Investigational ovarian cancer drug shows promise against platinum resistant disease

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A drug being developed as a treatment for ovarian cancer has shown single agent activity with durable disease control in some patients in a Phase-II clinical trial, an international research group has reported.

Dr Ursula Matulonis from Dana-Farber Cancer Institute in the USA reported the results of the single-agent trial of the drug, called MLN8237, in a poster at the 35th Congress of the European Society for Medical Oncology (ESMO).

MLN8237 selectively inhibits an enzyme known as Aurora A kinase, which is a member of a family of kinase enzymes involved in normal cell division. Researchers have found that Aurora A kinase is over-expressed in some cancer cells, leading to growth of cancers.

"In epithelial ovarian cancer, Aurora A kinase has been reported to be frequently upregulated or overexpressed, and associated with worse clinical outcome," Dr Matulonis said. "This is why an effective Aurora A Kinase inhibitor is a potential new therapy to be used alone or in combination with other standard agents such as paclitaxel."

In addition to ovarian cancer, the Aurora A kinase gene is amplified or overexpressed, or both, in other cancers including colon, breast, pancreatic, and bladder cancers, as well as certain lymphomas, leukemias and myeloma.

Unlike other aurora kinase inhibitors currently being studied, MLN8237

selectively targets aurora A Kinase and can be administered orally, Dr Matulonis said.

In the current study, sponsored by Millennium Pharmaceuticals, American, French, Italian and Polish researchers treated 31 patients whose cancer was resistant or refractory to platinum-based chemotherapy and who had tried at least three other therapies. Twenty-five patients had ovarian cancer, 5 had primary peritoneal cancer, and one had Fallopian tube carcinoma.

"The patients enrolled to this study all had progression after platinum-containing regimens which is the mainstay of ovarian cancer treatment," Dr Matulonis said. "Patients with 'platinum resistant' recurrent ovarian cancer represent a large unmet medical need."

The patients received MLN8237 in 21-day cycles: seven days of twice-daily 50mg treatment, followed by a 14-day break. Three patients had a partial response to the treatment, and 5 had stable disease that was sustained for at least four 21-week cycles, the researchers report.

"The most important finding from this study was the fact that MLN8237 demonstrates single-agent activity in ovarian cancer with encouraging durable disease control in some patients," Dr Matulonis said.

Several patients have remained on the study drug for over 12 months, she noted. "I personally have a patient on this current study who has been on MLN8237 for now more than 12 months. She is doing remarkably well."

The fact that multiple patients had stable disease or response suggests that future development of MLN8237 in combination with other active agents may be a promising avenue to investigate, the researchers said.

"These durable responses are encouraging since all of the patients enrolled on this study have failed platinum. Because of the other durable responses reported in other MLN8237 studies, this all helps support the prediction that this is a new mechanism to fight cancer, and the MLN8237 drug does not appear to share mechanisms for resistance to other available drugs."

The researchers noted that the drug had various toxicities. The most common serious toxicities included neutropenia, stomatitis, leucopenia, thrombocytopenia and fatigue, which were generally reversible during the 14-day break in treatment. Five patients discontinued due to adverse events.

The fact that the drug has shown some efficacy in treating drug-resistant ovarian cancer "is worth exploring further," noted Professor Stan Kaye, Professor of Medical Oncology at the Royal Marsden Hospital.

Provided by European Society for Medical Oncology

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