

Medtronic

Engineering the extraordinary

Advances in hemodialysis

Supra HFR Advanced Therapy



Please refer to the Instruction for Use of Supra HFR procedure packs and included components (that are medical devices CE0123) for the available instruction, contraindications, warnings and precautions, together with User manuals of Flexya and Formula machines.

Supra HFR

Challenges with Extracorporeal Renal Replacement Today

Removal of a
Wide
Spectrum of toxins,
especially
large

Preservation of
Nutritional
Status

Counteract the
effects
of
Inflammation



1. Maduell F, Moreso F, Pons M, et al. High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. *J Am Soc Nephrol*. 2013;24(3):487-497.
2. Cobo G, Lindholm B, Stenvinkel P. Chronic inflammation in end-stage renal disease and dialysis. *Nephrol Dial Transplant*. 2018;33(suppl 3):iii35-iii40.
3. Piccoli GB, Nielsen L, Gendrot L, Fois A, Cataldo E, Cabiddu G. Prescribing hemodialysis or hemodiafiltration: when one size does not fit all the proposal of a personalized approach based on comorbidity and nutritional status. *J Clin Med*. 2018;7(10):331.
4. Tonelli M, Wiebe N, Guthrie B, et al. Comorbidity as a driver of adverse outcomes in people with chronic kidney disease. *Kidney Int*. 2015;88(4):859-866.
5. Vega A, Quiroga B, Abad S, et al. Albumin leakage in online hemodiafiltration, more convective transport, more losses? *Ther Apher Dial*. 2015;19(3):267-71.
6. Ahrenholz PG, Winkler RE, Michelsen A, Lang DA, Bowry SK. Dialysis membrane-dependent removal of middle molecules during hemodiafiltration: the beta2-microglobulin/albumin relationship. *Clin Nephrol*. 2004;62(1):21-8.
7. Palleschi S, Ghezzi PM, Palladino G, et al. Vitamins (A, C and E) and oxidative status of hemodialysis patients treated with HFR and HFR-Supra. *BMC Nephrol*. 2016;17(1):120.
8. Esquivias-Motta E, Martín-Malo A, Buendia P, et al. Hemodiafiltration with endogenous reinfusion improved microinflammation and endothelial damage compared with online-hemodiafiltration: a hypothesis generating study. *Artif Organs*. 2017;41(1):88-98

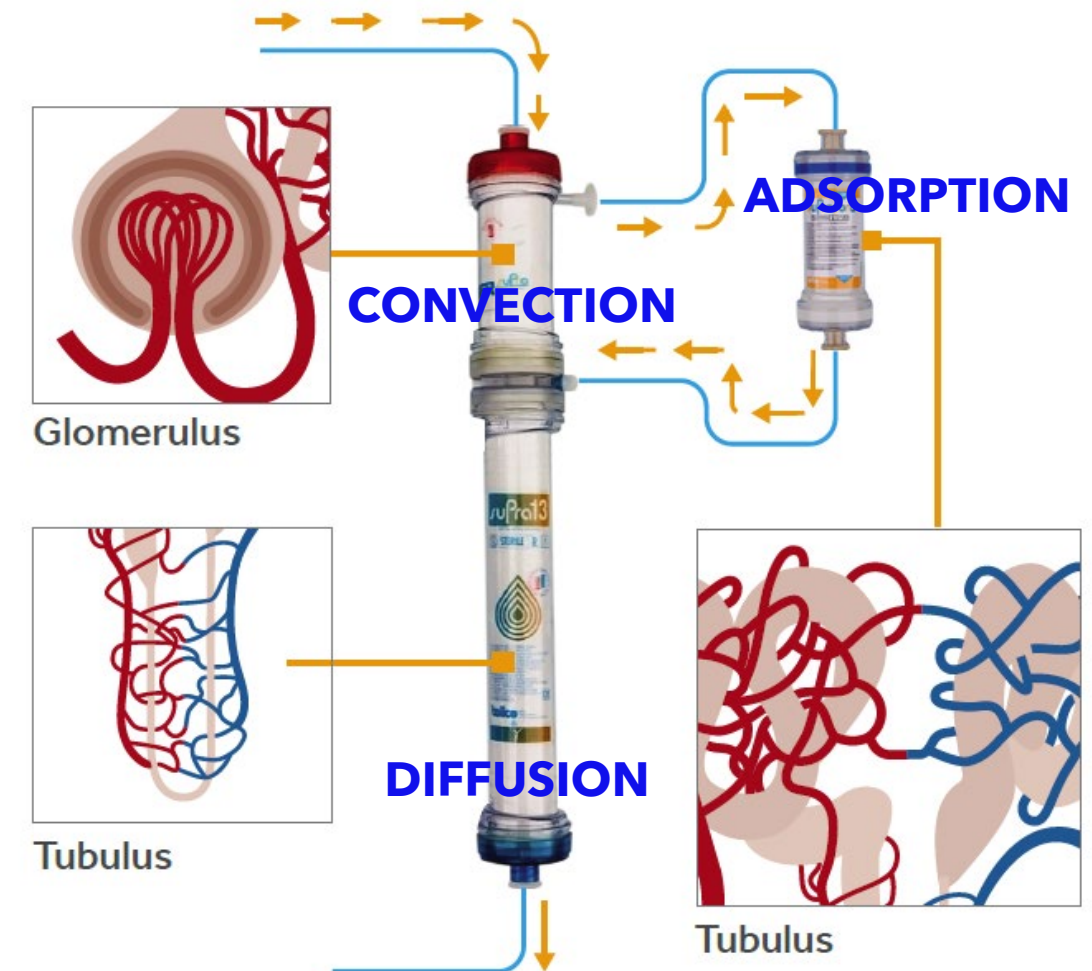
Supra HFR

Technical design

Supra HFR is the HDF therapy based on the HFR (**H**emodia**F**iltration with endogenous **R**einfusion) concept that mimics the physiology of the human kidney. The substitution fluid is **endogenous** because obtained by regeneration of the same own patient ultrafiltrate.

Convection, diffusion and adsorption are the three separated purification mechanisms grouped in two devices^{1,2}:

- **a double-chamber filter**
- **a resin adsorbent cartridge.**



1. Palleschi S, Ghezzi PM, Palladino G, et al. Vitamins (A, C and E) and oxidative status of hemodialysis patients treated with HFR and HFR-Supra. *BMC Nephrol.* 2016;17(1):120.

2. Esquivias-Motta E, Martín-Malo A, Buendia P, et al. Hemodiafiltration with endogenous reinfusion improved microinflammation and endothelial damage compared with online-hemodiafiltration: a hypothesis generating study. *Artif Organs.* 2017;41(1):88-98.

Supra HFR

Adsorption focus: how does the resin work

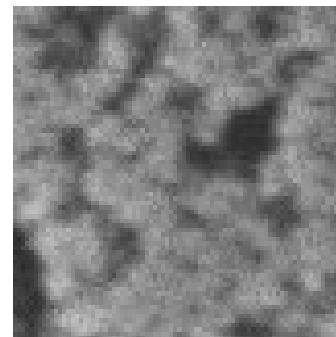
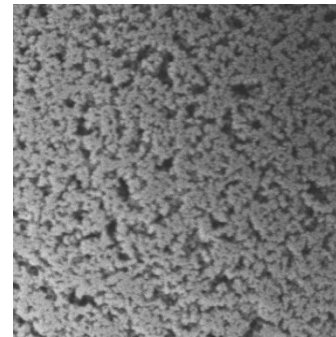
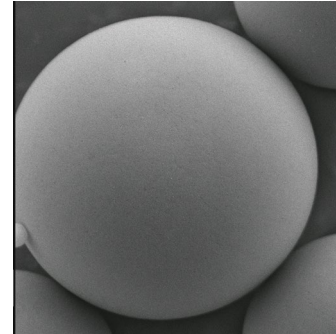
Hydrophobic styrene resin inside the cartridge

Different affinities based on chemical, physical or electrical interactions allows resin to adsorb molecules.

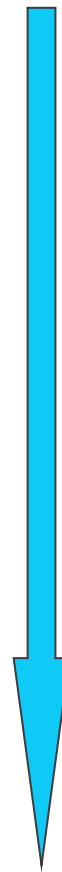
Typical adsorbed molecules: β 2-microglobulin, homocysteine, angiogenin, PTH, myoglobin several chemokines and cytokines

The resin structure offers high sorbent surface area (up to 700 m²/g) thanks to many pores and channels.




The resin has been proven not to retain albumin and essential physiological molecules.

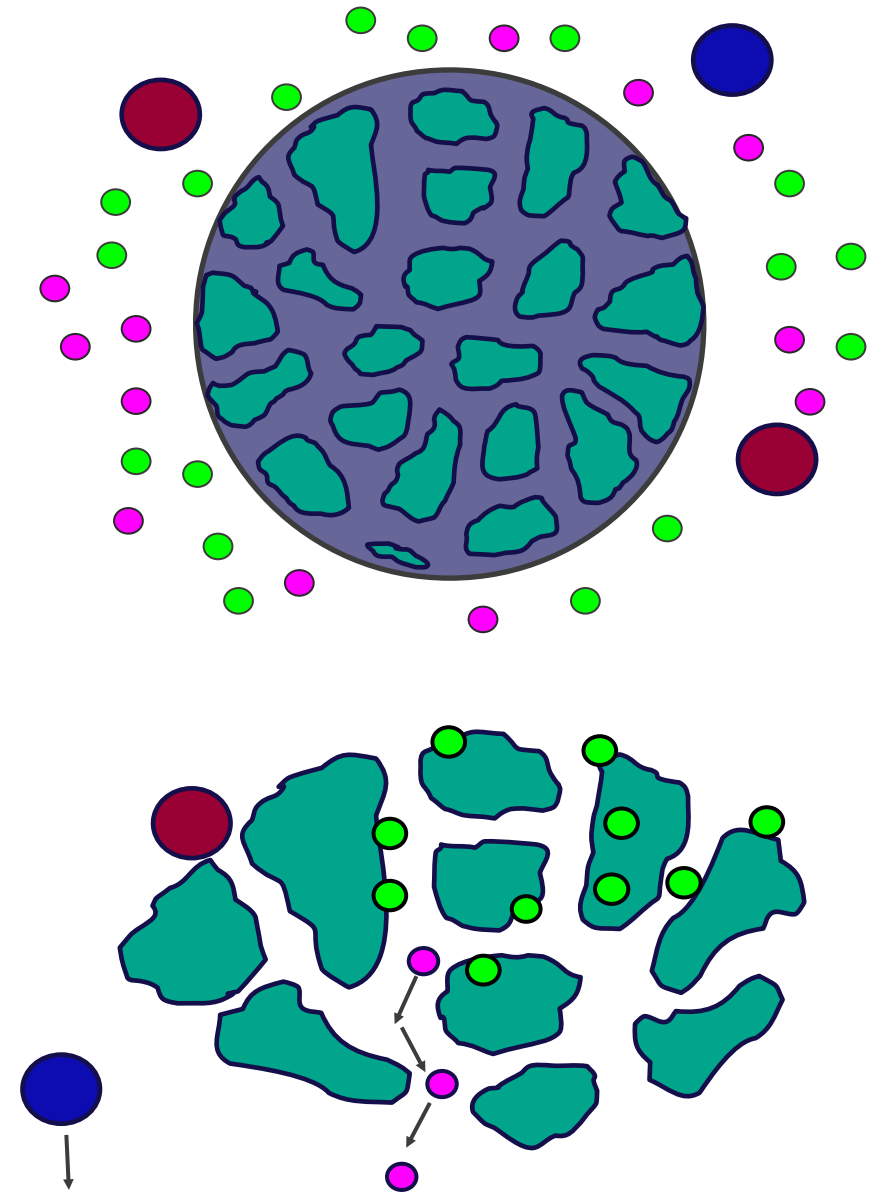


micro



nano

-  Big molecules with affinity to resin bind at surface
-  Small molecules with affinity to resin diffuse internally where they are adsorbed
-  Molecules without affinity to resin are eluted

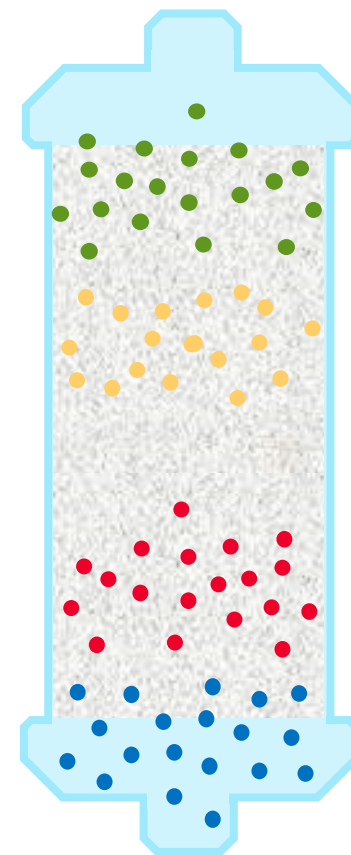
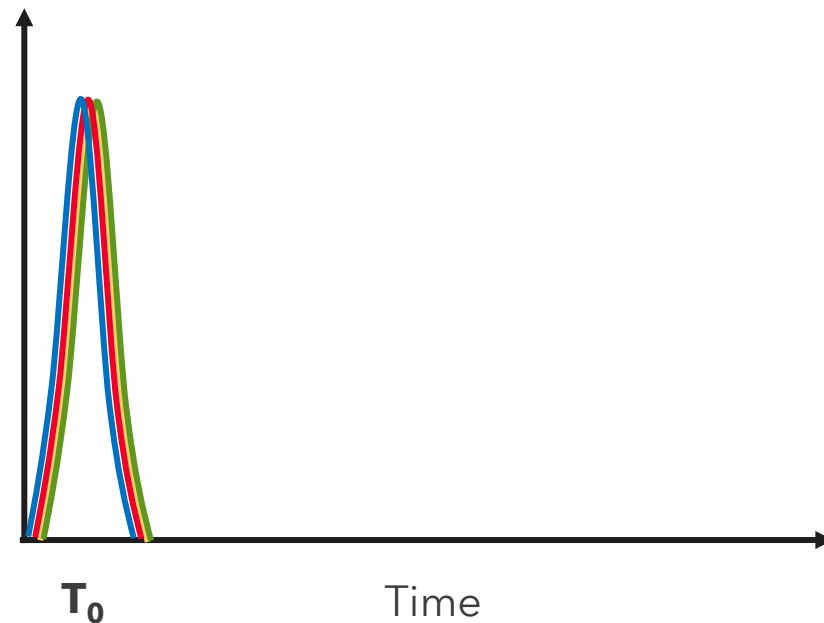


Supra HFR

Adsorption Focus: chromatography column

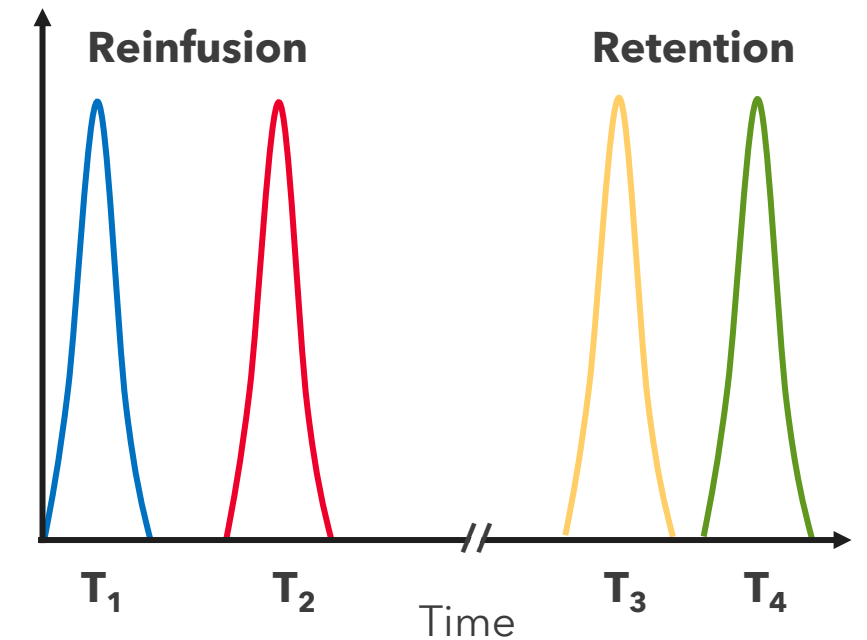
Sorbent cartridge performs as a **chromatography column**

Different molecules contained in the ultrafiltrate enter at the same time inside the cartridge



Molecules with little or no affinity to the resin have a short elution time and are reinfused to the patient.

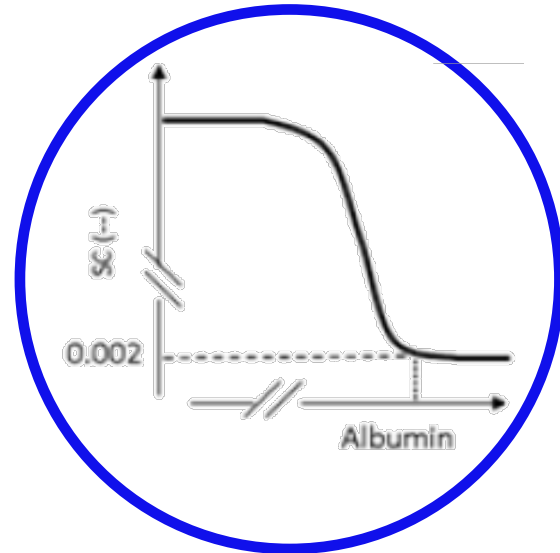
Those with high affinity to the resin, have a longer elution time or are completely retained by the resin.



Supra HFR

Permeability of the convective stage membrane

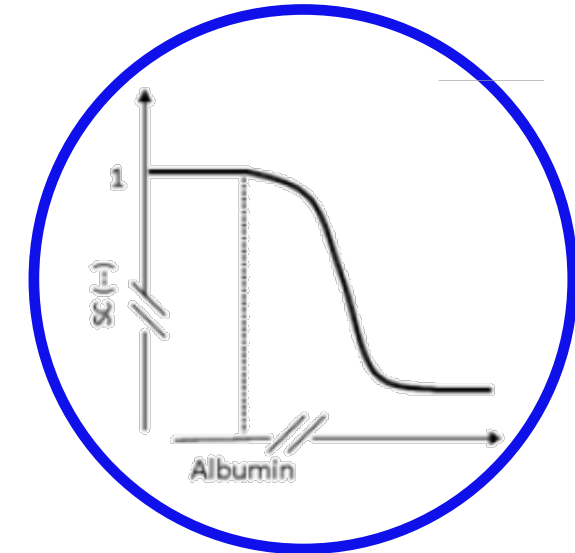
High Flux membrane



Synclear 02™ membrane



Plasma membrane



	TNF- α	IL-6	AAG	Albumin
Molecular weight	Monomer 17 kDa, trimer 51 kDa	23-26 kDa	41-41 kDa	66,5 kDa
Stokes radii	monomer 1.9 nm / trimer 2,3 nm	2 nm	3,5 nm	3,5 nm
Polyphenylene H	31%	9%	1%	0%
Synclear 02	74%	35%	11%	3%

Extraction percentage of different molecules with different membranes

Supra HFR convective chamber is equipped by Synclear 02™ membrane

The expansion of the permeability over the standard high flux is allowed by the selective resin adsorption.

Supra HFR therapy is an advanced alternative to HDF online.

Supra HFR

Main clinical results

Evaluation design

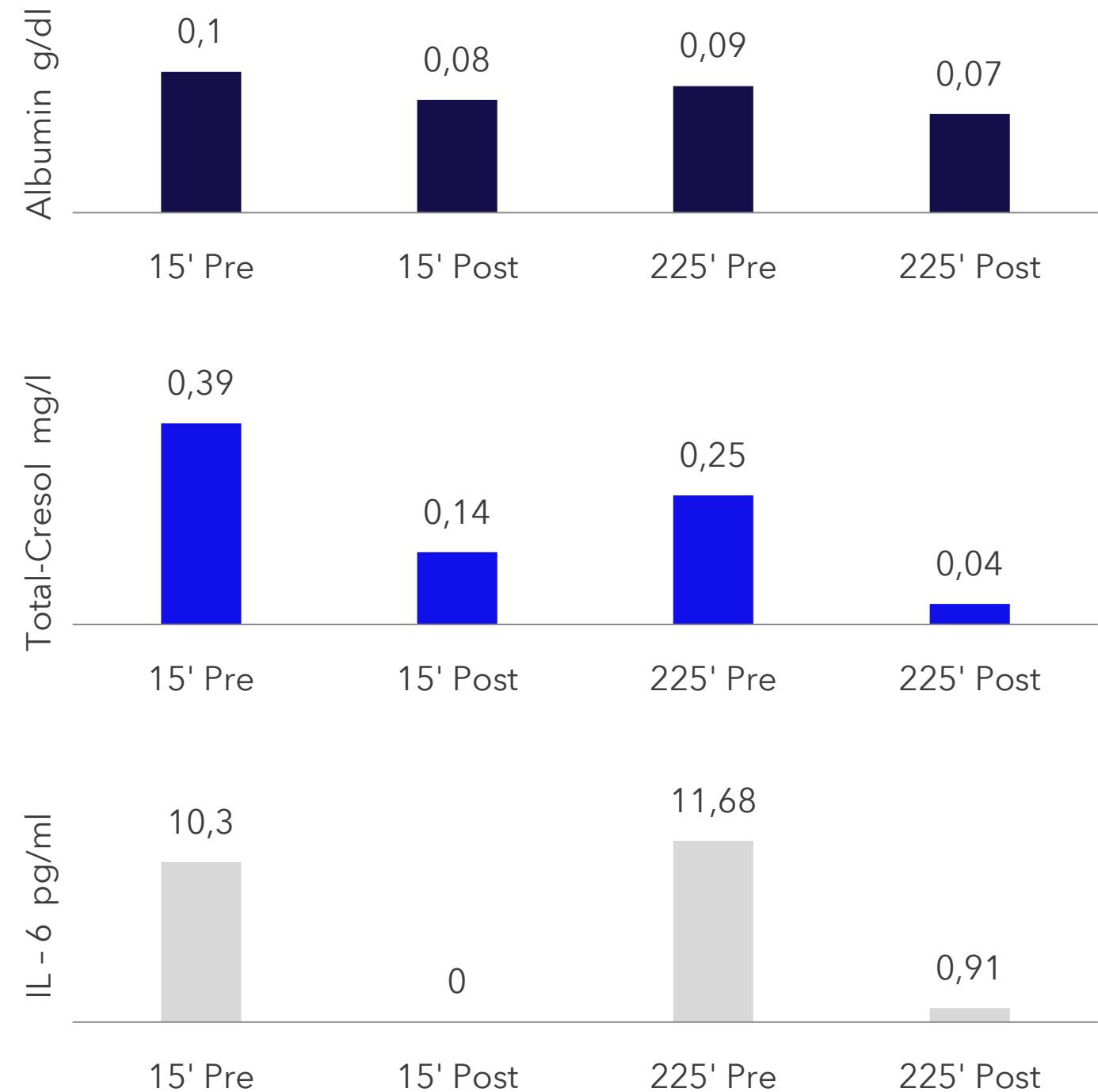
- 12 ESRD patients three times weekly hemodialysis
- Single dialysis session evaluation
- Pre and post cartridge sampling 15' and 225'

Investigation focus

- Retention capacity of the resin along a 4 hours session
- P-cresol, IL-6 and albumin

Remarkable outcomes

- **Effective removal of protein bound toxins, cytokines and albumin saving along the whole dialysis session**
 - Significant adsorption of P-cresol and IL-6
 - No albumin retention



Riccio E, Cataldi M, Minco M, et al. Evidence that p-cresol and IL-6 are adsorbed by the HFR cartridge: towards a new strategy to decrease systemic inflammation in dialyzed patients? *PLoS One*. 2014; 9(4):e95811

Supra HFR

Main clinical results

Evaluation design

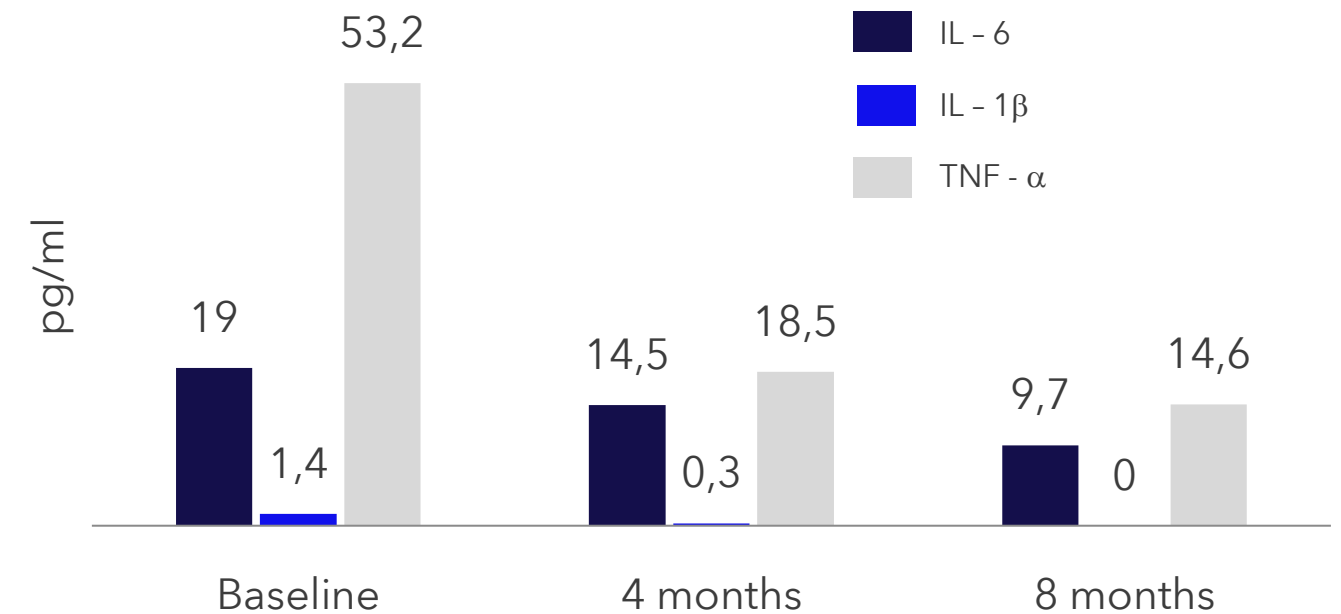
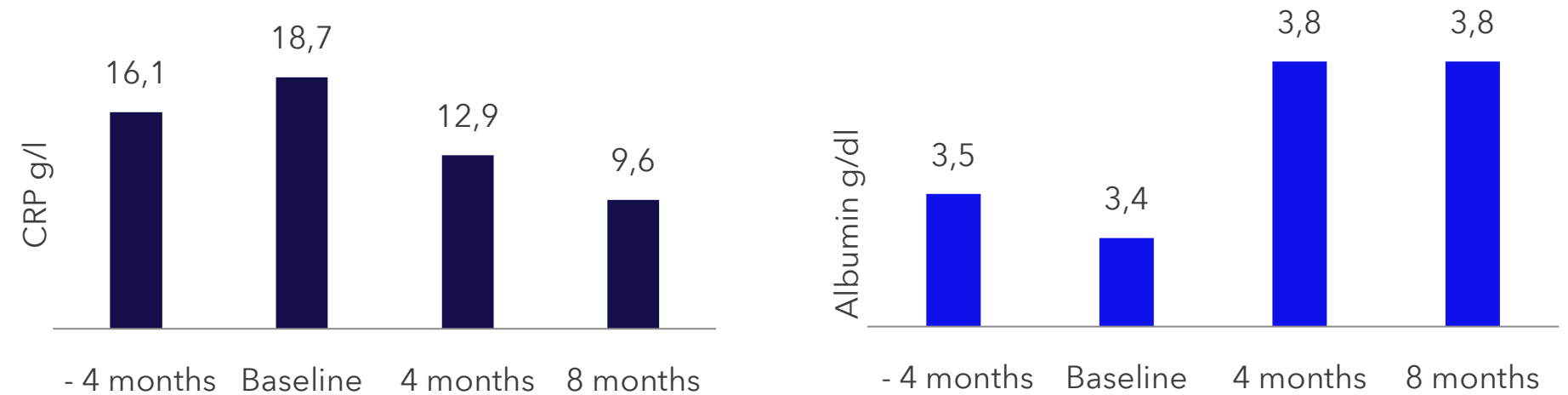
- 24 patients (>6 months HD)
- CRP > 5 mg/L
- Albumin <4 g/dL
- Pre dialysis serum sampling at 0, 4, 8 months in Supra HFR

Investigation focus

- Long terms effect on
 - Inflammation
 - Albumin levels

Remarkable outcomes

- **Medium long terms benefits in improving inflammation, increasing blood purification and improving nutritional status**
- In 4 and 8 months periods
 - serum levels of CRP, IL-6, IL-1b, TNF-a decreased
 - Albumin levels significantly increased



Borrelli S, Minutolo R, De Nicola L, et al. Effect of hemodiafiltration with endogenous reinfusion on overt idiopathic chronic inflammation in maintenance hemodialysis patients: a multicenter longitudinal study. *Hemodial Int.* 2014;18(4):758-766.

Supra HFR

Main clinical results

Evaluation design

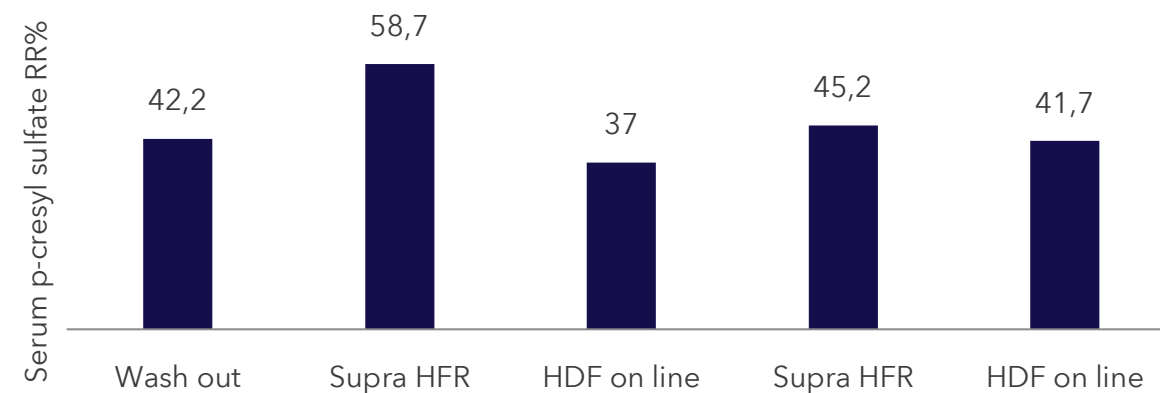
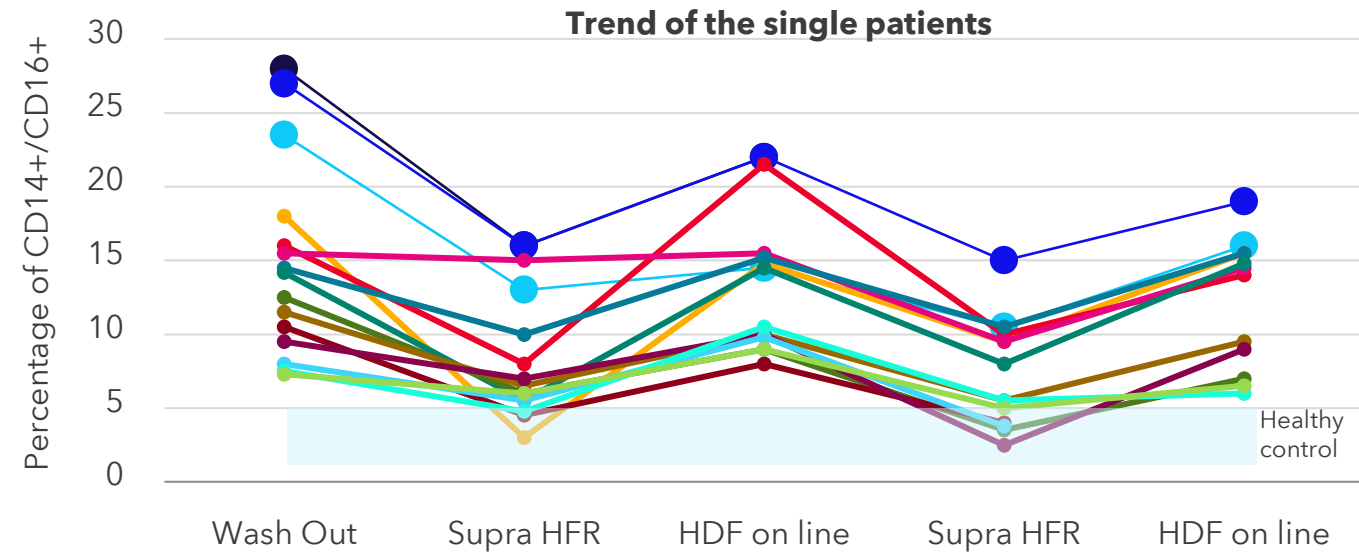
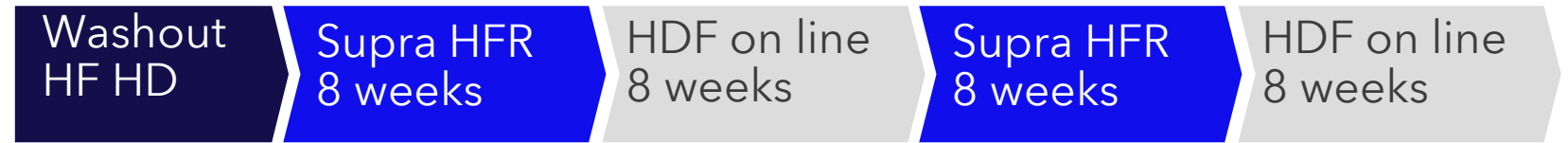
- Perspective crossover study
- 16 patients
- 4 periods 8 weeks long
- Comparison vs HDF on line

Investigation focus

- Effectiveness comparison in
 - Improvement of inflammatory status
 - Impact on endothelial damage
 - Uremic toxins removal

Remarkable outcomes

- **Improvement of the inflammatory status up to achieve healthy control levels**
- The study design and the results allow to relate strong benefits of Supra HFR compared to HDF on line in most all the targets



Esquivias-Motta E, Martín-Malo A, Buendia P, et al. Hemodiafiltration with endogenous reinfusion improved microinflammation and endothelial damage compared with online-hemodiafiltration: a hypothesis generating study. *Artif Organs*. 2017;41(1):88-98.

Meaningfully removes large molecular weight and protein-bound toxins¹⁻³

Benefits of Supra HFR therapy includes blood purification in a wide range of molecular size so suitable for treating patients with high concentration of large molecular weight toxins and of protein-bound toxins

Preserves beneficial molecules^{1,4}

Benefits of Supra HFR therapy includes preservation of beneficial molecules such as aminoacids and vitamins.

Improves inflammatory conditions^{1,2}

Benefits of Supra HFR therapy includes reduced inflammation. CRP, IL-6 and several inflammatory markers decrease.

Improves quality of life⁵

Benefits of Supra HFR therapy include improved quality of life.



1. Esquivias-Motta E, Martín-Malo A, Buendia P, et al. Hemodiafiltration with endogenous reinfusion improved microinflammation and endothelial damage compared with online-hemodiafiltration: a hypothesis generating study. *Artif Organs*. 2017;41(1):88-98.
2. Cuoghi A, Caiazza M, Monari E, et al. New horizon in dialysis deuration: characterization of a polysulfone membrane able to break the 'albumin wall'. *J Biomater Appl*. 2015;29(10):1363-1371.
3. Riccio E, Cataldi M, Minco M, et al. Evidence that pcrisoland IL-6 areadsorbed by the HFR cartridge: towards a new strategy to decrease systemic inflammation in dialyzed patients? *PLoS One*. 2014;9(4):e95811
4. Palleschi S, Ghezzi PM, Palladino G, et al. Vitamins (A, C and E) and oxidative status of hemodialysis patients treated with HFR and HFR-Supra. *BMC Nephrol*. 2016;17(1):120.
5. Solano FG, Bellei E, Cuoghi A, Caiazza M, Bruni F. Radical improvement of signs and symptoms in systemic lupus erythematosus when treated with hemodiafiltration with endogenous reinfusion dialysis. *Case Rep Nephrol Dial*. 2015;5(1):106-112.

Q&A

Thank you

Important: Please refer to the package insert for complete instructions, contraindications, warnings and precautions.

© 2022 Medtronic. Medtronic, Medtronic logo, and Engineering the extraordinary are trademarks of Medtronic. ™* Third-party brands are trademarks of their respective owners. All other brands are trademarks of a Medtronic company.

EMA-RC-2200027-era-22-advtherapies-on-booth-presentation-en-we-6931121

Medtronic

Bellco S.r.l.

Via Camurana, 1 - 41037 Mirandola (MO) Italy

Tel: +39 0535 29111

www.bellco.net