Identifying patients who benefit most from immune suppressant

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A new analysis may help doctors identify breast cancer patients who will benefit from treatment with the immune suppressant drug everolimus, say French researchers at the 4th IMPAKT Breast Cancer Conference in Brussels, Belgium.

Everolimus is currently used as an immunosuppressant to prevent patients rejecting transplanted organs and in the treatment of renal cell cancer. Research is also being conducted into the drug's use in other cancers, including breast cancer.

Dr Thomas Bachelot, from Centre Leon Berard in Lyon and colleagues analyzed data from the TAMRAD study, published two years ago[1]. This was the first study to show that in patients whose cancer progressed after treatment with the aromatase inhibitor drug tamoxifen, the time-to-progression could be delayed by the addition of everolimus.

The new study aimed to identify which biological characteristics of the patient's primary tumor could be used to identify those for whom everolimus would be most effective. "This is of great importance, as everolimus is quite toxic and you don't want to give this drug if you're not sure the patient will benefit from it," Dr Bachelot explained.

"The interesting thing is that we did not find what we expected," Dr Bachelot said. The researchers had hypothesized that patients who would benefit the most from this treatment would be those with high expression levels of phosphatidylinositol 3-kinases (or PI3Ks), a family

of enzymes involved in cellular functions such as cell growth and proliferation.

"But the opposite seems to be true," Dr Bachelot said. In patients with low PI3K levels, median time-to-progression exceeded 30 months, while in those with high levels, median survival was 6.4 months.

"At the same time, we also found that the low expression of a protein that normally block mTOR activation, LKB1, was associated with a good response to everolimus, while patients with normal levels of this protein did not have the same good response. Those results suggest that patients with an activation of mTOR that is not dependent on PI3K are the ones who may benefit the most from everolimus."

"These are exiting results, as they may allow for a better selection of patients who should receive this very effective but sometimes toxic drug," Dr Bachelot said. The results need to be validated on an independent and larger cohort of patients before any definitive conclusion can be reached, he noted. The researchers hope this will be done in coming months.

Commenting on the study which he was not involved in, Dr Angelo Di Leo, from Hospital of Prato, Italy, former IMPAKT Co-Chair, said: "These are very attractive results, but still preliminary. For the time being we do not have molecular markers that can be used in clinical practice to select patients candidate to this treatment. It will be important to test the identified markers of response to everolimus, in particular PI3K, in the context of the recently presented large phase-III trials."

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