01 - 03 DÉCEMBRE 2021
21e CONGRÈS NATIONAL
Exercer et enseigner la médecine générale
CNGE COLLÈGE ACADÉMIQUE
Grand Palais LILLE
#CNGE2021
www.congrescnge.fr

DOI: 10.1002/prp2.844

PRP BRITISH PHARMACOLOGICAL SOCIETY

ORIGINAL ARTICLE

Benefits and adverse effects of sacubitril/valsartan in patients with chronic heart failure: A systematic review and meta-analysis

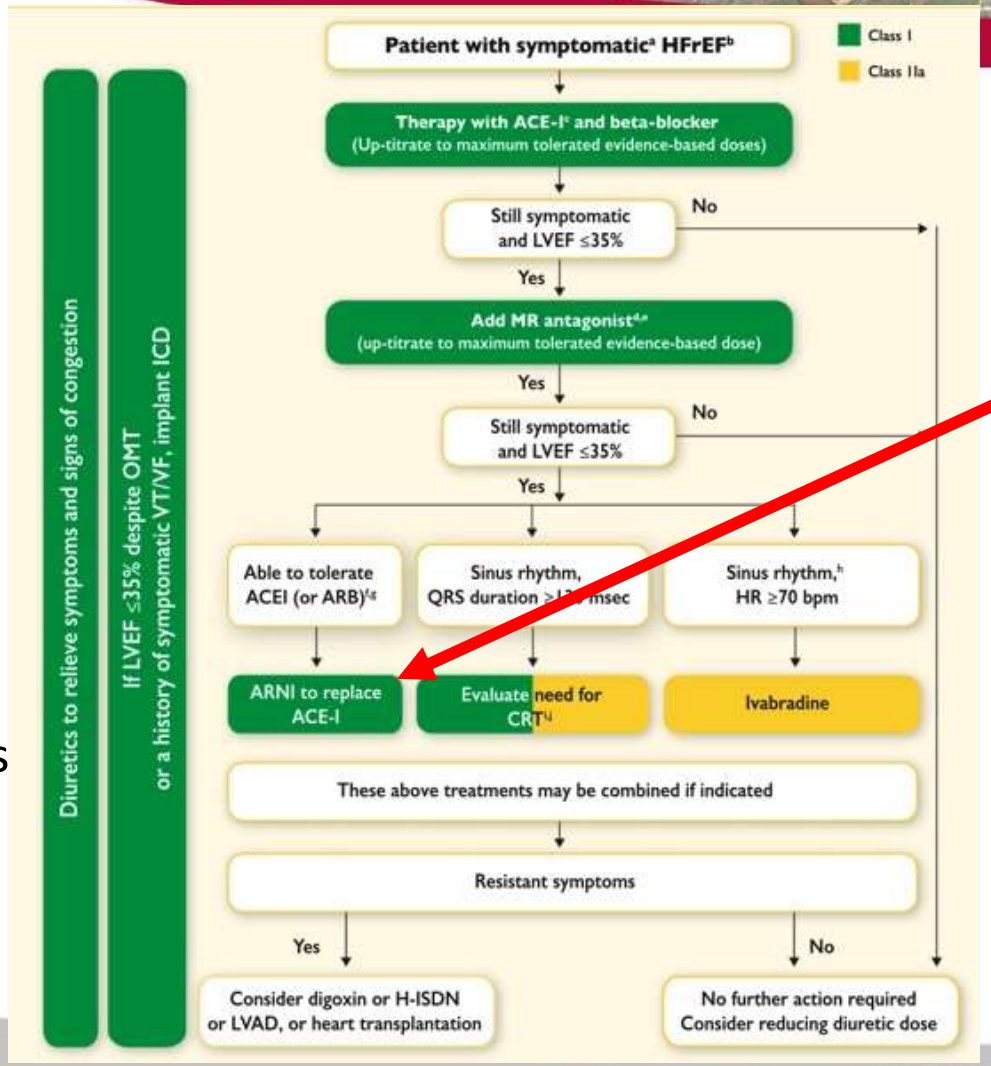
Elodie Charuel[1,2] | Thibault Menini[1,2] | Sabrina Bedhomme[2,3] | Bruno Pereira[4] | Nathalie Piñol-Domenech[5] | Suzy Bouchant[1] | Rémy Boussageon[6] | Sylvaine Bœuf-Gibot[1] | Helene Vaillant-Roussel[1,2,4]

CONTEXTE

Insuffisance cardiaque

1-2 % population des pays développés

>10% après 70 ans



ARNI
sacubitril/valsartan
Entresto®

CONTEXTE

REB : Reconstruire the Evidence Base

Quelles données ?

1 seul ECR : PARADIGM-HF, 2014

METHODE

Revue de la littérature

PubMed

Embase®

Cochrane Library

Méta-analyse

Review Manager 5.4

PRISMA
TRANSPARENT REPORTING OF SYSTEMATIC REVIEWS AND META-ANALYSES

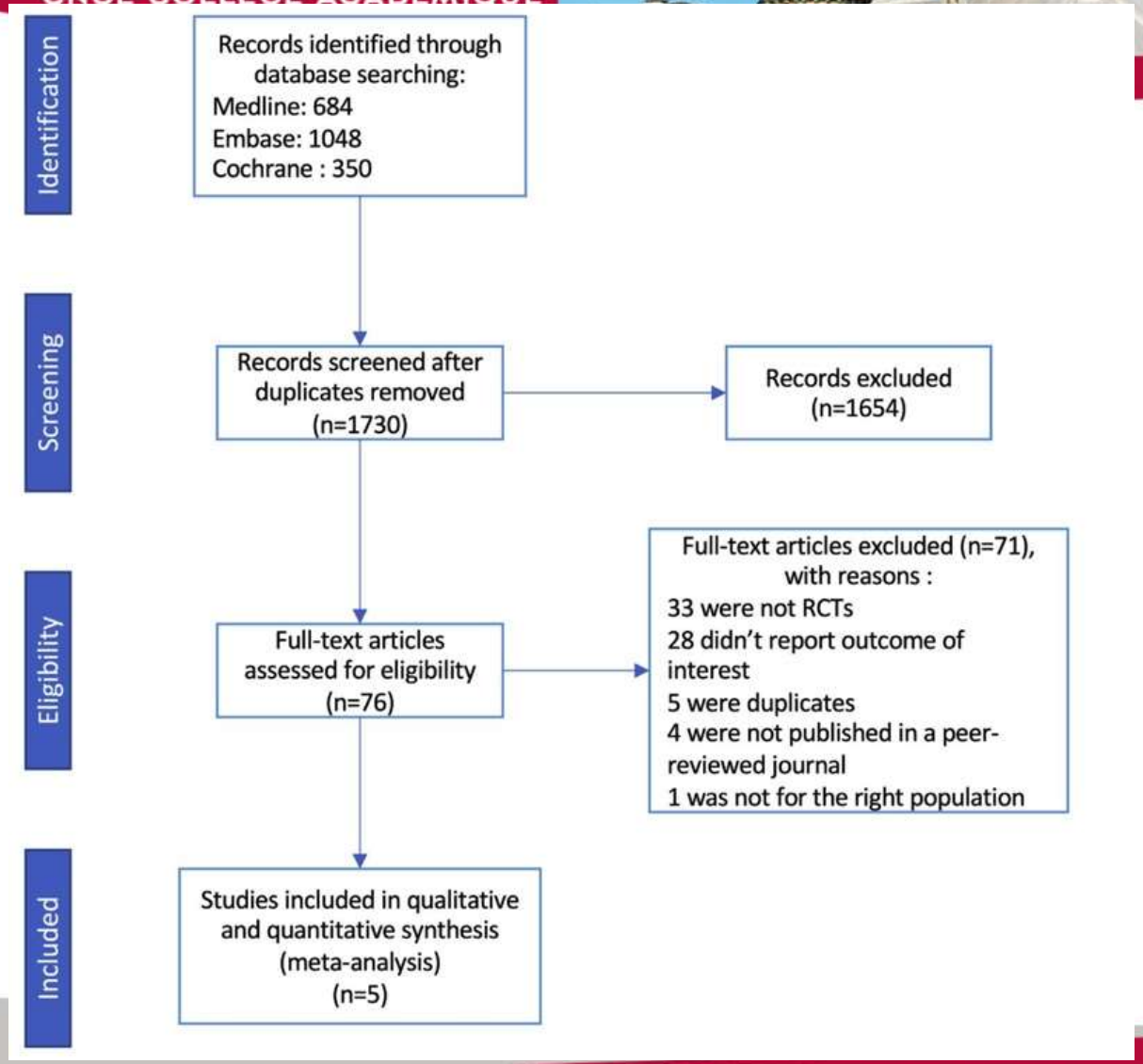
Analyse des biais RoB 2

Gradation des preuves

RATING QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

GRADE: an emerging consensus on rating quality of evidence and strength of recommendations

RESULTAT : prisma diagram



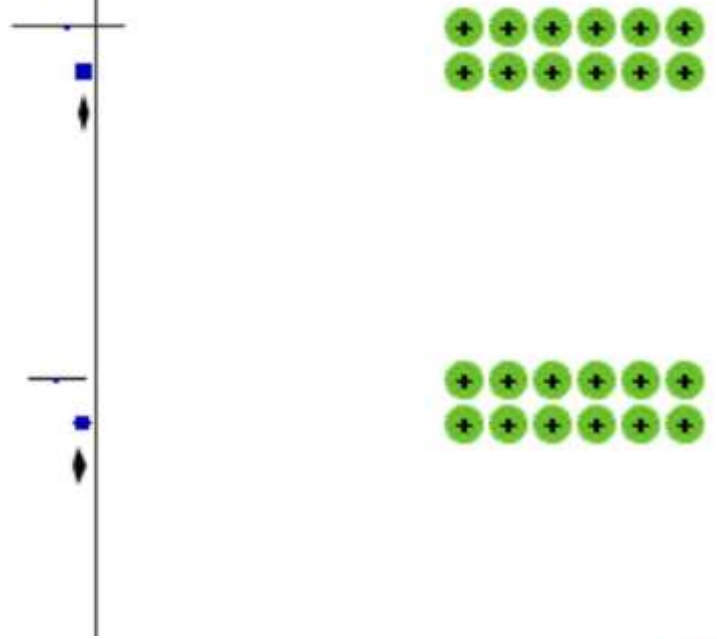
RESULTATS

TABLE 1 Characteristics of the included studies

Included studies	Drug	Control	Patients	Population	Mean duration follow-up (months)	Primary outcomes of the ECR	RR All-cause mortality
PARADIGM-HF, 2014	Sacubitril/ Valsartan	Enalapril	8442	HFrEF	27	Death from cardiovascular causes or hospitalization for heart failure	0.86 [0.78, 0,94]
PIONEER-HF, 2019	Sacubitril/ Valsartan	Enalapril	882	HFrEF	2	Time-averaged proportional change in NT-proBNP	0.67 [0.30, 1.47]
EVALUATE-HF, 2019	Sacubitril/ Valsartan	Enalapril	464	HFrEF	3	Central aortic stiffness	N.A.
PARAGON-HF, 2019	Sacubitril/ Valsartan	Valsartan	4822	HFpEF	35	Hospitalizations for heart failure and death from cardiovascular causes	0.97 [0.85, 1.12]
PARAMOUNT-HF, 2012	Sacubitril/ Valsartan	Valsartan	149	HFpEF	8	Change in NT-proBNP	0.51 [0.05, 5.57]

RESULTATS : HFrEF

Study or Subgroup	sacubitril/valsartan Events	Total	enalapril Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 All-causes mortality						
PIONEER-HF 2019	10	440	15	441	0.5%	0.67 [0.30, 1.47]
PARADIGM-HF 2014	711	4187	835	4212	26.2%	0.86 [0.78, 0.94]
Subtotal (95% CI)		**4627**		**4653**	**26.7%**	**0.85 [0.78, 0.93]**
Total events	721		850			
Heterogeneity: Chi² = 0.38, df = 1 (P = 0.54); I² = 0%						
Test for overall effect: Z = 3.46 (P = 0.0005)						
1.1.2 First hospitalization for worsening heart failure						
PIONEER-HF 2019	35	440	61	441	1.9%	0.58 [0.39, 0.85]
PARADIGM-HF 2014	537	4187	658	4212	20.6%	0.82 [0.74, 0.91]
Subtotal (95% CI)		**4627**		**4653**	**22.6%**	**0.80 [0.72, 0.89]**
Total events	572		719			
Heterogeneity: Chi² = 2.93, df = 1 (P = 0.09); I² = 66%						
Test for overall effect: Z = 4.29 (P < 0.0001)						



Risk of Bias: A B C D E F

1.1.5 Symptomatic hypotension

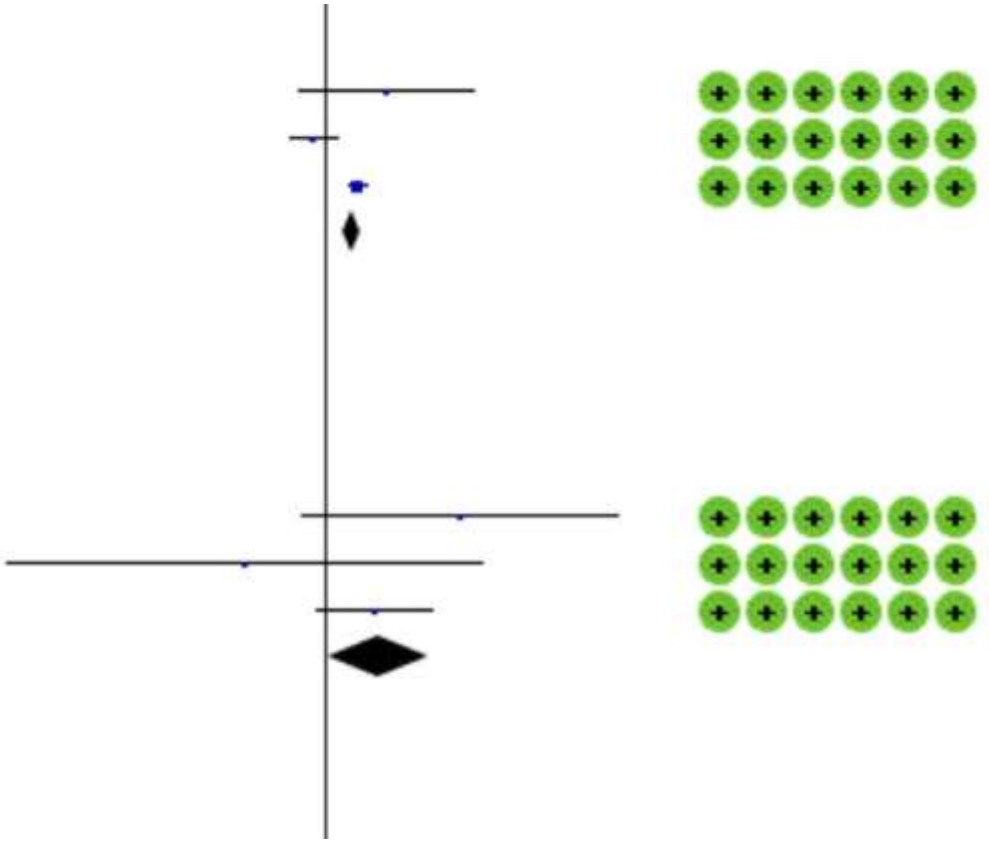
EVALUATE-HF 2019	9	231	4	233	0.1%	2.27 [0.71, 7.27]
PIONEER-HF 2019	56	440	66	441	2.1%	0.85 [0.61, 1.18]
PARADIGM-HF 2014	588	4187	388	4212	12.2%	1.52 [1.35, 1.72]
Subtotal (95% CI)		**4858**		**4886**	**14.4%**	**1.43 [1.28, 1.60]**
Total events	653		458			

Heterogeneity: Chi² = 11.17, df = 2 (P = 0.004); I² = 82%
Test for overall effect: Z = 6.28 (P < 0.00001)

1.1.6 Angioedema

PIONEER-HF 2019	6	440	1	441	0.0%	6.01 [0.73, 49.74]
EVALUATE-HF 2019	0	231	1	233	0.0%	0.34 [0.01, 8.21]
PARADIGM-HF 2014	19	4187	10	4212	0.3%	1.91 [0.89, 4.11]
Subtotal (95% CI)		**4858**		**4886**	**0.4%**	**2.05 [1.04, 4.03]**
Total events	25		12			

Heterogeneity: Chi² = 2.26, df = 2 (P = 0.32); I² = 11%
Test for overall effect: Z = 2.08 (P = 0.04)



Gradation des preuves

Sacubitril / valsartan

Population	No. of studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias		Control	RR (95% CI)	Quality
HFrEF	All-cause mortality Two (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Likely publication bias[f]	721/4627	850/4653	0.85 [0.78, 0.93]	⊕⊕⊕O Moderate
	First hospitalization for worsening heart failure Two (RCTs)	No serious risk of bias	Serious inconsistency[d]	No serious indirectness	No serious imprecision	Undetected	572/4627	719/4653	0.80 [0.72, 0.89]	⊕⊕⊕O Moderate
	Worsening renal function Three (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[e]	Likely publication bias[f]	166/4874	187/4903	0.89 [0.73, 1.09]	⊕⊕⊕O Moderate
	Hyperkalemia Three (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[e]	Likely publication bias[f]	762/4874	798/4903	0.96 [0.88, 1.05]	⊕⊕OO Low
	Symptomatic hypotension Three (RCTs)	No serious risk of bias	Serious inconsistency[d]	No serious indirectness	No serious imprecision	Likely publication bias[f]	653/4858	458/4886	1.43 [1.28, 1.60]	⊕⊕OO Low
	Angioedema Three (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[e]	Likely publication bias[f]	25/4858	12/4886	2.05 [1.04, 4.03]	⊕⊕OO Low
	Congestive heart failure Three (RCTs)	Serious risk of bias[a]	Serious inconsistency[d]	No serious indirectness	Serious imprecision[e]	Likely publication bias[f]	144/4643	162/4670	0.89 [0.72, 1.11]	⊕OOO Very Low
HFpEF	All-cause mortality Two (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[e]	Undetected	343/2556	351/2541	0.97 [0.85, 1.11]	⊕⊕⊕O Moderate
	Worsening renal function Two (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Undetected	36/2556	71/2541	0.50 [0.34, 0.75]	⊕⊕⊕⊕ High
	Hyperkalemia Two (RCTs)	Serious risk of bias[b]	No serious inconsistency	No serious indirectness	Serious imprecision[e]	Undetected	328/2535	370/2519	0.88 [0.77, 1.01]	⊕⊕OO Low
	Symptomatic hypotension Two (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Undetected	408/2556	284/2541	1.43 [1.24, 1.65]	⊕⊕⊕⊕ High
	Angioedema Two (RCTs)	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[e]	Undetected	15/2556	4/2541	3.43 [1.20, 9.78]	⊕⊕⊕O Moderate
	Congestive heart failure Two (RCTs)	Serious risk of bias[c]	No serious inconsistency	No serious indirectness	Serious imprecision[e]	Undetected	90/2568	89/2554	1.01 [0.75, 1.34]	⊕⊕OO Low

DISCUSSION

+

Valeurs absolues

Prise en compte des effets indésirables

Aide Bibliothécaire

Analyse des biais ROB 2

GRADE

−

80% des publis indexées dans Medline, intérêt des autres sources ?
Et la littérature grise ?

HFmrEF ?

Peu d'études, molécule récente mais…

ECR bon moyen évaluer pour les effets indésirables ?

Comparaison avec la littérature existante

- ***Zang et al, August 2020***

+ 1 étude = mitral regurgitation / echographic criteria : (OR) reaching 0.83 [0.74, 0.92]

OR non représentatif d'une taille d'effet ?

Effets indésirables HFpEF et HFrEF confondus = 2 populations différentes !

- ***Spanella et al., 2020*, ESC heart failure**

rôle protecteur fonction rénale / patients âgés et HFpEF

Utilité pour la MG ?