



SPECIAL REPORT

By Sally Wardle

Meet Bob – living proof that lung cancer isn't the death sentence it once was...

LUNG cancer was once considered pretty much a death sentence. Just two decades ago, it was near-impossible to treat. Doctors had only a handful of drugs at their disposal – and most patients were given just months to live.

A mere 17 per cent of those diagnosed with lung cancer in 1990 were alive a year later, and scientific progress in treating it had also stalled. Even as the discovery of new treatments for breast and bowel cancer helped boost survival rates, the outlook for those with lung cancer remained bleak. Today it is still the UK's biggest cancer killer, accounting for one in five of all cancer deaths, but now – at last – there is reason for hope.

Over the past decade, thanks to huge leaps in scientific understanding, an arsenal of highly targeted lung cancer treatments have been developed. Now a new analysis of US data, published in The New England Journal Of Medicine, reveals promising signs that this could be leading to a drop in deaths from the most common form of the disease.

Deaths from non-small-cell lung cancer, which accounts for about eight in ten cases, have been gradually declining over the past few decades due to fewer people smoking (the main cause of lung cancer). However, from 2013, as new treatments were launched, the decline in deaths doubled, with rates plummeting by almost 20 per cent in three years.

Experts soon expect to see a similar trend in the UK, where doctors report that patients are surviving longer than ever before thanks to medical breakthroughs. 'When I started as a consultant nearly 15 years ago, lung cancer was a next-to-impossible disease to treat,' says Professor Sanjay Popat, consultant oncologist at London's Royal Marsden Hospital.

'There was no hope, people were downbeat and patients would say, "What is the point?" But we now have a much deeper understanding of the biology of the disease. We have newer treatments and we have new surgical and radiotherapy techniques.'

'And as a consequence, people who would on average pass away within less than a year historically are now living in excess of two years, three years, even five years. It is absolutely fantastic to see.'

WITH about 47,000 people diagnosed every year in the UK, lung cancer is one of the most common types of the disease. Though smoking is thought to be responsible for about 70 per cent of cases, it can also occur in people who have never smoked due to exposure to harmful chemicals, other substances and pollution.

In its early stages, lung cancer often causes few symptoms. But as it progresses, patients may develop a persistent cough, bring up blood and experience aches, pains and breathlessness. Because of the vague symptoms early on, it is often picked up when it has already spread to other parts of the body.

'Once the cancer has spread beyond the lung, the majority of patients will die from their disease,' explains Professor Charles Swanton, Cancer Research UK's chief clinician and a lung cancer doctor at University College London Hospitals NHS Foundation Trust.

Previously, people with advanced lung cancer would be treated with chemotherapy drugs. However, they were rarely effective and were accompanied by gruelling side effects, including sickness and fatigue, that tarnished the last months of patients' lives.

But over the past ten years, targeted drugs, which come in pill form and work by interfering with the

way cancerous cells multiply and grow, have gained UK approval for the treatment of advanced non-small-cell lung cancer. Now, samples taken from tumours are tested to see if there are specific genetic mutations that can be targeted with these newly available drugs.

Prof Popat says: 'About 15 to 20 per cent of patients with advanced lung cancer have some sort of genetic change in their tumour that can be targeted. "That isn't a genetic change that is inherited from their parents, or one that they can pass on to their children, but it is a genetic change in the tumour itself, driving it to grow and divide and multiply and replicate. There are now simple, straightforward tablets that can switch off the effect of that genetic change, causing the whole cancer to implode."

Some targeted lung cancer drugs, including erlotinib and gefitinib, are directed at a mutation called the epidermal growth factor receptor (EGFR), which causes tumours to grow rapidly. About ten to 15 per cent of non-small-cell lung cancer patients have this mutation, and studies

have shown these treatments can add months to lives.

Earlier this month, osimertinib – also called Tagrisso – became the latest drug for EGFR-positive non-small-cell lung cancer to be approved by UK regulator the

National Institute for Health and Care Excellence (Nice) after trials showed it could stall cancer growth for even longer.

According to Prof Swanton, about half of patients with an EGFR mutation now live for three years or more thanks to such drugs. 'When you've got a patient with an EGFR mutant lung cancer, you breathe a sigh of relief because you know there is a very good chance they will benefit from this new class of drugs,' Prof Swanton says.

More recently, immunotherapy treatments, which stimulate the immune system to attack cancerous cells, are helping even more

lung cancer patients live for longer. Pembrolizumab, also known as Keytruda, was in 2016 the first immunotherapy treatment for non-small-cell lung cancer approved for use on the NHS. It affects a molecule called PD-1, which is found on the surface of T-cells – a type of white blood cell that help the body fight infection. This activates them to attack tumour cells.

According to data presented earlier this month at the European Society for Medical Oncology's virtual congress, almost a third of patients with advanced non-small-cell lung cancer treated with pembrolizumab lived longer than five years. This compares with just 16 per cent of those treated with chemotherapy. 'It's a complete game-changer,' says Prof Popat.

And in cancer clinics, doctors are already seeing how effective these drugs can be. 'We've had miraculous outcomes,' says Prof Swanton. 'Patients are alive today who would not have been a decade ago.'

One such patient is Bob Pain, 65-year-old, who runs a graphics printing business, was diagnosed in

2015 after scans picked up a shadow on his left lung. The ex-smoker underwent surgery to have half the lung removed, followed by chemotherapy. Tests showed he was free of cancer, but in early 2018 he began developing worrying symptoms.

'I started to get pain in my back and hip,' Bob recalls. 'I had just started doing yoga in an effort to get fitter after my illness, so put it down to that. Then, on Good Friday, I fainted suddenly.'

'My wife Lisa called an ambulance and I was taken to A&E, where they did loads of tests. "The doctors eventually let me go, as there didn't seem to be anything wrong. But when I told my chest consultant, he organised a scan, which revealed a big mass on my lung and my liver.'

The cancer had returned, and this time it had spread to his liver and bones – stage four. He was left in agony and struggled to move.

In June 2018, Bob started treatment with pembrolizumab, covered privately by his health insurance – and after just a few months, scans showed the tumours in his liver and lung had reduced by half. 'It was staggering,' Bob says. 'It felt like I'd won the Lotto jackpot. It was just incredible.'

Recent scans have shown that Bob is clear of cancer – even in his bones – and the difference in his health is remarkable. 'Now I do yoga two or



WINNER: Bob Pain, who was saved by a new treatment, with friends at the Epsom Derby in 2018

three times a week,' he says. 'And I walk four or five miles, three or four times a week.'

Bob, who is currently raising funds for The Royal Marsden Cancer Charity by walking 26 miles over 26 days, adds: 'It is looking good. With stage four lung cancer, they don't say you are in remission, but this is the nearest best equivalent.'

Early-stage treatments have also improved in recent years. Patients are now offered stereotactic radiotherapy on the NHS which delivers a high dose of radiation to the tumour, sparing patients surgery.

Progress in treating the most aggressive form of the disease, small-cell lung cancer, which accounts for about one in ten cases, has lagged far behind.

'The prognosis is very poor – the average patient lives just nine months from diagnosis,' says Dr Charles Escru, consultant at The Clatterbridge Cancer Centre and Honorary Research Fellow at the University of Liverpool.

Chemotherapy works briefly in many but the cancer soon returns, and most targeted treatments have also proved ineffective. But research found that adding immunotherapy to chemotherapy can

boost survival. This year NICE approved immunotherapy drug atezolizumab, also called Tecentriq, given with chemotherapy for patients with advanced small-cell lung cancer. More than half of patients are alive a year later, and a third after 18 months. 'Although the survival benefit may seem small, this is a huge breakthrough,' says Dr Escru.

Retired market trader Paul Bird, 62, from Leicester, started the treatment after being diagnosed with small-cell lung cancer in February. 'I wasn't a smoker and have always been fit and sporty,' he says. 'But I had started coughing and getting out of breath just walking to the pub or up a hill.'

Scans revealed a tumour in one of his bronchial tubes, which lets air into the lungs, and he was told he had just five months to live. But after five months of treatment, his tumour had shrunk from 2.5in to 1.37in. 'Now I can walk 18 holes of the golf course, which I couldn't

have done before,' he says. 'Whatever this drug is doing, it's definitely helping.'

Unfortunately, there is a 'but', as the UK continues to grapple with Covid-19. Cancer Research UK says the pandemic has led to

14,000 fewer patients receiving urgent referrals for lung cancer tests since March. The charity warned that some symptoms, such as a new cough or breathing problems, could be mistaken for coronavirus, resulting in delays seeking treatments. Almost half of GPs have also reported problems when ordering chest X-rays. Prof Swanton says early diagnosis is key. 'If the NHS clogs up again because of Covid admissions... the collateral damage to cancer care and patients with new diagnoses could be immense.'

Additional reporting: Hilary Freeman

COVID Q&A

Those second wave rumours – and why Italy is faring better

Q So, is this the second wave of Covid-19 or not?

A There's no doubt that the UK is seeing a steep rise in the number of people testing positive for Covid-19.

In recent weeks, the numbers have started to climb rapidly. The fear – as outlined in a public broadcast last week by Sir Patrick Vallance, the Government's Chief Scientific Adviser, and Professor Chris Whitty, Chief Medical Officer for England – is that these cases will grow uncontrollably. This is likely to have an effect on hospital admissions, which are already starting to creep up, and deaths. The number of Britons in hospital with the virus has risen by more than 50 per cent since last week.

In their address, Sir Patrick and Prof Whitty warned that the number of people infected could double every seven days, leading to as many as 50,000 cases per day by mid-October. But some experts say this prediction is implausibly quick.

In the meantime, Imperial College London data suggests a doubling of infections every seven to eight days. This was based on 136 positive tests from 150,000 swabs between August 22 and September 7.

Critics say this is too low a number of positive tests to reliably compute trends – and that it may not reflect the current picture.

'Some people say it's not a second wave, because actually, the first wave never went away,' says Paul Hunter, professor of medicine at the University of East Anglia. 'The fact is, we are seeing a major resurgence of the infection, and whether it's part of the first wave or second – those are purely words.'

It's important to remember, though, that we are not in the same place as we were in the spring. At the peak of the pandemic, the Government reported there were more than 6,000 daily infections, but the true number is estimated to have been much higher.

Experts at the London School of Hygiene and Tropical Medicine say it may even have topped 100,000 in March. Back then, only some people with symptoms – mainly those in hospitals – were being tested.

So while the two 'waves' may appear alarmingly similar on a graph, it's not accurate to compare them at all. The rise in cases now is an early warning – one which we did not have the benefit of at the start of the year – that the

virus is spreading. And it gives the Government, and population, time to act.

Prof Hunter says new measures introduced last week should help slow the rise in infections, and stop cases rising so steeply. But he adds: 'I personally doubt that they will, by themselves, reverse the epidemic this side of Christmas.'

Q France and Spain are seeing a second wave – why isn't Italy too?

A Cases of Covid-19 have risen steeply in France and Spain, with both reporting more than 10,000 new infections a day. Meanwhile Italy, which was hit harder than most European countries in March, appears to have things under control.

While the number of infections there has been creeping up, levels have remained fairly consistent over the past month, and not topped 2,000. It is faring better than the UK too.

Last week, Boris Johnson suggested the difference was because Britain was 'a freedom-loving country'. But Italy's President Sergio Mattarella hit back, saying Italians 'love freedom, but we also care about seriousness'.

Exactly why France, Spain and the UK are faring so differently to Italy is not clear. But experts say it could be that Italian rules on mask-wearing in public are strictly adhered to and enforced by police and officials.

The country is also offering rapid Covid-19 tests at some airports. And although they are less accurate than the one used in the UK, they can provide a result in 30 minutes.

Italy's test and trace system is also thought to be working well. However, it is too soon to suggest that the country will escape unscathed this time.

Q Has the virus mutated, making it more – or less – dangerous now?

A Every time a virus infects a person, it makes new copies of itself to attack other cells, and during this process mistakes can be made that result in changes.

In fact, most of the time, mutations don't make much difference to how the virus behaves. Sir Patrick said the virus that causes Covid-19 had 'genetically moved a bit' but stressed this had not changed its ability to infect people or cause disease and death.

CANCER FACTS

More than 1.7 million lives are lost globally to lung cancer every year.

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