# CONVINCE

#### Comparison of high-dose HDF and high-flux HD.

#### Peter J Blankestijn for the CONVINCE study group.





# **Disclosure of Interest**

Do you have, or have you had during the past 2 years, any formal association with a company or other interested party?

Yes, speakers and advisory fees payed directly to the institution

Do you have, or have you had during the past 2 years, received any grants from an entity

No

Do you have, or have you had during the past 2 years, received any non-financial support from an entity?

No

Are you a member (current) of any kind of committee, board, WG, etc. of another scientific association with similar aims as ERA

No

# **Rationale 1**

In HDF diffusion and convection are combined as driving forces for uremic toxin removal.

HDF with online production of substitution fluid offers a modality to allow day to day use of HDF. Substitution fluid is most often delivered in postdilution mode.

Four RCTs addressed the question whether online HDF offers any clinical benefit. No definitive answer was produced. However, the individual participant meta-analysis provided directions for further research.





#### **Risk of mortality by achieved volume in 4 RCTs**

		Online HDF Convection Volume delivered BSA-standardized in L /1.73 m <sup>2</sup> per treatment session			
	Hemodialysis	<19	19–23	>23	
All-cause mortality					
Adjusted	1	0.83 (0.66; 1.03)	0.93 (0.75; 1.16)	0.78 (0.62; 0.98)	
CVD mortality					
Adjusted	1	0.92 (0.65; 1.30)	0.71 (0.49; 1.03)	0.69 (0.47; 1.00)	
Infections					
Adjusted	1	1.50 (0.92; 2.46)	0.97 (0.54; 1.74)	0.62 (0.32; 1.19)	
Sudden Death					
Adjusted	1	1.09 (0.69; 1.74)	1.04 (0.63; 1.70)	0.69 (0.39; 1.20)	

EuDial Pooling Project, N=2793, median follow up 2.5 y Nephrol Dial Transplant 2016; 31: 978-984

# Rationale 2

So, there is some suggestion that online HDF in post dilution mode may offer clinical benefit. However, definitive proof is lacking.

Nephrology community is divided in believers and non-believers. Acceptance of the therapy shows great geographical variability.

When call H2020-SC1-2016-2017 under the topic SC1-PM-10-2017: "Comparing the effectiveness of existing healthcare interventions in the adult population" was presented, we designed CONVINCE.

Rationale and design papers: BMJ open 2020: 10; e033228 Nephrol Dial Transplant 2022; 37: 1006-13



# Methods 1: CONVINCE

Prospective randomized international multicenter clinical trial

Objectives	Description		
Primary Objective	to <b>compare HDF</b> when delivered consistently in high-dose, with high-flux <b>HD</b> treatment in terms of <b>all-cause mortality</b> .		
Secondary Objectives	<ol> <li>Compare treatments in terms of cause specific morbidity and mortality.</li> <li>Assess <b>PRO-s</b> to capture patient perspectives and compare between treatments.</li> <li>Assess cost effectiveness of high-dose HDF.</li> </ol>		



### Methods 2

Funded: The CONVINCE study was solely and exclusively supported by the European Commission Research & Innovation, Horizon 2020 grant no 754803.

Registered: International Clinical Trial Registry Platform, NTR 7138 CRO: Julius Clinical, the Netherlands (www.juliusclinical.org)

Inclusion criteria:

- likelihood to achievement of the 23L convection volume (= total ultrafiltration volume, i.e. sum of substitution volume and net UF volume to achieve dry weight)
- ability to complete the patient reported outcome assessments Exclusion criteria:
- the expected general aspects





# Methods 3

Primary outcome: all cause mortality

Secondary outcomes:

Cause specific mortality Composite of fatal and non-fatal CV events All-cause and infection related hospitalizations Kidney transplantation Patient reported outcomes

Statistical analysis:

Cox proportional hazards modelling Competing risk modelling when appropriate (sec outcomes)





# **Results: participating 61 clinics in 8 countries**



#### **Results**







#### **Baseline characteristics**

	HDF N=683	HD N=677
Age (years)	62,5±13	62,3±13
History of CV disease	43%	47%
Diabetes	34%	37%
Dialysis vintage (median)	35 months	30 months
Vascular access: Native fistula catheter	82% 13%	82% 14%
Previous kidney transplantation	14%	12%



### **Convection volume across visits for the HDF group**



Average levels during the trial



#### Variation in Kt/V per session across visits



Average levels during the trial and mean difference over time between treatment arms obtained through linear mixed models using the on trial measurements with adjustments for baseline measurements and trial site included as random effect. Values are means (95% CI).



#### **Primary and secondary outcomes**

	HDF (N)	Risk per 100/py	HD (N)	Risk per 100/py	Hazard ratio (95% CI)
Death from any cause	118	7,1	148	9,2	0,77 (0,65-0,93)
Cardiovascular death	31	1,9	37	2,3	0,81 (0,49-1,33)
Non-CV death	87	5,3	111	6,9	0,76 (0,59-0,98)
Infection + COVID Infection - COVID	38 23	2,3 1,4	54 33	3,6 2,1	0,69 (0,49-0,96) 0,82 (0,42-1,59)
Kidney transplantation	75	4,8	71	4,7	1,01 (0,71-1,44)

### Kaplan Meier curves for overall survival





#### **Exploratory subgroup primary outcome analyses**

Subgroup	High-Dose Hemodia- filtration	High-flux Hemodialysis	High-Dose Hemodia- filtration	High-flux Hemodialysis	Hazard Ratio (95% CI)	
	no. of events	/no. of patients	rate/100	0 person-yr		
Death from any cause						
Age						
<50 yr	2/121	8/119	0.64	2.57 🚽	<b>⊢∎</b> ;I	0.25 (0.06-1.05)
50 to 65 yr	49/264	43/250	7.61	7.13	<b>⊢⊢</b> +	1.05 (0.75-1.49)
>65 yr	67/298	97/308	9.59	13.92	⊢∎1	0.68 (0.53-0.89)
Sex						
Male	83/436	97/420	7.94	9.82	⊢∎}	0.81 (0.65-1.01)
Female	35/247	51/257	5.74	8.17	<b>⊢</b> i	0.70 (0.47-1.02)
Preexisting cardiovascula disease	r					
No	43/387	66/361	4.40	7.52	⊢∎	0.58 (0.42-0.79)
Yes	75/296	82/316	11.06	11.17	<b>⊢₽</b> (	0.99 (0.76-1.28)
Preexisting diabetes						
No	54/453	76/426	4.72	7.24	⊢ <b></b>	0.65 (0.48-0.87)
Yes	64/230	72/251	12.50	12.81	⊢∎	0.97 (0.72-1.31)
Residual urinary output						
<1000 ml/24 hr	12/52	12/52	9.23	12.32	▶	0.76 (0.37-1.59)
≥1000 ml/24 hr	6/30	6/30	3.26	4.05	⊢∎►	1.59 (0.56-4.45)
Vascular access						
Fistula	97/558	123/557	7.16	9.23	⊢-₩	0.77 (0.64–0.94)
Graft or catheter	21/125	25/120	6.98	8.93		0.78 (0.45–1.34)
Dialysis vintage						
<2 yr	37/267	51/281	5.59	7.56	<b>⊢₽</b> <u>†</u>	0.73 (0.53-1.00)
2 to 5 yr	34/207	49/207	6.94	9.96	<b>⊢⊢</b>	0.70 (0.46-1.06)
>5 yr	46/207	48/188	9.18	10.86		0.85 (0.64–1.15)
Death from cardiovascular						
causes	10/207	14/261	1.02	1.50		0.76 (0.25 1.64)
Yes	12/38/	14/301	2.80	2.12		0.70 (0.35-1.64)
103	19/290	23/310	2.80	3.13	0.25 0.50 1.00 1.50 2.00	0.09 (0.40-1.05)



High-Dose Hemodiafiltration Better High-Flux Hemodialysis Better

#### Perspectives

- High volume online HDF can be delivered over prolonged period of time
- All-cause mortality: considerable beneficial effect
- Cause specific: interpretation with caution: not powered
- Limitation: some level of patient selection:
  - >23L/session + PRO assessment
- No reason for safety concern
- Next : comprehensive analysis of patient reported outcomes in the same dataset. In total > 10.000 sets of questionnaires.



#### Conclusion

- Online HDF, when delivered in a dose > 23L convection volume per session in post-dilution mode, resulted in a lower risk of death as compared to standard HD.
- This finding allows for a wider spread acceptance of this treatment modality.

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#### **CONVINCE** consortium



# !!!!!!! Thank you very much!!!!!!!!!!

#### **CONVINCE steering committee**



#### Available on the NEJM website starting 13.15 h CET today!



#### The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

#### Effect of Hemodiafiltration or Hemodialysis on Mortality in Kidney Failure

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