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MEETING ABSTRACTS Open Access

Rituximab combined with liposomal doxorubicin (R-Dox) in HIV-infected patients with severe Kaposi sarcoma-associated herpes virus (KSHV) associated multicentric Castleman disease (MCD)

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Background

MCD is characterized by inflammatory symptoms, splenomegaly, adenopathy, hypoalbuminemia, hyponatremia, and cytopenias. MCD in HIV-infected patients is generally KSHV-associated. No standard therapy exists. Rituximab has activity, but monotherapy may be insufficient in severe disease and can be associated with worsening of Kaposi's sarcoma (KS).

Methods

Patients with symptomatic MCD received rituximab 375 mg/m^2 plus liposomal doxorubicin 20 mg/m^2 every 21 days until substantial clinical improvement or disease progression. This regimen is being evaluated prospectively within an MCD natural history protocol. Additional therapy, employing agents with antiviral activity (discussed below), was generally employed to consolidate or maintain responses. Clinical, biochemical, and radiographic responses were evaluated using protocol-defined criteria. Overall complete response (CR) required normalization of all MCD-related abnormalities.

Results

Patient characteristics: 12 (1 woman, 11 men) patients completed R-dox. Median age, 43 (34-55); median number of prior therapies 2 (0-8). Diffuse adenopathy (12); median spleen (cm), 18.5 (12.5-28). Concurrent KS (5). All were receiving concurrent combination antiretroviral therapy. Baseline laboratory values, median (range): CD4 cells/μL, 291 (21-1598); C-reactive protein (mg/dL), 9.9 (0.4-21); albumin (mg/dL), 2.7 (1.5-3.3); sodium (mEq/L), 133 (126-136); platelets (K/μL), 70 (10-377); hemoglobin (gm/dL), 9.4 (6.8-12.2). Median cycles received 4.5 (3-9) (Table 1)

With 9 patients receiving additional therapy after R-dox; IFNα (6), high-dose zidovudine + valganciclovir (2), additional liposomal doxorubicin (1); 6 additional patients achieved overall CR (total 75%). KS responded in 4/5 (80%). With 31.4 months median potential followup (actual 5.5+ to 47+), estimated 2-year progression-free survival and overall survival are 61.1% and 78.6%, respectively. 8/12 (67%) remain symptom free, while 3 had recurrent MCD flares (months 7, 10, 17) responding to additional R-Dox. One had progressive MCD and worsening KS during cycle 6 and died at month 6. At autopsy, primary effusion lymphoma was discovered. One patient died at month 17 of sepsis unrelated to therapy. Select toxicities: 9 infusion reactions (Gr. 1 = 3, Gr. 2 = 4, Gr. 3 = 2) with the first dose

Table 1 Best response with R-Dox

Response Category	Complete Response	Partial Response	Stable Disease
Clinical	12 (100%)	-	-
Biochemical	10 (83%)	1 (8%)	1 (8%)
Radiographic	6 (50%)	6 (50%)	-
Overall	3 (25%)	6 (50%)	3(25%)

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of rituximab; 6/60 cycles complicated by neutropenia (Gr. 2 = 5, Gr. 3 = 1), no infectious complications.

Conclusions

R-Dox is effective in treating severe KSHV-MCD or MCD with concurrent severe KS. Evaluation of R-Dox in KSHV-MCD is ongoing.

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