New cancer drug shows potential in patients with BRCA mutations

June 6 2013

(Medical Xpress)—A new cancer drug designed to be effective in tumours with faulty BRCA genes has generated impressive responses in an early-stage clinical trial.

The drug, called BMN 673, targets DNA repair in cancer cells, and is designed specifically to attack tumours that have been left vulnerable by genetic mutations.

A small study involving Newcastle University found the drug was well tolerated by patients and showed 'excellent anti-tumour activity', the team has announced.

The trial results were presented at the American Society of Clinical Oncology (ASCO) meeting in Chicago, US, late yesterday. The trial was funded by US firm BioMarin Pharmaceutical and also involved several institutions in the USA.

The trial results covered 70 patients with a range of cancers – including ovarian or peritoneal, and breast. Patients with cancers linked to BRCA mutations saw the most substantial improvement.

The researchers used different measures of the drug's effect on tumour instability and breakdown. One was a clinical score called RECIST, which includes a range of measures such as whether visible lesions, or cracks, appear in the walls of tumours after treatment. Some 11 of 25 evaluable ovarian cancer patients with BRCA mutations had a RECIST-

positive response to treatment, as did seven of 18 breast cancer patients with BRCA mutations. Signs of some clinical benefit were seen in several more patients.

BRCA mutations reduce cells' ability to repair their DNA, and when inherited substantially increase the risk of developing a range of cancers, including breast, ovarian and prostate.

No targeted treatments have yet been approved specifically for use in patients who have inherited BRCA mutations.

BMN 673 – which is yet to be given a trade name – is one of a handful of a family of molecules called PARP inhibitors which are under development for the treatment of cancer. BMN 673 is one of the most promising PARP inhibitors currently being tested in clinical trials.

Nicola Curtin, Professor of Experimental Therapeutics at the Northern Insitute for Cancer Research at Newcastle University, said: "PARP inhibitors are an exciting class of drug because they are specifically designed to exploit a malfunction in DNA repair that is caused by mutations in BRCA genes. BMN 673 is the most potent PARP inhibitor in clinical development. We saw evidence of PARP inhibition in samples from patients on very low doses of BMN 673 and several patients responded well and the drug was well tolerated."

Study researcher Professor Johann de Bono, Professor of Experimental Cancer Medicine at The Institute of Cancer Research, London, and Honorary Consultant in Medical Oncology at The Royal Marsden, said: "Patients with germline BRCA-associated tumours have no targeted treatment options, and there is a real need for these to be developed. Our promising study showed that BMN 673, a potent member of a family of potential drugs called PARP inhibitors, had excellent anti-tumour activity.

"It's one of a range of new-style cancer therapies that target specific molecular defects in tumours and offer the potential of more personalised treatments to patients, including those with BRCA mutations."

Researchers now plan a larger, Phase 3 clinical trial of BMN 673 to further explore its potential effectiveness.

Provided by Newcastle University