

et al. 2003). Re-treatment of Bexxar responders on relapse with a second schedule of Bexxar induced a CR in 22% and a partial response in 34%, with a median of 10.7 months TTP (Kaminski *et al.* 2003). A cautionary note is that an incidence of sMDS of 4.1% per annum has been seen in this small patient group so far. Whether this reflects their 'end of the road' status or a side-effect of Bexxar remains to be seen. A randomised phase III trial is testing CHOP + Bexxar vs. CHOP-R in FL patients, following encouraging results in a phase II SWOG study (Press *et al.* 2003). In June 2003, the US FDA approved Bexxar for the treatment of CD20 positive, rituximab-refractory and chemotherapy-relapsed FL. At the time of writing a European licence has not yet been granted.

Zevalin (^{90}Y Ibritumomab Tiuxetan)

In the pivotal, phase III randomised study of Zevalin vs. rituximab, 143 patients with relapsed or refractory indolent or transformed NHL (79% FL) the primary endpoints of OR and CR rates were significantly in favour of Zevalin (80 and 34% vs. 56 and 16%, p for OR = 0.002 and p for CR = 0.04, respectively) (Witzig *et al.* 2002). Despite follow-up of 29 months, only a trend for longer TTP is seen in the Zevalin arm FL patients due to the study being underpowered for this unplanned analysis (10.6 vs. 10.1 months in all patients and 15.0 vs. 10.2 months in the FL patients only, respectively). Yet production of higher OR and CR rates has to translate into prolonged TTP and ultimately OS if the natural history of the disease is to be altered. More recent data suggest that Zevalin may indeed alter TTP. Thirty seven per cent of the 211 patients with relapsed, refractory or transformed indolent B-cell NHL treated in the 4 studies which led to the US registration of Zevalin in February 2002 have experienced remissions of >12 months, with TTP of 29.3 months (range 12.7 to 75.5+ months) (Witzig *et al.* 2003). Reduced dose Zevalin has proven safe in a phase I study conducted in NHL patients relapsing following an autograft (Vose *et al.* 2003). Furthermore, Zevalin produced OR and CR rates of 74 and 15% in 54 heavily pre-treated FL patients who were rituximab refractory or had relapsed <6 months after responding to rituximab (Witzig *et al.* 2002). The TTP was estimated at 6.8 months.

Use of myeloablative doses of ^{131}I -anti-CD20 (B1; Bexxar) \pm ^{131}I -anti-CD37 (MB-1) has been explored in Seattle, resulting in \approx 85 per cent overall and \approx 75 per cent complete response rates (Press 1999). The estimated progression-free survival at six years was 51 per cent for those with low-grade NHL (Liu *et al.* 1998). The same centre has reported superior efficacy (both 5 year PFS: 48 vs. 29% and OS: 67 vs. 53%, respectively) of high dose Bexxar compared with high-dose chemotherapy \pm TBI in patients with relapsed follicular lymphoma (Gopal *et al.* 2003). However, this study was a retrospective comparison of consecutively treated patients and requires prospective randomised confirmation. The logistics and cost of patient isolation for \approx ten days to protect others from patient radioactivity temper the encouraging results of

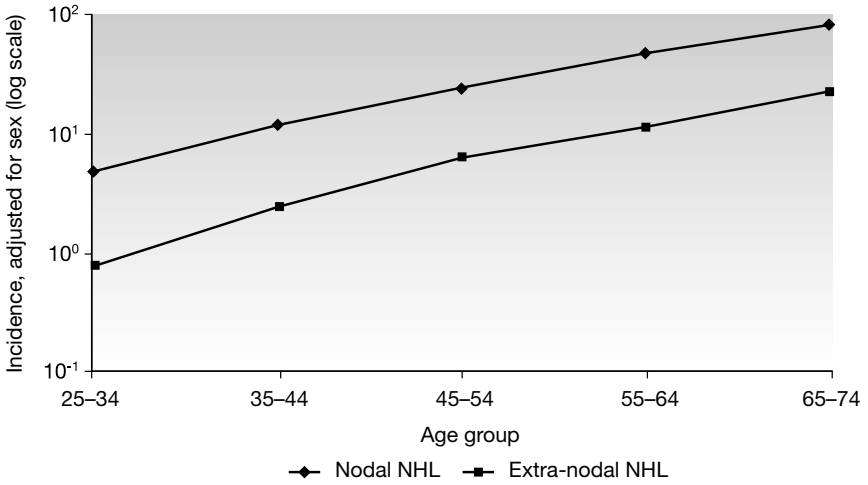


Figure 1.2 Age-specific incidence/100,000 of nodal and extra-nodal non-Hodgkin's lymphomas in the USA.

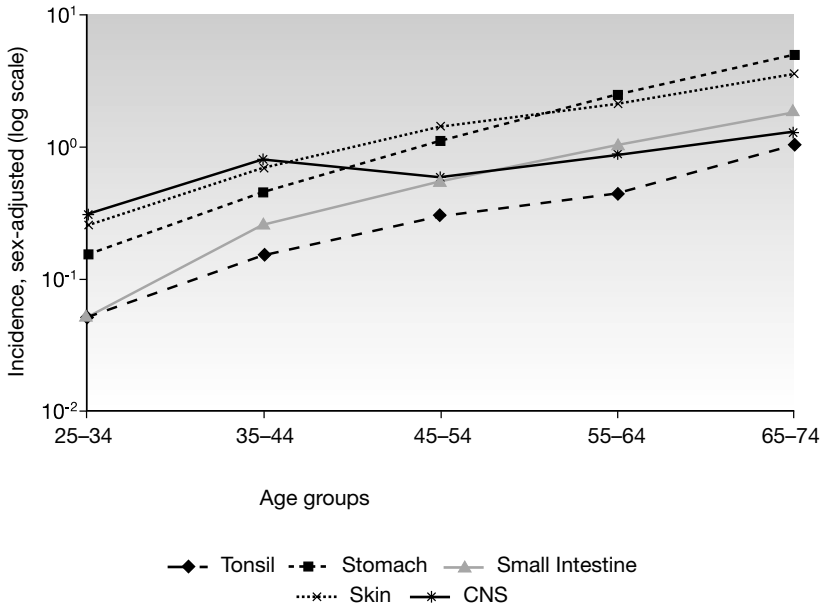


Figure 1.3 Age-specific incidence/100,000 of extra-nodal non-Hodgkin's lymphomas in the USA, by site.

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