

## LETTER TO THE EDITOR

## Reply to “Comparison of four medium cut-off dialyzers”

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We would like to thank Krieter and Wanner for their kind remarks on our recently published study [1]. The authors have raised some interesting issues, and we are grateful for the opportunity to address them.

First, we agree with the authors that, with a molecular weight of 45 kDa and a Stokes' radius of 2.8 nm, the lambda free light chain ( $\lambda$ FLC) dimer is a particularly interesting biomarker, because it is ideally suited to characterize the typical cut-off range of medium cut-off (MCO) dialysis membranes. Both kappa and lambda light chains, 22 and 45 kDa, respectively, could be considered a good differential marker of depuration efficacy, especially  $\lambda$ FLC in the 40–45 kDa molecular weight range, where there are no clear differentiating markers.

Second, Krieter and Wanner wonder whether the  $\lambda$ FLC determinations used in our study were based on an assay with monoclonal or polyclonal antibodies. Indeed, we should have specified the assay used to determine FLCs in our study. There are two main FLC assays: N Latex FLC (Siemens, Marburg, Germany), based on the use of a monoclonal specific antibody, and Freelite® (The Binding Site, Birmingham, UK), based on polyclonal specific antibodies and used for nephelometric or turbidimetric instrument platforms. In our study, serum concentrations of  $\kappa$  and  $\lambda$ FLC were measured by nephelometry on a BN™ II System analyzer (Siemens Healthineers), using the Freelite® Human Lambda and Kappa Free kits for use on the Siemens BN™ II, references LK018.T and LK016.T, respectively (The Binding Site). This test is a sensitive latex-enhanced immunoassay based on polyclonal antisera. We agree with the authors that the  $\lambda$ FLC polyclonal assay would be better suited to detect differences between high-flux and MCO dialyzers.

Assuming that only the polyclonal assay is appropriate for discriminating between the hemodialysis efficacy of different MCO dialyzers, it must be asked whether our results are comparable and coherent. A study of six patients by Krieter *et al.* [2] found a  $\lambda$ FLC reduction ratio (RR) of  $28 \pm 4\%$  with ELISIO HX17 (surface area 1.7 m<sup>2</sup>) and  $39 \pm 13\%$  with Theranova 400 (surface area 1.7 m<sup>2</sup>). Our study of 23 patients [1] obtained a  $\lambda$ FLC RR of  $44.0 \pm 8.0\%$  with ELISIO HX19 (surface area 1.9 m<sup>2</sup>) and  $48.3 \pm 7.4\%$  with Theranova 400. These slightly higher values can be partly explained by differences in the prescription parameters of the dialysis treatment: dialyzer surface area, blood flow (300 vs  $439 \pm 26$  mL/min) and dialysis duration (240 vs  $288 \pm 17$  min). Results consistent with these two studies have recently been published by Martínez-Miguel *et al.* [3]. Their study, with 14 patients, blood flow 384 mL/min and dialysis duration 227 min, obtained a  $\lambda$ FLC RR of  $35.9 \pm 10.1\%$  with ELISIO HX21 (surface area 2.1 m<sup>2</sup>) and  $45.5 \pm 10.0\%$  with Theranova 500 (surface area 2.0 m<sup>2</sup>).

Considering that the values of free  $\lambda$ FLC RR varied between 20% and 60% in our study [1], there were no significant differences in the  $\lambda$ FLC RRs between the four MCO dialyzer treatments, and all of them were significantly higher than those obtained with high-flux HD treatments and significantly lower than those obtained with hemodiafiltration. Therefore,  $\lambda$ FLC could be considered a good differential marker of dialysis treatment efficacy, as it allows clear discrimination between high-flux HD, MCO dialyzer hemodialysis and high-volume hemodiafiltration treatments.

We would like to thank Krieter and Wanner again for their interest in our study.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no financial support for the project. F.M. has received consultancy and lecture fees from Baxter, Fresenius Medical Care, Medtronic, Nipro, Toray and Vifor. The other authors declare no conflicts of interest.

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