.7	88.6	93.4	
Probability of efficacy, %	58.0	66.5	51.8	
Survival to hospital discharge				
No./total (%)	723/1011 (71.5)	402/563 (71.4)	321/448 (71.7)	354/521 (67.9)
Adjusted odds ratio (95% CrI)	1.27 (0.99-1.62)	1.30 (0.97-1.72)	1.18 (0.86-1.62)	1 [Reference]
Adjusted absolute risk difference, % (95% CrI)	5.0 (-0.2 to 9.5)	5.4 (-0.7 to 10.5)	3.5 (-3.4 to 9.5)	
Major bleeding[c,e]				
No./total (%)	21/1002 (2.1)	11/559 (2.0)	10/443 (2.3)	2/517 (0.4)
Adjusted odds ratio (95% CrI)	2.97 (1.23-8.28)[f]	2.34 (0.93-5.93)	2.50 (0.95-6.56)	1 [Reference]
Adjusted absolute risk difference, % (95% CrI)	0.8 (0.1-2.7)[f]	0.5 (0.0-1.9)	0.6 (0.0-2.1)	
Probability of harm, %	99.4[f]	96.5	96.9	

JAMA avril 2022

REMAP-CAP – conclusion

- Pas d'impact sur les traitements de support
- *Probable* augmentation de la **survie jusqu'au congé**

  + Sous-groupe **anticoagulation NON-thérapeutique**

COR	LOE	
2b	B-R	11. In select critically ill patients hospitalized for COVID-19, add on treatment with an antiplatelet agent to prophylactic dose LMWH/UFH is not well established but might be considered to reduce mortality.[36,50]

jth juillet 2022

JAMA avril 2022

RECOMMENDATIONS AND GUIDELINES

ISTH guidelines for antithrombotic treatment in COVID-19

Sam Schulman[1,2] | Michelle Sholzberg[3] | Alex C. Spyropoulos[4,5] | Ryan Zarychanski[6] | Helaine E. Resnick[7] | Charlotte A. Bradbury[8] | Lisa Broxmeyer | Jean Marie Connors[9] | Anna Falanga[10,11] | Toshiaki Iba[12] | Scott Kaatz[13] | Jerrold H. Levy[14] | Saskia Middeldorp[15] | Tracy Minichiello[16] | Eduardo Ramacciotti[17,18] | Charles Marc Samama[19] | Jecko Thachil[20] | on behalf of the International Society on Thrombosis and Haemostasis

J Thromb Haemost. 2022;20:2214–2225.

DOI:10.1111/jth.15808
jth juillet 2022

COVID-19 et traitement anti-thrombotique

- Soins **non critiques** avec **D-dimères élevés** HEP-COVID, étude multi-plateforme (ATTAC-ACTIV4a-REMAPCAP):
  + Bénéfice de l'anticoagulation pour la survie sans **traitement de support** et événements **thrombotiques**
  + Effets **nuisibles** inhibiteurs **P2Y12** chez population avec anticoagulation **thérapeutique** (ACTIV-4a)
- Soins **intensifs**
  + **Pas de bénéfice** à l'anticoagulation **thérapeutique** (pour les traitements de support)
  + **Possible bénéfice** de survie à l'hospitalisation avec **antiplaquettaires** (REMAP-CAP)
- Bénéfice **à confirmer** des **anticoagulants** oraux directs à la **sortie** de l'hôpital chez patient avec facteurs de risque TEV additionnels (MICHELLE)

RÉSUMÉ

- **Gliflozines** pour le traitement de **l'insuffisance cardiaque**
- Nouvelle classe thérapeutique pour le traitement de l'**obésité** (**GIP / GLP-1**)
- **Gliflozines** et **Finerenone** pour le traitement des néphropathies avec albuminurie
- **Bénéfice CV** aux **ARGLP-1** dans une population à **risque CV faible**
- Traitement de l'**hypertriglycéridémie**
  + **IPE** pour réduire les événements cardiovasculaires
  + **Fibrates** limités à la prévention des **pancréatites** et traitement de la **rétinopathie**

RÉSUMÉ

- *Possible* bénéfice d'une dose **HBPM intermédiaire post partum** pour prévenir les EP et les phlébites superficielles chez les femmes avec ATCD de TEV
- Rôle des **antiplaquettaires** limité chez patients hospitalisés avec la COVID-19
  + *Possible* augmentation de la survie à l'hospitalisation au prix d'une augmentation des saignements surtout si combinaison avec anticoagulation thérapeutique

suppléments

Treatment for Mild Chronic Hypertension during Pregnancy

N Engl J Med 2022;386:1781-92.

CHAP

- Étude ouverte multicentrique à répartition aléatoire
- 2408 femmes enceintes < 23 semaines avec hypertension non sévère
- Seuil traitement de 140/90 versus 160/105

CHIPS

Variable	Less-Tight Control (N = 493)	Tight Control (N = 488)	Adjusted Odds Ratio (95% CI)‡
Small-for-gestational-age newborns — no./total no. (%)¶			
Birth weight <10th percentile	79/491 (16.1)	96/488 (19.7)	0.78 (0.56–1.08)
Birth weight <3rd percentile	23/491 (4.7)	26/488 (5.3)	0.92 (0.51–1.63)

nejm mai 2022
nejm janvier 2015

CHAP - résultats

Outcome	Imputation Analysis (N = 2408)*		Complete-Case Analysis (N = 2325)†			
	Adjusted Risk Ratio (95% CI)	P Value	Active Treatment	Control	Risk Ratio (95% CI)	P Value
			no./total no. (%)			
Primary composite outcome	0.82 (0.74–0.92)	<0.001	353/1170 (30.2)	427/1155 (37.0)	0.82 (0.73–0.92)	<0.001
Preeclampsia with severe features	0.80 (0.70–0.92)		272/1170 (23.3)	336/1155 (29.1)	0.80 (0.70–0.92)	
Medically indicated preterm birth at <35 wk	0.73 (0.60–0.89)		143/1170 (12.2)	193/1155 (16.7)	0.73 (0.60–0.89)	
Placental abruption	0.88 (0.49–1.59)		20/1170 (1.7)	22/1155 (1.9)	0.90 (0.49–1.64)	
Fetal or neonatal death at <28 days	0.81 (0.54–1.22)		41/1170 (3.5)	50/1155 (4.3)	0.81 (0.54–1.21)	
Safety outcome						
Small for gestational age						
<10th percentile	1.04 (0.82–1.31)	0.76	128/1146 (11.2)	117/1124 (10.4)	1.07 (0.85–1.36)	0.56
<5th percentile	0.89 (0.62–1.26)	0.51	58/1146 (5.1)	62/1124 (5.5)	0.92 (0.65–1.30)	0.63

nejm mai 2022

CHAP - conclusion

- Grosse étude en médecine obstétricale
- Bénéfice pour des **critères d'évaluation pertinents**

  + Pré-éclampsie, naissance pré-terme < 35 semaines
- **Sécurité fœtale** avec traitement anti-hypertenseur

THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA

Antihypertensive therapy is recommended for pregnant women with an average systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, regardless of the hypertensive disorder of pregnancy (*strong, moderate*).

CHAP

A diastolic blood pressure of 85 mm Hg should be targeted for pregnant women on antihypertensive therapy with chronic or gestational hypertension (strong, moderate), and a similar target, considered for women with preeclampsia (*conditional, low*).

CHIPS

jogc mai 2022

nejm mai 2022

AHA SCIENTIFIC STATEMENT

Hypertension in Pregnancy: Diagnosis, Blood Pressure Goals, and Pharmacotherapy: A Scientific Statement From the American Heart Association

Hypertension. 2022;79:e21–e41.

Guideline		Hypertension in pregnancy diagnosis*	Treatment threshold, mm Hg	Treatment target, mm Hg
ACOG	2013[1] 2019[2] 2020[3]		≥160/105 with diagnosis of chronic hypertension[1] ≥160/110 if acute[3]/chronic hypertension[2]†	120–159/80–105[1] 120–159/80–109 if chronic[2]†
World Health Organization	2018[142] 2020[143]	Not defined	Not specified‡	Above lower limits of normal[143]
National Institute for Health and Care Excellence	2019[144]		≥140/90	≤135/85
Society of Obstetricians and Gynaecologists, Canada	2018[145] 2020[146]		≥140/90[145,146]	DBP, 85[145,146] <140/90+comorbidities[145]
International Society for the Study of Hypertension in Pregnancy	2018[110]	Plus the absence of preeclampsia features	≥140/90 in office ≥135/85 at home	110–140/85
European Society of Cardiology	2018[147]	"Antenatally unclassified" if first BP measure >20 wk of gestation	≥150/95 ≥140/90+end-organ damage/gestational hypertension	Not specified
Society of Obstetric Medicine of Australia and New Zealand	2014[148]		≥160/100 ≥140/90, optional	Based on clinician assessment

hypertension février 2022

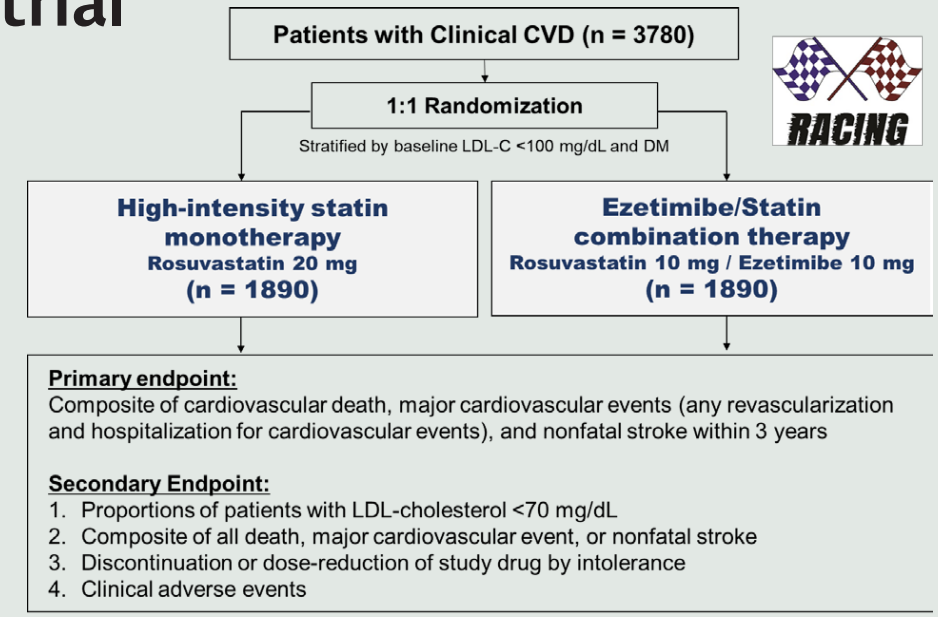
Long-term efficacy and safety of moderate-intensity statin with ezetimibe combination therapy versus high-intensity statin monotherapy in patients with atherosclerotic cardiovascular disease (RACING): a randomised, open-label, non-inferiority trial

- Multicentrique en Corée du sud, non-infériorité, répartition aléatoire, ouverte, initiée par les investigateurs du Centre de recherche cardiovasculaire, conduite
- Patients avec **maladie cardiovasculaire** et indication de statine à haute dose pour une **cible C-LDL < 1.7 mM**

- Question de l'étude:
  + Une statine à dose **modérée** en combinaison avec **Ezetimibe** est-elle non-inférieure à une statine à dose **élevée**?
- Rosuvastatin 10 mg + Ezetimibe 10 mg versus Rosuvastatin 20 mg
- 3780 patients suivis durant 3 ans
- Seuil de non-infériorité 2% de différence absolue entre les deux groupes (erreur alpha unilatérale 5%)

lancet juillet 2022

Long-term efficacy and safety of moderate-intensity statin with ezetimibe combination therapy versus high-intensity statin monotherapy in patients with atherosclerotic cardiovascular disease (RACING): a randomised, open-label, non-inferiority trial



doi.org/10.1016/ S0140-6736(22)00916-3
lancet juillet 2022

	Moderate-intensity statin with ezetimibe combination therapy (n=1894)	High-intensity statin monotherapy (n=1886)	Absolute difference (90% CI)	Hazard ratio (95% CI)	p value
Primary endpoint					
Composite of cardiovascular death, major cardiovascular event, or non-fatal stroke	172 (9·1%)	186 (9·9%)	−0·78% (−2·39 to 0·83)		
Secondary efficacy endpoint					
Composite of all-cause death, major cardiovascular event, or non-fatal stroke	186 (9·8%)	197 (10·4%)	−0·62% (−2·28 to 1·03)	0·94 (0·77 to 1·15)	0·94
Individual clinical endpoint					
Cardiovascular death	8 (0·4%)	6 (0·3%)	0·10% (−0·28 to 0·50)	1·34 (0·46 to 3·85)	0·59
All-cause death	26 (1·4)	22 (1·2)	0·21% (−0·44 to 0·86)	1·19 (0·67 to 2·09)	0·56
Major cardiovascular events	153 (8·1%)	167 (8·9%)	−0·78% (−2·31 to 0·75)	0·91 (0·73 to 1·14)	0·41
Coronary artery revascularisation	91 (4·8%)	89 (4·7%)	0·09% (−1·10 to 1·27)	1·02 (0·76 to 1·37)	0·88
Percutaneous coronary intervention	87	89	..	..	..
Coronary artery bypass surgery	4	0	..	..	..
Peripheral artery revascularisation	8 (0·4%)	7 (0·4%)	0·05% (−0·35 to 0·46)	1·15 (0·42 to 3·16)	0·79
Hospitalisation for ischaemic heart disease	142 (7·5%)	150 (8·0%)	−0·46 (−1·93 to 1·01)	0·94 (0·75 to 1·19)	0·62
Stable angina or unstable angina	120	133	..	..	..
Acute myocardial infarction	22	17	..	..	..
Hospitalisation for heart failure	14 (0·7%)	19 (1·0%)	−0·27% (−0·83 to 0·28)	0·74 (0·37 to 1·47)	0·39
Hospitalisation for peripheral artery disease	8 (0·4%)	7 (0·4%)	0·05% (−0·35 to 0·46)	1·15 (0·42 to 3·16)	0·79
Non-fatal stroke	15 (0·8%)	14 (0·7%)	0·05% (−0·47 to 0·58)	1·07 (0·52 to 2·22)	0·85
Ischaemic stroke	11 (0·6%)	11 (0·6%)	−0·002% (−0·47 to 0·47)	0·99 (0·43 to 2·31)	1·0
Haemorrhagic stroke	4 (0·2%)	3 (0·2%)	0·05% (−0·25 to 0·37)	1·34 (0·30 to 5·97)	0·70

Différence absolue (95% IC)

-2.69-1.13

lancet juillet 2022

RACING - conclusion

- Ajouter Ezetimibe à une statine à dose modérée semble être non-inférieur à une statine à dose élevée
  + Incluant des critères d'évaluation pertinents (mortalité CV)
  + Malgré un taux d'événements plus faible que prévu
  + Population Corée du sud

lancet juillet 2022

Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

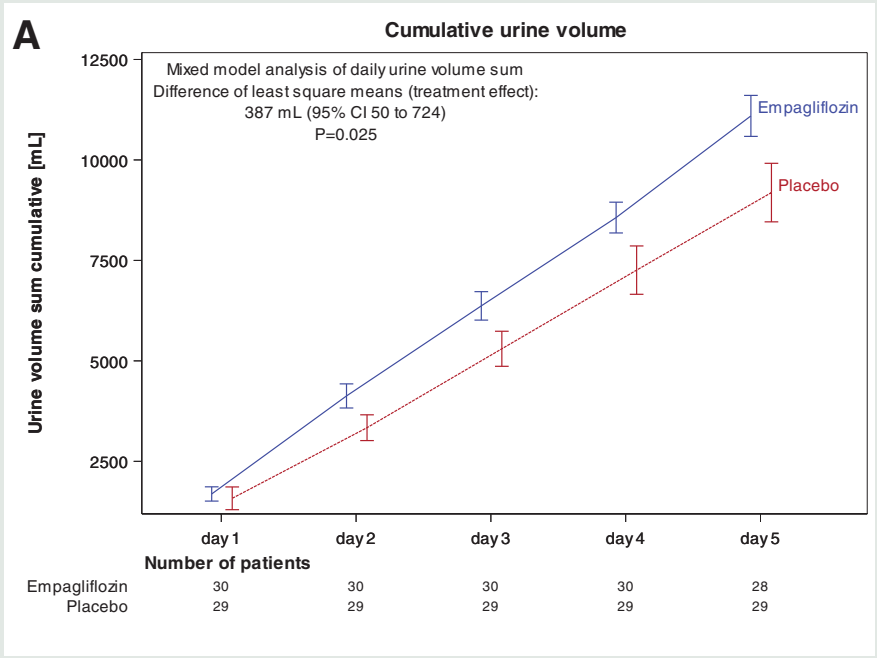
*RECOVERY Collaborative Group**

* 34% recevaient HBPM à dose « plus élevée »

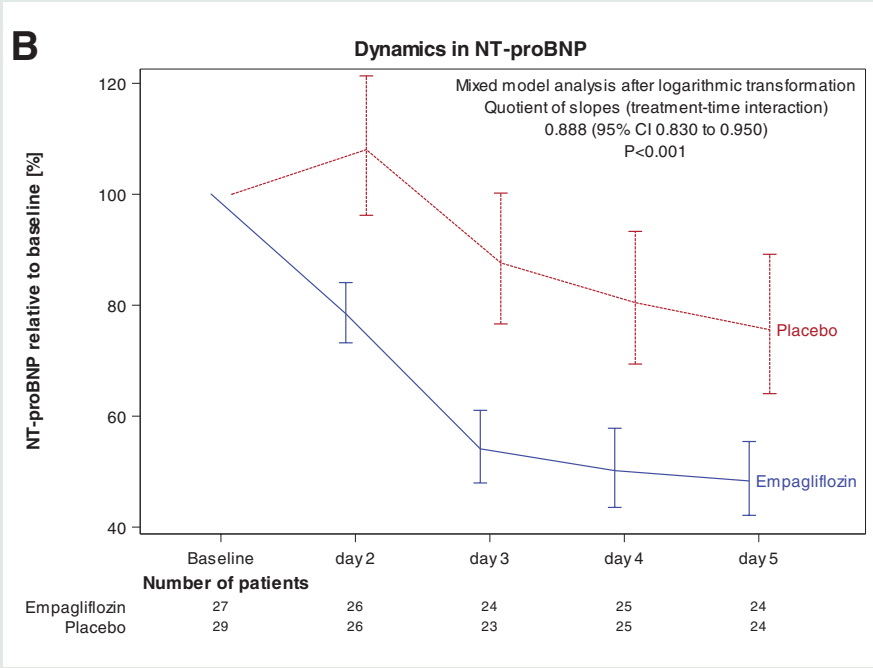
	Treatment allocation		RR (95% CI)	p value
	Aspirin (n=7351)	Usual care (n=7541)		
Primary outcome				
28 day mortality	1222 (17%)	1299 (17%)	0·96 (0·89–1·04)	0·35
Secondary outcomes				
Median time to being discharged alive (IQR), days	8 (5 to >28)	9 (5 to >28)	..	..
Discharged from hospital within 28 days	5496 (75%)	5548 (74%)	1·06 (1·02–1·10)	0·0062
Receipt of invasive mechanical ventilation or death*	1473/6993 (21%)	1569/7169 (22%)	0·96 (0·90–1·03)	0·23
Invasive mechanical ventilation	772/6993 (11%)	829/7169 (12%)	0·95 (0·87–1·05)	0·32
Death	1076/6993 (15%)	1141/7169 (16%)	0·97 (0·90–1·04)	0·39
Subsidiary clinical outcomes				
Use of ventilation	1131/4936 (23%)	1198/5036 (24%)	0·96 (0·90–1·03)	0·30
Non-invasive ventilation	1101/4936 (22%)	1162/5036 (23%)	0·97 (0·90–1·04)	0·36
Invasive mechanical ventilation	296/4936 (6%)	325/5036 (6%)	0·93 (0·80–1·08)	0·35
Successful cessation of invasive mechanical ventilation	135/358 (38%)	135/372 (36%)	1·08 (0·85–1·37)	0·54
Renal replacement therapy	273/7291 (4%)	282/7480 (4%)	0·99 (0·84–1·17)	0·93

lancet janvier 2022

Effects of Early Empagliflozin Initiation on Diuresis and Kidney Function in Patients With Acute Decompensated Heart Failure (EMPAG-HF)



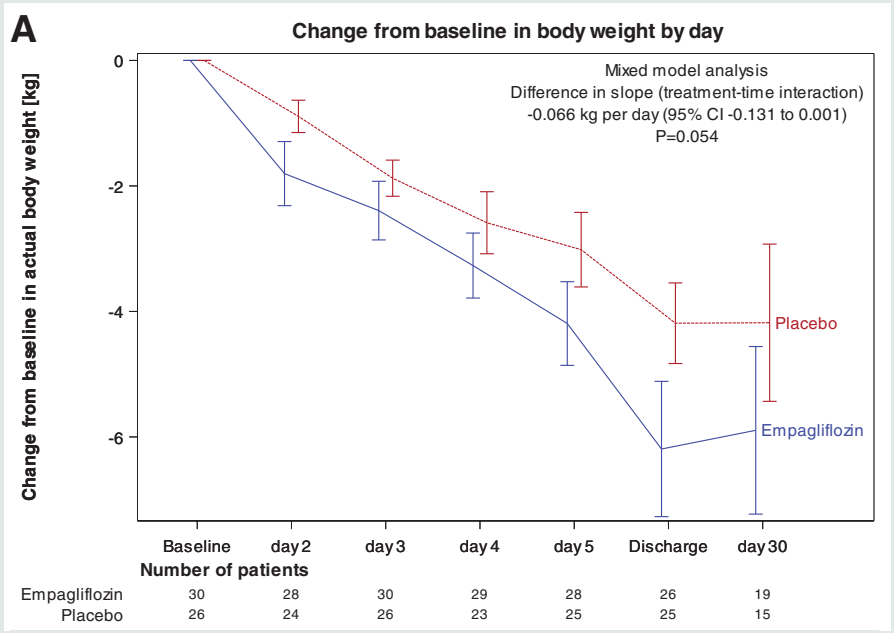
diurèse



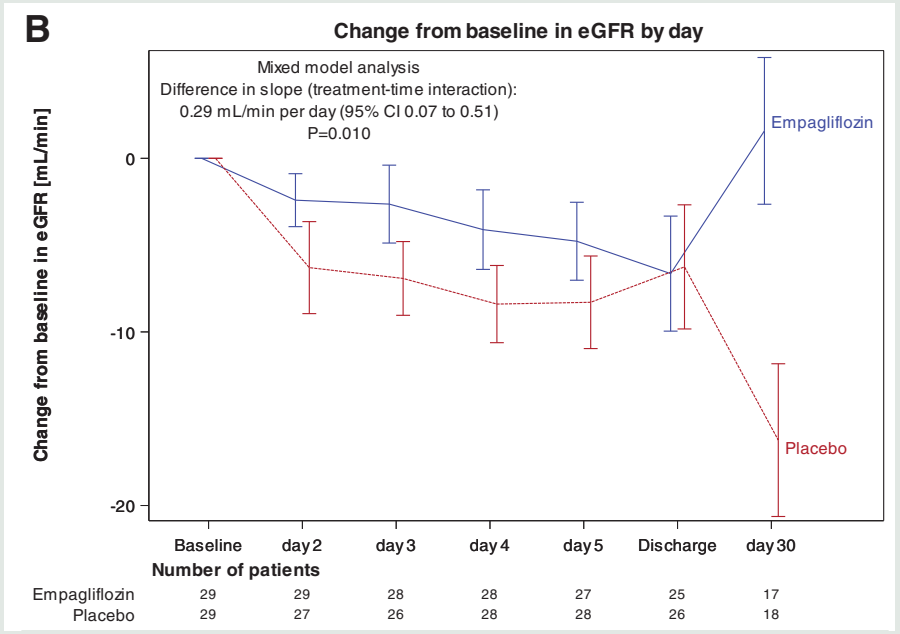
NT-proBNP

Circulation juillet 2022

Effects of Early Empagliflozin Initiation on Diuresis and Kidney Function in Patients With Acute Decompensated Heart Failure (EMPAG-HF)



poids



Fonction rénale

Circulation juillet 2022

Empagliflozin in Patients with Chronic Kidney Disease

The EMPA-KIDNEY Collaborative Group*

Streamlined design

RCT:
Empagliflozin 10 mg once daily
vs. matching placebo

Inclusion criteria:
eGFR ≥ 20, < 45 mL/min/1.73 m^2;
or ≥ 45, < 90 and uACR ≥ 200 mg/g

Composite primary outcome:
- CV or renal death
- Maintenance dialysis or kidney transplant
- Sustained eGFR < 10 mL/min/1.73 m^2 or sustained ≥ 40% eGFR decline

Baseline characteristics

n = 6609

Mean age 64 (SD 14) years

33% ♀
67% ♂

8 countries:
Europe, N. America and Asia

eGFR, mL/min/1.73 m^2:
Mean 37.5 (SD 15)
78% with eGFR < 45
34% with eGFR < 30

Primary renal diagnoses:
31% diabetic nephropathy
25% glomerular disease
22% ischaemic/hypertensive
12% other and 10% unknown

uACR, mg/g:
Median 412 (IQR 94–1190)
48% with uACR < 300

Comorbidity:
46% diabetes
27% cardiovascular disease

Conclusion

The EMPA-KIDNEY trial has recruited a large, widely generalizable CKD population with high proportions of the types of people without diabetes and with low eGFR or uACR who have not been included in previous trials of SGLT2i. Results are anticipated in 2022.

DOI:10.1056/NEJMoa2204233
nejm novembre 2022

EMPA-KIDNEY – résultats

Outcome	Empagliflozin (N = 3304)		Placebo (N = 3305)		Hazard Ratio (95% CI)*	P Value
	no. (%)	*no. of events/100 patient-yr*	*no. (%)*	*no. of events/100 patient-yr*		
Primary outcome: progression of kidney disease or death from cardiovascular causes	432 (13.1)	6.85	558 (16.9)	8.96	0.72 (0.64–0.82)	<0.001
Key secondary outcomes†						
Hospitalization for heart failure or death from cardiovascular causes	131 (4.0)	2.04	152 (4.6)	2.37	0.84 (0.67–1.07)	0.15
Hospitalization for any cause‡	—	24.8	—	29.2	0.86 (0.78–0.95)	0.003
Death from any cause	148 (4.5)	2.28	167 (5.1)	2.58	0.87 (0.70–1.08)	0.21
Other secondary outcomes						
Progression of kidney disease	384 (11.6)	6.09	504 (15.2)	8.09	0.71 (0.62–0.81)	
Death from cardiovascular causes	59 (1.8)	0.91	69 (2.1)	1.06	0.84 (0.60–1.19)	
End-stage kidney disease or death from cardiovascular causes§	163 (4.9)	2.54	217 (6.6)	3.40	0.73 (0.59–0.89)	

nejm novembre 2022

Autres articles d'intérêt

Piccini JP, Caso V, Connolly SJ, et al. Safety of the oral factor Xia inhibitor asundexian copared with apixaban in patients with atrial fibrillation (PACIFIC-AF): a multicentre, randomised, double-blind, double-dummy,dose-finding phase 2 study.

***Lancet* 2022 Apr 9;399(10333):1383-1390.**

Douketis JD et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.

***CHEST* 2022; 162(5):e207-e243.**

Autres articles d'intérêt

Castellano JM, Pocock SJ, Bhatt DL, et al. Polypill strategy in secondary cardiovascular prevention. ***N Engl J Med*** **2022;387:967-977**

Yoshimura S, Sakai N, Yamagami H, et al. Endovascular therapy for acute stroke with a large ischemic region. ***N Engl J Med*** **2022;386:1303-13.**

Bearne LM, Volkmer B, Peacock J, et al; the MOSAIC Trial Collaboration. Effect of a home-based, walking exercise behavior change intervention vs usual care on walking in adults with peripheral artery disease: the MOSAIC randomized clinical trial. ***JAMA.*** **2022;327(14):1344-1355.**

Autres articles d'intérêt

Kuroda M, Tamiya E, Nose T, et al. Effect of 15-mg edoxaban on clinical outcomes in 3 age strata in older patients with atrial fibrillation: a prespecified subanalysis of the ELDERCARE-AF randomized clinical trial.

***JAMA Cardiol*. 2022;7(6):583-590.**

Kearon C, de Wit K, Parpia S, Schulman S, SpencerF A, Sharma S et al. Diagnosis of deep vein thrombosis with D-dimer adjusted to clinical probability: prospective diagnostic management study

***BMJ* 2022;376:e067378.**

Autres articles d'intérêt

Menon BK, Buck BH, Singh N, et al. Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non- inferiority trial.

***Lancet* 2022; 400: 161–69**

Gao P, Wang T, Wang D, et al. Effect of stenting plus medical therapy vs medical therapy alone on risk of stroke and death in patients with symptomatic intracranial stenosis: the CASSISS randomized clinical trial. ***JAMA*. 2022;328(6):534-542.**

Devereaux PJ et al; POISE-3 Investigators. Tranexamic Acid in Patients Undergoing Noncardiac Surgery. ***N Engl J Med* 2022 May 26;386(21):1986-1997.**

Autres articles d'intérêt

Chang RW, Tucker LY, Rothenberg KA, et al. Incidence of ischemic stroke in patients with asymptomatic severe carotid stenosis without surgical intervention. ***JAMA*. 2022;327(20):1974-1982.**

Banovic M, et al; AVATAR Trial Investigators. Aortic Valve Replacement Versus Conservative Treatment in Asymptomatic Severe Aortic Stenosis: The AVATAR Trial. ***Circulation*. 2022 Mar;145(9):648-658.**

Abramson BL et al. Canadian Cardiovascular Society 2022 Guidelines for Peripheral Arterial Disease. ***Can J Cardiol*. 2022 May;38(5):560-587.**

Autres articles d'intérêt

Mackenzie IS, Rogers A, Poulter NR, Williams B, Brown MJ, Webb DJ, Ford I, Rorie DA, Guthrie G, Grieve JWK, Pigazzani F, Rothwell PM, Young R, McConnachie A, Struthers AD, Lang CC, MacDonald TM; TIME Study Group. Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study): a prospective, randomised, open-label, blinded-endpoint clinical trial. ***Lancet.*** **2022 Oct 22;400(10361):1417-1425.**

International Consensus Meeting on Venous Thromboembolism (problèmes orthopédiques). ***J Bone Joint Surg.*** **March 16th 2022; vol 104 issue Suppl 1**

Autres articles d'intérêt

Tao C, Nogueira RG, Zhu Y, et al. Trial of endovascular treatment of acute basilar-artery occlusion. ***N Engl J Med*** **2022;387:1361-1372.**

Liu D, Huang Y, Huang C, Yang S, Wei X, Zhang P, Guo D, Lin J, Xu B, Li C, He H, He J, Liu S, Shi L, Xue Y, Zhang H. Calorie Restriction with or without Time-Restricted Eating in Weight Loss. ***N Engl J Med*** **2022;386:1495-1504.**

Delgado-Lista J et al. Long-term secondary prevention of cardiovascular disease with a Mediterranean diet and a low-fat diet (CORDIOPREV): a randomised controlled trial.

Lancet **2022 May 14;399(10338):1876-1885.**

Autres articles d'intérêt

Greenberg SM, Ziai WC, Cordonnier C, Dowlatshahi D, Francis B, Goldstein JN, et al; American Heart Association/American Stroke Association. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association.

***Stroke*. 2022 Jul;53(7):e282-e361.**

Woller SC, Stevens SM, Kaplan D, Wang TF, Branch DW, Groat D, Wilson EL, Armbruster B, Aston VT, Lloyd JF, Rondina MT, Elliott CG. Apixaban compared with warfarin to prevent thrombosis in thrombotic antiphospholipid syndrome: a randomized trial. ***Blood* Adv. 2022 Mar 22;6(6):1661-1670.**

Autres articles d'intérêt

CRISTAL Study Group, Sidhu VS et al. Effect of Aspirin vs Enoxaparin on Symptomatic Venous Thromboembolism in Patients Undergoing Hip or Knee Arthroplasty: The CRISTAL Randomized Trial.

***JAMA*. 2022 Aug 23;328(8):719-727.**

Agarwal R, Sinha AD, Cramer AE, Balmes-Fenwick M, Dickinson JH, Ouyang F, Tu W. Chlorthalidone for Hypertension in Advanced Chronic Kidney Disease.

***N Engl J Med.* 2021 Dec 30;385(27):2507-2519.**

Autres articles d'intérêt

UK TAVI Trial Investigators, Toff WD et al. Effect of Transcatheter Aortic Valve Implantation vs Surgical Aortic Valve Replacement on All-Cause Mortality in Patients With Aortic Stenosis: A Randomized Clinical Trial. ***J***

***AMA*. 2022 May 17;327(19):1875-1887.**

Devereaux PJ et al; VISION Cardiac Surgery Investigators. High-Sensitivity Troponin I after Cardiac Surgery and 30-Day Mortality.

***N Engl J Med.* 2022 Mar 3;386(9):827-836.**

Autres articles d'intérêt

Vaduganathan M, Docherty KF, Claggett BL, Jhund PS, de Boer RA, Hernandez AF, Inzucchi SE, Kosiborod MN, Lam CSP, Martinez F, Shah SJ, Desai AS, McMurray JJV, Solomon SD. SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials.

Lancet. **2022 Sep 3;400(10354):757-767.**