Commentary

# An in silico approach to treating "the right patient with the right drug at the right dose at the right time"

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Biomarkers that predict responses to anti-cancer drugs are required to establish personalized cancer medicine, which is defined by the United States Federal Drug Administration as treating "*the right patient with the right drug at the right dose at the right time*" (1). In this issue, Dr. Wang and colleagues report a gene expression signature that predicts the efficacy of ZD-6474 (vandetanib) in 89 lung cancer cell lines (2) using a data set deposited in the cancer cell line encyclopedia (3). This was an in silico study; therefore, the results require validation in tumor samples from lung cancer patients treated with ZD-6474. However, the study provides a good example of a method of identifying candidate biomarkers that predict responses to anti-cancer drugs.

ZD-6474 is a selective inhibitor of VEGFR, RET, and EGFR tyrosine kinases, and its efficacy in lung cancer has been tested in several randomized clinical trials, including ZODIAC (NCT00312377; vandetanib ± docetaxel), ZEAL (NCT00418886; vandetanib ± pemetrexed), ZEPHYR (NCT00404924; vandetanib *vs*. placebo), and ZEST (NCT00364351; vandetanib *vs*. erlotinib). Recent *in vitro* and *in vivo* studies indicate that the *EGFR* mutation and *RET* fusion (both oncogenic) are genetic biomarkers that predict the efficacy of vandetanib (4-7). However, although recent retrospective evaluation of tumor samples from those trials confirmed the utility of *EGFR* mutations, it did not clearly validate the *RET* fusion (8,9). Thus, there may be several as yet undefined cellular contexts that modify the efficacy of vandetanib.

As the authors point out, a randomized clinical trial accompanied by a comprehensive omics study is the best way to identify predictive biomarkers for a particular drug; however, such studies are not easy to execute in practice. In particular, the limited quantity and quality of biopsied tumor tissues from advanced cancer patients who are scheduled to receive chemotherapy is a problem. A combination of full-omics data from cancer cell lines and focused-omics analysis of tumor specimens will facilitate the identification of predictive biomarkers that are useful in a clinical setting.

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*Ethical Statement:* The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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