As a result of these findings, we have re-analysed the results of the 23 published studies on height and breast cancer risk [2]. Adding to these the study of Tavani and colleagues there have been nine which found no association between height and breast incidence and 14 which showed a positive relationship, with taller women being at higher risk. None of the negative studies were prospective compared with eight (57%) of the positive publications. Within the studies which showed no association, height was self-reported in eight (89%). In contrast, in the positive studies, only four (29%) used self-reported height as a risk factor (χ^2 (Yates correction) = 5.75, $P < 0.01$).

These findings suggest that misreporting of extremes of height may be a common human failing. Whether this has any gender basis cannot be determined from these results. Certainly we should not underestimate the impact of personal feelings about being too short or too tall in terms of inaccuracy of self-reporting of height in those who perceive themselves as having stature outside of the 'normal' range. Adult height will depend upon a variety of both genetic and environmental factors. Interestingly, a recent study has suggested that women with *BRCA-1* mutations were more likely to have low birth weight and length [3]. This effect was present in women born between 1936 and 1971, suggesting that this was unaffected by changes in nutrition. Hence, it is possible that the increased risk associated with height is a marker of environmental exposure to both nutrients and carcinogens. Future epidemiological studies examining risk factors should avoid self-reported height estimates and rely instead upon objective measurement of stature.

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The EORTC Phase II Study of Iproplatin in Advanced Osteogenic Sarcoma

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Osteosarcoma of the extremities, recognised usually as a high grade tumour, affects mainly children and young adults. During the last few decades, the introduction of aggressive cisplatin-based combination chemotherapy has dramatically improved long term survival to 65% [1]. Iproplatin (*cis*-dichloro-*trans*-dihydroxy-bis(isopropyl-amin)platinum IV) was introduced in the 1980s as a new second generation platinum compound, which had shown less nephro- and neurotoxicity than cisplatin in preclinical studies and phase I trials [2, 3]. Early results suggested moderate activity of the drug in several tumours, even if these were considered as chemorefractory [4–6]. In this study, iproplatin was evaluated in the treatment of advanced and relapsing osteosarcomas.

Patients with histologically proven, measurable, pretreated metastatic osteosarcoma were investigated in this study. The other eligibility criteria were: patients' informed consent, WHO performance status ≤ 2, age 5–55 years, as well as adequate renal, liver and haematological function tests (white blood cell count (WBC) $> 4.0 \times 10^9$/l, platelet count $> 125 \times 10^9$/l). Pretreatment investigations included a complete medical history, physical examination, laboratory data (haemoglobin, WBC and platelet count, clinical chemistry),

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chest X-ray and initial measurement investigations (computed tomography (CT) scan or ultrasound of intra-abdominal or mediastinal masses). A complete blood count was repeated weekly and the haematological toxicity analysis was based on nadir counts.

Iproplatin, given at a dose of 240 mg/m^2 intravenously (i.v.) on day 1, in an i.v. infusion within 60 min, every 4 weeks, was continued until progression or the occurrence of unacceptable toxicity. Treatment was postponed if the WBC count was $< 3.0 \times 10^9$ or the platelet count was $< 100 \times 10^9$ on day 1, until recovery above these values with a maximum delay of 3 weeks. Patients were evaluated after two courses. Response and toxicity were defined according to the WHO criteria [7].

19 patients from 12 institutions were registered into the trial. 4 patients (21%) were ineligible because of inadequate baseline data. The median age of the 15 eligible patients was 18 years (range 12–25 years). One patient (7%) had a performance status of 0, 7 (47%) had a performance status of 1 and 7 (47%) had a performance status of 2. Prior local treatment consisted of: surgery only in 11 patients (73%), radiotherapy only in 1 patient (7%) and combination of both in 2 patients (13%). One patient (7%) had no prior local treatment. All patients received prior systemic treatment, with cisplatin-based first line chemotherapy given in 14 patients (in 7 patients as an adjuvant and in 7 patients for advanced disease), the last patient received a methotrexate-based regimen. The marker lesions followed were the primary tumour in 7 patients, lung metastases in 14 patients and soft tissue metastases in 3 patients.

A median of two treatment cycles (range one to three) were administered. In 1 patient (7%) stabilisation of disease lasting for 3 weeks was reported. Treatment failures were seen in 14 patients (93%) with early progression observed in 6 patients (40%) and early death in 1 patient (7%). Iproplatin at the given dose was well tolerated. Grade 3 or 4 thrombocytopenia was observed in 3 patients (20%). No severe leucopenia was reported. Except for grade 3 vomiting seen in 6 patients (40%), no other severe non-haematological toxicity was observed.

In this single-armed, non-randomised trial, no response to iproplatin in a group of cisplatin pretreated patients with advanced osteosarcomas was observed. We conclude therefore, that at this dose and schedule iproplatin cannot be recommended for treatment of cisplatin pretreated osteosarcoma.

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