Bibliographic reference	**Tack et al 2011 (REF ID: 65)** **Al-toma et al 2007 (REF ID: 251)** **Note: Tack (2011) study was an extension of the Al-toma (2007) study.**
Study type	Case series
Study quality	Very low quality
Number of patients	Total number of eligible patients = 18
Patient characteristics	**Inclusion criteria** • Patients aged <70 years and diagnosed with RCD type II • Showed no response to one or two courses of cladribine for 5 consecutive days. • A lower percentage of aberrant T cells was allowed in the presence of ulcerative jejunitis. **Exclusion criteria** • Enteropathy-associated T-cell lymphoma (EATL) was excluded (based on the diagnosis according to the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues). • Patients with severe concomitant cardiac, pulmonary, renal or hepatic disease. • Patients with active uncontrolled infection and HIV positivity. **Diagnosis of RCD type II**

<table>
<tr><th>Bibliographic reference</th><td>Tack et al 2011 (REF ID: 65)
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<tr><td></td><td>

The diagnosis of RCD II was based on persisting or recurring symptoms and small intestinal villous atrophy after a former good response despite strict adherence to a gluten-free diet for at least 1 year.
Furthermore, the clinically validated cut-off value of 420% aberrant IEL detected by flow cytometric analysis was used to distinguish RCD type I and type II.

Patient characteristics
Total number of eligible patients = 18
The median time between cladribine treatment and auto-SCT = 6.25 months.

All patients entered the treatment protocol, however 5 patients did not make it to auto- SCT: i) unsuccessful leukapheresis = 2; ii) progression into EATL occurred before stem cells could be collected = 3

Median follow-up time for the 13 auto-SCT patients = 26 years (range: 10 to 67 months)
<table>
<tr><th></th><th>Transplanted (n=13)</th><th>Nottransplanted (n=5)</th></tr>
<tr><td>Gender: Female/Male</td><td>7:6</td><td>3:2</td></tr>
<tr><td>Age at CD diagnosis (years): Median (range)</td><td>50 (37–68)</td><td>63 (45–66)</td></tr>
<tr><td>Age at RCDII diagnosis (years): Median (range)</td><td>58 (42–68)</td><td>64 (47–70)</td></tr>
<tr><td>Age at (intention to) auto-SCT (years): Median (range)</td><td>59 (43–68)</td><td>65 (52–70)</td></tr>
<tr><td>Treatment before auto-SCT:
Cladribine
Azathioprine/Prednisone</td><td>
13
3</td><td>
5
2</td></tr>
<tr><td>Time between cladribine and auto-SCT (months): Median (range)</td><td>6.25 (3–30)</td><td></td></tr>
<tr><td>Follow-up time (months): Median (range)</td><td>26 (10–67)</td><td>5.5 (1–12.5)</td></tr>
</table>
</td></tr>
<tr><th>Intervention</th><td>Autologous hematopoietic stem cell transplant (Auto-SCT)</td></tr>
</table>

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	• Mobilization of hematpoietic progenitor cells from the BM into the peripheral blood was achieved using G-CSF injection daily for at least 4 days without preceding chemotherapy. • The conditioning regimen consisted of fludarabine administered orally for 5 days (40 mg/m2 per day) and intermediate dose melphalan (administered i.v., 2 days, 70 mg/m2 per day) • At day 0 stem cells were reinfused. • All patients received standard antibacterial and antifungal prophylaxis during neutropenia and trimethoprim–sulfamethoxazole gluten free syrup 480–960 mg daily until 6 months after transplantation. • Total parenteral nutrition and blood and platelet transfusions were given if indicated.
Comparison	N/A
Length of follow up	Median in months (range) = 26 (10–67)
Location	Recruitment: between March 2004 and February 2010 Tertiary hospitals: Amsterdam = 15; Italy = 1; Germany = 1; Portugal = 1 (total 18 eligible) (locations for the 13 patients who went through Auto-SCT were not reported)
Outcomes measures and effect size	**Mortality:** Transplant group = 23% (3/13) Nottransplant group = 100% (5/5) [all died within a median follow-up of 5.5 months (range 1–12.5 months)]. (death due to EATL: Transplant group = 1; Nottransplant group = 4) **Overall survival after auto-SCT (unresponsiveness to cladribine therapy):** Transplant group: Overall 3-year survival = 80% Overall 4-year survival = 66% **Complete histological remission (defined as Marsh 0 or I):** Transplant group = 38% (5 of 13)

Bibliographic reference	**Tack et al 2011 (REF ID: 65)** **Al-toma et al 2007 (REF ID: 251)** **Note: Tack (2011) study was an extension of the Al-toma (2007) study.**
	Aberrant intestinal T lymphocytes: Transplant group (median percentage): Before = 45%; After = 54% All transplanted patients reached follow-up of almost 1 year to assess remission status. Within 1 year after auto-SCT, the majority of patients (11 of 13) showed impressive clinical improvement with normalization of stool frequency, disappearance of gastrointestinal symptoms and normal levels of or improvement of ≥1 point in BMI, albumin and/or Hb. **All patients had a WHO performance status of 0 at the end of follow-up:** Before ASCT: 7/13 (54%) After ASCT: 13/13 (100%)
Source of funding	This study was supported by an unrestricted grant from AstraZeneca.
Comments	Very small number of cases, no comparison to other treatment due to the narrow inclusion criteria (RCD type II, unresponsive to cladribine therapy), a proportion of the patients had EATL. Hence, the limited inconclusive evidence cannot be generalised to the overall RCD patients.