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‘ACOPP’ chemotherapy for frontline treatment of older patients with Hodgkin lymphoma - a pilot study

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THE beatson WEST OF SCOTLAND CANCER CENTRE

NHS The Newcastle upon Tyne Hospitals NHS Foundation Trust

INTRODUCTION

Approximately 20% of patients with Hodgkin lymphoma (HL) are aged 60 years or older. There is no standard of care for such patients, who have a markedly inferior prognosis compared with younger counterparts and are underrepresented in clinical trials. BEACOPP chemotherapy has been demonstrated to be highly effective in frontline HL management, but when used in older patients (even at non-escalated doses) there is an unacceptable rate of toxicity-related death. We proposed that a modification of the BEACOPP regime by removing bleomycin and etoposide and dose reduction of cyclophosphamide (‘ACOPP’) would potentially be a well-tolerated and effective regimen for older HL patients.

AIM

This pilot study investigated the feasibility of ACOPP chemotherapy for frontline management of older patients with HL who were deemed unfit for more intensive management approaches (e.g. ABVD).

METHOD

Fifteen patients with histologically confirmed Hodgkin lymphoma (Beatson West of Scotland Cancer centre n=12, Newcastle n=3) were treated between March 2018-January 2020. *Table 1* describes the ‘ACOPP’ dosing regime, with comparison to other regimens used in HL.

Table 1 – Breakdown of chemotherapy drugs and doses included in ACOPP with comparison to other HL regimens

ABVD (28 days)	escBEACOPP (21 days)	ACOPP (21 days)	ChlVPP (28 days)	VEPEMB (28 days)
Doxorubicin 25mg/m2 D1/15	Doxorubicin 35mg/m2 D1	Doxorubicin 35mg/m2 D1		Mitoxantrone 6mg/m2 D15
	Cyclophosphamide 1250mg/m2 D1	Cyclophosphamide 650mg/m2 D1	Chlorambucil 6mg/m2 D1-14	Cyclophosphamide 500mg/m2 D1
	Etoposide (IV) 200mg/m2 D1-3			Etoposide (oral) 60mg/m2 D15-19
Dacarbazine 375mg/m2 D1/15	Procarbazine 100mg/m2 D1-7	Procarbazine 100mg/m2 D1-7	Procarbazine 100mg/m2 D1-14	Procarbazine 100mg/m2 D1-5
	Prednisolone 40mg/m2 D1-14	Prednisolone 40mg/m2 D1-14	Prednisolone 40mg/m2 D1-14	Prednisolone 30mg/m2 D1-5
Bleomycin 10,000 units/m2 D1/D15	Bleomycin 10,000 units/m2 D8			Bleomycin 10,000 units/m2 D15
Vinblastine 6mg/m2 D1/D15	Vincristine 1.4mg/m2 D8	Vincristine 1.4mg/m2 D8	Vinblastine 6mg/m2 D1/D8	Vinblastine 6mg/m2 D1
	G-CSF D9-recovery	G-CSF D9-13		

Interim imaging after two cycles was mandated – either with PET-CT (preferred) or standard CT if PET unavailable. Details of toxicity, hospital admissions and outcome were prospectively recorded.

RESULTS

Baseline characteristics:
The median age of the 15 patients was 76 (range 58-92), 9/15 (60%) were male and 13/15 (87%) had advanced stage disease. The median IPS of patients with advanced disease was 3. The median ECOG performance status of all patients was 1, with CIRS-G comorbidity score ranging from 5-13 (median 9, lymphoma diagnosis excluded).

Deliverability:

Table 1 – Details of number of cycles received, dose delays and reductions and hospital admissions during therapy

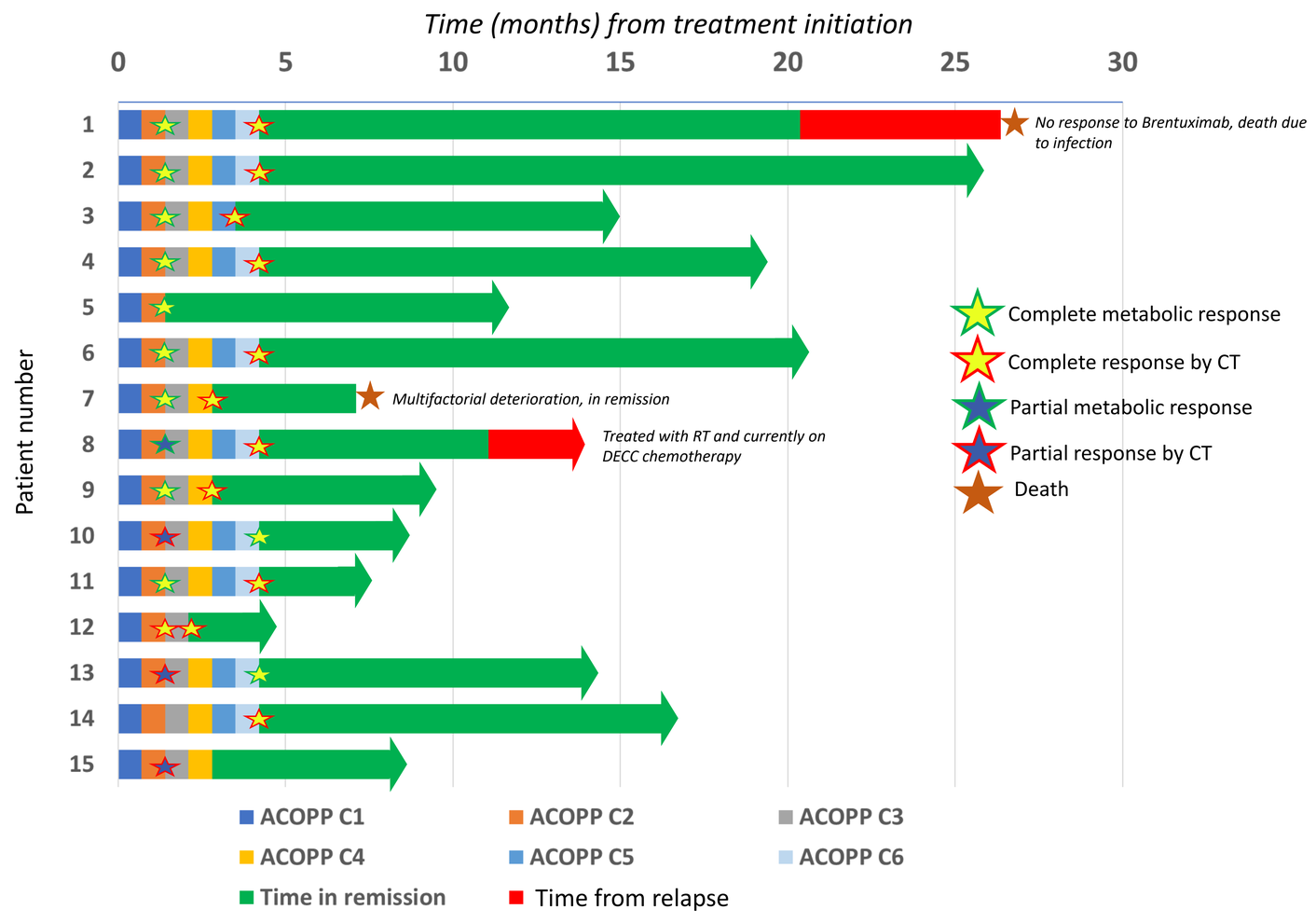
	No. patients (% of total n=15)
Received 6 cycles	9 (60%)
Reasons for <6 cycles	*1.Frailty, new diagnosis PD* *2.Frailty, struggling with tabs* *3.Frailty, postural hypotension* *4.Recurrent LRTI, COVID pandemic* *5.Early stage* *6. Pain/immobility from vertebral fractures*
≥1 delay ≥7 days	9 (60%)
2 delays ≥7 days	1 (7%)
Dose reductions	3 (20%) *1. Vincristine C3 – CVA/postural hypotension* *2. Vincristine C6 – vocal cord palsy* *3. Vincristine C3 – peripheral neuropathy*
Hospital admissions (any):	11 (73%)
1	3
2	6
3	1
4	0
5	1

Table 2 – Toxicity details and grading

Toxicity	No. patients (% of n=15)
Neutropenia:	9 (60%)
Grade 1	1
Grade 2	0
Grade ≥3	8
Febrile neutropenia	3 (20%)
Thrombocytopenia:	8 (53%)
Grade 1	4
Grade 2	0
Grade ≥3	4
Anaemia:	13 (87%)
Grade 1	3
Grade 2	2
Grade ≥3	8
Neuropathy:	8 (53%)
Grade 1	4
Grade 2	4
Grade ≥3	0

Responses:

Figure 3 – Response timeline for all 15 patients at data cut-off 1st October 2020, median follow up for all patients = 13 months



CONCLUSIONS

- **‘ACOPP’ can be safely delivered to older patients with co-morbidity in the outpatient setting (median age 76, median CIRS-G 9 in this series).**
- **Toxicity was mainly haematological but manageable:**
  - **20% experiencing febrile neutropenia, no platelet transfusions**
- **High response rates are encouraging in this small series with 12/15 patients (80%) alive and in first remission at median follow up of 13 months.**