There is ongoing progress in the understanding of the molecular basis and subgroups of pancreatic cancer, but therapeutic target alterations are rare and treatment options are still mainly based on classic cytotoxic drugs. In The Lancet Gastroenterology & Hepatology, Jean-Bapiste Bachet and colleagues report the findings from their non-comparative, randomised first-line phase 2 trial in 114 previously untreated patients with metastatic pancreatic cancer, assigned (2:1) to either the experimental combination of simplified leucovorin and infusional fluorouracil plus nab-paclitaxel or to gemcitabine plus nab-paclitaxel. The primary endpoint of more than 50% of participants in the leucovorin and fluorouracil group being alive and progression free at 4 months was reached (at 4 months, 40 [56%, 90% CI 45–66] of 72 patients in the leucovorin and fluorouracil group were alive and free from disease progression; 21 [54%, 40–68] of 39 patients in the gemcitabine group were also alive and progression-free at 4 months). Both regimens were tolerable, although their toxicity profiles differed markedly: more hepatic and haematological toxicities occurred in the gemcitabine group and more febrile neutropenia, mucositis, paresthesia, alopecia, and hand–foot syndrome occurred in the leucovorin and fluorouracil group. Overall, the study results warrant further study of the simplified leucovorin and infusional fluorouracil plus nab-paclitaxel combination.

For patients with pancreatic cancer who are intolerant or have disease progression while on adjuvant or palliative gemcitabine, simplified leucovorin and infusional fluorouracil plus nab-paclitaxel could be considered an additional treatment option beyond the combinations of infusional fluorouracil–folinic acid with oxaliplatin or nanoliposomal irinotecan. Evidence from clinical trials suggests that gemcitabine is equally as efficacious as infusional fluorouracil–folinic acid; because of the different toxicity profiles of leucovorin and fluorouracil plus nab-paclitaxel and gemcitabine plus nab-paclitaxel regimens, each with a low risk of grade 4 adverse effects, both might provide the backbone for experimental multiple-drug combinations in advanced pancreatic cancer.

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I have received fees for advice and talks from Celgene and Shire.


Direct-acting antivirals for acute HCV: how short can we go?

Treatment for individuals with hepatitis C virus (HCV) infection has evolved rapidly, with combinations of two or more different classes of direct-acting antivirals for 8–12 weeks achieving sustained virological response (SVR) in more than 95% of treatment-naive, non-cirrhotic individuals with chronic HCV infection.1–3

In this context, the optimal management of acute HCV infection is uncertain. With little data available, recent international guidelines support a fairly conservative approach, with the American Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD–IDSA) guidelines advocating the same regimens for acute HCV as recommended for chronic HCV, while the European Association for the Study of the Liver (EASL) guidelines suggest sofosbuvir plus an NS5A inhibitor for 8 weeks, with a longer duration of...
12 weeks for those with HIV or baseline HCV RNA higher than 1 000 000 IU/mL.

Trials are underway to fill this evidence gap, assessing short duration direct-acting antiviral regimens in acute (<6 months) and recent (<12 months) HCV infection. Preliminary results following 4 weeks and 6 weeks of sofosbuvir–ledipasvir for acute HCV infection in HIV patients, whereas SVR was lower in Rockstroh and these individuals might prevent onward transmission, including those with acute and recent HCV, including DAHHS-2 (NCT02600325) and REACT (NCT02625909).

Access to HCV treatment for people at high risk of onward transmission, including those with acute and recent HCV infection, should be a priority. As we begin to explore the use of ultrashort direct-acting antiviral therapy in acute and recent HCV infection, one question persists: how short can we go?

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Restrictive blood transfusion for gastrointestinal bleeding

Since 1990, global life expectancy has increased by an average 6·3 years, ranging from 3.8 to 8.3 years across continents.1 This striking result was achieved in many fields of preventive and clinical medicine, without a dominant impact of any single measure or field. Major improvements were noted in areas such as trauma care, oncology, and cardiovascular medicine. The latter, for instance, led to the current situation in many western countries where more patients die of chronic heart failure than of acute myocardial infarction. In gastroenterology, we have seen similar improvements: in gastrointestinal oncology for instance, the median survival of patients with advanced colorectal cancer (one of the most common malignancies) strongly increased from only 6 months with best supportive care to more than 2 years with combination treatment.2 However, such improvements were not achieved for all gastroenterological conditions. Mortality associated with gastrointestinal bleeding (the most common gastrointestinal emergency) only marginally improved. New techniques, such as endoscopic haemostasis, continuous profound acid suppression, and interventional radiology, have been introduced. At the same time, the average patient profile changed from elderly patients with drug-related ulcers and comorbidity to elderly patients with recent hepatitis C virus infection: The DARE-C II study. Hepatology 2016; 64: 1921–21.

The paper by Ayodele Odutayo and colleagues4 in The Lancet Gastroenterology & Hepatology further marks the borders of this narrow path of optimal management of patients with acute upper gastrointestinal bleeding by focusing on transfusion policies. Restrictive transfusion, usually at a haemoglobin threshold of 70–80 g/L, has been studied in various other conditions, including trauma, myocardial infarction, septicaemia, stroke, and bone marrow failure. Another recent meta-analysis5 included 31 trials with 12,587 patients with a range of conditions. Restrictive transfusion led to 43% fewer patients transfused, without affecting mortality (RR 0.97, 95% CI 0.81–1.16).6

The meta-analysis by Odutayo and colleagues4 included five randomised trials with 1965 patients, comparing restrictive versus liberal transfusion for acute upper gastrointestinal bleeding. Restrictive transfusion was indeed associated with fewer transfusions, and with lower risks of rebleeding and mortality. It prevented one rebleed per 24 patients and one death per 45 patients with a bleed, although each with large confidence intervals. This finding is relevant because of the high incidence of upper gastrointestinal bleeding and its significant morbidity and mortality. The data support the existing guideline on management of non-variceal upper gastrointestinal bleeding,7 which recommends transfusion at a haemoglobin threshold of 70 g/L.

However, this meta-analysis is limited by the paucity of original studies. Three of the five studies included were small, contributing only 7% of all patients. One of the two other studies was designed to determine the impact of restrictive transfusion.8 The other instead aimed to assess the feasibility of a multicentre, cluster randomised trial,9 with an unblinded design. In that