

# Matching targeted therapies to tumor's specific gene mutations key to personalized cancer treatment

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(Medical Xpress) -- Customizing targeted therapies to each tumor's molecular characteristics, instead of a one-size-fits-all approach by tumor type, may be more effective for some types of cancer, according to research conducted by The University of Texas MD Anderson Cancer Center.

MD Anderson's Phase I findings were presented today on the opening press program of the 47th Annual Meeting of the American Society of Clinical Oncology. Apostolia-Maria Tsimberidou, M.D., Ph.D., associate professor in MD Anderson's Department of Investigational [Cancer Therapeutics](#), and the study's principal investigator, presented the data.

Marking the largest scale on which this approach has been examined to date, the study analyzed the results of matching targeted therapies with specific gene mutations in patients. The data indicated that this strategy was associated with higher rates of response, survival and failure-free survival than observed in non-matched patients.

## Pairing Patient and Treatment

"This preliminary study strongly suggests that molecular analysis is needed to use the right drug for the right patient. Up to this point, we have treated tumor types, but this study shows we cannot treat all patients with a tumor type the same way. We need to take into

consideration a number of factors, and this study suggests that a personalized approach is needed to improve clinical outcomes for patients with cancer," said Tsimberidou.

The identification of pathways involved in carcinogenesis, metastasis and [drug resistance](#); new technologies enabling tumor molecular analysis; and the discovery of targeted therapies have stimulated research focusing on the use of targeted agents as part of a personalized medicine approach, she said.

"Over the past decades, a personalized medicine approach using [Gleevec](#) has changed the way we treat [chronic myeloid leukemia](#), as well as [survival rates](#)," said Razelle Kurzrock, M.D., professor and chair of MD Anderson's Department of Investigational Cancer Therapeutics. "We wanted to apply a similar approach to solid tumors."

## Research Methods and Results

In the initial analysis, Tsimberidou analyzed 1,144 patients with metastatic or inoperable cancer underwent testing for molecular aberrations at MD Anderson. Their median age was 58, and the median number of prior treatments was four. Of these patients, 460 had one or more gene aberration, including:

- 10 percent with a PIK3CA mutation
- 18 percent with a KRAS mutation
- 8 percent with a NRAS mutation
- 17 percent with a BRAF mutation
- 3 percent with an EGFR mutation
- 2 percent with a CKIT mutation
- 21 percent PTEN loss
- 37 percent a p53 mutation

Patients with gene aberrations were treated on clinical trials with matched targeted agents, when available. Regimens included one or more therapies targeting PIK3CA, mTOR, BRAF, MEK, multikinases, KIT or EGFR. Outcomes of patients with gene aberrations treated with matched therapy were compared with those patients with gene aberrations who were not treated with matched therapy because of issues such as: eligibility, study availability; insurance coverage and/or logistical problems with the study calendar.

For the 175 patients with one aberration, the response rate was 27 percent with matched targeted therapy. The response rate was 5 percent in 116 patients when treated with non-matched therapy.

Patients who received matched targeted therapy had median survival of 13.4 months, while median survival for patients treated with unmatched targeted therapy was nine months. Median failure-free survival in patients who received matched targeted therapy was 5.2 months, compared to 2.2 months for patients who received unmatched targeted therapy.

## **Further Research Needed**

These preliminary results merit further investigation and confirmatory, prospective studies are needed, especially because the study was not a randomized study and therefore biases could influence the results.

"MD Anderson's goal is to better understand the biology involved in each patient's carcinogenesis by testing each tumor for genetic abnormalities driving tumor growth to guide treatment selection. This strategy will lead to the optimization of personalized therapy," Tsimberidou said.

Another goal is to match targeted therapies to patients earlier in treatment.

"When Gleevec was first introduced, it was tested in patients in blast crisis and the response rate was about 15 percent. In contrast, when tested in the front line setting, and with the introduction of similar but increasingly potent second- and third-generation drugs, patients' response rate was close to 100 percent, and now their expected survival is 25 years and counting," said Kurzrock. "Ultimately, to best match treatments to patients and offer the most therapeutic benefit, assessing a patient's molecular markers has to become the standard at diagnosis."

## **About the Phase I Program – The Time is Now**

MD Anderson's Phase I program is the largest of its kind and accounts for the majority – but not all – of the institution's earliest clinical studies. In 2010, of the 11,000 patients who participated in MD Anderson clinical trials, more than 1,150 were enrolled in one of the 120 Phase I trials in the program.

Currently, tumors are tested up for up to 12 molecular aberrations, but at the rate technology is rapidly advancing, Kurzrock expects that number to climb to more than 100 in the near future.

Patients treated in the Phase I Program are typically very ill and all other approved therapies have failed them. Yet they are 'fighters' who are willing to try anything, including studies not specific to their diagnosis to test the effectiveness of a new drug, drug combination or delivery method, said Kurzrock.

"This study affirms what we in the cancer community have been talking about for a decade – matching drugs to patients," said Kurzrock. "The time is now. The drugs are here. The technology is here, and with our program at MD Anderson we can bring the two together in hopes to offer the most personalized care for our patients."

Provided by University of Texas M. D. Anderson Cancer Center

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