Results of a phase II study of brentuximab vedotin in the first line treatment of Hodgkin lymphoma patients considered unsuitable for standard chemotherapy (BREVITY)

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were 3-year progression-free survival(PFS), 3-year overall survival(OS), and toxicity. Response was assessed using the revised International Workshop Criteria. Toxicity was graded according to the Common Terminology Criteria for Adverse Events v4.0.

Results: 41 patients were enrolled from Oct 2013 to Aug 2015. 36 patients were evaluable for response. The baseline clinical characteristics were as follows: the median age, 45 years (range: 18-75 years); >60 years, 13.5%; female, 30.6%; ECOG PS >1, 13.9%; stageI/II, 86.1%; elevated LDH, 27.8%. After 2 cycles of GAD-M, ORR in all and stageI/II were 94.4% (34/36) and 100% (31/31), respectively. CR rate were 50% (18/36) and 54.8% (17/31), respectively. After 6 cycles ORR in all and stageI/II were still 94.4% (34/36) and 100%(31/36), respectively. CR rate increased to 83.3% (30/36) and 90.32% (28/31), respectively. At median follow-up of 23.3 months, 3-year PFS was 72.1%(Figure 1A), 3-year OS was 76.3% (Figure 1B). According to the stage, 3-year PFS for stage I/II and III/IV were 77.3% and 40.0%, respectively. 3-year OS were 79.3% and 60.0%, respectively. The most common hematologic adverse event of grade 3/4 was anemia (52.8%). The major non hematologic side effects were hypoalbuminemia (100%), increased transaminases (88.9%) and hyperbilirubinaemia (52.8%). Although grade 1/2 nonhematologic toxicities were frequent during GAD-M treatment. Grade 3/4 toxicities were few. One patients died of treatment related toxicity, who was 61-year-old man died of electrolyte disorders caused by severe vomiting. Other patients didn't suffer from this adverse event.

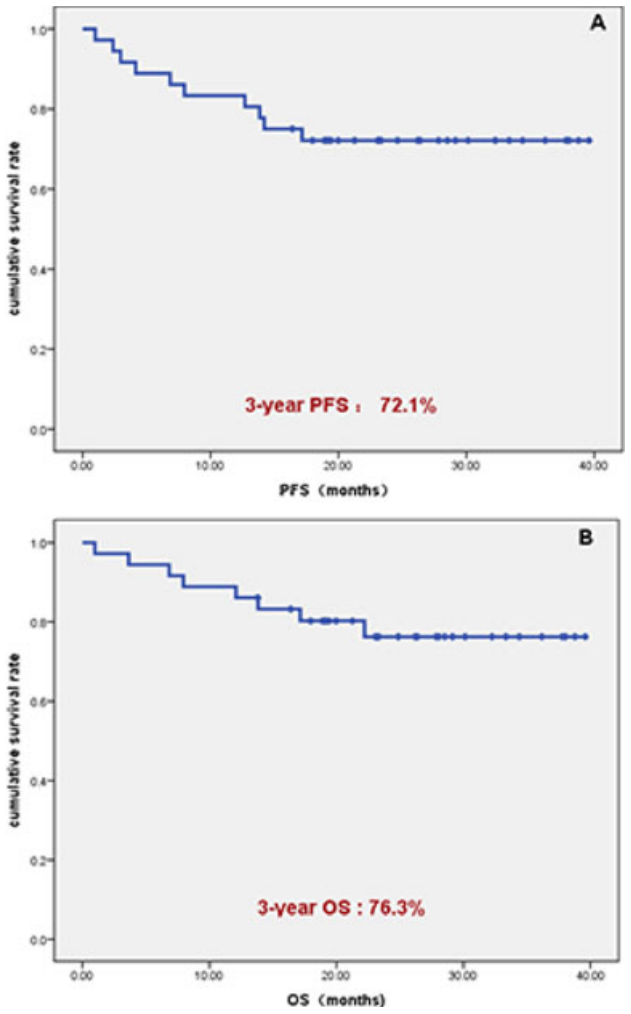

Figure 1: The survival curves of PFS and OS.

Conclusions: These results demonstrate that GAD-M regimen provides a high ORR in newly diagnosed ENKTL, especially for stageI/II. GAD-M with EIFRT for ENKTL in stageI/II was feasible, although most patients experienced recoverable liver dysfunction and anemia during the protocol treatment.

Keywords: gemcitabine; L-asparaginase; methotrexate (MTX).

"FOCUS ON…" SESSION: TARGETING CD30 IN HODGKIN LYMPHOMA

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RESULTS OF A PHASE II STUDY OF BRENTUXIMAB VEDOTIN IN THE FIRST LINE TREATMENT OF HODGKIN LYMPHOMA PATIENTS CONSIDERED UNSUITABLE FOR STANDARD CHEMOTHERAPY (BREVITY)

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Introduction: Standard treatment for Hodgkin lymphoma (HL) is poorly tolerated in older patients and results are disappointing. Brentuximab vedotin (BV) is a CD30 targeted antibody-drug conjugate licenced for the treatment of relapsed or refractory HL on the basis of excellent safety and efficacy demonstrated in the pivotal phase 2 clinical trial. BREVITY trial was designed to evaluate the efficacy and tolerability of BV monotherapy in previously untreated patients (pts) with HL unfit for standard treatment due to age, frailty or co-morbidity.

Methods: This response adaptive phase II, Simon 2-stage, single arm study required 30 evaluable pts. Primary outcome was complete metabolic response (CMR, Deauville Score 1-3) by centrally reviewed PET-CT after 4 cycles of BV. Secondary outcomes included PFS, OS, toxicity and comorbidity assessment (CIRS-G). Inclusion criteria were

TABLE 1

Patient Characteristic	n=38 Median (Range)
Age	76 (59, 90)
CIRS-G Score No. categories endorsed Severity Total score	3 (0, 7)1.5 (0, 3)6 (0, 11)
	n (%)
GenderMale Female	22 (57.9)16 (42.1)
StageStage 2 Stage 3 Stage 4	7 (18.4)13 (34.2)18 (47.4)
B symptoms	27 (71.1)
Bulky Disease	5 (13.2)
Extranodal disease	22 (57.9)
ECOG Performance Status0 1 2 34	3 (7.9)16 (42.1)11 (28.9)7 (18.4)1 (2.6)

previously untreated HL stage 2 (with B symptoms and/or mediastinal bulk) to stage 4 with cardio-respiratory compromise (at any age), or ECOG PS ≤3 and considered unfit for standard chemotherapy (in pts ≥60 yrs). BV dose was 1.8 mg/kg every 3 weeks, reduced to 1.2 mg/kg for toxicity. Pts responding after 4 doses of BV continued to a maximum of 16 cycles if CT/PET-CT every 4 cycles confirmed ongoing response. Pts also underwent exploratory blinded PET-CT after cycle 2.

Results: 38 pts were recruited from Feb 2014-Oct 2015 at 12 UK centres; demographics are shown in Table 1. 35 treated pts were evaluable for toxicity, 31 were evaluable for response. A median of 4 cycles was given (range 1-16). Dose was reduced in 28 cycles across 14 pts due to toxicity and 11 pts stopped treatment due to adverse events (AEs). 716 AEs were reported, 626 (88%) were grade 1/2. 27 (77%) pts had at least one AE ≥ grade 3, most commonly infection, myelosuppression or neuropathy. CMR at PET4 was 26% (95% CI 14, 43) and overall objective response was 84% (95%CI: 67, 93). There was a significant correlation of interim PET2 with PET4 (Rho = 0.67, $p < 0.001$) with a CMR rate at PET 2 of 32% (95% CI 17, 52). To date 28 of 31 evaluable pts have progressed and median PFS is 7.4 months (95% CI 5.3, 10.2).

Conclusions: In this study BV monotherapy produced a high overall response rate although the CMR rate after 4 cycles did not meet the pre-specified 40% level, and PFS was short. Toxicity was greater than in the pivotal study in a younger/fitter population and led to treatment termination in some pts. A follow-on study aims to improve CMR and PFS by using a lower dose of BV in combination with other agents.

Keywords: brentuximab vedotin; elderly; Hodgkin lymphoma (HL).

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BRENTUXIMAB VEDOTIN CONSOLIDATION TO REDUCE RADIATION USE IN PATIENTS WITH LIMITED STAGE NON-BULKY HODGKIN LYMPHOMA: AN UPDATE FROM a PHASE 2 CLINICAL TRIAL

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Background: HL is one of the most common cancer types in young adults. Although approximately 90% of limited stage HL patients are projected to be cured with standard chemotherapy with or without radiation, many do not live their expected life span due to delayed treatment–related complications that include secondary malignancies and cardiovascular disease. Given the risks associated with current therapies for HL, novel treatment strategies are urgently needed to reduce the use of radiation as well as conventional chemotherapy drugs while improving upon current standard of care outcomes.

Methods: In this phase 2 multicenter study, patients with previously untreated limited stage HL received ABVD induction followed by BV consolidatoin **(NCT01578967)**. The primary objective was to estimate the proportion of patients who achieve PET-negative disease after ABVD followed by BV. The goal was to achieve negative PET and avoid radiation in >85% of patients. Patients received 2 to 6 cycles of ABVD based on their baseline risk factors and the interim PET scan result. Approximately 6 weeks after induction, 1.8 mg/kg of BV was given every 3 weeks for 6 cycles.

Results: Forty one patients were enrolled from April 2012 through December 2015. Out of 40 evaluable patients, the median age was 29 years (range 19 – 68), and 45% presented with unfavorable disease. Thirty seven out of 40 patients (92.5%) received ≤4 cycles of ABVD (27.5% received 2 cycles) prior to BV consolidation. One patient received radiation due to disease progression. BV-related grade ≥ 3 toxicities included neutropenia (7.5%), peripheral neuropathy (2.5%) and rash (2.5%). There was one death due to sepsis and hepatic failure, a very rare but known complication of BV, and all reported ≥ grade 4 toxicities were associated with this event. After 2 cycles of ABVD, 72.5% of patients achieved PET-negative disease (Deauville score < 3), and 37 out 39 evaluable patients (94.9%, CI: 88 – 100%) were PET-negative after the completion of BV. The estimated 2-year progression free (PFS) and overall survival rates were 92% and 97%, respectively, with a median follow up of 22 months. All 37 patients who achieved

TABLE 1 PET results in HL patients who received ABVD followed by BV Consolidation

	Interim-PET2 (n = 40)	Post BV (n = 39)
Deauville 1	13	18
Deauville 2	16	19
Deauville 3	8	1
Deauville ≥ 4	3	1

HL, Hodgkin lymphoma; PET, positron emission tomography; HL, Hodgkin lymphoma; ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; BV, brentuximab vedotin; Interim-PET-2, PET scan after 2 cycles of ABVD; Post BV, PET scan after 6 cycles of BV