Selected gene mRNA expression is not predictive of improved overall survival

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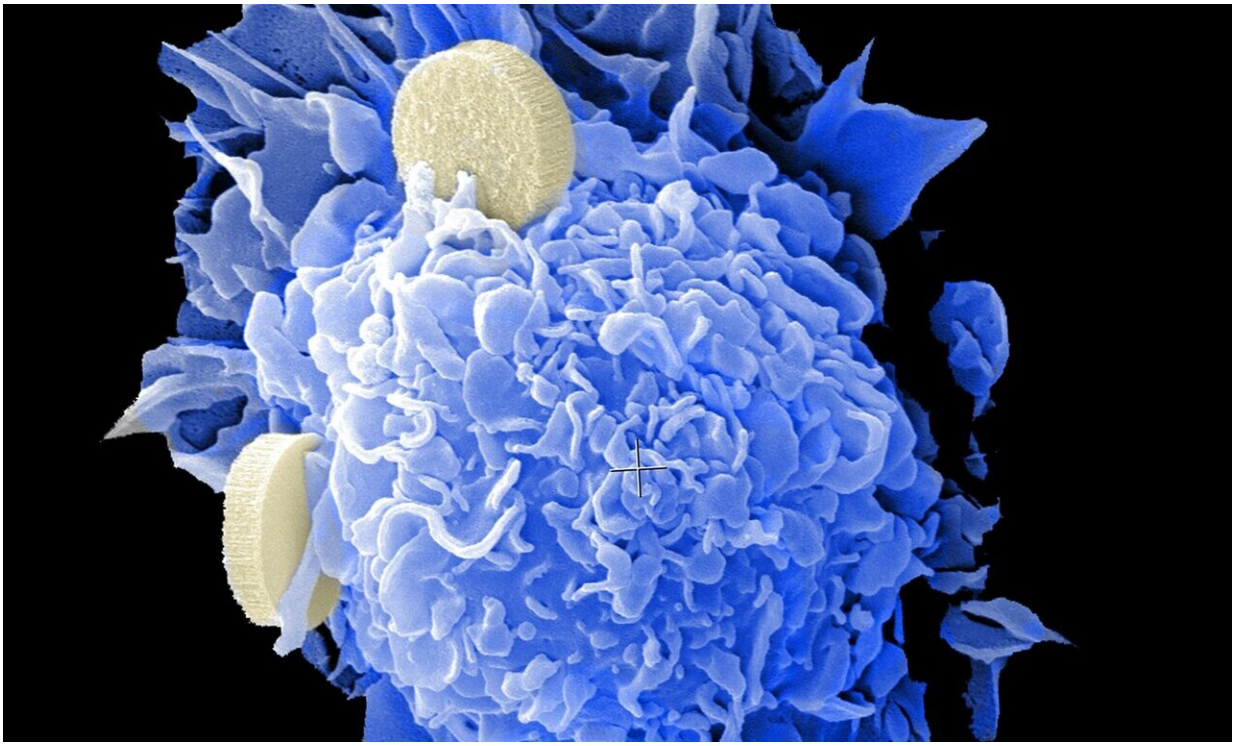

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A phase III study examining whether messenger (m)RNA expression correlated with sensitivity or resistance to chemotherapy did not confer a statistically significant advantage in overall survival for patients with resected stage II-III non-small cell lung cancer (NSCLC), according to research presented at the International Association for the Study of Lung

Cancer World Conference on Lung Cancer.

Lung cancer researchers and clinicians have sought methods to improve chemotherapy's modest 5% overall survival rate for patients with NSCLC. Dr. Silvia Novello, professor of medical oncology at the University of Torino at San Luigi Gonzaga Hospital, Orbassano, Italy, and a large group of European researchers evaluated the predictive utility of the mRNA expression levels of molecular markers, mRNA expression levels of molecular markers, excision repair cross-complementing group ERCC1 and thymidylate synthase (TS).

The primary research aim of the study was to investigate if adjuvant pharmacogenomic-driven approach was able to improve overall survival in completely resected NSCLC.

The researchers randomly assigned 773 patients from 31 Italian and German centers (one in Poland) within 5-8 weeks after radical surgery, adopting a unique study design. Genomic analyses were performed soon after surgery and then patients were randomly assigned in each of the four genomic subgroups to investigator's choice of platinum-based chemotherapy or to tailored treatments defined by biomarkers.

Because cisplatin activity is supposed to be limited in presence of high ERCC1 expression levels, patients allocated to tailored treatment received or single-agent docetaxel if TS level was high (n = 148) or pemetrexed if TS was low (n = 43). In the subgroup with low ERCC1 expression levels, patients received cisplatin/gemcitabine if TS level was high (n = 101) or cisplatin/pemetrexed if TS was low (n = 92). The most frequent doublets used in the control arm were cisplatin/gemcitabine (n = 159) and cisplatin/vinorelbine (n = 123) (others, n = 28) .

Median follow-up time was 28.2 months. The estimated median overall survival in the control arm was 83.5 months vs 96.4 months in the

tailored arm (95% CI: 0.55-1.04; hazard ratio (control vs tailored) was 0.76).

"In completely resected stage II-III NSCLC, tailoring adjuvant chemotherapy on the basis of the mRNA expression of selected genes does not confer a statistically significant survival advantage in terms of overall survival and relapse-free survival. Toxicity was less commonly reported in the customization arms," Novello reported.

"The ITACA study is the largest adjuvant study tailored to ERCC1/TS status, and the results have been long-awaited," said IASLC President Dr. Tetsuya Mitsudomi. "This trial should be praised for the mandated genomic analysis that was accomplished within a reasonably short timeframe before random assignment. In addition, this trial confirmed that there is no biomarker strong enough to predict the efficacy of cytotoxic chemotherapy; however, the concept of customizing adjuvant therapy according to the genomic status of patients' tumors is valid, leading to the recent demonstration in the ADAURA study of the superiority of osimertinib in delaying the postoperative recurrence of disease in patients with EGFR-mutated NSCLC."

Provided by International Association for the Study of Lung Cancer