Highlights from this issue

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LUMINAL

A global consensus report on fistulising peri-anal Crohn's disease

The World Congress of Gastroenterology 2013, held in Shanghai, called for the development of state-of-the-art, evidence based views for designated areas of gastroenterology. An expert consensus group was formed and developed a consensus on the classification, diagnosis and multidisciplinary treatment of perianal fistulising Crohn's disease (pCD), based on best available evidence (***see page 1381***). The group carried out a systematic literature review; statements were formed, discussed and approved in multiple rounds. Consensus was defined as at least 80% agreement among voters. Evidence was assessed using the modified GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria. Based on a multidisciplinary approach, items relevant for fistula management were identified and algorithms on diagnosis (see figure 1) and treatment of pCD were developed. This is an important document that is relevant to all clinicians involved in managing Crohn's Disease patients.

A practical gene signature for determining prognosis for colorectal cancer

The advent of robust methods to determine gene expression profiles in cancer has led to the discovery of a number gene signatures in colorectal cancer that identify cancers with good and poor prognosis. However, most of these profiles have not moved into the clinic, in part because of the practical challenges of working with RNA in the clinical setting. Chang and colleagues have addressed this limitation of current gene profiles by developing a validated immunohistochemistry (IHC) signature for determining the prognosis of colorectal cancer. Using RNA microarray data, they found five signatures with high concordance and reproducible prognostic value. They then integrated these results into a sub-network and found a signature that included GRB2, PTPN11, ITGB1, and POSTN. A prognosis score that used IHC results of these four genes had better prognostic values for 5-year disease-free survival than did tumour-node-metastasis staging in discovery and validation cohorts. Their prognosis score was also effective at identifying patients most likely to respond to chemotherapy. This exciting advance has substantial potential to move quickly into the clinic and to improve the care of patients with colorectal cancer.

A better way to treat pancreatic cancer?

Pancreatic cancer is one of the most lethal cancers, in part because of the lack of effective medical therapies. Current chemotherapy regimens provide modest survival benefit. Novel effective therapies are needed for the treatment of this disease, which has led to efforts to design targeted therapies directed at gene mutations present in these cancers. Although oncogenic KRAS mutation appears to be the usual initiating molecular event in pancreatic cancer, the progression of this cancer appears to depend on mutations in other genes, such as phosphatase and tensin homolog (*PTEN*), which then leads to activation of signalling pathways, like the mammalian Target of Rapamycin (*mTOR*) signalling pathway. Morran *et al* have now found in mouse models of pancreatic cancer that the combination of oncogenic KRAS and inactivated *PTEN* leads to cancers that are highly dependent on activated *mTOR* signalling (***see page 1481***). This discovery is particularly exciting because targeted therapies that inhibit the *mTOR* signalling pathway are rapidly moving into the clinic and may be especially effective in the treatment of pancreatic cancers that have oncogenic KRAS and inactivated *PTEN*.

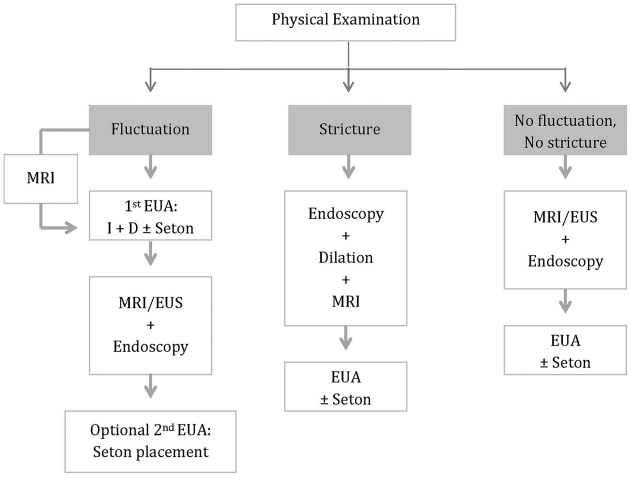

Figure 1 Diagnostic algorithm for pCD.

HEPATOLOGY

New insights into HCV infection of human hepatocytes

Cellular systems are of great importance to study mechanisms of HCV infection. Unfortunately, the viral constructs available as yet are mainly cell clones derived from hepatocellular carcinoma (HCC) and do not reflect the broad spectrum of HCV diversity. Using primary human hepatocytes a French group has established a reliable system of infection with sera from HCV infected patients ***(see page 1490)***. They observed large inter-individual differences of infectiousness. Importantly, HCV sera with low concentrations of cytokines involved in inflammation and immune response were most infectious. This authentic system based on primary liver cells will become a valuable tool for further research for example, for testing novel antiviral drugs against various HCV genotypes. Please also read the expert commentary by T Pietschmann ***(see page 1375)***.

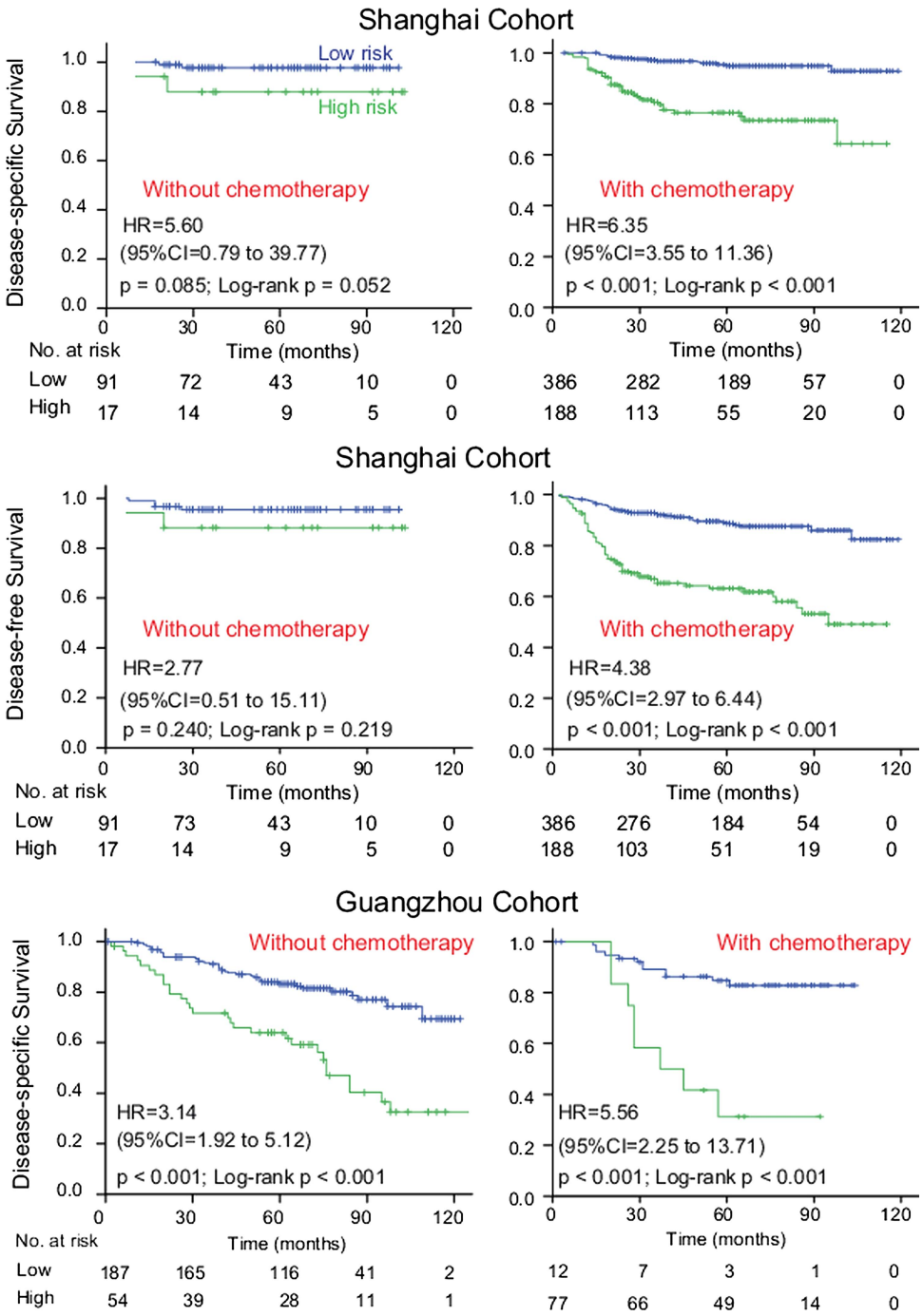

Figure 2 Combined analysis of the Shanghai cohort and the Guangzhou cohort examining the association between the scores of IHC signature and survivals of stages II and stage III colorectal carcinoma patients with postoperative chemotherapy.

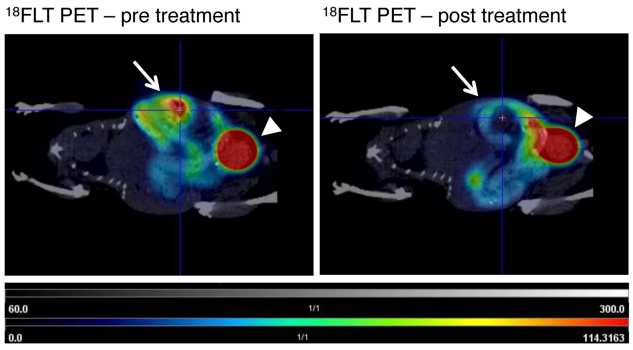

Figure 3 (C) Representative 18FLT positron emission tomography (PET)-CT images show the PET signal emitted from the pancreatic tumour (white arrows) as well as excreted tracer in the bladder (arrowheads) in a mouse with pancreatic cancer at time of presentation (left panel), and after 4 days rapamycin treatment (right panel).

Complex role of p21 in HCC

P21, a cyclin dependent kinase inhibitor traditionally has been considered as a tumour suppressor. The role of p21 in HCC is poorly understood and controversially discussed. In an animal model with chronic cholestasis this interesting study from Germany suggests a dual role of p21 for liver regeneration and carcinogenesis ***(see page 1501)***. Whereas p21 was required for hepatocyte proliferation during chronic liver injury it also promoted tumour development. Moreover in human HCC p21 expression was associated with poor prognosis. These exciting findings are covered by an insightful commentary on ***(see page 1372)***.