Effects of cetuximab combined with afatinib on the expression of KDR and AQP1 in lung cancer

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ABSTRACT. In this study, we examined the effect of cetuximab (epidermal growth factor receptor monoclonal antibody) combined with afatinib (epidermal growth factor receptorand human epidermal growth factor receptor 2 tyrosine kinase irreversible inhibitor) on the apoptosis of A549 cells and on kinase domain receptor (KDR) and aquaporin 1 (AQP1) expression in A549 cells. A549 cells were cultured in RPMI-1640 and then divided into 4 groups: control group, 1-nM cetuximab group, 25-μM afatinib group, and 1-nM cetuximab + 25-μM afatinib group. After incubation for 48 h, the cell inhibition rate, cell cycle distribution, and invasive ability of A549 cells before and after treatment were examined using MTT, flow cytometry, and transwell assays, respectively. Gene and protein expression levels of KDR and AQP1 were detected by reverse transcription-polymerase chain reaction and western blot analysis. Cetuximab and afatinib significantly inhibited A549 cell growth. Their combination produced greater growth inhibition ($P < 0.01$). Cetuximab and afatinib both induced the apoptosis of A549 cells, and their combination produced a higher apoptosis rate ($P < 0.01$). Compared with monotherapy, cetuximab in combination with afatinib induced G1 phase arrest and downregulated the gene and protein

expression of KDR and AQP1 ($P < 0.05$). Cetuximab in combination with afatinib synergistically inhibited the growth and migration of cells and downregulated the gene and protein expression of KDR and AQP1, indicating that a combination of cetuximab and afatinib is a potential strategy for lung cancer therapy.

Key words: Apoptosis; Aquaporin-1; Cetuximab; Kinase domain receptor; Afatinib

