AST Journal Club
"IgG Endopetidase in Highly Sensitized Patients Undergoing Transplantation"

Additional Q& A
Speaker: Stanley Jordan, MD, FASN, FAST • Cedars-Sinai Medical Center, Los Angeles
Moderator: Leonardo Riella, MD, PhD • Harvard Medical School, Boston

Q: What was the reason to give rituximab following Campath-given Campath depletes B-cells?

A: This is a very good question. Others have offered that Thymo also depletes B-cells and could be effective as an anti-B-cell agent. However, this has not been our experience. For example, we have transplanted highly sensitized patients who have no DSAs at transplant and seen rapid rebound of DSAs within 1-2 weeks post-transplant even though they received Campath induction. Thus, we feel this is not adequate and rituximab has a better capacity to deplete B-cells. I am attaching a manuscript that shows the responses of T & B cells post-transplant in highly-HLA sensitized patients receiving rituximab and campath.

Q: Can you re-dose IdeS? Anti-idiotypic Ab?

A: This is also a good question and as yet unanswered question. We know that IdeS is an immunogenic protein that can elicit immune responses. However, to date, we have seen variable immune responses (unpublished) with many patients showing no antibodies and others strong antibodies after ideS treatment. It is theoretically possible to re dose, but we are not sure if this will be effective. More importantly, Hansa Medical is working on developing a new IdeS that will be much less immunogenic and hopefully can be reused. I think this will likely improve our ability to provide longer and possibly repeat therapies to remove deleterious antibodies.

Q: How many doses of IVIg and rituximab do you give post-op?

A: Currently, we give only one dose of each as shown in the protocol. If the patient develops dn DSAs or rebound DSAs, we would re-treat with IVIg + rituximab X 1 dose. However, this has been infrequent.

Q: How about a patient with a prior Strep infection? Can IdeS be used?

A: Yes, as most patients have had prior Strep infections, we did not check anti-IdeS status as an entry criteria for the study. We did this initially, and identified only 2 patients who had detectable antibodies to IdeS. Thus, it seems a fairly low incidence, at least in LA. There is some concern about IgE antibodies to IdeS, as this may cause anaphylactic reactions, but we did not see this in our study. Further analysis will help better define this problem.

Q: Can IdeS be used in proliferative GN with monoclonal IgG deposits? Or to prevent recurrence of PGNMID after transplant?

A: This question is now being investigated. Patients with anti-GBM disease are being treated with IdeS as a monotherapy in a study in Sweden. This will help us better understand the utility of IgG endopeptidase in preventing injury by anti-GBM IgG antibodies. I think this is going to be an important area of IdeS research and certainly it would be potentially useful to prevent autoantibody injury to allografts in patients who have pathogenic IgG autoantibodies reactive with renal antigens pre-transplant.

Q: If post-op you see increase in DSA, would you prefer IdeS instead of PLEX

A: This is a distinct possibility. This of course would be best for those patients who have unexpected ABMR with rapidly increasing DSAs. IdeS might be preferable to PLEX due to the rapidity of removal of DSAs, (especially complement activating DSAs) and the lack of IdeS effect on coagulation factors that might be removed by PLEX. We look forward to doing these studies.