Figitumumab has anti-tumor activity in Ewing's sarcoma

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A preliminary study of the anticancer drug figitumumab has found that it has antitumour activity in Ewing's sarcoma—a cancer which affects mainly teenage boys. The results have led to the drug's progression to a Phase 2 trial in patients with Ewing's sarcoma, which has recently finished recruiting. These are the conclusions of an Article published Online First in the Lancet Oncology. The study is by Dr Johann S de Bono, The Institute for Cancer Research (ICR), Sutton, UK, and The Royal Marsden NHS Foundation Trust, Sutton, UK, and colleagues.

Ewing's sarcoma is a rare disease in which cancer cells are found in the bone or soft tissue, most commonly the pelvis, femur, humerus, and ribs. It occurs most commonly it male teenagers with a male to female ratio of 1.6 to 1.

Data from preclinical studies have suggested that Ewing's sarcoma, and some other sarcoma subtypes, are dependent on the insulin-like growth factor signalling pathway. Figitumumab is a drug which targets the insulin-like growth-factor-1 receptor (IGF-1R). This phase I study was carried out to assess the effects of figitumumab in these sarcoma subtypes.

Between January, 2006, and August, 2008, patients with refractory, advanced sarcomas received figitumumab (20 mg/kg) in two groups within a phase 1 trial. The first cohort (15 patients) included patients with multiple sarcoma subtypes, age 18 years or older, and the second cohort (14 patients) consisted of patients with refractory Ewing's

sarcoma, age nine years or older. The primary endpoint was to assess the safety and tolerability of figitumumab.

Of the 29 patients that were enrolled, 16 had Ewing's sarcoma, and the 29 received a total of 177 cycles of treatment (median 2, mean 6, range 1□□). In terms of adverse events, grade 3 deep venous thrombosis, grade 3 back pain, and grade 3 vomiting were each noted once in individual patients; one patient had grade 3 or 4 raised liver enzymes. The only other grade 4 adverse event was raised concentrations of uric acid, noted in one patient. A total of 28 patients were assessed for response; two patients, both with Ewing's sarcoma, had objective responses (one complete response and one partial response) and eight patients had disease stabilisation (six with Ewing's sarcoma, one with synovial sarcoma, and one with fibrosarcoma) lasting four months or longer.

The authors say: "Figitumumab is well tolerated and has antitumour activity in Ewing's sarcoma, warranting further investigation in this disease."

They conclude: "Our results show that figitumumab can be safe for both adult and paediatric sarcoma patients, and has single-agent antitumour activity in different sarcoma subtypes, including Ewing's sarcoma. Phase 2 studies of figitumumab and other anti-IGF-R agents in Ewing's sarcoma and other sarcoma subtypes are now completing accrual and rational combinations with other treatments are also being pursued."

In an accompanying Reflection and Reaction comment, Dr Jeffrey A Toretsky, Georgetown University, Washington DC, USA, and Dr Richard Gorlick, The Albert Einstein College of Medicine of Yeshiva University, The Children's Hospital at Montefiore, Bronx, NY, USA, say: "With several different companies developing IGF-1R inhibitors, there could be ample opportunity to optimise clinical benefit from IGF-1R blockade, although the development of these antibodies may be

complicated. Five-drug chemotherapy is routine in the treatment of Ewing's sarcoma, therefore improvement in outcome for these patients will likely require demonstration of the feasibility of combining the antibody with standard chemotherapy. Ultimately, a phase 3 randomised study investigating the benefit of this combination might provide the proof of activity that will achieve the IGF-1R-pathway promise."

Source: Lancet