Can we predict neo-adjuvant therapy response in patients with osteosarcoma?

Osteosarcoma (OS) is a malignant primary tumor of bone affecting adolescents and young adults. There are few if any molecular markers to predict its behavior and prognosis. In our study we investigated the relationship of expression of different molecular markers in osteosarcoma tumors before treatment to pathologic necrotic response after neo-adjuvant chemotherapy. In summary, deletion of RB1 (72%), gain of RUNX2 (68%), deletion of TP53 (52%), deletion 18q23 (48%) by molecular studies and p16-negative by IHC (38%) were common findings. Most abnormalities, particularly RB1 and TP53 deletions and RUNX2 gain, did not correlate with chemotherapy response. IHC p16-negative status correlated strongly with failed chemotherapy response (15/40). Alterations of 18q correlated slightly with poor response (p=0.0796). Poor response cases included 3 cases with deletion of 18q23, 3 cases with LOH for 18q23 and 1 case with copy gain (trisomy 18). Comparison of 18q genomic abnormalities in cases with a favorable versus poor response suggested a smallest region of overlap for a negative factor at 18q23. In conclusion we identified complex genotypes in the OS samples with frequent occurrence of previously identified biomarkers such as deletion RB1, deletion TP53, deletion 18q23 and gain of RUNX2. Comparison of genomic findings to p16-negative status and chemotherapy response revealed p16-negative status to be the best overall indicator of a poor chemotherapy response, with the poorest responders being both p16 negative and altered for 18q23. Additional studies are warranted to validate these findings and further characterize the role of CDKN2A and other factors that influence response to therapy in osteosarcoma patients.

Biography

Dariusz Borys is an Associate Professor of Pathology and Orthopedic Surgery, Head of Orthopedic and Pediatric Pathology and Director of Digital Pathology at Loyola University Chicago. He has received his Doctor of Medicine from the University of Wroclaw, Poland in 1994 and completed a Residency program in Anatomic Pathology at County General Hospital in Wroclaw, Poland in 1995. He has completed his Postdoctoral research at the University of Arizona, Tucson, Arizona in 1998. He continued on with and completed Residency training in both Anatomic Pathology and Clinical Pathology at University of Illinois at Chicago in 2001. He has received a Pediatric Pathology Fellowship at New York University, New York in 2005 and followed that with an Orthopedic Pathology Fellowship at NYU Hospital for Joint Diseases, New York in 2006. After completing his Fellowships, he becomes Faculty Member in the rank of Assistant Professor at University of California and then he finally moved to Loyola University Chicago in 2013. At LUMC he is appointed as an Associate Professor of Pathology and Orthopedic Surgery and is serving as the Head of Orthopedic and Pediatric Pathology and Director of Digital Pathology. Currently his research focuses on the molecular markers in diagnostic, prognostic and targeted therapy in osteosarcoma.

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