

# Medium-Cut-off (MCO) Membranes Reduce Inflammation In Chronic Dialysis Patients: a randomized, controlled “First in Man“-Trial

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## Background

Mortality in dialysis patients might be related to reduced clearance of pro-inflammatory mediators. A new MCO membrane with better permeability for molecules up to 45 kDa was tested clinically for the first time.

## Methods:

The randomized crossover trial in 48 patients compared MCO to High-flux (HF) dialysis of 4 weeks duration each plus 8 weeks extension phase.

Primary endpoint was the gene expression of TNF- $\alpha$  and IL-6 in peripheral whole blood, secondary endpoints were plasma levels of specified inflammatory mediators and cytokines.

## Results:

The primary end point TNF- $\alpha$ - and IL6 mRNA in leucocytes was reduced to a greater extent with MCO.

A significant difference between MCO and HF after 4 weeks was observed for sTNF-R1, kappa and lambda free light chains, albumin, urea and Lp-PLA2 (table 1).

After a significant drop after four weeks of MCO dialysis, albumin concentrations stabilized after 12 weeks (table 2).

## Conclusions:

MCO membranes modulate inflammation in dialysis patients.

Enhanced removal of soluble mediators influences the transcription of pro-inflammatory cytokines in peripheral leukocytes.

These results encourage further investigations with longer treatment periods and clinically relevant endpoints.

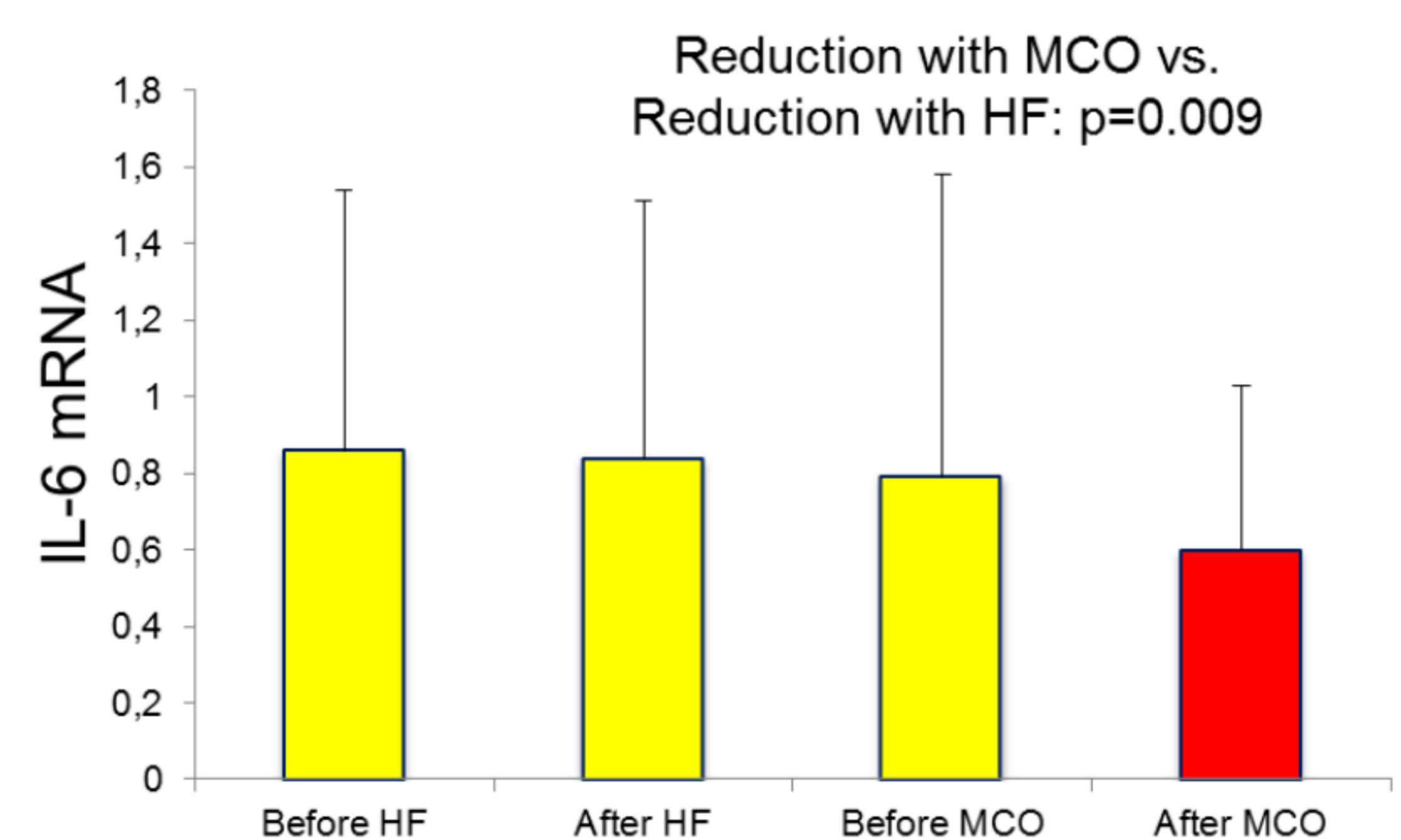
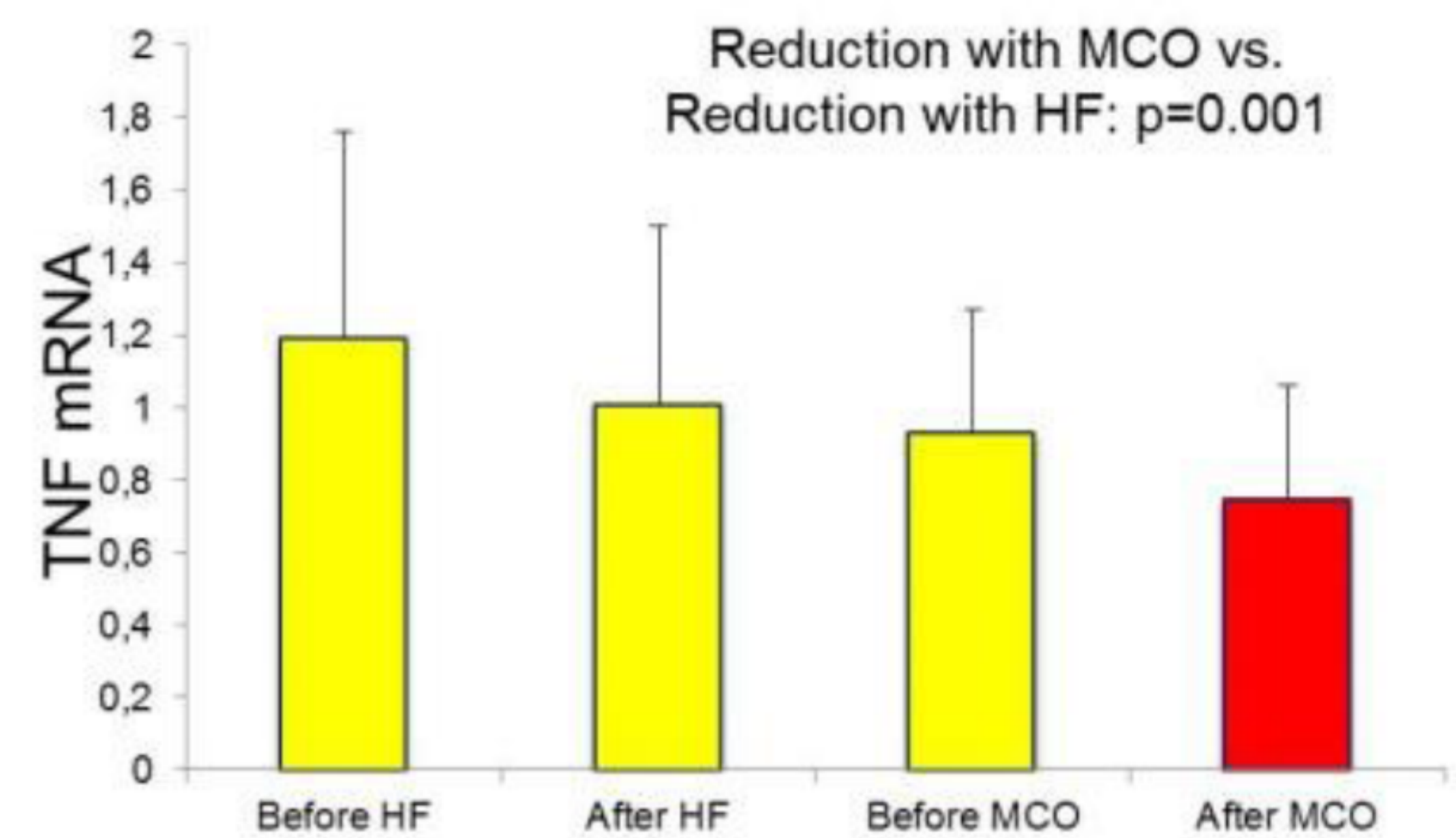
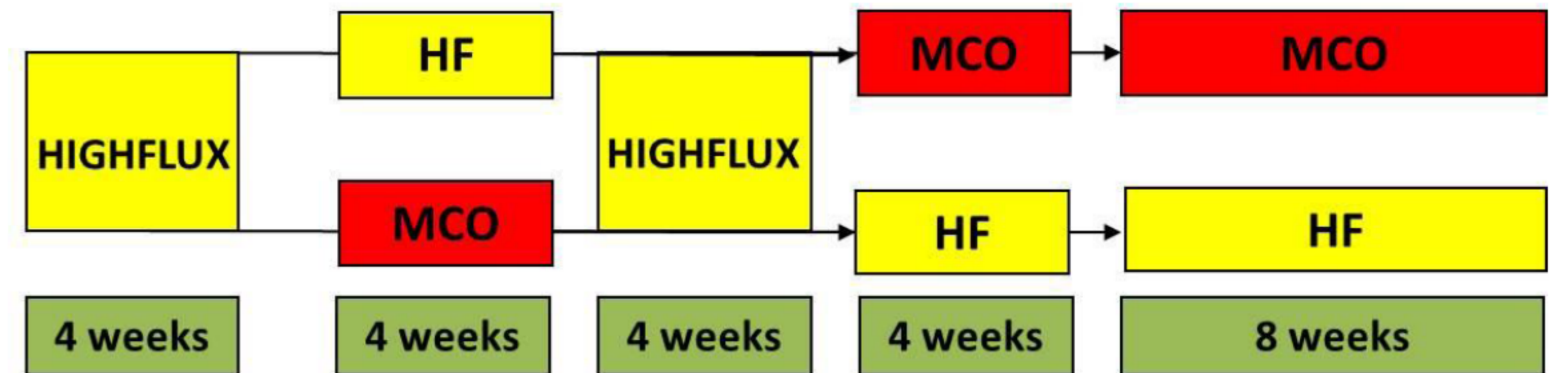


Table 1 : Long-term plasma levels before and after 4 weeks treatment with High-flux / MCO. Shown are only parameters with a significant change after the MCO-period. \*= $p < 0.05$  vs. T=0; \*\*= $p < 0.01$  vs. T=0

	High-flux		MCO		p MCO vs HF
	T=0	T= 4 weeks	T=0	T= 4 weeks	
Clinical parameters					
Albumin g/l	36.6 $\pm$ 3.2	37.5 $\pm$ 2.7	37.0 $\pm$ 3.6	35.3 $\pm$ 3.7**	< 0.001
CRP mg/l	13.4 $\pm$ 25.5	9.6 $\pm$ 15.7	15.3 $\pm$ 30.0	9.3 $\pm$ 14.5	n.s.
Beta2M mg/l	27.0 $\pm$ 9.1	26.1 $\pm$ 8.6	26.9 $\pm$ 8.4	25.7 $\pm$ 8.1**	n.s.
TNF-/TNFR-Family					
sTNF-R1 ng/ml	13.3 $\pm$ 4.7	12.9 $\pm$ 4.7	13.0 $\pm$ 4.4	11.0 $\pm$ 3.7**	0.01
TNF- $\alpha$ pg/ml	23.4 $\pm$ 7.3	22.2 $\pm$ 6.0	24.1 $\pm$ 8.1	20.6 $\pm$ 5.8**	n.s.
Main cytokines					
IFN- $\gamma$ pg/ml	16.0 $\pm$ 19.7	14.4 $\pm$ 17.8	17.5 $\pm$ 19	11.8 $\pm$ 12**	n.s.
IL-10 pg/ml	59 $\pm$ 355	47 $\pm$ 280	51 $\pm$ 287	65 $\pm$ 402**	n.s.
IL-6 pg/ml	9.8 $\pm$ 20.5	5.5 $\pm$ 4.5*	9.0 $\pm$ 13.2	6.0 $\pm$ 5.9**	n.s.
Other					
FLC kappa mg/l	134 $\pm$ 65	140 $\pm$ 77	137 $\pm$ 65	120 $\pm$ 54**	0.003
FLC lambda mg/l	91 $\pm$ 42	91 $\pm$ 44	95 $\pm$ 46	79 $\pm$ 36**	< 0.001
Lp-PLA2 ng/ml	180 $\pm$ 90	185 $\pm$ 108	156 $\pm$ 76	189 $\pm$ 101**	0.026

Table 2: Primary endpoints and plasma levels of Albumin and CRP during the 8 weeks extension phase

	High-flux		MCO	
	Start	End	Start	End
Albumin g/l	37.6 $\pm$ 2.3	37.9 $\pm$ 3.5	35.7 $\pm$ 4.5	36.4 $\pm$ 3.9
CRP mg/l	5.7 $\pm$ 6.5	7.2 $\pm$ 8.5	12.6 $\pm$ 18.8	16.9 $\pm$ 48.4
TNF- $\alpha$ mRNA	1.06 $\pm$ 0.67	1.03 $\pm$ 0.43	0.80 $\pm$ 0.25	0.87 $\pm$ 0.31
IL-6 mRNA	1.00 $\pm$ 0.85	0.89 $\pm$ 0.73	0.53 $\pm$ 0.29	0.62 $\pm$ 0.42

