

Prediction of Response and Progression in Multiple Myeloma with Serum-free Light Chains (sFLC): Corroboration of the International Myeloma Working Group (IMWG) Criteria

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Background

The serum free light (sFLC) assay was proposed as a tool for the assessment of response in patients with non-secretory or oligosecretory MM and patients with primary amyloidosis. Response and progression criteria have been proposed by the International Myeloma Working Group (IMWG), but have not been thoroughly validated.

Patients and Methods

Electronic records of patients with multiple myeloma enrolled in various clinical trials at the Cleveland Clinic Taussig Cancer Center between 4/2004 and 12/2006 were reviewed. Response to treatment and progression were assessed using the European Blood and Bone Marrow Transplantation (EBMT) criteria (table 1) and the sFLC criteria (in patients with evaluable involved sFLC; iFLC ≥ 10 mg/dl (≥ 100 mg/l)). sFLC responses were defined using the IMWG criteria (table 2).

Response Definitions

Complete Remission (CR)	Disappearance of all evidence of serum and urine M-components on electrophoresis as well as by immunofixation studies.
Partial Remission (PR)	A greater than 50% reduction in the serum paraprotein, and if present, a greater than 90% reduction in the urine light chain excretion.
Stable disease (SD)	A stable serum and urine paraprotein (within 25%).
Progressive disease (PD)	25% increase in serum paraprotein or plasmacytoma

Table 1. Response definition by the EBMT criteria

Partial Remission (PR)	50% or greater decrease in the difference of the involved and uninvolved free light chain.
Stable Disease (SD)	Less than 50% decrease and less than 25% increase in the difference between the involved and uninvolved serum free light chain
Progressive disease (PD)	Greater than 25% increase in the difference between the involved and uninvolved serum free light chain

Table 2. Response definition using the sFLC criteria of IMWG

Results

The median age of the 89 identified patients was 61 years (range 41-87) and 58 patients (65%) were males. The involved light chain was kappa in 67 pts (75%). Table 3 summarizes the patients demographics and baseline laboratory evaluations. By EBMT criteria, 4 patients had a complete remission, 22 patients had a partial remission, 34 patients had stable disease, 26 patients had progressive disease and 3 were inevaluable (table 4). Only 43 of the 89 pts (48%) had an involved FLC ≥ 10 mg/dL; of which 14 had a PR, 8 had SD, 18 had PD, and 3 were inevaluable. Table 5 reviews the test characteristics for sFLC assay for the prediction of response or progression.

	N=89
Age (years), Median (range)	61 (41-87)
Gender, % Males	65%
Heavy chain, %	
IgG	67%
IgA	24%
Light chain, % Kappa	75%
Baseline $\beta 2$ microglobulin, mg/dL Median, (range)	3.6 (1.4-47.7)
Baseline creatinine, mg/dL Median, (range)	1.1 (0.6-7.7)

Table 3. Patients characteristics at baseline

	Sensitivity	Specificity	PPV	NPV
Response	81% (51-94%)	83% (65-92%)	64% (38-83%)	92% (68-98%)
Progression	93% (68-98%)	80% (62-91%)	72% (49-87%)	95% (78-99%)

Table 5. Test characteristics of the sFLC assay. PPV/NPV: positive/negative predictive value

	N=89
Involved sFLC > 10 mg/dL, N (%)	43 (48%)
sFLC response, N (%)	
PR	14 (32%)
SD	8 (19%)
PD	18 (42%)
Not evaluable	3 (7%)
EBMT response, N (%)	
CR	4 (5%)
PR	22 (25%)
SD	34 (38%)
PD	26 (29%)
Not evaluable	3 (3%)

Table 4. Classification of responses according to the EBMT and sFLC criteria

Conclusions

The sFLC reliably predicts response and progression in MM. However, half the pts had an involved sFLC that would not be considered evaluable by IMWG criteria, which limits its potential use.

References

- 1- Durie B et al.. Leukemia 2006; 20(9): 1467-73.
- 2- Blade J et al. British Journal of Haematology 1998;102:1115-23.