Development of an Integrated Risk Prediction Model of Taxane-induced Peripheral Neuropathy within SWOG S1714

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Taxanes play an important role in the treatment of early-stage breast cancer. Chemotherapy induced peripheral neuropathy (CIPN) is a complication of taxane therapy and can lead to treatment dose reduction or discontinuation, which may ultimately affect overall survival, and can substantially impact quality of life and functional status in survivors. The trajectory of CIPN symptoms is not well described.

SWOG S1714 enrolled participants 18 years or older with Stage I-III primary non-small cell lung, primary breast, or primary ovarian/fallopian tube/peritoneal cancer starting treatment with a taxane-based regimen. Participants with baseline neuropathy were eligible to enroll. Neuropathy was assessed with the patient-reported European Organization for Research and Treatment of Cancer QLQ-CIPN20 (CIPN-20). The occurrence of clinically meaningful sensory neuropathy was defined as an increase of 8 or more points (on a 0-100 scale, with a higher score indicating more severe symptoms) between baseline and follow-up in the sensory neuropathy subscale of the CIPN-20. Assessments occurred at baseline and at 4, 8, and 12 weeks +/-14 days and 24, 52, 104, and 156 weeks +/- 28 days after registration.

Among N=1336 enrolled participants, 1321 were eligible (99%). Of the eligible participants, we will report on the 1198 (90.7%) with breast cancer. The median age was 55 years (range 23-84) and 99.3% were female. The breast cancer cohort included 72.2% White, 11.7% Black, 4.9% Asian, and 11.0% Hispanic/Latino participants. Paclitaxel (every week for 12 weeks or every 2 weeks for 8 weeks) was administered to 56.2% and docetaxel (every 3 weeks for 12-18 weeks) to 43.8%. The mean baseline patient-reported CIPN-20 sensory neuropathy subscale score was 6.2 (standard deviation 12.0). Through one full year of follow up, 1084 participants (90.5%) were evaluable for sensory neuropathy at any time point. At individual assessment times, clinically meaningful sensory neuropathy was reported by 18.7% of participants at week 4, 33.0% at week 8,46.3% at week 12, 44.8% at week 24, and 47.4% at week 52. Clinically meaningful sensory neuropathy at one or more assessments was reported by 67.8% of participants.

In this large prospective cohort of racially/ethnically diverse participants with breast cancer receiving taxane-based therapy, 2 out of every 3 experienced clinically meaningful sensory neuropathy symptoms during the first year of treatment and nearly 50% continue to experience clinically meaningful sensory neuropathy symptoms at the end of the first year. Given the high incidence of symptoms during taxane treatment and persistence of symptoms after treatment completion, it is critical to develop effective methods to predict, prevent, and treat this toxicity. Our R37 grant provides funding for biomarker (genetics, kinetics, nutrients, metabolites, lipids) analyses to build an Integrated CIPN Risk Prediction Model. Funding: NIH/NCI/NCORP grant UG1CA189974 and NIH/NCI grant 1R37CA277043-01.