Alemtuzumab in the treatment of steroid refractory acute graft-versus-host disease

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Type of Session: Scientific

Background
Corticosteroid therapy is the mainstay of treatment for graft versus host disease ("GVHD"). This condition is typically manifested by gut, skin, and liver toxicity. Unfortunately, steroid medications have significant side effects that in turn can have negative consequences in terms of post-transplant morbidity, prompting ongoing searches for newer, less toxic treatment modalities. Alemtuzumab, a humanized monoclonal antibody to the cell surface marker CD52, has thus far been tried mainly as a means of preventing GVHD. Only a few patients have actually been treated with this antibody, thus this study was initiated to assess the efficacy and safety of alemtuzumab in the setting of steroid-refractory GVHD.

Materials and Methods
- Prospective, multicenter study
- Patients enrolled from December 2004 to May 2006 (n=13)
- A fludarabine-based reduced-intensity conditioning (RIC) regimen was used.
- The hematopoietic cells were obtained from HLA-identical siblings in 12 cases, while one patient and a stem cell from umbilical cord blood in one patient.
- All but one received CSA and MTX for GVHD prophylaxis.
- Patients all had steroid-refractory grade II-IV acute GVHD
- Treatment consisted of Campath 1H 10mg given subcutaneously on days 1-5.
- Primary Endpoint:
  - Efficacy of alemtuzumab (Campath 1H) after exclusion of other severe HST-related complications.
- Secondary Endpoints:
  - Side effects and incidence of infectious complications

Results
- Median age was 33 years old (range 1-59 years)
- GVHD was classified as grade II in 8 patients, grade III in 5 patients, and grade IV in 2 patients
- Predominant organ affected was gut in 6 cases, skin in 7, liver in 4, and combination of gut and skin in 4 patients
- In 6 of the 13 patients, the clinical manifestations of GVHD were noticed after the first 100 days of hematopoietic stem cell transplant (HSCT)
- Complete resolution of GVHD was seen in 23%; Partial response was seen in 62%; No responses were seen in 15%
- Six of the 13 patients were able to decrease steroid use
- Five patients developed CMV (pp65) reactivation, and 3 of them were successfully treated with valciclovir/ganciclovir
- All patients maintained complete chimerism during and after alemtuzumab therapy.
- With median follow-up of 5 months (range 1-18 months), 8 patients remain alive, 3 without evidence of GVHD.
- Of the five patients that died, 3 were from GVHD, and the others due to infectious complications.

Author’s Conclusions
- This preliminary study suggests that alemtuzumab is a well-tolerated agent and has a beneficial effect in the treatment of refractory GVHD. As this is only a pilot study, additional investigation is needed.
Nonetheless, the study suggests that this modality could be used early in the management of patients with GVHD in order to improve quality of life and reduce the long-term side effects of corticosteroids.

**Clinical/Scientific Implications**

- This paper reports on a novel use of alemtuzumab, an anti-CD52 humanized, monoclonal antibody commonly used for GVHD prophylaxis.
- By demonstrating its relative safety and efficacy through this small, modified "phase I/II"-type trial, the authors have opened the potential for alemtuzumab use in the second-line setting.
- Furthermore, given the significant toxicities inherent to corticosteroid use in the post-transplant population, the results shown here offer promise for alemtuzumab as a potential first-line therapeutic option.

See the patient-oriented summary of this study

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