

**Innovations thérapeutiques :  
dans la maladie coronaire  
dans le diabète  
dans l'insuffisance cardiaque**

**Pr Olivier Hanon**  
**Hôpital Broca, Paris**

# Traitements anti thrombotiques ?

**Aspirine**

**Clopidogrel**

**Prasugrel**

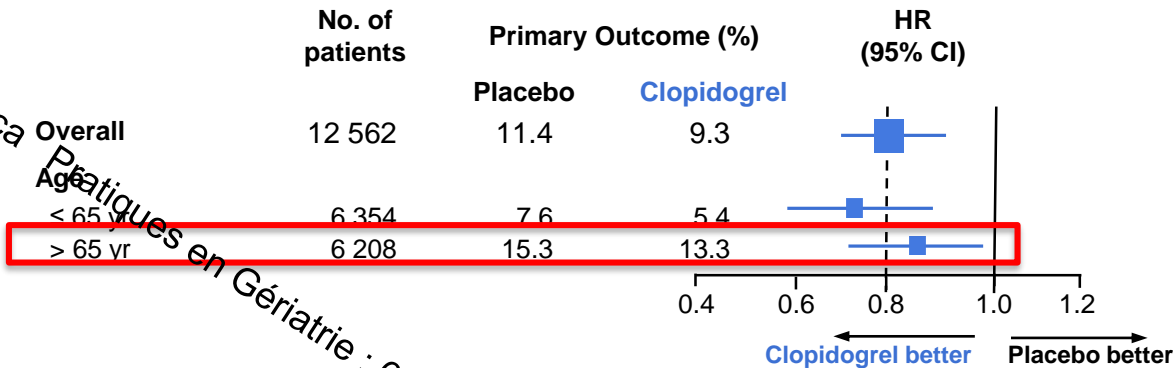
**Ticagrelor**

**SCA : bithérapie pendant 1 an**

# Efficacité du Clopidogrel chez les patients âgés

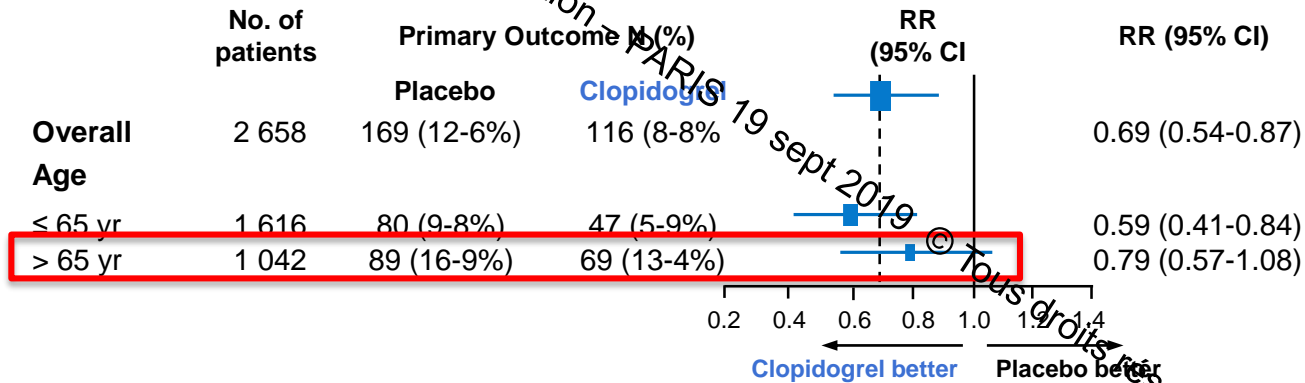
Journée Scientifique de Broca  
Etude **CURE**<sup>1</sup>

**Critère Primaire :**  
mortalité CV  
ou IDM ou AVC  
(suivi moyen à 9 mois)



Etude **PCI-CURE**<sup>2</sup>

**Critère Primaire :**  
mortalité CV ou IDM  
ou revascularisation  
en urgence à 30 jours  
(suivi moyen 8 mois)



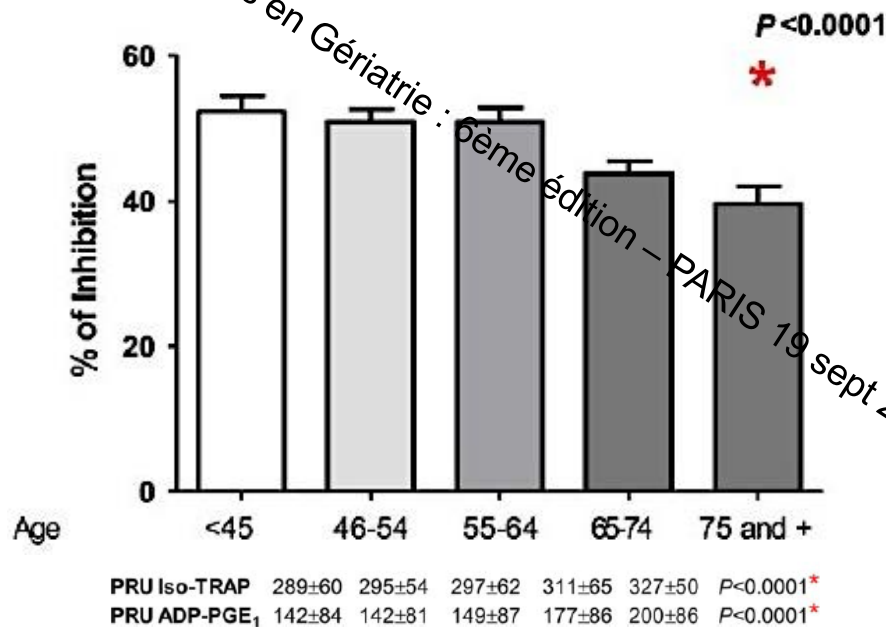
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1. Yusuf S. N Engl J Med 2001;345:494-502. 2. Mehta SR. Lancet 2001;358:527-33.

# Réponse au Clopidogrel chez les patients âgés

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**SENIOR-PLATELET**  
 Etude

**Inhibition plaquettaire  
 avec 75mg de Clopidogrel**



➤ **La réponse au Clopidogrel est significativement diminuée chez les patients âgés**

## Bon usage des agents antiplaquettaires

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Pour le **prasugrel**, la survenue significativement plus fréquente d'accidents hémorragiques chez les sujets de plus de 75 ans a conduit à **contre-indiquer ce médicament après 75 ans en France** (alors qu'il est autorisé dans certains pays à demi-dose).

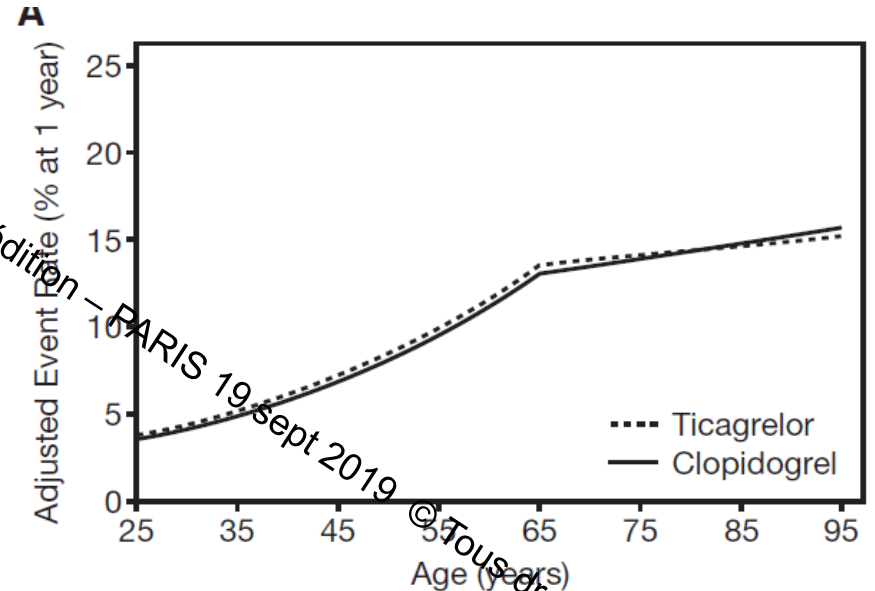
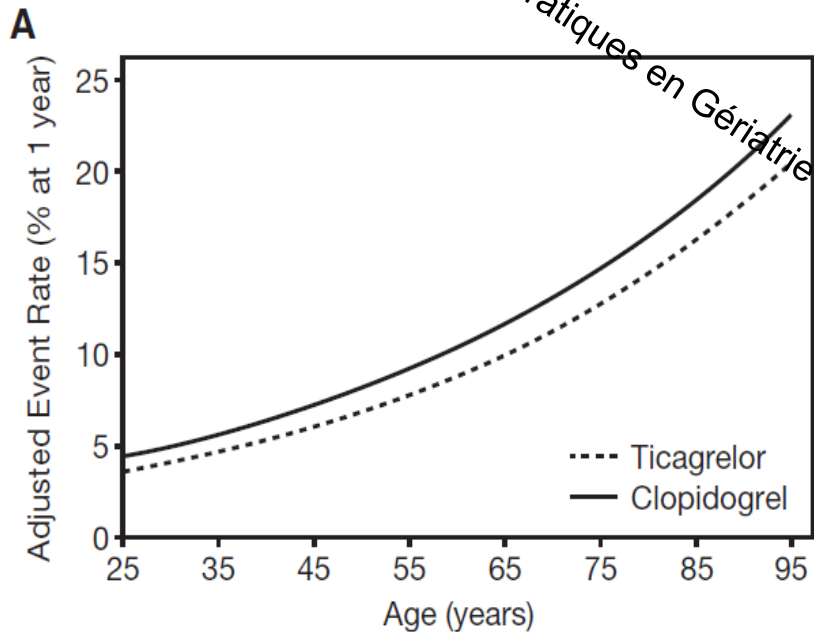
# Ticagrelor Versus Clopidogrel in Elderly Patients With Acute Coronary Syndromes: A Substudy From the Prospective Randomized PLATelet Inhibition and Patient Outcomes (PLATO) Trial

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Pratiques en Gériatrie

Primary composite outcome CV death/MI/stroke

Overall major bleeding



# Outcomes in patients treated with ticagrelor or clopidogrel after acute myocardial infarction: experiences from SWEDEHEART registry

N= 45 073 ACS patients enrolled into Swedish Web system of Evidence-based care in between 1 January 2010 and 31 December 2013.

**Table 2** Association between use of ticagrelor vs. clopidogrel and outcomes

Event	Ticagrelor	Clopidogrel	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
<b>Primary outcome</b>				
Death, MI, or stroke	11.7	22.3	0.49 (0.46–0.53)	0.85 (0.78–0.93)
<b>Secondary outcomes</b>				
Death	5.8	12.9	0.43 (0.39–0.47)	0.83 (0.75–0.92)
MI	6.1	10.8	0.52 (0.47–0.58)	0.89 (0.78–1.01)
Stroke	1.8	3.8	0.53 (0.44–0.63)	0.81 (0.65–1.01)
<b>Risk of bleeding</b>				
Admission with bleeding	5.5	5.2	1.0 (0.92–1.20)	1.20 (1.04–1.40)

# Efficacy and safety outcomes of ticagrelor compared with clopidogrel in elderly Chinese patients with acute coronary syndrome

A double-blinded, randomized controlled study

Patients older than 65 years, with ACS, F up 12 months

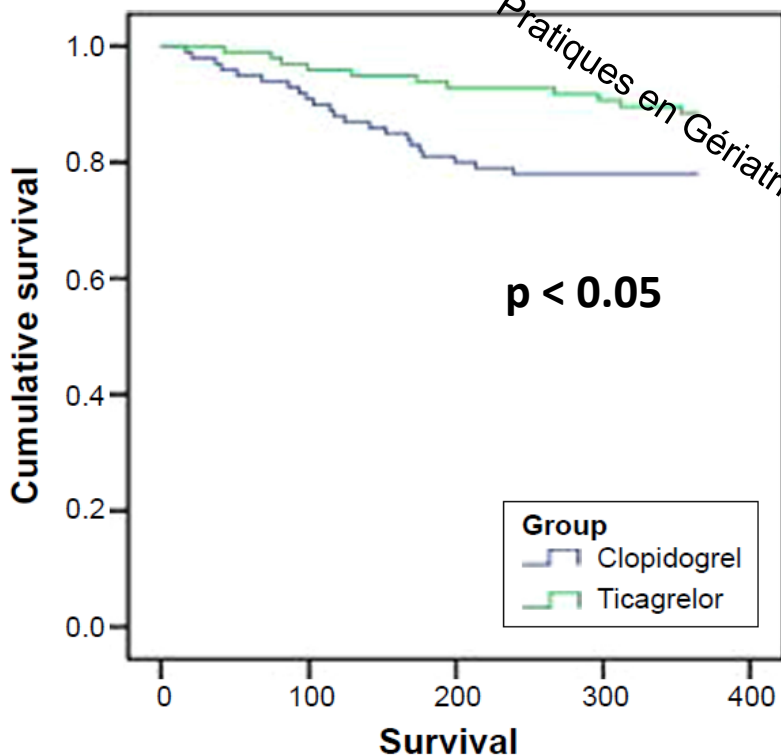


Figure 1 Kaplan-Meier estimate of composite of CV death/MI/stroke for all patients using clopidogrel or ticagrelor.

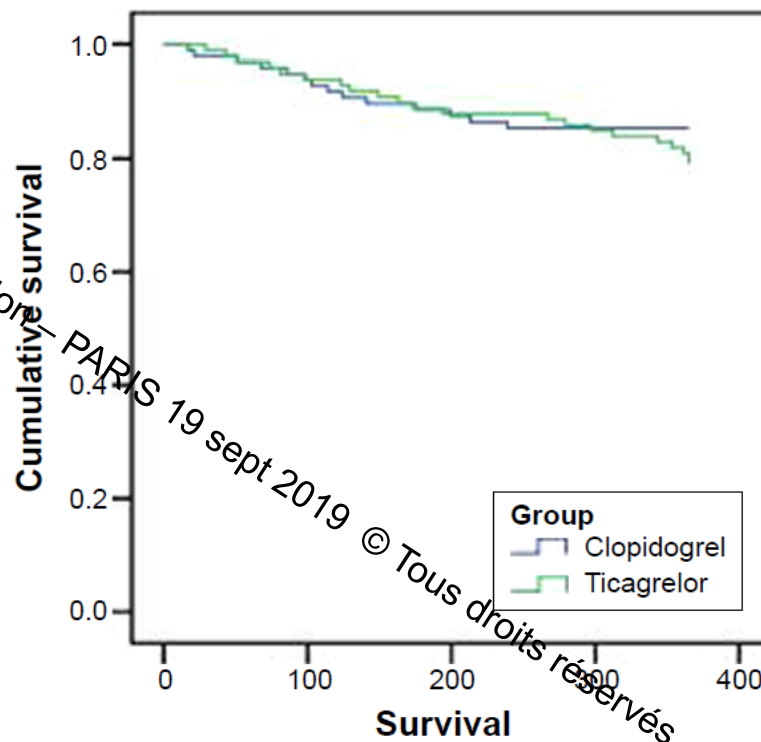


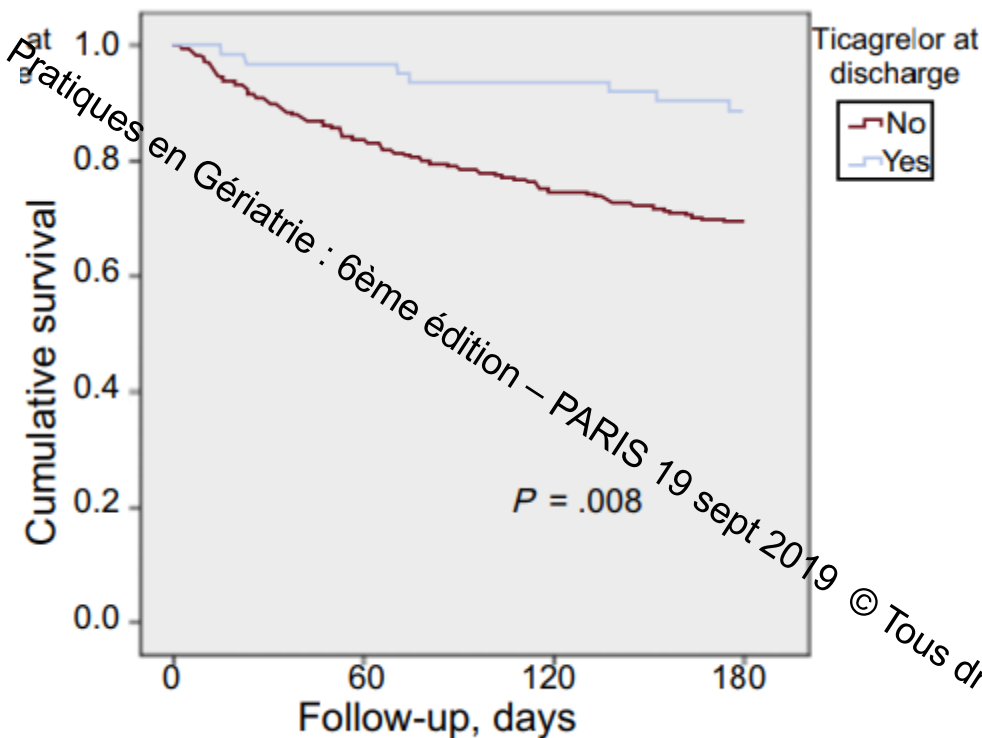
Figure 2 Kaplan-Meier estimate of bleeding for all patients using clopidogrel or ticagrelor.



# Clinical Characteristics and Prognosis of Very Elderly Patients With Acute Coronary Syndrome Treated With Ticagrelor: Insights From the LONGEVO-SCA Registry

Patients aged 80 years with NSTEMI from 44 Spanish hospitals

Readmission



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# Durée de la bithérapie chez le sujet très âgé :

## 1 an ou 3-6 mois

P2Y <sub>12</sub> inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk.	IIb	A
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Ticagrelor 60 mg b.i.d preferred over other oral P2Y<sub>12</sub> inhibitors for DAPT continuation >12 months in post-MI

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# 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases



**ESC**  
European Society  
of Cardiology

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# Cardiovascular risk categories in patients with DM

## Very high-risk

Patients with DM and established CVD  
or other target organ damage<sup>a</sup>  
or three or more major risk factors<sup>b</sup>  
or early onset T1DM of long duration (>20 years)

## High-risk

Patients with DM duration  $\geq 10$  years without target organ damage<sup>a</sup> plus  
any other additional risk factor<sup>b</sup>

## Moderate-risk

Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10  
years, without other risk factors

<sup>a</sup> proteinuria, renal impairment defined as  $eGFR \geq 30 \text{ mL/min/1.73m}^2$ .

<sup>b</sup> age, hypertension, dyslipidemia, smoking, obesity.

# Type 2 DM - Drug naïve patients

ASCVD, or high / very high CV risk (target organ damage or multiple risk factors)\*

+

-

**SGLT2 inhibitor or GLP-1 RA Monotherapy§**

**Metformin Monotherapy**

If HbA<sub>1c</sub> above target

If HbA<sub>1c</sub> above target

Add Metformin

DPP-4i    GLP-1 RA    SGLT2i if eGFR adequate    TZD

If HbA<sub>1c</sub> above target

If HbA<sub>1c</sub> above target

- Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
- DPP-4i if not on GLP-1 RA
- Basal insulin
- TZD (not in HF pat)
- SU

SGLT2i or TZD    SGLT2i or TZD    GLP-1 RA or DPP-4i or TZD    SGLT2i or DPP-4i or GLP-1 RA

If HbA<sub>1c</sub> above target

Continue with addition of other agents as outlined above

If HbA<sub>1c</sub> above target

- Consider the addition of sulfonylurea OR basal insulin:
- Choose later generation SU with lower risk of hypoglycaemia
  - Consider basal insulin with lower risk of hypoglycaemia

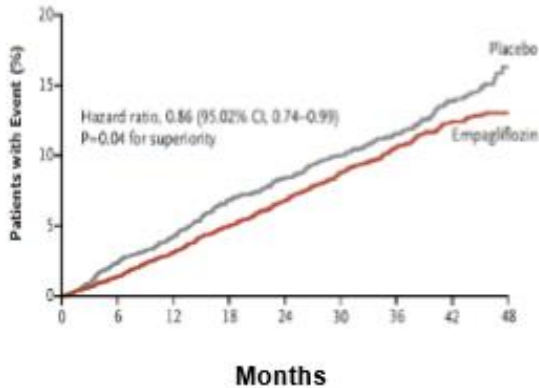
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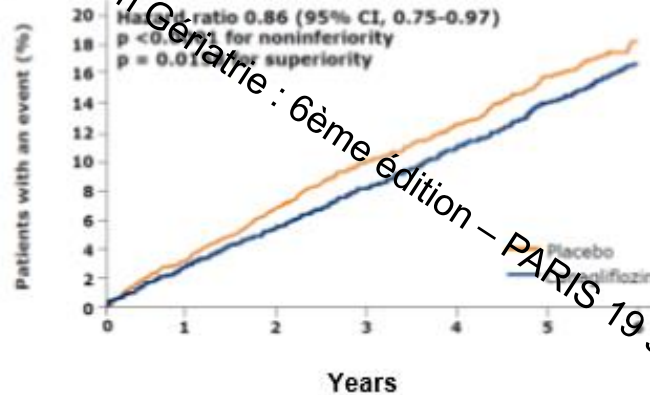
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# CVOTs with SGLT2 inhibitors (3P-MACE endpoint)

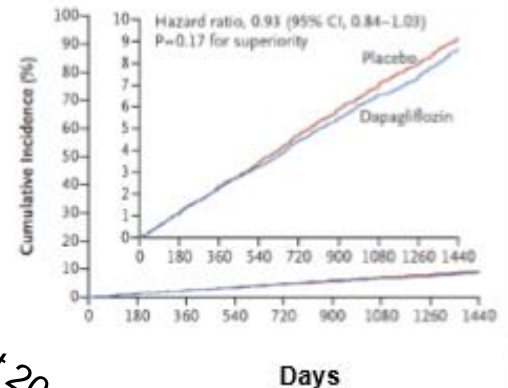
### EMPA-REG Outcome<sup>1</sup>



### CANVAS Program<sup>2</sup>



### DECLARE<sup>3</sup>



1. Zinman B et al. N Engl J Med. 2015
2. Neal B et al. N Engl J Med 2017
3. Wiviott SD et al. N Engl J Med 2018

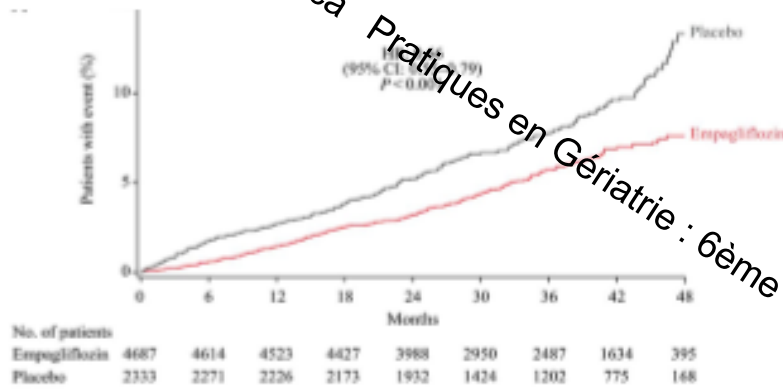
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# CVOTs with SGLT2 inhibitors

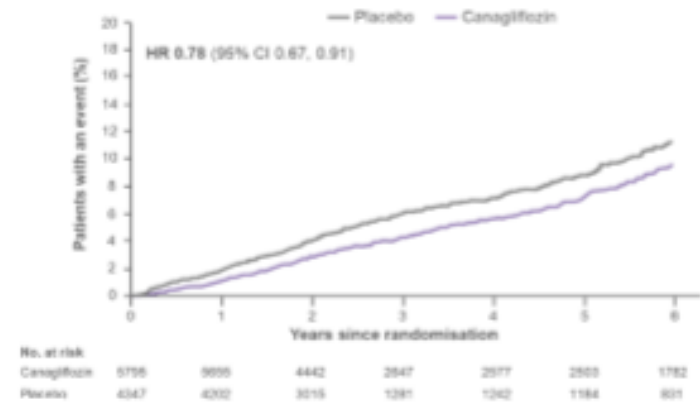
## (HF hospitalization and CV death)

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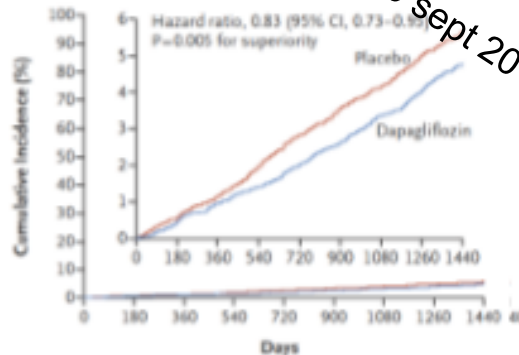
### EMPA-REG Outcome<sup>1</sup>



### CANVAS Program<sup>2</sup>



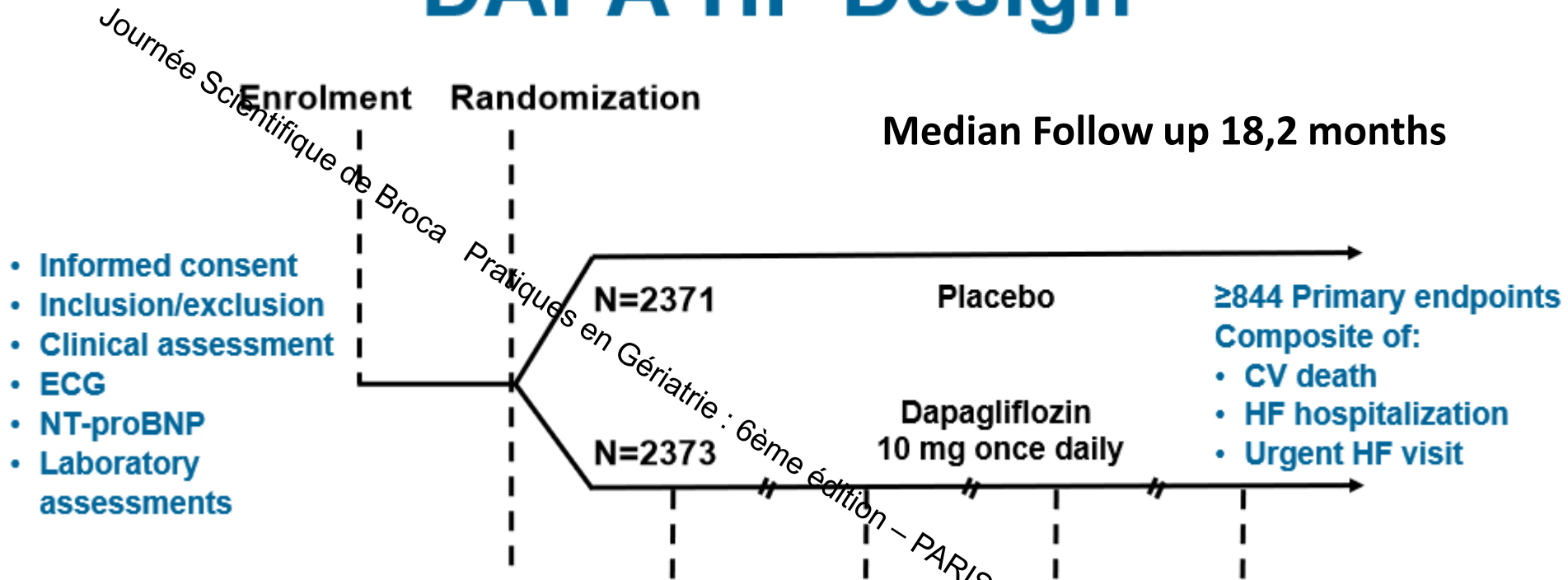
### DECLARE



1. Zinman B et al. N Engl J Med. 2015
2. Neal B et al. N Engl J Med 2017
3. Wiviott SD et al. N Engl J Med 2018

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# DAPA-HF Design

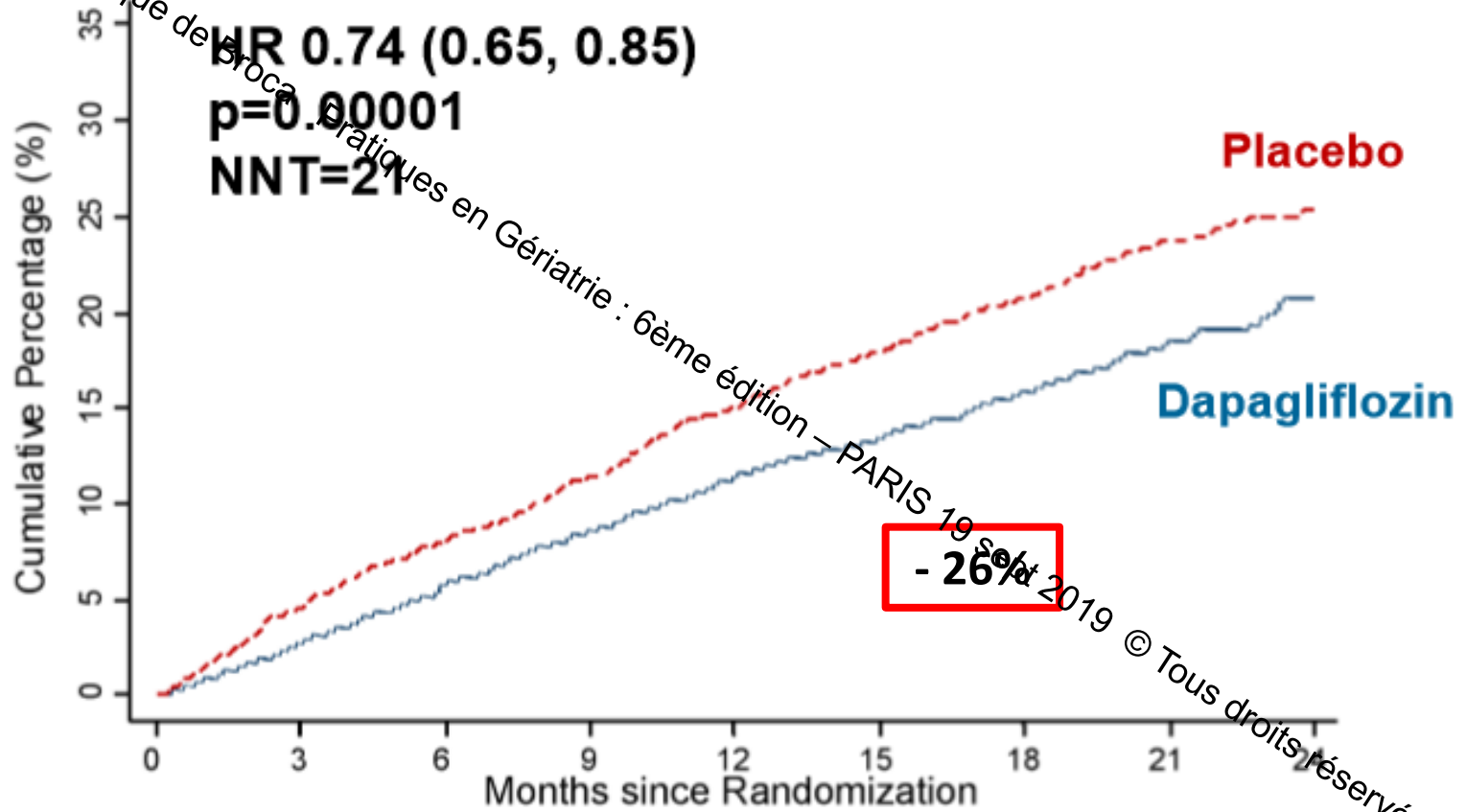


- **Informed consent**
  - **Inclusion/exclusion**
  - **Clinical assessment**
  - **ECG**
  - **NT-proBNP**
  - **Laboratory assessments**
- **Key inclusion criteria:** Symptomatic HF; EF  $\leq 40\%$ ; NT-proBNP  $\geq 600$  pg/ml (if hospitalized for HF within last 12 months  $\geq 400$  pg/mL; if atrial fibrillation/flutter  $\geq 900$  pg/mL)



# Primary composite outcome

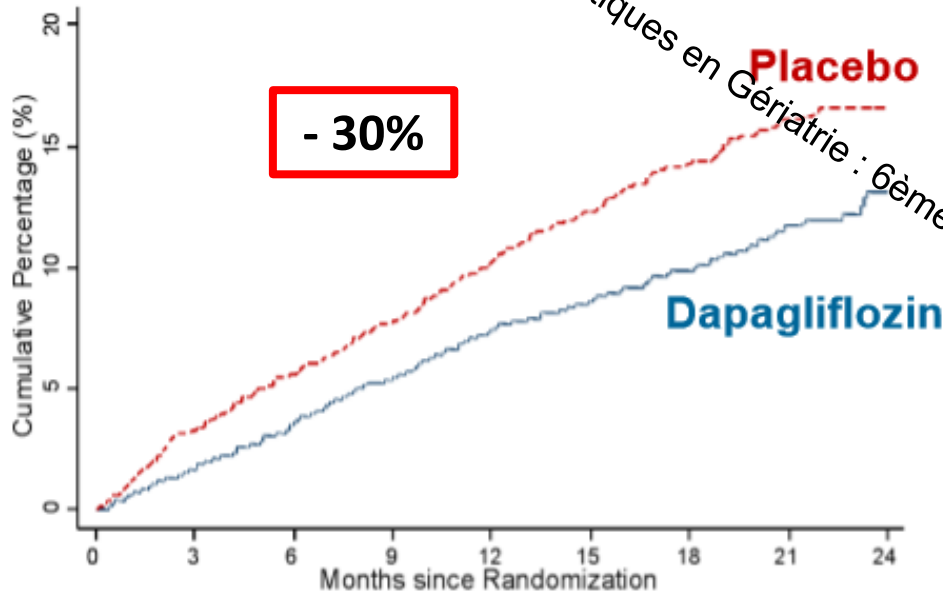
CV Death/HF hospitalization/Urgent HF visit



# Components of primary outcome

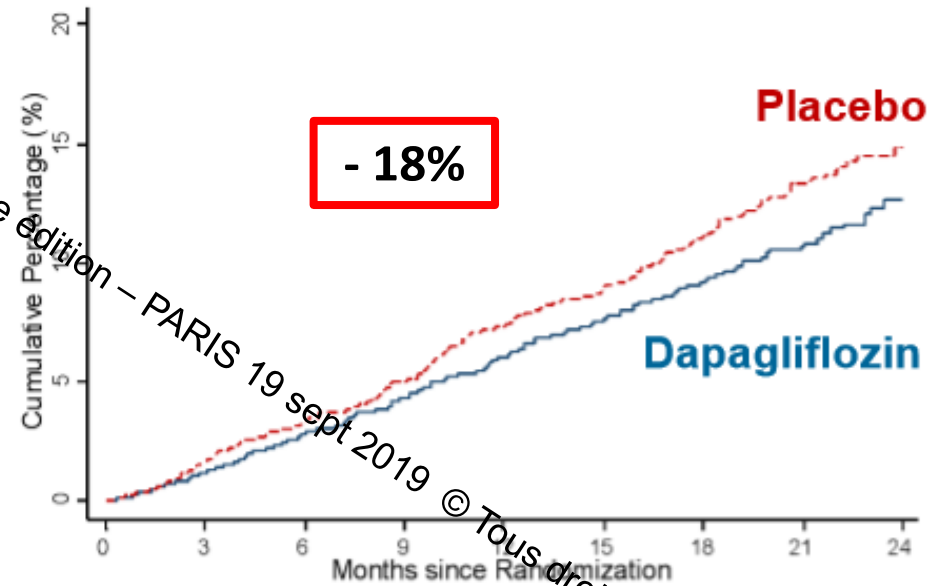
## Worsening HF event

HR 0.70 (0.59, 0.83); p=0.00003

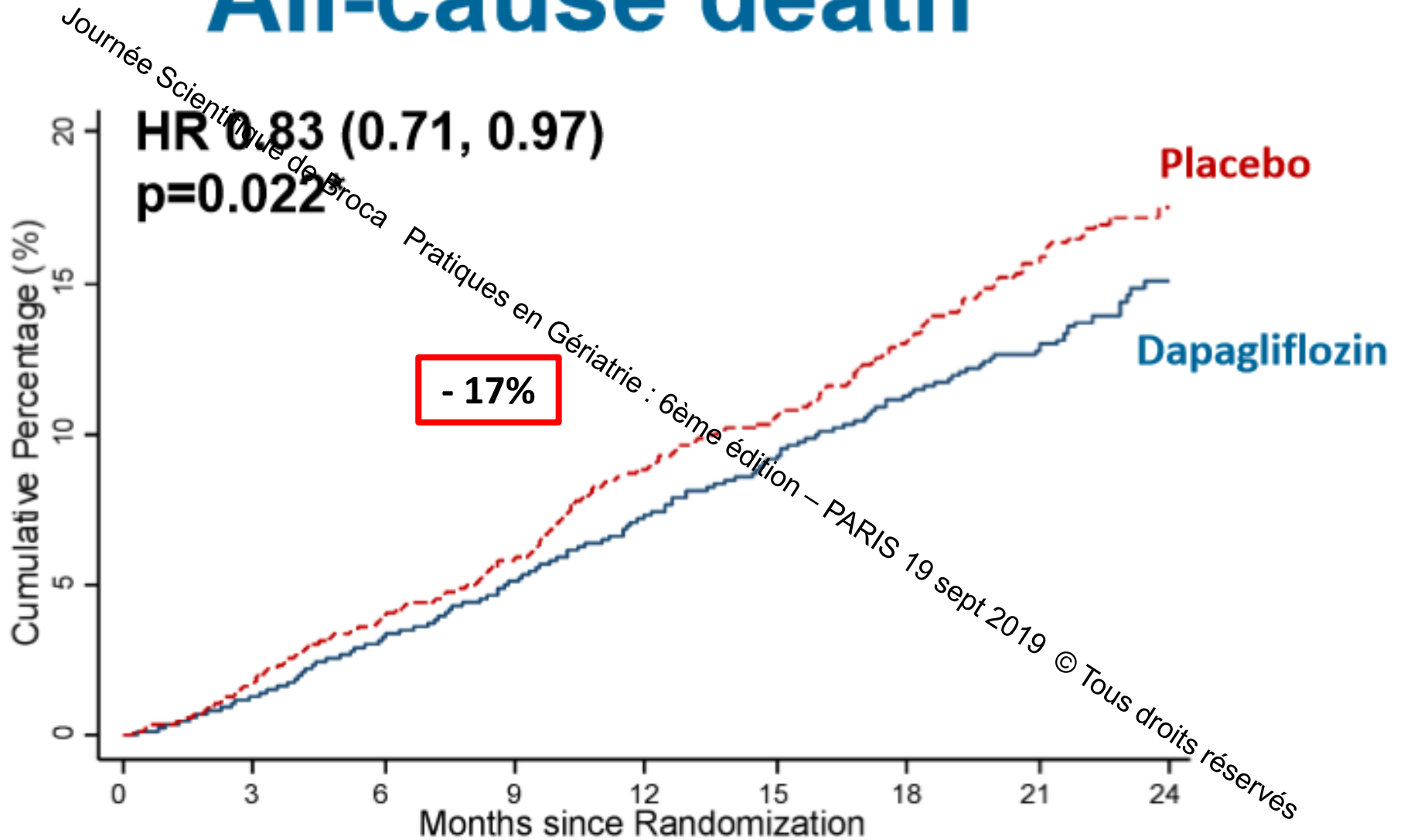


## Cardiovascular death

HR 0.82 (0.69, 0.98); p=0.029

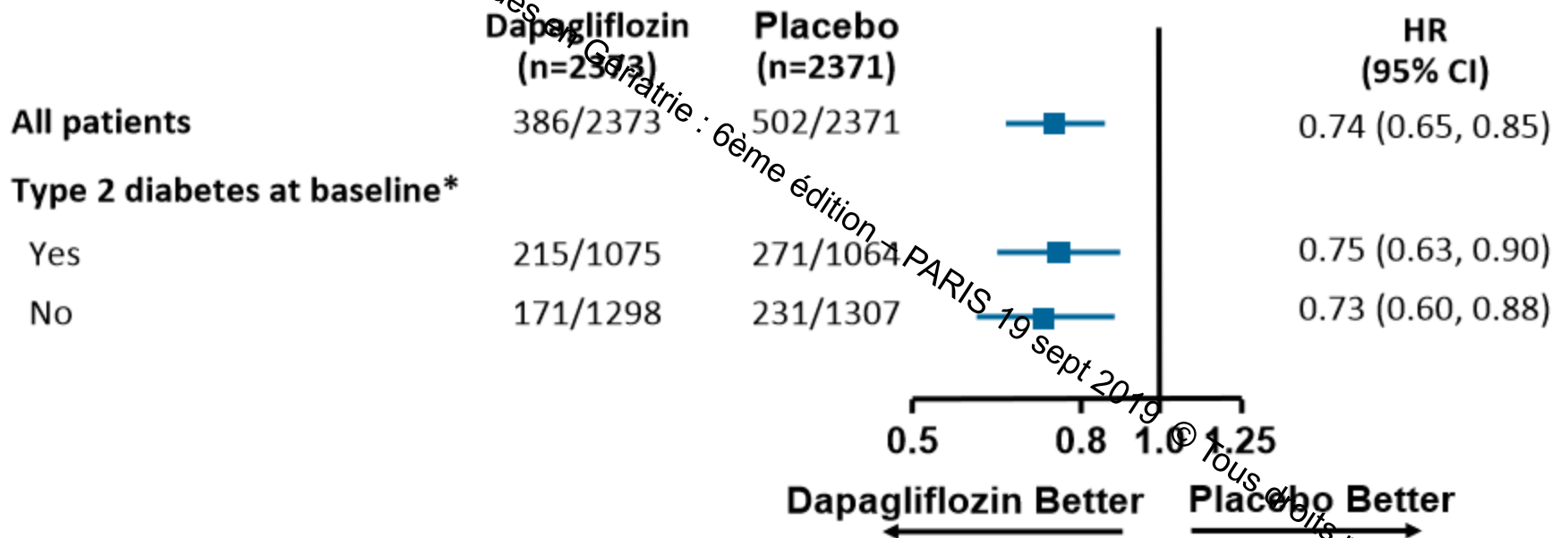


# All-cause death



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# No diabetes/diabetes subgroup: Primary endpoint



\*Defined as history of type 2 diabetes or HbA1c  $\geq 6.5\%$  at both enrollment and randomization visits.

# Summary and conclusions

- Dapagliflozin reduced the risk of worsening heart failure events and cardiovascular death, and improved symptoms, in patients with HFrEF, when added to standard therapy
- The relative and absolute risk reductions in death and hospitalization were substantial, clinically important, and consistent across important subgroups, including patients **without T2D**
- Dapagliflozin was well tolerated and the rate of treatment discontinuation was low
- Dapagliflozin offers a new approach to the treatment of **LVEF HFrEF**

# Conclusions

- **Les thérapeutiques du patient âgé à haut risque vasculaire changent**
  - **Coronarien :**
    - **Ticagrelor**
  - **Diabétique :**
    - **Inhibiteurs SGLT2**
    - **Agonistes GLP1**
  - **Insuffisance cardiaque :**
    - **IEC/BB/Sacubitril-valsartan/Fer**
    - **Inhibiteurs SGLT2**
- **Mais peu de données après 80 ans,**  
**=> Besoin d'études spécifiques +++**