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THE ADDITION OF RITUXIMAB TO CODOX-M/IVAC CHEMOTHERAPY IN THE TREATMENT OF HIV-ASSOCIATED BURKITT LYMPHOMA IS SAFE WHEN USED WITH CONCURRENT cART

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BACKGROUND

Historically, there has been a difference in the treatment of lymphoma according to HIV status[1] but since the advent of combined anti-retroviral therapy (cART) similar rates of overall survival have been demonstrated in the treatment of Hodgkin's Disease and Diffuse Large B-cell Lymphoma, leading to a change in practice and the use of standardised intensive regimes[2,3].

CODOX-M/IVAC chemotherapy is commonly used to treat Burkitt Lymphoma (BL) and in the HIV negative population, rituximab often added with suggested survival benefits[4]. Concerns over increased toxicity in an already immunocompromized population[5,6] have prevented its routine use in people living with HIV (PLWH). There are however few studies looking specifically at this[7].

AIMS

1) To assess whether the addition of rituximab to CODOX-M/IVAC chemotherapy is safe in PLWH in terms of treated related toxicity and mortality.
2) To assess whether rituximab increases treatment efficacy.

METHOD

Retrospective review of all HIV-BL treated in five London centres (Chelsea & Westminster, Kings College, Royal Free, St Bartholomew's & University College London Hospitals) between 2003 and 2013. The standard CODOX-M/IVAC regime[8,9] (+/- rituximab) was used with 2 alternating cycles of CODOX-M (cyclophosphamide, vincristine, doxorubicin and methotrexate) and IVAC (ifosfamide, etoposide and cytarabine). All patients received cART.

RESULTS

91 individuals (74 male) were treated, 49 received CODOX-M/IVAC and 42 R-CODOX-M/R-IVAC. There was no significant difference in baseline characteristics between groups. The median follow-up for the whole group is 41 months (range: 4-109). At BL diagnosis, the median CD4 count was 244 cells/mm^3 (range: 0-864) and 40 (44%) patients were newly diagnosed HIV positive. 32 (35%) were previously established on cART and 20 (63%) had undetectable plasma HIV viral loads.

Toxicity

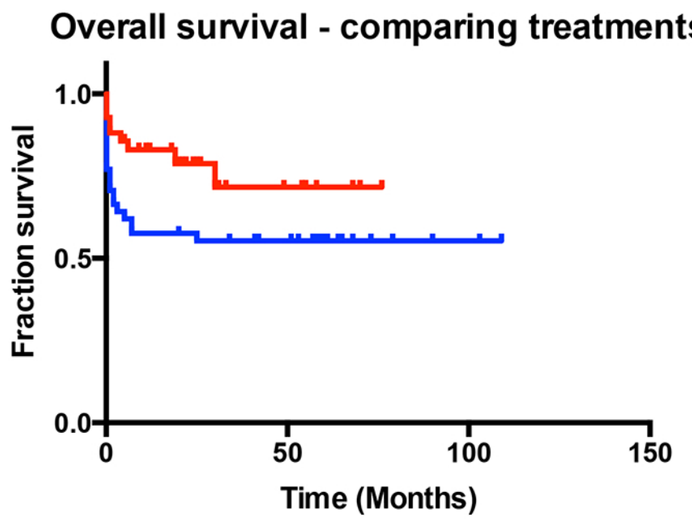
The addition of rituximab did not confer any significant increase in grade 3/4 toxicity such as infections, mucositis, diarrhea, renal impairment and tumor lysis syndrome. Opportunistic infections were infrequent with 2 confirmed and 1 suspected fungal chest infections, (all received R-CODOX-M/R-IVAC). There were 5 cases of CMV reactivation requiring treatment (x3 R-CODOX-M/R-IVAC, x2 CODOX-M/IVAC, all without end organ disease). There was no increase in bone marrow suppression with a similar length of neutropenia and GCSF use in both groups. Comparative measurements of HIV viral load, CD4 count, hemoglobin, platelet and white cell counts during and after treatment were not significantly different. There was no increase in inpatient hospital stay (94 vs. 103 days, p=0.58).

	CODOXM	RCODOXM	p-value	IVAC	RIVAC	p-value
Total Cycles	66	77		56	64	
Grade 3/4 Infection	74.24%	64.94%	*0.23*	58.93%	56.25%	*0.62*
Grade 3/4 Mucositis	22.73%	35.06%	*0.11*	3.57%	3.13%	*0.89*
Grade 3/4 Diarrhea	9.09%	14.29%	*0.34*	5.36%	4.69%	*0.87*
Grade 3/4 Tumor Lysis	4.55%	7.79%	*0.43*	0.00%	0.00%	*>0.99*
Grade 3/4 Renal failure	6.06%	5.19%	*0.83*	0.00%	1.56%	*0.35*
Median days neutropenic	9.5	10.5	0.21	5	6	0.29
Median days of GCSF required	5	7	0.69	5	6	0.55

Survival & Efficacy

60 patients were alive at last follow-up. The two-year overall survival is 68%. The overall survival is greater for patients receiving rituximab (2 year OS 72% (95%CI: 0.22-0.92, hazard ratio 0.46) vs. 55% (95%CI: 1.1-4.5, hazard ratio 2.2) (logrank p=0.04). The 2 year progression free survival (PFS) was greater in the rituximab cohort [2 year PFS 81% (95%CI 0.21-0.99, hazard ratio 0.46) vs. 55% (95%CI 1.0-4.8, hazard ratio 2.2);logrank p=0.04].

Of the 31 deaths, 6 were due to sepsis (x4 CODOX-M/IVAC, x2 R-CODOX-M/R-IVAC), 15 from progressive disease, 4 from disease relapse and 2 were HIV-related. Four deaths were unrelated to treatment of which 2 occurred while the patients were in complete remission. There was no significant difference in toxic deaths or disease relapse between groups (p=0.137)



CONCLUSION

Our multicenter analysis is the largest to date in this population and showed that the addition of rituximab to CODOX-M/IVAC chemotherapy confers no increase in toxicity and significantly improved OS and PFS in PLWH with BL who receive concomitant cART. BL should be treated with the same chemotheraputic approach regardless of HIV status.

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