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Real World Experience With Brentuximab Vedotin in Relapsed/Refractory CD30 Positive Lymphoma: Outcomes in 33 Patients After Prolonged Follow-up At a Single UK Centre

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Abstract: Brentuximab vedotin (BV), a CD30 targeted antibody drug conjugate, has demonstrated impressive activity in both Hodgkin lymphoma (HL) and anaplastic large cell lymphoma (ALCL) in phase II studies. Real world experience in a number of named patient programmes (NPP) have been reported but few long-term outcomes have been described. Here we describe clinical outcomes for a group of 33 patients (pts) that received BV via a NPP or following conditional licensing by the European Medicines Agency. We update previously reported outcomes for 24 pts (Gibb et al, Haematologica 2013) with more than 3 years additional follow-up and 9 new pts.

Thirty-three pts with CD30+ T-cell lymphoma who were relapsed or refractory after previous chemotherapy or auto-transplant, had a positive PET-CT scan and deemed suitable for systemic therapy were treated. Response was assessed using PET-CT after 4 (PET4) and 8 cycles (PET8). Of the 33 pts included, 18 (55%) were female with median age (range) of 40 years (21-77). Twenty-four pts had HL, 8 ALCL and 1 angio-immunoblastic T-cell lymphoma. The median (range) number of prior systemic therapies was 2 (1-5) of which 15 had prior radiotherapy and 9 had received an autotransplant.

Pts received a median of 5 cycles of BV (range 1-16) at a dose of 1.8mg/kg once every 3 weeks. The overall response rate (ORR) was 61%. By histology the ORR was 63% in both HL (15/24) and ALCL (5/8), and 0% in angio-immunoblastic T-cell lymphoma (AITL) (0/1). Complete response rate was 24% (HL n=4, ALCL n=4); this was higher in the ALCL group (50%, 4/8) than the HL group (17%, 4/24). Overall, the best response was seen at PET4 in all but 1 pt with HL who improved to CR at PET8.

Of the 25 pts who were eligible for allotransplant (allo-T), 8 (32%) proceeded to allo-T without further systemic therapy. Median number of cycles of BV received prior to allo-T was 6 (range 5-8). Responses to BV were either CR (n=5) or PR (n=3), 2 of whom received consolidation radiotherapy. Seven pts were assessed for toxicity and outcomes following allo-T (n=1 lost to follow-up after transferring to another centre). After a median follow-up of 25.3 months (range 2.4 - 59.8) 5 pts are still alive. Acute graft versus host disease (GvHD) was seen in 5 pts (71%); this involved the skin (grade 1-2, n=5), gut (grade 2-3, n=3) or liver (grade 1, n=1). Chronic GvHD was seen in 3 pts (43%). Two pts had overlap syndrome. Six pts experienced bacterial and viral infections that were successfully treated in all but 1 pt. One further pt died following severe GvHD.

Of the pts that did not receive an allo-T, 14 had an inadequate response (PD at PET4 n=3, PD at PET8 n=7, PD or death before PET4 n=3, SD n=1). A further 3 pts declined allo-T, 2 of these had achieved CR and remain alive (1 progression-free) at 23.0 and 56.1 months of follow-up. Four pts proceeded to allo-T after additional systemic therapy.

In pts with relapsed/refractory CD30+ve lymphoma treated with BV outside a clinical trial protocol we have shown that response rates and toxicity are broadly comparable with the published phase II trial data. Best long term outcomes were seen in pts that achieved CR and/or underwent allotransplant with 6 pts in this category (18% of entire cohort) alive and
disease-free up to 5 years later. We conclude that prolonged survival is possible after BV in a proportion of real world pts whose prognosis is conventionally regarded as extremely poor.

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