Value of Serum Free Light Chain Testing for the Diagnosis and Monitoring of Monoclonal Gammopathies in Hematology (MKG405)

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Objectives

- To review the applications of free light chain assays (Freelite™)
- Discuss the interpretation and utility of FLC (free light chain) assays for use in routine clinical practice.

Method and Interpretation

The highly sensitive quantification of free κ and free λ concentrations is performed on nephelometric or turbidimetric platforms.

Diagnosis

"...based on the accumulated evidence, a serum panel consisting of free light chain testing with serum protein electrophoresis or serum immunofixation is optimal for the up-front diagnosis of monoclonal gammopathies without the need for urine testing."

Monitoring Response to Treatment

The review discusses the benefits of monitoring response to treatment with the serum FLC assays which is shown here in Table 1.

Prediction of Progression in MGUS/Solitary Plasmacytoma

"Importantly, risk-stratification models have been developed that incorporate results of free light chain testing with other risk factors to provide powerful predictive factors."

Prognosis in Myeloma

The available literature indicates that serum FLC assays are powerful predictors of outcome in Myeloma.

Table 1	**Benefits of Measuring Free Light Chains to Monitor Response to Treatment**
Benefit	Detail
Incorporated into Response Criteria Guidelines	Baseline studies needed for all patients for later assessment of stringent CR; more frequent sampling for patients who were unmeasurable using other methods
Rapid Indication of Response	Involved free light chain concentration decreases weeks before intact Ig levels decrease
Sensitive Assessment of Residual Disease	Abnormal free light chain levels can persist despite negative immunofixation
Dose Reduction	Assess adequacy of response after dose reduction or (early) discontinuation of treatment
Early Marker of Relapse	Detection of relapse is possible months before immunofixation converts to positive
Identification of Free Light Chain Escape	A shift in secretion from intact Ig to free light chain can occur with relapse; periodic monitoring with serum free light chain testing can detect free light chain escape
Prognostic Indicator	Free light chain reduction by ≥ 50% or normalisation of the involved free light chain concentration after treatment signals better prognosis in AL amyloidosis

Conclusion

The review concludes that FLC assays in combination with electrophoresis methods can eliminate the need for urine testing in the diagnosis of monoclonal gammopathies. The point is also made that the majority of patients with oligosecretory myeloma can now be included in clinical trials due to the incorporation of the FLC assays into the International Uniform Response Criteria and states:

"Endorsement of the use of the free light chain assays as one component in the assessment of stringent CR to treatment in the international uniform response criteria attests to the high sensitivity of this technology to detect minimal residual disease."

The author also goes onto discuss the future applications of FLC assays in relation to prognosis, measurement of time to response and as a tool to identify patients with molecular aberrations leading to uncontrolled FLC synthesis and release.

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