Title of case study: The use of alemtuzumab in stem cell and organ transplantation

1. Summary of the impact

Alemtuzumab, a humanised therapeutic antibody, is a major addition to the repertoire of immunosuppressive agents used for organ and stem cell transplants. Administered as an induction agent in a short course of treatment, alemtuzumab reduces the incidence of graft rejection without preventing recovery of the patient’s ability to fight infection. Alemtuzumab also decreases graft versus host disease, a vital factor in the treatment of aplastic anaemia and acute leukaemias. Furthermore, its important role in minimising immunosuppressive therapy helps prevent treatment-associated problems for the patient. Currently used off-licence for transplants, alemtuzumab improves patient survival and healthcare.

2. Underpinning research

Effective immunosuppression of the host immune system plays a pivotal role in the successful transplantation of organs or stem cells. While a successful transplant requires the patient’s immune system to be suppressed, to minimise both short and long-term graft versus host disease (GVHD), the immune system must still retain its ability to reconstitute itself to fight infection. The humanised anti-CD52 monoclonal antibody alemtuzumab was created in Cambridge University in the 1980s but extensively developed as an immunosuppressant in the period 1994-2007 by Professor Herman Waldmann and colleagues after they moved to Oxford University. Short-term use of alemtuzumab depletes lymphocytes actively involved in causing GVHD and organ rejection, but allows the patient's haematopoietic stem cells to survive enabling immune recovery. Funding from the Medical Research Council and the USA-based companies LeukoSite Inc and ILEX Oncology enabled the production of clinical grade alemtuzumab in Oxford for use in clinical trials.

The efficacy of alemtuzumab in reducing the immune response to donor organs (minimising graft rejection) was demonstrated in a variety of settings, including kidney and liver transplants. In 1999 Professor Waldmann reported that while the use of alemtuzumab was of equivalent benefit to conventional triple therapy (cyclosporine or tacrolimus, azathioprine and prednisolone) in kidney transplants, it had the additional advantage of minimising treatment for the patient1. Later reports confirmed that alemtuzumab was safe and effective, allowing long-term remission, and was beneficial when compared to conventional triple therapy2. Its use during the induction period prior to transplant permitted low levels of cyclosporine A to be used for maintenance therapy, reducing treatment-associated adverse side effects.

The value of alemtuzumab was also highlighted in allogeneic stem cell transplants in diseases such as Hodgkin’s lymphoma and myeloma3. Its use minimised the administration of toxic immunosuppressive drugs during the pre-transplant conditioning treatment whilst still resulting in durable long-term remission. The immunosuppressive activity did not significantly affect the transplanted stem cells responsible for repopulating, or engraftment of the immune system4. Yet another important aspect of alemtuzumab concerned its effectiveness at depleting lymphocytes through ‘in the bag’ techniques. The removal ex vivo of T cells using this technique outside the patient has been shown to be a simple and reliable method for the prevention of GVHD5.

In 1995, Oxford University established a User Group consisting of bone marrow transplant centres from the UK, Europe, Israel, Australia and South Africa. This informal group met annually until 2007 and provided data from more than 4,264 patients to be pooled to develop effective treatment protocols6. Oxford also maintained the group databases, performing and reporting the beneficial and adverse effects of alemtuzumab.
3. References to the research


Funding for research: Funding of approximately £6.3M until 2007 was awarded in grants from the Medical Research Council, and the USA-based companies LeukoSite Inc. and ILEX.

4. Details of the impact

The number of organ and stem cell transplants taking place is increasing year by year. In 2010, in the USA alone, 16,898 kidney and 6,291 liver transplants were performed while in excess of 50,000 stem cell transplants are performed annually worldwide. Although more than 90% of renal transplants survive for one year, this figure drops to less than 50% after 10 years, thus emphasising the urgency for the availability of improved therapies for supporting transplant patients.
The increasing use of alemtuzumab (now manufactured by Genzyme), used off-label, continues to represent a major advance forward in the field of tissue transplantation. Used increasingly in the induction period, it is considered to be ‘the most potent currently used lymphoid depleting antibody’⁹.

The Users’ Group meetings, organised by the University of Oxford and clinical teams involved in transplantation, have provided invaluable information that continues (i.e. post-2008) to be critical for the effective use of alemtuzumab. The establishment of this resource for clinicians, and the efficacy of the antibody, have resulted in alemtuzumab being recognised as an important therapeutic antibody not only for allogeneic organ transplants including kidney¹⁰, heart¹¹ and intestinal transplants¹², but also in stem cell transplants in diseases such as lymphoma¹³, acute leukaemia¹⁴ and aplastic anaemia¹⁵.

The use of alemtuzumab continues to have major impacts in the following areas:

- Improvements in the conditioning treatments used before stem cell transplants or as part of the induction period prior to organ transplantation. The use of alemtuzumab reduces the intensity of these regimes, with faster recovery of the immune system’s ability to fight infection, and fewer adverse health problems, such as cancer, diabetes or bone disease.
- The promotion of improved survival of patients following transplantation due to reduced acute and chronic GVHD, and fewer deaths arising from infection.

The outcome of alemtuzumab use is a reduction in treatment-associated toxicity for the patient. Combined with its selective immunosuppressive properties, this has resulted in patients requiring less hospitalisation, and has increased access to cost-effective treatment.

Current treatment costs of the recognised off-licence use of alemtuzumab (brand name Campath, MabCampath, Campath-1H or Lemtrada) currently manufactured by Sanofi-Aventis/Genzyme are greatly reduced compared to many other transplant therapeutic regimens currently in use. For example, when used as an induction agent in kidney transplants, the cost of alemtuzumab is approximately £264 compared to £1684 - £3100 for other therapeutic monoclonal antibodies¹⁶.

5. Sources to corroborate the impact


The inclusion of alemtuzumab in heart transplants results in increased freedom from graft rejection despite reduced therapy (including the use of steroids).


Paper reporting that the use of alemtuzumab in visceral transplantation permitted improved graft success with 91% and 75% patients surviving after 1 and 5 years, respectively.


Paper describing the use of alemtuzumab in conditioning treatment prior to stem cell transplantation in follicular lymphoma.


Paper describing the use of alemtuzumab in myeloid leukaemia and its efficacy in reducing GVHD.


Paper describing the value of (intravenous/subcutaneous) alemtuzumab in 50 patients with aplastic anaemia in reducing GVHD.


Analysis of kidney transplants in 1233 patients in 10 trials.