Rituximab to Treat Children with CD20 positive Lymphoma or Leukemia – Choose Protocol and Dose Wisely

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To the editor:

We read recent article on increased toxicities due to Rituximab in children with Burkitt lymphoma (BL) in India with interest (1). Rituximab usage in children is a double-edged sword (2). We have few comments about the present study (1).

Authors treated group C patients with central nervous system disease and group B patients with poor response on Day 8 with LMB96 protocol (21 patients and 15 received Rituximab). Of the 15 patients who were treated with Rituximab and LMB96 (R-LMB96) protocol, 9 are alive and disease free (60%) and toxic deaths were 2/15 (13%). For 6 patients treated on LMB96 alone, 3 are alive and disease free (50%) and 2/6 (33%) had toxic deaths. So, children who had worst disease had better outcomes if treated with R-LMB96 rather than LMB alone. This in agreement with published findings from the original trial which showed EFS 93% at 3-yr vs. 75% reported in LMB96 group C (3). Authors have modified original protocol which might have affected its efficacy.

Rest of the 64 patients were treated as per MCP842 protocol (total 8 courses of cycle A & B). Later 7 patients on MCP842 switched due to poor response to salvage LMB96. Of the remaining 57 patients, 20 received Rituximab of whom 13 are alive and disease free (65%) and 7/20 (35%) had toxic deaths. Of 37 patients treated without Rituximab, 30 are alive and disease free (81%) and toxic deaths were 3/37 (8%). So, patients treated with Rituximab and MCP842 (R-MCP842) protocol had high rate of toxic deaths. Rituximab increases CD19+ lymphocyte depletion 35−fold, with methotrexate and cyclophosphamide (4). So, giving 8 cycles of R-MCP842 might have depleted B cells to very low level leading to higher infection rate and mortality.

To minimize side-effects and reduce costs low-dose Rituximab (100 mg fixed dose once weekly for 4 weeks) has been used in several autoimmune diseases, including immune thrombocytopenia and autoimmune hemolytic anemia (5). Adding Rituximab to the acute lymphoblastic leukemia (ALL) chemotherapy protocol improved the outcome for younger adults with CD20-positive, Ph-negative ALL (6). At our centre we have switched to low dose Rituximab (100 mg/m2/dose) for all children with relapsed CD20 positive ALL. Here we share our experience of treating 11 such children. Mean age was 11 year (range 5-16 years). Of them 64% underwent allogeneic stem cell transplantation (SCT). One child who relapsed after SCT achieved remission again after giving Rituximab alone and maintained remission for 3 years on 3-monthly maintenance rituximab. Median doses given were 4 per child (range 2-16). Immunoglobulin deficiency was noted in 5 (44%) and all received replacement therapy. Infusion reactions were noted and one child needed oxygen and intensive care but recovered in 24 hours. There was one toxic death due to pneumonia post-SCT with corona virus. Two remained refractory and 2 relapsed. Six children are alive and disease free at median follow up of 24 months (range 2-48 months). It's feasible and safe to administer low-dose Rituximab along with chemotherapy in the developing world setting.

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