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Addition of bendamustine to Brentuximab vedotin leads to improved complete metabolic remission rates in children, adolescents and young adults with relapsed and refractory classical Hodgkin lymphoma: a retrospective, single centre series

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INTRODUCTION

- The majority of children and young adults with classical Hodgkin lymphoma (cHL) are cured with first line treatment. Treatment failure rates with paediatric regimens are ~10% in early stage, and 15 to 20% in advanced stage[1]
- Cure may be achieved in relapsed or refractory (R/R) cHL with salvage therapy, when achieving complete metabolic remission (CMR) on FDG-PET CT is highly predictive for continuing progression free survival (PFS)[2]
- Brentuximab vedotin (Bv) used as monotherapy in children and young people with R/R cHL achieved a 33% CMR rate[3]
- Bendamustine used as monotherapy in adults achieved a CMR rate of 33%[4]
- A number of studies in adults have reported superior outcomes with the combination of Bv plus bendamustine, with a CMR rate of 76% in a phase 1/2 study[5]
- Less data exists about use in the paediatric, teenage and young adult population
- The combination of bendamustine and Bv (Bv+B) received approval at UCLH's Institutional Use of Medicine Committee, subject to regular audit of response and toxicity

AIM OF THE AUDIT

- To examine response, outcome and toxicity data for 29 children and young people aged under 30 years, treated consecutively with Bv+B at UCLH, as second line or greater salvage for R/R cHL
- Patients were treated between May 2015 and December 2019

PATIENT CHARACTERISTICS

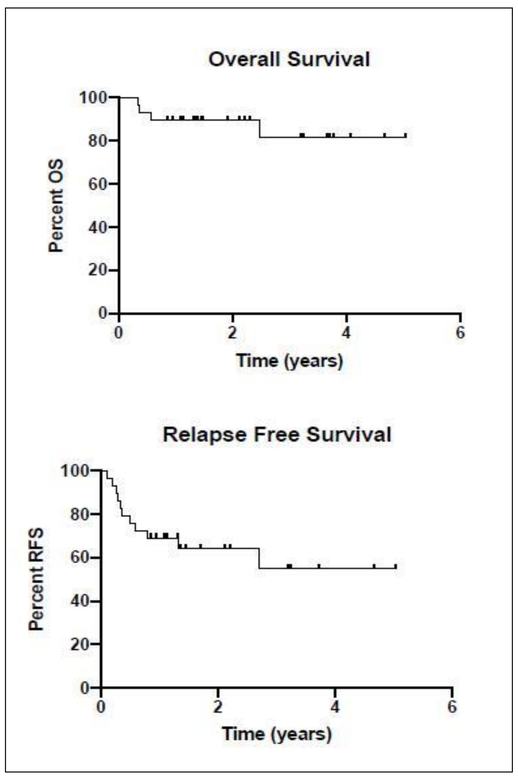
	Patients n (%) Total = 29
Age at start of Bv+B therapy, years: **Median (range)**	***21 (9-28)***
Male **Female**	***17 (59)*** ***12 (41)***
Response to primary therapy: **Early relapse** **Late relapse** **Primary refractory**	 ***2 (7)*** ***7 (24)*** ***20 (69)***
Number of prior treatment lines: **Median (range)** **2** **3** **4**	 ***2 (24)*** ***23 (79)*** ***4 (14)*** ***2 (7)***
Previous treatment: **Bv monotherapy** **Prior radiotherapy** **Prior ASCT**	 ***3 (10)*** ***5 (17)*** ***4 (14)***

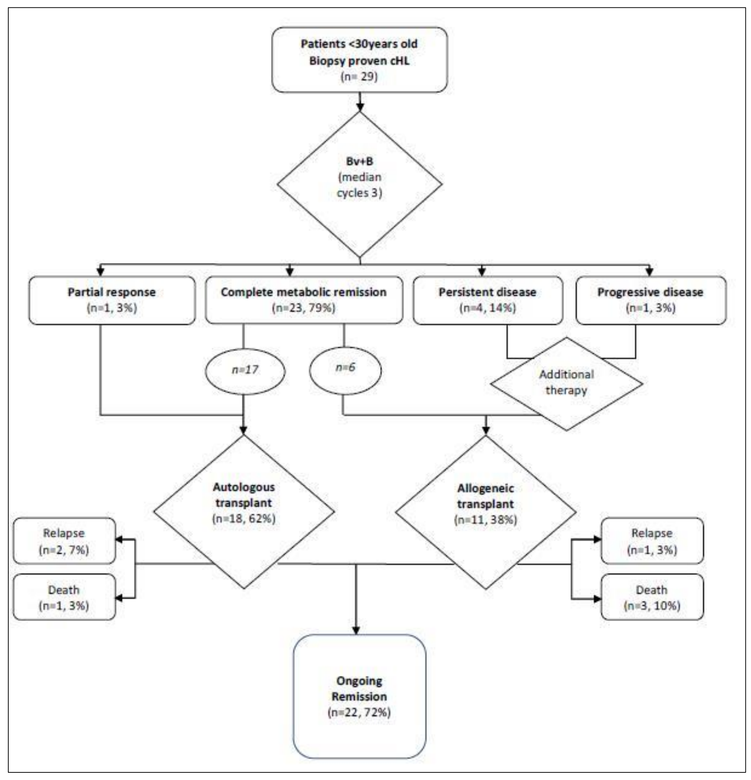
TREATMENT

- Patients received 90mg/m2 bendamustine on days 1 and 2, and 1.8mg Bv on day 2 of a 21 day cycle
- Median number of cycles was 3 (1-6)
- Response was assessed by PET CT after 2/3 cycles with CMR defined as Deauville 1, 2 or 3

OUTCOMES

- Overall response rate 83% (24/29)
- Complete metabolic remission 79% (23/29)
- At median follow up of 20 months:
  - Median PFS and overall survival (OS) not reached
  - Estimated PFS at 24 months = 64%; estimated OS at 24 months = 90%





TOXCITY DATA

- 66% (19/29) experienced grade 3 or 4 (G3/4) toxicity (per CTC criteria) including:
  - Cytopenias: neutropenia (31%), anaemia (7%) and thrombocytopenia (3%)
  - Nausea: G3/4 in one patient, of any grade in 38% of patients
- Neuropathy occurred in 10% (3/29); in all cases was G1
- Infusion reactions (IRRs) affected 52% (15/29) : G1/2 in 34% (10/29) and G3/4 in 17% (5/29):
  - Occurred mainly on day 1 of cycle 2, during or after the bendamustine infusion
  - UCLH premedication regimen was amended to 100mg IV methylprednisolone + 10mg IV chlorphenamine on day 1 and day 2, with overnight admission for observation on day 1 cycle 2 (previously IV steroid on day 2 only, prior to Bv)
  - Since premedication amendment, 11 patients treated:
    - 5 (45%) experienced IRRs but of maximum G2
    - A further patient, not included in this series as Bv+B treatment is ongoing, experienced G3 reaction with fever, hypotension and rash

CONCLUSIONS

- This series indicates that combination Bv+B is a highly active salvage regimen for children and young adults with R/R cHL, achieving an ORR of 83%, and CMR in 79% of patients
- IRRs are an important toxicity, especially on day 1 of cycle 2. An amended pre-medication protocol has reduced severity and frequency of IRRs, although severe reactions can still occur
- Although this data is retrospective and non-randomised, the CMR rates are higher than those reported with either drug used as single agent providing a bridge to SCT with the majority of patients achieving a pre-transplant CMR

REFERENCES

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