Trialling tailored treatments for colorectal cancer

An EU-funded project completing pan-European clinical trials on a molecular approach to bowel cancer diagnosis and treatment marks a further step towards personalised and better medical care for patients - potentially saving lives.

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Colorectal cancer (CRC) is the second most common cause of cancer death. In Europe, every year around 450 000 people are diagnosed with CRC and 200 000 die. Spread of the cancer to other parts of the body (metastasis) is common. It is particularly deadly because it has no early visible symptoms and thus diagnosis is often too late.

The EU-funded MERCURIC project is performing a clinical trial on an innovative combination of treatments to combat advanced CRC. In doing so, it is moving away from traditional one-size-fits-all chemotherapy treatments. Instead, it recognises that cancer is a heterogeneous disease: cancer cell behaviour is different for different patients and can change with time – for example, building resistance to a treatment.

“That individual cancers have different responses to standard treatments and can become resistant to treatment is well known,” explains MERCURIC project coordinator Sandra Van Schaeybroeck of Queen’s University Belfast, UK.

“But so far we had few effective responses in these ‘hard-to-treat tumours’ as the underlying mechanisms of resistance were little understood. Today, we know much more about the molecular and genetic heterogeneity of CRC and other cancers. This means we can ‘profile’ cancers in individuals and in groups of patients, over time, allowing more effective, tailored treatments.” MERCURIC is an example of the ‘stratified medicine’ approach which is gaining much interest from health systems across the world. Using new profiling techniques, patient subgroups can be better matched to targeted treatments. This saves lives, reduces costs and is a step towards fully personalised medical treatments. The MERCURIC clinical trials are aimed at a subgroup of CRC sufferers with poor survival rates – those with particular types of aggressive tumours.

Aberrant behaviour

Certain aggressive cancers are driven by the action of MEK proteins. There are anti-MEK treatments. However, as single agent treatments, these have shown very poor responses in

CRC. Earlier research by MERCURIC partners indicated that an aberrant protein called c-MET causes this resistance to MEK treatment.

“C-MET fills a useful function in the body, for example in controlling tissue growth and wound healing,” explains Van Schaeybroeck. “However, when it becomes aberrant and active, it sends uncontrolled growth signals causing resistance to treatments and metastasis to other organs.”

Significantly, the research also showed that when an anti-MET drug is added to the anti-MEK treatment, the cancer cells die.

MERCURIC is undertaking phase 1 and 2 clinical trials on CRC patients with specific aggressive tumours, using combinations of anti-MET and anti-MEK drugs. The phase 1a trials are now completed, reports Van Schaeybroeck.

“We now know the safe dosage and the treatment schedule. Currently, we are into phase 1b: investigating the response of the tumours to this novel tailored treatment combination,” she says.

Later, a phase 2 trial will be performed to show the effect of this treatment in over 100 CRC sufferers from across Europe.

It’s in the blood

Also in phase 1b, the researchers are developing a genetic blood test to determine whether a CRC patient could benefit from this new, combined treatment.

“Diagnosis can involve time-consuming and painful biopsies and time is critical in cancer treatment,” explains Van Schaeybroeck. “By using biomarkers, such as mutated cancer DNA found in blood, we will create a tool to understand when a combined drug treatment is needed – in real time, without waiting for an available operating room. In this way, treatment can be given and adjusted as and when it is needed, not when resources are available.”

As well as offering welcome benefits to future CRC sufferers, the MERCURIC project is also an example of where medical treatment is heading.

“Made-to-measure treatments are becoming possible because of the growing understanding of the genetic and molecular nature of cancers and disease in general,” says Van Schaeybroeck.

“MERCURIC focuses on a particular sub-group of CRC patients. However, this ‘stratified’ approach beginning with a genetic and molecular profile of a patient can, and is, increasingly applied to many cancers and other disease groups.”

Project details

- Project acronym: **MERCURIC**
- Participants: **UK (Coordinator)**, Spain, Belgium, Ireland, France, Italy, Czech Republic
- Project N°: 602901
- Total costs: € 8 096 788
- EU contribution: € 5 999 994
- Duration: December 2013 to November 2020

See also

Project website: https://www.mercuric.eu/
Project details:
https://cordis.europa.eu/project/rcn/110280_en.html

View the article online:
http://ec.europa.eu/research/infocentre/article_en.cfm?artid=48076