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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Protective Role of Oxaliplatin Among Platinum-Based Therapies in the Development of Therapy-Related Myeloid Neoplasms

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Introduction

As a DNA-damaging agent, platinum-based chemotherapy serves as a cornerstone in cancer treatment. However, its widespread use has been associated with increased incidence of therapy-related myeloid neoplasms (t-MNs). Among the three most commonly used platinum chemotherapies - cisplatin, carboplatin, and oxaliplain - oxaliplatin presents a distinctive clinical usage and toxicity profile. Predominantly utilized in treating gastrointestinal tract (GI) cancers, oxaliplatin manifests a distinct toxicity pattern when compared to its counterparts. This variance is supported by a previous study that postulated oxaliplatin-induced cytotoxicity primarily results from ribosomal stress as opposed to a DNA-damage response (Bruno et al. Nature Medicine 2017). Further, epidemiological and anecdotal data suggest a lower incidence of t-MNs associated with oxaliplatin. In this study, we aimed to investigate and compare the clinical manifestations, molecular phenotypes, and patient outcomes associated with t-MNs following exposure to various platinum-based therapies.

Methods

All patients clinically diagnosed with t-MNs between 2008 and 2022, based upon a presentation with a myeloid neoplasm (AML or MDS) with any previous cancer associated with exposure to platinum-based chemotherapy, at a single center were analyzed. Descriptive statistics were used to compare the clinical and molecular profiles between the groups of patients receiving different types of platinum.

Results

153 patients were found to have been diagnosed with t-MNs during the study time period following platinum exposure. 45 (29.4%) had been exposed to only cisplatin, 72 (47.1%) to carboplatin alone, 9 (5.9%) to oxaliplatin alone, 25 (16.3%) to both cisplatin and carboplatin, and 1 each (0.7%) to carboplatin or cisplatin in combination with oxaliplatin. The most frequent primary cancers included non-Hodgkin lymphoma (19.6%), followed by ovarian (14.4%), breast (11.8%), and lung (7.8%). Median time from platinum exposure to t-MN diagnosis was 2.7, 3.5, and 3.6 years for patients having previously received only cisplatin, carboplatin, or oxaliplatin respectively (P value not significant between oxaliplatin vs. cisplatin or vs. carboplatin). In regard to MDS/AML diagnosis ratio, there was no significant difference between cisplatin-only, carboplatin-only, and oxaliplatin-only t-MNs. Cytogenetics data and gene mutation data were available in 139 patients. Del 5q/-5 and/or Del7q/-7 were numerically rare in oxaliplatin-only t-MNs compared to cis-only (22.2% vs. 43.9%, P = 0.285) or carbo-only t-MNs (22.2% vs. 48.4%, P = 0.171). Also, complex karyotype was only found in 1 patient (11%) in oxaliplatin-only t-MNs, whereas 51% and 58% of cisplatin-only and carboplatin-only t-MNs were found to have complex karyotype. Despite the low frequency of complex karyotype in oxaliplatin-only t-MNs, *TP53* mutations were prevalent and found in 56%, 60%, and 60% of cisplatin-only, carboplatin-only, and oxaliplatin-only t-MNs, respectively (no statistical difference among the groups). Median overall survival (OS) was not significantly different among the three groups.

Conclusion

In the patients with t-MNs post-platinum exposure, oxaliplatin-induced t-MNs represented only 6% of the entire cohort, with a significantly lower incidence of t-MN-associated chromosomal abnormalities (del5q/-5, del7q/-7, and complex karyotype). This discrepancy cannot be solely attributed to the less frequent use of oxaliplatin in comparison to other platinum agents. The findings underscore the protective role of oxaliplatin in the development of t-MNs, warranting further investigation in both clinical practice and biological mechanism.

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