

# Free light chain clearance on immune and inflammatory response in CKD patients (FIREFLIES Study) A FIRST THREE MONTH FOLLOW UP

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## OBJECTIVES

Free light chain immunoglobulins (FLC) accumulate in the sera of patients with renal failure as result of a reduced or abolished clearance and may be considered as members of the family of uremic toxins. We hypothesized that a new hemodiafiltration system, SUPRA could reduce levels of FLC in hemodialyzed patients.

Supra is a new therapy form Bellco that utilizes separated convection, diffusion and adsorption. A two-stage filter is applied that consists of a "high cut off" membrane Synclear 0.2 filter in the first convective stage and a low-flux polyphenylene filter in the second diffusive stage to enhance complete separation of convection from diffusion. An additional effect of FLC reduction is expected on the immunological and inflammatory parameters. Aim of the multicenter FIREFLIES study is the evaluation of SUPRA therapy on long-term reduction of FLCs levels. Moreover is expected an improvement, due to FLCs reduction, on the immunological and inflammatory parameters.

## METHODS

Within a cohort of 147 patients (selected for pre-screening) and on the basis of inclusions criteria of this protocol (i. e. active inflammatory and immunological diseases determine exclusion) were enrolled 27 patients (16M, 11F) with a mean age of 70±12 years, in 5 Dialysis centres.

A wash out period of 2 weeks in Bicarbonate-Dialysis (BD) was followed by a six month of SUPRA treatment (4 hours, three times per week). Plasma Samples were collected at beginning of the dialysis session after three month and at the end of the study (Fig 1).

After Three months pre dialysis levels of FLCs  $\kappa$ , FLCs  $\lambda$  and  $\beta$ 2M were determined by nephelometric assays (FREELITE; The Binding Site, Birmingham, UK); TGF  $\beta$ -1 and CFD were evaluated by Solid Phase Sandwich ELISA (Quantikine ELISA kit, R&D System, Minneapolis, MN, USA).

## STUDY DESIGN

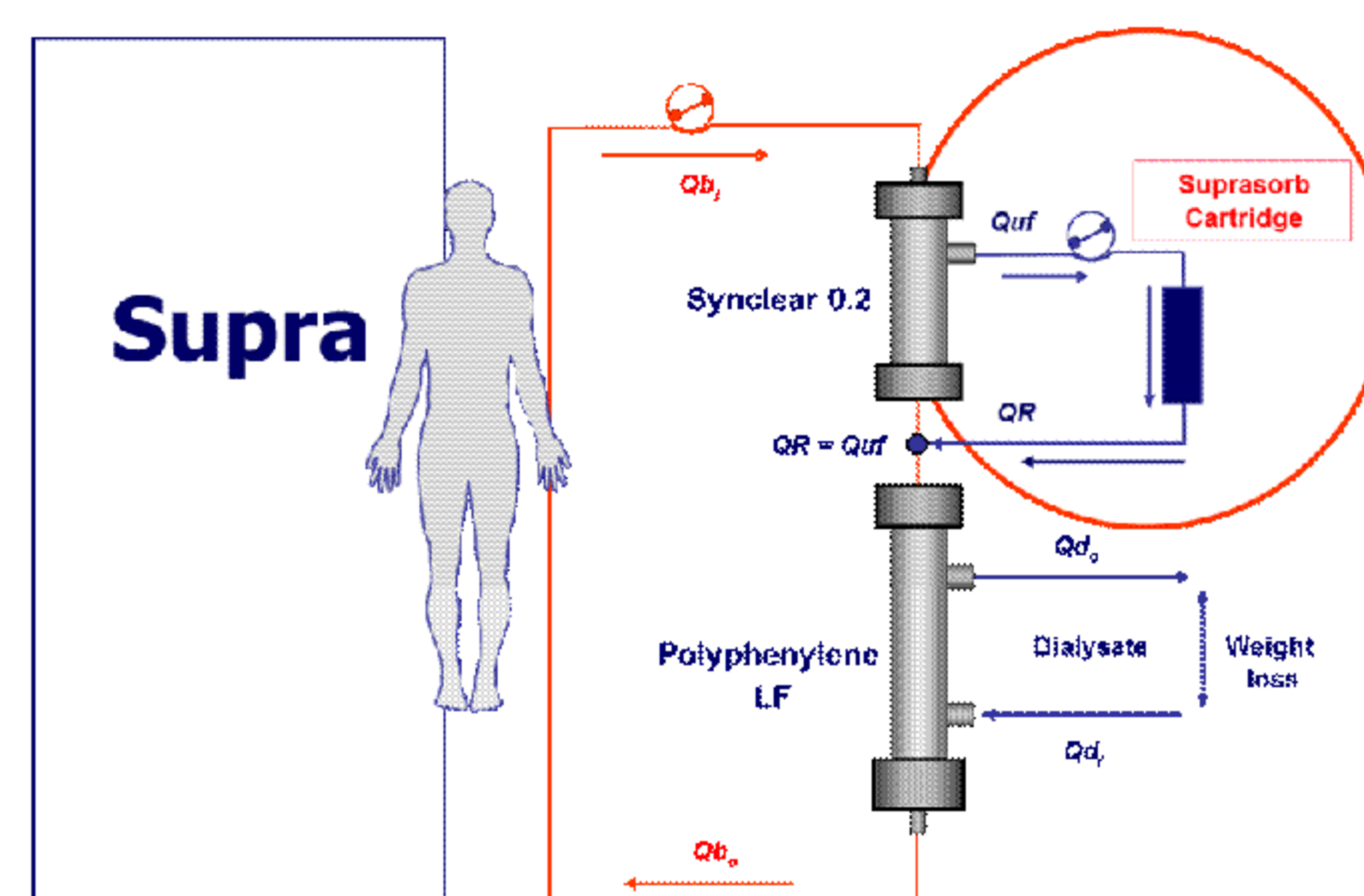


Fig 1. The Supra Scheme; In the convective phase of the first stage, plasmatic water passes through a sorbent cartridge containing 80 ml of hydrophobic styrene resin (Suprasorb; Bellco Srl, Mirandola, Italy) constituted by numerous pores and channels that add to its extensive surface area.

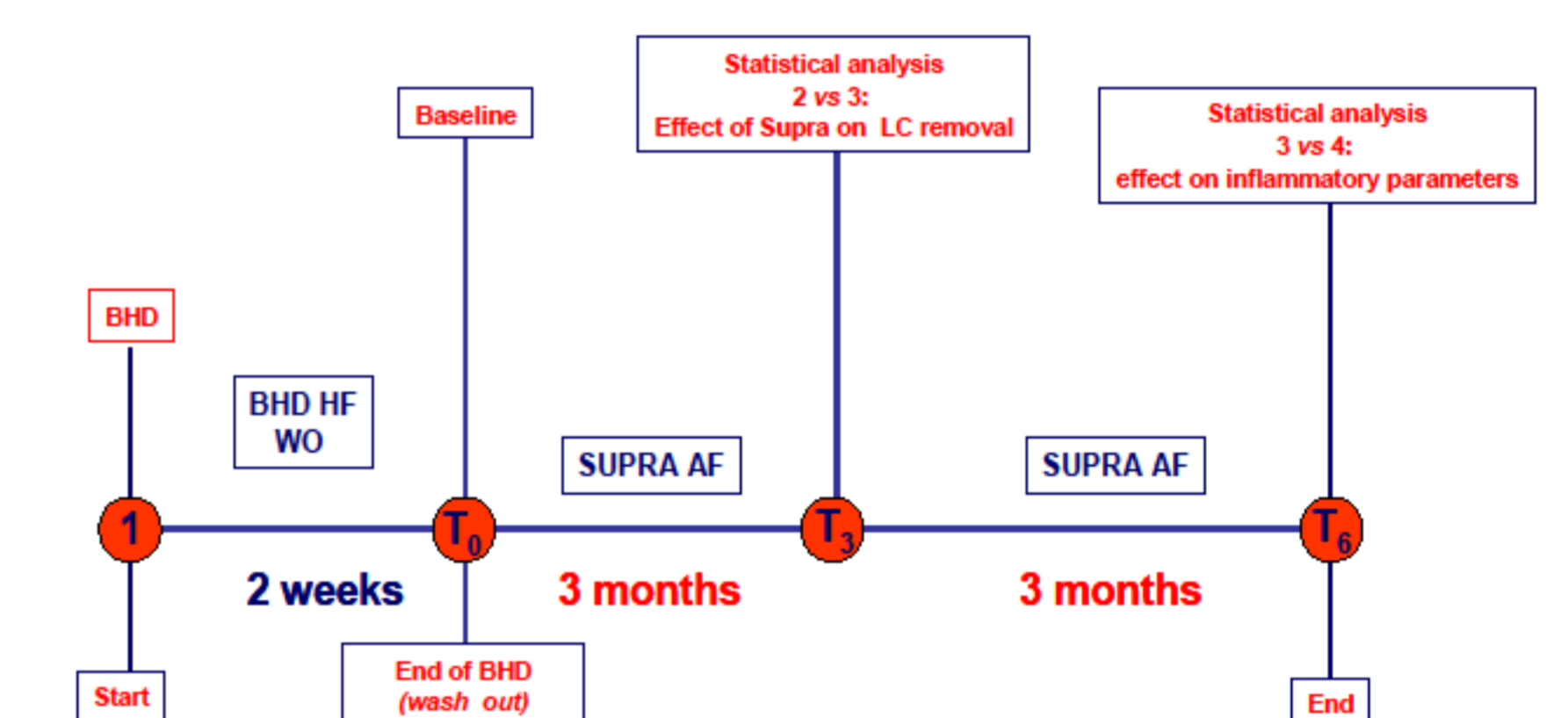


Fig 2. study design. Sampling will be made in the central treatment of the week, in order to eliminate any effect of accumulation in the long period. Is not indicated any variation of the current drugs therapy.

## RESULTS

Here we present a preliminary and partial results on FLCs level in the twenty-seven patients that have completed the first three month of the study. The results shown a statistically significant reduction for FLCs  $\kappa$ , FLCs  $\lambda$ ,  $\beta$ 2M, TGF $\beta$ -1; and Complement Factor D (CFD) with the respect to the basal value (Table 1). Another marker, such as FLCs  $\kappa/\lambda$  ratio, not shows significantly variation between T0 and T3 (1.90±0.14 vs 1.80±0.12) confirming that the SUPRA technique is able to remove both  $\kappa$  and  $\lambda$  free light chain.

A linear correlation have been found between  $\beta$ 2M and both  $\kappa$  and  $\lambda$  FLC's, that become statistically significant after three month of Supra treatment.

| Molecule               | Basal       | After 3 month | P            |
|------------------------|-------------|---------------|--------------|
| FLC's $\kappa$ (mg/l)  | 292.0±33.1  | 246.0±26.4    | 0.0002 (***) |
| FLC's $\lambda$ (mg/l) | 154.1±15.7  | 138.7±11.9    | 0.001 (*)    |
| $\beta$ 2M (mg/L)      | 40.45±2.16  | 32.52±1.26    | <0.0001(***) |
| TGF $\beta$ 1(mg/L)    | 0,028±0,002 | 0,021±0,002   | 0.0008 (***) |
| CFD(mg/L)              | 27.43±1.56  | 25.00±1.24    | 0.009 (**)   |

Table 1. Molecules behaviour at basal level and after three month of SUPRA treatment

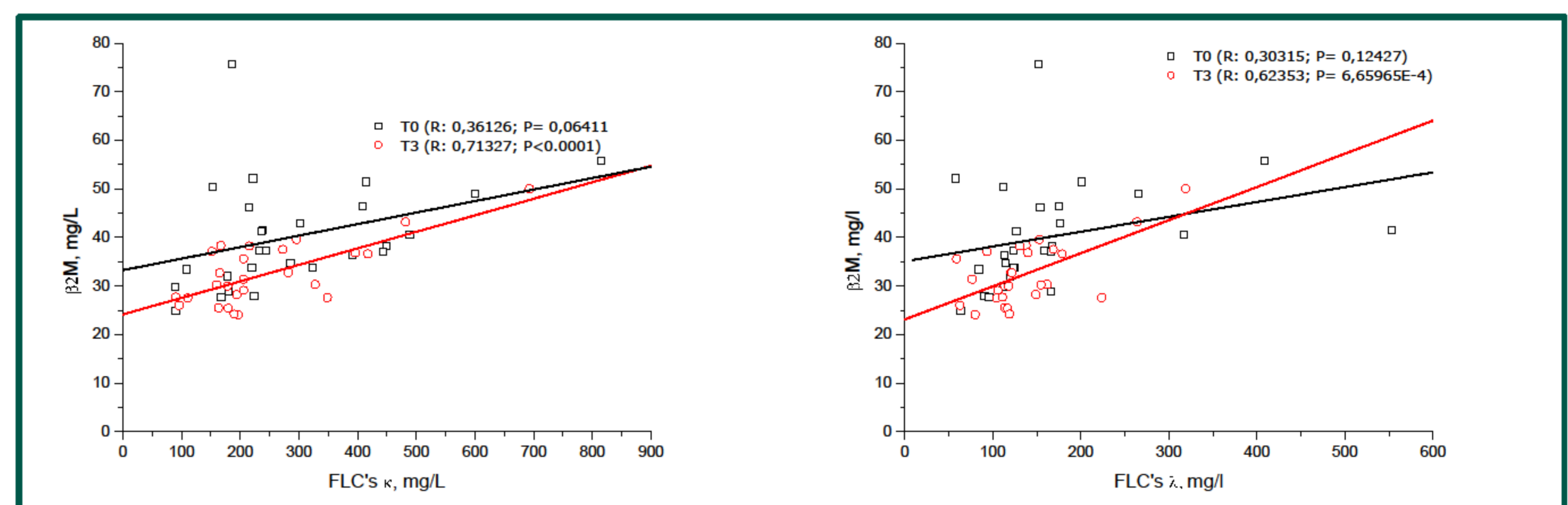


Fig 3. Linear correlation between  $\beta$ 2 microglubulin and FLC's  $\kappa$  and  $\lambda$  pre-dialysis serum value (T0 vs T3)

## CONCLUSIONS

The first three month follow up of the study confirm that SUPRA treatment is able to reduce the FLCs serum concentration as well as  $\beta$ 2M, TGF  $\beta$ 1 and CFD; The second end point, the reduction of inflammatory status of the patients, will be evaluated in next three month.

## REFERENCES

- Cohen G, Rudnicki M, Schmalldienst S, Hörl WH. Effect of dialysis on serum/plasma levels of free immunoglobulin light chains in end-stage renal disease patients. *Nephrol Dial Transplant*. 2002 May;17(5):879-83
- Testa A, Dejoie T, Lecarrer D, Wratten M, Sereni L, Renaux JL. Reduction of free immunoglobulin light chains using adsorption properties of hemodiafiltration with endogenous reinfusion. *Blood Purif*. 2010;30(1):34-6.
- Katzmann JA, Abraham RS, Dispenzieri A, Lust JA, Kyle RA. Diagnostic performance of quantitative kappa and lambda free light chain assays in clinical practice. *Clin Chem*. 2005 May;51(5):878-81.
- Hutchison CA, Harding S, Mead G, Goehl H, Storr M, Bradwell A, Cockwell P. Serum free-light chain removal by high cutoff hemodialysis: optimizing removal and supportive care. *Artif Organs*. 2008 Dec;32(12):910-7.