Increased toxicities in children with Burkitt lymphoma treated with Rituximab – Experience from a tertiary cancer centre In India

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Abstract

Background: Even though rituximab has emerged as the standard of care for management of high risk paediatric burkitt lymphoma(BL) its safety in children from the low-middle income countries (LMICs) remains to be proven. We herein report our experience of using rituximab in patients with BL treated in our institute. Patients and Methods: All patients diagnosed of BL between January-2015 through December-2017 were treated in a risk stratified manner with either modified MCP-842 or modified LMB protocol. Patients with poor response to MCP 842 were shifted to LMB-salvage regimen. In addition, rituximab was given for selected patients of LMB group B or C. Result: Forty-two(49.4%) of 85 analyzed patients with BL received rituximab [Median dose:1500(Range:375-1875) mg/m2]. The incidence of febrile neutropenia(p=0.02), pneumonia(p=0.005), Intensive care unit admissions(p=0.002) and toxic deaths(p=0.04) were higher amongst BL patients who received rituximab. Pneumonia was fatal in 11 of 16(69%) patients who received rituximab. The mortality was 100% for patients who developed recurrent pneumonia after completion of treatment. On multivariate analysis, rituximab continued to be significantly associated with toxic deaths, HR:11.45(95\%CI: 1.87-70.07; p=0.008). The addition of rituximab to intensive chemotherapy resulted in an inferior 1-year event free survival $(49.4\pm8.1\%$ vs $79.3\pm6.5\%$;p=0.025) and 1-year overall survival $(63.1\pm8.5\%$ vs $91.8\pm4.5\%$;p=0.007). Also, the addition of rituximab did not improve 1-year relapse free survival $(78.3\pm7.3\%$ vs $83.9\pm6.0\%$;p=0.817). Conclusion: The potential immunomodulatory effect of rituximab and increased susceptibility to infections in patients from LMICs being treated under resource-constrained situations has to be carefully considered while choosing this drug in the treatment BL.

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N=85 MCP-842 LMB-96 (N=64)(N=21)1-TD 1-TD 1-Pr 1-Pr Post 2cycles PET-CT (N=81) PR (N=16) CR (N=46) PR (N=7) CR (N=12) Continued on MCP-842 (N=9) Continued on MCP-842 (N=46) Continued on LMB-96 LMB-S (N=7) +R (N=6) +R (N=8) -R (N=1) -R (N=34) +R (N=6) -R (N=1) +R (N=9) -R (N=3) -R (N=1) +R (N=12) TD-4 Pr-0 TD-0 Pr-1 TD-2 Pr-2 TD-0 Pr-0 TD-0 TD-0 TD-0 TD-0 TD-0 TD-3 Pr-1 Pr-1 Pr-1 Pr-1 Pr-1 Pr-0 End of treatment PET-CT CR-4 PR-1 CR-4 PR-0 CR-5 PR-0 CR-1 PR-0

TD-1 Re-1 AIR-6 (67%)

AIR-2 (67%)

Figure 1: Flow diagram with treatment, response assessment and outcome in patients with Burkitt lymphoma

R: Rituximab CR: Complete Response PR: Partial Response TD: Toxic Deaths Pr: Progressive Disease Re: Relapse AIR: Alive in Remission

AIR-0

AIR-4 (50%)

AIR-0

AIR-9 (75%)

AIR-30 (88%)

TD-2 Re-1 AIR-2 (33%)