Scientists establish a foot in the door in precision medicine for oesophageal cancer

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Credit: University of Aberdeen

Scientists at the Universities of Aberdeen and Dundee have established a foot in the door in finding new, precision treatments for patients with oesophageal cancer, one of the hardest forms of the disease to treat.

Professor Russell Petty, Chair of Medical Oncology in the University of Dundee School of Medicine led the decade long study into oesophageal cancer while at the University of Aberdeen. This research has culminated in a diagnostic test to establish which patients might benefit from a specific treatment. This can help predict which class of drugs may act to extend and improve quality of life for some patients.

By identifying which patients will benefit from being treated with the drug gefitinib – and just as importantly identifying those who get no benefit from it – clinicians can focus on the best treatment plans in each case.

A clinical trial initiated by Professor Petty and colleagues in 2007 involving 450 patients in 50 hospitals across the United Kingdom looked at their responses to gefitinib. The researchers saw dramatic improvements in some patients who lived well beyond their initial prognosis of only weeks or months to live, in some cases by around 18 months to two years, and had improved quality of life.

Professor Petty explained: "After starting the trial we quickly observed very dramatic responses in some patients with improvement of their symptoms, and while not curative the responses were durable, lasting many months, for example up to two years in some cases.

"These responses to gefitinib were transformative to patients in this situation, moving them from being severely ill, with rapidly deteriorating health and within a few months of the end of their life, to a much improved condition where we had control of their cancer's growth and symptoms and they could return to 'normal life' with their families."

However, these responses occurred only in a minority, and the overwhelming majority of patients gained no benefit from gefitinib.

The research team carried out a detailed genetic analysis of biopsies of the patients' tumours to establish why some patients responded so well. As a result they have now developed a diagnostic test - the EGFR FISH test - that identifies those patients who will benefit from taking the drug.

Professor Zofia Miedzybrodzka, Chair in Applied Medicine at the University of Aberdeen who led the genetic testing part of the study explained: "By examining why some patients responded very well to gefitinib while others didn't, we have also learned more about how oesophageal cancer develops and what makes it so difficult to treat successfully,"

An estimated 455,000 individuals worldwide are

diagnosed annually with oesophageal (or esophageal in American English) cancer and the rate has risen over the last four decades.

The disease has been notably resistant to treatment. While significant advances in treatment for other cancers have led to improved survival rates – around 50 per cent of patients with breast cancer, and 60 per cent of those with colon cancer, now recover – the rate for oesophageal cancer is only around 15 per cent.

Professor Petty clarified: "This research is extremely important because oesophageal cancer can be very aggressive and, without treatment or with ineffective treatment, many patients will unfortunately only have a short time to live.

"It is important to treat people with the medicine most likely to control the cancer first time around, as we may not get a second chance. Gefitinib, for example, only benefits around 1 in 10 patients, so it was vital we developed the test to identify which patients would and would not benefit.

"In those patients where we know gefitinib will not work, we can avoid proceeding with an ineffective treatment and give them the opportunity to try alternatives.

"This really is a foot in the door which will help us get better and more effective treatments for oesophageal cancer, using the same kind of precision treatment approaches which are already being applied in some other cancers.

"My hope is that our work is the end of the beginning in finding a range of precision treatments for patients with oesophageal cancer, which will lead to much better survival rates or extension of life."

Professor Petty added, "Gefitinib was the best of this class of medicine at the time we started our trial. Better drugs have since emerged in the same class, known as EGFR inhibitors, and our hope is that the same test we have developed to identify the patients that benefit from gefitinib will also work with these newer drugs."

The results of the research are reported in the *Journal of Clinical Oncology*, the leading journal in the field.

Provided by University of Aberdeen