GENETIC VARIATION AND CHEMOTHERAPY RESPONSE IN LYMPHOMA PATIENTS

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Background: Older adults with Non-Hodgkin lymphoma (NHL) frequently receive reduced dose or less-aggressive chemotherapy regimens. There is a need to identify patients who may receive antitumor benefit from the full dose of anthracycline without experiencing dose limiting toxicity. Our aims were to identify the percentage of patients who received the standard dose of anthracycline, evaluate the frequency of single nucleotide polymorphisms (SNPs) involved in the anthracycline metabolic pathway, and to evaluate the association of those SNPs with treatment tolerability in community dwelling NHL patients.

Methods: Iowa residents age 45 and older with newly diagnosed diffuse large B-cell or grade 3 follicular lymphoma were eligible. Participants underwent tests for cognition and frailty at baseline and at 6 months. Genomic DNA was extracted from saliva samples. 31 SNPs were determined using Pyrosequencing and Real-Time PCR. Medical records were reviewed for clinical variables. Statistical analysis was done using JMP 9.0.2 software.

Results: 66 patients were enrolled with a mean age of 67.2 years (range 45-86 years). Genotypes were completed for all 58 who returned saliva kits. DNA concentration ranged from 0.0027 to 10.13 µg/µl. All SNPs were in Hardy Weinberg Equilibrium. As expected, an increase in age was associated with lower total dose delivered and lower delivered dose intensity. Our analyses indicated that the GG genotype (n=35) of the SNP rs471692 in Topoisomerase 2A received a higher total dose of the anthracycline compared to the AG or AA (n=14) ($p = 0.014$, Welch's ANOVA). One patient of the GG genotype had dose reduction (1 out of 35) compared to 3 patients in the AA or AG genotype (3 out of 12).

Conclusions: We were able estimate the frequencies of SNPs in NHL patients treated in a community care setting. SNPs in the doxorubicin pathway might be predictive in selecting patients who will better tolerate and thus benefit from anthracycline treatment.