Background: Despite advances in supportive care, patients undergoing standard chemotherapy for breast cancer face not only significant side effects, but also the risk of treatment-induced side effects. Current methods for predicting risk are inconsistent and/or unreliable. Because the biology and pathophysiology of many side effects is regulated by the synergistic interaction of simultaneously expressed genes, we reasoned that a novel approach to risk prediction could be achieved by the development of clusters of SNPs defined by BNs. The present study was designed to assess the feasibility of identifying SNPs that were associated with regimen-related diarrhea, oral mucositis, nausea and vomiting, fatigue, cognitive dysfunction, and neuropathy. In patients with breast cancer treated with dose-dense AC+T, the primary end point was an area under the receiver operating characteristic curve (aROC) >0.8.

Methods: After informed consent, 78 patients with breast cancer who had received at least 3 cycles of (DD) AC+T were enrolled and saliva samples were collected. Salivary DNA was isolated and analyzed on Illumina Omni microarrays (2.5×10⁶ SNPs). Standard supportive therapy for prevention and management of side effects was provided. The frequency and severity of diarrhea, oral mucositis, nausea and vomiting, fatigue, cognitive dysfunction, and neuropathy, and nausea and vomiting were determined using Patient Care Monitor©, a validated patient-reported symptom assessment tool, was used to measure the frequency and severity of diarrhea, CINV, cognitive dysfunction, oral mucositis, peripheral neuropathy, and fatigue. Side effects were considered to be significant if rated at a score ≥ 4.

Results: The incidence of clinically significant side effects was higher than anticipated by the literature and is reported in Table 1 along with the accuracy and aROC. Seventy-eight subjects with histologically proven breast cancer who were treated with at least 3 cycles of DD AC+T provided informed consent and were enrolled in the study. Subjects provided a saliva sample using a DNA Genotek collection tube from which DNA was extracted. SNP expression was determined using Illumina Omni microarrays with a chip size of 2.5×10⁶ SNPs. Each patient received standard supportive care with chemotherapy. Patient Care Monitor®, a validated patient-reported symptom assessment tool, was used to measure the frequency and severity of diarrhea, CINV, cognitive dysfunction, oral mucositis, peripheral neuropathy, and fatigue. Side effects were considered to be significant if rated at a score ≥ 4. Using algorithms based on Bayesian methodological programming, predictive networks were developed for each of the 6 side effects using Bayesian methods including 10-fold internal cross-validation.

Conclusions: Sixty-eight subjects with histologically proven breast cancer who were treated with at least 3 cycles of DD AC+T provided informed consent and were enrolled in the study. Subject provided a saliva sample using a DNA Genotek collection tube from which DNA was extracted. SNP expression was determined using Illumina Omni microarrays with a chip size of 2.5×10⁶ SNPs. Each patient received standard supportive care with chemotherapy. Patient Care Monitor®, a validated patient-reported symptom assessment tool, was used to measure the frequency and severity of diarrhea, CINV, cognitive dysfunction, oral mucositis, peripheral neuropathy, and fatigue. Side effects were considered to be significant if rated at a score ≥ 4. Using algorithms based on Bayesian methodological programming, predictive networks were developed for each of the 6 side effects using Bayesian methods including 10-fold internal cross-validation.

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