13. Post-transplant Lymphoproliferative Disorder

- AST Infectious Diseases Community of Practice summary of recommendations and supporting data that guide the prevention, diagnosis and treatment of PTLD in the solid organ transplant recipient. Relevant aspects of non-PTLD EBV syndromes are also addressed.

- Retrospective review of 11 transplant recipients (4 kidney, 1 heart, 1 kidney-pancreas, 4 single-lung, and 1 bilateral lung) at two U.S. centers diagnosed with PTLD treated with rituximab. Immunosuppressive therapy was reduced in dose or discontinued in all patients at the discretion of the managing physician. Three patients received a course of acyclovir.
- The overall response rate was 64% (6 complete remission, 1 partial remission, 2 progressive disease, and 2 deaths) and 55% complete remission rate.

- Phase 2 study conducted at 15 French and 4 Belgian centers between May 2000 and December 2001. Forty-six patients with untreated B-PTLD that were not responding to tapering of immunosuppression were included and 43 patients (18 kidney, 11 heart, 7 liver, 4 lung, and 3 heart-lung) were analyzed.
- Treatment consisted of 4 weekly injections of rituximab at 375 mg/m². Immunosuppressive drugs were stopped if possible, or dosage reduced by at least 50% and/or the number of drugs reduced to no more than two. At day 80, 37 (86%) patients were alive and the response rate was 44.2%, including 12 complete response. The overall survival rate at 1 year was 67%.

- Comprehensive review of hematologic cancers, including PTLD, following solid organ transplant.

- Comprehensive review of PTLD following solid organ transplant and hematopoietic stem cell transplant with a focus on management. Provides overview of ongoing clinical trials of novel agents.

- A comprehensive review of PTLD in adult transplant recipients, including solid organ transplant and bone marrow transplant.
- Retrospective review of SOT patients diagnosed with PTLD at a single U.S. center between December 1970 and May 2003. Early PTLD was defined as PTLD that occurs within 1 year post-transplant. The authors concluded that patients with early PTLD were likely to be EBV+, CD20+, and more commonly involved the grafted organ.

- A report of a single U.S. center’s utilization for rituximab in PTLD as salvage therapy on long-term outcomes. The authors found poor response rates and survival rates compared to other studies. The patients in the analysis had a high tumor burden and did not receive surgical interventions prior to rituximab.

- The Organ Procurement and Transplant Network/United Network for Organ Sharing database was reviewed for individuals who developed PTLD and underwent retransplant from 1987 through 2004.

- A multi-center, prospective study investigated the use if rituximab in 17 patients with PTLD (5 heart, 4 kidney, 4 lung, and 4 liver) between 1999 and 2002. Patients were treated with four weekly doses of 375 mg/m² of rituximab. Immunosuppressive therapy was reduced in all patients prior to their entry into the study protocol. Complete remission was achieved in 9 patients (52.9%) with a mean duration of 17.8 months; interestingly, these 9 PTLD cases were EBV-associated. The mean overall survival period was 37.0 months with 11 patients still living at the time of publication.

- A retrospective study evaluating the impact of rituximab on PTLD response and survival in a single center cohort. PTLD cases between 1984 and 2009, including heart, kidney, liver, and lung transplant recipients were included (n=24). Chemotherapy regimen was up to physician’s choice along with reduction in immune suppression. Nearly 50% of patients were switched to sirolimus for immunosuppression after PTLD diagnosis but the authors did not find this change to impact response to treatment or survival within the study time period. The median time to diagnosis in this series was beyond 5 years after transplantation.
• Overall response rate (ORR) was 62% (66% rituximab vs. 50% non-rituximab; p = 0.5). R-CHOP-like regimens were used most frequently (72% of patients treated with rituximab). Median overall survival was 64 months (CI 95% 31-96). OS was significantly increased in patients treated with rituximab (p = 0.01; CI 95% rituximab 58-79 months; non-rituximab 1-30 months).


• Retrospective review of solid organ recipients diagnosed with PTLD between August 1988 and June 2008 at a single U.S. center. Of 162 adult patients diagnosed, 148 were evaluated. Patients were treated with either reduced immunosuppression (RI) alone (n=67), surgical excision followed by RI (n=30), or other first line therapies with or without RI (n=51).
• The study demonstrated a 45% response rate from RI alone, with the majority being complete response. There was a 32% acute rejection rate with RI-containing regimens with some requiring a second transplant. Of note, monomorphic PTLD was diagnosed in 63% patients treated with RI alone vs. 39% patients treated with other first-line therapies, implying a selection of patients with monomorphic PTLD for treatment with RI alone (p=0.011). The study also identified the following risk factors for poor response: bulky disease, advanced stage, and older age.


• PTLD guidelines from a joint working group established by the Haematology subgroup of the British Committee for Standards in Haematology (BCSH) and the British Transplantation Society (BTS). This review details the therapeutic options recommended including reduction in immunosuppression, transplant organ resection, radiotherapy and chemotherapy.


• A retrospective review of 8 kidney transplant recipients who developed PTLD and subsequently underwent retransplantation from 1963 to December 2012 at a single U.S. center. After a median follow-up of 62.5 months (range 2-125 months) allograft survival was 87.5% (7 functioning grafts, 1 failed graft from chronic rejection), with no recurrence of PTLD. Three patients died from causes other than PTLD.


• A comprehensive review of PTLD in pediatric intestinal transplant recipients in regard to pathology, presentation, and management. Also provides a summary of cases reviewed from the literature.

A multi-center, prospective, phase II study of 16 patients with biopsy-proven PTLD after any organ allograft (excluding lung) transplantation. A sequential approach was used in this study, starting with reduction in immunosuppression, escalating to interferon alpha2b, and finally to chemotherapy. The response rate to reduced immunosuppression was 0/16 complete remission and 1/16 (6%) partial remission. Six of the 16 patients (38%) had documented rejection during the period of reduced immunosuppression. 13 patients underwent treatment with IFN alpha with 2/13 (15%) complete remission and 2/13 (15%) partial remission. Lastly, 7 patients proceeded to ProMACE-CytaBOM chemotherapy with 67% complete remission.


Prospective, multicenter, open-label, phase II trial evaluating 152 CD20+ PTLD patients who failed reduced immunosuppression. All patients received rituximab whereby on day 50, if patients were complete responders would continue rituximab monotherapy. All others would receive R-CHOP. The study concluded that treatment stratification into rituximab or R-CHOP consolidation on the basis of response to rituximab induction is safe and effective.


International multicenter open-label phase 2 trial, treatment-naive adult solid-organ transplant recipients diagnosed with CD20-positive PTLD who had failed to respond to upfront immunosuppression reduction received four courses of rituximab (375 mg/m² IV) once a week followed by 4 weeks without treatment and four cycles of CHOP every 3 weeks. In case of disease progression during rituximab monotherapy, CHOP was started immediately.

The primary endpoint was treatment efficacy measured as response rates in all patients who completed treatment with rituximab and CHOP, per protocol, and response duration, in all patients who completed all planned therapy and responded. Secondary endpoints were frequency of infections, treatment-related mortality, and overall survival.


Retrospective review of 42 adult patients treated with either reduced immunosuppression (RI) with or without surgical resection of all known disease. 63% (19/30) responded to RI alone with multivariate analysis indicating elevated LDH, organ dysfunction, and multi-organ involvement as risk factors for poor responders of RI. At the median follow-up of 147 weeks, 55% of patients were alive with 50% in complete remission.