New and emerging regenerative approaches for gastrointestinal disease

The gastrointestinal system consists of the digestive tract and its accessory organs. It is responsible for the digestion and metabolism of food, and the absorption of the resulting nutrients. The gastrointestinal system consists of the mouth, pharynx, oesophagus, stomach, small and large bowel, and anus. The accessory organs include the tongue, salivary glands, pancreas, liver and gallbladder and biliary tract.

Common gastrointestinal conditions include stomach, pancreas and colorectal cancer; inflammatory bowel disease (ulcerative colitis and Crohn’s disease); perianal fistula; faecal incontinence and liver disease.

We searched horizon scanning and commercial databases, clinical trial registries and UK-based regenerative medicine networks and organisation for new and emerging regenerative approaches for the treatment of gastrointestinal diseases. We included technologies in late phase clinical trials with evidence of recent activity on clinical trial databases. We also included cell-based extracorporeal bioartificial liver assist devices which, although they do not fall into the definition of a regenerative approach, use a cellular approach. We excluded technologies for diseases of the mouth, pharynx and salivary glands.

Findings and regenerative approach

We found 20 new and emerging regenerative technologies. Of these eight (40%) were in development for cancer, six (30%) for liver disease, and two (10%) each for fistula, inflammatory bowel disease and faecal incontinence. The graph overleaf shows the clinical trial phase for each disease group. The full HSRIC report gives the names and details of the technologies we identified.

The identified technologies used regenerative approaches which differed by the disease:

- all cancers are being targeted by cell therapies which aim to increase immune stimulation with or without genetic modification to the cells, or genetic modification of cells leading to localised drug activation,
- inflammatory bowel disorders are being targeted using cell therapy aiming to stimulate exogenous repair, and
- all other disorders are being targeted using cell therapy with cell transplantation or with extracorporeal cell therapy devices.

For cancer, four products are in development for colorectal cancer (one phase III, one phase II/III and two phase II), three for pancreatic cancer (one phase III and two phase II) and one for oesophageal cancer (phase II).
Products in phase III trials

We found five technologies in phase III commercially-sponsored clinical trials, four of which are likely to be licensed through the EMA ATMP regulations route.

The final product in phase III trials is an extracorporeal liver assist device (ELAD) from Vital Therapies. This product was reported not to have reached its survival primary endpoint in an earlier trial in this patient group (company website), but showed promise in younger patients without significant kidney and blood clotting dysfunction. Vital Therapies are in the planning stages for a trial in a more constrained group of patients with alcohol induced liver decompensation (VTI-308, NCT02612428).

Conclusions

Regenerative techniques in gastrointestinal disease appear to be moving on from ‘simple’ stem cell transplantation to the use of cells in more complex approaches. These include the stimulation of immune and exogenous repair systems in inflammatory bowel disease where there are known inflammatory components of the condition, and the targeting of specific tumour antigens in cancer. The regenerative approach in conditions such as perianal fistula and faecal incontinence, without an inflammatory component, remains with the transplantation of allogeneic or autologous condition-relevant stem cells.

HSRIC will monitor the identified products through later clinical development, informing key health service and research policy and decision makers when appropriate. In April 2015, HSRIC wrote a briefing on: CX601 for perianal fistula associated with Crohn’s disease.

For further details of the technologies we identified and references, please read the full NIHR HSRIC report which is free to download.