

“This is really exciting!” Professor Christian Ottensmeier from Southampton University tells us. “We’re taking a drug being tested by a pharmaceutical company in a group of patients and trying it in a completely different group”.

Professor Ottensmeier is leading an exploratory clinical trial to test a new drug, initially developed as a leukaemia drug, in patients with cancers of the head and neck.

And this is only possible thanks to our [Centre for Drug Development](#) (CDD) team, who have led pioneering ‘first-in-man’ trials for the last 25 years, and who have built a series of vital relationships with pharmaceutical companies. This allows them to run a [pioneering scheme](#) that makes experimental new drugs available to patients via clinical trials.

The scheme, run jointly with our commercial arm – [Cancer Research Technology](#) – is simple; pharmaceutical companies allow us to carry on developing experimental drugs they have either de-prioritised, or are only testing in certain groups of patients.

Let’s take a closer look at the new trial, and how this ingenious approach is working out the drug’s potential in treating head and neck cancer.

Meet AMG 319

The experimental drug, named AMG 319, is made by the pharmaceutical company Amgen, and it’s designed to switch off a molecule in our cells called PI3K δ (that funny squiggle is the Greek letter ‘delta’).

PI3K δ is mainly found in white blood cells, and can affect our immune response by controlling the expansion of armies of B and T cells in response to an infection. When it’s switched on, it allows white blood cells to multiply rapidly.

This is the first time the drug has been tested as an immune-boosting weapon against solid tumours

– Professor Christian Ottensmeier

But rapid cell division is also a hallmark of cancer. So Amgen has been testing the drug’s effectiveness in treating blood cancers where white blood cells are dividing uncontrollably, like certain types of [leukaemia](#) and [lymphomas](#).

But could this drug have other uses? Researchers in our Southampton Centre – led by Professor Ottensmeier – are world-renowned for their studies into how our immune system can be harnessed to treat cancer. The ability of AMG 319 to switch off certain types of white blood cells led the project team to have a bright idea. Could this drug actually be used to help our immune systems fight other types of cancer?

“This is the first time the drug has been tested as an immune-boosting weapon against solid tumours,” says Ottensmeier. “We specialise in treating head and neck cancers at Southampton hospital – we know the immune system plays an important role in this type of cancer, and the timing of standard treatment for these patients gives us the perfect opportunity to test this new drug”.

Pushing the immune detonation button

In recent years, it's become clear that patients with more immune cells in their head and neck tumours generally have a better outlook.

"Certain types of immune cells, for example those known as 'killer' T cells, can recognise a tumour as bad news," says Ottensmeier. "They respond like they do to an infection and destroy the cancer cells.

But, as Ottensmeier explains, with immune cells, it's not always 'more is better' – our immune systems are held in a delicate balance by a range of different cells.

"Another type of T cell, called a 'regulatory' T cell, spots that the cancer cells are still part of 'us' and dampens down the flames of the 'killer' T cells response."

So could reducing the levels of these regulatory cells help the 'killer' T-cells do their jobs?

Lab experiments from before the launch of the trial showed that blocking PI3Kδ with AMG 319 did indeed stop the 'regulatory' T cells from suppressing the immune response, but didn't affect the 'killer' T cells' ability to destroy cancer cells.

"So getting the right type of immune cells into the tumour and responding to it could be critical in switching the environment from defence to attack mode – helping patients to kill cancer cells using their own immune system," says Ottensmeier.

Opening a window of opportunity

The drug has already been tested in a [phase I trial](#) by Amgen, so doctors know it's safe and what doses they can give patients.



It's a 'window of opportunity' trial – Dr Emma King

The new clinical trial, which will be open in Poole, Southampton and Liverpool, will include around 50 patients whose cancer tests negative for [human papilloma virus](#) (HPV) – this is because infection with the virus has an effect on the immune response, so might skew the trial results.

"Patients are randomly assigned to two groups," explains Dr Emma King, the lead doctor overseeing the trial at Poole. "About a third gets a placebo (dummy) treatment, and the rest are given AMG 319."

But patients on the trial don't miss out on any of the normal treatments they'd be given for head and neck cancer. "It's a 'window of opportunity' trial," explains King. This means the trial takes advantage of a natural break after a patient's diagnosis to test out a new treatment.

In the case of head and neck cancers, patients initially need a biopsy, so doctors can determine what kind of tumour it is and whether it can be removed surgically. Patients who need surgery have around a three week wait after their biopsy, and this provides a 'window' to test the potential of AMG 319.

"Patients are given AMG 319, or the placebo, for at least 21 days. When we operate to remove the tumour, we're going to compare it to the sample we took at the biopsy. And what we're looking for is a change in the number of white blood cells in the tumour", says King.

Proof of principle

This clinical trial is still at an early stage and being used to test the waters for potential bigger trials.

Professor Ottensmeier explains what they are hoping to achieve. "Giving a patient AMG 319 for just 21 days is, in reality, unlikely to have any clinical benefit for those taking part in the trial. But it will help us to understand if it has potential benefit for patients in the future," he says.

If the results are positive, and more 'killer' white blood cells are found in the tumours after treatment, the next step will be testing the drug in bigger clinical trials.

"Then we can start asking the question of whether it can help shrink tumours, or stop cancer coming back after surgery, improving survival for head and neck cancers."

And on the flip side of the coin, if the results are negative, the researchers have still gained valuable knowledge. "We'll know there's no point in testing it further. The patients involved have not lost out on any standard treatments, and we can focus our energy on other drugs," Ottensmeier explains.

Hopes for the future

"I'm very glad to see more research being done for patients with head and neck cancers, because not many doctors and scientists work in this field," Dr King tells us. "Only around three in 10 patients with HPV-negative head and neck cancers are still alive five years after their diagnosis, so there's an urgent need for better treatments."

"Sadly, people are often diagnosed at quite a late stage, which not only has an impact on their chances of surviving, but means treatments need to be more aggressive, and often come with debilitating side effects."

I'm very glad to see more research being done for patients with head and neck cancers, because not many doctors and scientists work in this field

– Dr Emma King

Dr King and Professor Ottensmeier both hope that immunotherapies like AMG 319 could help shrink tumours, making surgery and radiotherapy easier, more effective, sparing more healthy tissue and reducing the risk of the cancer coming back.

And they are optimistic that, in the bigger picture, immunotherapies like this will help turn cancer into a disease that can be safely managed by doctors over long periods, rather than one people die from.

“We’re testing the treatment for people with head and neck cancers because we have this window of opportunity and we get tumour samples pre and post-treatment,” says Ottensmeier. “But it could potentially be effective against all types of solid tumours.”

On top of this, speculates Dr King, because of how AMG 319 works, it could help boost the effectiveness of existing immunotherapy drugs.

“One of the most frustrating things to come out of clinical trials testing immunotherapies for patients with other types of cancers is that not all respond to these drugs,” she says, “The best results show that only around half of patients benefit. One of our goals is to find out if combining AMG 319 with other immunotherapies increases the number of patients who do well on these treatments.”

It’s an exciting trial and, if the results are positive, it could mean a new treatment option will be available to patients with head and neck cancer and boost the number who survive this type of the disease. And further in the future, it could make existing immunotherapies effective for more people and help treat a wide range of different cancers.

These are still early days but nothing would be achieved without the bright minds of our researchers and the collaboration between CDD and pharmaceutical companies working to get experimental drugs into clinical trials.

Emma

[back to previous article](#)