Vintafolide combination for ovarian cancer

Ovarian cancer ranks second among gynaecological malignancies in the USA and Europe. Initial response rates to platinum-based chemotherapy are relatively high; however, most patients will subsequently develop resistant disease for which present therapies offer modest benefit. Unlike normal tissues, most ovarian cancers over-express high-affinity folate receptors.

In PRECEDENT, a phase 2 international trial for patients with platinum-resistant ovarian cancer, the folate receptor-targeting drug vintafolide (folic acid-desacetyl-vinblastine monohydrazide conjugate) was added to standard therapy with pegylated liposomal doxorubicin (PLD). Median progression-free survival (PFS) for participants receiving vintafolide plus PLD was 5·0 months compared with 2·7 months for PLD alone (hazard ratio 0·63, 95% CI 0·41–0·96; p=0·031). In the subgroup of patients with 100% of lesions expressing the folate receptor, median PFS was 5·5 months with combination therapy and 1·5 months with single-drug PLD (0·38, 0·17–0·85; p=0·013). Participants in the PLD-only group with 100% folate receptor-positive lesions had the shortest median PFS of any subset.

First author R Wendel Naumann (Levine Cancer Institute, Charlotte, NC, USA) described the merits of vintafolide, "a folate conjugated to a chemotherapy drug. This conjugate is not active in the blood, and normal cells don't express the folate receptor. The conjugate binds to the folate receptor on the tumour, undergoes endocytosis, and the active drug is then cleaved from the carrier in the cell."

For this study, 149 participants with measurable disease were randomly assigned in a 2:1 ratio to combination or single-drug therapy. At 28-day intervals, patients were intravenously administered vintafolide (2·5 mg three times a week, in weeks 1 and 3) plus PLD (50 mg/m² on day 1), or PLD alone (identical dose and schedule). The vintafolide and PLD combination was well tolerated.

"This study is a good example of targeted therapy", said David Mutch (Washington University School of Medicine, St Louis, MO, USA). "These two agents act by disparate mechanisms."

Naumann noted that a phase 3 study with this drug combination is currently underway, "The PROCEED trial is similar to the phase 2 trial in design, with the exception that each patient will undergo a scan before the patient goes on study to show all the lesions in the body and the level of the folate receptor."

Judith A Gilbert

Steve Gschmeissner/Science Photo Library

Published **Online**
October 25, 2013
http://dx.doi.org/10.1016/S1470-2045(13)70505-9

For the **study** see *J Clin Oncol* 2013; published online Oct 14. DOI:10.1200/JCO.2013.49.7685

Nab-paclitaxel shows promise in pancreatic cancer

A phase 3 study has shown that the addition of albumin-bound paclitaxel (nab-paclitaxel) to gemcitabine improved outcomes for patients with metastatic pancreatic cancer.

Daniel Von Hoff (Translational Genomics Research Institute, Phoenix, AZ, USA) and colleagues randomly assigned 431 patients to receive nab-paclitaxel plus gemcitabine and 430 to receive gemcitabine alone. Median overall survival, the primary endpoint, was 8·5 months in the nab-paclitaxel plus gemcitabine group and 6·7 months in the gemcitabine group (hazard ratio [HR] 0·72, 95% CI 0·62–0·83; p<0·001). 1-year survival was 35% in the nab-paclitaxel plus gemcitabine group versus 22% in the gemcitabine group; at 2 years, it was 9% versus 4%, respectively. Treatment-related adverse events of grade 3 or higher, including neutropenia, leucopenia, and fatigue, were more common in the nab-paclitaxel plus gemcitabine group than in the gemcitabine group. Peripheral neuropathy was also more common with nab-paclitaxel plus gemcitabine than with gemcitabine alone—70 patients who received the doublet chemotherapy had peripheral neuropathy, compared with three treated with gemcitabine alone.

David Cunningham and Elizabeth Smyth (The Royal Marsden, London, UK) told *The Lancet Oncology* that the study was "adequately powered to [show] a modest improvement in overall survival in a disease where few drugs have demonstrated benefit and gemcitabine has been a treatment standard for more than 20 years." As a result, they believe that "this combination is likely to become a standard treatment for patients with this disease…adding to the treatment options available for pancreatic cancer, which includes FOLFIRINOX (for selected patients) and other gemcitabine-based doublet chemotherapies."

Philip A Philip (Karmanos Cancer Center, Wayne State University, Detroit, MI, USA), concluded: "Now that the activity of nab-paclitaxel has been established in patients with metastatic pancreatic cancer, additional work is necessary to determine its role in the adjuvant setting and in patients with locally advanced unresectable pancreatic cancer. The value of nab-paclitaxel in older patients or those who have performance status less than 80% also needs to be determined. Finally, determination of tumor biomarkers that would predict response or lack of it in patients treated with nab-paclitaxel must also be developed to improve patient selection."

Holly Baker

Published **Online**
October 25, 2013
http://dx.doi.org/10.1016/S1470-2045(13)70506-0

For the **study** see *New Engl J Med* 2013; published online Oct 16. DOI:10.1056/NEJMoa1304369