**Clinical Area:** Oncology; Allogenic bone marrow transplant for low-grade Lymphoma (LGL) and chronic lymphocytic leukemia (CLL).

**Keywords:** Low-grade lymphoma, chronic lymphocytic leukemia, allogenic bone marrow transplantation (BMT).

**Reference:** Toze CL, Shepherd JD, et al. Allogenic bone marrow transplantation for low-grade lymphoma and chronic lymphocytic leukemia. *Bone Marrow Transplantation* 2000; 25: 605-612

**Study Type:** Case Series.

**Study Aim:** Report the results for 26 patients with LGL or CLL receiving allogenic bone marrow transplant at Vancouver General Hospital since 1985.

**Outcomes**

- *Primary:* Overall survival and event-free survival, the endpoint events were death relapse, or a second BMT.
- *Secondary:* Acute and chronic graft-versus host disease (GVHD).

**Design**

- *Number of subjects:* N=26 (n=18 with LGL and n=8 with CLL)
- *Method of subject selection (inclusion/exclusion criteria):* Age $\leq$50-55 years (related donor), and $\leq$45-50 years (unrelated donor), with refractory or recurrent disease, Karnofsky performance score (KPS) $\geq$80%, adequate pre-transplant organ function, with ejection fraction $\geq$ 40%, forced expiratory volume in 1second $\geq$60%, aspartate transaminase $\leq$4 times upper normal with no evidence of cirrhosis or active hepatitis.
- *Consecutive patients?* Not discussed.
- *Description of study population:* The age ranged from 20 to 53 years, with a median of 42 years. 50% of the patients were men and 50% were women. The interval from diagnosis to the BMT ranged from 4.4 to 154 months with a median of 22 months. 20 patients (77%) had stage IV disease and 22 (85%) had never achieved a remission. The median number of prior treatment was 3.
- *Exposure/Intervention:* All patients had a thorough work-up including tissue biopsy for histological staging, bone marrow aspirate and biopsy, scans, ECG, x-rays, biochemistry, ventriculograms, pulmonary function tests, and others. 23 (88%) of the patients then underwent total body irradiation, and 3 (12%) were given busulphan as conditioning regimens before the transplant. In 19 (73%) patients, the donor marrow source was an HLA matching sibling, in 6 (23%) patients the donor was unrelated, and in one patient, it was syngeneic. 25 (96%) of the patients then received GVHD prophylaxis. This was not given to the patient with a syngeneic donor.
- *Source of outcome data (e.g. patient self-report, doctor report, lab results):* Clinical and lab evaluation. Regimen-related toxicity was evaluated in 8 organ systems according to Bearman criteria. Acute GVHD was staged and graded according to the Seattle and Minnesota systems, and chronic GHVD with the Glucksberg criteria.
- *Length of follow-up:* 0.1-6 years with a median of 2.4 years.
- *Completeness of follow-up:* Not all patients were followed-up for the same period of time.

**Validity:**

- *Is the study type appropriate for the question(s) being asked?* This is not a study, just a report of the results of BMT done in at Vancouver General Hospital since1985.
- *Were patients similar with respect to baseline characteristics?* Yes.
- *Was the intervention and other aspects of patient care similar for all patients (or for all patients in a defined subgroup)?* Yes.
- *Was the process of observation likely to affect the outcome?* Probably not.
- *Did an objective observer assess outcomes and were outcome measurements consistent?* Not discussed.
- *Was follow-up duration appropriate?* No
- *Was follow-up rate sufficient?* Not discussed.

**Conclusions regarding validity of methods:**
This case series had some advantages like having inclusion criteria, and well-defined outcomes. However, it had a small sample size, and a variable duration of follow-up. Like all case series, there were several internal validity threats including selection bias, non-blinding, and lack of a control or comparison group.

**Results**
Patients: N=26

| | |
|---|---|
| Survival | |
| Alive | 16 (61.5%) |
| Died | 10 (38.5%) |
| Regimen related toxicity | 4 (40%) |
| GVHD + infection | 2 (20%) |
| Progressive multifocal leukoencephalopathy | 1 (10%) |
| Refractory/recurrent disease | 3 (30%) |
| | |
| Remission | |
| Complete | 18 (69%) |
| No remission | 4 (15%) |
| Not evaluable | 2 ( 8%) |
| Too early to evaluate | 1 ( 4%) |
| Questionable | 1 ( 4%) |

**Authors' Conclusions:**
The authors concluded that allogenic bone marrow transplant is feasible and gives durable complete remissions among patients who do not respond to conventional therapies. The authors recommended more studies with longer follow-up.

**Reviewer's Conclusions:**
This case series found a relatively high survival, and complete remission rates among patients, with refractory or recurrent CLL or LGL, after receiving an allogenic bone marrow transplantation. However, due to the study design, it is not possible to determine whether this intervention is more effective than an alternative intervention, or no intervention.