Effective Health Care

Serum Free Light Chain Assay Analysis
Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Serum free light chain assay analysis for the diagnosis, management, and prognosis of plasma cell dyscrasias will go forward for refinement as a systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase.

- When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

Topic Description

Nominator: Health care professional association

Nomination Summary: The nominator presents a series of questions for a review on the effectiveness of serum free light chain (FLC) assay analysis to guide the diagnosis, management, and prognosis of plasma cell dyscrasias. In particular, they are interested in multiple myeloma (MM), including nonsecretory multiple myeloma (NSMM), and either free light chain type or intact immunoglobulin (INMM); amyloidosis (AL); and monoclonal gammopathy of undetermined significance (MGUS), all of which have been traditionally screened for and diagnosed using both serum and urine by electrophoresis along with immunofixation to identify the heavy and light chain components.

Population(s): Any patient diagnosed with one of the B-plasma cell dyscrasias (i.e., MM, free light chain or intact immunoglobulin, AL, MGUS, or NSMM). Additionally, undiagnosed patients presenting with any of the non-specific complaints associated with these diseases (i.e., bone issues, elevated urine/serum protein, anemia, fatigue, or renal dysfunction), including patients being ruled out during a routine physical.
Intervention(s): Serum FLC analysis.
Comparator(s): Traditionally used serum and urine protein electrophoresis and immunofixation.
Outcome(s): Comparative diagnostic, prognostic, and therapeutic accuracy; cost savings (e.g., decreased length of stay and number of clinic visits); decreased whole body scans or bone marrow biopsies; earlier detection of patient relapse; improved treatment, survival, and quality of life.

Key Questions from Nominator:

1. Is there improved diagnostic and/or therapeutic accuracy for FLC analysis in conjunction with serum electrophoresis as compared with the current practice of performing urine and serum electrophoresis for diagnosis and therapy monitoring?
2. What are the economic implications of routinely measuring serum FLC in conjunction with serum electrophoresis for diagnosis and/or therapy as opposed to the current practice of serum and urine electrophoresis?
3. What is the diagnostic and/or therapeutic monitoring utility of the κ/λ ratio?
4. What are the day-to-day biological variables, such as renal function, that affect the utility of FLC measurements?
5. Can FLC results by different manufacturers be standardized?
6. Can FLC reference ranges by different manufacturers be standardized?
7. Can FLC reliably be used as an independent risk factor for progression to MM in MGUS patients?
8. If patients at risk for progression from MGUS to MM can be identified, does this measurably affect survival or quality of life?
9. Can the ability to measure FLC, with their shorter half lives, improve treatment protocol selection?
10. If FLC affects treatment protocol selection in a timelier manner, does this lead to a change in survival or quality of life?
11. Can the increased sensitivity of FLC identify patient relapse earlier?
12. If relapse can be identified earlier, does this improve survival?
13. Does the increased sensitivity of FLC in AL and NSMM improve treatment and survival?
14. Are the number of bone marrow biopsies and/or whole body scans decreased in NSMM when FLCs are measured?
15. Are there cost savings such as decreased length of stay or number of clinic visits in MM patients when FLC is used as compared to the current practice of serum and urine electrophoresis?

Considerations

- The topic meets all EHC Program selection criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)

- Recent studies have shown the potential for the serum FLC assay measurements to replace urine electrophoresis and to also reduce the need for serum immunofixation in the screening and diagnosis of some plasma cell dyscrasias. Also, recent studies have reported a potential for serum FLC assays to allow for earlier detection of light chain type plasma cell dyscrasias. Some experts agree that urine tests are no longer necessary as part of the initial screening algorithm for identifying a disease in which serum monoclonal immunoglobulins are increased; however, some believe they may still be required for specific disease diagnosis and monitoring. Serum FLC assay is not supported as a stand alone test or as a replacement for usual management. Testing algorithms have changed with the development of the serum FLC assays, introducing variation in practice.

- Consensus guidelines exist for this topic; however, the evidence base for serum FLC assay analysis for plasma cell dyscrasias has not been systematically reviewed. Therefore, this topic will move forward as a new systematic review.