Hope for me, and for others who come after

Award-winning article explores the impact of a new network of early trial centres

Delays in getting promising new treatments into trials are slowing progress in cancer care and failing patients who have run out of options and are running out of time. This article, which earned freelance journalist **Victoria Lambert** a Best Cancer Reporter Award, looks at what UK efforts to cut these delays has meant for three patients with advanced cancer.

"Death is a huge, vicious dog. We are trapped together in an alleyway, and every day I must stare him in the face, and challenge him. I must attack him first, with all my strength, and every weapon at my disposal. I have to – if I turned for one moment, if I lost my courage, if I tried to run away instead, he would chase me and he would leap on me, he would savage me and he would kill me."

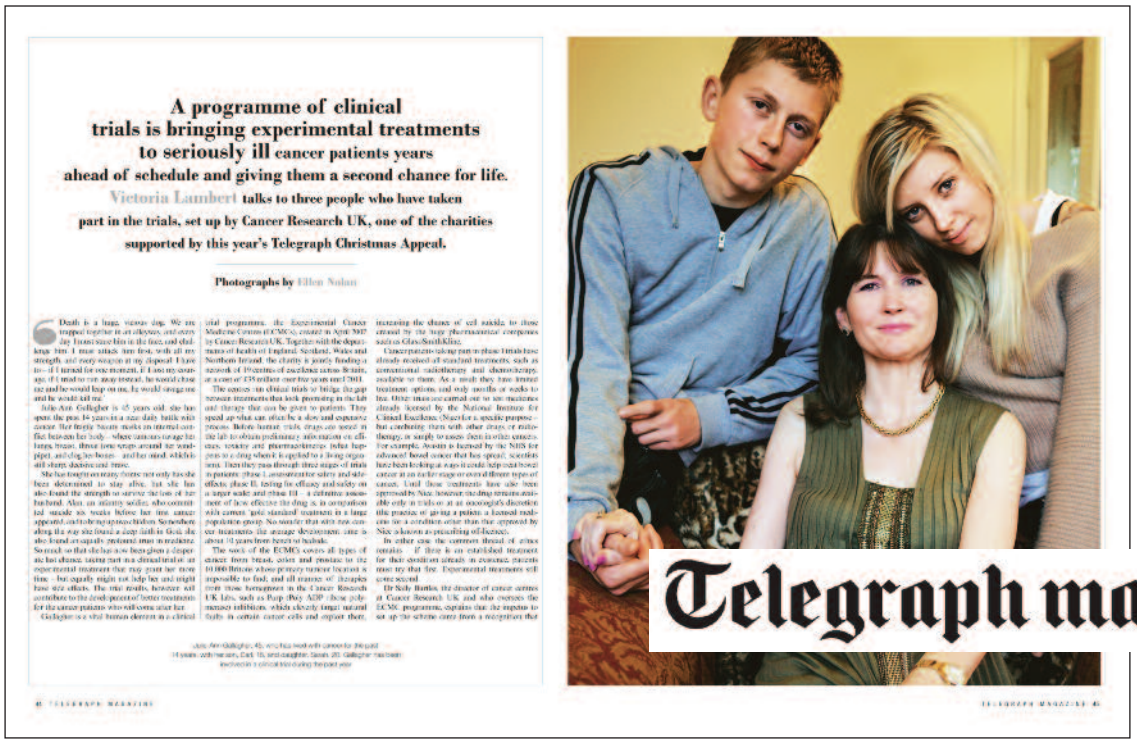
Julie-Ann Gallagher is 45 years old; she has spent the past 14 years in a near daily battle with cancer. Her fragile beauty masks an internal conflict between her body – where tumours ravage her lungs, breast, throat (one wraps around her windpipe), and clog her bones – and her mind, which is still sharp, decisive and brave.

She has fought on many fronts: not only has she been determined to stay alive, but she has also found the strength to survive the loss of her husband, Alan, an infantry soldier, who committed suicide six weeks before her first cancer appeared, and to bring up two children. Somewhere along the way she found a deep faith in God; she also found an equally profound trust in medicine. So much so that she has now been given a desperate last chance, taking part in a clinical trial of an experimental treatment that may grant her more time – but equally might not help her and might have side-effects. The trial results, however, will contribute to the development of better treatments for the cancer patients who will come after her.

ELLEN NOLAN

Victoria Lambert

Gallagher is a vital human element



A programme of clinical trials is bringing experimental treatments to seriously ill cancer patients years ahead of schedule and giving them a second chance for life.

Victoria Lambert talks to three people who have taken part in the trials, set up by Cancer Research UK, one of the charities supported by this year's Telegraph Christmas Appeal.

Photographs by Ellen Nolan

Telegraph magazine

The patient's voice. Given that fears about safety and exploitation form the framework for many drug development stories, this article was important in providing an alternative perspective: that of patients with advanced cancer, for whom access to drug trials offers their only hope

in a clinical trial programme, the Experimental Cancer Medicine Centres (ECMCs), created in April 2007 by Cancer Research UK. Together with the departments of health of England, Scotland, Wales and Northern Ireland, the charity is jointly funding a network of 19 centres of excellence across Britain, at a cost of £35 million over five years until 2011.

The centres run clinical trials to bridge the gap between treatments that look promising in the lab and therapy that can be given to patients. They speed up what can often be a slow and expensive process. Before human trials, drugs are tested in the lab to obtain preliminary information on efficacy, toxicity and pharmacokinetics (what happens to a drug when it is applied to a living organism). Then they pass through three stages of trials in patients: phase I, assessment for safety and side-effects; phase II, testing for efficacy and safety on a larger scale; and phase III – a definitive assessment of how effective the drug is, in comparison with current 'gold standard' treatment in a large population group. No wonder that with new cancer treatments the average development time is about 10 years from bench to bedside.

The work of the ECMCs covers all types of cancer, from breast, colon and prostate to the 10,000 Britons whose primary tumour location is impossible to find; and all manner of therapies from those home-grown in the Cancer Research UK labs, such as Parp (Poly ADP ribose polymerase) inhibitors, which cleverly target natural faults in certain cancer cells and exploit them, increasing the chance of cell suicide, to those created by the huge pharmaceutical companies such as GlaxoSmithKline.

Cancer patients taking part in phase I trials have already received all standard treatments, such as conventional radiotherapy and chemotherapy, available to them. As a result they have limited treatment options, and only months or weeks to live. Other trials are carried out to test medicines already licensed by the National Institute for Clinical Excellence (NICE) for a specific purpose – but combining them with other drugs or radiotherapy, or simply to assess them in other cancers.

For example, Avastin is licensed by the NHS [National Health Service] for advanced bowel cancer that has spread; scientists have been looking at ways it could help treat bowel cancer at an earlier stage or even different types of cancer. Until those treatments have also been approved by NICE, however, the drug remains available only in trials or at an oncologist's discretion

(the practice of giving a patient a licensed medicine for a condition other than that approved by NICE is known as prescribing off-licence).

In either case the common thread of ethics remains – if there is an established treatment for their condition already in existence, patients must try that first. Experimental treatments still come second.

Dr Sally Burtles, the director of cancer centres at Cancer Research UK and who oversees the ECMC programme, explains that the impetus to set up the scheme came from a recognition that while superb cancer centres already existed in Britain, a network was needed to draw them together and to encourage collaboration: "We wanted to speed up the development of new drugs, and we knew that by providing specialist resources we could improve the system we had." The programme is also an excellent way to ensure that each centre can concentrate on its own oncological specialty, while ensuring that patients get the most appropriate new therapy for them. Patients can be referred between centres depending on their ability to travel, or receive their treatment close to home.

Cancer Research UK facilitates the ECMC programme, and in 2011 its results will be peer-reviewed, the official test of whether it has been a success. Prof Ruth Plummer, the clinical professor of experimental cancer medicine based at Newcastle University, believes that the network has been enormously positive – in the first year, 400 trials took place, by year three (2008) that number had doubled, and by the end of this year it will no doubt have expanded exponentially again. "It has really made the UK research situation attractive to the global pharmaceutical companies; one recently contacted me to ask if we had the facilities to take on a major trial. If not, they would take it to Europe. A few emails later, I was able to inform the company that we were more than set up to take on the work." Plummer also points out that Britain is the only country to have such a network, although other countries are watching closely – and a similar EU-wide scheme is in the process of being set up.

Agreeing to go on to a trial was a surprisingly easy choice for 21-year-old Calum Elliot, because it seemed a bonus – both for him and others. "I was more than happy," he says, "whatever the side-effects or results. It was good to think that my experience might make it easier for other young people who are diagnosed like me." Two years ago, Elliot, a plasterer, started having episodes when he would become mentally 'absent' for a few moments; his family – mother, Jane, 40; stepfather, Craig Watson, a 43-year-old driver; and his 17-year-old sister, Danielle, with whom he still lives in a flat close to Glasgow airport – and his friends spotted that he simply didn't respond to anything – conversation or action – for two to three minutes at a time. These moments might occur in the pub or playing football, or even when watching his team, Glasgow Rangers. Concerned, in 2008 his mother took him to the GP, who referred him to a specialist. An MRI scan revealed a tiny abnormality on the left side of his brain and epilepsy was diagnosed. For the next year and a half, Elliot took anti-epileptic drugs but the drugs did not stop the seizures, which had become weekly.

For Elliot the toughest news was being told that his driving licence would be suspended (as it is with all epilepsy sufferers on safety grounds). Not long after, he suffered an episode at work and was 'let go' four weeks later. Yet he still didn't feel ill and played football with an understanding team and league mates (who took him to the side when a seizure struck and allowed him back on to the pitch when he 'came round'). Then, in September this year, Elliot's doctors sent him for a routine MRI scan; he was called in for an appointment to discuss it the next day. The night before, he suffered a terrible headache and began vomiting. His mother drove him straight to the hospital. "I was given a CT scan that showed there was bleeding on the brain,' he says. 'The doctor who I had been due to see the next day showed up to see me. He explained he was a surgeon; I guess he must have known already he would need to operate on me."

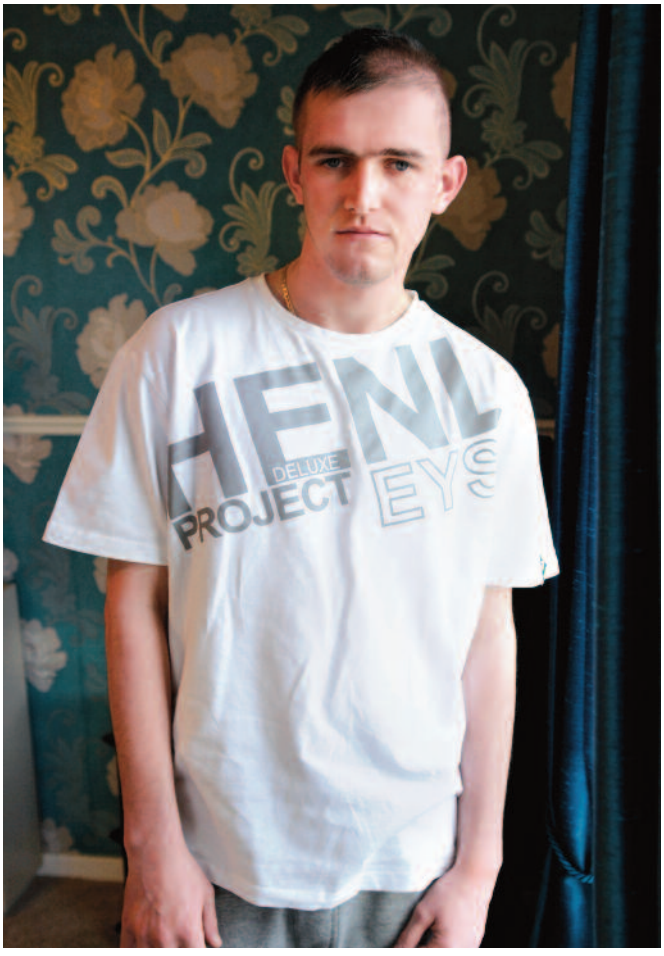
Elliot underwent a five-hour operation: the small spot on the original MRI scan from 2008 had grown into a 2 cm tumour, and after 90% was removed, leaving a small horseshoe-shaped scar on the left side of his head, it was proved malignant. Of the diagnosis itself, Elliot says now, "That's something you don't want to hear. But you have to deal with it and be strong." His stepfather says, "We told everyone that first day – friends and family and especially Calum's granny; they're very close and that was the hardest bit, I think."

Elliot was warned that his was one of the worst cases the surgeon had seen – a grade 4 glioblastoma (one of the most aggressive brain tumours at its most advanced state – cancers are graded 1 to 4 in severity). But Elliot was immediately offered the chance to go on a trial organised by an ECMC locally as – incredibly – a blood sample showed that his DNA matched the exact requirements of a new drug. He would be the first person in the world to try a vaccine created in a Glasgow lab that aims to boost the body's own defences.

Prof Jim Cassidy, who runs the ECMC at the University of Glasgow with his fellow oncologist Prof Jeff Evans, believes that there are tremendous benefits to the scheme. "We have always been good at research and at clinical care here; establishing the ECMC helps us bring the two together, so not only does bench get close to bedside, but we can also work the other way round. We can take samples from patients who are undergoing experimental medicine and see what the drug is doing to the tissue or tumour, to see how it succeeds or fails. It's not trial and error, it is trial and understanding."

Calum Elliot needs to have 13 injections in the course of the trial and has already had nine. He is undergoing a course of radiotherapy that will be over before Christmas, and chemotherapy, which will last until April.

"I was warned to expect side-effects but I'm fine," he says. "The injections which go into my upper thigh sting for 10 minutes but that's it. I haven't even lost much hair from the other treatments." Overall he feels fit, eats well, and has had no 'episodes' since the operation. He goes clubbing with his friends, drinks 'in moderation' and is planning a four-day weekend in Butlins Skegness to celebrate the end of the radiotherapy. It will be a few months before Elliot knows whether the experimental treatment has worked – when he is scanned a few weeks after the end of radiotherapy. It will not be until a second MRI another six weeks later that an accurate result will emerge – but he seems to be focused less on getting through the course and more on counting down the days until he regains his driving licence.



ELLEN NOLAN

Calum Elliot, 21, has been taking part in a trial that aims to limit the aggressive tumour in his brain by boosting his body's natural defences

In the South Yorkshire town of Penistone, 72-year-old Terry Windle is also waiting to see if his experimental cancer treatment has worked. Slim and healthy-looking, he could easily pass for a decade younger. The home he shares with his wife, Kathy, 58, a retired pharmacist, is decorated with paintings and photographs of motorsport – he has spent his life designing, building and racing motorbikes. Next year Windle plans to cross the US on a Harley-Davidson ("It'll be me and a couple of other fellows: one's 70-odd and the other's 84. We can't wait"). But before he can buy the plane ticket, he has to have a check-up with his oncologist at St James's Hospital in Leeds, an ECMC where he received treatment for his ocular melanoma – an incredibly rare cancer that first appeared in his eye 29 years ago.

"I should have died then," Windle says, enormously cheerful. "But I didn't even know it was cancer. I'd had problems with my sight playing squash, and I was sent to hospital, where they found a tumour on the back of the right eyeball, which they removed. No one said the tumour might be malignant."

"It was good to think that my experience might make it easier for other young people"

"My condition can be managed. It's extraordinary. I'm not even considered terminally ill any more"

ELLEN NOLAN

Terry Windle, 72, with his wife, Kathy, at their home in Penistone, South Yorkshire. Terry has had a successful outcome to his clinical trial treatment at St James's Hospital in Leeds, which 'teaches' immune cells to kill melanoma cells

Then 23 years later, in 2004, Windle started experiencing unusual stomach pains; that August he was sent for an MRI. A specialist told him they had found a tumour on his liver, which they intended to remove within a fortnight. "I wasn't that surprised. A few years before, a friend had undergone the same eye experience – an extraordinary coincidence. He had been warned it was cancer and that it might spread to his liver, which it duly did, and he died. So I had begun asking questions and learnt that ocular melanoma usually kills you within five years. By my own reckoning I should have been dead by 1986." However, a series of regular monthly, three-monthly, and six-monthly CT scans showed no recurrence. "I just got on with life," he says. But the cancer did recur in 2006, first in his navel in the form of an inoperable tumour, and then a lump on the back of his neck. "They sat me down in 2007, and said, it's months, not years now. You're 69, pack in your work and enjoy what time you have left – we can do nothing."

But they did suggest that Windle could join the ECMC at St James's Hospital, and in the summer of 2008 he was invited to join a phase I trial for gene therapy for ocular melanoma which had spread to the liver. The trial was of a new treatment called a PolyMEL DNA vaccine. It works by teaching immune cells to recognise certain proteins (antigens) made by melanoma cells. Theoretically, the immune cells will then kill the melanoma cells.

"I had three jabs over a few weeks – that's all – just like any other vaccine in my arm." While he waited to see if it would work, Windle spent the next year building a shining Lotus racing car from a kit.

The results appear to be good – his oncologist has told him the cancer has "stalled". And despite his tumours, which all appeared in the two years preceding the trial (one in the muscle of his shoulder, one in his breast, one on his side, two in the lungs and one by the navel), he looks fit and well, and is planning another skiing trip. "From what I can gather this has completely stalled them; I can't be cured, but my condition can be managed. That will do for me. It is extraordinary. I'm not even considered terminally ill any more."

Julie-Ann Gallagher, who lives in Bishops Waltham, Hampshire, cannot make the same bold statement. Like Windle, her experience has been extraordinary, her endurance inexplicable. But unlike Windle and Elliot, she has also undergone lengthy bouts of pain and discomfort – and she looks as ill as she is. We talk in her sitting-room – family photographs of her daughter, Sarah, now 20, a fitness instructor, and son, Carl, 15, who intends to take up an apprenticeship in plumbing after school, are proudly displayed on a table.

Gallagher is wrapped in myriad layers, furry boots and a fleecy blanket. The temperature is nearly as cold inside her small council house as it is out. Gallagher has spent most of her adult life fighting cancer and raising her children alone; she hasn't been able to develop a career or save for infirmity. "I can't afford to put the heating on yet," she says. "I told Carl, we must wait until it is really necessary. We simply can't afford it." She looks blue-grey with cold. Advanced cancer patients are not allocated winter heating support as pensioners are – an issue that the cancer support charity Macmillan is campaigning on strongly. It is the only occasion that Gallagher shows her frustration at her lot. "I'm never warm – the

tumours in my lungs feel like icicles, and the only time I know the sensation of heat is when I'm in hospital undergoing an iodine transfusion."

Gallagher first developed cancer at the age of 31, in August 1996, when six weeks after her husband's death (he suffered, she believes, from manic depression) she found a lump in her left breast "the size of a piece of coal; one day there was nothing, the next this thing. It felt like it had smaller tumours, like grapes, hanging off it. I have no doubt it was due to the extreme shock and stress of my situation. I was the widowed mother of six-year-old Sarah and Carl, then aged 18 months." Her GP took one look and sent her the same day to a specialist. "The breast sister appeared with dread in her eyes – I thought, I am going to follow my husband." That was the first and last moment of self-pity she allowed herself. "I thought, I must fight this for my children – they don't deserve this."

Moreover, she wanted them to understand that, despite their father's suicide, life is worth choosing. She underwent a mastectomy and reconstructive breast surgery, but the tumour, which was a grade 2/3, had already spread to her lymph glands. She underwent six months of chemotherapy, and began taking tamoxifen to prevent it recurring. "I lost my hair but I didn't care; I even stopped wearing the wig I was given, when Carl pulled it off in the supermarket. Nothing mattered but surviving." Her breast sister warned her, "It will come back, you may get 10 years if you're lucky."

Gallagher shakes her head. "That wasn't enough time for me, but it made me start planning. I promised my daughter I would be at her wedding, which, last year, I was."

She began to feel well, fit and strong, and launched a business, selling decorative gold and silver nipple 'jewellery' for mastectomy sufferers. Life was briefly good. "And then, in 2004, I came last in the parents' race on sports day – I had no puff. A few days later, I raced a parking warden back to my car, and lost, feeling breathless." Her doctor ordered an X-ray, and Gallagher admitted that she had felt a lump on her neck, too.

A tumour had appeared, wrapping itself around her jugular vein and the windpipe next to it. A tiny patch of cancer cells had somehow survived, undetectably hidden behind the reconstructed breast, and had spread – not only to her windpipe, but also pitting both lungs.

The tumour on her side was cut out, but although she was offered chemotherapy, Gallagher was told that there was no hope of recovery. "When I said, 'Don't you bet on it,' they told me, 'That's what all the patients say.'"

Gallagher refused to give in. She underwent a year of very gruelling chemo. Then, in 2006, her oncologist announced there was no more she could do for Gallagher and told her firmly that she should not expect to collect her pension. "I think if you get secondary cancer you become a nuisance; they know what to do with primary and they know how to support you, but once you get to my stage, it's so different."

Gallagher was not prepared to give up – she moved to Southampton University Hospital, and after demanding to try something, was given hormone therapy, which had to be injected painfully into her stomach to slow down her ovaries, which seemed to be fuelling the growth of the cancer. By 2008 she was becoming more breathless. "I could smell death on myself – my lungs were filling up with fluid and I was drowning." An operation to drain her lungs worked but left her ill; she lost a stone in weight.

A scan revealed the cancer was now in her spine and hips, and her body was clearly too weak for chemo to be considered. It was time to stop the agonising injections too – Gallagher simply couldn't stand them. "I was so close to death last Christmas, I know that,' she says. But then a small miracle happened. 'I was asked to join the ECMC trial at Southampton University Hospital for a drug called zoledronate, which is given intravenously once a month."

Her consultant oncologist, Jennifer Marshall of Southampton University Hospital Trust, explains this is a trial of a bisphosphonate therapy, principally used in osteoporosis patients as it strengthens bones and helps to reduce bone pain. "We have learnt that it possibly also has an anticancer effect, too," she explains, "hence the idea for a randomised trial."

"And in Julie-Ann's case, while we couldn't 'cure' the bone cancer," Marshall says, "we could at least put her on the trial and do something about the pain she was suffering while hopefully protecting her from fractures."

Gallagher recalls, "After the first infusion I felt relief. I just felt better, somehow." But after six months, her veins collapsed to the extent that injections were no longer an option. She was taken off the trial as she could not carry on, but prescribed off-licence another form of bisphosphonate therapy called ibandronate, which she takes in tablet form once a day.

"Although Julie-Ann was not on the trial for the full period of two years, it did reduce her pain and continues to – nor has she suffered any breaks, so I think for her you could say it has been successful," Marshall says.

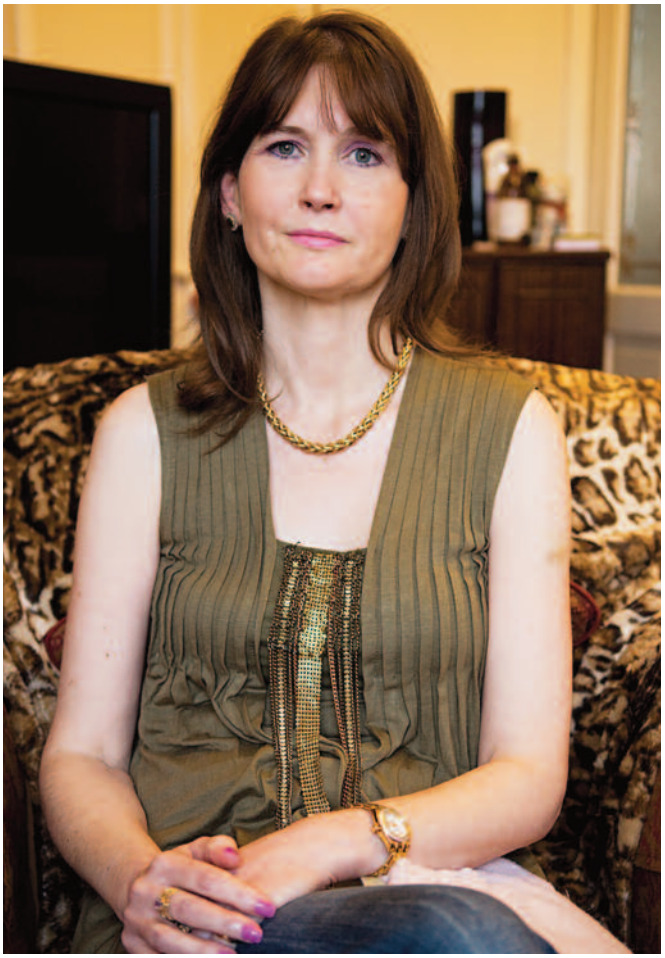
Gallagher is now busy planning Christmas and looking forward to her

"Without these new drugs, cancer would have taken me. But I'm not ready to go yet. I love life"

son's 16th birthday, and then her daughter's 21st. Jennifer Marshall is happy to keep looking out for new trials because, she explains, "Julie-Ann's defied the odds; we just want to give her as good a quality of life as possible and keep her well."

Part of the problem with any cancer is its mutability. "Tumours change and become resistant," Dr Sally Burtles explains, "which is why single drugs, however good they may be when they get passed by NICE, are often more effective when we start trying them in combinations with other drugs or radiotherapy. Plus much of the work done in ECMCs is the search for biomarkers: these are the factors in our DNA that mean once we understand them we can start to anticipate who will do best from which drug before treatment even begins."

Highly personalised treatment is the future, she confirms. "We call it stratification: ultimately the aim is that every individual will be treated according to the exact genetic code of their cancer. Obviously there is still much work to be done, but I have no doubt this will come." As for the ECMCs, she admits that it is too early to talk of general success rates; that will be decided after peer review in 2011, but she anticipates that the project will be deemed a success.



ELLEN NOLAN

Julie-Ann Gallagher, 45, mother to 15-year-old Carl and 20-year-old Sarah, has lived with cancer for the past 14 years. Gallagher has been involved in a clinical trial during the past year

Prof Ruth Plummer admits she is sometimes in awe of the patients who join the ECMC's nationwide trials. "It is very humbling to meet these people who want to join our studies; they know they are often incurable and many are running out of options. We have to be really honest about what they are doing but they accept that this is unknown territory. They say – I know this may not help me but maybe it will help someone in the future. It makes our centres very positive places to be. And there is a very low refusal or dropout rate on the trials. It is unusual for anyone to decide not to join in if they physically can."

None of the three people interviewed knows for certain if their treatment has been a "magic bullet" either, yet all would take up the offer to do another trial. Even Gallagher, for whom the future does not look so hopeful, feels blessed. "I am grateful for the 14 years I have had. I am grateful I have seen my daughter's wedding. But you have to help yourself and make your own luck. Last Christmas I felt I didn't have long – but I am still here and I have no doubt that getting the bisphosphonate therapy has helped.

"Without these new drugs, cancer would have taken me, but I am not ready to go yet. I love life. And I still hold out hope for a miracle cure."

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