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INTER-B NHL RITUX 2010 TRIAL FOR CHILDREN/ADOLESCENTS WITH HIGH-RISK MATURE B-CELL NON-HODGKIN'S LYMPHOMA/ACUTE LEUKAEMIA: SAFETY AND EFFICACY IN PATIENTS TREATED WITH RITUXIMAB AND LMB CHEMOTHERAPY.

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Keywords: Burkitt's lymphoma, Children, Lymphoma therapy, Rituximab

Veronique Minard-Colin[1], Anne Auperin[2], G. A. Amos Burke[3], Sarah Alexander[4], Rafael Delgado[5], Salvatore Buffardi[6], Anne Uyttebroeck[7], Catherine Bollard[8], József Zsiros[9], Monika Csoka[10], Bernarda Kazanowska[11], Alan K Chiang[12], Arnaud Verschuur[13], Rodney R. Miles[14], Andrew Wotherspoon[15], Donald A. Barkauskas[16], Keith Wheatley[17], Gilles Vassal[18], Peter Adamson[19], Thomas G. Gross[20], Catherine Patte[18], Marta Pillon[21]

[1] Pediatric and Adolescent hematology and Oncology, Gustave Roussy, Villejuif, France
[2] Unit of Biostatistics and Epidemiology, Gustave Roussy, Villejuif, France
[3] Department of Paediatric Haematology, Oncology and Palliative Care, cambridge university hospitals NHS Foundation Trust, Cambridge, United Kingdom
[4] Division of Haematology/Oncology, Hospital for Sick Children, Toronto, Canada
[5] Pediatric Hematology and Oncology, University of Valencia, Valencia, Spain
[6] Pediatric Hematology and Oncology, A.O.R.N. Santobono–Pausilipon, Napoli, Italy
[7] Pediatric Hematology and Oncology, University Hospitals Leuven, Leuven, Belgium
[8] Center for Cancer and Immunology Research, Children's National Health System and The George Washington University, Washington, United States
[9] Princess Máxima Center for Pediatric Oncology, Princess Máxima Center for Pediatric Oncology, Ultrecht, Netherlands
[10] 15. Pediatric Hematology and Oncology, Semmelweis University, Budapest, Hungary
[11] Department of Pediatric Bone Marrow Transplantation, Oncology, and Hematology, Wroclaw Medical University, Wroclaw, Poland
[12] Department of Paediatrics and Adolescent Medicine, Li Ka Shing Faculty of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, Hong Kong
[13] Pediatric Hematology and Oncology, La Timone, APHM, Marseille, France
[14] Department of Pathology and ARUP Laboratories, Huntsman Cancer Institute, Salt Lake City, United States
[15] Pathology Department, The Royal Marsden NHS, London, United Kingdom
[16] Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, United States
[17] Cancer Research UK Clinical Trials Unit, Institute of Cancer and Genomic Sciences, College of Medical and Dental Sciences, Birmingham, United Kingdom
[18] Department of Pediatric and Adolescent Oncology, Gustave Roussy, Villejuif, France
[19] Global Head, Oncology Development & Pediatric Innovation at Sanofi, Cambridge, United States
[20] Department of Pediatrics, Center for Cancer and Blood Diseases, Children's Hospital Colorado, Aurora, United States
[21] Pediatric Hematology and Oncology, University of Padova, Padova, Italy

Background:

The addition of rituximab to standard Lymphomes Malins B (LMB) chemotherapy improved survival of children and adolescents with high-risk mature B-cell non-Hodgkin's lymphoma and mature acute leukemia (B-NHL/AL) in the international randomized phase III trial Inter-B NHL ritux 2010 (NCT01516580).

Aims: After the first interim analysis, randomization was stopped for efficacy and additional patients were subsequently enrolled and treated with R-LMB for planned secondary aims. Here we report the total cohort of patients treated with R-LMB.

Methods:

From December 2011 to June 2017, 298 patients < 18 years with high-risk B-NHL (stage III with LDH level>2N, stage IV) and B-AL were included in the Inter B-NHL Ritux 2010 study and allocated to the R-LMB arm: 164 were reported in the publication (NEJM 2020;382:2207-19) of the randomized part of the study (Main R-cohort) and there are 134 additional patients (Additional R-cohort). Rituximab was given (375 mg/m^2) on days -2 and 1 during the first 2 chemotherapy courses and on day 1 of the 2 following courses (total 6 infusions). Therapeutic groups were as follow: B: Stage III or IV, central nervous system negative; C1: Stage IV/B-AL cerebrospinal fluid (CSF) negative; C3: CSF positive. The endpoint event-free survival (EFS) is defined as the minimum time between inclusion and detection of residual viable tumor cells after the second consolidation course (primary refractory disease), relapse, progressive disease, second cancer, or death from any cause, or the date of the last follow-up for patients who did not have any event.

Results:

Median age was 8 years (interquartile range (IQR) 5-12). 88% patients had Burkitt lymphoma (BL). 48% were in group B, 40% in C1 and 12% in C3. 94% patients received at least 6 rituximab administrations. The median follow-up was 45 months (IQR 34-57). There were 20 events (13 treatment failures: primary refractory disease or progression or relapse, 5 toxic deaths, 2 second cancers (histiocytic sarcoma, melanoma)). Seven treatment failures occurred in patients of therapeutic group B, 3 of group C1 and 3 of group C3. All relapses, except one, occurred during the first 10 months. 4-year EFS was 93.0% (95%CI 89.4% to 95.5%) (93.9% in main R-cohort, 91.3% in additional R-cohort). 16 deaths occurred (7 disease-related, 8 toxic deaths at first or further line, 1 from histiocytic sarcoma). 4-year overall survival (OS) was 94.2% (95%CI 90.7% to 96.4%) (95.1% in main R-cohort, 92.0% in additional R-cohort). Among patients with BL, 9 had treatment failures (6 in group B, 2 in group C1, and 1 in group C3) and 7 died. The most frequent grade ≥ 3 acute adverse events after prephase were febrile neutropenia (93%), infection (58%), and stomatitis (78%). One year after inclusion, 102 (59%) of 173 evaluated patients for immunoglobulin level had low IgG level.

Summary/Conclusion:

Rituximab in addition to standard LMB therapy achieved outstanding EFS and OS in both randomized and additional parts of the trial in children/adolescents with high-risk B-NHL/AL with significant acute toxicity and hypoglobulinemia. However, some very rare patients still have resistant disease and very poor outcome, notably those with Burkitt lymphoma.

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