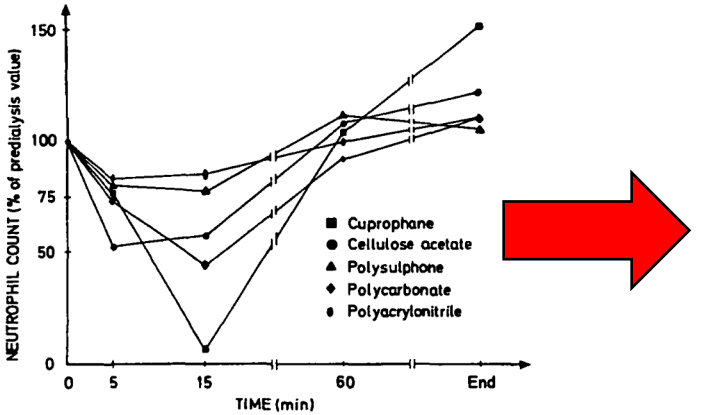
61ST ERA CONGRESS
STOCKHOLM & VIRTUAL
MAY 23-26, 2024

The CompAct-HD trial reports a persistent inflammatory profile in patients undergoing haemodialysis, acutely exacerbated with each treatment

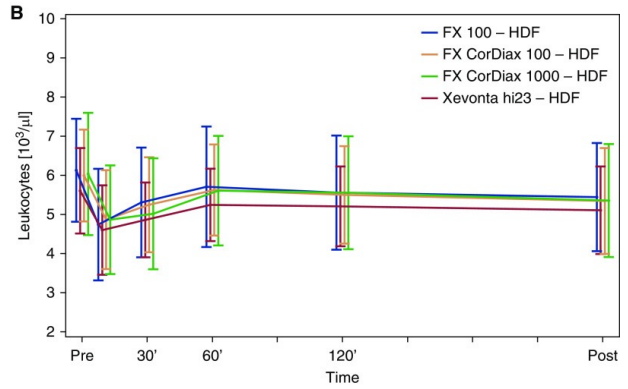
Dr Duha Ilyas[1,2]
Clinical Research Fellow at Manchester Royal Infirmary
PhD Student at University of Manchester, UK

"Bio-incompatibility" in Haemodialysis

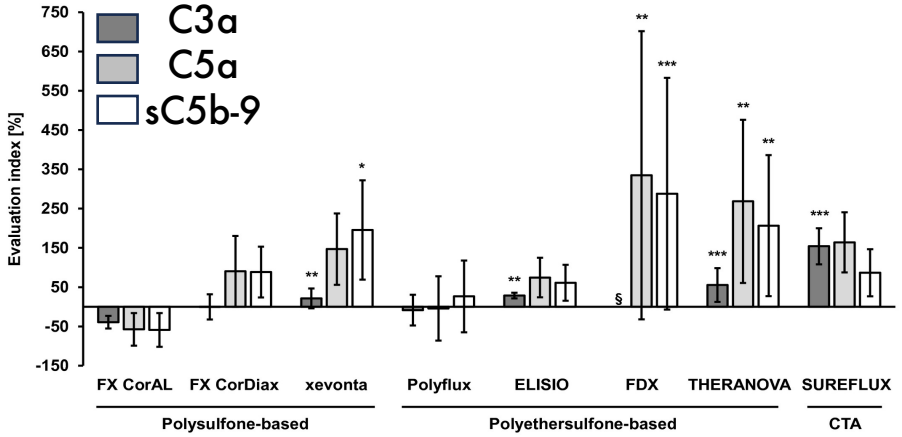
A haemocompatible device is one that must be capable of coming into contact with blood without causing any clinically adverse reactions.



1988: A comparison of neutrophil changes amongst 5 haemodialysis membranes



2020: Assessing the haemocompatibility of high flux polysulfone membranes used today



Despite advances in technology, activation of the immune system remains a problem today.

Methods

Trial set up:

Large multicentre trial recruiting patients undergoing chronic haemodialysis

- 6 blood samples collected for each patient.
- Clinical data was simultaneously collected.
- Mobile lab unit used for prompt sample processing

Inclusion Criteria:

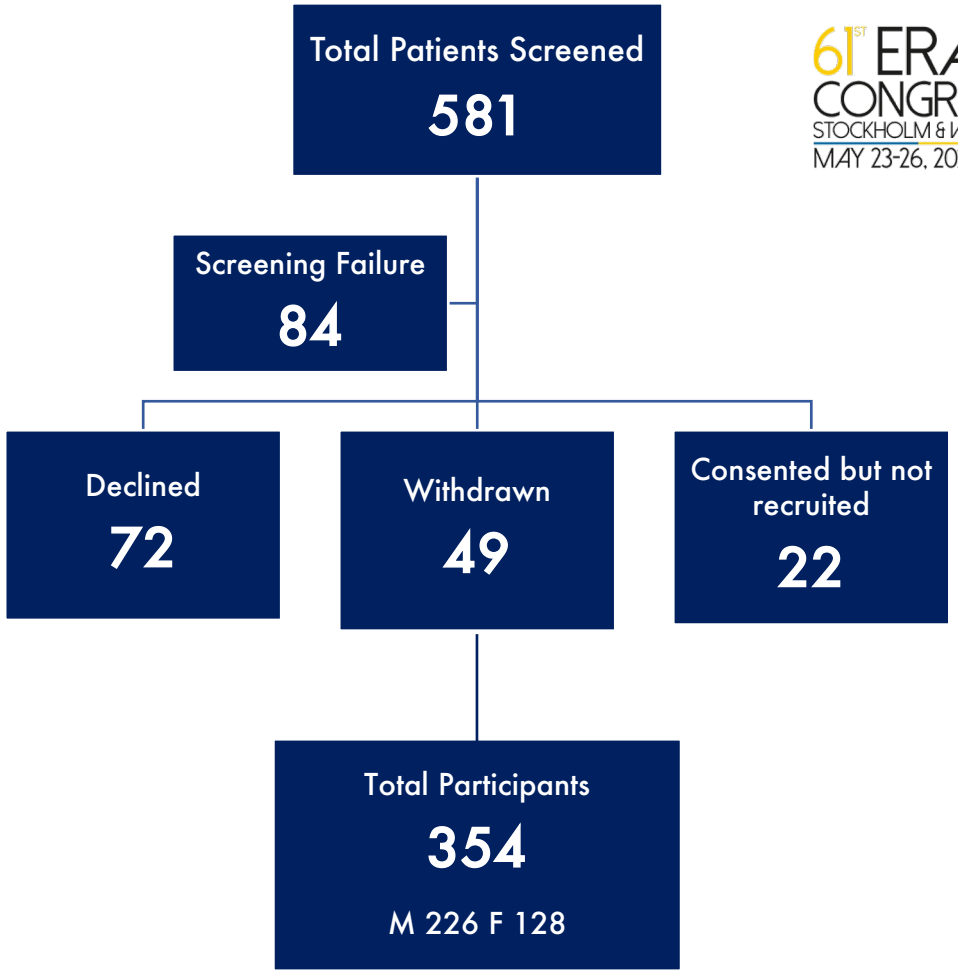
- Adult patients
- Undergoing chronic haemodialysis

Exclusion Criteria:

- Recent or active infection (within 28 days)
- Known blood borne virus
- Pregnancy

Sample handling and analysis:

- All samples were frozen within 50 minutes of collection until analysis
- Highly multiplexed assays were used for analysis of 27 biomarkers of inflammation.
- Single point samples from 14 healthy donors were analysed simultaneously for comparison



61ST ERA CONGRESS STOCKHOLM & VIRTUAL MAY 23-26, 2024

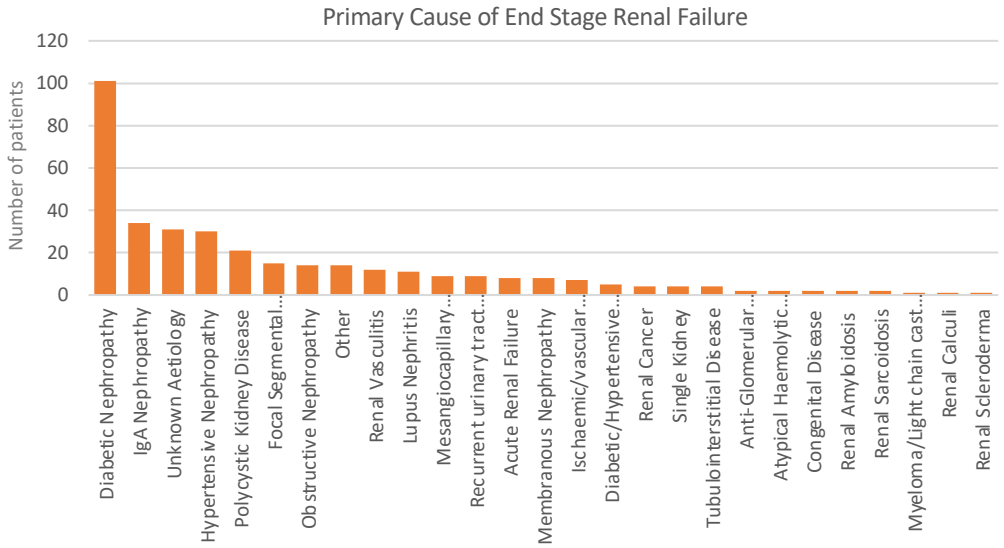
Complement Proteins

C1q C2 MBL C4 C4b C3 C3b/iC3b C5 C5a C9 FH Properdin FD FI FB

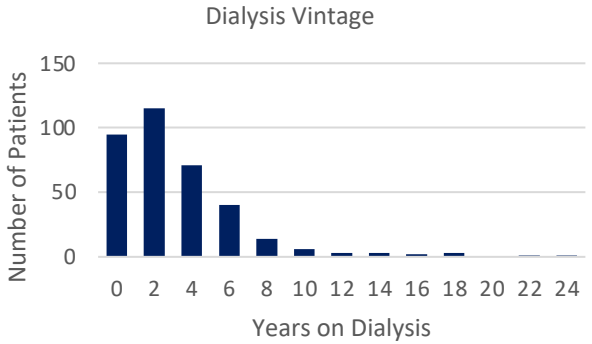
Cytokines + Growth Factors

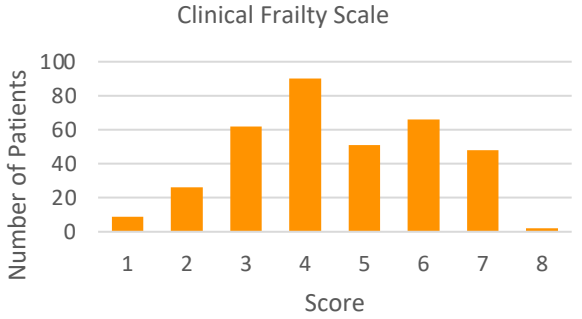
G-CSF, IFN-γ Il-1β Il-2 IL-4 IL-6 IL-8 IL-10 MCP-1 IL-12p40 Ilp-70 TNF-α IP-10

Results



Baseline Characteristics	Total (N = 354)
Age	61.6(46.1-77.1)
Male	226(63.8%)
Ethnicity	
Arab	1(0.3%)
Asian/Asian British	70(19.8%)
Black/Black/British	39(11%)
Mixed	5(1.4%)
Other	5(1.4%)
White	234(66.1%)
Access	
Tunnelled Line	180(50.8%)
Graft	1(0.3%)
Fistula	173(48.8%)
Dialyser	
Fresenius Classix	144(40.7%)
Fresenius CorDiax	141(39.8%)
Nipro Sureflux	67(18.9%)
Baxter Theranova	2(0.6%)

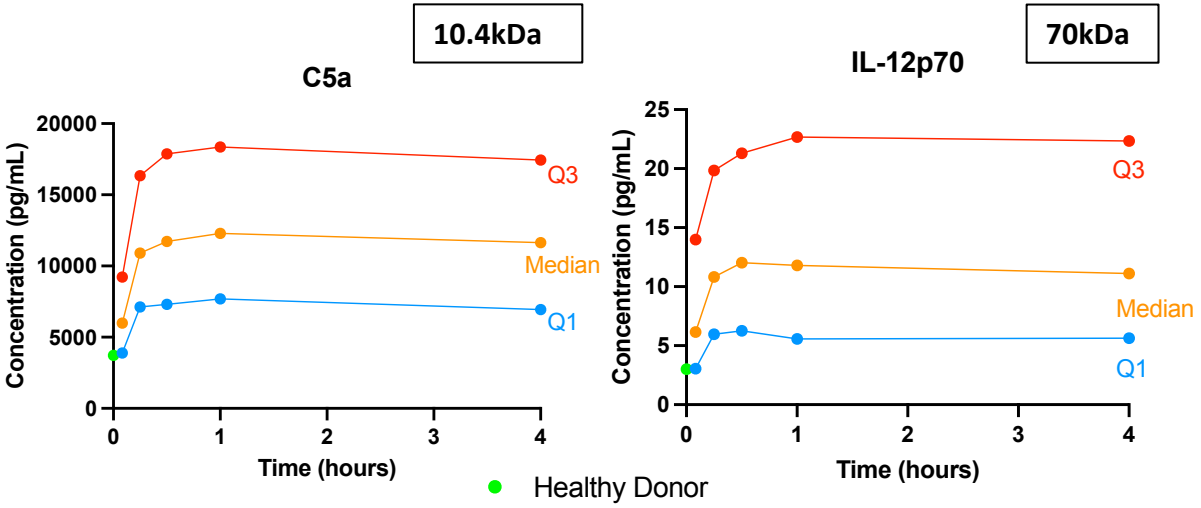




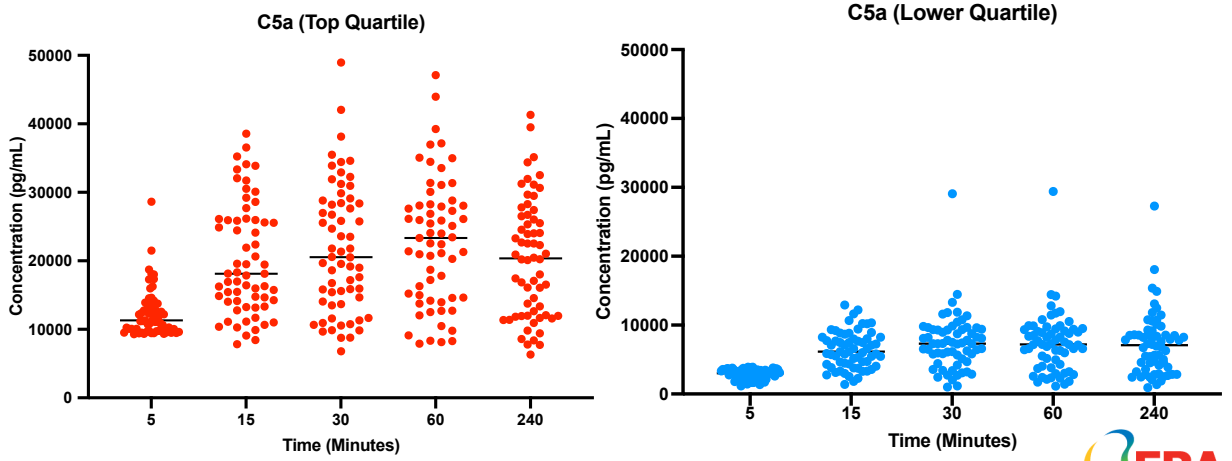
61ST ERA CONGRESS
STOCKHOLM & VIRTUAL
MAY 23-26, 2024

Clinical data was analysed for 354 patients recruited from 8 dialysis units across Greater Manchester

An acute rise in both complement proteins and cytokines can be seen in the first 30 minutes from the start of haemodialysis.

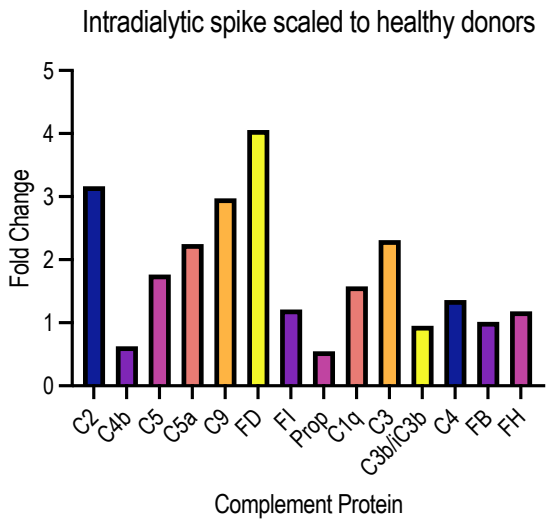


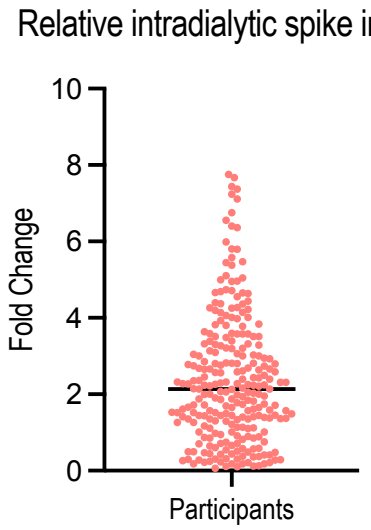
Patients follow their trajectory during the course of the session allowing them to be classified into low, medium and high responders.



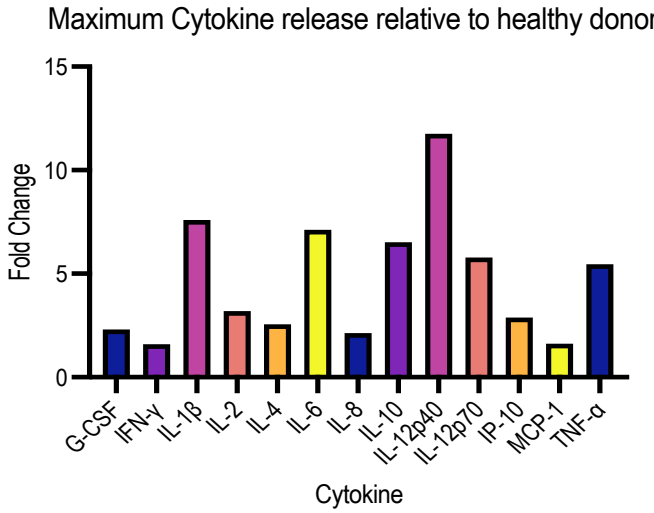
Discussion

An intradialytic spike could be seen for the majority of complement proteins relative to healthy donors.





Similarly, a relative increase in cytokines could be seen amongst dialysis patients despite loss during treatment.



Cytokine	MW
IL-12p40	40kDa
IL-1B	17.5kDa
IL-6	21-28kDa
IL-12p70	70kDa
IL-10	18.5kDa
TNF-a	17.4kDa

Conclusions

- An acute inflammatory temporal response can be seen in patients undergoing haemodialysis with ultrapure water using high flux membranes.
- Patients can be categorized into low, medium or high responders based on level of response during dialysis.
- Patients exhibiting high levels of immune activation are likely to be at a greater risk of complications from chronic inflammation.
- We can use this work to identify patients most likely to benefit from targeted, therapeutic interventions i.e. complement inhibitors.

Acknowledgements

Co-authors:

Elizabeth Blackburn[3], Andy Herbert[3], Leonard Ebah[1,2], Jennifer Mackie[3], Thomas Lindsay[1], Sandip Mitra[1,2]

[1]Manchester Foundation Trust
[2]University of Manchester
[3]Invizius Ltd

References:

- C. Heierli, M. Markert, P. H. Lambert, T. Kuwahara, J. P. Wauters, On the Mechanisms of Haemodialysis-induced Neutropenia: A Study with Five New and Re-used Membranes, *Nephrology Dialysis Transplantation*, Volume 3, Issue 6, 1988, Pages 773–783, https://doi.org/10.1093/oxfordjournals.ndt.a091753
- Wagner, Stephan; Zschätzsch, Sebastian; Erlenkoetter, Ansgar; Rauber, Lena; Stauss-Grabo, Manuela; Gauly, Adelheid. Hemocompatibility of Polysulfone Hemodialyzers – Exploratory Studies on Impact of Treatment Modality and Dialyzer Characteristics. Kidney360 1(1):p 25-35, January 2020. | DOI: 10.34067/KID.0000342019
- Melchior, P., Erlenkötter, A., Zawada, A.M., Delinski, D., Schall, C., Stauss-Grabo, M., Kennedy, J.P., 2021. Complement activation by dialysis membranes and its association with secondary membrane formation and surface charge. Artificial Organs 45, 770–778.. https://doi.org/10.1111/aor.13887