In this issue

A new prognostic marker for breast cancer?

The genes *TSC1* and *TSC2* encode the putative tumour suppressor proteins hamartin and tuberin, respectively. Germ line mutation in either *TSC* gene leads to the development of the heritable tuberous sclerosis disorder that is characterised in part by the presentation of solid tumours. So far, the role of tuberin and hamartin in tumour suppression has been linked to mainly renal and brain solid tumours that are common in tuberous sclerosis. In this issue of EJC, as part of an ongoing study of tumour suppressor gene expression, Jaing and colleagues have investigated *TSC1* and *TSC2* expression in human breast cancers. Both hamartin and tuberin were strongly expressed in normal mammary epithelial cells. However, in invasive tumour tissues, the levels of both proteins were significantly reduced. Tumours from patients who developed recurrence and died had significantly lower levels of tuberin compared with those who remained disease free. Likewise, hamartin levels were significantly lower in patients with metastasis, recurrence and mortality. In contrast to the *TSC2* tuberin gene, DNA analysis showed that hamartin *TSC1* gene promoter was heavily methylated in tumours. The authors conclude that reduced expression of *TSC1*gene regulated by promoter hypermethylation is associated with an unfavourable clinical outcome in patients with breast cancer.

Strengthening the link: Choroid plexus tumour and mutant *TP53*

Choroid plexus brain tumours are extremely rare, typically diagnosed in early childhood and represents about 1% of all paediatric cancers. These tumours have been found in many familial cancer syndromes including Li-Fraumeni where patients have germ line *TP53* gene mutations. In this issue of EJC, Krutilkova and colleagues report on five new families of patients with childhood choroid plexus carcinomas carrying germ line mutations in the *TP53* gene. The identification of these families adds further support to the view that the presence of this type of brain tumour is indicative of having acquired *TP53* mutations. Importantly however, only one of the families conformed to the criteria of Li-Fraumeni syndrome and only three met the Chompret criteria for germ line *TP53* mutation testing. In two families, there was no family history of cancer and they did not meet any clinical criteria for *TP53* genetic analysis. The authors suggest that *TP53* gene testing should be considered in all patients with choroid plexus carcinoma. The association of childhood choroid plexus carcinoma with germ line *TP53* mutations can have important consequences for the relatives of the patients who can be at increased risk of cancer and can also have practical implications for patient treatment.

Clinical response: To confirm or not to confirm

Response rate is the most widely used surrogate marker for anticancer drug activity and is fundamental to clinical oncology research. Several guidelines exist to ensure that response assessment is uniform and consistent. All guidelines state that once a clinical response is observed, it must be confirmed by repetition after a minimum interval from the initial observation. Nonetheless, on careful analysis, the rationale for requiring response confirmation is neither clear nor self-evident. In this issue of EJC, Perez-Gracia and colleagues report on the results of a study designed to compare the validity of response rate assessment determined with or without secondary confirmation. Using specified criteria, nine trials of a single cytotoxic drug including 416 patients were selected from a pharmaceutical database. Objective response rates were assessed by single or two separate evaluations. The results show that response rates determined by single assessments were similar to the results gained when secondary conformation was required. In each of the trials analysed, the observed Kappa coefficient reflected concurrence between the two methods. The authors assert that assessing response rate without confirmation may be a valid, cheaper and easier protocol, but concede that their results should be confirmed by additional studies.

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