IN BRIEF

IBS

Remotely delivered cognitive behavioural therapy superior to treatment as usual for IBS

Cognitive behavioural therapy (CBT) can reduce IBS symptom scores; however, the current availability of this therapy is poor and uncertainty exists in its long-term effectiveness and optimum mode of delivery. In a randomized controlled trial in primary and secondary care conducted in the South of England, the clinical effectiveness of telephone-delivered CBT (TCBT) and web-delivered CBT (WCBT) for IBS were compared with treatment as usual (TAU). Out of 1,452 patients with refractory IBS screened for eligibility, 558 were allocated to one of the three treatment groups. After 12 months follow-up, the co-primary outcomes of IBS Symptom Severity Score and Work and Social Adjustment Score were both significantly decreased ($P \leq 0.002$) in the groups receiving TCBT and WCBT compared with TAU. The trial shows that sustained improvements to IBS symptoms can be achieved with remotely delivered therapies that could increase CBT availability in isolated or resource-poor locations.

ORIGINAL ARTICLE Everitt, H. A. et al. Assessing telephone-delivered cognitive–behavioural therapy (CBT) and web-delivered CBT versus treatment as usual in irritable bowel syndrome (ACTIB): a multicentre randomised trial. *Gut* https://doi.org/10.1136/gutjnl-2018-317805 (2019)

VIRAL HEPATITIS

HCV-infected lungs and hearts can be safely transplanted into non-infected individuals

The transplantation of organs from donors with hepatitis C viraemia is typically avoided, but the advent of direct-acting antiviral (DAA) agents could prevent transmission of HCV to the recipient and enable the use of HCV-infected organs. In a US-based open label trial, 44 patients without HCV infection received organ transplantations (36 lungs, 8 hearts) from HCV-infected donors, immediately followed by a 4-week regimen of a pangenotypic DAA agent. Of the 35 patients with at least 6 months of follow-up, all had excellent graft function with a sustained undetectable hepatitis C viral load from ~2 weeks after transplantation. Thus, this approach of preventing establishment of HCV infection with DAA therapy could increase the available donor organ pool.

ORIGINAL ARTICLE Woolley, A. E. et al. Heart and lung transplants from HCV-infected donors to uninfected recipients. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1812406 (2019)

IBD

CT-P13 biosimilar is non-inferior to infliximab

Anti-TNF therapy is effective in IBD but the high costs of some biologic agents necessitate the development of biosimilar drugs. CT-P13 is a biosimilar of the anti-TNF agent infliximab and has been approved for patients with IBD on the basis of extrapolation in other indications, but a direct comparison of infliximab with a biosimilar for patients with IBD was lacking. Now, in a phase III randomized controlled trial, 220 patients with Crohn's disease and naive to biologic agents were allocated to groups receiving CT-P13 or infliximab for 1 year, with a switch in therapy at week 30. After 6 weeks, the proportion of patients with a ≥70-point decrease in Crohn's Disease Activity Index scores were similar in groups receiving CT-P13 or infliximab, establishing non-inferiority for CT-P13. Over the full study period, treatment-emergent adverse events were also similar between the groups.

ORIGINAL ARTICLE Ye, B. D. et al. Efficacy and safety of biosimilar CT-P13 compared with originator infliximab in patients with active Crohn's disease: an international, randomised, double-blind, phase 3 non-inferiority study. *Lancet* **393**, 1699–1707 (2019)

LIVER

Mutational landscape in liver disease — fit for regeneration?

A new study published in *Cell* has used deep sequencing to offer insights into the mutational landscape of human chronic liver disease, identifying recurrent mutations. Moreover, in vivo CRISPR–Cas9 screening in a mouse model validated the functional relevance of these somatic mutations, demonstrating roles in hepatocyte fitness and liver regeneration.

"It is now clear that normal tissues such as blood, skin and oesophagus harbour a large number of somatic mutations, something previously thought to be more exclusive to cancer," explains author Hao Zhu. "In the setting of chronically diseased livers, we identified a broad range of recurrent mutations, many of which were in genes not known to be involved in cancer," he says, adding that there was a knowledge gap in the field as to whether mutations in normal cells within solid organs are functional and can alter cellular physiology or regeneration.

Zhu and colleagues performed whole-exome sequencing of liver samples from 82 individuals (one normal liver sample, with the remainder from patients with chronic liver disease including cirrhosis). Author Tao Wang's team led the bioinformatics analyses, which revealed a complex mutational landscape with extensive mutational burden and heterogeneity. Further ultra-deep sequencing identified recurrent mutations in *PKD1*, *PPARGC1B*, *KMT2D* and *ARID1A* in diseased livers. Notably, the number and volume of clones carrying mutations increased as a function of fibrosis stage and level of liver damage.

To further examine the functional relevance of these mutated genes, the researchers established an in vivo CRISPR–Cas9 screen of 147 genes in *Fah*-knockout mice, which

BIOMATERIALS

Turning up the heat on gastrointestinal delivery systems

Two new temperature-responsive drug delivery systems have been developed. Proof-of-concept experiments in pigs demonstrated that the devices could deliver drugs to the oesophagus and stomach and, upon addition of warm water as a stimulus, the biomaterials within changed shape or disassembled for easier passage through the gastrointestinal tract.

"Gastrointestinal devices are being applied broadly across clinical indications ranging from cancer to systems for drug delivery and energy harvesting," explains first author Sahab Babaee. Control of such devices with certain triggers (such as pH) can improve their functionality and the researchers reasoned that ingestion of warm water (at 55°C) could act as a trigger for temperature-responsive elements.

Using pigs as a large-animal model, Babaee and colleagues first characterized temperature changes across the upper gastrointestinal tract. They identified two zones where temperature could be controlled using high volumes of warm water (100–250 ml), the oesophagus and stomach, and tailored device development to these regions.

Combining mechanical metamaterials and thermoresponsive elements (e.g. shape-memory nitinol) in their design, two different prototype devices were developed. Inspired by a blooming flower, the capsule-sized oesophageal system opened up to reveal millineedles attached to 'petal' arms that could deliver drugs to the oesophageal mucosa and, after ingestion of warm water, reverted to its original capsule shape to pass through to the stomach. For prolonged large-dose gastric drug delivery, a highly flexible macrostructure could deform into a cylindrical shape to pass through the oesophagus before forming a