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IN BRIEF

BREAST CANCER

Enzalutamide—a new treatment for ER-positive disease

The androgen receptor (AR) is expressed widely in breast cancer and has been proposed as a therapeutic target in patients who do not express the oestrogen receptor (ER). However, its role in women with ER-positive tumours is uncertain. The AR inhibitor, enzalutamide, exerts its effects by preventing nuclear localization of the AR. Now, a study in 192 women with ER-positive breast cancer has shown that the AR:ER ratio is a significant predictive factor for risk of breast cancer. A high AR:ER ratio demonstrated a fourfold increased risk of failure to respond to tamoxifen treatment, and the AR:ER ratio was an independent predictor of disease-free survival and disease-specific survival. In breast cancer xenograft models, enzalutamide was also shown to inhibit oestradiol-mediated cell growth, indicating that this agent could be used to treat AR-positive tumours, regardless of the ER status.

Original article Cochrane, D. R. *et al*. Role of the androgen receptor in breast cancer and preclinical analysis of enzalutamide. *Breast Cancer Res*. doi:10.1186/bcr3599

PANCREATIC CANCER

Frondoside A enhances the effects of gemcitabine

Pancreatic cancer has a very poor prognosis. Gemcitabine is the current standard therapy, but more-effective treatments are needed. A study in human pancreatic cancer cell lines has shown that the triterpenoid, frondoside A, when combined with gemcitabine, could serve as a promising new treatment approach for treatment of this disease. In an athymic mouse model, tumour growth was significantly reduced with the gemcitabine–frondoside A combination compared with either drug alone, even when gemcitabine was used at the lowest dose tested (4 mg/kg). These results indicate that this combination might provide clinical benefit in patients.

Original article Al Shemaili, J. *et al*. Frondoside A enhances the antiproliferative effects of gemcitabine in pancreatic cancer. *Eur. J. Cancer* doi:10.1016/j.ejca.2014.01.002

BREAST CANCER

Overcoming resistance with dual HER2 blockade

Although many treatment advances in breast cancer have been made, resistance inevitably develops. Activating mutations in *PIK3CA* that occur in patients with *HER2* amplification can often confer resistance to anti-HER2 therapies. Using the SNaPshot assay, researchers have idenitifed 'hotspot' *PIK3CA* mutations in cells resistant to the HER2 inhibitor lapatinib. They showed that the *PIK3CA* mutations partially uncouple PI3K signalling from HER2, and that resistance could be overcome by using the pan-PI3K inhibitor BKM120. In mice with *HER2*-amplified tumours, dual HER2 blockade with trastuzumab and lapatinib resulted in tumour regression, and the addition of BMK120 further improved tumour regression. The combination of PI3K inhibition with dual HER2 blockage seems to circumvent resistance to HER2 inhibitors, providing a rationale to further explore this strategy.

Original article Rexer, B. N. *et al*. Direct inhibition of PI3K in combination with dual HER2 inhibitors is required for optimal antitumor activity in HER2+ breast cancer cells. *Breast Cancer Res*. doi:10.1186/bcr3601