



Serum free light chain (FLC) measurements are useful under the following circumstances:

- A. Evaluation for monoclonal gammopathy.
- B. Monitoring of monoclonal gammopathies during treatment.

A. Evaluation for monoclonal gammopathy

Serum Freelite™ FLC analysis should be used alongside serum protein electrophoretic tests. Results are considered abnormal when they fall outside the following normal ranges:

- Serum kappa (κ) concentrations: 3.3–19.4 mg/L**
- Serum lambda (λ) concentrations: 5.7–26.3 mg/L**
- Serum κ/λ ratio: 0.26–1.65**

Results will fall into the following categories:

1. **Normal samples.** Serum κ, λ and κ/λ ratio are all within the normal ranges. If accompanying serum and urine electrophoretic results are normal, it is most unlikely that the patient has a monoclonal gammopathy.
2. **Abnormal κ/λ ratios.** Support the diagnosis of a monoclonal gammopathy and require an appropriate tissue biopsy. Borderline elevated ratios occur with renal impairment and may require appropriate renal function tests.
3. **Low concentrations of κ, λ or both.** Indicate bone marrow function impairment.
4. **Elevated concentrations of both κ and λ with a normal κ/λ ratio.** May be due to the following:
 - Renal impairment (common).
 - Over-production of polyclonal FLCs from inflammatory conditions (common).
 - Biclonal gammopathies of different FLC types (rare).
5. **Elevated concentrations of both κ and λ with an abnormal κ/λ ratio.** Suggest a combination of monoclonal gammopathy and renal impairment.

It may be helpful to assess the results using a κ/λ logarithmic plot that includes the normal ranges and patient results from various disease groups (Figure 1).

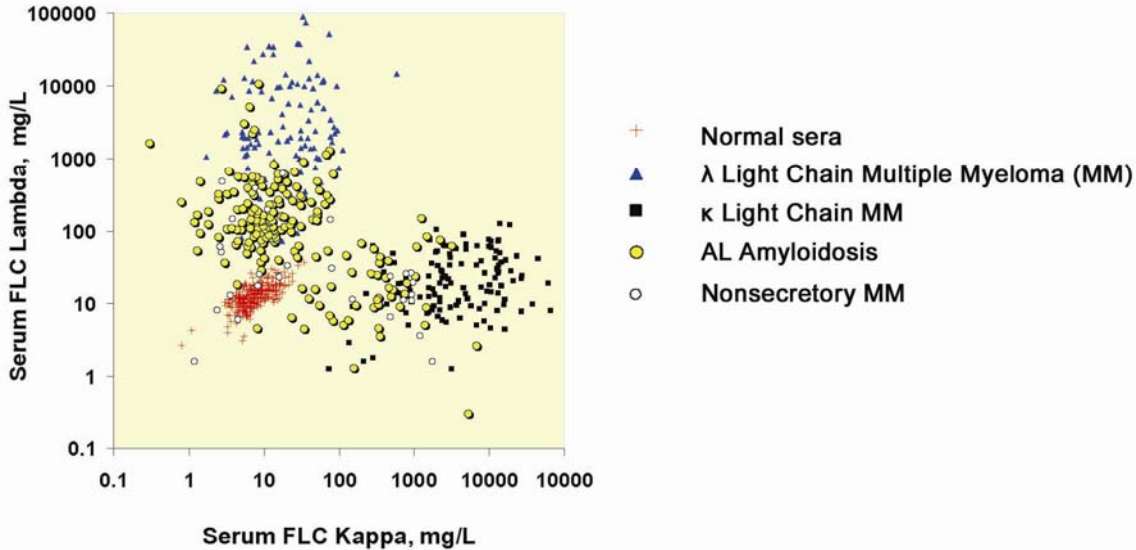


Figure 1. Logarithmic plot of serum FLC results.¹

B. Monitoring of monoclonal gammopathies during treatment

Patients with monoclonal gammopathies can be monitored serially using the tumor (“involved”) FLC concentration and the κ/λ ratio.

Response criteria for patients with multiple myeloma

Results of the Freelite™ FLC assay have been incorporated into the newly published “International Uniform Response Criteria” for patients with multiple myeloma.² The sections of these criteria relevant to the serum FLC analyses are:

- **Measurable disease:** abnormal ratio and involved FLC ≥ 10 mg/dL (≥ 100 mg/L). This definition is particularly salient for patients who do not have measurable disease with serum protein electrophoresis (SPEP), 24-h urine protein electrophoresis (UPEP) or quantitative immunoglobulin analysis.
- **Stringent complete response:** normal FLC ratio.
- **Partial response:** $\geq 50\%$ decrease in the difference between involved and uninvolved FLC levels among patients with unmeasurable M protein using SPEP, 24-h UPEP or quantitative immunoglobulin analysis.
- **Progressive disease:** in patients without measurable serum and urine M protein levels, the difference between involved and uninvolved FLC levels is measured. The absolute increase must be ≥ 10 mg/dL (≥ 100 mg/L).
- **Relapse from complete response:** abnormal FLC ratio and/or involved FLC ≥ 100 mg/L.

Response criteria for patients with AL amyloidosis

The following response criteria have been agreed for AL amyloidosis:³

- **Complete response (CR):** normal κ/λ ratio, serum and urine immunofixation negative.
- **Partial response (PR):** if FLC > 100 mg/L at baseline, \downarrow by $\geq 50\%$.
- **Progression from CR:** abnormal κ/λ ratio (FLC concentration must double).
- **Progression from PR or stable:** increase in involved FLC by 50% to > 100 mg/L.

References

1. Bradwell AR. Serum Free Light Chain Analysis, 4th Edition, The Binding Site, Ltd., Birmingham, UK, 2006.
2. Durie BGM, Harousseau JL, Miguel JS, *et al.* International Uniform Response Criteria for Multiple Myeloma. *Leukemia*.2006;20(9):1467-73.
3. Gertz MA, Comenzo R, Falk RH, *et al.* Definition of organ involvement and treatment response in immunoglobulin light chain amyloidosis (AL): a consensus opinion from the 10th International Symposium on Amyloid and Amyloidosis, Tours, France, 18-22 April 2004. *Am J Hematol*. 2005;79:319-328.

Note. These guidelines are recommendations only. Final interpretation of results of the Freelite™ assay is to be determined by the clinician(s) caring for each patient following review of all available clinical information and current diagnostic and management guidelines. These interpretation guidelines are subject to revision and updates.

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