LIFE SCIENCES INDUSTRY REPORT 2025

PART 5: ONCOLOGY

Uncover the transformative trends that will drive the life sciences industry ahead, backed by expert commentary and data-driven insights.

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Editors' introduction

When we think of cancer, we think of a fight: a battle between a patient and a mutation to their biology, a transformation – a hijacking – on the cellular level. Indeed, cancer doesn't just take over a person's physical body, but their very life. Therefore, a critical focus on the very language of cancer has sharpened, an awareness of the importance of utilising words, vocabulary that is easily accessible for patients who may be overwhelmed by an excess of complex information. Similarly, navigation of cancer survivorship and ameliorating care options for those in the post-operative and multi-stage therapeutic phases of their disease and maintaining quality of life throughout has been more keenly assessed and addressed.

Furthermore, for oncology generally, last year was a 12-month period in which the potential of combination treatments was embraced with both hands, so to speak, research outcomes explored with an air of excitement at scientific conferences, and news frequently scattered with the potential of desiloing and collaborating instead. In short, a discourse is underway that seems very much to be heading towards meeting unmet needs, especially in the less common cancers. But it cannot be done alone.

In Part 5 of the Life Sciences Industry Report 2025, we look at just some of all this: from an interview with CEO of Vittoria, Nicholas Siciliano, discussing the future of CAR-T, to CK9 inhibitors and the possibilities there for disrupting cancer cell growth, as well as the applicability of mRNA vaccine technology when it comes to revolutionising cancer care. Part 5 also offers insight on the other side of things, HCP engagement and bringing awareness to physicians about drug development and treatment possibilities – and tackling the challenge of a decline in accessibility to healthcare practitioners in this regard.

With market data, including top-performing oncology drugs, and key takeaways from the year, an R&D focus that brings to its core the patient perspective is what became clear last year, and not only in oncology. Nonetheless, that essentially mutually beneficial understanding looks set to deepen in 2025, and beyond, across the breadth of the life sciences.

Eloise McLennan
Deep Dive Editor

Nicole Raleigh
Web Editor

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Life Sciences Industry Report 2025 Part 5:
Oncology

Market growth

The US oncology market is projected to grow from $104 billion in 2023 to $177 billion by 2028, with a CAGR of 11%.

Leading companies

Key players in the US oncology space include Merck, BMS, AstraZeneca, AbbVie, and Roche.

Sales channels

Non-retail channels dominate oncology drug sales, accounting for 88% of total sales, followed by mail order at 11%.

Top oncology drugs

The top five oncology drugs by treatment cost per patient are Revlimid ($470,901), Ibrance ($231,196), Darzalex ($201,877), Keytruda ($187,103), Opdivo ($118,355).

Biologics impact

Darzalex and Enhertu (biologics) are expected to drive market growth in 2028, contributing approximately $9 billion to the market.

Data and insights powered by EVERSANA

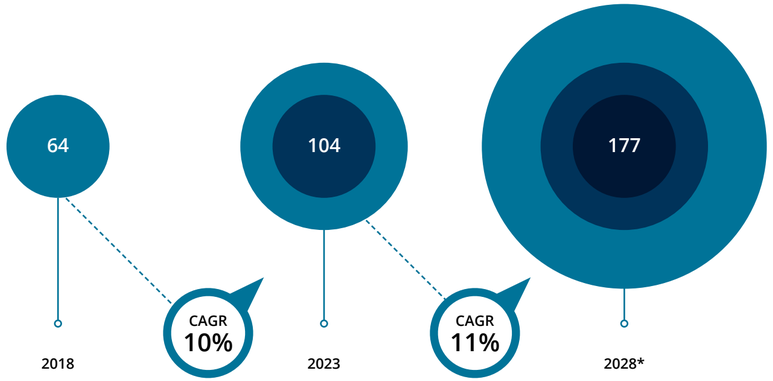
Performance of the US oncology market - 2023

The US oncology market has been forecasted to grow with a CAGR of 11% in the period of (2023 to 2028)

The US oncology market is projected to grow from $104bn in 2023 to $177bn by 2028, registering a CAGR of +11%

Note that growth rate here is 2% more than the US pharmaceutical market which has been forecasted to grow at 9%.

Some of the top pharmaceutical companies in the US dealing in oncology space include Merck, BMS, Astrazeneca, Abbvie and Roche.



Source: Secondary Research & Evaluate Pharma (Accessed on Mar, 2024)
*** Based on forecast on Evaluate Pharma*

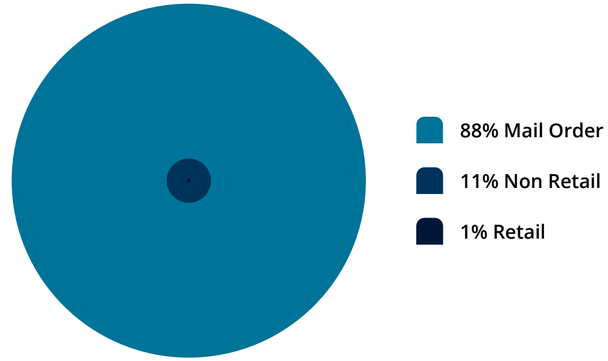
Sales by channel in oncology - 2023

The majority of sales (88%) are through non-retail channels, with mail order accounting for a significant portion (11%)

The non-retail channel significantly dominates drug sales, comprising approximately 88% of total sales

Following non-retail, mail order stands as the second-largest channel, representing 11% of drug sales

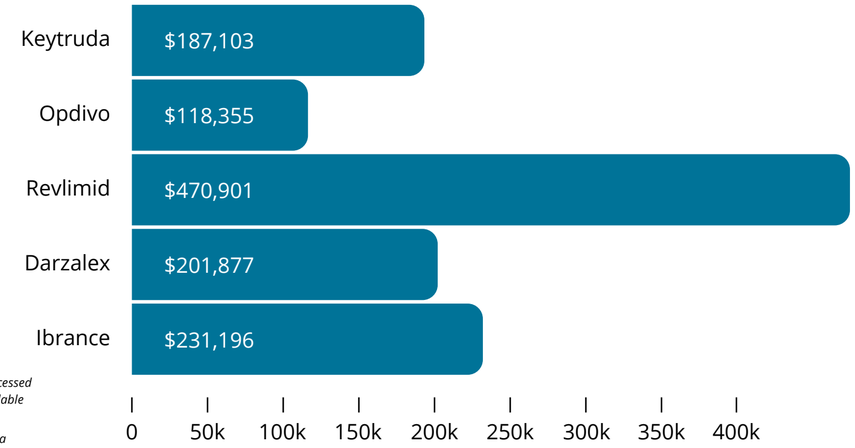
Retail channels hold a minimal share of 1% of sales, while the long-term channel has the least sales among all the channels



Source: Metys (top products covering 80% of the market)

Patient distribution & treatment cost per patient (Top 5 drugs)

Keytruda is seeing continuous gradual increase in patient count YoY compared to other drugs

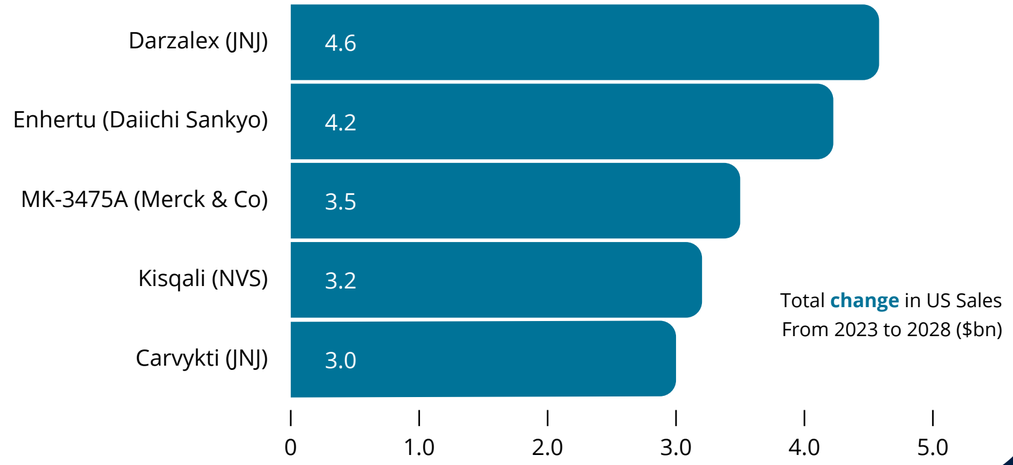


Source: EVERSANA Open Claims Data accessed on 19 December 2024 (2024 data is available till Oct' 2024)

Cost per Patient Source: Evaluate Pharma (Accessed on 19 December 2024)

Key growth drivers & breakers (oncology) by 2028

Darzalex & Enhertu (Biologics) will continue to drive the market growth in 2028, adding ~$ Bn 9 to the market



Source: Evaluate Pharma (Accessed on 19 December 2024)

Words matter: The power of language in cancer discussions

The priority for any individual diagnosed with cancer is to be provided an effective therapy as quickly as possible. However, Ben Hargreaves finds that, alongside treatment, there is a need to understand how language can influence both patient behaviour and outlook towards their therapy.

Patient centricity has been defined as putting the patient first in open and sustained engagement, with the aim of respectfully and compassionately achieving the best outcome for the patient and their family. The ways in which patient centricity can be applied have broadened beyond early utilisations in clinical trials to a range of areas, such as device design and the growing role of patient organisations.

One area where this is important, and particularly complicated, is in oncology. Cancer is the most feared of all conditions. Due to this, there is a huge amount of R&D going into creating new treatments and discovering new ways of treating cancer.

However, alongside the rush to treat the disease, there is also an awareness of the smaller elements that can make a patient's treatment journey more manageable or more difficult. This can be produced by something as simple as the language used during the treatment and diagnosis process. Words have the power to influence a patient's outlook, and that alone should be enough to draw focus to the area.

The power of words

This change is happening, as the use of language is understood to be particularly relevant for cancer patients. It is common to hear terms used for cancer and patients that are not used in other disease areas. Language has emerged that relies on 'fighting' terms to describe the treatment process: being in a 'battle' with cancer, 'surviving' a diagnosis, and 'losing their battle' with the disease. For some people, the outlook of physically confronting the disease may be of use, but how helpful this type of description is for broad populations is now being researched more.

A study by the University of South California found that using terms such as 'battle' or 'war' to describe being treated for cancer led people to feel that the process must be difficult, and painful to treat. Further, the surveyed participants felt they would not be able to control the disease or do anything to stop it from occurring – which is particularly dangerous, given the number of lifestyle factors that increase the risk of cancer.

The importance of the issue has also seen major companies that produce cancer treatments conduct research to understand better ways to engage compassionately with patients. Novartis released findings from its study, 'My Cancer. My Words', at the end of last year. The company surveyed over 2,000 people living with cancer in the US and the UK, and healthcare professionals (HCPS), to explore how the use of language affects people living with cancer.

The aim of the study was to understand how people reacted to specific words and phrases commonly used in relation to cancer and treatment. Researchers compiled the frequency of words associated with cancer, as well as

The words and metaphors people use to talk about cancer can feel worlds apart from any other disease.

what phrases they associated with cancer, and whether words and phrases would be associated with a positive or negative impact on treatment choices. And pharmaphorum received comment from a Novartis spokesperson to better understand the company's aims for carrying out the research.

"The words and metaphors people use to talk about cancer can feel worlds apart from any other disease. By teaming up with a multidisciplinary committee of experts, as well as surveying patients and physicians in the UK and US, we wanted to investigate how much words really matter, and to what extent language might even affect cancer outcomes. Our aim is to inspire more people living and working with cancer to explore this issue with us, and to create greater debate about the under-recognised – yet critical – role words can play in cancer treatment," the spokesperson stated.

Individual reactions

Novartis' survey found two-thirds of patients (67% of 1871) and almost all healthcare providers (88% of 142) believed that language impacts their lives or the lives of those living with the disease. Among the findings, people living with cancer most commonly associated 'cancer' with 'death', 'chemotherapy', 'pain', and words that are used to describe fear and anxiety – this held true for all types of cancer, and for however long they had lived with it.

The research also focused on identifying the differences that existed between the respondents based in the UK and the US. One finding was that nearly all metaphors were perceived to have a negative impact on treatment choice by UK participants, which did not hold true for those in the US. Novartis provided the example of the word 'warrior', which half of respondents in the UK identified as having a negative impact on their ability to choose a treatment, but was mostly found to have a positive impact on those in the US.

Worse than simply having a negative impact on treatment choice, the 'war' terminology frequently deployed may create a feeling of impotence in those where recovery is not possible. In a study with women diagnosed with metastatic breast cancer, the results found that women responded to diagnosis as an 'unfair fight' because of its incurable nature. Instead, the participants preferred to emphasise 'living life' with their diagnosis, rather than fighting it.

No perfect solution

A conclusion that Novartis' study drew was that there were no universally 'perfect words'; even words that could be regarded as neutral, such as 'patient', elicited both a positive and negative reaction. The focus, then, must be on understanding the individual's language preference. One lesson to be taken is that some people will be helped by identifying as a warrior, while others may prefer language that highlights that they are living a normal life, regardless of their diagnosis.

In terms of how Novartis will apply the study on its work in the future, the spokesperson offered: "In the short term, we hope it will inspire more people living and working with cancer to explore this important issue with us. However, the questions it raises are complex. How we can build on this research with the community over the longer-term is something we're discussing with our committee of experts, and we welcome wider input."

As with many complex issues, there is no single correct answer. Simply having the discussion over what word choices would be suitable for the patient is the right path forward to create a flexible, individual-orientated language for use with people living with cancer.

About the author

Ben Hargreaves is an established freelance life sciences writer, whose experience includes such publications as the BioProcess Insider, BioPharma-Reporter, BioSpace, Outsourcing-Pharma, pharmaphorum, and Motley Fool, among others.

Life after cancer: Navigating survivorship and mental health

When we think of cancer, we think of a fight: a battle between a patient and a mutation to their biology, a transformation – a hijacking – on the cellular level. Indeed, cancer doesn't just take over a person's physical body, but their very life.

The word "cancer" brings to mind diagnosis – and the mental impact of that on the person, who becomes "patient" thereafter, and their families – as well as the treatment possibilities, and the recovery, the regathering of strength post those therapies, and – sometimes, hopefully, when effective – pulling through and making it to "the other side", so to speak: the cancer in remission.

In short, when it comes to journeying through cancer care, there seems to have been prolific, yet strangely finite, consideration of that path, ceasing when it comes to post-treatment. Screening and diagnosis to treatment and remission have been covered, but what about what happens after that? What about cancer survivorship? The good news is that a shift in the state of affairs is occurring.

In the aftermath of cancer: Fear of the unknown

June was National Cancer Survivors' month. As the National Cancer Institute (NCI) defines it, cancer survivorship as a term applies to those who have faced cancer, undergone treatment, and survived – but, importantly also, continued onwards "through the balance of [their] life".

This notion of balance is key. To survive cancer is not necessarily to be free of the disease; life, indeed, can very much be lived with cancer. After all, the essential nature of "survival" is to continue to live or exist in spite of an accident, ordeal, or challenging circumstances. It is under such stresses, though, that we change. Therefore, it stands to reason that post-treatment care for cancer patients should evolve to parellel these changes.

After cancer treatment has "completed", real-life adjustments can be considerable, taking a toll not only on the body, but on a patient's mental health. A study published in Medical Clinics of North America as far back as 2017 noted the negative mental health aspects of survivorship: that there was fear and hypervigilance to physical sensations – known as "fear of recurrence" (FOR) – and that cancer survivors "have numerous sources of distress that increase their potential for adjustment reactions". That "distress" becomes an umbrella term for myriad and divergent symptoms, ranging, according to the National Comprehensive Cancer Network (NCCN), "from common feelings of vulnerability, sadness, and fears of recurrence to disabling depression, anxiety, trauma, panic, and existential crisis." That's a pretty broad remit, and certainly not insignificant when it comes to consideration of cancer survivorship care.

The same study suggested screening, not only for cancer recurrence, but for mental health needs. The NCCN itself has guidelines for screening distress to assist healthcare professionals with this, a commonly recommended measure being the Distress Thermometer (DT), a simple oral or printed measure that asks the patient to rate their distress from 0 = no distress to 10 = extreme distress. If a patient scores four or higher, further screening may be needed.

The burgeoning field of cancer survivorship research

Cancer survivorship research, such as that conducted at Imperial College London, focuses on the health and wellbeing of people who are living with, through, and beyond a cancer diagnosis, recognising at the same time the impact of cancer on family members, friends, and caregivers.

This field of research has sprung up because – happily – cancer survival in the UK has doubled over the last 40 years. It is estimated that some four million people will be living with or after cancer by 2030. However, it is a double-edged sword: a greater number of cancer survivors means a greater number of people living with the after-effects of the disease and its treatment. It is for this reason that supporting people to live with and beyond cancer is a major focus of the NHS Long Term Plan for Cancer. Indeed, the National Cancer Research Initiative has recently published Cancer Research Priorities for Living With and Beyond Cancer.

Fear of recurrence (FOR) is palpable, a beastly nightmare that poses a threat in waking and in sleep, seeping through the fabric of the family unit – exacerbated by the fact that late effects might not exhibit for months or years following the last treatment. These effects can include cardiovascular and pulmonary issues, bone loss, changes to sight and hearing, lymphoedema, and additional problems.

The same Medical Clinics of North America study mentioned above also noted the extensive Childhood Cancer Survivor Study (CCSS), which tracked over 20,000 survivors across the US. While most survivors did not meet the criteria for a diagnosis of post-traumatic stress disorder (PTSD), many survivors did report post-traumatic stress symptoms. Certainly, adult and young adult (AYA) survivors (normally, 15 to 39 years of age) are increasingly recognised as a group with emotional needs that differ from either childhood cancer survivors or older adults, and FOR is common in this bracket.

What is important to note is that physical symptoms can be associated with depressive symptoms. In other words, FOR and its ilk can become a case of “directed energy”: think it, and it shall happen. One example in the Medical Clinics of North America study was oral cancer survivors, who reported dental health, problems with smelling, and issues with range of motion – all associated with both depressive and anxiety symptoms. In terms of treatment for cancer survivors, however, when it comes to mental health conditions, which the study notes “can linger for up to 10 years after treatment” – cognitive behavioural therapy (CBT) has been shown to be effective in reducing mood symptoms, while mindfulness-based approaches have demonstrated efficacy in reducing anxiety and depressive symptoms.

Furthermore, according to a Phase 3 study led by researchers at the University of Pittsburgh School of Medicine, and supported by the National Cancer Institute, run at the UPMC Hillman Cancer Center in Pittsburgh and published in The Lancet, cancer patients who receive specialised mental health support as part of their treatment plan are more likely to see improvement in quality of life and pain reduction, as well as fatigue and depression.

Importantly, the study showed that, even if the collaborative care intervention was offered to patients for free, hospitals could expect to save some $4 million or more for every 250 patients. Mental health treatment for cancer survivors, it suggested, results in fewer emergency room visits, fewer readmissions to hospital within 90 days, and a shortening of the length of hospital stays themselves – all benefits that reduce costs to healthcare systems.

Shaping the future of cancer survivorship care and support

The National Cancer Survivorship Resource Center (The Survivorship Center) is a collaboration between the American Cancer Society and the George Washington University Cancer Institute. Funded by a five-year cooperative agreement from the Centers for Disease Control and Prevention (CDC), its goals are to shape the future of cancer survivorship care and improve the quality of life of cancer survivors as they transition from treatment to recovery.

Merck & Co (known as MSD outside of the US and Canada) is a pharma company striving to provide similar support. The World Cancer Day motto, “Alone we are strong. Together we can be unstoppable.”, urges the necessity of collaboration, and 2024 has been an important year for the Close The Care Gap campaign, which advocates equitable access to cancer treatment. Notably, Merck has collaborated with the American Cancer Society’s Building

Expertise, Advocacy, and Capacity for Oncology Navigation (BEACON) initiative for several years, also, supporting global health institutions in low- and middle-income countries (LMICs) by fostering the creation and integration of cancer patient navigation programmes to address disparities in cancer care. Additionally, by harnessing AI, ML, and other technologies, the company insists personalised cancer care can be supported in ways that were not possible before; for example, digital healthcare platforms, which can enhance patient education and help support adherence, while cultivating community support, including such CBT programmes as mentioned above.

A case study – Breast cancer and the enlightened patient experience

Let's turn, though, to a real-life example of cancer survivorship: Bethan Brookes, a journalist who wrote a personal blog about her cancer, and who permitted reference to her journey in this feature, is now in remission. However, her life was turned upside down on the 13th January 2021, when she was diagnosed with advanced HER2-positive Stage 3 breast cancer. Three weeks later, she had had a mastectomy ("Show up. Breathe. Trust", the name of the blog, was Brookes' mantra on the morning of her mastectomy); all of the lymph nodes on her left-hand side were also removed (15 out of 20 had shown signs of cancer). This was followed over subsequent months by gruelling chemotherapy rounds, radiotherapy, and drug therapy.

The blog, in fact, became Brookes' own form of therapy, her mental health journey through cancer survivorship – and an online location to which other cancer survivors could come, read and relate, share their stories, and build a community of care.

To follow Brookes' journey through her blog is to accompany her through "spiralling fears" following a mere "four-minute call (rather than a face-to-face appointment)" due to the COVID-19 pandemic, to understand that "nothing can prepare you for the diagnosis", but that there is a calming effect within simple, clearly defined instructions for patients undergoing surgery and post-operative care. Of course, an operation is just "a launch pad" for the "odyssey" that cancer is. The diagnosis changes everything and "fear loomed large in the shadows".

After an all-clear post-mastectomy, there was a separation that Brookes felt from normalcy, feeling that she had "finally stepped over the threshold into a different space. The club that no-one wants to be part of. The cancer club. And through the cancer club lens, the world looks different." Indeed, that club contains "a seemingly endless continuum of tests and scans, nail-biting waits for results, and follow-up appointments." What saw her through the early days, though, was the allocation of a MacMillan breast cancer nurse.

Such support is deeply required by patients who have no clear inkling of the parameters of time left them post-treatment, as much as during: Will it be five years? Five months? The psychological impact is intense. The expression "every moment counts" is a pressing one for the survivorship group, and for their nearest and dearest. In Brookes' case, she shares that there came a point where, with hesitancy, her 16-year-old son asked whether he could see his mother's mastectomy, asked with "courage and emotional maturity" – highlighting that, when it comes to adapting to the cancer journey, it is not just the patient who is forced into accepting transformation – a "brutal transition" – of life as they had come to know it.

While Brookes herself is stoical about the loss of one of her breasts – "They fed my children and sustained new life. They have done their job, and, for me, losing one will not significantly diminish my experience of life." – she is also consciously aware of the stigma and, sometimes assumed, sympathetic distress of "other people" about such a loss for a woman. And that can

include survivors' own partners and children. But it is, as Brookes states, all too easy "to choose to retreat into a place of separateness", to seek refuge in the "quiet loneliness" of the disease. The cancer survivor's journey is frequently not a solo one; rather, it is one embarked upon hand in hand with a loved one, there to provide support in the darkest hours.

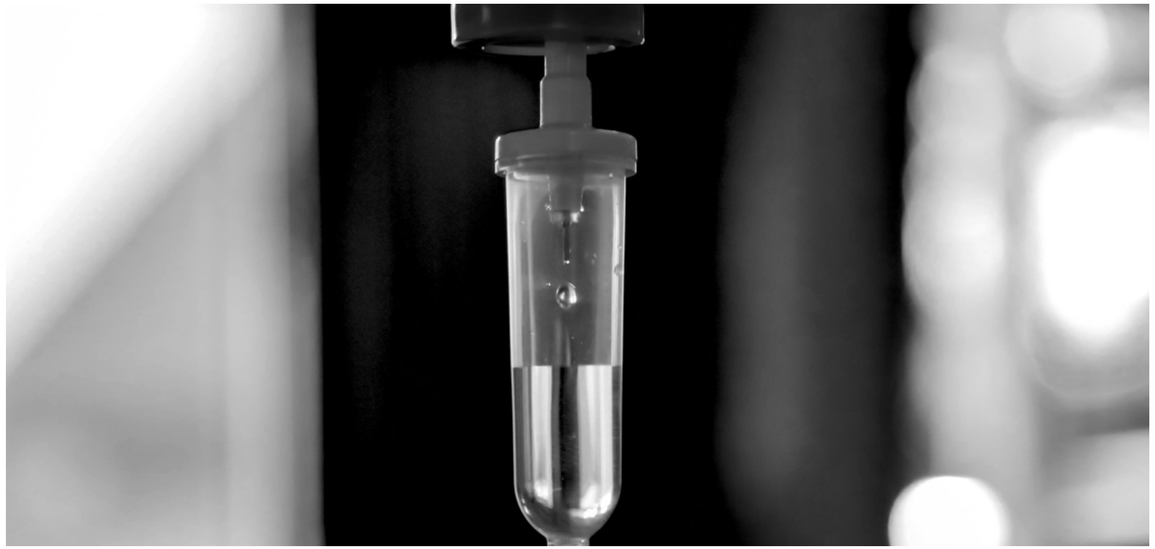
Sadly, that is not always the case, however, and a retrospective longitudinal study conducted over 10 years and published in the Journal of the National Comprehensive Cancer Network found that loneliness and social isolation were associated with a higher risk of mortality among cancer survivors, according to the UCLA Loneliness Scale. A total of 3,371 cancer survivors with 5,711 person-years of observation were included in the study and most of them were long-term survivors, diagnosed over two years prior to the survey. The variables of male sex, non-White race/ethnicity, unmarried status, less education, more health conditions (other than cancer), and feeling depressed in the past year were linked to a higher probability of feeling or being "lonelier".

Survivorship: No battles, but acceptance

Support and community are key words, then, in cancer survivorship. So, while naming her drugs after her children's favourite Avengers characters and glutting on Schitt's Creek to see her through long and gruelling chemotherapy sessions seems formidable in the concept of fighting cancer, it is notable that Brookes would beg to differ with the notion of "fighting", per se. Instead, for her "using the language of war feels neither helpful, nor wise [...] To be at war with the cancer implies a zero sum game. Cancer or no cancer. Win or lose. You beat it or it beats you." What is to be submitted to, rather, is an acceptance, a "surrender to the process."

Survivorship for Brookes is a crossroads of an ending and a beginning. After "one mastectomy with full lymph clearance, 27 intravenous infusions, 21 sessions of radiotherapy, 16 doses of targeted therapy, 36 self-administered injections, [and] a bucket full of drugs" she finished her treatment, yet noting that NICE guidelines state she should not receive any monitoring scans. Rather, she – as are other such survivors – is advised to carry on with life, "hope for the best, and 'wait for any symptoms of secondaries' (which will mean [...] Stage 4 cancer)." The onus, then, falls on the patient, a health responsibility brusquely handed back. So, while Brookes takes on the importance of stress reduction, a largely plant-based diet, supplementation, and exercise – and prioritises tasks dependent on energy available on any one day whilst in recovery, from treatment, from trauma – it's all too clear that "modern oncology focuses on treating us once we have been diagnosed with cancer," looking ever for a cure, rather than prevention, or healing post-fact.

Brookes' automatic and "underlying suspicion" was that it was all about cost-saving. The reality is, however, that repeated scans are not good for the body: the risks of developing a fatal cancer from a CT scan are about one in 2,000. Yet, the risks are not the same for every cancer, nor each individual. Personalisation



is, indeed, also key. There is, furthermore, the consideration that, with any secondary cancer that might be found via a scan, care then becomes palliative, focused on improving quality of life, as it is “incurable”.

Brookes has since opted for a contralateral mastectomy, not wanting reconstruction. It’s not about risk reduction, but about “symmetry” – again, this notion of balance, of stability, of control over one’s body once more. Yet, while Brookes notes the sense of “an identity in free fall” and repeated moments of return to the trauma of her experience, survivorship – like the cancer experience itself – is unique to each individual.

Cancer survivorship: Personal in so many ways

In a landmark 1985 report published on cancer survivorship, physician Fitzhugh Mullan described his own battle with cancer and the unique issues that lay ahead for survivors of malignancies. In the report, he observed three “seasons of survival”: acute survival (diagnosis to completion of initial treatment); extended survival (the period of anxiety over possible recurrence); and permanent survival (recognising the likelihood of having been cured).

The outcomes for cancer survivors vary on many levels. As a 2021 Canadian study published in Current Oncology noted, of the 44 participants who took part – 11 survivors, seven family/friend caregivers, 18 healthcare providers, and eight decision-makers – 13 stakeholder-relevant outcomes were identified and categorised into the domains of psychosocial, physical, economic, informational, and patterns and quality of care.

In 1996, the Office of Cancer Survivorship (OCS) was established to promote a better understanding of and the ability to address the unique needs of the growing population of cancer survivors. Housed within the NCI’s Division of Cancer Control and Population Sciences, the OCS works to enhance the quality and length of survival of those diagnosed with cancer and to minimise or stabilise adverse effects experienced during cancer survivorship. The office supports research that both examines and addresses the long- and short-term physical, psychological, social, and economic effects of cancer and its treatment among cancer survivors and their families.

Cancer survivorship research under the OCS includes a variety of funding mechanisms, such as Investigator Initiated Applications (R01s), Small Grant Programs (R03s), and Requests for Applications (RFAs), as well as collaborations within NCI and other organisations regarding survivors' needs for education, communication, and appropriate medical and supportive care.

Refocusing the cancer club lens

There yet exist further barriers to accessing what is clearly necessary mental health support as a cancer survivor, including stigma, lack of integration between oncology and mental healthcare systems, and financial constraints. To this end, endeavours such as the Working With Cancer Pledge, for example, ensure a supportive and positive work environment that is inclusive, respectful, and safe, providing beneficial, informational resources.

Additionally, if a cancer survivor goes on to develop another condition separate from the oncological, the impact on their care is considerable. Nonetheless, despite these challenges, there exist evidence-based interventions for mental health in survivorship, too, such as psychotherapy, pharmacological treatments, peer support, and lifestyle interventions. Therefore, there needs to be a call for greater collaboration – again, one of those key words – between oncology and mental health professionals; and a greater call for education on the availability of these interventions.

At the end of the day, it should be remembered that many cancer survivors spotlight the gratitude they feel for each new day that dawns: the value in life and living, in friends and family, and the necessity of community in fighting the fight (or the process of acceptance and submission) and carrying on – through treatment, and beyond – is invaluable.

About the author

Nicole Raleigh is pharmaphorum's web editor. Transitioning to the healthcare sector in the last few years, she is an experienced media and communications professional who has worked in print and digital for over 18 years.

Insider insights: Vittoria CEO Nicholas Siciliano on the future of CAR-T

Unlocking the full potential of CAR-T cell therapies remains one of the most exciting and actively pursued frontiers in cancer research today. While the emergence of these innovative therapies has generated immense interest, there is a pressing need to push beyond the hype to confront the very real challenges limiting their efficacy and accessibility, driving continuous innovation to enhance these potentially curative treatments.

In this exclusive interview, Deep Dive editor Eloise McLennan sat down (virtually) with Vittoria Biotherapeutics' CEO and co-founder, Nicholas Siciliano, to gain an insider's perspective on the state of the CAR-T field. Here, he shares his insights into the key challenges that must be addressed to propel this revolutionary modality forward into what he calls the "second inning" of CAR-T treatments.

Eloise McLennan:

How did you get into the field of cell therapy?

Nicholas Siciliano:

For the last 15 years or so, I've had a front-row seat to all the advances in cell and gene therapy and the technologies being translated at Penn [University of Pennsylvania, Philadelphia]. It's been really exciting.

I took a non-traditional path out of my doctoral degree. I co-founded a molecular diagnostic company in the greater Philadelphia area called Invisible Sentinel. It was with technology that I actually invented. We didn't spin it out of a university. Because of that, we had to take a "non-traditional" financing route. Long story short, [we] got it funded by a few high-net-worth individuals back in the 2008 market downturn, who thought it was less risky to invest in two first-time entrepreneurs than leave their money in the stock markets.

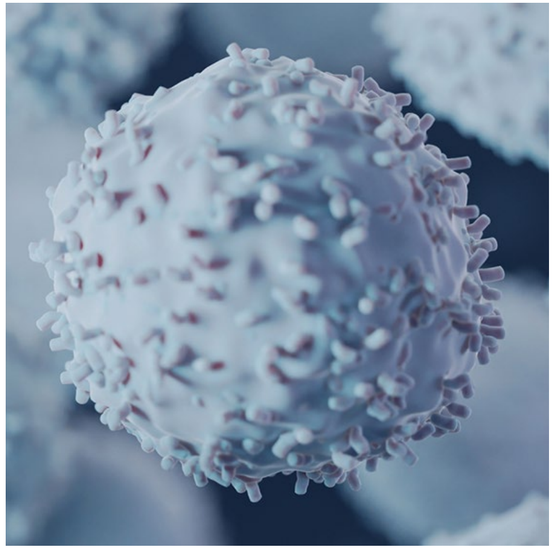
That was a great experience. It taught me a lot. It also plugged me into the network here in Philadelphia, of entrepreneurs and investors. On my travels, I met an individual by the name of Bruce Peacock – one of the premier life sciences executives, arguably in the country. He and I partnered about six or seven years ago on forming NewCos out of the greater Philadelphia ecosystem. It was through that endeavour that we came across the underlying technology for Vittoria.

Could you give us a brief overview of where we are at the moment in terms of CAR-T cell therapies?

We're in the second inning of what I believe is a game that's going to go well into extra innings. With the initial translational work done at Penn with what is now Kymriah, the excitement level was really high. Then again, it took some time to really dig in and understand, how can we apply this to other indications? How can we make it better for B-cell malignancies? Then there was a lot of early excitement around allogeneic therapies.

Unfortunately, some of the initial clinical results were not what everyone had aspired for. That's an interesting dynamic because I believe there's a place for both autologous and allogeneic therapies in the future of this modality. What I'm seeing now is this emergence of a third class that I like to term, "enabled autologous".

You may never get the same type of curative potential from an allogeneic that you would with autologous, but again, with autologous, there are still many drawbacks with logistics, and challenges. I think enabled autologous is trying to bridge that gap.

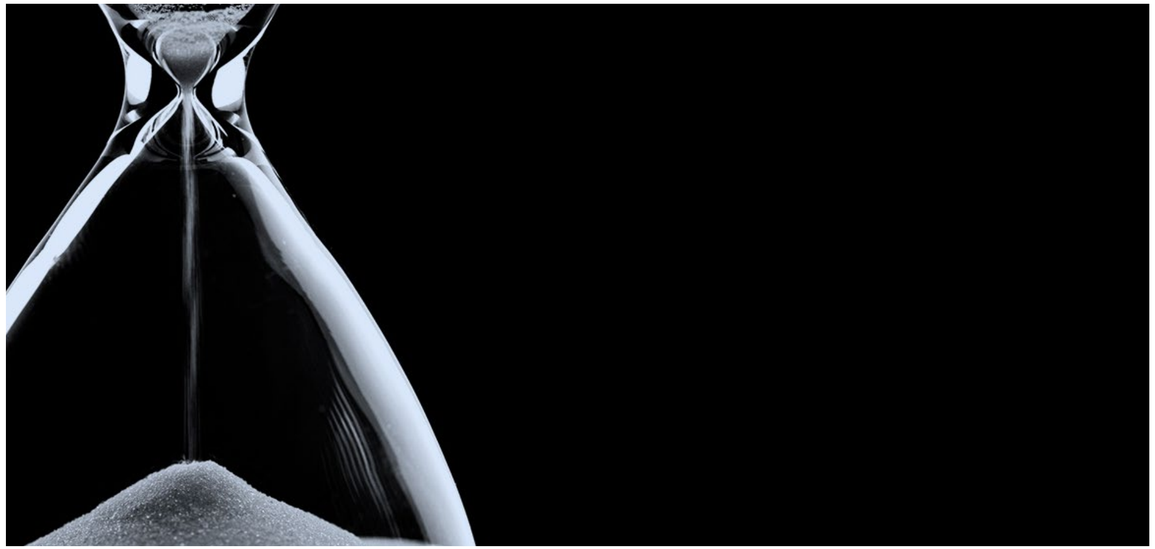


What are the most significant challenges currently facing CAR-T cell therapies in terms of efficacy and patient outcomes?

One of the challenges with the first-generation products is that we see complete responses in 30% to 40% of the patients. It'd be great to double that number. Obviously, we'd aspire for 100%. Increasing effectiveness is always top of mind.

Some drivers around that current shortfall are: Do the CAR-Ts expand for every patient? How can we confer enhanced proliferative properties? One of the strongest correlates so far is that early expansion of the CAR-Ts in the patient is important to achieve a complete response.

The second is the durability of the CAR-Ts. Often, what you see are the partial responses and then the patients relapse. Often, that's due to the T-cells becoming exhausted. Anything we can do to make them more resistant to exhaustion and have them be active longer in the patient will be important to increase that. Then, on the other side, there's the manufacturing and logistics piece, but I'll pause there to see if there's anything more you want to talk about therapeutically.



The high relapse rate is a significant concern in CAR-T therapies. What are the primary factors contributing to this issue, and what advancements are being made to address it?

One of the challenges with targeting a pan antigen – whether it be CD19 for B-cells or BCMA – is antigen escape. One of the things that drives that escape in general with cancer is selective pressure and time. Therapies that do a better job clearing tumours sooner rather than later, such as getting more exhaustive clearance early on, will help prevent things like antigen escape.

There are unrealised checkpoint pathways. One that we work on at Vittoria is the CD5 signalling pathway, which can potentially unlock or harness the patient's natural immune response to the tumours.

That might even be a new approach that you see. We see some of that with engineered TIL [tumour-infiltrating lymphocyte] therapies now, but I think we can apply it to engineered T-cell therapies like CAR-T and TCR-T.

The high cost of CAR-T cell therapies is a significant barrier to widespread adoption. What steps are being taken within the industry to reduce these costs?

Some of that's going to come just generally with economies of scale as this becomes more of a common modality. The cost of the drug substances needed to make these products, the cost of the associated labour, all of that will benefit from some economy of scale. The big needle mover will be the automation of these processes, particularly autologous processes.

By trimming days off the ex vivo manufacturing process, you do a few things. One is you reduce the labour costs, you reduce the time required in a GMP clean room facility. But interestingly, shorter manufacturing times for autologous cell therapies also confer a functional benefit to the resulting drug product. It actually makes the drug product more potent.

The less time a patient's cells spend outside of their body and in an artificial and external

environment, the less exhausted they become and the better they do. By shortening the ex vivo manufacturing processes, you can also significantly lower the required dose in many cases – this is the case of Vittoria – because the expansion winds up happening in the patient, rather than in the manufacturing process. That's also important.

Beyond blood cancers, what new applications of CAR-T therapies are currently being explored by researchers and developers?

Some of the hottest indications or applications being talked about now are in immunology. Really exciting work is ongoing with lupus patients and other immunology applications, Graves' disease, for example, where B-cells are mediating the pathogenic effect.

At Vittoria, again, we've also taken an eye to that. Our second programme right now has a huge potential application in lupus. It also addresses one of the inherent safety issues with all of the first-generation B-cell-targeted CAR-Ts, in that it would specifically target the pathogenic B-cells and spare healthy B-cells in immunology applications.

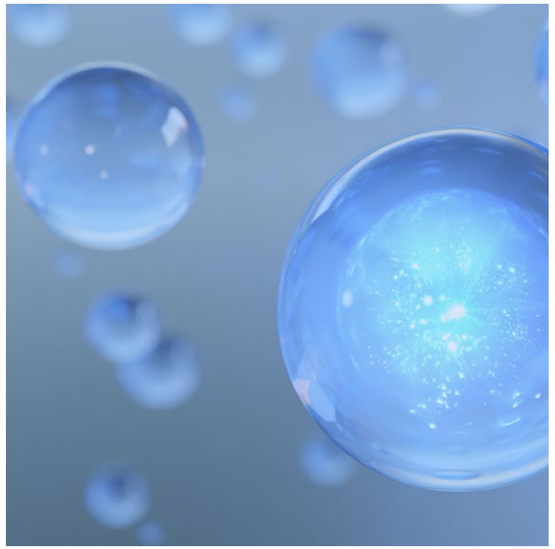
In oncology, it would specifically target the malignant cells and spare the patient's healthy B-cells. That, I think, is a really interesting dynamic and one of the, again, areas where we'll start to see improvement in the space – call it on-target, off-tumour issues.

What are the key regulatory challenges facing CAR-T therapies? How can industry work with regulators to try and overcome them without impacting what patients are able to receive?

You know what? I'd like to take this opportunity to pay a compliment to the FDA. They've made a significant effort to be thoughtful about some of these newer game-changing modalities like cell and gene therapy and build into what has been historically a very rigid infrastructure.

Now, the reality is, as a drug developer and just drug developers in general, the agency will never move fast enough because we want to be able to advance these technologies at lightning speed. But, over the last couple of years, I've seen a real effort to try to create pathways for accelerated approvals. One of the big challenges you have in this space, just again inherently, is that the technology is advancing so quickly that it becomes dynamic to manage the regulations.

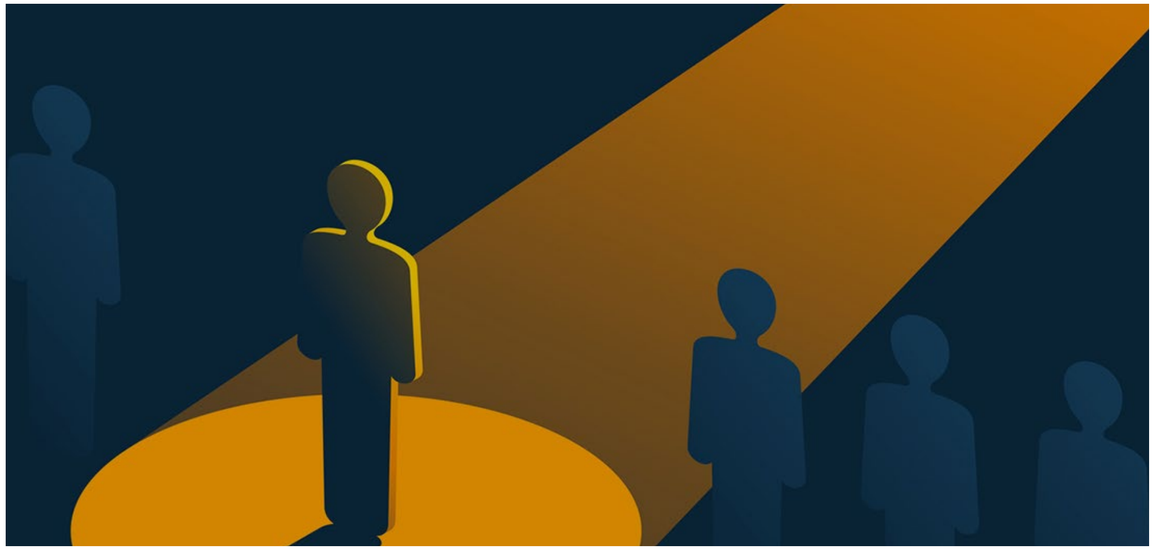
We all take a lot of responsibility playing in this space right now because it's going to be up to us to, one, get it right and, two, avoid major pitfalls that would, again, push the agency to become more restrictive.



You've called this era of cell therapy the "second inning", what innovations or research initiatives are addressing current limitations to push us into the third inning?

One of the inherent challenges is that there are just so many targets. There's an opportunity to get much more, I'll call it, 'surgical' with antigenic targets. I think you're seeing some of that with the TCR-T therapies, too, looking at epitopes in the context of MHC receptors.

There's also this concept of cell therapy unlocking the patient's naturally occurring anti-tumour T-cells and immune cells to create additional effector populations of cells in the patient. That's something that we're working on at Vittoria that we're really excited about. That could be a real game-changer.



Finally, what excites you most about the future of CAR-T therapies, and what potential advancements or breakthroughs do you foresee in the next few years?

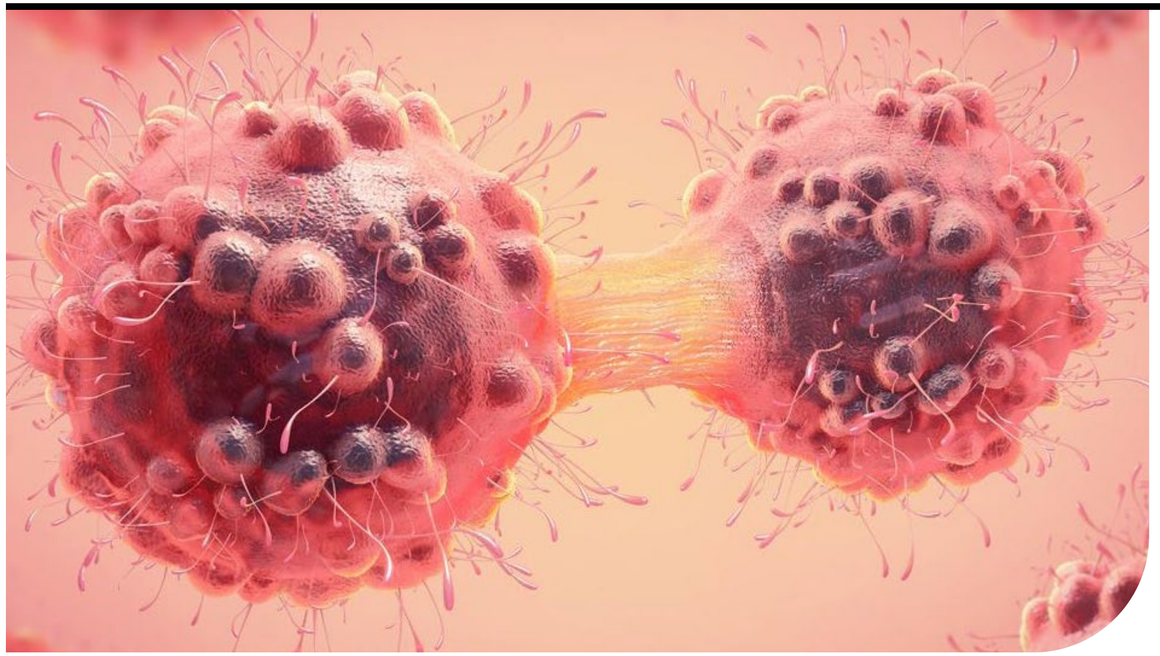
I think in the next couple of years, we're going to see this modality solve for some of the "holy grails" in the space, such as solid tumour treatments and metastatic tumours.

I think we are moving in the right direction to start to make some progress there. Again, some of that comes with armouring technologies or the work we do at Vittoria with our SENZA5 platform to be able to overcome resistance and immunosuppression.

Breaking into the solid tumour paradigm – that's probably the next big near-term milestone to fall.

About the author

Eloise McLennan is the editor for pharmaphorum's Deep Dive magazine. She has been a journalist and editor in the healthcare field for more than five years and has worked at several leading publications in the UK.



CDK9 inhibitors: Disrupting cancer cell growth and the treatment paradigm

We have made significant strides in cancer treatment in the last decade and a half. Patients are living longer than ever before, largely due to the innovations developed within our biotech and pharma industry.

But our work is nowhere near done. Patients relapse or develop resistance to medications and, even in some cancers with approved targeted therapies - such as peripheral T-cell lymphoma (PTCL), which accounts for ~5%–10% of all lymphomas (NIH) - the National Comprehensive Cancer Network (NCCN) guidelines still recommend a clinical trial or chemotherapy and radiation.

Moving beyond chemotherapy and radiation

For patients with PTCL, and frankly patients with most types of cancers, chemotherapy historically has a low complete remission rate and many quality-of-life impacting side effects, including bone marrow toxicity called myelosuppression, peripheral neuropathy, and infections. PTCL also has one of the highest rates of relapse. Once patients relapse, medicine options are extremely limited, and many move on to try experimental drugs in investigational clinical trials.

Patients deserve better, they deserve options, and we're at a point in scientific discovery as a biopharma industry that, if we come together and focus, we can deliver patients safe, well-tolerated, and curative cancer treatments. I believe Cyclin-Dependent Kinase 9 (CDK9) inhibitors are one modality that will bring us a step closer to that future.

By targeting the fundamental processes that enable cancer cell survival, CDK9 inhibitors offer a highly attractive and sought-after cancer therapy in haematologic malignancies, particularly in lymphomas.

CDK9: An appealing target for cancer therapy

CDK9 is a key regulator of transcriptional elongation and has been shown to modulate the expression and activity of oncogenes. Aberrations in CDK9 activity have been observed in multiple types of cancers and, due to its key role in the progression of malignant cell phenotypes, CDK9 has emerged as a novel prognostic marker and an appealing target for cancer therapy. CDK9 inhibitors have shown clinical potential to selectively stop the abnormal growth of cancer cells and, in some cases, induce cancer cell death, all while sparing normal cells and leading to fewer side effects.

CDK9 inhibitors also offer a modality to potentially overcome resistance and extend the half-life of existing treatments, by targeting a different pathway and providing an alternative method to combat the cancer cells that have grown resistant to another medicine. Furthermore, CDK9 inhibitors show low toxicity in clinical studies, making them an ideal combination agent, as they are not likely to add to the patient treatment burden.

Using PTCL as an example, which I know well due to my familiarity with the space and biology, PTCL is a group of rare, aggressive blood cancers that develop from the uncontrolled

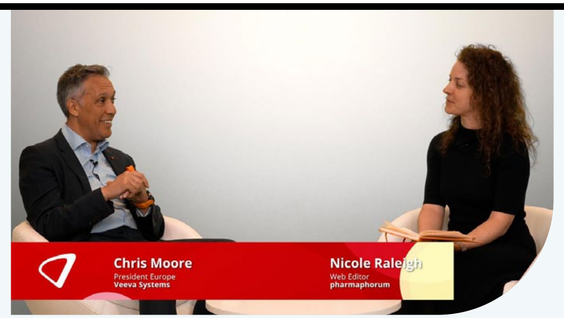
growth and division of mature T-cells. If we can inhibit (block) CDK9, we essentially cut off the cancer cells' supply of necessary growth signals, making it harder for the cancer cells to grow and survive and for the cancer to spread. Unlike with chemotherapy and radiation, this targeted approach spares the healthy cells and, in cancers like PTCL where patients fall ill extremely quickly, this could be less harsh on their immune system and hopefully lead to less off-target side effects. Clinical trial data validates this hypothesis, and I believe this approach can be replicated across many different types of cancers.

Enitociclib, which we're evaluating at my current company, Vincerx Pharma, as a standalone therapy and as a combination agent through a collaboration with the National Institutes of Health (NIH), is a timely example of the promise of CDK9 inhibitors. The positive data from our Phase 1 combination study of enitociclib plus venetoclax and prednisone gives me hope in not only enitociclib, but in CDK9 inhibitors as a drug class – hope in the ability to provide patients and physicians with a multitude of durable, safe treatment options and improve patient outcomes.

Our industry owes cancer patients medicines that enable them to thrive, not just survive, and I believe CDK9 inhibitors will help get us there.

About the author

Steven Bloom is the chief business officer of Vincerx. A seasoned executive with 35 years of experience in the healthcare industry, prior to joining Vincerx Pharma he held senior roles at Eli Lilly and Company, overseeing marketing, patient advocacy, and corporate affairs. He also helped build and scale start-ups like Inflexxion and Pharmetrics, before the latter was acquired by IMS Health. Bloom led business development activities at ZIOPHARM Oncology and served as chief strategy officer at VERASTEM Oncology, also, playing a key role in acquiring duvelisib, which was approved by the FDA in September 2018 for the treatment of CLL and FL. Additionally, he has served as chief business officer at Boston Pharmaceuticals and, most recently, at Transgene. Bloom graduated from Northeastern University College of Pharmacy in 1984 and has been an American Cancer Society Road to Recovery driver since 2008. He is currently Chairman of the Board of Directors of the CLL Society.



In conversation with Chris Moore: Declining HCP access

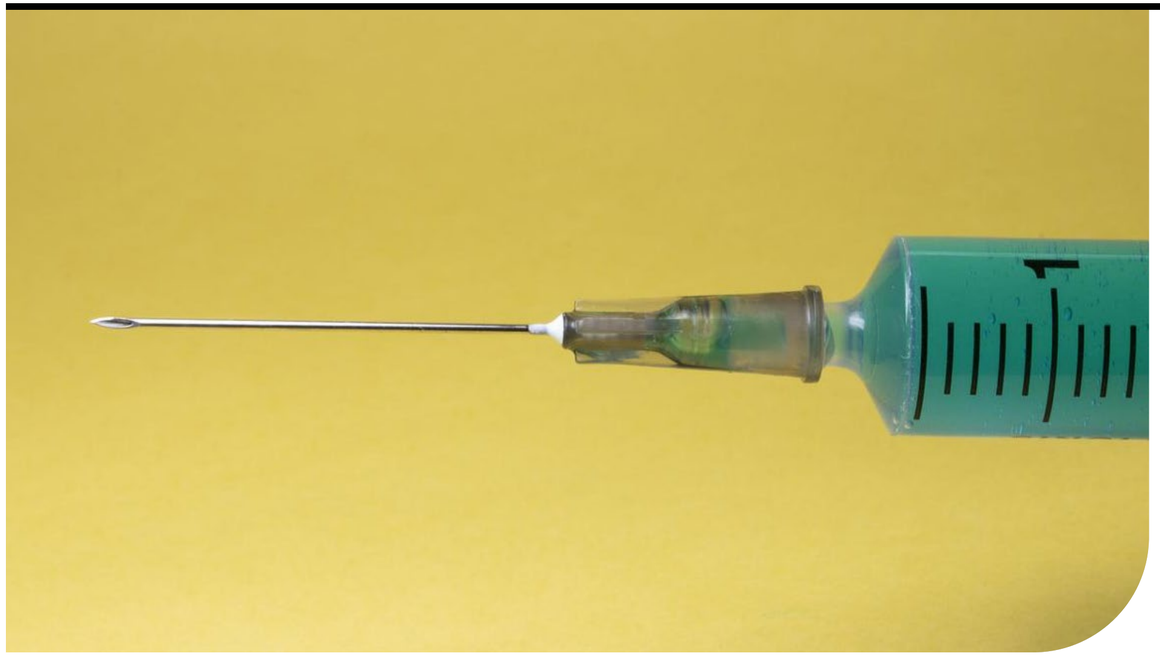
During the 10th anniversary of the Veeva R&D and Quality Summit, held in Madrid in June, web editor Nicole Raleigh sat down with Chris Moore, president of Europe for Veeva Systems, to discuss the global trend in declining HCP access and how a more coordinated approach across functions can help.

With less than half of HCPs now accessible, a Veeva Pulse Field Trends Report analysed why, looking at over 600 million interactions and activities, and finding that HCP access has returned to its pre-pandemic state due in part to HCPs being more selective across specialties.

Moore discusses how one connected resource across sales, marketing, and medical teams can build more relevant and trusted relationships with HCPs and, through such a coordinated engagement model, facilitate a positive upwards trend in HCP access again.

You can read more about the event overall here. You can also view another conversation between them on the event itself here.

And be sure to watch the video discussion here to find out more.



Beyond COVID-19: mRNA vaccines aim to revolutionise cancer care

mRNA vaccines, pivotal in the fight against COVID-19, are now emerging as a promising innovation in cancer treatment. As clinical trials advance, Ben Hargreaves finds the technology is poised to revolutionise oncology treatment by offering personalised, targeted therapies for various cancer types.

For the pharmaceutical industry, the pandemic can now be viewed as having provided temporary boosts: in terms of revenue, reputation, and cooperation. One innovation emerging from the industry in this period, however, has shifted from being a potential therapeutic option to a validated, permanent approach: mRNA technology. mRNA vaccines quickly became a core part of the vaccine strategy and proved that the technology had promise within infectious diseases.

With the significant revenue generated by COVID-19 vaccines, the rest of the mRNA vaccine pipeline has been accelerated forward. As a result, the potential global market for the technology is estimated to grow to be worth $68 billion by 2030. Such large revenue projections are fuelled by the therapeutic areas that companies developing mRNA vaccines are currently focusing on, with cancer being the next big target.

Vaccines against cancer

There are many different types of vaccines against cancer, such as the human papillomavirus (HPV) vaccine, which reduces the risk of cancer by protecting against HPV types that lead to cervical cancer. For mRNA vaccines, there are various ways that they can be used against cancer, including in adoptive T-cell therapies, therapeutic antibodies, and immunomodulatory proteins, as well as cancer vaccines.

The latter holds particular promise for cancer immunotherapy because they can stimulate and boost pre-existing immune responses to tumour antigens, increasing tumour cell recognition and clearance. This could allow for mRNA vaccines to be used as monotherapies or be used in combination with other anti-cancer agents.

mRNA vaccines also hold an advantage in being able to be tailored to each patient, with the ability to identify the mutations specific to each patient and thereby create an individualised cancer vaccine to target them. This may help the patient by preventing cancer return after surgery by stimulating the patient's immune system to recognise and destroy remaining cancer cells.

Trials begin

In August, the first patient in the UK received a lung cancer vaccine that is being investigated on this basis. The mRNA vaccine, known as BNT116, is being developed by BioNTech and is targeting the treatment of non-small cell lung cancer (NSCLC). The phase 2 trial will recruit 130 participants across seven countries, with six of the sites located in the UK. Patients enrolled in the trial will be at different stages of NSCLC lung cancer, from early stage disease before surgery or radiotherapy to stage 4 or recurrent lung cancer.

The objective of the trial is to determine the safety and tolerability of the mRNA vaccine. The trial will test the vaccine as a monotherapy,

while certain patients will also be given established chemotherapy or immunotherapy treatments in combination with the vaccine. According to BioNTech, the immunotherapy is Sanofi and Regeneron's Libtayo (cemiplimab), a PD-L1 checkpoint inhibitor.

Sarah Benafif, medical oncology consultant and leader of the study at University College London Hospitals, said: "The strength of the approach we are taking is that the treatment is aimed at being highly targeted towards cancer cells. In this way, we hope that in time we are able to show that the treatment is effective against lung cancer whilst leaving other tissues untouched."

A recent study noted several advantages that mRNA cancer vaccines hold in the development process, with the development of such treatments being relatively fast and cheaper compared to conventional vaccines. Other benefits outlined included that they are not produced with pathogen particles, decreasing the risk of undesired immune responses, and that the clinical trials to date have generated reliable immune responses, high efficacy, and were well-tolerated.

Expanding pipeline

The targeting of lung cancer is particularly significant given that it is the type of cancer most commonly diagnosed and responsible for the most deaths globally. However, this type of therapy could be applied to various types of cancer and is already being tested in this capacity. In July, BioNTech posted phase 2 results that showed a different mRNA vaccine candidate, BNT111, alongside Sanofi and Regeneron's Libtayo (cemiplimab), a PD-L1 checkpoint inhibitor, was able to achieve a statistically important improvement in the overall response rate for the combination treatment for advanced melanoma.

Another company that scored an approval for its mRNA COVID-19 vaccine, Moderna, is also progressing its pipeline of candidates against cancer. The bulk of its targets within cancer utilise its mRNA-4157 vaccine candidate to target various cancer types in combination with PD-1 therapy, with oncology indications including melanoma, NSCLC, cutaneous squamous cell carcinoma, and others. Each of these potential combination treatments have progressed to phase 2 or further.

With PD-1/L1 treatments being effective treatments for a wide range of cancers, the hope is that an mRNA vaccine boosting this efficacy further could aid cancer patients to remain cancer-free. There is also the financial angle to any successful combination therapy, if it could prove itself to outperform checkpoint inhibitors alone then it could become a standard of treatment in certain areas. Considering that PD-1/L1 are some of the most lucrative drug treatments across the industry, this could be a major coup for any mRNA developer that manages to successfully co-develop such a treatment.

"We hope that in time we are able to show that the treatment is effective against lung cancer whilst leaving other tissues untouched"

- Sarah Benafif.

The last hurdle

This approach should soon be going in front of the FDA, with Moderna and Merck's mRNA-4157/Keytruda (pembrolizumab) combination having three years of data to potentially back up a filing for accelerated approval in melanoma. Earlier this year, FierceBiotech reported that Peter Marks, director of the FDA's Center for Biologics Evaluation and Research, had said that the agency is ready to review mRNA vaccines, on a similar basis to CAR-T treatments.

The necessity for the agency to clarify that it is ready to review the potential products highlights the complexity facing regulators with these products. As outlined by a recent paper, challenges exist when it comes to commercialising this novel class of therapies. The authors state that the regulatory framework for a drug modality with a diverse range of applications is unclear. In addition, they add that there is a need for the harmonisation of definitions across regulatory agencies, with mRNA vaccines sometimes labelled as gene therapy, while others refer to gene silencing and gene delivery via RNA molecules as RNA therapeutics. With some mRNA approaches also using AI to personalise each vaccine to the patient, there are also questions about how to regulate a product that can differ each time it is delivered.

As such, this novel approach will require significant flexibility on the part of global agencies and will likely need adaption to regulations should they prove effective enough to be approved. With a number of mRNA therapeutics targeting indications in oncology, such hurdles will be faced down in the short term. In the long term, mRNA vaccines could change the way that cancer is treated.

About the author

Ben Hargreaves is an established freelance life sciences writer, whose experience includes such publications as the BioProcess Insider, BioPharma-Reporter, BioSpace, Outsourcing-Pharma, pharmaphorum, and Motley Fool, among others.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