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A Multicenter Phase 2 Study Incorporating High-Dose Rituximab into the CODOX-M/IVAC Regimen for Untreated Burkitt's Lymphoma (BL): Examination of Correlative Serum and CSF Rituximab Levels

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Background: Two-year survival rates for adult BL remain <60-65%. Furthermore, there is a paucity of data adding Rituximab to CODOX-M/IVAC therapy and virtually no data regarding the significance of serum or cerebrospinal fluid (CSF) levels.

Methods: Twenty-five BL patients were enrolled. Patients had low-risk (LR) or high-risk (HR) disease; LR patients received 3 CODOX-M cycles, while HR had 4 alternating CODOX-M/IVAC cycles (Mead et al. Blood 2009). Rituximab (500mg/m^2) was given x 2 doses each cycle. Correlative analyses of paired serum and CSF Rituximab levels were obtained for cycles 1+3 at 24+72 hours.

Results: There were 20 HR and 5 LR patients and median age was 44 years (range, 23-70). 3 HR and 1 LR patient were HIV+, while 15% of HR patients had CNS disease. Additionally, 35% of HR patients had bulk >10 cm and 40% had bone marrow involvement. Myelosuppression and mucositis appeared comparable with prior CODOX-M/IVAC data. The overall remission rate after 2 cycles was 100% with 67% complete remission. At 34-month median follow-up, 2-year PFS and OS rates for all patients were 86% and 86%, respectively (LR 2-year PFS and OS: both 100%; HR 2-year PFS and OS: both 82%). Further, the 2-year PFS and OS for HR, HIV-negative patients were 91% and 91%, respectively (disease-specific survival 100%). Two patients died from progressive disease (both HIV+ HR). The median serum and CSF rituximab levels for these patients were compared with patients without relapse (***Table 1***). Interestingly, cycle 1, 24-hour serum Rituximab levels were significantly higher among patients without relapse compared with the two patients who relapsed/died (P=0.042). Cycle 3, 24-hour Rituximab levels were of borderline significance (P=0.06).

Conclusions: The integration of Rituximab into CODOX-M/IVAC was associated with excellent survival rates, especially for HIV-negative BL. Further investigation of the predictive value of serum Rituximab levels is warranted.

Table 1. Rituximab Levels for Patients Without and With Disease Relapse.

Chemotherapy cycle/hours after R infusion	Median serum R level (ng/ml) for pts without relapse	Serum R level for 2 pts with relapse		Median CSF R level (ng/ml) for pts without relapse	CSF R levels for 2 pts with relapse	
		Pt #1	Pt #2		Pt #1	Pt #2
C1/24h	258,135	170,770	91,180	104	277	23
C1/72h	139,425	60,470	29,780	253	220	133
C3/24h	306,400	162,190	224,360	246	274	N/A
C3/72h	218,850	149,680	135,450	196	378	580

Abbreviations: C, cycle; h, hours; pt, patient; R, Rituximab.

Figure 1. Survival for High-Risk, HIV-Negative BL.