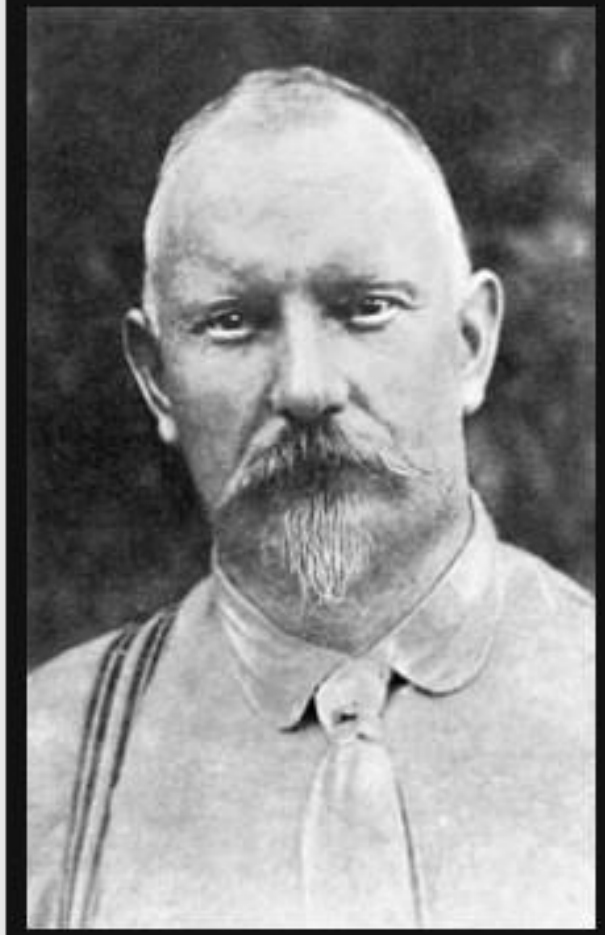
Quoi de neuf en dialyse?

Pierre Delanaye, MD, PhD
Université de Liège
Service de Dialyse
CHU, Sart Tilman, Liège, BELGIQUE

Conflits d’intérêts

- Consultance: ARK sciences, IDS
- Présentations rémunérées dans les 5 dernières années:
  Bayer, Amgen, Sanofi, Ménarini, Frésénius, Roche



Nul n'est censé ignorer la Loi... Il y a plus de deux cent mille lois !

(Jules Renard)

1	Journal of the American Society of Nephrology : JASN	journal	4.597 Q1	8	Current Opinion in Nephrology and Hypertension	journal	1.381 Q1
2	Nature Reviews Nephrology	journal	4.223 Q1	9	Seminars in Nephrology	journal	1.224 Q1
3	Kidney International	journal	3.331 Q1	10	American Journal of Nephrology	journal	1.211 Q1
4	Clinical Journal of the American Society of Nephrology	journal	2.950 Q1	11	Advances in Chronic Kidney Disease	journal	1.175 Q1
5	American Journal of Kidney Diseases	journal	2.475 Q1	12	Journal of Nephrology	journal	1.151 Q1
6	Nephrology Dialysis Transplantation	journal	1.865 Q1	13	CKJ: Clinical Kidney Journal	journal	1.092 Q1
7	Kidney International Supplements	journal	1.730 Q1	14	Journal of Renal Nutrition	journal	1.018 Q1

- Top 100
- Médecine
- Pas de journaux de “review”

Journal	Position	Facteur d'impact	Nombre de papiers traitant de dialyse
New England Journal Medicine	3	70,670	3
Lancet	4	59,102	0
JAMA	9	51,273	3
Nature	13	43,070	0
Science	14	41,037	0
Lancet Oncology	19	35,386	0
World Psychiatry	22	34,024	0
Nature Medicine	31	30,641	0
Lancet Neurology	33	28,755	0
BMJ	38	27,604	0
Lancet Infectious Diseases	39	27,516	0
Lancet Diabetes & Endocrinology	48	24,540	0
European Heart Journal	56	23,239	1
Circulation	58	23,054	2
Lancet Respiratory Medicine	59	22,992	0
JAMA Oncology	61	22,416	0
JAMA Intern Med	74	20,768	7
Nature Reviews Nephrology	78	19,684	
Annals of Internal Medicine	80	19,315	2
Gastroenterology	81	19,233	0
Intensive Care Medicine	82	18,967	1
Journal of Hepatology	83	18,946	1
Journal of the Amercian College of Cardiology	86	18,639	1
Lancet Psychiatry	88	18,329	0
Gut	92	17,943	0
European Urology	99	17,298	0

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European Urology	99	17,298	0

- Recherche originale
- Article « complet »
- Dialysés sont la « cible » principale ou importante de l’article

Journal	Position	Facteur d'impact	Nombre de papiers traitant de dialyse
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~~Lancet~~	~~4~~	~~59,102~~	~~0~~
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~~Nature~~	~~13~~	~~43,070~~	~~0~~
~~Science~~	~~14~~	~~41,037~~	~~0~~
~~Lancet Oncology~~	~~19~~	~~35,386~~	~~0~~
~~World Psychiatry~~	~~22~~	~~34,024~~	~~0~~
~~Nature Medicine~~	~~31~~	~~30,641~~	~~0~~
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~~Gut~~	~~92~~	~~17,943~~	~~0~~
~~European Urology~~	~~99~~	~~17,298~~	~~0~~


PROMO
Jupiler
BRASSERIE
BREWED AND CANNED IN BELGIUM
BIERE · BIER

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis

S.D. Barbar, R. Clere-Jehl, A. Bourredjem, R. Hernu, F. Montini, R. Bruyère, C. Lebert, J. Bohé, J. Badie, J.-P. Eraldi, J.-P. Rigaud, B. Levy, S. Siami, G. Louis, L. Bouadma, J.-M. Constantin, E. Mercier, K. Klouche, D. du Cheyron, G. Piton, D. Annane, S. Jaber, T. van der Linden, G. Blasco, J.-P. Mira, C. Schwebel, L. Chimot, P. Guiot, M.-A. Nay, F. Meziani, J. Helms, C. Roger, B. Louart, R. Trusson, A. Dargent, C. Binquet, and J.-P. Quenot, for the IDEAL-ICU Trial Investigators and the CRICS TRIGGERSEP Network*

N Engl J Med. 2018 Oct 11;379(15):1431-1442.

- RCT, ouverte, multicentrique
- Choc septique avec IRA sévère
- Stratégie d'épuration précoce (12h) or tardive (48h)
- 488 patients randomisés (246 « early » et 242 « late »)
- Mortalité à 90 jours

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Early Strategy (N=246)	Delayed Strategy (N=242)
Age — yr	69.3±11.6	68.7±12.8
Sex — no. (%)		
Male	142 (58)	154 (64)
Female	104 (42)	88 (36)
Body-mass index†	28.8±7.7	29.0±8.3
Coexisting conditions — no. (%)		
Chronic renal failure	32 (13)	44 (18)
Hypertension	145 (59)	137 (57)
Diabetes	80 (33)	69 (29)
Congestive heart failure‡	20 (8)	20 (8)
Chronic respiratory failure	19 (8)	10 (4)
Chronic liver disease	31 (13)	31 (13)
Immunosuppression	69 (28)	74 (31)
Median days in hospital before ICU admission (IQR)	1 (1–2)	1 (1–3)
SAPS II at ICU admission§	65.1±16.5	64.1±15.6
SOFA score at enrollment¶	12.2±2.9	12.4±2.9
Exposure to at least one nephrotoxic agent within 4 days before randomization — no. (%)	128 (52)	106 (44)
Multiple organ support in ICU — no. (%)		
Invasive mechanical ventilation	219 (89)	213 (88)
Vasopressor support with norepinephrine or epinephrine	246 (100)	242 (100)
Inotropic support with dobutamine	52 (21)	58 (24)
Extracorporeal membrane oxygenation	1 (<1)	9 (4)

Diagnostic criteria for acute kidney injury at the failure stage of the RIFLE classification — no. (%)‖		
Oliguria	86 (35)	80 (33)
Anuria	83 (34)	88 (36)
Serum creatinine 3 times the baseline level**	156 (63)	149 (62)
Serum creatinine before ICU admission — mg/dl**	1.01±0.49	1.06±0.50
Serum creatinine at enrollment — mg/dl	3.21±1.48	3.40±1.60
Blood urea nitrogen — mg/dl	59.2±26.9	63.1±30.0
Serum potassium — mmol/liter	4.3±0.8	4.5±0.9
Serum bicarbonate — mmol/liter	17.7±5.0	17.7±4.5
Fluid balance before enrollment — ml/24 hr	3194±2352	3211±2244

Table 2. Primary and Secondary Outcomes.*

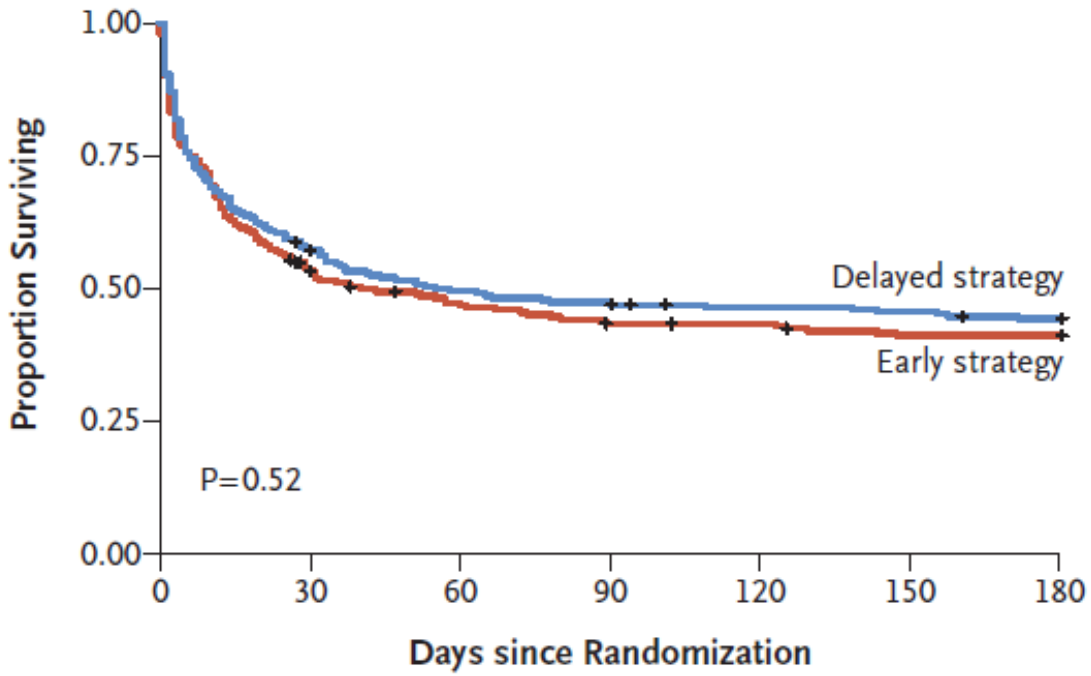
Variable	Early Strategy (N = 246)	Delayed Strategy (N = 242)	P Value
Primary outcome			
Secondary outcomes			
Median time from diagnosis of failure-stage acute kidney injury to initiation of renal-replacement therapy (IQR) — hr†	7.6 (4.4–11.5)	51.5 (34.6–59.5)	<0.001
Patients who received renal-replacement therapy — no. (%)	239 (97)	149 (62)	<0.001
Patients in the delayed-strategy group who received emergency renal-replacement therapy before 48 hr, according to criterion — no. (%)‡		41 (17)	

Table 2. Primary and Secondary Outcomes.*

Variable	Early Strategy (N = 246)	Delayed Strategy (N = 242)	P Value
Primary outcome			
Secondary outcomes			
Death at 28 days — no. (%)	111 (45)	102 (42)	0.48
Death at 180 days — no./total no. (%)	143/236 (61)	134/235 (57)	0.37
Median time from diagnosis of failure-stage acute kidney injury to initiation of renal-replacement therapy (IQR) — hr†	7.6 (4.4–11.5)	51.5 (34.6–59.5)	<0.001
Patients who received renal-replacement therapy — no. (%)	239 (97)	149 (62)	<0.001
Patients in the delayed-strategy group who received emergency renal-replacement therapy before 48 hr, according to criterion — no. (%)‡		41 (17)	

Table 2. Primary and Secondary Outcomes.*

Variable	Early Strategy (N = 246)	Delayed Strategy (N = 242)	P Value
Primary outcome			
Death at 90 days — no./		3/238 (54)	0.38
Secondary outcomes			
Death at 28 days — no. (		102 (42)	0.48
Death at 180 days — no.		4/235 (57)	0.37
Median time from diagn of renal-repla		(34.6–59.5)	<0.001
Patients who received re		149 (62)	<0.001
Patients in the delayed-s ment therapy		41 (17)	



No. at Risk

Delayed strategy	242	137	117	112	107	105	101
Early strategy	246	127	109	99	98	92	92

- STARRT-AKI en cours avec 2866 patients inclus
- AKIKI2 en cours avec 810 patients

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intravenous Iron in Patients Undergoing Maintenance Hemodialysis

Iain C. Macdougall, M.D., Claire White, B.Sc., Stefan D. Anker, M.D., Sunil Bhandari, Ph.D., F.R.C.P., Kenneth Farrington, M.D., Philip A. Kalra, M.D., John J.V. McMurray, M.D., Heather Murray, M.Sc., Charles R.V. Tomson, D.M., David C. Wheeler, M.D., Christopher G. Winearls, D.Phil., F.R.C.P., and Ian Ford, Ph.D., for the PIVOTAL Investigators and Committees*

N Engl J Med. 2019 Jan 31;380(5):447-458.

- RCT, multicentrique, ouverte, non-infériorité
- Hémodialyse chronique, stratégie de traitement en Fer (Saccharose, Venofer)
- Haute dose « proactive » IV (400 mg/mois) versus stratégie réactive (dose entre 0 et 400 mg/mois)
- 2,141 patients randomisés (1093 « proactive) et 1048 « reactive »), suivi médian de 2,1 années
- Composite: infar non fatal, AVC non fatal, hospi pour DC et mortalité

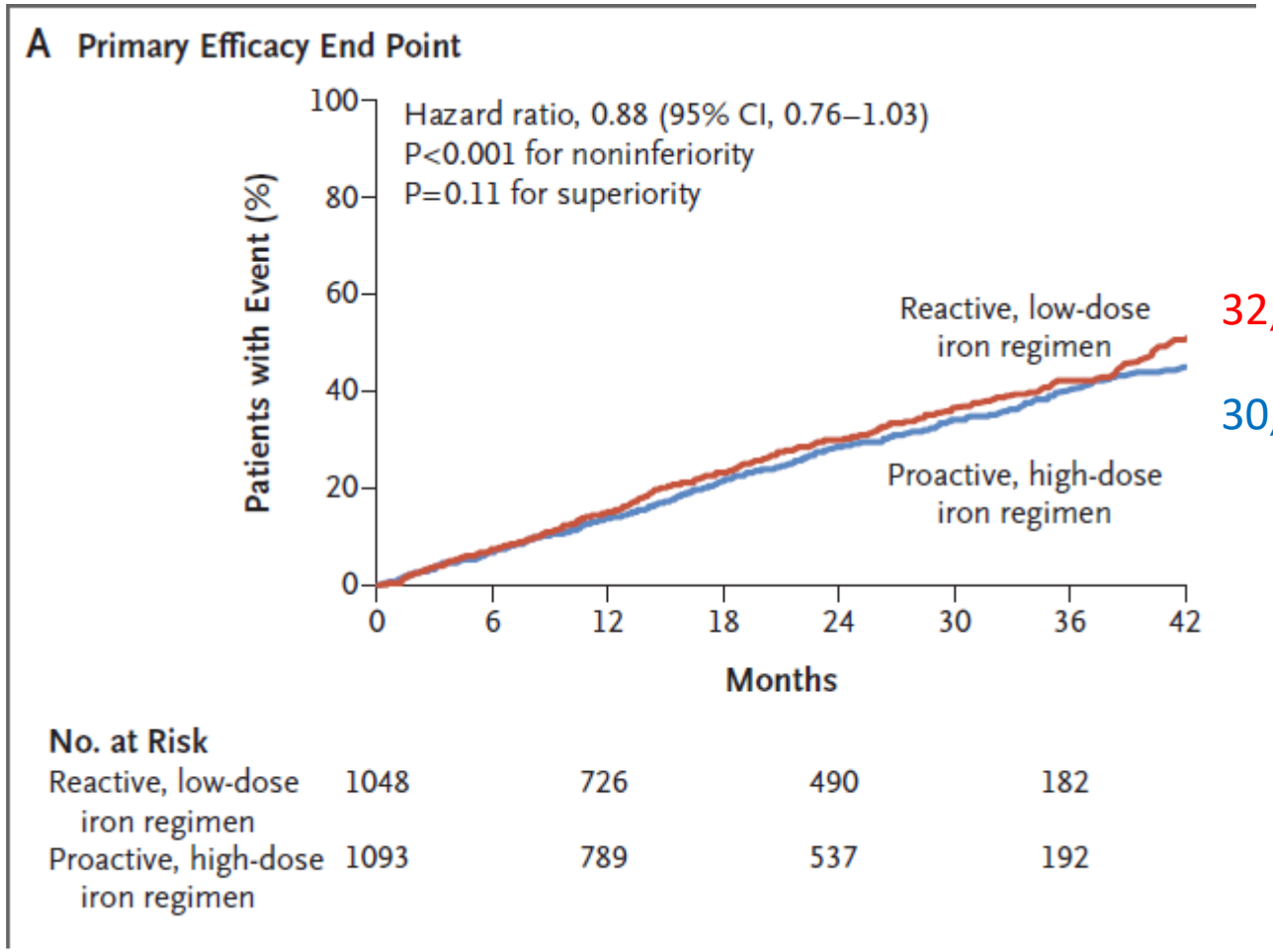
Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Proactive, High-Dose Iron Regimen (N=1093)	Reactive, Low-Dose Iron Regimen (N=1048)
Age — yr	62.7±14.9	62.9±15.1
Male sex — no. (%)	710 (65.0)	688 (65.6)
Race — no. (%)†		
White	868 (79.4)	830 (79.2)
Black	93 (8.5)	97 (9.3)
Asian	96 (8.8)	89 (8.5)
Other	36 (3.3)	32 (3.1)
Median duration of dialysis treatment (IQR) — mo	4.9 (2.8–8.4)	4.8 (2.8–8.1)
Vascular access — no. (%)		
Dialysis catheter	449 (41.1)	428 (40.8)
Arteriovenous fistula or graft	644 (58.9)	620 (59.2)
Cardiovascular disease — no. (%)		
Atrial fibrillation	96 (8.8)	68 (6.5)
Heart failure	41 (3.8)	45 (4.3)
Hypertension	804 (73.6)	753 (71.9)
Hyperlipidemia	277 (25.3)	258 (24.6)
Peripheral vascular disease	92 (8.4)	95 (9.1)
Previous myocardial infarction	97 (8.9)	87 (8.3)
Previous stroke	85 (7.8)	91 (8.7)
Diabetes — no. (%)	494 (45.2)	456 (43.5)
Smoking status — no. (%)		
Current smoking	145 (13.3)	104 (9.9)
Former smoking	261 (23.9)	284 (27.1)
Never smoked	687 (62.9)	660 (63.0)
Weight — kg	81.3±21.0	82.9±20.9
Body-mass index‡	28.5±7.1	29.0±6.7
Blood pressure — mm Hg§		
Systolic	145±24	145±24
Diastolic	74±14	74±15
Hemoglobin — g/dl	10.6±1.4	10.5±1.4
Median serum ferritin concentration (IQR) — μg/liter	214 (132–305)	217 (137–301)
Median transferrin saturation (IQR) — %	20 (16–24)	20 (16–24)
Median C-reactive protein level (IQR) — mg/liter	6.0 (3.3–13.9)	7.0 (4.0–15.0)
Median dose of erythropoiesis-stimulating agent (IQR) — IU/wk¶	8000 (5000–10,000)	8000 (5000–12,000)
Primary cause of kidney failure — no. (%)		
Diabetic nephropathy	363 (33.4)	349 (33.5)
Glomerular disease	191 (17.6)	203 (19.5)
Hypertension	129 (11.9)	106 (10.2)
Tubulointerstitial disease‖	113 (10.4)	88 (8.4)
Renovascular disease	64 (5.9)	83 (8.0)
Polycystic kidney disease	62 (5.7)	55 (5.3)
Other	61 (5.6)	68 (6.5)
Unknown	110 (10.1)	96 (9.2)

P=0,03

P=0,04

Plus d'IEC/Sartans dans le groupe "reactive" (30,3 vs 25,3%)



32,7%

30,5%

31 % d'infections dans les deux groupes (idem pour autres ES)

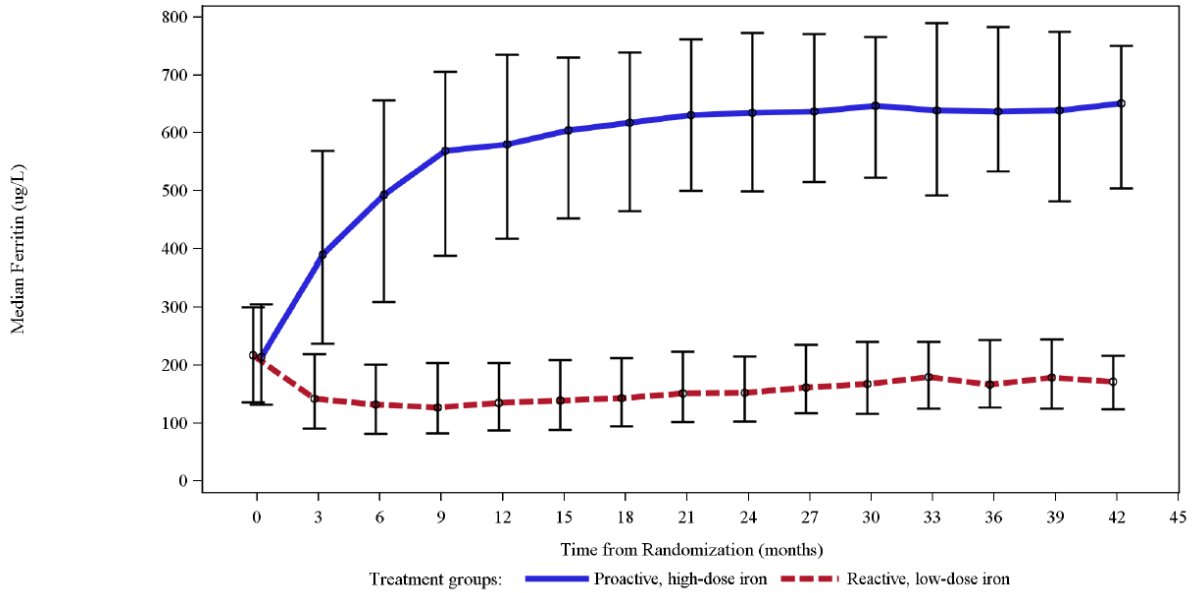
Doses médianes mensuelles

FER: 264 versus 145 mg

EPO: 29,757 versus 38,805 U (soit -19,4%)

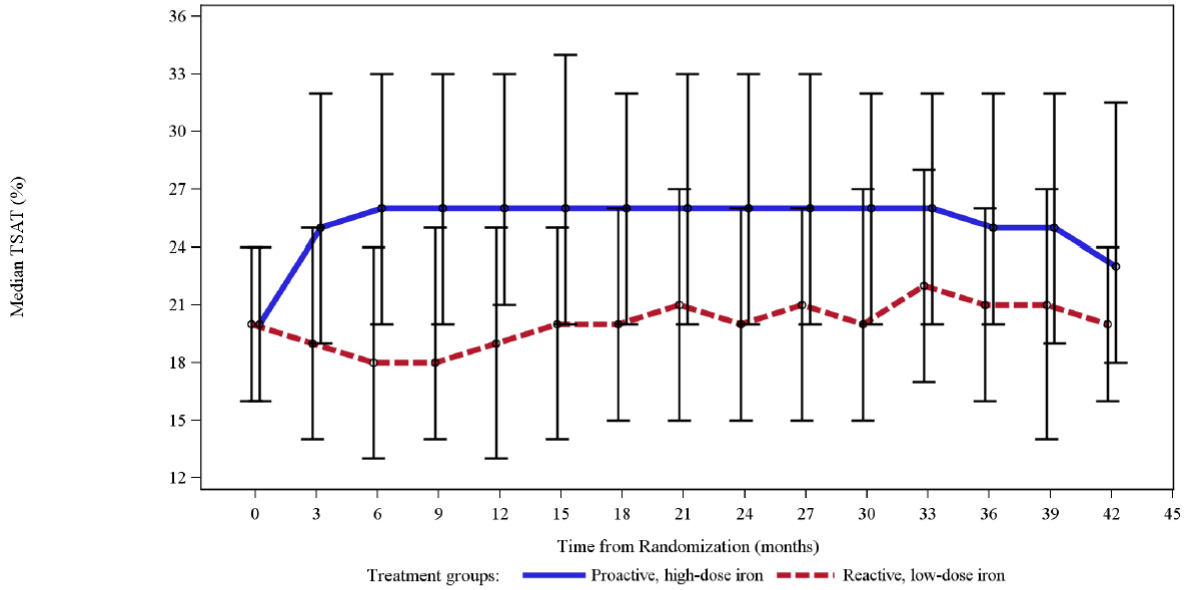
Moins de transfusions dans le groupe « proactive »

Figure S7. Median Serum Ferritin Concentration over Time.



Number of patients															
Proactive, high-dose iron	1093	1005	946	887	822	769	715	655	584	481	376	287	206	134	96
Reactive, low-dose iron	1048	972	897	831	766	701	648	603	527	438	365	279	211	135	79

Figure S8. Median Transferrin Saturation over Time.



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Reactive, low-dose iron	1048	972	897	831	766	700	648	603	527	438	364	278	210	135	79

Data presented as median (lower quartile, upper quartile). TSAT denotes transferrin saturation.

ORIGINAL ARTICLE

Roxadustat Treatment for Anemia in Patients Undergoing Long-Term Dialysis

N. Chen, C. Hao, B.-C. Liu, H. Lin, Caili Wang, C. Xing, X. Liang, G. Jiang, Zhengrong Liu, X. Li, L. Zuo, L. Luo, J. Wang, M. Zhao, Zhihong Liu, G.-Y. Cai, L. Hao, R. Leong, Chunrong Wang, C. Liu, T. Neff, L. Szczech, and K.-H.P. Yu

N Engl J Med. 2019 Sep 12;381(11):1011-1022.

- RCT, multicentrique, ouverte, non infériorité
- Inhibiteur de HIF prolyl hydroxylase en hémodialyse chronique
- 2/1, Roxadustat (100 ou 120mg PO, 3X/sem) versus EPOα (Pas de FER IV, PO permis)
- 304 patients randomisés (256 terminent), 26 semaines
- Variation moyenne d'hémoglobine entre la baseline et la moyenne d'Hg observée entre 23 et 27 semaines

Maxwell PH, Nat Rev Nephrol, 2016, p157

Table 1. Demographic, Clinical, and Laboratory Characteristics of the Patients at Baseline (Intention-to-Treat Population).*

Characteristic	Roxadustat (N=204)	Epoetin Alfa (N=100)
Age — yr	47.6±11.7	51.0±11.8
Male sex — no. (%)	126 (61.8)	58 (58.0)
Type 2 diabetes — no. (%)	30 (14.7)	17 (17.0)
Weight — kg	62.8±11.8	61.5±9.9
Hemoglobin		
Mean value — g/dl	10.4±0.7	10.5±0.7
Distribution — no. (%)		
<10.0 g/dl	56 (27.5)	29 (29.0)
≥10.0 g/dl	148 (72.5)	71 (71.0)
Baseline epoetin alfa dose		
Mean value — IU/wk	7582±2931	7597±2931
Distribution — no. (%)		
<8000 IU/wk	99 (48.5)	50 (50.0)
≥8000 IU/wk	105 (51.5)	50 (50.0)
Dialysis method — no. (%)		
Hemodialysis	182 (89.2)	89 (89.0)
Peritoneal dialysis	22 (10.8)	11 (11.0)

Ferritin		
Mean value — μg/liter	498.5±487.4	420.1±406.8
Distribution — no./total no. (%)		
≥200 μg/liter	136/203 (67.0)	62/100 (62.0)
100 to <200 μg/liter	24/203 (11.8)	19/100 (19.0)
<100 μg/liter	43/203 (21.2)	19/100 (19.0)
Transferrin — g/liter	1.89±0.46	1.91±0.39
Total iron-binding capacity — μmol/liter	47.4±11.4	48.3±9.0
C-reactive protein — no. (%)†		
≤ULN	158 (77.5)	80 (80.0)
>ULN	46 (22.5)	20 (20.0)
Blood pressure		
Systolic — mm Hg	148.1±16.1	148.4±16.5
Diastolic — mm Hg	85.3±9.8	84.2±10.7
Cholesterol		
Total — mg/dl	168.2±42.9	165.1±41.4
LDL — mg/dl	95.1±34.8	90.1±29.4
HDL — mg/dl	43.3±12.0	44.5±15.1
LDL:HDL	2.33±1.00	2.17±0.85

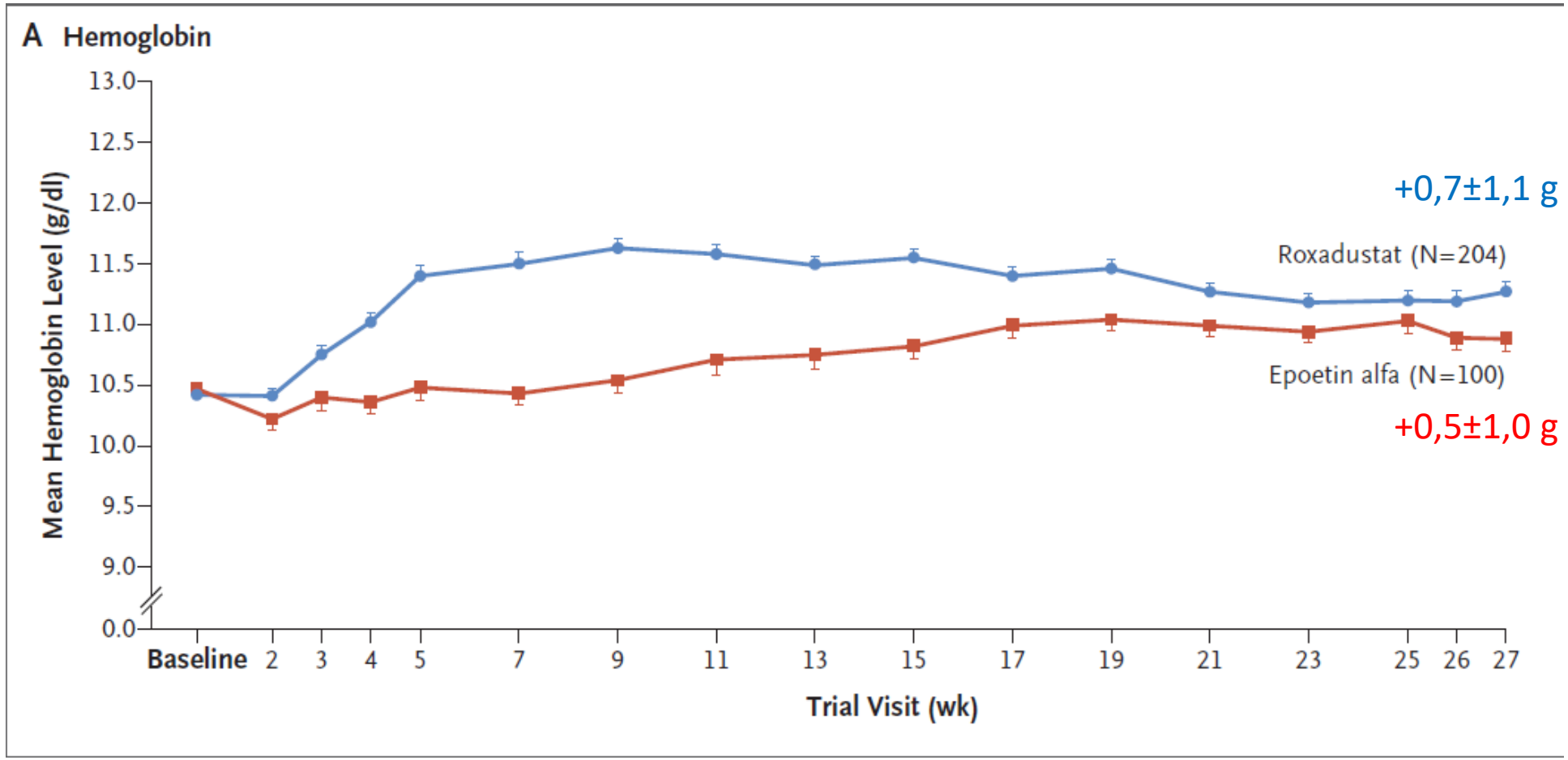

A Hemoglobin
Mean Hemoglobin Level (g/dl)
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
0.0
Baseline
2
3
4
5
7
9
11
13
15
17
19
21
23
25
26
27
Trial Visit (wk)
Roxadustat (N=204)
Epoetin alfa (N=100)
+0,7±1,1 g
+0,5±1,0 g

Table 2. Mean Change from Baseline in Iron Biomarker Levels at Week 27 (Intention-to-Treat Population).*

Variable	Roxadustat		Epoetin Alfa		Treatment Difference (95% CI)
	End-of-Treatment Assessment	Change from Baseline	End-of-Treatment Assessment	Change from Baseline	
Iron					
No. of patients	160	160	94	94	
Mean (μmol/liter)	15.2±8.1	0.1±8.3	10.6±4.0	−3.7±7.2	
Least-squares mean (μmol/liter)		0.6±0.7		−3.9±0.5	4.4±0.7 (3.0 to 5.9)
Transferrin					
No. of patients	160	160	94	94	
Mean (g/liter)	2.29±0.66	0.40±0.48	1.86±0.45	−0.04±0.36	
Least-squares mean (g/liter)		0.38±0.05		−0.05±0.04	0.43±0.05 (0.32 to 0.53)
Total iron-binding capacity					
No. of patients	160	159	94	93	
Mean (μmol/liter)	57.4±16.5	10.0±11.9	46.6±11.3	−1.1±9.0	
Least-squares mean (μmol/liter)		9.5±1.2		−1.2±1.1	10.7±1.3 (8.1 to 13.3)
Transferrin saturation					
No. of patients	160	159	94	93	
Mean (%)	28.0±15.8	−5.7±15.4	23.0±8.5	−7.6±13.8	
Least-squares mean (%)		−4.5±1.2		−8.7±1.0	4.2±1.4 (1.5 to 6.9)
Ferritin					
No. of patients	160	160	94	94	
Mean (μg/liter)	373±470	−119±208	294±294	−136±220	
Least-squares mean (μg/liter)		−99±19		−133±21	35±24 (−12 to 82)

* Plus–minus values are means ±SD or least-squares means ±SE. Baseline values are provided for patients who had paired values at week 27 for comparison. To convert the values for iron to micrograms per deciliter, divide by 0.1791.

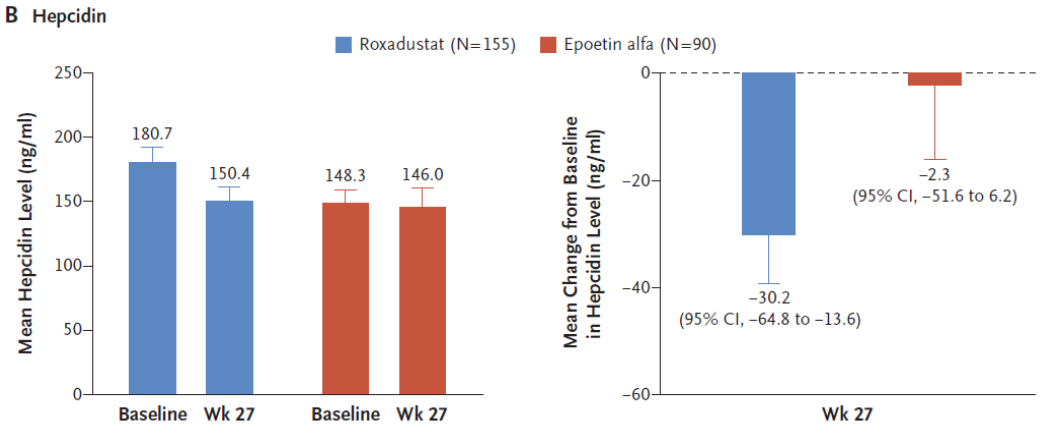


Table 3. Adverse Events Occurring in at Least 5% of Patients in Either Treatment Group and All Serious Adverse Events (Intention-to-Treat Population).*

Event	Roxadustat (N = 204)	Epoetin Alfa (N = 100)	Total (N = 304)
	number of patients (percent)		
Adverse events			
Any adverse event during treatment	96 (47.1)	38 (38.0)	134 (44.1)
Upper respiratory tract infection	37 (18.1)	11 (11.0)	48 (15.8)
Hypertension	25 (12.3)	16 (16.0)	41 (13.5)
Hyperkalemia†	15 (7.4)	1 (1.0)	16 (5.3)
Chest discomfort‡	13 (6.4)	0	13 (4.3)
Vomiting	12 (5.9)	2 (2.0)	14 (4.6)
Asthenia	12 (5.9)	2 (2.0)	14 (4.6)
Alanine aminotransferase increased	11 (5.4)	4 (4.0)	15 (4.9)
Dizziness	10 (4.9)	6 (6.0)	16 (5.3)
Hypotension	10 (4.9)	6 (6.0)	16 (5.3)
Muscle spasms	5 (2.5)	5 (5.0)	10 (3.3)

Serious adverse events, according to system organ class§			
Any serious adverse event during treatment	29 (14.2)	10 (10.0)	39 (12.8)
Blood or lymphatic system disorder	1 (0.5)	0	1 (0.3)
Cardiac disorder	5 (2.5)	1 (1.0)	6 (2.0)
Endocrine disorder	1 (0.5)	0	1 (0.3)
Gastrointestinal disorder	2 (1.0)	0	2 (0.7)
Hepatobiliary disorder	2 (1.0)	0	2 (0.7)
Immune system disorder	2 (1.0)	0	2 (0.7)
Infection or infestation	5 (2.5)	3 (3.0)	8 (2.6)
Injury, poisoning, or procedural complication¶	7 (3.4)	5 (5.0)	12 (3.9)
Metabolism or nutrition disorder	1 (0.5)	0	1 (0.3)
Nervous system disorder	3 (1.5)	0	3 (1.0)
Product issue	0	1 (1.0)	1 (0.3)
Renal or urinary disorder	4 (2.0)	0	
Reproductive system or breast disorder	1 (0.5)		
Vascular disorder	2 (1.0)		

42 patients (20,5%) dans le groupe roxadustat ont arrêté le traitement versus 6 (6%) dans le groupe EPO

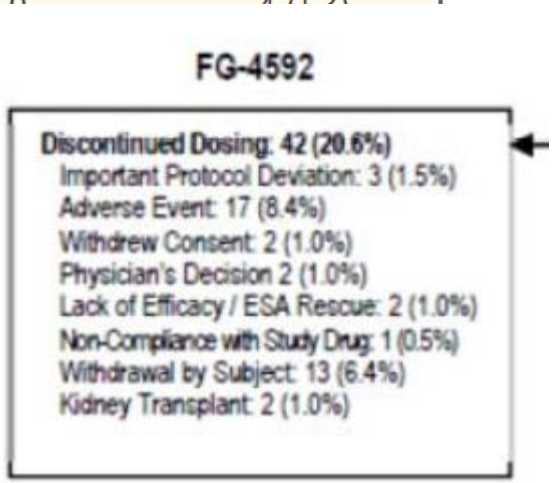


Table 1 | **Clinical trials of small-molecule PHD enzyme inhibitors**

Molecule	Phase	Administration	NCT reference	Study design (primary outcome)	Treatment duration (study dates)	Renal disease category
FG-2216	II	Oral	NA	–	–	–
FG-4592 ASP1517 Roxadustat	III (US/EU)	Oral, 1–3 times weekly	02174731	Randomized open label versus epoetin α, 1,425 patients (major adverse cardiac events)	1–2 years* (7/2014–2/2017)	HD or PD
			02174627	Randomized double-blind versus placebo, 2,600 patients (major adverse cardiac events)	1–2 years* (6/2014–2/2017)	CKD not on dialysis
			02021318 (DOLOMITES)	Randomized open label versus darbepoetin α, 570 patients (Hb response without rescue therapy)	2 years (2/2014–7/2017)	CKD not on dialysis
			01887600 (ALPS)	Randomized double-blind versus placebo, 600 patients (Hb response without rescue therapy)	1–2 years (5/2013–6/2016)	CKD not on dialysis
			02052310 (HIMALAYAS)	Randomized open label versus epoetin α, 750 patients (mean Hb change from baseline)	1–3 years (12/2013–6/2017)	Incident HD or PD
			02273726	Randomized open label versus epoetin α, 600 patients (mean Hb change from baseline)	1–3 years (12/2014–6/2017)	Stable HD or PD
			02278341 (PYRENEES)	Randomized open label versus epoetin α and darbepoetin α, 750 patients (mean Hb change from baseline)	2 years (11/2014–7/2018)	Stable HD or PD
			01750190	Randomized double-blind versus placebo, 600 patients (Hb response without rescue therapy)	≥1 year (11/2012–6/2017)	CKD not on dialysis
	II (Japan)	Oral, 3 times weekly	01964196	Randomized double-blind versus placebo, 100 patients (rate of rise in Hb)	28 weeks (8/2013–3/2015)	CKD not on dialysis
BAY85-3934 Molidustat	IIb	Oral, once daily	02021409 (DIALOGUE 2)	Randomized open label versus darbepoetin α, 120 patients (change in Hb)	16 weeks (1/2014–9/2015)	CKD not on dialysis
			01975818 (DIALOGUE 4)	Randomized open label versus epoetin α or β, 188 patients (change in Hb)	16 weeks (1/2013–9/2015)	Stable HD
			02021370 (DIALOGUE 1)	Randomized double-blind versus placebo, 120 patients (change in Hb)	16 weeks (2/2014–9/2015)	CKD not on dialysis
			02055482 (DIALOGUE 3)	Long-term extension of NCT02021409/02021370 (change in Hb)	≤3 years (6/2014–11/2018)	CKD not on dialysis
			02064426 (DIALOGUE 5)	Long-term extension of NCT 01975818 (change in Hb)	≤3 years (6/2014–11/2018)	Stable HD
GSK1278863 Daprodustat	IIb	Oral, once daily	01977573	Randomized single-blind versus epoetin, 252 patients (change in Hb)	24 weeks (10/2013–5/2015)	CKD not on dialysis
			01977482	Randomized double-blind versus active control, 217 patients (change in Hb)	24 weeks (11/2013–2/2015)	Stable HD
	IIa	Oral, once daily	02075463	Open label, 20 patients‡ (change in Hb)	16 weeks (6/2014–3/2016)	HD hypo-responsive to epoetin
			02019719	Randomized double-blind versus placebo, 97 patients (change in Hb)	4 weeks (11/2013–8/2014)	Stable HD in Japanese patients
			01587924	Randomized double-blind versus rhEPO, 86 patients (change in Hb)	4 weeks (5/2012–5/2013)	Stable HD
			01587898	Randomized double-blind versus placebo, 74 patients (change in Hb)	4 weeks (5/2012–5/2013)	CKD not on dialysis
			01047397	Randomized single-blind versus placebo, 107 patients (change in Hb)	4 weeks (3/2010–2/2011)	Stable HD and CKD not on dialysis
AKB-6548	IIb	Oral, once daily or 3 times weekly	01906489	Randomized double-blind versus placebo, 210 patients (percentage achieving Hb ≥11.0 or ≥1.2 g/dl increase from baseline)	20 weeks (7/2013–10/2014)	CKD not on dialysis
	II	Oral, once daily or 3 times weekly	02260193	Non-randomized open label, 90 patients (change in Hb)	16 weeks (9/2014–7/2015)	Stable HD
JTZ-951	I	Oral, once daily	NA	–	–	–

Maxwell PH, Nat Rev Nephrol, 2016, p157

Research

JAMA | Original Investigation

Association of Medicaid Expansion With 1-Year Mortality Among Patients With End-Stage Renal Disease

Shailender Swaminathan, PhD; Benjamin D. Sommers, MD, PhD; Rebecca Thorsness, BA; Rajnish Mehrotra, MD, MS; Yoojin Lee, MS, MPH; Amal N. Trivedi, MD, MPH

JAMA. 2018 Dec 4;320(21):2242-2250.

Research

JAMA | Original Investigation

Association Between Dialysis Facility Ownership and Access to Kidney Transplantation

Jennifer C. Gander, PhD; Xingyu Zhang, PhD; Katherine Ross, MPH; Adam S. Wilk, PhD; Laura McPherson, MPH; Teri Browne, PhD; Stephen O. Pastan, MD; Elizabeth Walker, MS; Zhensheng Wang, PhD; Rachel E. Patzer, PhD, MPH

JAMA. 2019 Sep 10;322(10):957-973.

Research

JAMA | Original Investigation

Effect of Oral Alfacalcidol on Clinical Outcomes in Patients Without Secondary Hyperparathyroidism Receiving Maintenance Hemodialysis

The J-DAVID Randomized Clinical Trial

The J-DAVID Investigators

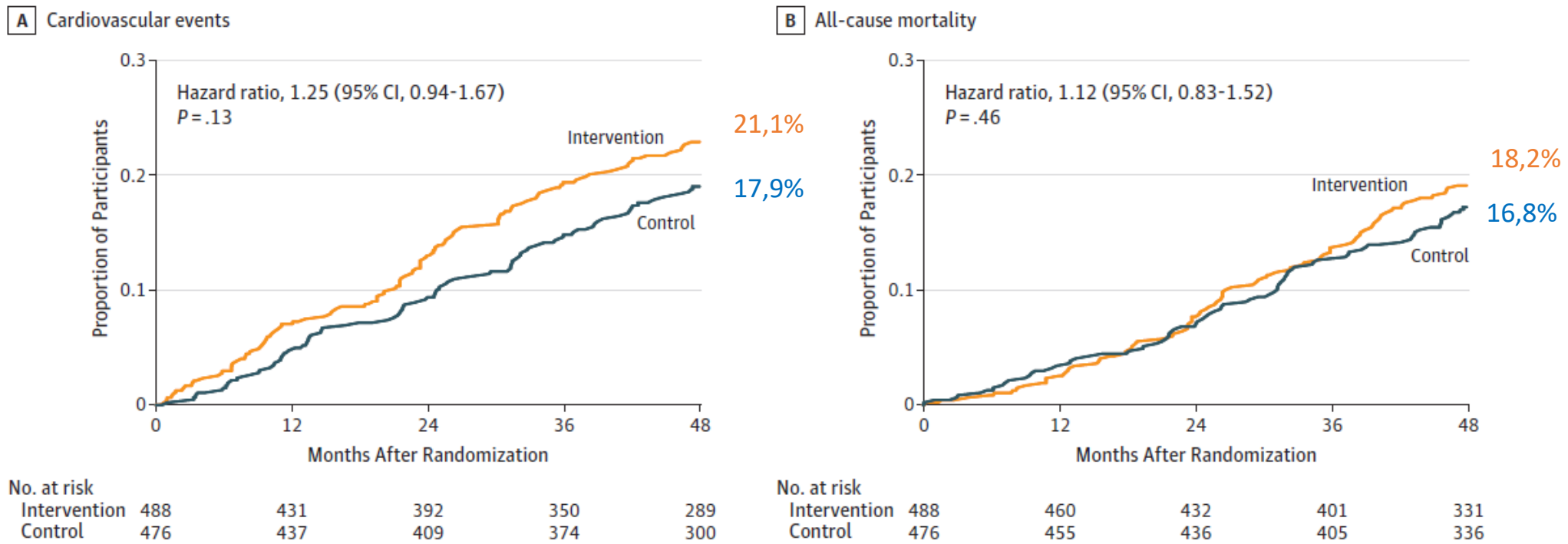
JAMA. 2018 Dec 11;320(22):2325-2334.

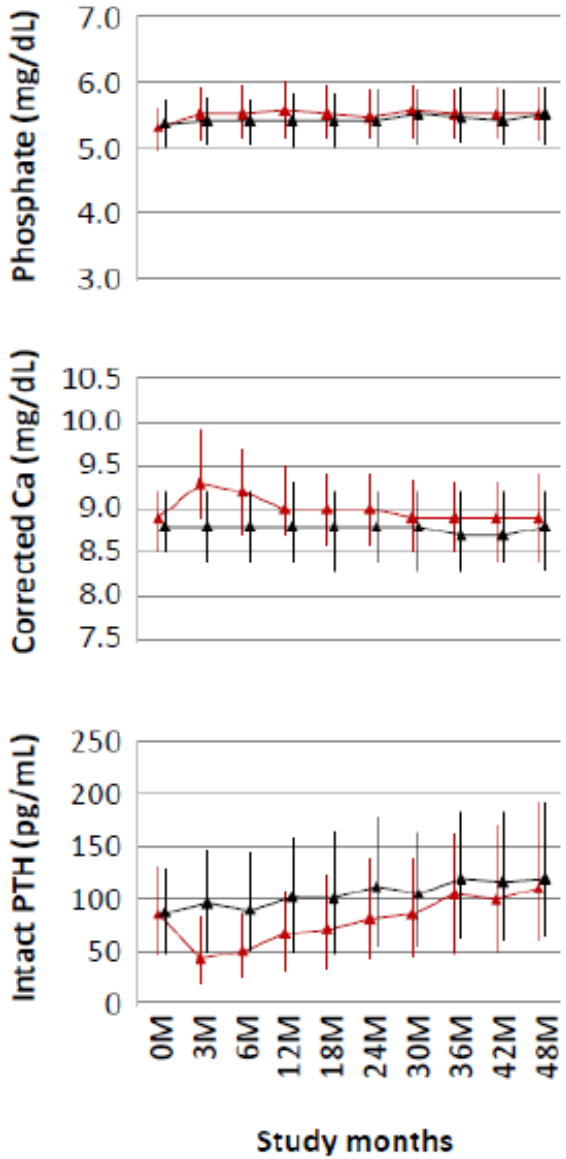
- RCT, multicentrique, ouverte
- Alfacalcidol pour les effets pléiotropes potentiels de la vitamine D (PTH≤180pg/ml)
- Alfacalcidol, 0,5 µg/j en hémodialyse
- 964 patients (488 vitamine D et 476 groupe contrôle), suivi fixe de 4 années
- Composite: événements CV fatal ou non (infar, DC, AVC, rupture/dissection aorte, amputation, mort subite), intervention au niveau coronarien, intervention au niveau MI

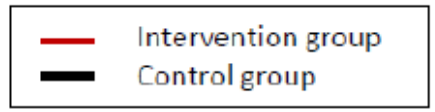
Table 1. Baseline Characteristics of Participants in a Study of the Effect of Oral Alfacalcidol in Patients Receiving Hemodialysis

Characteristic	Oral Alfacalcidol Group (n = 488)	Control Group (n = 476)
Age, median (IQR), y	65 (58-71)	65 (58-71)
Men, No. (%)	301 (61.7)	277 (58.2)
Women, No. (%)	187 (38.3)	199 (41.8)
Duration of hemodialysis, mean (IQR), y	6 (2-10)	5 (2-11)
Diabetic nephropathy, No. (%)	207 (42.4)	204 (42.9)
History of cardiovascular disease, No. (%)	127 (26.0)	117 (24.6)
Blood pressure		
Systolic, No.	486	476
Median (IQR), mm Hg	145 (130-160)	148 (134-160)
Diastolic, No.	486	475
Median (IQR), mm Hg	74 (67-82)	74 (68-83)
Pulse rate, bpm	72 (66-78)	72 (66-78)
Dialysis, median (IQR), h per wk	12 (12-12)	12 (12-12)
Single pool Kt/V[a]		
No.	477	465
Median (IQR)	1.41 (1.23-1.61)	1.44 (1.20-1.64)
Dialysate calcium concentration, No. (%), mEq/L		
2.5	130 (26.6)	121 (25.4)
3.0	333 (68.2)	331 (69.5)
Other	25 (5.1)	24 (5.0)
Height, cm		
No.	478	468
Median (IQR)	160 (154-167)	161 (153-167)
Body weight, kg		
No.	487	
Median (IQR)	54.5 (48.2-61.5)	53.9 (47.5-61.9)
BMI		
No.	477	468
Median (IQR)	21.1 (19.0-23.4)	21.1 (19.1-23.3)
Laboratory parameters, median (IQR)		
C-reactive protein, mg/dL		
No.	427	414
Median (IQR)	0.10 (0.05-0.30)	0.10 (0.05-0.26)
Serum albumin, g/dL		
No.	487	476
Median (IQR)	3.8 (3.5-3.9)	3.8 (3.5-4.0)
Serum calcium, mg/dL	8.9 (8.5-9.2)	8.8 (8.5-9.2)
Corrected calcium, mg/dL	9.1 (8.8-9.5)	9.1 (8.7-9.5)
Phosphate, mg/dL	4.6 (3.9-5.2)	4.7 (4.0-5.4)
Intact parathyroid hormone, pg/mL	85.1 (45.2-130.0)	86.1 (47.0-127.4)
Use of medication for MBD in CKD, No. (%)		
Calcium carbonate	412 (84.4)	392 (82.4)
Sevelamer hydrochloride	153 (31.4)	155 (32.6)
Lanthanum carbonate	69 (14.1)	49 (10.3)
Cinacalcet hydrochloride	27 (5.5)	29 (6.1)
Active vitamin D sterol	0 (0.0)	0 (0.0)

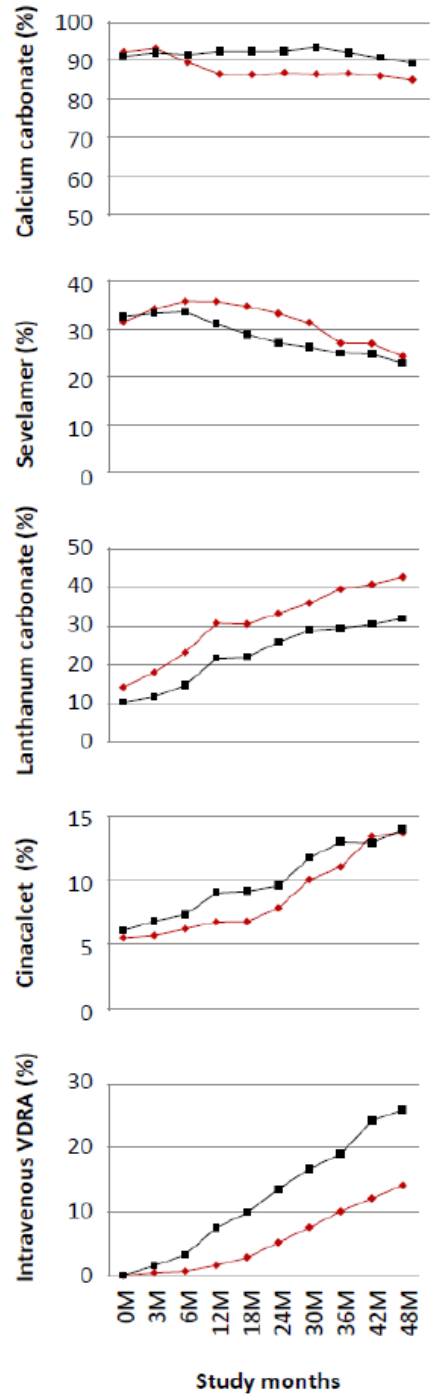
Figure 2. Primary and Secondary Outcomes







Pas de données sur
25-OH vitamin D



ESC European Society of Cardiology
European Heart Journal (2019) **40**, 887–898
doi:10.1093/eurheartj/ehy422

CLINICAL RESEARCH
Prevention and epidemiology

Cause of kidney disease and cardiovascular events in a national cohort of US patients with end-stage renal disease on dialysis: a retrospective analysis

Michelle M. O'Shaughnessy[1]*, Sai Liu[1], Maria E. Montez-Rath[1], Richard A. Lafayette[1], and Wolfgang C. Winkelmayer[2]

Eur Heart J. 2019 Mar 14;40(11):887-898.

- Observationnelle, rétrospective, USRDS
- Tout patient dialysé sous Medicare après 91 jours, suivi de 5 ans
- Critère composite: infar, AVC ischémique, mort CV

Final cohort (n= 658,168):

Adults aged 18-100 years with first dialysis treatment 1997-2014, remaining on dialysis at 91 days post-dialysis initiation, and with ESRD attributed to IgAN (n=9828), FSGS (n=27,029), MN (n=5660), MPGN (n=3718), LN (n=12,398), vasculitis (n=5023), DN (n=567,778) or ADPKD (n=26,734)

- DN sont plus âgés que les IgA: 63,2 versus 46,2 ans
- DN sont moins greffés que les IgA: 49,3 versus 8,1%
- Critère primaire plus fréquent pour: DN 40,1 versus 10,3%

Table 2 Cardiovascular event rates from 91 days to 5 years and 90 days after dialysis initiation, among US patients with end-stage renal disease attributed to glomerular disease, diabetic nephropathy, or autosomal dominant polycystic kidney disease

	Percent with event	Number of events	Years at risk	Event rate (per 100 person-years)
Composite event (fatal or non-fatal cardiovascular event)				
IgAN	7.82	769	22 895	3.36
FSGS	15.21	4111	71 440	5.75
MN	19.08	1080	14 671	7.36
MPGN	16.22	603	9311	6.48
LN	13.24	1641	33 237	4.94
Vasculitis	17.02	855	11 886	7.19
DN	33.19	188 455	1 314 229	14.34
ADPKD	12.62	3375	69 296	4.87

Table 3 Hazard ratios (95% confidence intervals) for cardiovascular events from 91 days to 5 years and 90 days after dialysis initiation, among the US patients with end-stage renal disease attributed to glomerular disease, diabetic nephropathy, or autosomal dominant polycystic kidney disease

	Primary GN subtypes				Secondary GN subtypes		Non-GN comparator groups	
	IgAN	FSGS	MN	MPGN	LN	Vasculitis	DN	ADPKD
Composite event								
Model 1	Ref	1.95 (1.80–2.10)	2.48 (2.27–2.72)	2.02 (1.82–2.25)	1.69 (1.55–1.84)	2.49 (2.25–2.74)	4.95 (4.61–5.31)	1.58 (1.46–1.71)
Model 2	Ref	1.72 (1.59–1.85)	1.84 (1.68–2.02)	1.70 (1.53–1.89)	2.09 (1.92–2.28)	1.63 (1.48–1.80)	3.53 (3.29–3.78)	1.24 (1.15–1.34)
Model 3	Ref	1.71 (1.58–1.84)	1.82 (1.67–2.00)	1.69 (1.52–1.88)	2.09 (1.92–2.27)	1.62 (1.47–1.79)	3.47 (3.24–3.72)	1.24 (1.15–1.34)
Model 4	Ref	1.68 (1.56–1.81)	1.79 (1.63–1.96)	1.65 (1.48–1.84)	1.97 (1.80–2.14)	1.61 (1.46–1.78)	3.13 (2.91–3.36)	1.25 (1.16–1.35)
Model 5	Ref	1.65 (1.53–1.78)	1.67 (1.52–1.83)	1.55 (1.40–1.73)	1.86 (1.71–2.03)	1.55 (1.41–1.71)	2.97 (2.77–3.20)	1.29 (1.19–1.39)

Circulation

ORIGINAL RESEARCH ARTICLE

Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States

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Circulation. 2018 Oct 9;138(15):1519-1529.

- Observationnelle, rétrospective, USRDS
- Contexte de fibrillation auriculaire (non valvulaire) chez le dialysé
- Patients sous apixaban ou sous warfarine (« matched cohort », 1/3 soit 2,351 et 7,053)
- AVC ischémique ou embolie, saignement majeur, saignement GI, saignement intracrânien ou mort

Table 1. Actions and pharmacokinetics of NOACs

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct inhibitor of thrombin	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
Serum half-life, h	12–17	5–9	12	10–14
Renal clearance, %	80	36	25	50
Blood test	TT or ECT	Anti-Xa activity	Anti-Xa activity	Anti-Xa activity
Specific reversal agents	• Idarucizumab • Aripazine	• Andexanet alpha • Aripazine	• Andexanet alpha • Aripazine	• Andexanet alpha • Aripazine
Dialysable	Yes	No	No	No

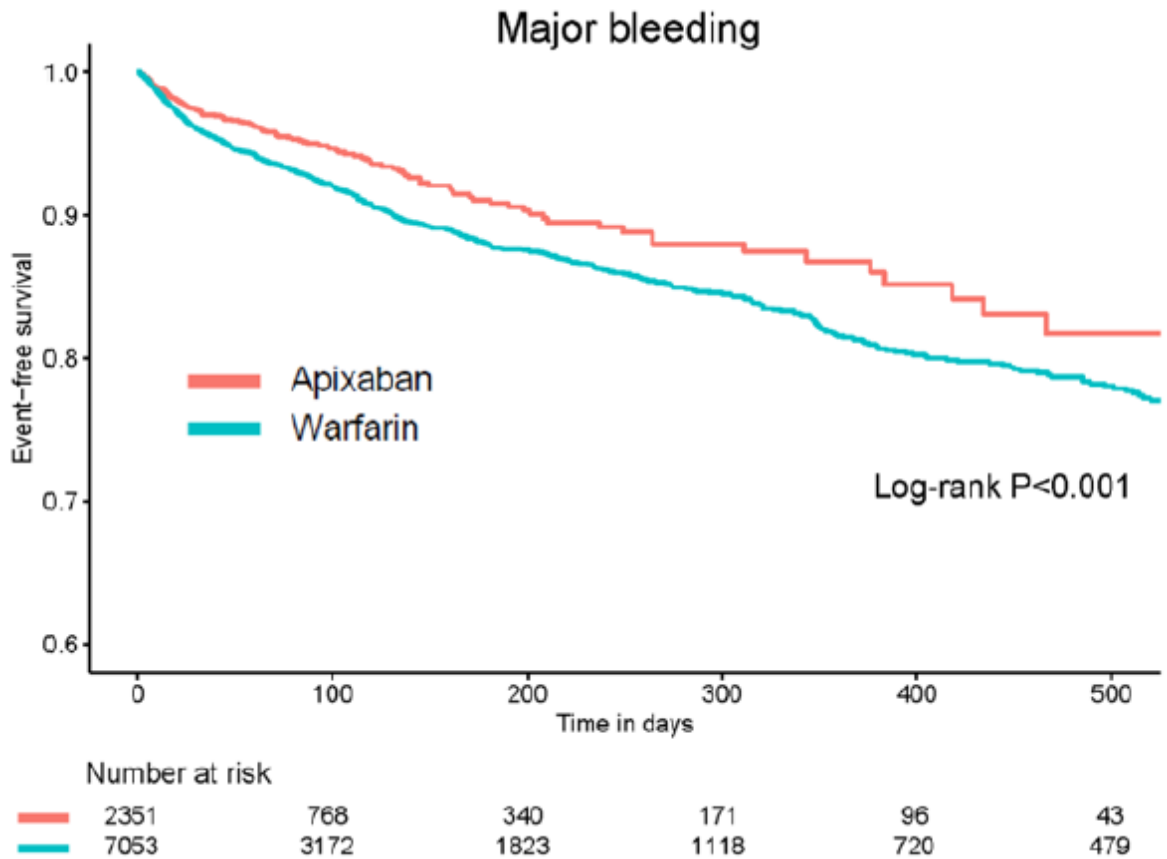
CKD Stage	GFR (mL/min)	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
1	>90	✓	✓	✓	✓
2	90-60	✓	✓	✓	✓
3	59-30	✓ ESC: GFR 30-49 mL/min ⇨ reduced dose	✓ ESC: GFR 30-49 mL/min ⇨ reduced dose	✓	✓ ESC: GFR 30-49 mL/min ⇨ reduced dose
4	29-15	FDA: reduced dose / EMA: Contra-indicated	✓ reduced dose	✓ reduced dose*	✓ reduced dose
5 5D	<15 Dialysis	Contraindicated	Contraindicated	FDA: full to reduced * dose / EMA: Contra-indicated	Contraindicated

* : If two of the following criteria are present : serum creatinine ≥ 1.5 mg/dl, age ≥ 80 years, body weight ≤ 60kg

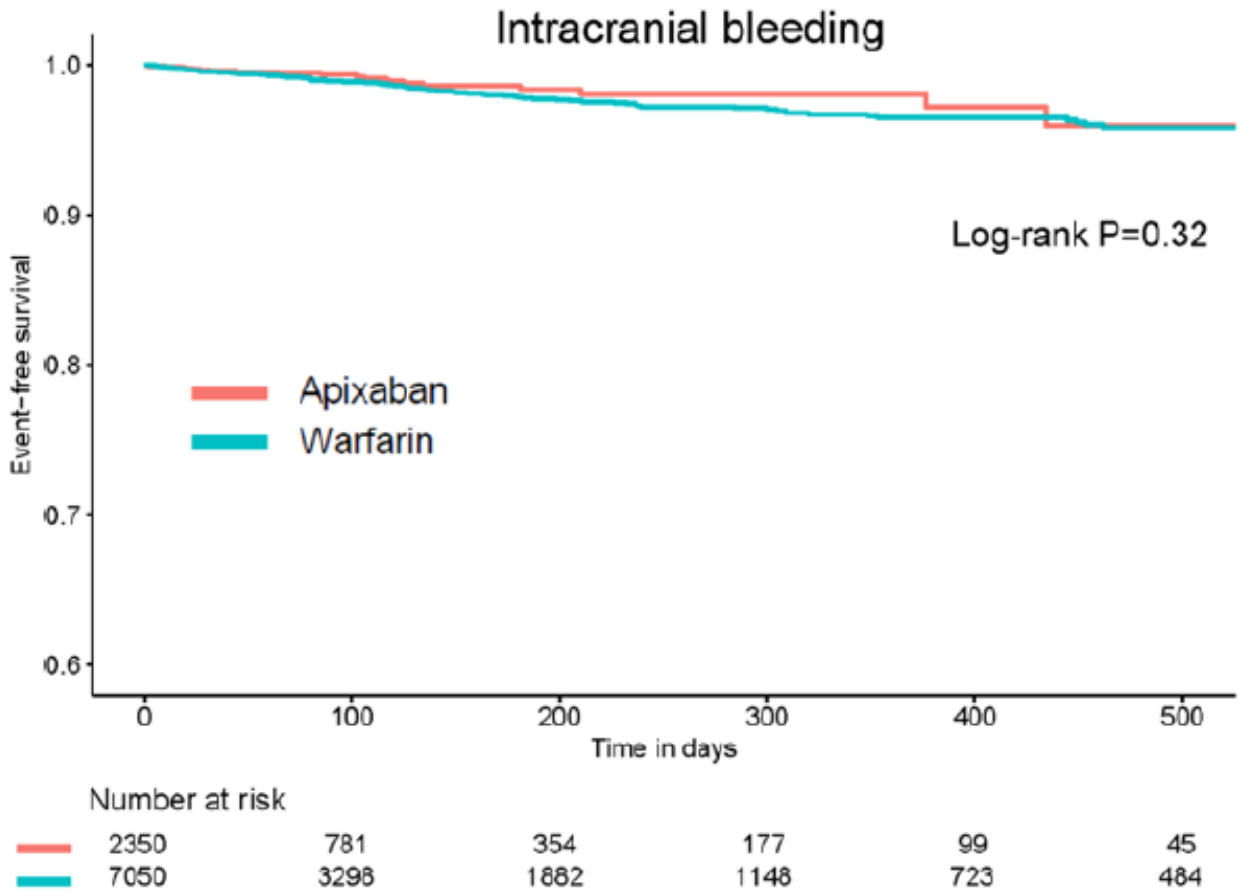
Table 1. Baseline Characteristics in the Overall Eligible Population

Variable	Overall (n=25 523)	Apixaban (n=2351)	Warfarin (n=23 172)
Demographics			
Age, y	68.22 (11.89)	68.87 (11.49)	68.15 (11.93)
Male	13 852 (54.3)	1280 (54.4)	12 572 (54.3)
Race			
White	16 837 (66.0)	1595 (67.8)	15 242 (65.8)
Black	7458 (29.2)	604 (25.7)	6,854 (29.6)
Other	1228 (4.8)	152 (6.5)	1076 (4.6)
Nephrology care			
Dialysis modality			
Hemodialysis	24 146 (94.6)	2216 (94.3)	21 930 (94.6)
Peritoneal dialysis	1377 (5.4)	135 (5.7)	1242 (5.4)
Time on dialysis, y			
<1	7196 (28.2)	656 (27.9)	6540 (28.2)
1 to <2	2949 (11.6)	240 (10.2)	2709 (11.7)
2 to <3	2759 (10.8)	256 (10.9)	2503 (10.8)
≥3	12 619 (49.4)	1199 (51.0)	11 420 (49.3)
Private insurance	3898 (15.3)	416 (17.7)	3482 (15.0)

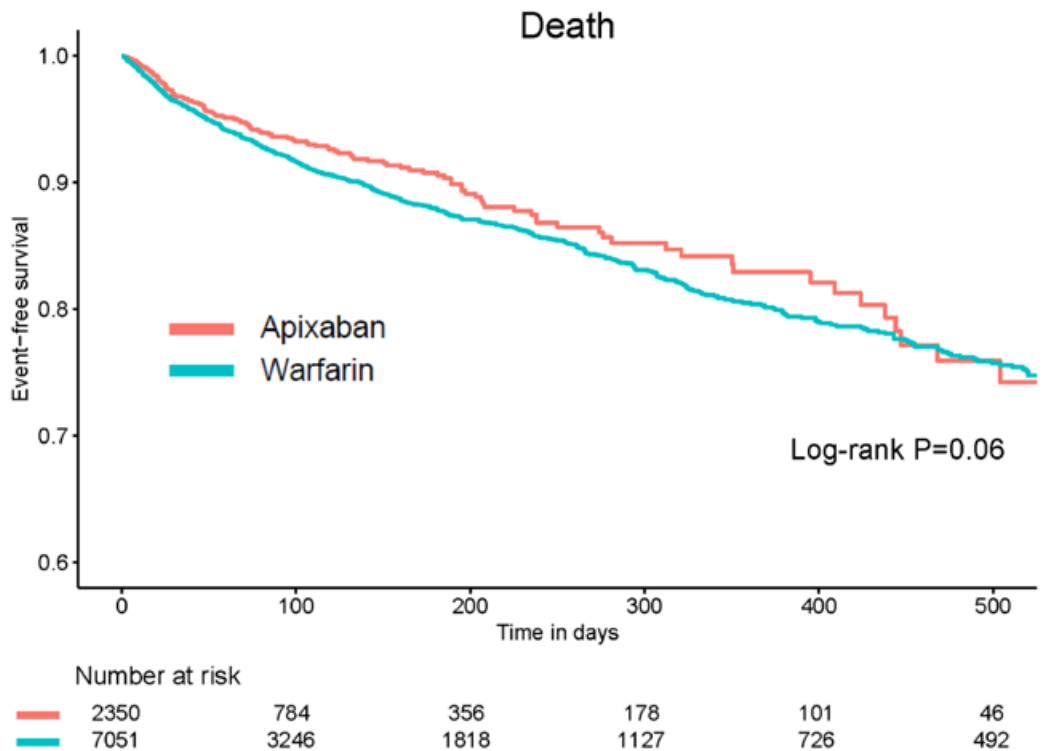
Apixaban approuvé par FDA en dialyse en 2013
En 2015, 26,6% des patients nouvellement anticoagulés le sont avec apixaban

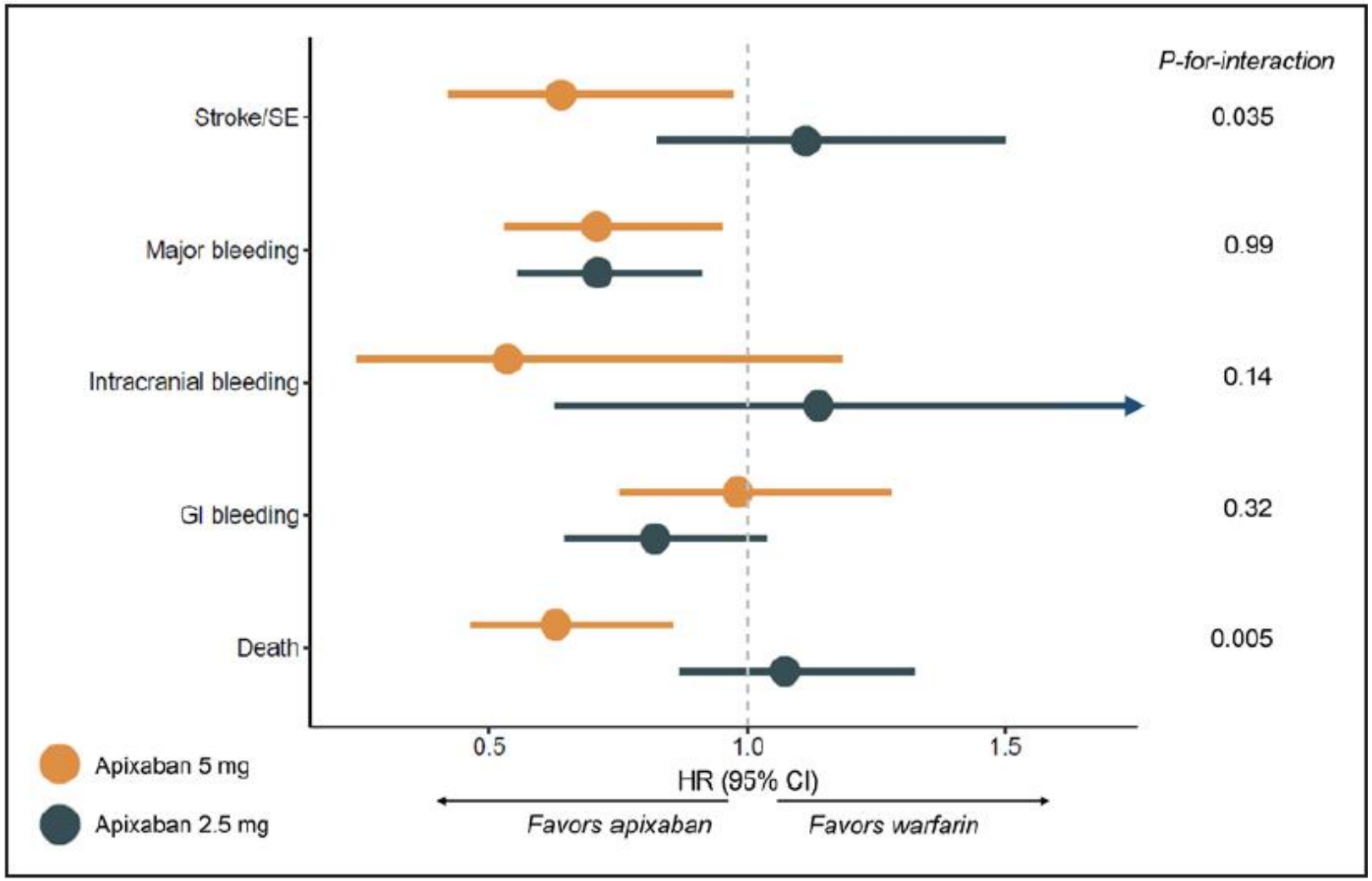

Major bleeding
Event−free survival
1.0
0.9
0.8
0.7
0.6
Apixaban
Warfarin
Log-rank P<0.001
0
100
200
300
400
500
Time in days
Number at risk
2351 768 340 171 96 43
7053 3172 1823 1118 720 479

-30%



3,1/100 patients/an


Death
1.0
0.9
0.8
0.7
0.6
Event−free survival
Apixaban
Warfarin
Log-rank P=0.06
0
100
200
300
400
500
Time in days
Number at risk
2350 784 356 178 101 46
7051 3246 1818 1127 726 492


P-for-interaction
Stroke/SE
0.035
Major bleeding
0.99
Intracranial bleeding
0.14
GI bleeding
0.32
Death
0.005
0.5
1.0
1.5
HR (95% CI)
Favors apixaban
Favors warfarin
Apixaban 5 mg
Apixaban 2.5 mg

Circulation

ORIGINAL RESEARCH ARTICLE

Prophylactic Use of Implantable Cardioverter-Defibrillators in the Prevention of Sudden Cardiac Death in Dialysis Patients

The Prospective, Randomized, Controlled ICD2 Trial

Circulation. 2019 Jun 4;139(23):2628-2638.

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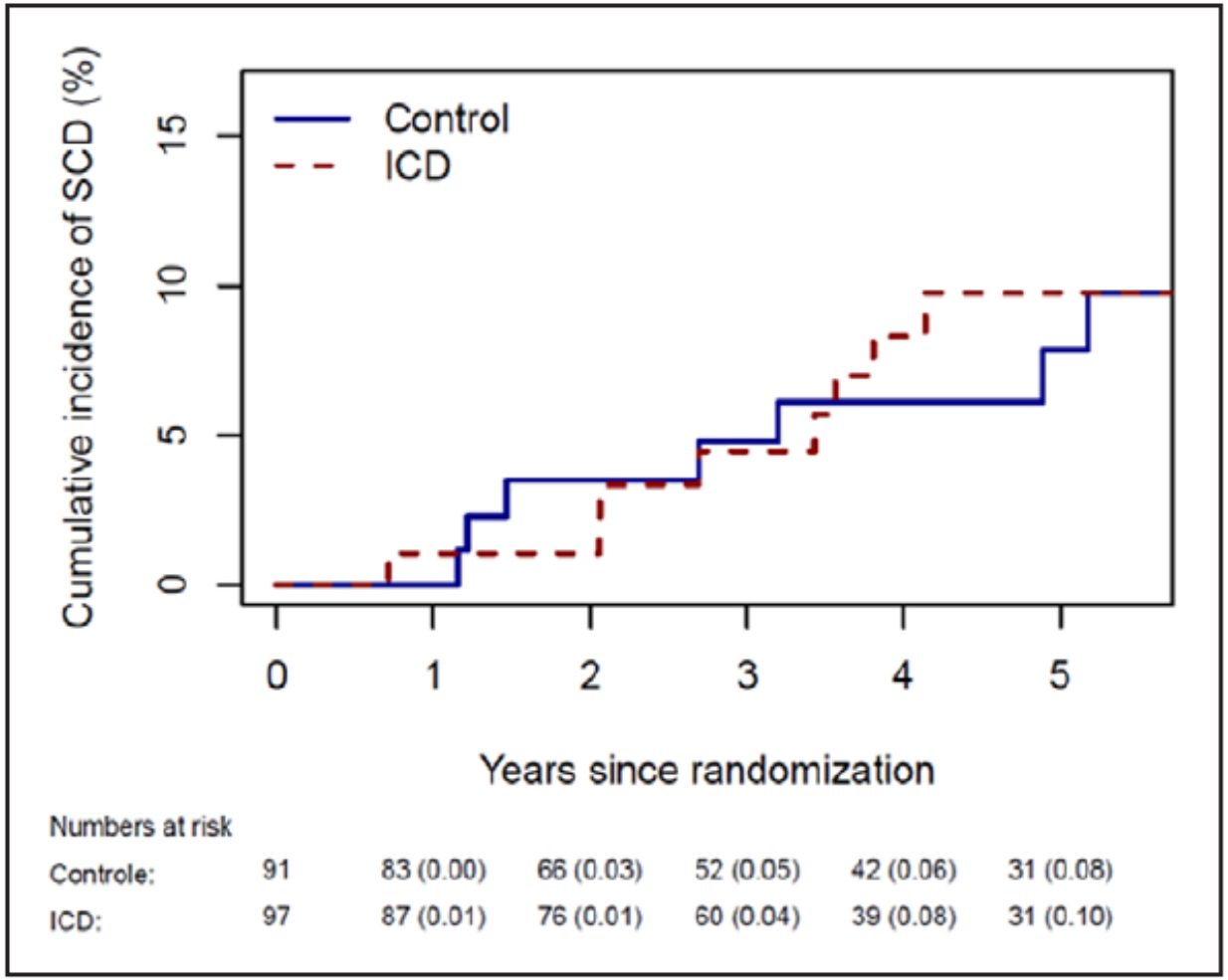
Bastiaan van Dam, MD, PhD
Charles A. Herzog, MD
Martin J. Schalij, MD, PhD
Ton J. Rabelink, MD, PhD
For the ICD2 Trial Investigators

- RCT, monocentrique, ouverte
- Pace défibrillant prophylactique en dialyse et FE≥35%
- 188 patients randomisés (97 « pacé » et 91 contrôle), suivi médian de 6,8 années
- Mort subite à 5 ans

Table 1. Baseline Characteristics (ITT Population)

Characteristic	ICD (n=97)	Control (n=91)
Men	74 (76.3)	69 (75.8)
Age, y	67 (62–74)	68 (61–74)
Body mass index, kg/m^2	28.0±5.4	27.2±4.7
Blood pressure, mm Hg		
Systolic	139±22	138±21
Diastolic	75±11	74±11
Heart rate, bpm	70±13	73±13
Dialysis		
Duration, mo	17 (10–27)	15 (10–27)
Modality		
Hemodialysis	71 (73.2)	63 (69.2)
Peritoneal dialysis	26 (26.8)	28 (30.8)
Kt/V urea per wk		
Hemodialysis	4.3 (3.6–5.2)	4.5 (3.8–5.1)
Peritoneal dialysis	2.2 (2.0–2.5)	2.6 (2.1–3.4)
Hemodialysis, d/wk	3 (3–3)	3 (3–3)
Symptoms		
NYHA I	59 (60.8)	56 (61.5)
NYHA II	25 (25.8)	25 (27.5)
NYHA III	9 (9.3)	6 (6.6)
Medical history		
Diabetes mellitus	34 (35.1)	38 (41.8)
Atrial fibrillation or flutter	25 (25.7)	17 (18.7)
Percutaneous transluminal coronary angioplasty	14 (14.4)	16 (17.6)
Coronary artery bypass graft	12 (12.4)	13 (14.3)
Myocardial infarction	23 (23.7)	27 (29.7)
Heart failure	4 (4.1)	5 (5.5)
Transient ischemic attack/ cerebrovascular accident	13 (13.4)	18 (19.8)
Hypertension	80 (82.5)	71 (78.0)
Hypercholesterolemia	54 (55.7)	43 (47.3)
Cardiovascular risk profile		
Family history of premature cardiovascular disease	34 (35.1)	30 (33.0)
Smoking		
Never	36 (37.1)	25 (27.5)
Current/former	61 (63.9)	66 (72.5)
Medication use		
β-Blocker	57 (58.8)	51 (56.0)
Angiotensin-converting enzyme inhibitor	20 (20.6)	19 (20.9)

Characteristic	ICD (n=97)	Control (n=91)
Angiotensin receptor blocker	33 (34.0)	24 (26.4)
Calcium antagonist	37 (38.1)	29 (31.9)
Statin	58 (59.8)	58 (63.7)
Insulin	16 (16.5)	20 (22.0)
Erythropoietin	82 (84.5)	72 (79.1)
Cause of end-stage renal disease		
Diabetic nephropathy	23 (23.7)	21 (23.1)
Hypertension	37 (38.1)	27 (29.7)
Cystic kidney	4 (4.1)	6 (6.6)
Glomerulonephritis	14 (14.4)	9 (9.9)
Other/unknown	19 (19.6)	28 (30.8)
Echocardiography		
LVEF ≥55%	58 (59.8)	45 (49.5)
LVEF ≥45% and <55%	26 (26.8)	30 (33.0)
LVEF ≥35% and <45%	13 (13.4)	16 (17.6)
Left ventricular hypertrophy	42 (43.3)	43 (47.3)



10,1% (total)

9,7%

7,8%

Figure 2. Five-year cumulative incidence of sudden cardiac death (SCD) per treatment group (intention-to-treat analysis).
The difference in SCD incidence was nonsignificant (*P*=0.55, log-rank test).
ICD indicates implantable cardioverter-defibrillator.

Table 3. Adverse Events (Based on Crude Rates) in the ICD Group (n=80)

Event	n (%)
Directly related to ICD implantation procedure	10 (12.5)
Pocket hematoma	2 (2.5)
Pocket infection	3 (3.8)
Post-ICD implantation bacteremia	1 (1.3)
Pneumothorax	0
Lead dysfunction	10 (12.5)
Lead dislocation	3 (3.8)
Lead perforation	1 (1.3)
Lead malfunction	6 (7.5)
Inappropriate shocks	4 (5.0)
Subclavian vein stenosis	3 (3.8)
ICD explantation	6 (7.5)
Attributable to bacteremia	4 (5.0)
Directly related to ICD implantation	1 (1.3)
Probably not related to ICD implantation	3 (3.8)

ICD indicates implantable cardioverter defibrillator.

Research

JAMA Internal Medicine | Original Investigation

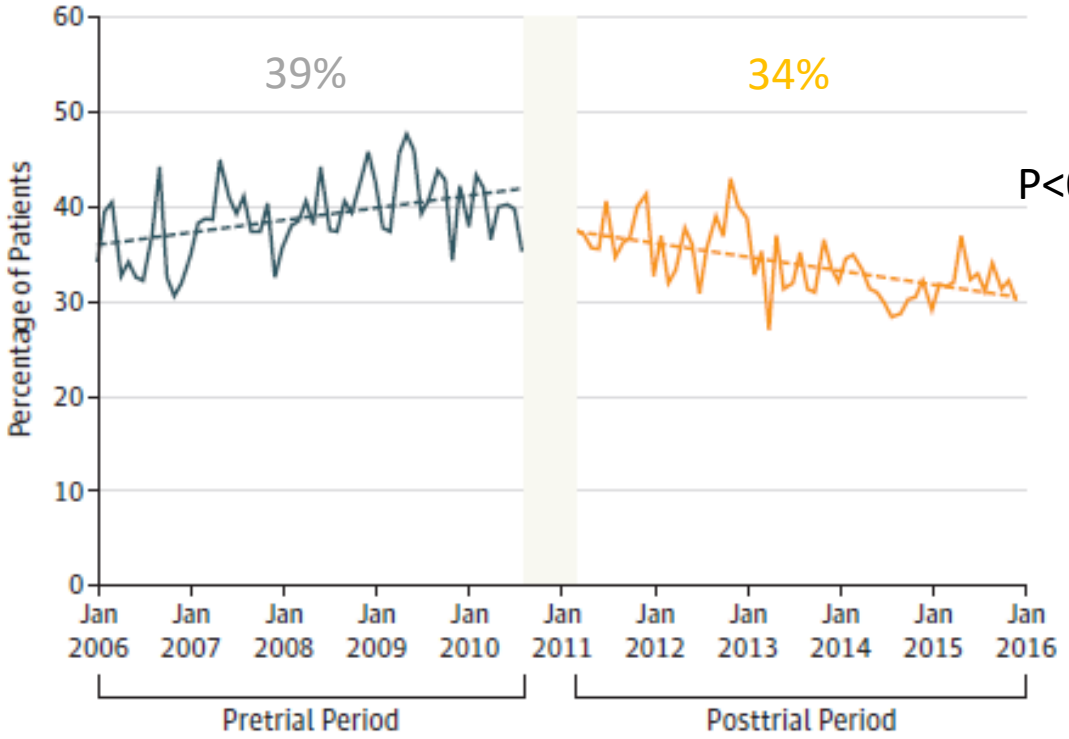
Association Between the Publication of the Initiating Dialysis Early and Late Trial and the Timing of Dialysis Initiation in Canada

Thomas W. Ferguson, MSc; Amit X. Garg, MD; Manish M. Sood, MD; Claudio Rigatto, MD; Elaine Chau, MBT; Paul Komenda, MD; David Naimark, MD; Gihad E. Nesrallah, MD; Steven D. Soroka, MD; Monica Beaulieu, MD; Ahsan Alam, MD; S. Joseph Kim, MD; Stephanie Dixon, PhD; Braden Manns, MD; Navdeep Tangri, MD

JAMA Intern Med. 2019 Jul 1;179(7):934-941.

- Observationnelle, rétrospective, registre canadien
- Les pratiques de dialyse sont-elles modifiées en termes de prise en charge depuis l'étude IDEAL?
- 28,468 patients (11,429 avant 17,039 après) avec au moins 90 jours de suivi néphrologique avant prise en charge et eGFR disponible (MDRD)

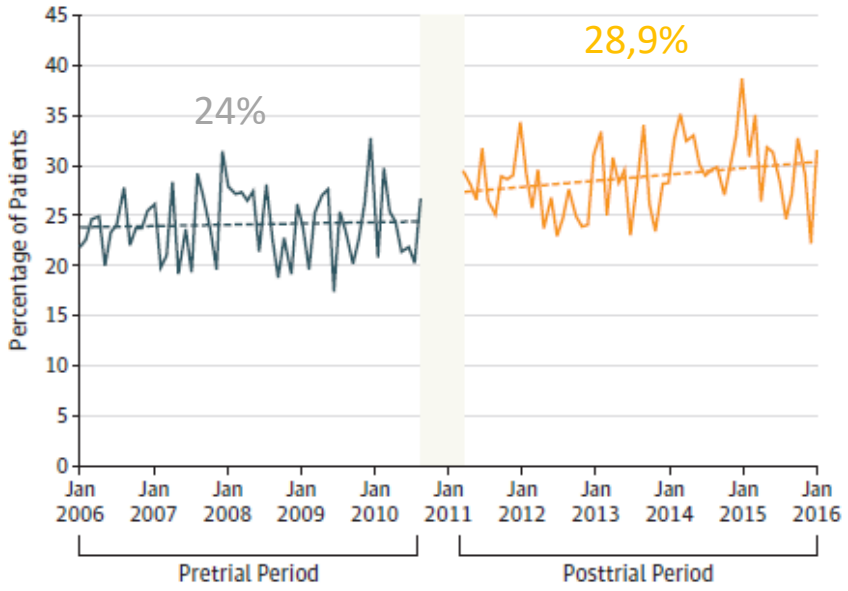
Figure 1. Percentage of Patients Initiating Dialysis Early Over Time eGFR>10.5 mL/min/1.73m²



P<0,001

P=0,08

Figure 2. Percentage of Patients Initiating Dialysis as an Acute Inpatient Over Time



Research

JAMA Internal Medicine | Original Investigation

Representativeness of Randomized Clinical Trial Cohorts in End-stage Kidney Disease
A Meta-analysis

Brendan Smyth, MBBS; Anna Haber, MBBS; Konlawij Trongtrakul, MD; Carmel Hawley, MMedSci; Vlado Perkovic, PhD; Mark Woodward, PhD; Meg Jardine, PhD

JAMA Intern Med. 2019 Jul 8. doi: 10.1001/jamainternmed.2019.1501. [Epub ahead of print]

- Comparaison RCT en dialyse entre 2007 et 2016 et données USRDS de 2011
- 189 RCT et 80,104 patients inclus
- USRDS: +500,000 patients
- Différence en âge (diabète et mortalité)

Table 2. Study Participant Characteristics Compared With USRDS

Characteristic	USRDS Value, %[a]	All RCTs, Mean (95% CI)	Trials, No.	*P* Value
Total No. of trials			189	
Age, y	61.2	58.9 (58.3-59.5)	187	<.001
Male sex	55.7	58.8 (57.5-60.0)	186	<.001
Comorbid diabetes	44.2	40.4 (36.9-43.8)	92	.04
Primary renal disease				
Diabetic nephropathy	44.2	27.4 (24.9-29.9)	89	<.001
Hypertension or vascular	29.0	20.7 (18.3-23.0)	78	<.001
Glomerulonephritis	9.5	25.5 (22.4-28.5)	84	<.001
Cystic kidney disease	2.6	5.3 (4.6-6.1)	51	<.001
Comorbidities at start of RRT, all modalities (2011-2013)				
Heart failure	29.8	19.9 (15.6-24.3)	33	<.001
Coronary artery disease	17.7	26.7 (22.1-31.4)	36	<.001
Cerebrovascular disease	8.8	11.1 (9.6-12.5)	30	.004
Peripheral vascular disease	12.0	15.2 (12.3-18.0)	26	.04
Hemoglobin, g/dL				
Prevalent hemodialysis	11.00	11.01 (10.83-11.19)	92	.88
Prevalent peritoneal dialysis	10.83			.05
Albumin, g/dL				
Incident, all modalities (2011-2013)	3.20	3.78 (3.73-3.82)	79	<.001
Vascular access				
Catheter	21.2	12.9 (10.3-15.5)	22	<.001
Mortality rate, per 100 patient-years (2011-2013)	18.6	8.9 (7.9-10.0)	126	<.001

Research

JAMA Internal Medicine | Original Investigation

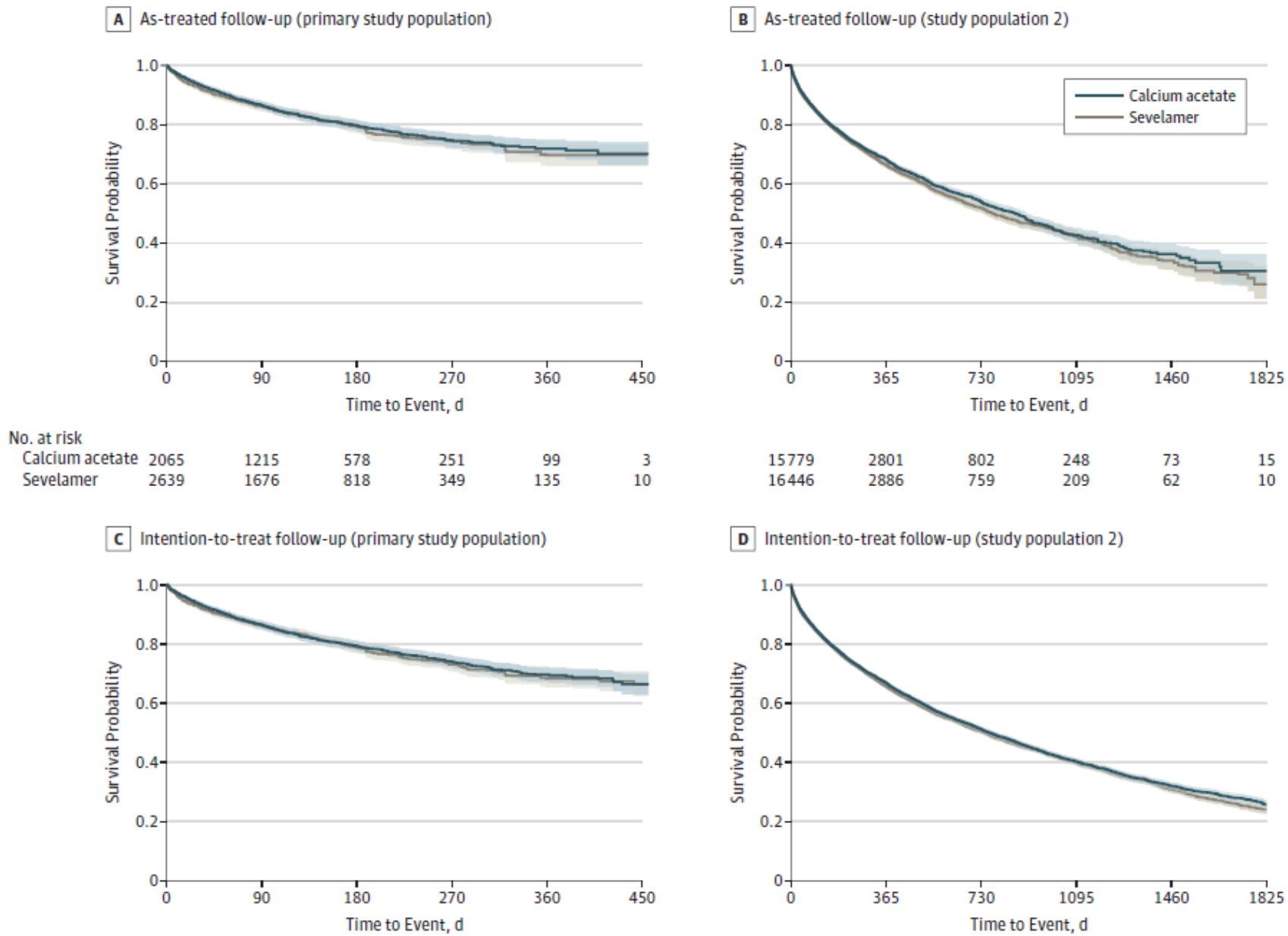
Cardiovascular Outcomes of Calcium-Free vs Calcium-Based Phosphate Binders in Patients 65 Years or Older With End-stage Renal Disease Requiring Hemodialysis

Julia Spoendlin, PhD, MPH; Julie M. Paik, MD, ScD; T. Tsacogianis, MPH; Seoyoung C. Kim, MD, ScD; Sebastian Schneeweiss, MD, ScD; Rishi J. Desai, MS, PhD

JAMA Intern Med. 2019 Jun 1;179(6):741-749.

- Observationnelle, rétrospective, cohorte USRDS
- Patients +65 ans, traitement par chélateurs débuté dans les 180 jours de la prise en charge en dialyse
- 2,647 (2,639) dans le groupe sevelamer et 2,074 (2,065) dans le groupe acétate de calcium
- Suivi maximal de 1,5 ans
- Mortalité CV, infar, AVC ischémique

Figure 1. Weighted Kaplan-Meier Curves for Cardiovascular Events



Research

JAMA Internal Medicine | Original Investigation

Assessment of Self-reported Prognostic Expectations of People Undergoing Dialysis

United States Renal Data System Study of Treatment Preferences (USTATE)

Ann M. O'Hare, MD; Manjula Kurella Tamura, MD; Danielle C. Lavallee, PhD; Elizabeth K. Vig, MD; Janelle S. Taylor, PhD; Yoshio N. Hall, MD; Ronit Katz, DPhil; J. Randall Curtis, MD; Ruth A. Engelberg, PhD

JAMA Intern Med. 2019 Jul 8. doi: 10.1001/jamainternmed.2019.2879. [Epub ahead of print]

Research

JAMA Internal Medicine | Original Investigation | SHARING MEDICINE

Care Practices for Patients With Advanced Kidney Disease Who Forgo Maintenance Dialysis

Susan P. Y. Wong, MD, MS; Lynne V. McFarland, PhD; Chuan-Fen Liu, PhD; Ryan J. Laundry, BA; Paul L. Hebert, PhD; Ann M. O'Hare, MD, MA

JAMA Intern Med. 2019 Mar 1;179(3):305-313.

Research

JAMA Internal Medicine | Original Investigation

Trends Associated With Large-scale Expansion of Peritoneal Dialysis Within an Integrated Care Delivery Model

Leonid V. Pravoverov, MD; Sijie Zheng, MD, PhD; Rishi Parikh, MPH; Thida C. Tan, MPH; Neelam Bhalla, MD; Chitra Reddy, MD; Joanna Mroz, MS, MPH; Tracy Y. Jonelis, MD; Alan S. Go, MD

JAMA Intern Med. 2019 Sep 9. doi: 10.1001/jamainternmed.2019.3155. [Epub ahead of print]

Research

JAMA Internal Medicine | Original Investigation

Association of Scheduled vs Emergency-Only Dialysis With Health Outcomes and Costs in Undocumented Immigrants With End-stage Renal Disease

Oanh Kieu Nguyen, MD, MAS; Miguel A. Vazquez, MD; Lakeesha Charles, LCSW; Joseph R. Berger, MD; Henry Quiñones, MD; Richard Fuquay, MD; Joanne M. Sanders, MS; Kandice A. Kapinos, PhD; Ethan A. Halm, MD, MPH; Anil N. Makam, MD, MAS

JAMA Intern Med. 2019 Jul 22. doi: 10.1001/jamainternmed.2019.1218. [Epub ahead of print]

Annals of Internal Medicine

REVIEW

Benefits and Harms of Oral Anticoagulant Therapy in Chronic Kidney Disease

A Systematic Review and Meta-analysis

Jeffrey T. Ha, MBBS; Brendon L. Neuen, MBBS(Hons); Lap P. Cheng, MBBS; Min Jun, PhD; Tadashi Toyama, PhD; Martin P. Gallagher, PhD; Meg J. Jardine, PhD; Manish M. Sood, MD; Amit X. Garg, PhD; Suetonia C. Palmer, PhD; Patrick B. Mark, PhD; David C. Wheeler, MD; Vivekanand Jha, MD; Ben Freedman, PhD; David W. Johnson, PhD; Vlado Perkovic, PhD; and Sunil V. Badve, PhD

Ann Intern Med. 2019 Aug 6;171(3):181-189. doi:

- Méta-analyse
- Balance risque/bénéfice de l'anticoagulation (AVK versus NOACs)
- Données de patients dialysés venant de 8 études, n=685
- « pas de données NOAC », pas de donnée en FA
- pas « d'évidence » à retirer de la méta-analyse

- RENAL-AF: Warfarine versus apixaban en hémodialyse (NCT02942407)
- AXADIA: Warfarine versus apixaban en hémodialyse (NCT02933697)
- AVKDIAL: AVK versus pas d’anticoagulation en hémodialyse (NCT02886962)

Annals of Internal Medicine

ORIGINAL RESEARCH

Comparative Efficacy of Therapies for Treatment of Depression for Patients Undergoing Maintenance Hemodialysis

A Randomized Clinical Trial

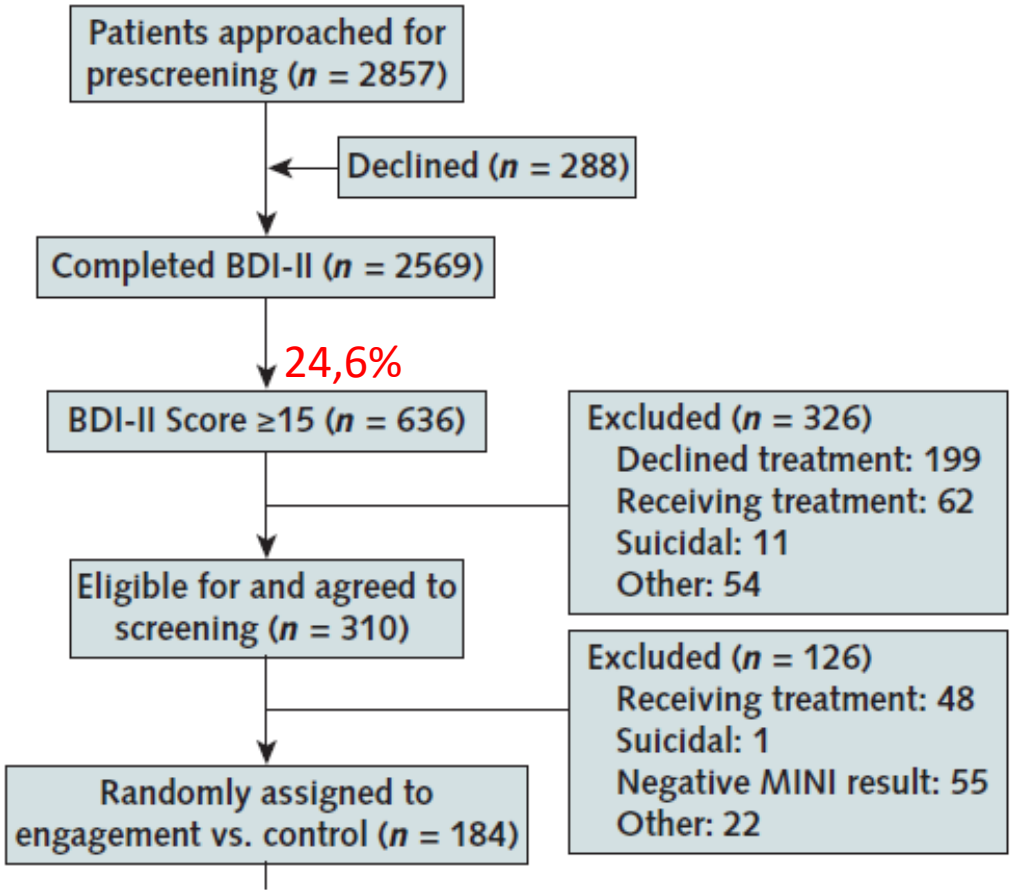
Rajnish Mehrotra, MD, MS; Daniel Cukor, PhD; Mark Unruh, MD, MS; Tessa Rue, MS; Patrick Heagerty, MS, PhD; Scott D. Cohen, MD, MPH; Laura M. Dember, MD; Yaminette Diaz-Linhart, MSW, MPH; Amelia Dubovsky, MD; Tom Greene, PhD; Nancy Grote, MSW, MEd, PhD; Nancy Kutner, PhD; Madhukar H. Trivedi, MD; Davin K. Quinn, MD; Nisha ver Halen, PhD; Steven D. Weisbord, MD, MSc; Bessie A. Young, MD, MPH; Paul L. Kimmel, MD; and S. Susan Hedayati, MD, MSc

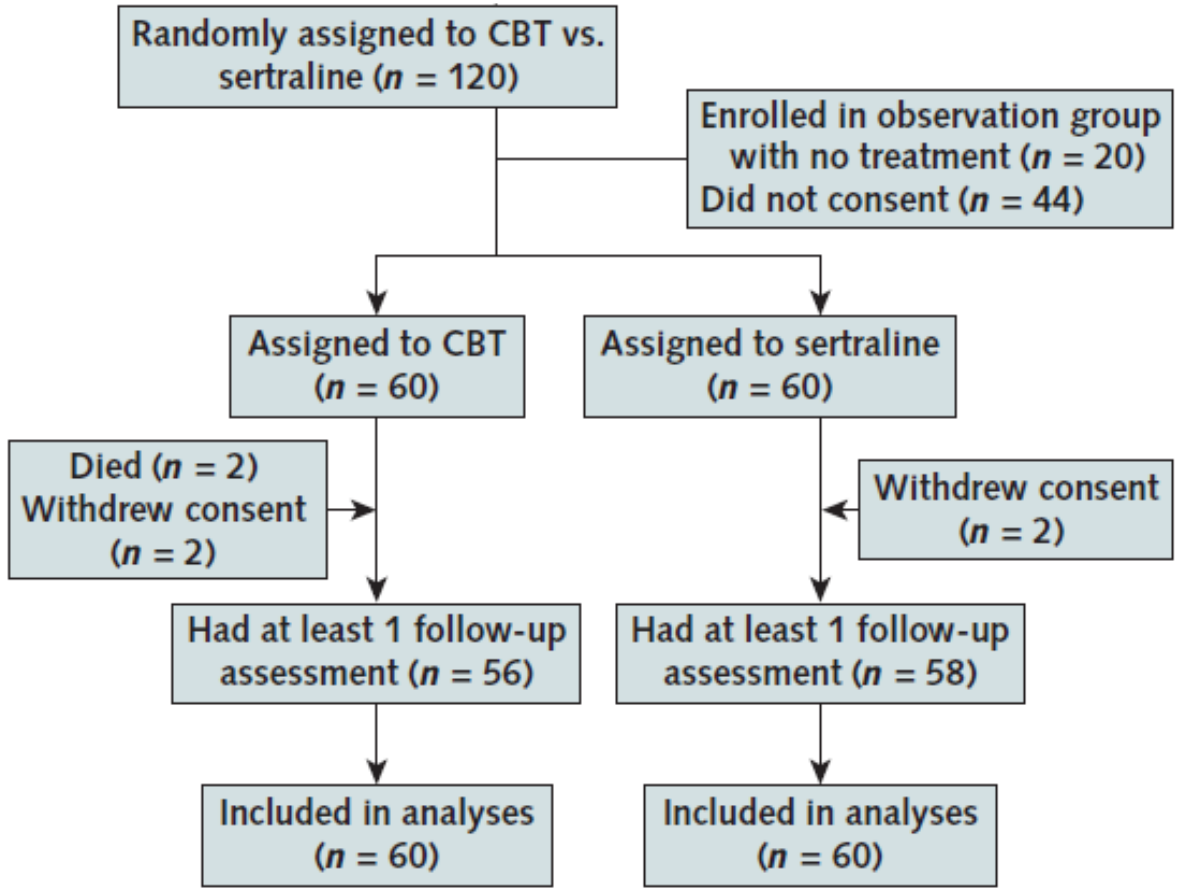
Ann Intern Med. 2019 Mar 19;170(6):369-379.

- RCT, multicentrique, ouverte
- Patients hémodialysés avec diagnostic de dépression sévère (scores)
- Thérapie cognitive/comportementale versus sertraline
- Phase 1: 8 semaines Phase 2: 12 semaines
- Phase 1: 180 patients Phase 2: 120 patients
- Phase 1: proportion de patients qui passent à la phase 2 (début du traitement)
- Phase 2: score de dépression QIDS-C à 12 semaines

Phase 1: pas de difference significative (66% versus 64% visite classique)

Figure 1. Enrollment, randomization, and follow-up.



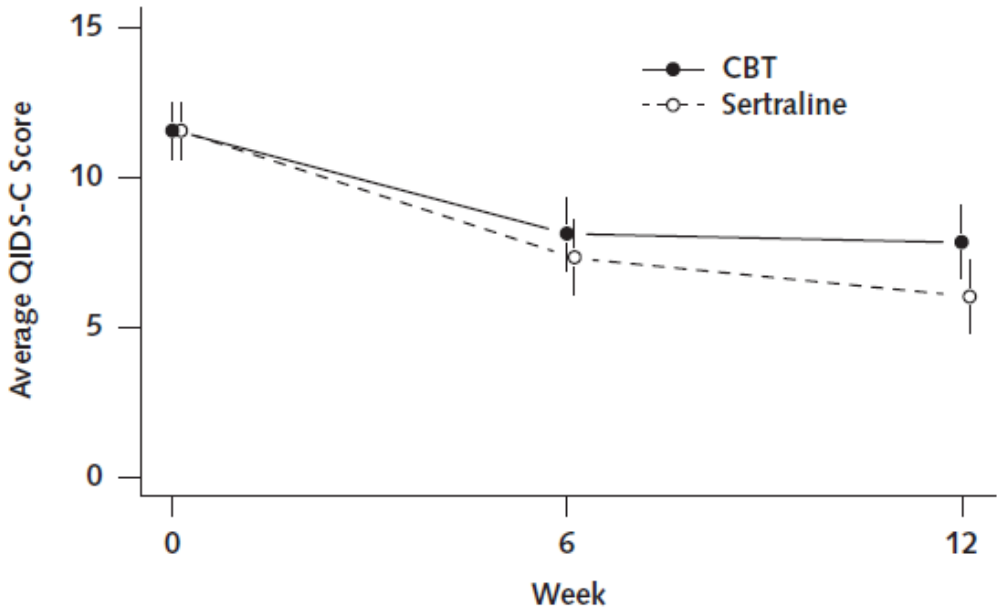

Randomly assigned to CBT vs. sertraline (n = 120)
Enrolled in observation group with no treatment (n = 20)
Did not consent (n = 44)
Assigned to CBT (n = 60)
Assigned to sertraline (n = 60)
Died (n = 2)
Withdrew consent (n = 2)
Withdrew consent (n = 2)
Had at least 1 follow-up assessment (n = 56)
Had at least 1 follow-up assessment (n = 58)
Included in analyses (n = 60)
Included in analyses (n = 60)

Supplementary Table 6. Prescribed dose of sertraline at each visit among the 60 patients randomized to drug therapy arm during the course of the 12-week treatment period

	0 week	2-week	4-week	6-week	9-week
Median Dose	25	100	150	150	100
% of patients taking drug	97	87	78	78	78
25 or 50 mg, %	97	17	8	8	10
100 mg, %	0	70	17	15	20
150 mg, %	0	0	53	17	12
200 mg, %	0	0	0	38	37

Psychothérapie: 80% ont eu 8 séances et 73% en ont eu 10

Figure 2. Longitudinal data on the primary outcome measure of QIDS-C scores among patients receiving hemodialysis with depression who were randomly assigned to CBT or sertraline treatment.



At each time point, for each treatment group, the data are presented as mean and 95% CI. CBT = cognitive behavioral therapy; QIDS-C = Quick Inventory of Depressive Symptoms-Clinician-Rated.

P=0,035

5 des 9 “secondary endpoints” meilleurs dans le groupe sertraline

Plus d’ES « mineur » dans le groupe sertraline

ORIGINAL

Association between intravenous contrast media exposure and non-recovery from dialysis-requiring septic acute kidney injury: a nationwide observational study

Yoshihisa Miyamoto[1], Masao Iwagami[2,3], Shotaro Aso[4], Hideo Yasunaga[4], Hiroki Matsui[4], Kiyohide Fushimi[5], Yoshifumi Hamasaki[1,6], Masaomi Nangaku[1,6] and Kent Doi[7*]

Intensive Care Med. 2019 Aug 26. doi: 10.1007/s00134-019-05755-2. [Epub ahead of print]

- Observationnelle, rétrospective, multicentrique
- Les patients hémofiltrés qui reçoivent du contraste récupèrent-ils moins bien au niveau rénal?
- Scanner à l'admission
- CVVH pour choc septique dans les 48 heures après l'admission
- 3,782 exposés au contraste (C+) et 6,119 non-exposés (C-)
- Traitement statistique complexe
- Mortalité et/ou dépendance à la dialyse

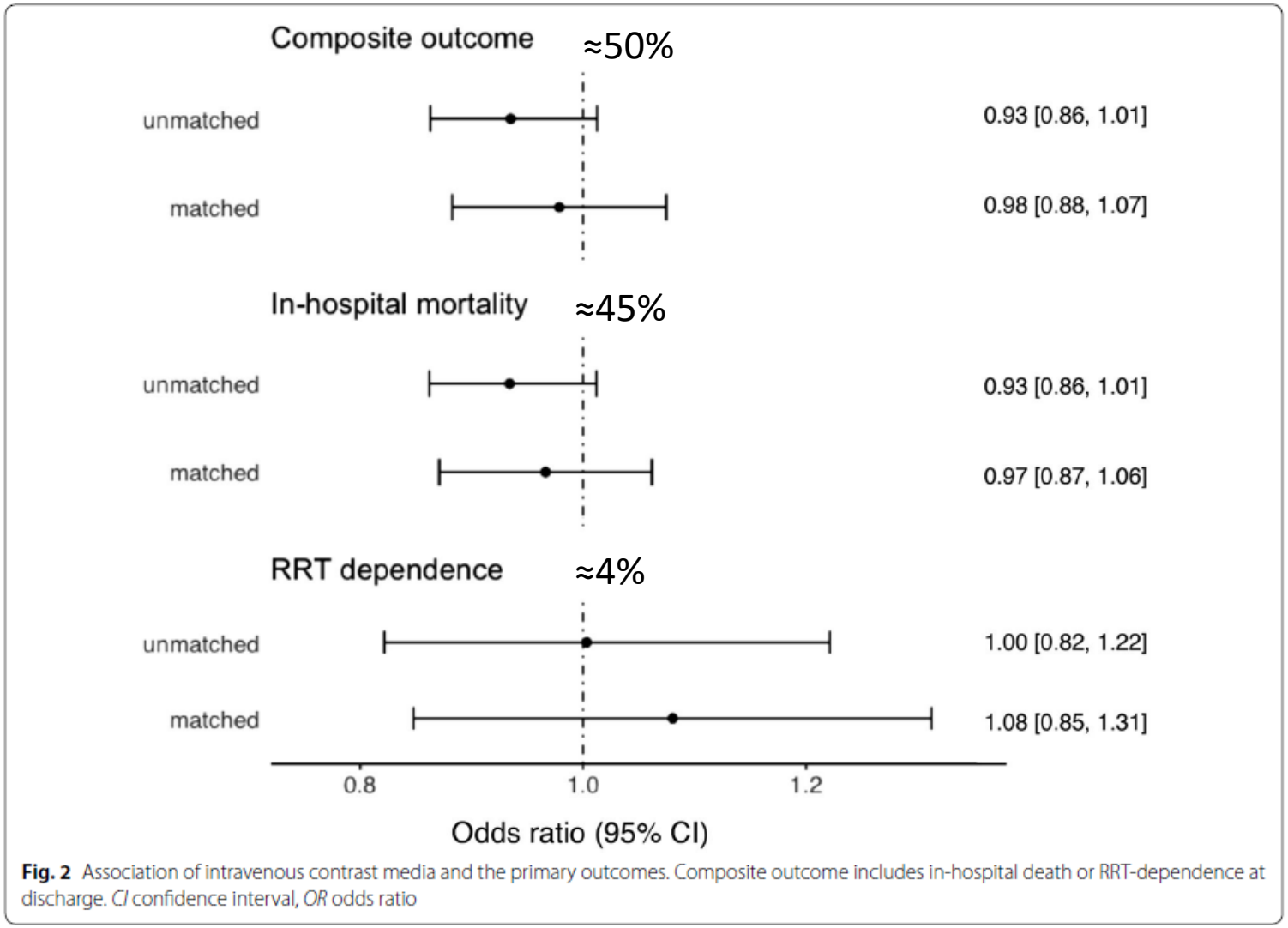


Fig. 2 Association of intravenous contrast media and the primary outcomes. Composite outcome includes in-hospital death or RRT-dependence at discharge. *CI* confidence interval, *OR* odds ratio

ARTICLE IN PRESS

Research Article
Viral Hepatitis

JOURNAL
OF HEPATOLOGY

Sofosbuvir/velpatasvir for 12 weeks in hepatitis C virus-infected patients with end-stage renal disease undergoing dialysis

Sergio M. Borgia[1,*], Janet Dearden[2], Eric M. Yoshida[3], Stephen D. Shafran[4], Ashley Brown[5], Ziv Ben-Ari[6], Matthew E. Cramp[7], Curtis Cooper[8], Matthew Foxton[9], Conrado Fernandez Rodriguez[10], Rafael Esteban[11], Robert Hyland[12], Sophia Lu[12], Brian J. Kirby[12], Amy Meng[12], Svetlana Markova[12], Hadas Dvory-Sobol[12], Anu O. Osinusi[12], Rafael Bruck[13], Javier Ampuero[14], Stephen D. Ryder[15], Kosh Agarwal[16], Raymond Fox[17], David Shaw[18], Shariq Haider[19], Bernard Willems[20], Yoav Lurie[21], Jose Luis Calleja[22], Edward J. Gane[23]

J Hepatol. 2019 Jun 11. pii: S0168-8278(19)30343-5. doi: 10.1016/j.jhep.2019.05.028. [Epub ahead of print]

- Phase 2, prospective, multicentrique, non-contrôlée
- Patients dialysés infectés par virus hépatite C
- 12 semaines de sofosbuvir/velpatasvir (400 mg/ 100 mg) (Epclusa©)
- 59 patients
- Réponse virologique (HCV RNA<15 UI/mL), 12 semaines après l'arrêt du traitement

Table 1. Baseline demographics and disease characteristics.

	Sofosbuvir/velpatasvir for 12 weeks (n = 59)
Mean age (range), yr	60 (33–91)
Male, n (%)	35 (59)
Race, n (%)	
White	31 (53)
Asian	18 (31)
Black or African American	6 (10)
American Indian or Alaska Native	2 (3)
Native Hawaiian or Pacific Islander	2 (3)
Mean body mass index (range), kg/m^2	26 (17–39)
HCV genotype, n (%)	
1	27 (46)
1a	15 (25)
1b	11 (19)
Other	1 (2)
2	7 (12)
3	19 (32)
4	4 (7)
6	2 (3)
Cirrhosis, n (%)	17 (29)
Mean HCV RNA level (range), log_{10} IU/ml	5.8 (3.1–7.7)
Prior HCV treatment experience, n/N (%)	13/59 (22)
Direct-acting antiviral-naive	
Pegylated interferon + ribavirin	6//13 (46)
Other	7/13 (54)
Type of dialysis, n (%)	
Hemodialysis	54 (92)
Peritoneal dialysis	5 (9)
Mean duration of dialysis (range), yr	7 (0–40)
Prior renal transplant, n (%)	19 (32)

Table 2. Treatment response.

	Sofosbuvir/velpatasvir for 12 weeks (n = 59)
SVR12, n (%)	56 (95)
Overall virologic failure, n (%)	2 (3)
Relapse	2 (3)
On-treatment virologic failure	0
Other, n (%)	1 (2)

SVR12, sustained virologic response rate 12 weeks after discontinuation of treatment.

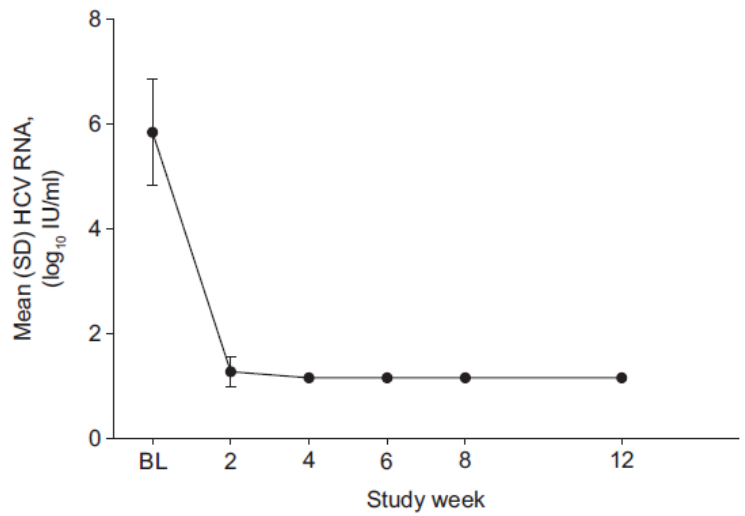


Fig. 1. Mean (± SD) HCV RNA levels from baseline through end of treatment. BL, baseline.

Table 3. Adverse events and laboratory abnormalities.

	Sofosbuvir/velpatasvir for 12 weeks (n = 59)
Any adverse event, n (%)	47 (80)
Grade 3 adverse events, n (%)[a]	7 (12)
Serious adverse events, n (%)[b]	11 (19)
Adverse events leading to sofosbuvir/velpatasvir discontinuation, n (%)	0
Deaths, n (%)	2 (3)
Adverse events occurring in ≥ 10% of patients, n (%)	
Headache	10 (17)
Fatigue	8 (14)
Nausea	8 (14)
Vomiting	8 (14)
Insomnia	6 (10)
Grade 3 or 4 laboratory abnormalities in > 1 patient, n (%)	
Creatinine	
Grade 3	1 (2)
Grade 4	14 (24)
Hyperglycemia[c]	
Grade 3	5 (9)
Hemoglobin	
Grade 3	4 (7)
Hyperkalemia	
Grade 3	2 (3)
Grade 4	1 (2)

[a] Cardiac failure congestive, device-related infection, headache, insomnia, neurilemmoma benign, pneumonia, and pubis fracture; all unrelated to study treatment.
[b] Anxiety, atrial fibrillation, cardiac failure congestive, cellulitis, depression, device-related infection, neurilemmoma benign, pneumonia, post procedural hemorrhage, post procedural swelling, pubis fracture, respiratory tract infection, and streptococcal bacteremia; all unrelated to study treatment.

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 22, 2019

PUBLISHED BY ELSEVIER

Transcatheter Aortic Valve Replacement in Patients With End-Stage Renal Disease

Molly Szerlip, MD,[a,*] Alan Zajarias, MD,[b,*] Sreekanth Vemalapalli, MD,[c] Matthew Brennan, MD,[c] Dadi Dai, PHD,[c] Hersh Maniar, MD,[b] Brian R. Lindman, MD,[d] Ralph Brindis, MD,[e] John D. Carroll, MD,[f] Mohanad Hamandi, MD,[a] Fred H. Edwards, MD,[g] Fred Grover, MD,[f] Sean O'Brien, PHD,[c] Eric Peterson, MD,[c] John S. Rumsfeld, MD, PHD,[f] Dave Shahian, MD,[h] E. Murat Tuzcu, MD,[i] David Holmes, MD,[j] Vinod H. Thourani, MD,[k] Michael Mack, MD[a]

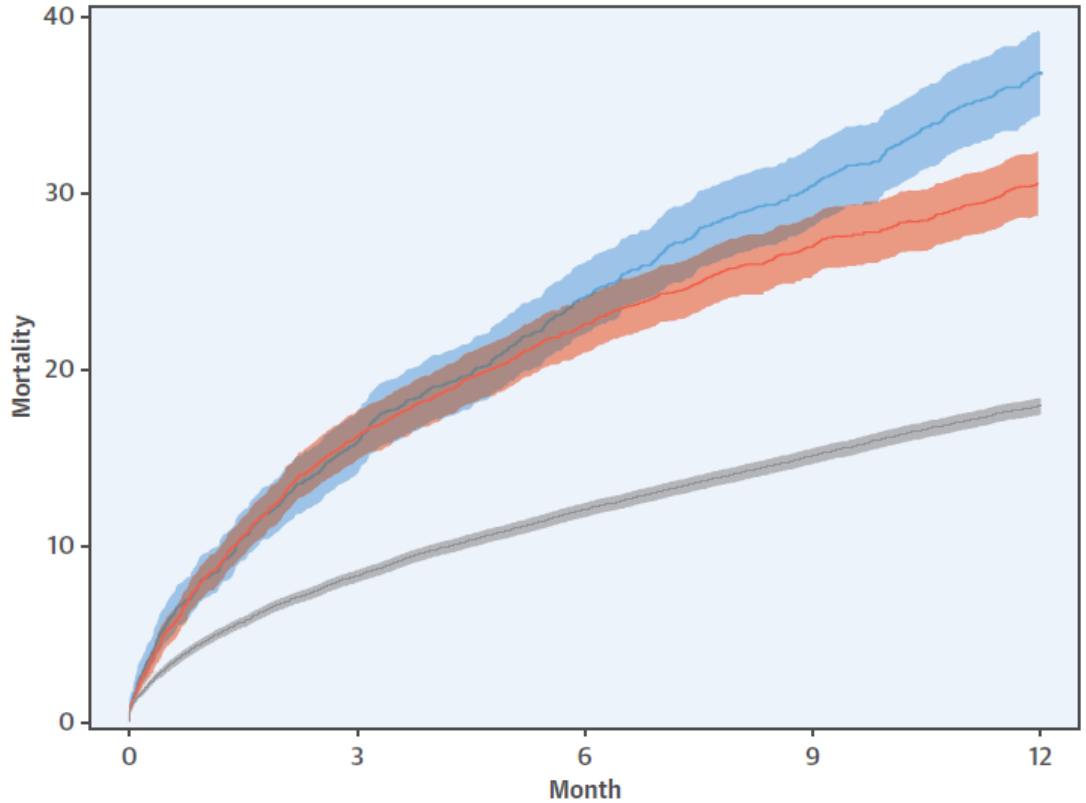
J Am Coll Cardiol. 2019 Jun 11;73(22):2806-2815.

- Registre (TVT), rétrospective
- TAVI pour sténose aortique chez patients dialysés versus non dialysés
- 3,053 dialysés versus 69,578
- Complications et mortalité à 1 an

TABLE 1 Baseline Characteristics of the Study Population

	Overall (N = 72,631)	No Dialysis (n = 69,578)	Dialysis (n = 3,053)	p Value
Age, yrs	83 (77-87)	83 (77-88)	76 (68-82)	<0.001
Male	37,925 (52.2)	36,089 (51.9)	1,836 (60.1)	<0.001
Race				<0.001
Caucasian	68,168 (93.9)	65,722 (94.5)	2,446 (80.1)	
African American	2,755 (3.8)	2,311 (3.3)	444 (14.5)	
Asian	859 (1.2)	783 (1.1)	76 (2.5)	
Other	849 (1.2)	762 (1.1)	87 (2.8)	
BSA, m^2	1.85 (1.68-2.02)	1.85 (1.68-2.02)	1.86 (1.70-2.03)	<0.001
Comorbidities				
Atrial fibrillation	29,542 (40.7)	28,301 (40.7)	1,241 (40.6)	0.977
COPD				<0.001
None/mild	52,535 (72.8)	50,559 (73.1)	1,976 (65.0)	
Moderate	9,770 (13.5)	9,262 (13.4)	508 (16.7)	
Severe	9,859 (13.7)	9,305 (13.5)	554 (18.2)	
Diabetes	27,203 (37.5)	25,503 (36.7)	1,700 (55.7)	<0.001
Hypertension	65,163 (89.7)	62,322 (89.6)	2,841 (93.1)	<0.001
PAD	22,162 (30.5)	20,934 (30.1)	1,228 (40.2)	<0.001
Prior MI	18,045 (24.8)	17,085 (24.6)	960 (31.4)	<0.001
Prior CABG	20,290 (27.9)	19,500 (28.0)	790 (25.9)	0.010
Prior PCI	25,369 (34.9)	24,193 (34.8)	1,176 (38.5)	<0.001
Heart failure				<0.001
NYHA functional class I-II	13,018 (17.9)	12,626 (18.1)	392 (12.8)	<0.001
NYHA functional class III-IV	58,908 (81.1)	56,274 (80.9)	2,634 (86.3)	<0.001
Stroke	8,794 (12.1)	8,352 (12.0)	442 (14.5)	<0.001
STS PROM, %	6.4 (4.2-9.9)	6.2 (4.1-9.5)	13.5 (8.9-20.6)	<0.001
Echocardiographic variables				
LVEF, %	58 (45-63)	58 (45-63)	55 (40-60)	<0.001
LVEF <45%	16,643 (22.9)	15,683 (22.5)	960 (31.4)	<0.001
AVA, cm^2	0.7 (0.6-0.8)	0.7 (0.6-0.8)	0.7 (0.6-0.8)	<0.001
Mean gradient, mm Hg	42 (35-51)	42 (35-51)	42 (35-50)	0.007
Moderate or severe MR	21,028 (29.0)	19,985 (28.7)	1,043 (34.2)	<0.001
Moderate or severe TR	17,466 (24.0)	16,513 (23.7)	953 (31.2)	<0.001
Laboratory variables				
Hemoglobin, g/dl	11.8 (10.5-13.0)	11.9 (10.6-13.1)	10.5 (9.5-11.5)	<0.001
Albumin, g/dl	3.7 (3.4-4.0)	3.7 (3.4-4.0)	3.5 (3.1-3.8)	<0.001

CENTRAL ILLUSTRATION 1-Year Patient Mortality Stratified by Renal Function Following Transcatheter Aortic Valve Replacement



Dialysis	1,733	1,463	1,203	938	735
Creatinine ≥2 w/o Dialysis	2,634	2,212	1,810	1,501	1,271
Creatinine <2 w/o Dialysis	39,782	36,509	30,757	25,755	21,737

Dialysis — Creatinine ≥2 w/o Dialysis — Creatinine <2 w/o Dialysis

Szerlip, M. et al. J Am Coll Cardiol. 2019;73(22):2806–15.

This figure shows 1-year mortality stratified by transcatheter aortic valve replacement patients who are on dialysis and who have creatinine ≥2 and <2 mg/dl.

TABLE 2 Procedural Characteristics and Outcomes

	Overall (N = 72,631)	No Dialysis (n = 69,578)	Dialysis (n = 3,053)	p Value
Complications				
In-hospital mortality	2,504 (3.4)	2,347 (3.4)	157 (5.1)	<0.001
O:E mortality	0.43	0.44	0.32	<0.001
Access complication	3,329 (4.6)	3,191 (4.6)	138 (4.5)	0.859
Major bleed	754 (1.0)	710 (1.0)	44 (1.4)	0.025
Stroke	2,226 (3.1)	2,143 (3.1)	83 (2.7)	0.255
Unplanned vascular surgery or intervention	2,714 (3.7)	2,601 (3.7)	113 (3.7)	0.912
LOS, days	5.0 (3.0-8.0)	5.0 (3.0-8.0)	6.0 (4.0-12.0)	<0.001


5 - 9 OCTOBRE 2020
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