Interpretation flow and sample results

The FLC test provides **3 numbers (kappa/lambda ratio, kappa & lambda)** and interpretation requires **examination of all 3 numbers in a stepwise manner**:

1. Is the kappa/lambda (κ/λ) **ratio** abnormal compared to the reference/normal/healthy range?

Abnormally **high** - suggests possible monoclonal light chains where **kappa (κ) is the "involved" chain**

Abnormally **low** – suggests possible monoclonal light chains where **lambda (λ) is the "involved" chain**

(Abnormal ratios may also be due to suppression of the "uninvolved" chain)

2. Verify by looking for the "**involved" chain elevation**. If elevated, then it is consistent with monoclonal light chains. If no elevation, then there is no evidence for monoclonal light chains by this method at this time.

3. Check the **"uninvolved" chain**. If low (suppressed), then this may explain the abnormal ratio if the "involved" chain is normal or low.

4. Any time you receive the next set of free light chain results for a patient (except when the lab switches manufacturer):

a) Compare the κ/λ ratio to the last κ/λ ratio result (or last few κ/λresults). If it is trending TOWARD the normal range from last time to this time, that is a good sign. If your κ/λ ratio from last time to this time is moving AWAY from normal, then that is not a good sign.

Be careful, ratio trends can be caused by changes in the "uninvolved" chain that skew the ratio in a way that does not reflect the disease direction. Also, consider whether your patient has been on treatment or not lately and other lab results.

b) Compare the "involved" light chain amounts from the last result to the current result. If it is trending TOWARD the normal range from last time to this time, that is a good sign. If your "involved" light chain amounts from last time to this time is moving AWAY from normal, then that is not a good sign.

c) Compare the "uninvolved" light chain amounts from the last result to the current result. Are changes in the "uninvolved" chain causing some of the trend changes in the ratio?

d) Compare the free light chain trends (ratio and "involved" chain) with the other lab results to see if they are trending the same way: SPEP, M spike levels, IgG, IgA, or IgM levels, Creatinine, Calcium, etc. This gives a more complete clinical picture.

5. Consider guideline cut-offs (i.e. involved/uninvolved FLC ratio ≥100 is changing to >70 for the Siemens assays and involved ≥100mg/L). This cutoff has also been validated for N Latex FLC assay (Henriot et. al. 2019 Clin Chem Lab Med). In addition, the International Myeloma Working Group has published a new risk stratification model (Mateos et al. Blood Cancer Journal (2020) 10:102) that uses a ratio >20 to be one of the 3 to 4 independent risk factors in the predicition of the progression probability. The decision to treat should not be based on the light chain numbers alone, but rather should be guided by complete clinical picture (including clinical symptoms and other lab and imaging tests).

["involved" chain is defined by the abnormal ratio. High ratio = kappa involved, Low ratio = lambda involved]

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Example Results between two different manufacturers with interpretations:

4	κ/λ ratio	Kappa	Lambda	Comments	
Previous method	0.08 (0.26-1.65)	1.21 (3.3-19.4)	15.3 (5.71-26.3)	• Low ratio suggests lambda clone • Kappa low • Lambda normal (no lambda clone)	• **Low ratio, likely due to kappa falsely low** • **No evidence of monoclonal FLCs by this method**
Siemens N Latex FLC	1.10 (0.53-1.51)	17.7 (8.24-28.9)	16.1 (9.1-32.6)	• Normal ratio • Normal kappa • Normal lambda	• **No evidence of monoclonal FLCs by this method**

18	κ/λ ratio	Kappa	Lambda	Comments	
Previous method	3.25 **(0.26-1.65)**	1.3 **(3.3-19.4)**	0.4 **(5.71-26.3)**	• High ratio suggests kappa clone • Kappa low • Lambda low	• **Elevated ratio but both kappa and lambda low** • **No evidence of monoclonal FLCs by this method**
Siemens N Latex FLC	13.95 **(0.53-1.51)**	22.6 **(8.24-28.9)**	1.62 **(9.1-32.6)**	• High ratio suggests kappa clone • Kappa normal • Lambda low	• **Elevated ratio due to low lambda** • **No evidence of monoclonal FLCs by this method**

22	κ/λ ratio	Kappa	Lambda	Comments	
Previous method	238.64 (0.26-1.65)	1260 (3.3-19.4)	5.28 (5.71-26.3)	• Abnormal high ratio suggests kappa clone • Kappa elevated • Lambda low	• **Elevated ratio and elevated kappa** • **Ratio skewed even higher due to low lambda** • **Evidence of monoclonal kappa FLC**
Siemens N Latex FLC	66.74 (0.53-1.51)	901 (8.24-28.9)	13.5 (9.1-32.6)	• Abnormal high ratio suggests kappa clone •Kappa elevated • Normal lambda	• **Elevated ratio and elevated kappa** • **Evidence of monoclonal kappa FLC but less exaggerated ratio compared to previous method**

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