Selective liquid biopsy yields interesting results

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COMMENT & ANALYSIS

Laboratory techniques that make genetic profiling and mutation monitoring of tumours more readily accessible than by direct tissue biopsy have recently been introduced. These techniques, based on the detection of circulating tumour DNA (ctDNA), have become known as liquid biopsies because they rely on peripheral blood sampling, write Bruno Damascelli, Vladimira Tichà, Elena Repetti and Tshering Dorji, Milan, Italy.

Detection of somatic mutations in circulating DNA is comparable to that obtained from tumour tissue biopsy, but with a direct therapeutic advantage in that the molecular diagnosis can be updated through noninvasive serial sampling. Liquid biopsy also includes detection of circulating tumour cells (CTCs) that can be characterised by immunofluorescence, contributing to a precise molecular diagnosis.

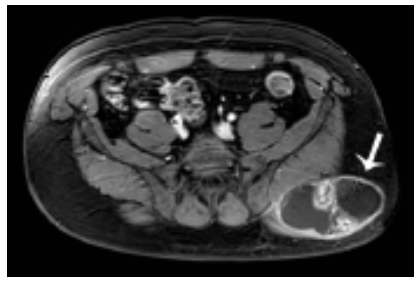

Figure 1: Pelvic MRI showing the tumour (arrow).

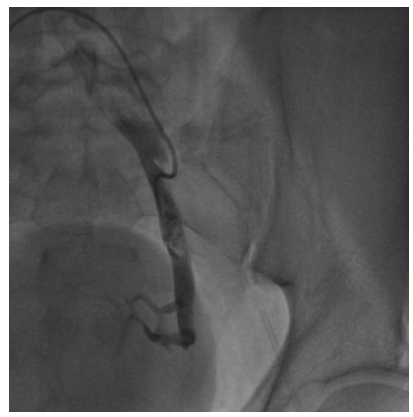

Figure 2: Selective catheterisation of the left hypogastric artery via contralateral femoral access.

The number of CTCs is small and a peripheral blood sample may contain only one tumour cell for every 600,000 nucleated cells. Likewise, fragmented DNA derived from tumours is found only in small amounts, mixed with DNA resulting from normal cell death, which accounts for at least 90%. Despite these limitations, liquid biopsy is gaining ground and has been internationally validated for non-small-cell lung cancer, melanoma and colorectal cancer.

Laboratory methods are improving daily and target sequencing and target mutation techniques are becoming increasingly effective in detecting a larger number of mutations and identifying single mutations of direct interest for targeted molecular therapy.

In just the same way as selective sampling is used for localisation of hormone-producing tumours, we decided to use selective venous catheterisation to overcome, in part, the dilution effect that ctDNA and CTCs undergo in peripheral blood. The circulation draining any part of the body can be reached by percutaneous venous mini-catheterisation via brachial, jugular or femoral puncture, according to standard interventional radiology practice. There are no contraindications to the procedure, which is carried out in an outpatient setting with acceptable invasiveness and can be repeated any number of times.

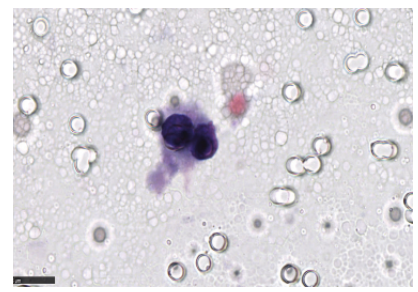

Figure 3: Cluster of two well-preserved tumour cells obtained by left hypogastric artery sampling.

In a preliminary clinical series, liquid biopsy carried out in parallel on selective and peripheral blood samples yielded interesting results. In the case of sarcoma of the left gluteus shown by way of example, target sequencing on a peripheral blood sample and on a selective sample from the left hypogastric artery showed a TP53 gene mutation, which can indicate tumour sensitivity to treatment with doxorubicin and ifosfamide. A tumour cell cluster was detected only in the selective sample (figures 1–3).

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CAVA trial to shed light on clinical and cost-effectiveness of routinely used central venous access devices

The world's largest randomised trial comparing three central venous access devices—peripherally inserted central catheters (PICCs), Hickman-type devices and chest wall ports—should provide definitive results in terms of their relative efficacy and cost-effectiveness, Jon Moss, Glasgow, UK, told CIRSE delegates.

The CAVA (Cancer and venous access) trial is a National Institute of Health Research- funded randomised controlled trial with associated qualitative research of venous access devices that deliver long-term chemotherapy. It is an open, multicentre trial with 17 participating UK sites involving 1,500 patients who received chemotherapy for three months, or more. The trial is currently recruiting and patients will be followed for a year.

"There are four randomisation options available for eligible patients (PICC vs. Port, PICC vs. Hickman, Hickman vs. Port, and PICC vs. Port vs. Hickman). The third option was the preferred one but if one device was not suitable for or refused by a patient the other two way comparisons could be used. The PICC vs. Hickman arm was a non-inferiority comparison, and the other options were a superiority comparison," said Moss, who is a professor of Radiology at NHS Greater Glasgow and Clyde.

Jon Moss

The primary outcome measure is complications. Secondary endpoints include venous thrombosis, re-intervention rates (device removal and replacement), interruptions to chemotherapy delivery, time to first complication and quality of life. Health-related quality of life including a novel device specific instrument and a full health economic analysis outcome, including cost effectiveness are being performed.

"To date, nearly 1,000 patients have been randomised, and the Hickman vs. Port comparison has been closed. The patient baseline characteristics consist of adults who are 18 years of age, or above, with either a solid or haematological malignancy who are to receive a course of chemotherapy lasting a minimum of three months. The three most common cancer types are colorectal, breast and pancreas in that order. The trial closes to recruitment in February 2018 with a maximum follow up of 12 months. The results should be available in early 2019," Moss told *Interventional News*.

CReST2 to compare uncovered with covered endoluminal stenting in patients with obstructing colorectal cancer

JAMES HILL

COMMENT & ANALYSIS

The CReST2 (Colorectal stenting trial 2) study aims to provide robust evidence as to whether or not covered or uncovered stents are better for patients with a large bowel obstruction caused by colorectal cancer who are to be treated with palliative intent, writes James Hill, Manchester, UK. Interventional radiologists will play an important role in making CReST2 a success and this is evident in the sites that have already opened to recruitment, he states.

Colorectal cancer is the second most common cause of cancer death in the UK. Each year, around 15% of people with colorectal cancer present with an obstruction. Surgery to resect the tumour is the preferred treatment if patients are fit enough and if the cancer is potentially curable. However, in many patients, their age, general health and the advanced state of their cancer means that this type of surgery is not appropriate. Self-expanding metal stent (SEM) placement is the preferred treatment for palliation of malignant colonic obstruction and is recommended by the UK's National Institute of Health and Care Excellence (NICE).

There are two designs of stent available: covered and uncovered. Uncovered stents may be at greater risk of ingrowth compared to covered stents, whereas covered stents may be at greater risk of migration. However, the balance of benefits and risks of the two stent types has not yet been reliably assessed. There have been no good quality randomised trials comparing covered and uncovered stents.

CReST2 is a five-year multicentre, randomised controlled trial funded by the National Institute for Health Research's (NIHR's) Health Technology Assessment (HTA) programme. Three hundred and fifty patients with a colonic obstruction secondary to colorectal cancer who are treated with palliative intent will be randomised to receive either a covered or an uncovered stent. To reduce bias, patients and all medical personnel except the person placing the stent will be blinded to allocation.

The co-primary outcome measures are quality of life, evaluated by the QLQ-C30 questionnaire at three months post-stenting and stent patency measured at six months post-stenting. Patients will be followed for a period of two years.

Eligibility

Patients aged 16 or over, with obstructing colorectal cancer, being treated with palliative intent are eligible for the trial. Patients with lesions at any site in the colon are eligible as long as stenting is considered feasible. Exclusion criteria are patients with low rectal cancer, patients being treated with antiangiogenic drugs, patients with impending or established perforation of the colon and patients who are pregnant.

In addition to answering questions about stent design, the trial will provide invaluable data about the efficacy and safety of stents in a large patient cohort within a clinical trial.

CReST2 builds on the success of CReST, the largest randomised trial performed to compare stenting with emergency surgery. CReST2 is open to recruitment and we would be delighted to welcome any interventional teams in the UK into the trial.

James Hill is a professor and consultant colorectal and general surgeon at Manchester Royal Infirmary and chief investigator for CReST2. CReST2 is sponsored by Manchester University NHS Foundation Trust. The views expressed are those of the author(s) and not necessarily those of the National Health Service, the NIHR or the Department of Health.