Session V: Prognostic, Predictive and Response Markers in WM

Abstract 129

Presenter: G. Yang

Soluble CD27 is a faithful marker of disease burden and is unaffected by the rituximab-induced IgM flare, as well as, plasmapheresis, in patients with Waldenström's Macroglobulinemia. B. T. Ciccarelli, G. Yang, E. Hatjiharissi, J. D. Soumerai, Z. R. Hunter, L. Ioakimidis, C. J. Patterson, R. J. Manning, L. Xu, S. Adamia, S. P. Treon; Dana-Farber Cancer Institute, Boston, MA, USA.

Backgound: Waldenström's macroglobulinemia (WM) is a B-cell, IgM-secreting lymphoplasmacytic lymphoma. In this disease, serum IgM levels are used to assess both progression and response to treatment. Rituximab is an important therapeutic, but one frequently associated with an induced IgM flare, which may complicate response assessment (Treon et al, Ann Oncol 2004). In addition, plasmapheresis is commonly employed and can further complicate this evaluation. We, therefore, sought to identify a novel marker of disease burden which could evade these common clinical challenges. Soluble CD27 (sCD27) is a TNF-family member secreted by WM cells, elevated in patients with WM, and supports tumor cell growth through the induction of CD40L on bone marrow mast cells (Ho et al, Blood 2008). As such, we attempted to delineate its potential as a faithful marker of disease burden in WM.
Methods: sCD27 levels were serially measured in 31 WM patients whose clinical outcomes (responder, stable disease, or progressive disease) were determined using consensus panel criteria based on concurrently-measured changes in serum IgM levels. Moreover, sCD27 levels were serially measured in 8 patients who had a rituximab-induced IgM flare, and in one patient, pre- and 48-hours post-plasmapheresis.
Results: Serial changes in sCD27 levels paralleled those of serum IgM levels in all outcome categories, and highly-correlated to serial changes in serum IgM levels ($r= 0.9760$; $p<0.0001$ by Pearson's correlation test). Moreover, in 8 patients who experienced an IgM flare related to rituximab, and eventually responded to therapy, IgM levels acutely rose from 3,515 to 5,270 mg/dL ($p=0.016$), while sCD27 levels declined from 174.1 to 155.9 U/mL ($p=0.10$). For the one patient undergoing plasmapheresis, IgM levels obtained 48 hours later declined from 4,770 to 2,370 mg/dL, whereas sCD27 levels showed minimal change (125.3 to 123.5 U/mL).
Conclusion: sCD27 is a faithful marker of disease burden and is unaffected by the rituximab-induced IgM flare, as well as, plasmapheresis in WM. The use of this marker may aid in correctly predicting clinical outcome in patients undergoing treatment with rituximab and/or plasmapheresis in WM.