Role of *XRCC1* gene polymorphisms in non-small cell lung cancer cisplatin-based chemotherapy, and their effect on clinical and pathological characteristics

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ABSTRACT. Non-small cell lung cancer (NSCLC) is the most common cancer globally. The XRCC1 protein interacts with ligase and poly(ADP-ribose) polymerase to repair cisplatin-induced DNA damage. The authors of previous studies have reported *XRCC1* Arg399Gln, Arg280His, and Arg194Trp polymorphisms and advanced NSCLC prognosis, but the results are inconclusive. We investigated the association between clinical outcome and *XRCC1* Arg399Gln, Arg280His, and Arg194Trp polymorphisms in advanced NSCLC patients treated with cisplatin. We recruited 252 patients with advanced NSCLC (TNM stages: IIIB and IV) and used polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) to genotype the polymorphisms. Patients with the TT genotype of *XRCC1* Arg194Trp showed a significantly better response to chemotherapy than those with the CC genotype. The GA+AA genotype of Arg194Trp

was correlated with better response to chemotherapy than the wild-type form. The TT genotype of Arg194Trp was associated with longer survival time than the CC genotype. The TT genotype of Arg194Trp was correlated with lower risk of death from all causes than the CC genotype. The Arg194Trp polymorphisms interacted with squamous cell carcinoma and affected overall survival of advanced NSCLC. However, there was no association between Arg399Gln and Arg280His polymorphisms and response to cisplatin-based chemotherapy and overall survival in advanced NSCLC. The results suggest that the TT genotype of Arg194Trp is significantly associated with better response to chemotherapy and longer overall survival of advanced NSCLC patients than the wild-type form. Our investigation offers insight into the influence of *XRCC1* gene polymorphisms on the treatment outcome of advanced NSCLC.

Key words: *XRCC1*; Arg399Gln; Arg280His; Arg194Trp; Cisplatin; Advanced NSCLC