

eMPORA III: Randomized comparison of dialyzer performance and hemocompatibility during hemodiafiltration

Götz Ehlerding, Wolfgang Ries, Manuela Kempkes-Koch, Ekkehard Ziegler, Petra Ronová, Mária Krizsán, Jana Verešová, Mária Böke, Ansgar Erlenkötter, Robert Nitschel, Adam M. Zawada, James P. Kennedy, Jennifer Braun, John W. Larkin, Natalia Korolev, Thomas Lang, Bertram Ottillinger, Manuela Stauss-Grabo and Bettina Griesshaber*

*Corresponding author:

Dr. Bettina Griesshaber

Fresenius Medical Care Deutschland GmbH

Global Biomedical Evidence Generation

Global Medical Office

Else-Kröner-Straße 1

61352 Bad Homburg, Germany

P +49 6172 268 6766

Bettina.Griesshaber@freseniusmedicalcare.com

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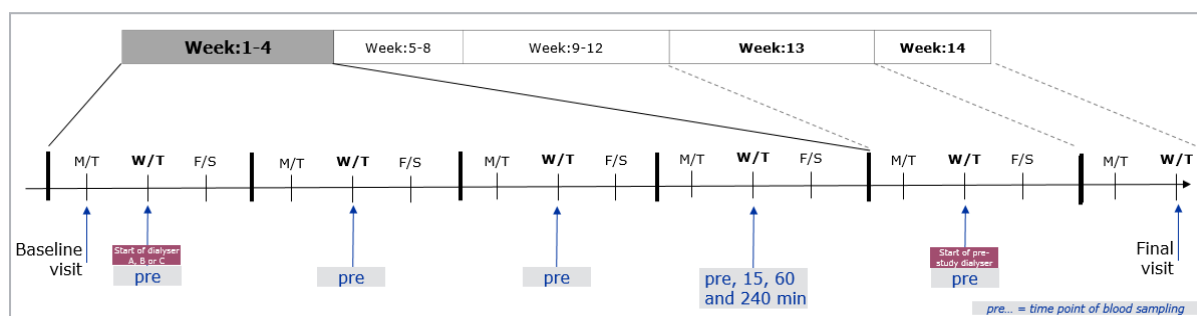
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Figure S1: Simplified study schedule: Change of dialyzers and blood sampling



M/T: Monday or Tuesday; W/T: Wednesday or Thursday; F/S: Friday or Saturday

Table S1: Methods for obtaining blood samples and analytical methods of investigated variables

Methods for obtaining blood samples • The pre-dialysis blood sample was obtained from the native arterial needle, before it was flushed or connected to the blood tubing. The venous blood samples were drawn slowly from the venous port – before the blood was diluted with the substitution solution – at the standard blood flow of approx. 300 mL/min, at running blood and dialysate. Arterial blood samples at the later timepoints were drawn at a temporarily reduced blood flow of 100 mL/min and at running dialysate.
Analytical methods of investigated variables • Creatinine: COBAS INTEGRA 400 plus analyzer (Roche, Mannheim, Germany) using CREJ2 method (Jaffé) • Urea: COBAS INTEGRA 400 plus analyzer (Roche, Mannheim, Germany) using UREAL method • Phosphate: COBAS INTEGRA 400 plus analyzer (Roche, Mannheim, Germany) using PHOS2 method • β2-microglobulin: COBAS INTEGRA 400 plus analyzer (Roche, Mannheim, Germany) using Tina-quant β2-microglobulin method • Myoglobin: COBAS INTEGRA 400 plus analyzer (Roche, Mannheim, Germany) using MYO2 method • C3a: C3a Plus MicroVue immunoassay (Quidel, San Diego, USA) • sC5b-9: sC5b-9 Plus MicroVue immunoassay (Quidel, San Diego, USA) • Hemoglobin, WBC/Leukocytes, PLT count: XN-1000 Pure analyzer (Sysmex, Kobe, Japan) • PMN elastase: PMN Elastase Human ELISA Kit (Thermo Fisher Scientific, Waltham, USA) • IL-6: Human IL-6 Quantikine ELISA Kit D6050 (R&D Systems, Minneapolis, USA) • IL-8: Human IL-8/CXCL8 Quantikine ELISA Kit D8000C (R&D Systems, Minneapolis, USA) • LTB-4: LTB4 Parameter Assay Kit KGE006B (R&D Systems, Minneapolis, USA) • sICAM-1: Human ICAM-1/CD54 Non-Allele-specific Quantikine ELISA Kit DCIM00 (R&D Systems, Minneapolis, USA) • hsCRP: COBAS INTEGRA 400 plus analyzer (Roche, Mannheim, Germany) using CRPHS method • β-TG: Asserachrom β-TG test (Diagnostica Stago, Asnières-sur-Seine, France) • TxB2: Thromboxane B2 Parameter Assay Kit KGE011 (R&D Systems, Minneapolis, USA) • MDA: Ultimate 3000 HPLC FLD (Thermo Fisher Scientific, Waltham, USA) • GSH-Px activity: Glutathione Peroxidase (GSH-Px) Activity Assay Kit E-bC-K096-M-96 (Elabsience, Houston, USA)

Table S2: Overview of Patient Reported Outcomes (PRO; Safety population)

		FX CorAL 600 (N=74)	FX CorDiox 600 (N=71)	xevonta Hi 15 (N=76)	Total (N=218)
Pittsburgh Sleep Quality Index (PSQI) by dialyzer					
PSQI	n	71	71	76	218
	Mean±SD	5.8±3.75	5.8±3.77	5.6±3.83	5.7±3.77
	Min, Median, Max	0.0, 5.0, 17.0	0.0, 6.0, 17.0	0.0, 5.0, 19.0	0.0, 5.0, 19.0
	LS mean difference [95% CI]	FX CorAL vs.	-0.07 [-0.54, 0.39]	-0.02 [-0.48, 0.44]	N/A
	p-value	FX CorAL vs.	0.7508	0.9346	N/A
Kidney Disease Quality of Life (KDQOL) Instrument Short Form v1.3					
KDQOL v1.3 “Fatigue domain”	n	71	71	76	218
	Mean±SD	63.7±20.35	64.2±22.78	63.6±21.32	63.8±21.41
	Min, Median, Max	10.0, 65.0, 100.0	0.0, 60.0, 100.0	10.0, 60.0, 100.0	0.0, 65.0, 100.0
	LS mean difference [95% CI]	FX CorAL vs.	-0.10 [-3.56, 3.36]	0.30 [-3.11, 3.72]	N/A
	p-value	FX CorAL vs.	0.9530	0.8605	N/A
Pruritus Numerical Rating Scale (PNRS) by dialyzer					
Peak PNRS	n	71	71	76	218
	Mean±SD	0.9±2.03	1.1±1.92	0.9±1.89	1.0±1.94
	Min, Median, Max	0.0, 0.0, 10.0	0.0, 0.0, 8.0	0.0, 0.0, 7.0	0.0, 0.0, 10.0
	LS mean difference [95% CI]	FX CorAL vs.	-0.08 [-0.42, 0.27]	0.08 [-0.26, 0.42]	N/A
	p-value	FX CorAL vs.	0.6558	0.6506	N/A
International Restless Legs Syndrome Study Group (IRLSSG) Rating Scale by dialyzer					
IRLSSG	n	71	71	76	218
	Mean±SD	3.4±6.66	3.2±5.89	2.9±6.24	3.2±6.24
	Min, Median, Max	0.0, 0.0, 28.0	0.0, 0.0, 19.0	0.0, 0.0, 25.0	0.0, 0.0, 28.0
	LS mean difference [95% CI]	FX CorAL vs.	0.24 [-0.83 1.32]	0.33 [-0.73 1.39]	N/A
	p-value	FX CorAL vs.	0.6533	0.5370	N/A

Legend: Max: maximum; Min: minimum; LS mean: Least Squares mean; N: number of patients; n: number of patients with data available; SD, standard deviation

LS mean difference shows the difference in the change in the PRO from baseline to the end of each period in reference to the FX CorAL 600 dialyzer (FX CorAL 600 vs. FX CorDiox 600, and FX CorAL 600 vs. xevonta Hi 15) with the and 95% confidence interval. The p-value indicates the level of statistical significance for the LS mean difference.

Questionnaires were collected at baseline at study start and at the end of each subsequent period, i.e., after patients had received 12 HDF sessions with each dialyzer. The questionnaires included:

Pittsburgh Sleep Quality Index (PSQI) ¹

- PRO assessment: perceived sleep quality
- Range: 0 (best sleep quality) to 21 (poorest sleep quality)
- Recall period: previous month

Kidney Disease Quality of Life (KDQOL) questionnaire v1.3, fatigue domain questions 9a, 9e, 9g, and 9i ²

- PRO assessment: perceived vitality/energy level
- Range: 0 (lowest vitality/energy) to 100 (highest vitality/energy)
- Recall period: previous month

Peak Pruritus Numerical Rating Scale (PNRS) ³⁻⁶

- PRO assessment: perceived severity of worst itch
- Range: 0 (no itch) to 10 (worst itch imaginable)
- Recall period: previous 24 hours

International Restless Legs Syndrome Study Group Rating Scale (IRLSSG) ⁷⁻⁹

- PRO assessment: perceived severity/impact of restless legs
- Range total score: 0 (no restless legs) to 40 (very severe restless legs)
- Recall period: previous week

Table S3: Anticoagulation by dialyzer (Safety population)

		Dialyzer		
		FX CorAL 600 (N=74)	FX CorDiax 600 (N=71)	xevonta Hi 15 (N=76)
Anticoagulation				
Clexane Bolus	[n (%)]	6 (8.1%)	5 (7.0%)	5 (6.6%)
	[dose (IU)]	3833 ± 1835	4200 ± 1789	4200 ± 1789
Non-Clexane LMWH Bolus	[n (%)]	20 (27.0%)	19 (26.8%)	21 (27.6%)
	[dose (IU)]	5493 ± 2129	5482 ± 2186	5593 ± 2125
Non-Clexane LMWH – 2 doses	[n (%)]	1 (1.4%)	1 (1.4%)	1 (1.3%)
	Bolus [dose (IU)]	8000	8000	8000
	Infusion [dose (IU)]	1000	1000	1000
UF heparin	[n (%)]	47 (63.5%)	46 (64.8%)	48 (63.2%)
	Bolus [dose (IU)]	2723 ± 1664	2663 ± 1606	2729 ± 1644
	Infusion [dose (IU)]	1447 ± 910.2	1486 ± 913.0	1469 ± 901.5

IU: International Units; LMWH: Low Molecular Weight Heparin; UF: Unfractionated.

Doses are presented as mean ± SD

Table S4: Overview of hemocompatibility markers: intra- and interdialytic changes (ITT population)

Variable (molecular weight) [unit]	Key indicator	INTRA					INTER		
		FX Coral 600	FX CorDiax 600	xevonta Hi 15	FX Coral vs FX CorDiax	FX Coral vs xevonta	FX Coral 600	FX CorDiax 600	xevonta Hi 15
		LS mean			p value	p value	p value		
Complement Activation									
C3a (9 kDa) [µg/L]	15 - pre	23.99	42.18	37.33	0.0034	0.0287	0.8331	0.7589	0.6983
	60 - pre	-0.52	5.70	7.13	0.3158	0.2095			
	240 - pre	-15.86	-16.51	-10.37	0.9159	0.3648			
	AUC - pre	-8.21	15.68	10.83	0.6069	0.6741			
sC5b-9 (1000 kDa) [µg/L]	15 - pre	38.51	45.47	53.42	0.3133	0.0283	0.9440	0.9842	0.6660
	60 - pre	45.50	52.13	78.16	0.3371	<0.0001			
	240 - pre	17.06	0.48	15.21	0.0162	0.7845			
	AUC - pre	128.60	119.20	192.15	0.7161	0.0126			
Cell activation / Inflammation									
WBC (leukocytes) [10^3/µL]	15 - pre	-0.56	-0.81	-0.67	0.0150	0.2456	0.9646	0.5769	0.7128
	60 - pre	-0.30	-0.21	-0.29	0.3837	0.9464			
	240 - pre	-1.00	-0.84	-0.76	0.1141	0.0139			
	AUC - pre	-2.17	-1.88	-2.10	0.3880	0.8282			
Monocytes [10^3/µL]	15 - pre	-0.20	-0.22	-0.25	0.5326	0.0116	0.6594	0.8033	0.6311
	60 - pre	-0.16	-0.17	-0.17	0.4999	0.6630			
	240 - pre	-0.26	-0.23	-0.20	0.1084	0.0017			
	AUC - pre	-0.77	-0.74	-0.71	0.5658	0.2817			
Lymphocytes [10^3/µL]	15 - pre	-0.15	-0.20	-0.16	0.0887	0.8665	0.6443	0.7618	0.8363
	60 - pre	-0.19	-0.23	-0.22	0.1618	0.3663			
	240 - pre	-0.15	-0.15	-0.12	0.9418	0.2596			
	AUC - pre	-0.69	-0.72	-0.64	0.7619	0.6770			
Neutrophiles [10^3/µL]	15 - pre	-0.15	-0.36	-0.25	0.0191	0.2576	0.9418	0.5225	0.6240
	60 - pre	0.10	0.23	0.12	0.1529	0.8862			
	240 - pre	-0.50	-0.39	-0.39	0.1894	0.2001			
	AUC - pre	-0.52	-0.21	-0.57	0.2557	0.8489			
Eosinophiles [10^3/µL]	15 - pre	-0.03	-0.04	-0.03	0.1950	0.3180	0.8403	0.5775	0.5077
	60 - pre	-0.02	-0.03	-0.03	0.1487	0.1970			
	240 - pre	-0.07	-0.07	-0.06	0.6110	0.0932			
	AUC - pre	-0.15	-0.18	-0.15	0.1686	0.6787			
Basophiles [10^3/µL]	15 - pre	-0.01	0.00	-0.01	0.0846	0.9949	0.8645	0.8976	0.8951
	60 - pre	-0.01	0.00	-0.01	0.3758	0.7125			
	240 - pre	-0.01	0.01	-0.01	0.3312	0.5988			
	AUC - pre	-0.03	-0.02	-0.03	0.3128	0.8955			
PMN elastase (30 kDa) [µg/L]	15 - pre	6.42	11.57	10.19	0.1193	0.2512	0.2030	0.3892	0.0987
	60 - pre	11.21	20.92	22.93	0.0031	0.0003			
	240 - pre	9.81	19.53	21.74	0.0030	0.0002			
	AUC - pre	40.9	61.30	71.05	0.1634	0.0361			

Variable (molecular weight) [unit]	Key indicator	INTRA					INTER		
		FX Coral 600	FX CorDiax 600	xevonta Hi 15	FX Coral vs FX CorDiax	FX Coral vs xevonta	FX Coral 600	FX CorDiax 600	xevonta Hi 15
		LS mean			p value	p value	p value		
IL-6 (22-28 kDa) [pg/mL]	15 - pre	-0.83	-0.60	-0.46	0.5947	0.3864	0.8061	0.4939	0.3074
	60 - pre	-1.28	-0.90	-1.02	0.3718	0.5301			
	240 - pre	-1.31	-0.66	-0.68	0.1288	0.1308			
	AUC - pre	-4.21	-2.96	-3.43	0.2945	0.5002			
IL-8 (8-9 kDa) [pg/mL]	15 - pre	-1.52	-1.94	-1.36	0.3756	0.7388	0.5802	0.4389	0.8236
	60 - pre	-3.15	-3.74	-3.24	0.2117	0.8392			
	240 - pre	-3.44	-4.48	-4.27	0.0285	0.0743			
	AUC - pre	-11.45	-13.36	-13.10	0.3710	0.4167			
LTB-4 (336 Da) [pg/mL]	15 - pre	160.6	219.4	178.4	0.0470	0.5391	N/A	N/A	N/A
	60 - pre	61.3	70.5	59.2	0.7553	0.9428			
	240 - pre	9.7	4.8	4.8	0.8686	0.8652			
	AUC - pre	200.4	228.0	190.1	0.5880	0.8364			
sICAM-1 (58 kDa) [µg/L]	15 - pre	11.56	6.61	3.68	0.4208	0.1929	0.3593	0.9772	0.6836
	60 - pre	0.05	0.39	7.93	0.9564	0.1934			
	240 - pre	-10.05	-3.34	-4.40	0.2736	0.3480			
	AUC - pre	-7.54	19.60	14.69	0.2285	0.3111			
hsCRP (25 kDa) [mg/L]	N/A	N/A	N/A	N/A	N/A	N/A	0.6172	0.5612	0.8872
Platelet Count / Activation									
PLT [10^3/µL]	15 - pre	-20.3	-23.9	-24.7	0.2241	0.1329	0.7218	0.5173	0.8168
	60 - pre	-25.2	-26.6	-29.4	0.6375	0.1505			
	240 - pre	-34.0	-33.8	-31.9	0.9406	0.4719			
	AUC - pre	-109.1	-108.8	-108.6	0.9756	0.9563			
β-TG (36 kDa) [IU/mL]	15 - pre	-12.5	10.9	16.6	0.0034	0.0002	0.6548	0.3104	0.2903
	60 - pre	-23.6	7.6	26.3	<0.0001	<0.0001			
	240 - pre	-38.5	-31.8	-27.2	0.4020	0.1496			
	AUC - pre	-96.4	-32.6	12.8	0.0286	0.0002			
TxB2 (371 Da) [µg/L]	15 - pre	0.66	0.42	0.34	0.0959	0.0259	0.4976	0.2590	0.9879
	60 - pre	-0.26	-0.23	-0.41	0.8589	0.2762			
	240 - pre	-1.04	-1.09	-1.09	0.7395	0.7517			
	AUC - pre	-1.80	-1.58	-2.07	0.7026	0.6365			
Oxidative Stress									
MDA (72 Da)	15 - pre	-0.02	-0.02	-0.03	0.9709	0.8214	0.8387	0.8336	0.7801
	60 - pre	-0.07	-0.06	-0.06	0.7674	0.7201			
	240 - pre	-0.08	-0.10	-0.08	0.4207	0.9878			
	AUC - pre	-0.22	-0.28	-0.24	0.3310	0.7488			
GSH-Px activity (22 kDa)	15 - pre	8.1	33.2	46.1	0.1203	0.0174	0.9073	0.6039	0.1869
	60 - pre	21.2	6.5	29.7	0.3646	0.5911			
	240 - pre	-8.1	-0.2	-22.9	0.6255	0.3486			
	AUC - pre	1.7	35.6	75.6	0.5816	0.2192			

Values indicate LS mean differences to the baseline (pre) values before the start of HDF. LS mean: Least Squares mean. Intradialytic: changes within a dialysis session. Interdialytic: changes over a dialysis period (12 sessions under one allocated dialyzer type). Shaded lines indicate parameters of key clinical interest for the variable. p-values formatted in bold script mark values <0.05 and the associated parameter. p-values are descriptive and not adjusted for multiple testing.

Table S5: Overview of Serious Adverse Events (SAEs), Adverse Events (AEs), and clinical safety (Safety population)

MedDRA SOC/PT	FX CorAL 600	FX CorDiax 600	xevonta Hi 15
Any SAE	2 (2.4) 2	4 (4.9) 5	3 (3.7) 3
Injury, poisoning and procedural complications	0 (0.0) 0	1 (1.2) 1	1 (1.2) 1
Femoral neck fracture	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Lower limb fracture	0 (0.0) 0	0 (0.0) 0	1 (1.2) 1
Cardiac disorders	0 (0.0) 0	0 (0.0) 0	1 (1.2) 1
Acute myocardial infarction	0 (0.0) 0	0 (0.0) 0	1 (1.2) 1
General disorders and administration site conditions	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Sudden cardiac death	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Infections and infestations	0 (0.0) 0	1 (1.2) 2	0 (0.0) 0
Cardiac valve abscess	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Endocarditis	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Metabolism and nutrition disorders	0 (0.0) 0	0 (0.0) 0	1 (1.2) 1*
Hyperkalemia	0 (0.0) 0	0 (0.0) 0	1 (1.2) 1*
Renal and urinary disorders	1 (1.2) 1	0 (0.0) 0	0 (0.0) 0
Cystitis hemorrhagic	1 (1.2) 1	0 (0.0) 0	0 (0.0) 0
Respiratory, thoracic and mediastinal disorders	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Dyspnea	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Surgical and medical procedures	1 (1.2) 1	0 (0.0) 0	0 (0.0) 0
Renal transplant	1 (1.2) 1	0 (0.0) 0	0 (0.0) 0
Any non-serious AE	4 (4.9) 4	3 (3.7) 4	1 (1.2) 1
Vascular disorders	2 (2.4) 2	1 (1.2) 1	1 (1.2) 1
Dialysis hypotension	2 (2.4) 2	1 (1.2) 1	1 (1.2) 1
Product issues	1 (1.2) 1	1 (1.2) 1	0 (0.0) 0
Thrombosis in device	1 (1.2) 1	1 (1.2) 1	0 (0.0) 0
Gastrointestinal disorders	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Vomiting	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Metabolism and nutrition disorders	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Hypovolaemia	0 (0.0) 0	1 (1.2) 1	0 (0.0) 0
Skin and subcutaneous tissue disorders	1 (1.2) 1	0 (0.0) 0	0 (0.0) 0
Pruritus	1 (1.2) 1	0 (0.0) 0	0 (0.0) 0
Overall N=82 Numbers indicate: No. of subjects (% of subjects) No. of events			
Clinical safety			
Repeated measurements of routine lab data and vital signs showed the patterns expected in patients undergoing state-of-the-art HDF. The mean hemoglobin concentration increased during HDF sessions (+0.6 g/dL overall), blood pressure decreased (systolic: -6.1 mmHg; diastolic: -2.2 mmHg), heart rate remained stable (+0.1 bpm), and body weight decreased (-2.1 kg). There were no conspicuous differences between dialyzers.			

HDF: Hemodiafiltration; MedDRA: Medical Dictionary for Regulatory Activities; PT: Preferred Term; SOC: System Organ Class.

* Related to the medical procedure. All other SAEs were neither considered related to the dialyzer nor to the medical procedure.

Section 1: Formulas for calculating $\beta 2$ -m Removal Rate (RR) and bloodside clearance K_b ; Statistical concept

$\beta 2$ -m RR [%] was calculated using the following formula¹⁰:

$$\beta 2\text{-m RR} = \left[1 - \frac{(1 - Hct_{240\min})}{(1 - Hct_{pre})} \frac{C_{\beta 2m, 240\min}}{C_{\beta 2m, pre}} \frac{Hct_{pre}}{Hct_{240\min}} \right] * 100$$

$Hct_{240\min}$ denotes the hematocrit as a proportion after 240 min of HDF, Hct_{pre} the hematocrit as a proportion at the start of HDF; $C_{\beta 2m, 240\min}$ denotes the $\beta 2$ -m concentration after 240 min of HDF, $C_{\beta 2m, pre}$ the $\beta 2$ -m concentration at the start of HDF. Thus, $\beta 2$ -m RR was corrected for concentration effects due to the dialysis treatment by considering the hematocrit.

Removal rates of other molecules (secondary performance endpoints) were calculated according to the same formula, using the concentrations of the molecule at the start and after 240 min of HDF.

Bloodside clearances K_b [mL/min] were calculated using the following formula (adapted from¹¹):

$$K_b = \frac{C_{art} \times Q_b (1 - Hct) - C_{ven} (Q_b (1 - Hct) - (Q_{sub} + Q_{UF}))}{C_{art}}$$

Hct denotes the arterial hematocrit as a proportion, Q_b [mL/min] the effective blood flow rate at the time clearance is calculated, Q_{sub} [mL/min] the HDF substitution rate, Q_{UF} [mL/min] the ultrafiltration rate, C_{art} [mg/dL] the plasma concentration before the dialyzer of the molecule whose clearance is to be calculated (arterial plasma), and C_{ven} [mg/dL] the plasma concentration after the dialyzer (venous plasma).

Non-clearance and non-removal related secondary variables were corrected for hematocrit (Hct) according to the following two formulas:

Blood cell counts:

$$C_t^{corr} = C_t \times Hct_{pre} / Hct_t$$

Markers of complement activation, markers of inflammation (except for blood cell counts), markers of oxidative stress, β -Thromboglobulin (β -TG), and Thromboxane (TxB2):

$$C_t^{corr} = C_t \times Hct_{pre} / Hct_t \times (100\% - Hct_t) / (100\% - Hct_{pre})$$

The corrections were calculated for each collection time point (t) except pre-dialysis values (pre).

The primary analysis consisted of the four parts listed below. It used a gate-keeping procedure to prevent inflation of the Type 1 error rate.¹² The first two steps, which were performed in parallel, implement the Bonferroni-Holm procedure. The overall one-sided α over all tests was 2.5%.

1. Non-inferiority comparison of FX CorAL versus FX CorDiax; non-inferiority margin $\delta = -5\%$.
2. Non-inferiority comparison of FX CorAL versus xevonta; non-inferiority margin $\delta = -5\%$.
3. Superiority comparison of FX CorAL versus xevonta.
4. Superiority comparison of FX CorAL versus FX CorDiax.

Assuming no carry over effect, a linear mixed model was used for the statistical analysis. This model included the fixed effects “period” and “dialyzer” and the random effects “center” and “patient”. The patients within each center identified the subjects with repeated measurements in the three periods. The comparison of the FX CorAL with each of the other two comparator dialyzers was done by defining contrasts or estimators of the fixed effect “dialyzer”.

The non-inferiority tests were based on the per protocol (PP) population which included all subjects who entered the study in accordance with each inclusion and exclusion criterion and who finished the study in accordance with the study protocol, without any major protocol deviations occurring. For validation purposes, this analysis was repeated on the intention to treat (ITT) population which included all patients who were randomized and for whom primary outcome data was available for at least one dialyzer. The superiority tests were performed on the ITT population and for validation on the PP population.

Analyses of secondary performance endpoints and PROs applied the same linear mixed model as described for the primary endpoint to calculate mean differences between FX CorAL and its comparators as well as the corresponding 95% confidence intervals.

Hemocompatibility markers were analyzed descriptively and compared between dialyzers, based on their concentration or activity profile over one HDF session. The analyses included *intradialytic* changes vs. the baseline (pre-)value at the *session’s* start. In addition, the eMPORA III study determined *interdialytic* changes: these are changes of the pre-values of the marker within one treatment *period*, which consisted of 12 sessions with one type of dialyzer.

Blood cell counts as well as hemocompatibility and activity markers were corrected for Hct changes over an HDF session. Missing values for all safety and efficacy endpoints were not replaced and described as a distinct category in tables. Based on the ‘missing at random assumption’, the linear mixed model allowed the modelling of incomplete data.

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