Trial Watch

INHIBITING SURVIVIN

A phase I, first-in-human study of YM155, a small-molecule inhibitor of the anti-apoptosis protein survivin, has indicated that the drug can be safely administered and might have anti-tumour activity.

A range of YM155 doses were administered for 127 cycles to 41 patients who had solid malignancies that were refractory to standard therapy or for whom there was no standard therapy. In general, toxicities were reversible, and severe toxicities were rare. At the maximum tolerated dose (MTD), the plasma concentrations of YM155 exceeded those shown to have anti-tumour activity in preclinical models. Indeed, several tumour responses were observed in patients receiving YM155 at or below the MTD. Of five patients with chemotherapy-refractory non-Hodgkin lymphoma, one complete and two partial responses lasting 8, 24+ and 48+ months were observed. Two of nine patients with hormone-refractory and docetaxel-treated prostate cancer had prostate-specific antigen responses.

The overall safety and pharmacokinetic profile of YM155 and its observed anti-tumour activity in several patients indicate that further clinical testing of this agent is warranted.

ORIGINAL RESEARCH PAPER Tolcher, A. W. *et al.* Phase I and pharmacokinetic study of YM155, a small-molecule inhibitor of survivin. *J Clin. Oncol.* 29 Sep 2008 (doi: 10.1200/JCO.2008.17.2064)

PRENATAL ENVIRONMENT AND BREAST CANCER RISK

It has been proposed that the hormones, for example oestrogen, and other biological factors that a baby is exposed to *in utero* (the prenatal environment) can affect breast cancer risk in adulthood, but findings from studies addressing this have been inconsistent. A collaborative group led by Isobel dos Santos Silva conducted a pooled analysis of individual participant data from 32 studies to investigate whether birth size (weight, length and head circumference), as a surrogate measure of the prenatal environment, influences breast cancer risk later in life.

Data were analysed for 22,058 women who developed breast cancer and 604,854 who did not. The authors found that birth weight, length and head circumference were all positively associated with risk of breast cancer in adulthood. Adjustment for each factor indicated that birth length was the strongest independent predictor of future risk. Women who were ≥51 cm long at birth had a 17% higher risk than those that were 49–50 cm at birth. Furthermore, the increased risk with birth size persisted when other established breast cancer risk factors were taken into consideration.

This study provides compelling evidence that there is a link between birth size and breast cancer risk. The authors estimate that high birth size could account for about 5% of all breast cancers in developed countries.

ORIGINAL RESEARCH PAPER dos Santos Silva, I. *et al.* Birth size and breast cancer risk: re-analysis of individual participant data from 32 studies. *PLoS Med.* **5**, e193 (2008)