pharmaphorum deepdive

Oncology

Plus: Innovations shaping the future of cancer treatment

ASCO 2022: top trends and developments

Realising the promise of cancer vaccines

Diversity by design: the importance of DE&I in oncology trials

July 2022

Contents

Deep Dive: Oncology 2022

As we have witnessed over the past three years, when life sciences companies, policymakers, and patient groups pull together towards a common goal, we are capable of remarkable achievements.

Now, we are faced with an opportunity to apply all that we have learned during the COVID-19 response, to tackle another, lingering opponent – cancer.

Over the past few decades, researchers have made tremendous strides in the fight against cancer in all its forms. With each new drug and therapeutic innovation added to the oncology diagnosis and treatment toolkit, patients and their caregivers are given a greater chance of combatting the disease.

Even in the most challenging of circumstances, realising the promise of emerging treatments remains a central value shared by all of our contributors. In this issue of Deep Dive, Advanced Clinical's Christopher Oelkrug takes us through the potential of therapeutic cancer vaccines, Nick Kenny and Dr Stephen Keith explain the importance of improving diversity in oncology trials, and Phesi's Dr Gen Li discusses new approaches to clinical trials in cancer.

From the insights shared within this issue, there is a clear sign that researchers, clinicians, and patients remain dedicated to realising a future without cancer. A worthy fight if ever there were one.

I hope you are staying safe.

Eloise

Eloise McLennan – editor, Deep Dive

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Communications & Commercialisation 2022
Plus:
• Key insights from ESMO 2022

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Immunotherapy: building the fourth pillar of cancer treatment

Cancer treatment has been traditionally characterised by surgery, chemotherapy, and radiation. However, in the late 20th century, a fourth element entered the mainstream: immunotherapies.

To appreciate and understand the promising future of immunotherapy in cancer treatment, it is important to reflect on the ground-breaking research and innovations that have paved the way for new cancer treatments over the past century. Here, we chart the remarkable history of immunotherapies and ongoing efforts to make them even more effective.

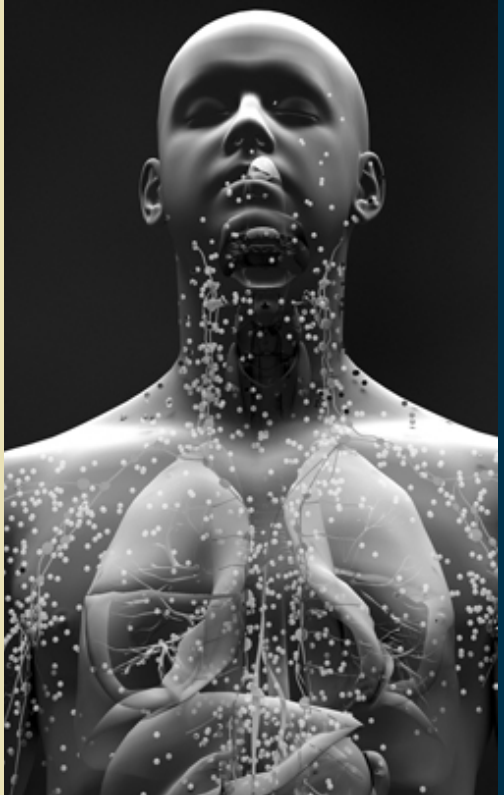
1860-1899

1868-1882

Fehleisen and Busch explore immune system modulation in cancer

The first scientific attempt to harness immune system modulation to combat cancer appeared in the 19th century after German physicians F Fehleisen and W Busch independently identified a link between accidental erysipelas infections in cancer patients and subsequent spontaneous tumour regression.

Building upon this hypothesis, both physicians sought to confirm this connection by intentionally injecting the erysipelas-causing Streptococcus bacteria into the tumours of several cancer patients. Following the infection, Fehleisen reported tumour shrinkage in three of the seven trial participants, indicating that the immune system had a modulatory role in treating cancer.



1891

William Coley develops first immunotherapy

The earliest case of cancer immunotherapy can be traced back to the late 1800s, when the New York bone surgeon and subsequent 'father of immunology' William Coley first attempted to leverage the immune system to treat cancer.

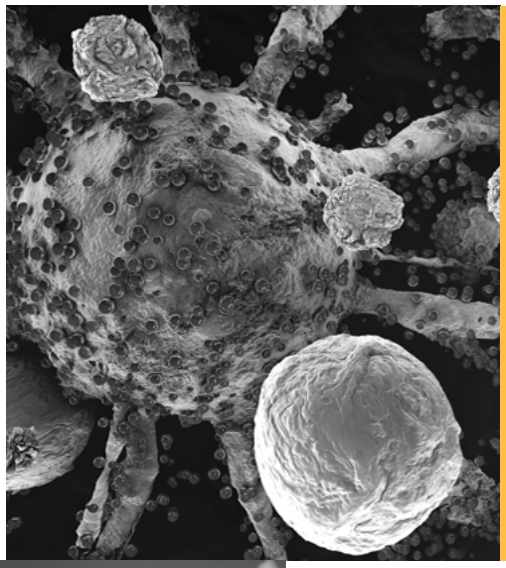
Similar to Fehleisen and Busch, Coley also observed similar patterns between acute bacterial infection and spontaneous tumour regression. Using this insight, he instigated a 40-year study, during which more than 1,000 cancer patients were injected with mixtures of live and inactivated Streptococcus pyogenes and Serratia marcescens bacteria, later known as 'Coley's toxins'.

1900-1950

1902

Early indications of CAR-T emerge

Although CAR-T therapy (see below) has substantially developed over the past few decades, an early example of the treatment appeared in the work of Dr Ferdinand Blumenthal and Dr E. von Leyden. In 1902, the duo attempted to treat patients using suspension derived from their own autologous tumour tissue culture. However, while some improvement was noted, the study did not result in significant tumour regression.



1907

Ehrlich's magic bullet theory

The achievements and contributions of the Nobel prize-winning German scientist Paul Ehrlich are well documented throughout the history of immunology. But in 1907, he put forward a hypothesis for a so-called 'magic bullet' of synthesised antibacterials designed to impact specific targets in the body. This initial idea formed the foundation for key cancer and immunotherapy developments, including chemoreceptor and chemotherapy concepts over the following century.

1940

Discovery of tumour-associated antigens

The 1940s were a turbulent period for immunotherapy research. Amid hesitancy in the medical community regarding the use of the treatment, fuelled by a general lack of understanding of the mechanism of action, newly approved chemotherapies began to gain prominence alongside the traditional surgical treatment approach.

However, despite this hesitancy, researchers used Ehrlich's early research into antibodies and antigens as a foundation for studies conducted on tumours derived from animal subjects. From these studies emerged a significant discovery: "tumour-associated antigens" (TAAs), which the immune system could potentially recognise.

This occurred in the context of hesitancy and scepticism in the medical community about the use of immunotherapies, because there was a lack of understanding about their mechanism of action; instead, chemotherapies, which started to be approved in the 1940s, became the preferred choice, alongside the traditional surgical approach.

1950-2000

1957

Discovery of interferon

While there is debate over who should be credited for the discovery of interferon – a cytokine produced by white blood cells – it is commonly accepted that the proteins were first identified by Scottish virologist Alick Isaacs and Swiss virologist Jean Lindenmann.

It was initially considered for use as a general anti-viral, however, subsequent research found interferon to be highly effective as an anti-cancer therapy in mice models.

1959

First example of a cancer vaccine emerges

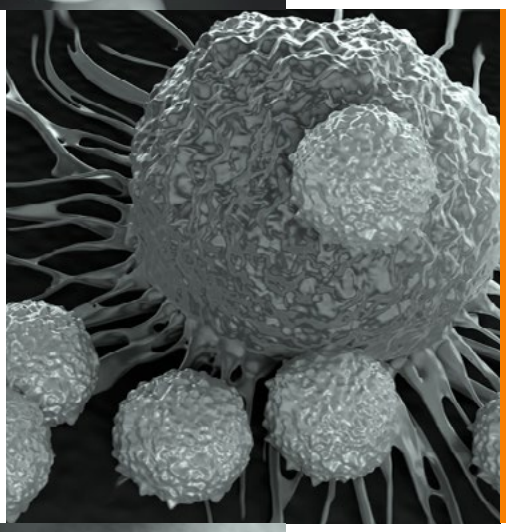
In the late 50s, the husband-and-wife team of Ruth and John Graham unveiled results from the first-ever cancer vaccine trial. The research included 114 patients with gynaecological cancers who were treated with an adjuvanted tumour lysate.

Although results showed a 22% incidence of remission or stable disease, the research received little attention from the medical community.

1967

Miller confirms existence of T cells

At just 30 years old, French-Australian immunologist Jacques Miller made a ground-breaking discovery, becoming the last person to identify the function of a human organ – the thymus. Then, just seven years later, he made an equally impressive discovery when he uncovered the presence of T cells and their role in mediating the immune response.



1976

Researchers unlock the promise of interleukins

While attempting to grow T cells in a culture, Researchers from the US National Institutes of Health's Intramural Research Program, led by renowned biomedical researcher Robert Gallo, identified the cytokine T cell growth factor, now known as interleukin-2 (IL-2). This broadened researchers' understanding of the immunology of T cells and revealed a direct way for oncologists to boost the patient's immune response to cancer.

1986

FDA approves first immunotherapy agent

Building upon the promise of interferon in oncology treatment, immunology achieved a significant milestone in 1986, when the first immunotherapy agent, an antitumor cytokine called interferon-alpha 2 (IFN-a2), was approved by the US Food and Drug Administration (FDA). Initially indicated for hairy cell leukaemia, the treatment was later green-lit for Stage IIb/III melanoma treatment.

1992/5

Rise of checkpoint inhibitors

Following the success of cytokine-based immunotherapies, scientists continued to seek other areas where the immune system could be leveraged against tumours. With the discovery of the PD-1 as an inducible gene on activated T-lymphocytes in 1992, Tasuku Honjo at Kyoto University in Japan made a significant contribution to the development of future PD-1/PD-L1 blocking therapies.

Drawing upon Jean-François Brunet's research of the first immune checkpoint molecule, CTLA-4, in 1897, a study led by Dr James Allison at the University of California, San Francisco, sought to clarify the ambiguities of the molecule's function. Through this study, Allison and his team pinpointed CTLA-4 as a critical immune checkpoint molecule that held strong potential as a future anti-cancer therapy target.

2000-2010

2002

Birth of CAR-T therapy

Although Dr Allison's research into the function and application of T cells in cancer treatment had greatly broadened the scientific understanding of the immune system. However, in 2002, Memorial Sloane Kettering Cancer Center scientists Michel Sadelain, Renier Brentjens, and Isabelle Rivière opted to push the boundaries of the T cell research even further by genetically engineering T cells with a chimeric antigen receptor (CAR).

This new approach paved the way for a new generation of immunotherapy treatments. Dubbed CAR-T therapy, these modified cells are programmed to help T cells attach to a specific cancer cell antigen on the surface of tumours.

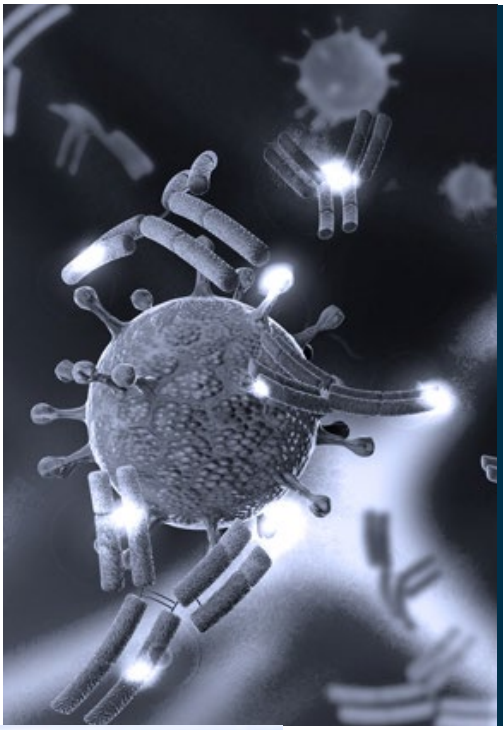
2011-2022

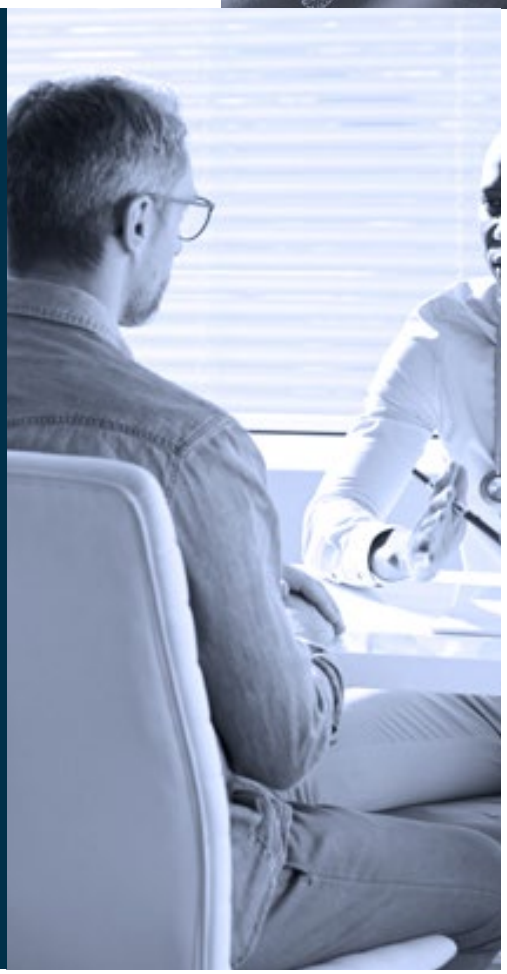
2011

First checkpoint inhibitor approved

In March 2011, Bristol Myers Squibb (BMS) made headlines as the first company to be granted market approval for its checkpoint inhibitor Yervoy (ipilimumab).

Yevory is a monoclonal antibody designed to activate the immune system by targeting CTLA-4 and disrupting the inhibitory mechanism that prevents T lymphocytes from identifying and destroying cancer cells. The FDA initially approved the therapy for melanoma indications; however, Yevory has since been granted approval for multiple designations by regulators around the world.





2017

FDA makes history with first CAR-T therapy approval

CAR-T therapy achieved a major milestone in late 2017 when Novartis's Kymriah (tisagenlecleucel) became the first gene therapy to receive FDA approval. The action ushered in a new approach to cancer treatment, using genetically modified autologous T cell immunotherapy to target and kill the cancer cells.

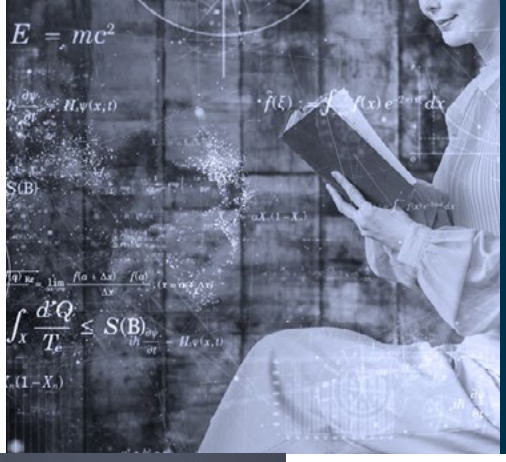
Initially designated for patients under 25 with refractory or relapsed B-cell precursor acute lymphoblastic leukaemia, the treatment has now been authorised for diffuse large B-cell lymphoma, a common form of non-Hodgkin lymphoma.

A few months later, Gilead's Yescarta (axicabtagene ciloleucel) became the second cell-based gene therapy approved by the FDA as a treatment for adults with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy.

2018

Researchers receive Nobel prize for checkpoint inhibitors

The importance of cancer immunotherapy was underlined in 2018 when James Allison and Tasuku Honjo were granted the Nobel Prize for their early work on CTLA4 and PD-1 checkpoint inhibitors, respectively.



2019

Enhertu scores first FDA approval

AstraZeneca/Daiichi Sankyo's Enhertu (trastuzumab deruxtecan) scored accelerated approval from the FDA to treat HER2-positive metastatic breast cancer after at least two prior therapies in late 2019. Since then, the antibody-drug conjugate has been cleared for use in approximately 40 countries.

2022

Killer innate-like T cells identified as 'soldier' for cancer therapy

Six years after the discovery of what scientists have dubbed 'killer innate-like T cells', researchers at the Sloan Kettering Institute in New York published a report in Nature, which identified that the immune cell 'soldier' could be a good target for immunotherapy, raising hopes that it might help narrow the gap between people who respond and those who do not.

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.

Realising the promise of cancer vaccines

For years, the promise of therapeutic cancer vaccines has intrigued researchers working in the oncology space. And for good reason.

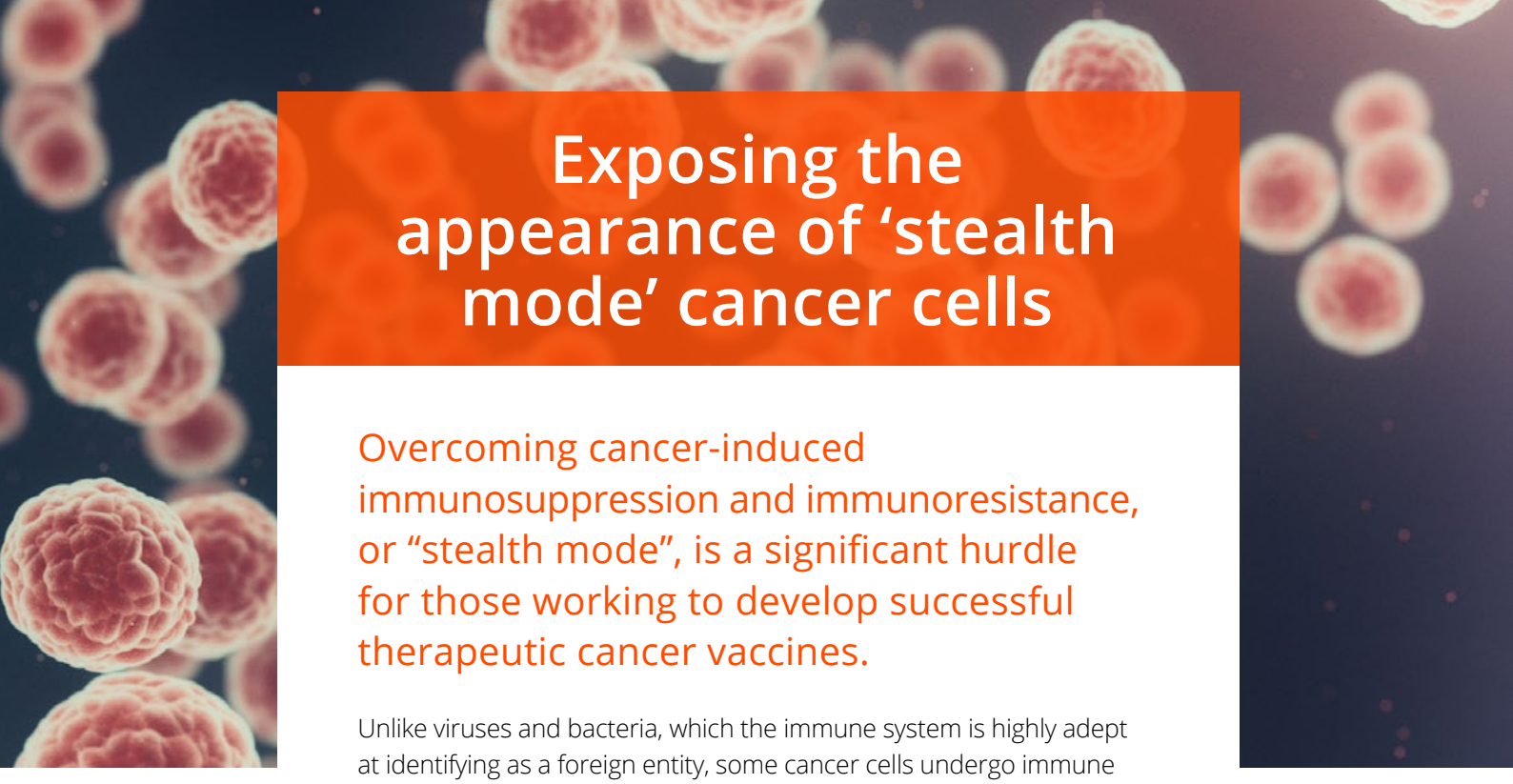
The concept of pre-emptively training the immune system to increase the frequencies of tumour-reactive T cells could be game-changing for cancer patients worldwide.

Preventative vaccines have already proven to be highly effective against certain cancer types. The Hepatitis B (HBV) vaccine and Human papillomavirus (HPV) vaccines are key examples. Comparatively, realising the potential of therapeutic vaccines has been a challenging journey, with disappointing trial results dampening initial enthusiasm.

But, despite initial setbacks, the therapeutic potential of these cancer vaccines is far from over. Buoyed by recent technological advancements and a broadened understanding of tumour-associated antigens, therapeutic vaccines have undergone a resurgence of interest.

For Christopher Oelkrug, director of business development for Advanced Clinical, it's an exciting time to investigate the clinical efficacy of therapeutic cancer vaccines. Particularly as recent results indicate that these treatments can help researchers address one of the biggest challenges in oncology – cancers' so-called 'stealth-mode'.

> "The tumour environment is really problematic," he explains. "Basically, tumours can go into 'stealth mode', which is not recognisable for the immune system. So, the ideal cancer vaccine has to overcome that immune suppression."



Exposing the appearance of 'stealth mode' cancer cells

Overcoming cancer-induced immunosuppression and immunoresistance, or "stealth mode", is a significant hurdle for those working to develop successful therapeutic cancer vaccines.

Unlike viruses and bacteria, which the immune system is highly adept at identifying as a foreign entity, some cancer cells undergo immune escape by MHC downregulation, immune checkpoint expression and/or tolerance inducing immune cells (Ma/Treg etc.) that makes them imperceptible to the immune system.

"The main challenge is to reactivate the immune system to see the tumour cell and recognise it as a threat," says Oelkrug. "Cancer cells express tumour associated antigens and/or neoantigens. Even if you use these as a vaccine, you don't really have an immunogenicity to them. You somehow have to increase that, so that the immune system gets primed."

Mobilising the immune system is a primary function of therapeutic cancer vaccines. Whereas preventative vaccines work to prevent healthy cells transforming into tumour cells through viral infections, therapeutic vaccines are specifically designed to target tumour-induced immunosuppression, exposing the camouflaged cancer cells and jump-starting the immune response.

> "Cancer vaccines have to induce humoral and cellular immunity," explains Oelkrug. "With traditional vaccines, you normally have a humoral immunity, but in the cancer setting, you want CD8 cytotoxic T cell-mediated cellular immunity so that you have cytotoxic T cells that can actually attack the tumour."

A decade of therapeutic innovation

Technological and scientific advancements have been instrumental in driving therapeutic cancer vaccine research.

Over the past decade, scientists have uncovered new information about the mechanisms that underpin immunotherapy treatments, including the advent of checkpoint inhibitors and mRNA vaccines. These breakthroughs have greatly expanded our understanding of the immune response to cancer and expanded the variety of patients eligible for immunotherapy treatments.

For Oelkrug, the disruption of COVID-19 has also contributed to growing interest and innovation in cancer vaccines. At the height of the pandemic, novel platforms received a surge of interest and investment, which ultimately led to the development and approval of a COVID-19 vaccine in just a few short months. Beyond the scope of this one disease, the mRNA vaccine technology has also been noted for its potential in developing cancer vaccines.

> "Companies that were working on the COVID-19 mRNA vaccines, have already been working on cancer vaccines in the past and already had clinical trials ongoing," he explains. "The next step is establishing the mRNA platform in the oncological field or as a therapeutic vaccine."

How vaccines work with established treatments

As it stands, there is no one-size-fits-all solution for oncology, and vaccines form just one piece of a wider puzzle when it comes to treating and eradicating cancer.

In the past, research into the efficacy and safety of therapeutic cancer vaccines analysed drug candidates as a standalone treatment. Ultimately, this yielded disappointing results. However, when studied as a combination therapy, alongside conventional treatments such as chemotherapy, results have proven far more promising.

Metronomic chemotherapy – the process of administering specific chemotherapy in a low dose – has been shown to eliminate immunosuppressive cells in the tumour microenvironment. When used alongside therapeutic vaccines, the two treatment approaches work in tandem to reveal the presence of a tumour to the immune system and stimulate a timely response.

"Combination is key here," says Oelkrug. "If you look at clinical trials to enhance the survival of patients, studies have shown that patients have an enhanced survival rate when they were treated besides the cancer vaccines, for example, with cyclophosphamide, which is a type of chemotherapy that depletes regulatory T cells in the tumour microenvironment and leads to an enhanced T cell infiltration.

> "With low dose metronomic chemotherapy, or other checkpoint inhibitors in a tandem therapy or combination of therapies, you are able to enhance the total immune response to the tumour," he says.

Addressing challenges through delivery systems

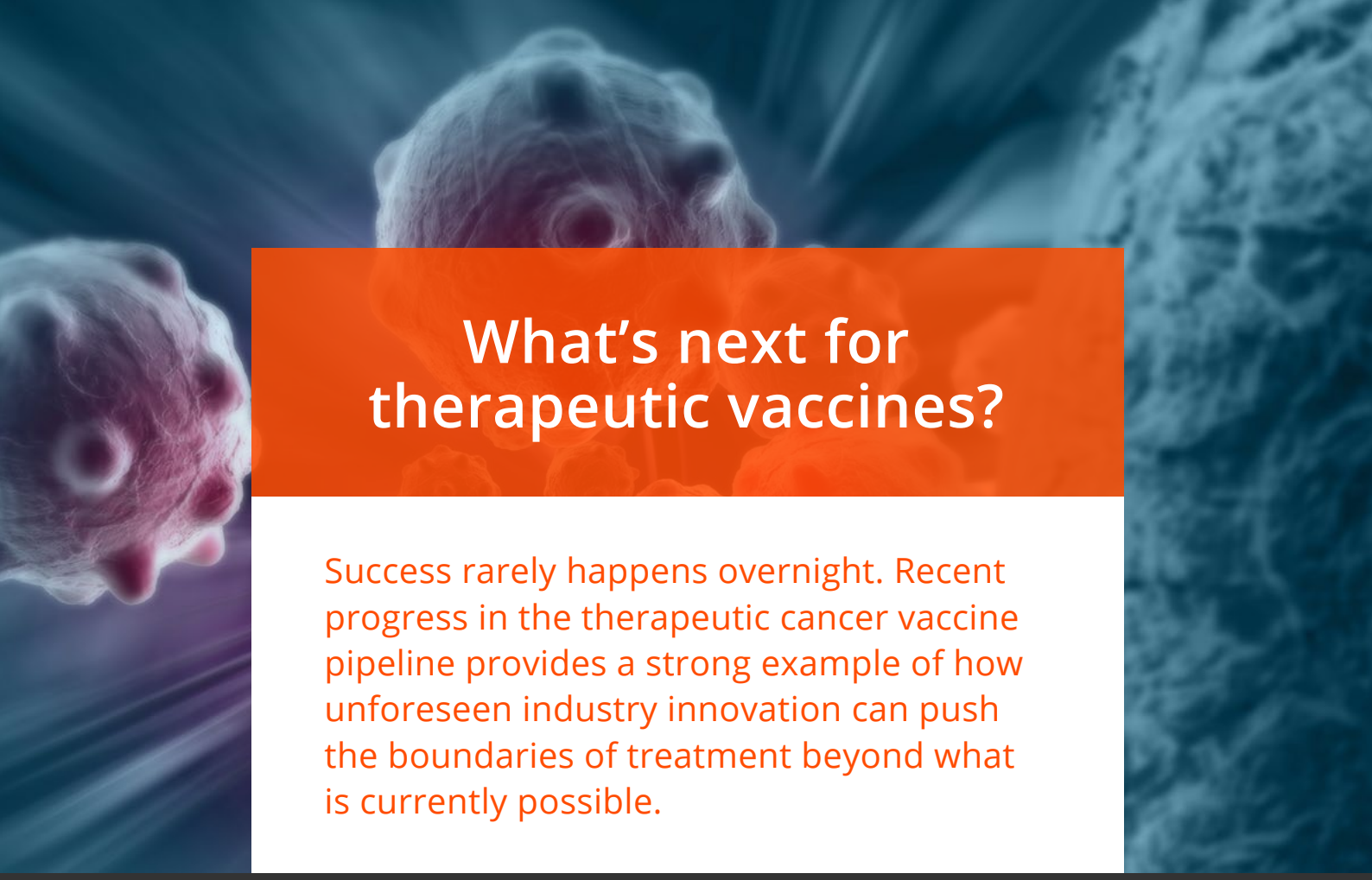
Developing a successful therapeutic vaccine for a complex and evolving target is an ambitious goal for researchers.

While cancer vaccines are promising immune-therapeutics for establishing immune surveillance, Oelkrug notes that further research and the translation into the clinic has to be conducted by identifying neoantigens, developing combination therapies, and optimising the current vaccine platforms before cancer vaccines become a potent strategy in immunotherapy.

"The main problem of older generations of cancer vaccines was the low level of antigen production," says Oelkrug. "Previous studies have shown an inefficient cellular delivery of plasmids when you look at, for example, DNA cancer vaccines, which led to an insufficient stimulation of the immune system.

"Therefore, you want to change different points within the whole development of cancer vaccines, and you can do that by the antigen design itself. You can look at different antigens, and the vector system you're using, such as viral vectors, the dose, and how the vaccine is actually delivered."

Moreover, it is important to acknowledge that cancer vaccines are more suitable for patients with a functioning immune system. Each patient will have individual needs, and while different routes of delivery make it possible to elicit specific immune responses, clinical trials of cancer vaccines should fully consider the patient's immune system function, risk of recurrence, and tumour burden.



What's next for therapeutic vaccines?

Success rarely happens overnight. Recent progress in the therapeutic cancer vaccine pipeline provides a strong example of how unforeseen industry innovation can push the boundaries of treatment beyond what is currently possible.

If the current trajectory of progress is maintained, therapeutic vaccines could become a reality for cancer patients around the world. Moreover, a greater understanding of the immune system will allow researchers to explore additional areas where vaccines could be impactful.

"More vaccines getting approved will lead to a huge impact on how we can treat cancer," says Oelkrug. "Getting away from really harsh treatments and looking at cancers that are not operable, or where the survival rate is really low."

For Oelkrug, this tenacity is an encouraging sign that further progress is attainable as each seemingly small step brings the industry and patients closer to the ultimate goal of eradicating cancer.

"There is no golden bullet to target tumour cells, like cancer," he concludes. "It's always the next challenge to try and get rid of them."

About the interviewee

Christopher Oelkrug is a director business development at Advanced Clinical. His main focus is on identifying new opportunities with clients to provide a better clinical experience. Based on his broad experience in Cancer Immunotherapy and Immunology and his entrepreneurial mindset, Christopher brings a unique perspective to novel developments within these therapeutic fields. He has a M.Sc. in cancer immunotherapy and was head of immunotherapy and oncology at a German research institute. Furthermore, Christopher is the holder of two patents in gut microbiome modulation and antibiotic resistance via IgY mediated therapy.

About Advanced Clinical

Advanced Clinical is a clinical development and strategic resourcing organisation committed to providing a better clinical experience across the drug development journey. Our goal is to improve the lives of all those touched by clinical research – approaching each opportunity with foresight, character, resilience, and innovation. Based on decades of experience, we help our clients achieve better outcomes by conducting candid conversations and anticipating potential issues through our customised solutions. Visit our website to learn more: www.advancedclinical.com.

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Phesi's Dr Gen Li: New approaches to clinical trials in cancer

Dr Gen Li, founder and president of Phesi, a provider of AI-powered clinical development analytics, products and solutions, discusses some of the latest challenges facing the industry, including why it is imperative that the design of clinical trials is data-driven.

How can a data-led approach to cancer clinical trial design help drug development?

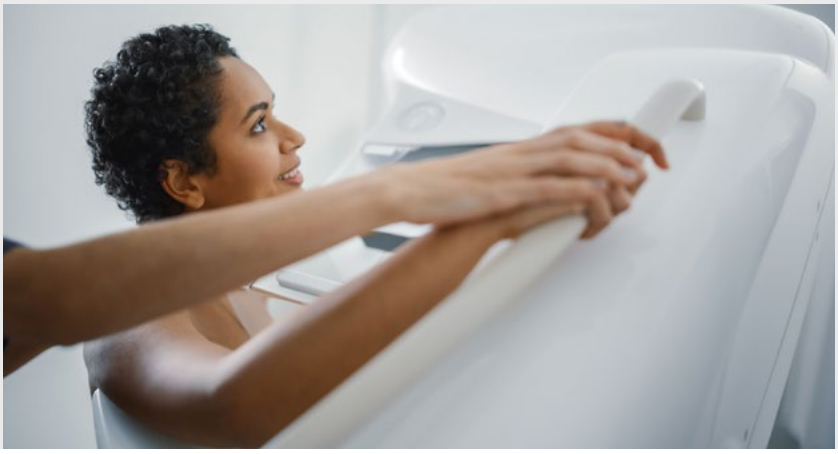
Dr Gen Li: All areas of the clinical development industry should be aiming to become more data led. Today, we have a wealth of data from clinical trials and patient records at our fingertips. Using such data to inform and optimise cancer trial design and execution, we can reduce patient burden and enable smarter clinical trials, as well as faster drug development.

Data helps investigators make confident decisions that are not based on gut instinct but on facts – such as which country is the best option for new sites and has the required concentration of patients matching your protocol.

Can you outline the findings from your recent big data analysis on breast cancer?

We've seen extensive research into breast cancer in recent years. In fact, our earlier analysis showed that in 2021, breast cancer was the most studied disease area, with more than 25,000 investigator sites recruiting for breast cancer clinical development. With this in mind, we wanted to investigate any trends that might be appearing in breast cancer clinical trials as they increase in number and sponsors continue to direct resources to breast cancer studies.

To do this, we analysed the data of 2,511,046 patients from 4,674 patient cohorts, mainly those who participated in clinical trials. Our analysis found that since 2014, the number of women younger than 60 years of age has tripled, from 30% to about 90%. We expected to see an increase in younger patients, correlating with progress we've made in the disease area in recent years – such as increased mammogram screenings and successful public health awareness campaigns. However, the increase in younger patients is substantial.



What are the implications of these findings for breast cancer trial designs moving forward?

Typically, younger patients are living with more aggressive forms of breast cancer, so it's vital that patient centricity is at the heart of any trial involving such individuals. One of the biggest challenges will be around potential fertility and pregnancy issues. These concerns might have been less of a priority before, but they will now need to be considered in order to convince patients to commit to trialling new treatments over the long term.

There will also be differences in a younger cohort to consider for trial design, including comorbidities and medication history. Sponsors must take advantage of existing patient and trial data to improve enrolment of patients that match protocols. Moreover, breast cancer trials must be dynamically designed around the complexities of this patient profile and be able to adjust in real-time.

What common challenges do sponsors face when designing cancer trials?

As we emerge from COVID-19, sponsors are faced with new challenges when designing any type of clinical trial. Essentially, sponsors are all selecting cohorts from the same limited pool of patients.

We are also seeing disruption in other areas and from other world events, such as the ongoing conflict in Ukraine – which is having a huge impact on clinical development in the region and neighbouring countries.

Another challenge for the industry is getting access to data and – once you have access – figuring out how to analyse data to unlock actionable insights when designing a trial. If you don't have access to a variety and volume of data, existing challenges – such as finding the right sites, countries, and patients – are only exacerbated.

How can synthetic data and digital twins optimise breast cancer trials?

Synthetic data is collated from similar or identical trials using the same agent to accurately model comparator or placebo outcomes. A synthetic data arm can be used in place of a placebo or comparator arm. This approach offers considerable benefits to the patient, in that it removes the ethically questionable placebo arm of a clinical trial. When patients are in chronic and severe pain, or advanced stages of a disease, placebo arms do nothing to relieve their symptoms – and are especially questionable if the patient has limited time to find an effective treatment.

Synthetic data also reduces the burden on sites and sponsors; fewer patients have to be recruited, and all patients who are recruited will be in the active arm of the trial. Patients are often afraid of being put on a placebo arm, which has long been a hurdle for patient recruitment.

Moreover, synthetic arms make use of the data available to the industry, analysing it to predict and model precise outcomes. They are best used in clinical trials where control group performance has been historically well characterised and where results have been consistent from trial to trial.

For example, trials in late-stage cancers or progressive genetic disorders where a patient's health would deteriorate were they to receive a placebo rather than the investigational treatment. Synthetic patient data can be used to define the boundaries of a trial, model and predict what types of patients should be included and excluded, and minimise or eradicate the need for placebo patient enrolment.

Why is patient centricity so central to clinical development?

Patient centricity directly impacts the commercial end of the sponsor, as well as the patients and research subjects along the way. If we can embrace a more patient-centric approach, we have the potential to make trials far less expensive and time and resource consuming, with less burden on the research subjects and the research sites. This is achievable when sponsors take a data-led approach to trials. By adopting a more modern outlook, we can have a profound impact on both patients and industry.

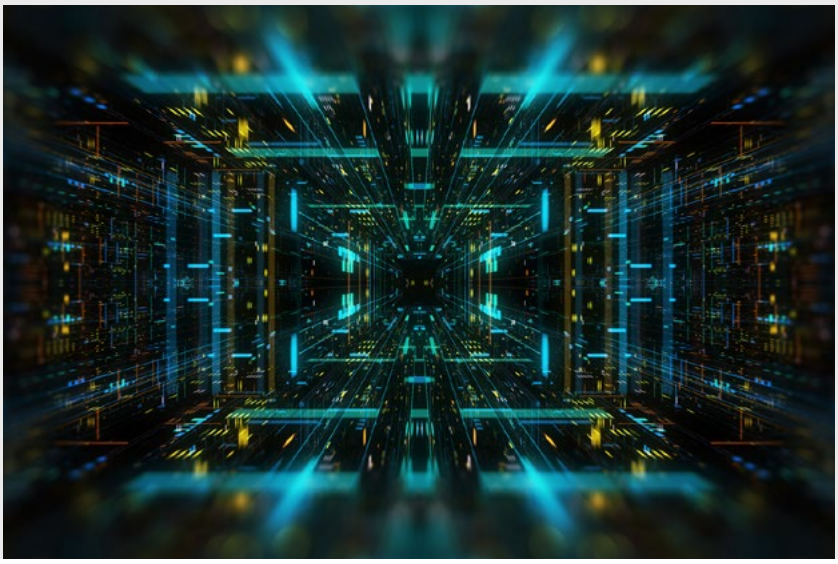
How do big data and AI inform your consultation process and improve clinical trial design?

By harnessing the power of real-time dynamic data and AI, we can enable our clients to maximise successful outcomes in drug development. With a data-led approach, sponsors can better predict the outcomes of a clinical trial, rather than relying on guesswork. Once a trial is underway, providing ongoing support enables sponsors to gain deep, real-time insights into how a clinical trial is running.

In this way, we enable confident decision making and rescue under-performing trials. Moreover, we empower clients to prioritise their portfolios and maximise commercial returns, with competitive intelligence, target product profile definitions and objective insights.

What future plans does Phesi have to enhance patient centricity and accelerate clinical trials?

We will continue working with clients on upcoming projects, keeping patient centricity at the heart of clinical development. Alongside this, we're always busy with our own research projects and publications. Our next analysis will take a deep dive into diversity in clinical trials, exploring the crucial role that diversity has to play in patient centricity.



About the interviewee

Dr Gen Li founded Phesi in 2007 with the aim of revolutionising clinical trials and the biopharmaceutical industry. Prior to founding Phesi in 2007, Dr Li was head of productivity for Pfizer Worldwide Clinical Development, a position he filled following Pfizer's acquisition of Pharmacia.

While at Pharmacia and Pfizer, Dr Li contributed significantly to the Centre for Medicines Research (CMR) International database for pharmaceutical R&D performance, ensuring the collection of key clinical trial parameters aligned with the critical path activities. Dr Li was also instrumental in creating the KMR productivity algorithms.

He earned his Ph.D. in Biochemistry from Beijing University, and an MBA from the Johnson Graduate School of Management at Cornell University.

About Phesi

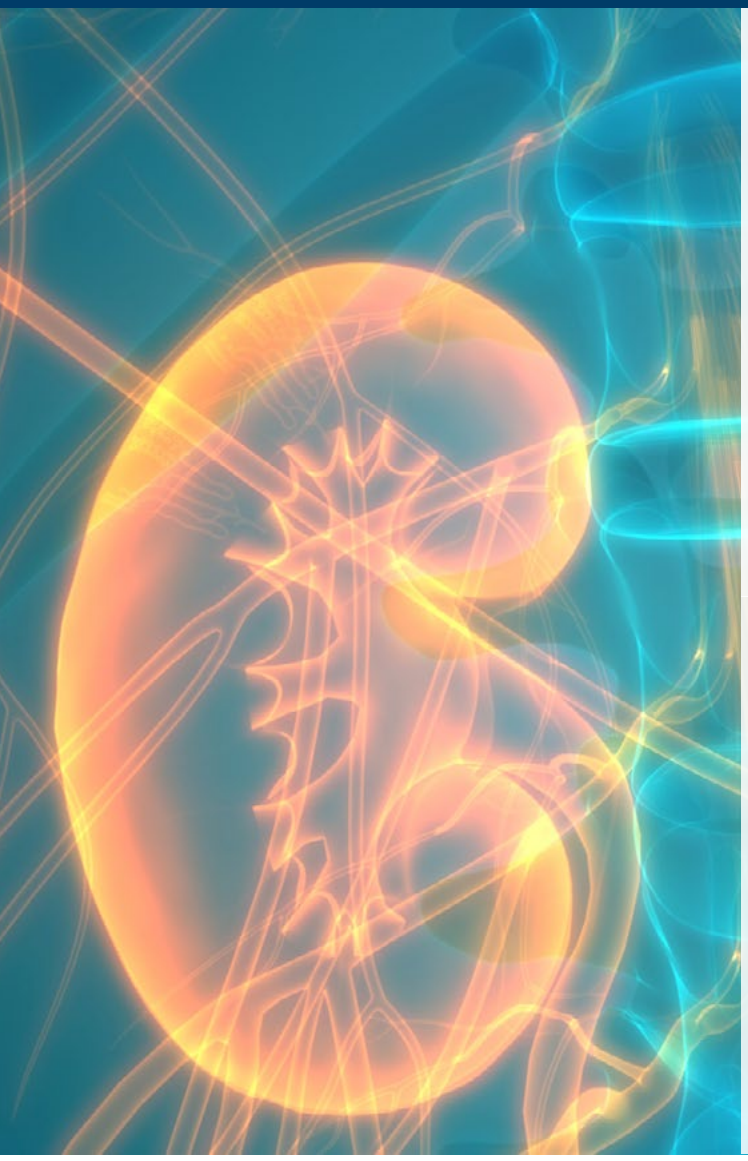
phesi
Patient-Centric Data Science

Phesi a data-driven provider of AI-powered clinical development analytics, products and solutions to the biopharmaceutical industry. The company's integrated offerings cover the entire clinical development process – from development planning and indication assessment to protocol evaluation, site selection, and trial implementation management.

Phesi has the world's largest real-time clinical development database; delivering patient-centric data science that enables biopharmaceutical companies to predict and optimise clinical development outcomes in any indication. Its database consists of 330,000 completed clinical trials, 604,000 completed research projects, >4.2 million physicians and >600,000 investigator sites worldwide.

Phesi delivers data, insights and answers, enabling smarter trials and faster cures. For more information, please visit Phesi.com.

The challenges and opportunities for kidney cancer care recovery



Kidney cancer care is rapidly approaching a tipping point in the UK. Despite being one of the 12 most common cancers in the UK, kidney cancer is the only one without dedicated guidelines and recommendations from the National Institute of Clinical Excellence (NICE). Instead, kidney cancer falls under the umbrella of urological cancer guidance, which is currently outdated by almost two decades.

In fact, according to Siew-Kwan Chang, Ipsen UK's Oncology Business Unit Head, the pressures of COVID-19 only exacerbated existing issues, exposing problems caused by the lack of dedicated guidance, gaps in data collection, a lack of holistic treatment pathways, insufficient investment, and the need for patient organisations providing psychosocial support for patients.

"Every day, 13 people die from kidney cancer" he explains. "The survival rate is not good – only around half of people diagnosed will survive their disease for five years or more."[i]

"In the UK, there is no holistic way of treating kidney cancer, and the guidelines are 20 years out of date.[ii] Despite ongoing efforts to improve kidney cancer care, we still fall far short of where we need to be and in order to make the change that is needed, the disease must be made a priority as a matter of urgency."

Ensuring that kidney cancer does not become the forgotten 'C' in post-pandemic recovery efforts is critical. And so, to evaluate the impact of COVID-19 on kidney cancer patients and explore opportunities to improve upon pre-pandemic care, Ipsen UK, in collaboration with Kidney Cancer UK, Queen's University Belfast and DATA-CAN, facilitated a roundtable of clinical experts and healthcare professionals. Using insight garnered from the roundtable report: **The Challenges and Opportunities for Kidney Cancer Care Recovery**, Ipsen has developed 11 recommendations to improve outcomes for patients, tackle the backlog, and provide high-quality kidney cancer care.

Understanding barriers to kidney cancer care recovery

While it is undoubtedly true that the arrival of COVID-19 significantly impacted research and treatment across oncology, concerns about perceived shortfalls in kidney cancer care emerged well before the pandemic first appeared on the radar of healthcare.

Approximately 46,000 people are living with some form of kidney cancer in the UK,[i] with an estimated 13,300 new cases diagnosed each year.[iii]

However, for many patients, accessing a definitive diagnosis is a lengthy and arduous process. In fact, according to Kidney Cancer UK, around 42% of patients received a late-stage diagnosis (stage 3 or 4), putting patients and their caregivers at a significant disadvantage in the fight to treat the disease.[i]

These alarming statistics directly challenge the NHS England faster diagnosis standard, which states that patients should not wait longer more than 28 days from referral to diagnosis.

"The NHS has a 28-day target from referral to diagnosis,"[iv] says Chang. "But 64% actually waited more than 28 days to get diagnosed, and 40% of those waited over three months."[i]

Delays in diagnosis and treatment are key contributors to the low-survival rate of kidney cancer. Approximately one in every 35 deaths from cancer in the UK is due to kidney cancer, and the nation has one of the worst five-year survival rates in Europe.[i]

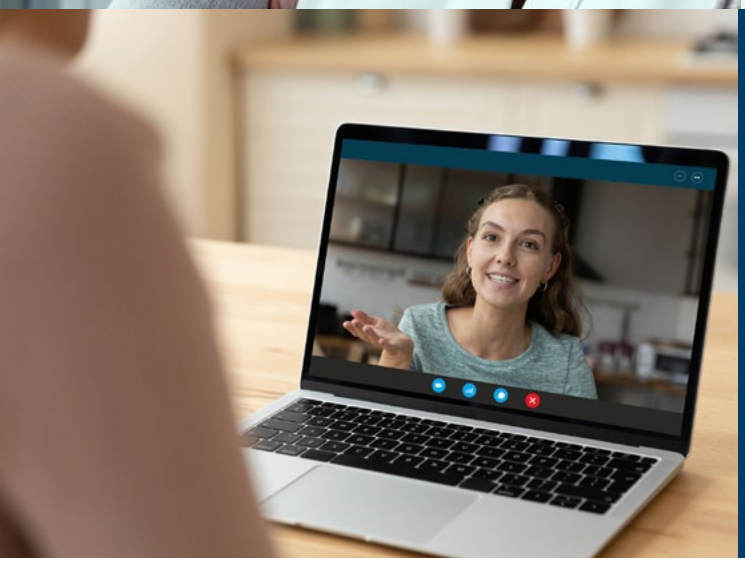
Ipsen recognises that this needs to change. As the UK works to resume pre-COVID oncology operations, it is vital to ensure that gaps in kidney cancer are addressed, starting with updating NICE guidelines.

Building back better: looking beyond the status quo

Over the past three years, the perfect storm of COVID-19, lockdowns and healthcare service delays have taken a toll on the mental health of cancer patients, their families, and their carers. According to the report, Kidney Cancer UK witnessed an 80% increase in calls to their careline, with people seeking more information about how COVID-19 will impact their condition or care.[v]

"For Ipsen, cancer and mental health are equally important," says Chang. "Patients need to have someone to talk to, to comfort them and reassure them that their cancers are well taken care of. That's the number one learning from COVID."

Using digital tools to expand the range of services available to patients would be beneficial in addressing mental health concerns. Participants also noted an uptake in digital tools throughout the pandemic, with remote consultations extending the methods of communication between patients and practitioners as physical consultations halted.



In addition to addressing mental health concerns, the data collected through digital tools provides researchers with critical information about the success and efficiency of treatments, which can be used to shape future kidney cancer and mental health services.

"Data can provide an objective picture of how well services are performing, not only in terms of outcomes but also as measures of process," says Chang. "The former tells us how well the total service is performing, but process measures provide vital information that tells us if a service can be improved, where it can be improved and to a great extent, how improvements can be made."

A call to action for kidney cancer guidance

The need to define 'good' in modern kidney cancer care is perhaps most evident in the report's call to action for NICE to develop tailored recommendations to guide the organisation of healthcare services for people with kidney cancer.

There is a good reason why this has become a focal point in rebuilding cancer care post-pandemic. Despite being the seventh most common form of cancer in the UK, with the lowest five-year survival rates across Europe, NICE guidance for how to diagnose and manage the disease is relegated to a four-page subset under the umbrella of urological cancer guidelines, published in 2002. While other cancer types included in the 2002 guidance, such as bladder cancer, have since been allocated comprehensive recommendations tailored to their specifications, NICE has yet to develop specific guidelines for kidney cancer care.

"The current guidelines are 20 years out of date,"[ii] explains Chang. "Kidney cancer is viewed as one of many cancers that oncologists need to manage, but we're not giving fair attention to kidney cancer alone."

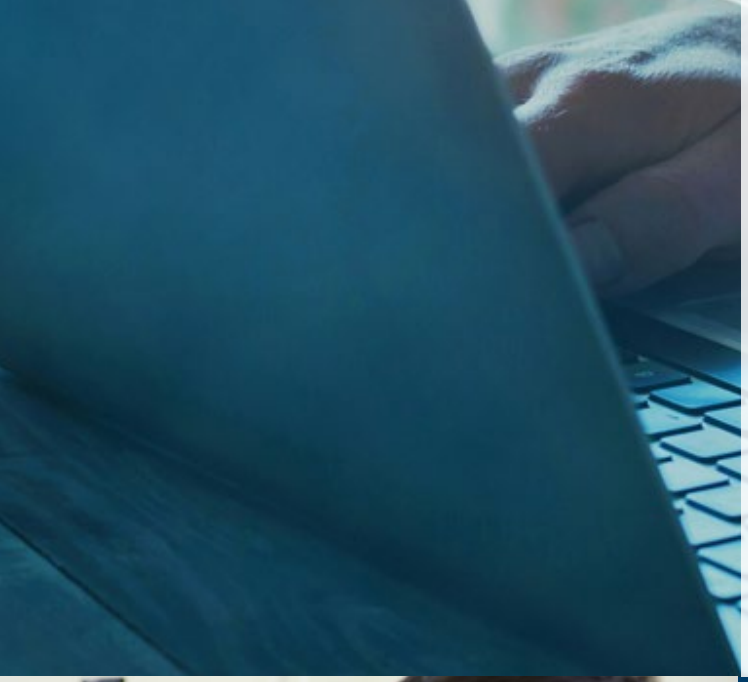
He continues: "Within cancer as a whole, trying to approach all types with a one-size-fits-all approach can also cause variations in service quality. Whilst there are certain similarities across all cancers and the underlying causes are basically the same, each type of cancer should be regarded as a separate condition."

From the responses detailed in the Ipsen-sponsored report, it is evident that the lack of relevant, up-to-date guidelines for kidney cancer care creates unnecessary barriers for both patients and clinicians working to combat the disease. As a result, significant unwarranted variations are present along the entire patient pathway in kidney cancer care[v]. This was further supported by the Kidney Cancer UK Accord, published in June 2022, which analysed the performance of kidney cancer services in the UK before the disruption of COVID-19.[vi]

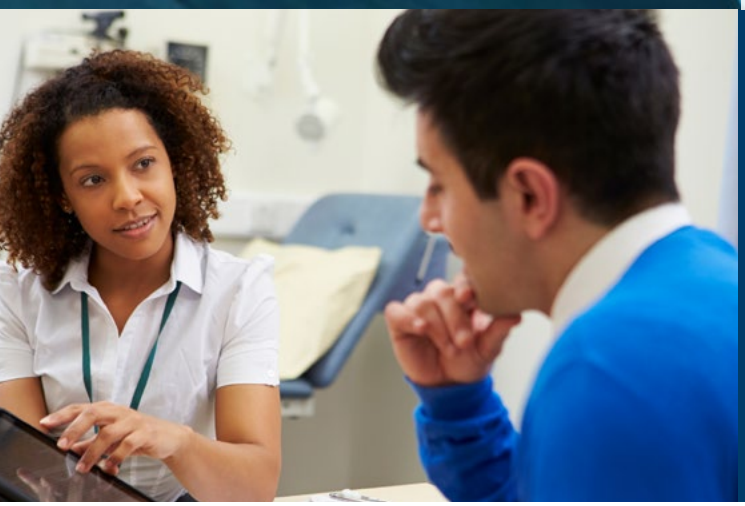
Results from the audit reflected the roundtable, with late diagnosis, variations in adherence to treatment pathways, and inconsistent regularity of check-ups after surgery highlighted as prominent issues caused by a lack of uniform guidelines.[vi]

Improving the treatment landscape

As illustrated in both the Kidney Cancer UK Accord and Ipsen's roundtable report, it is evident that the current landscape of kidney cancer care is in dire need of updated guidance and protocols if clinicians and patients in the UK stand a chance of achieving higher survival rates.



The report was well received by key industry figures, including Malcolm Packer, head of Charity Affairs and Communication at Kidney Cancer UK who stated: "Kidney Cancer UK welcomes this important report as it highlights the impact of COVID-19 on patients and services in the UK, including a diagnosis backlog, and lower rates of early-stage treatment. This in turn is causing the discovery of the disease to happen more often at its life-threatening, late stage. I would urge anyone showing symptoms – blood in urine, pain in your back/flank, or extreme fatigue – to contact their GP without delay."



With this call to action, it is hoped that NICE will extend kidney cancer the same individual guidance and recommendations they have provided for every other common form of cancer in the UK, giving clinicians the correct tools and pathways needed to effectively navigate the treatment environment. But as Chang highlights, driving policy change is only part of the puzzle. Every stakeholder across kidney cancer care must come together to help improve the treatment landscape for future generations.

"Upgrading the guidelines is the minimum that we need to do," he explains. "But the report is evidence that we are bringing people of a common interest together. Everybody is motivated with the same agenda: patient organisations, the NHS, and Cancer Alliance, we all have a role to play."

For more information, visit: www.kcuk.org.uk

i Kidney Cancer UK 2021 Patient Survey Report. Available: https://www.kcuk.org.uk/booklets/KCUK-patient-survey-2021/#page=2 Accessed: June 2022

ii NICE. Improving outcomes in urological cancers. Available at: https://www.nice.org.uk/guidance/csg2 Accessed: June 2022

iii Cancer Research UK. Kidney Cancer – incidence. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/incidence Accessed: June 2022

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v Kidney Cancer UK, Ipsen UK, DATA-CAN, Queen's University Belfast. The Challenges and Opportunities for Kidney Cancer Care Recovery. 2022.

vi Kidney Cancer UK Accord. Available: https://kcuk.org.uk/booklets/patient-consensus-2022/#page=1 Accessed: June 2022

About the author

Siew-Kwan Chang is the Oncology Business Unit Head at Ipsen UK. He has over 20 years' experience working within the pharmaceutical industry and started his career with Ipsen in 2004, working in Asia and Europe in both strategic and operational roles across global functions and local affiliates. Before entering the pharmaceutical industry, Siew-Kwan studied Pharmacy at Universiti Sains Malaysia.

About Ipsen

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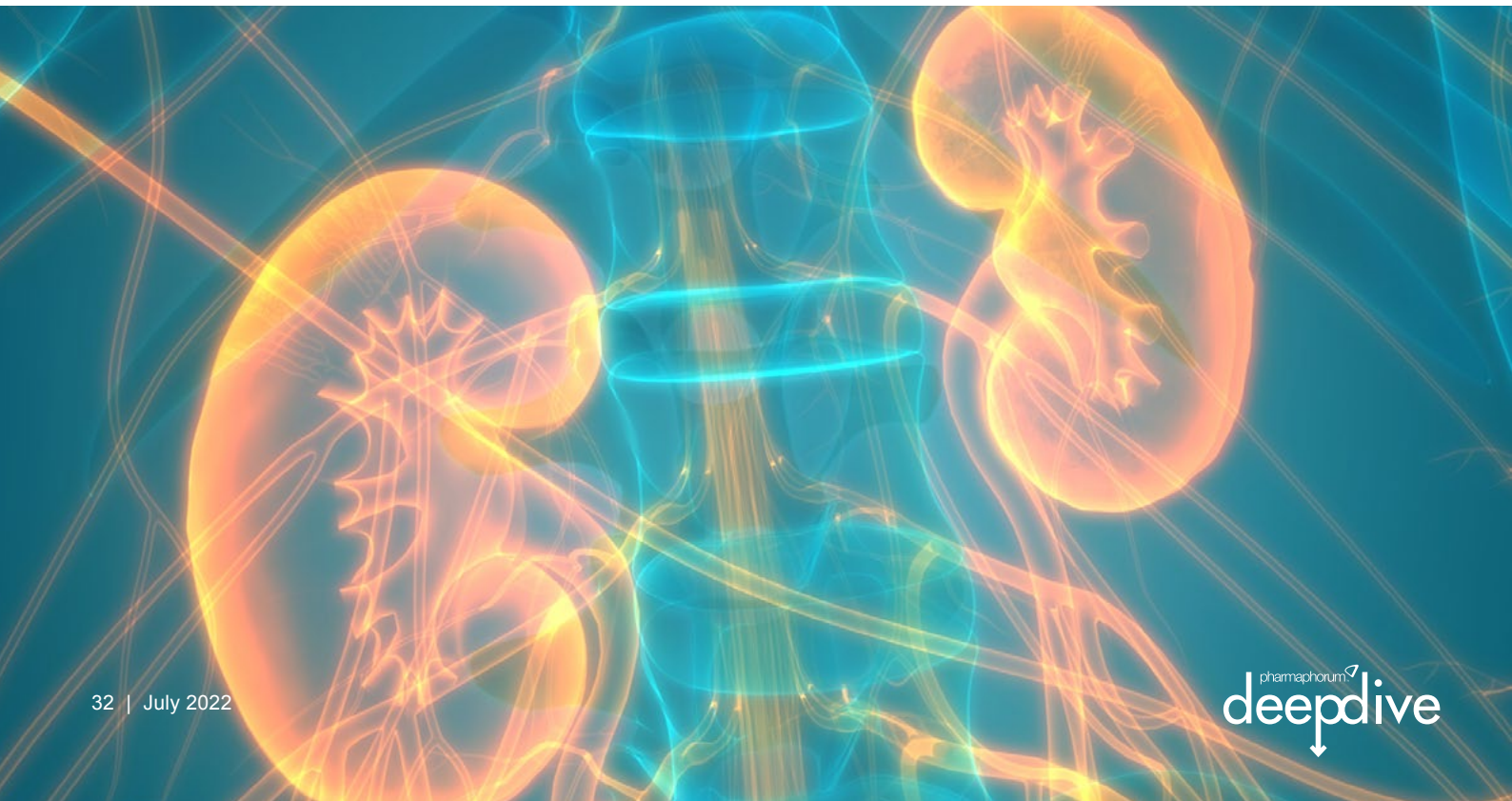
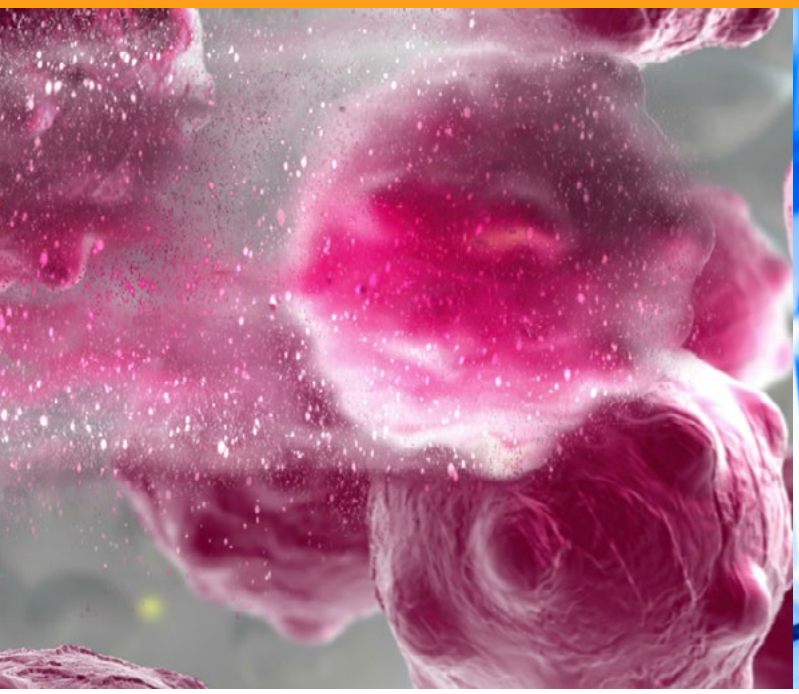
Our team in the UK is a core part of Ipsen's global biopharmaceutical business and is driven by the belief that patients don't have time to wait. We have a biotech mindset coupled with pharmaceutical capabilities and have invested in a robust business presence in the UK that spans the early stages of R&D (Abingdon, Oxford) through to in-house manufacturing (Wrexham, Wales) so we can effectively deliver on our promise to UK patients. As part of this investment in the heart of UK life sciences, we employ over 700 people across our three major UK sites, including our commercial headquarters in Bath Road, Slough.



Diversity by design: the importance of DE&I in oncology trials

"First, do no harm"; is an ethical axiom at the heart of medical research; physicians worldwide pledge to uphold the oath to serve patients. Clinical trials offer a practical example of how this value can be realised in drug development, reinforcing the importance of understanding and evaluating the safety and efficacy of new therapies in a controlled environment (clinical trials) before they reach patients at large.



However, within this clinical trial landscape there remains a significant ethical and scientific gap. For many years, clinical trials in oncology have almost exclusively catered to specific demographics when selecting trial subjects – namely White participants – a stark contrast to the reality of the diverse racial and ethnic populations that make up society – and, often, actual epidemiology and disease burden.

Under-representation of diverse populations in cancer clinical trials is a well-documented and unnecessary barrier to understanding the true safety and efficacy of novel treatments across population subgroups. Amid a growing body of evidence to support the need for Diversity, Equity, and Inclusion (DE&I) in oncology, there is a groundswell of final acknowledgement, awareness and, action that diversity is not an optional luxury in clinical research. It is an imperative.

"By not allowing everybody to have equal access, independent of who you are, where you live, what you look like, or what your ethnic background is, we're exacerbating the still significant lack of health equity in our medical systems," explains Nick Kenny, chief scientific officer at Syneos Health.

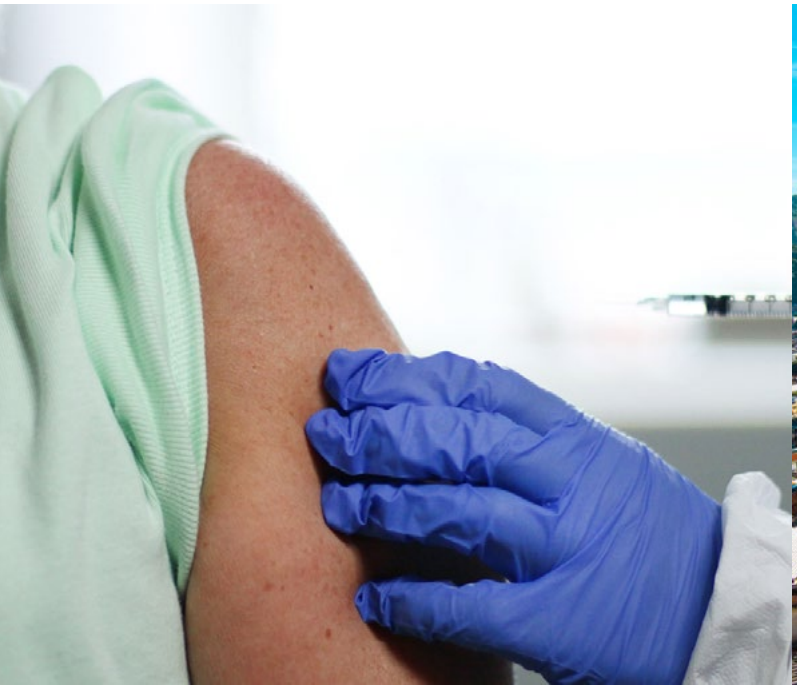
Understanding barriers to diversity in oncology trials

Despite ongoing calls (for decades) to address disparities in health and healthcare in the US, health inequity remains a prominent and unnecessary barrier to treatment for patients in marginalised communities. These discrepancies are mirrored in the clinical trial landscape, where traditional study designs – through lack of intentional design and awareness – cater disproportionately to the medical needs of White participants when evaluating the safety and efficacy of a potential new treatments.

The result of this conventional approach is an oncology trial landscape that, while not actively excluding participants along racial, gender, sexual, or age lines, unintentionally creates barriers to access for diverse populations – and a significant scientific and medical gap in our knowledge of how these new medicines will truly behave in the real world.

"Just asking people to join clinical trials is such a significant issue in particular communities," explains Dr Stephen Keith, senior medical director at Syneos Health. "If you ask African-American or Hispanic patients if they want to participate in clinical trials, more than half will say: 'Yes, we would like to do that', but if you're not asked, you can never get the opportunity.

"This is not just a moral issue," he continues. "This is scientifically and clinically significant because if a drug is labelled for an indication across all population groups, but yet you've not demonstrated the safety and effectiveness in at least most population groups, we're really doing a disservice to our patient population."



According to Dr Keith, patients in underserved communities face significant hurdles along the path to inclusion in oncology trials. For example, even if an individual is invited to participate in oncology research, that study may not be easy to reach in their community, or they may not be granted leave from work for the necessary time required for the trial and its assessments. When considered in isolation, such socio-economic barriers may seem relatively minor, but these factors result in well documented lower enrolment in studies and tragically low representation.

"If you look at the demographics of patients who were enrolled in all of the immuno-oncology drugs that have swept the market in the past few years, in some instances, less than 1% of those patients were minorities in the US," says Kenny. "Here is a complete class of drugs with novel mechanisms that are now in use across a broad range of cancers, and we actually don't really know how they're going to behave in specific patient sub-groups…leading to a blind spot of concern. We just don't know what we don't know."

Active listening: earning the trust of patients

Addressing the current imbalance in the US healthcare ecosystem cannot be achieved by the biopharmaceutical industry or healthcare providers alone. For both Drs Keith and Kenny, it is essential to include underserved communities in the conversation and actively listen to their lived experience and insight into systemic issues that prevent underrepresented communities from not only enrolling in clinical trials but in accessing healthcare in general.

"As an industry, we need to listen to patients," says Kenny. "We need patients to educate us about what they see when they look at what we do, what they don't understand, and what the barriers are.

"Soliciting these opinions and actually feeding the information into trial designs is critical," he continues. "You have to have this unique mindset that intentionally drives you to challenge all your prior assumptions and say, 'Can this protocol actually get to the right people? When I get it there, will they actually get in?'"

Here, a process of what Kenny calls 'reverse-education' can benefit both patients and industry experts. By actively listening to the community early in the trial development stage, companies can leverage a broader understanding of participant needs when selecting research sites and developing trial protocols.

"In drug development, the pressure is on to get patients into a trial, find out if the drug works, and either kill it or put it onto the market. Where and how you found those patients really was not given a whole lot of attention. It was all: 'we need to get this trial done and evaluate things quickly'," says Dr Keith.

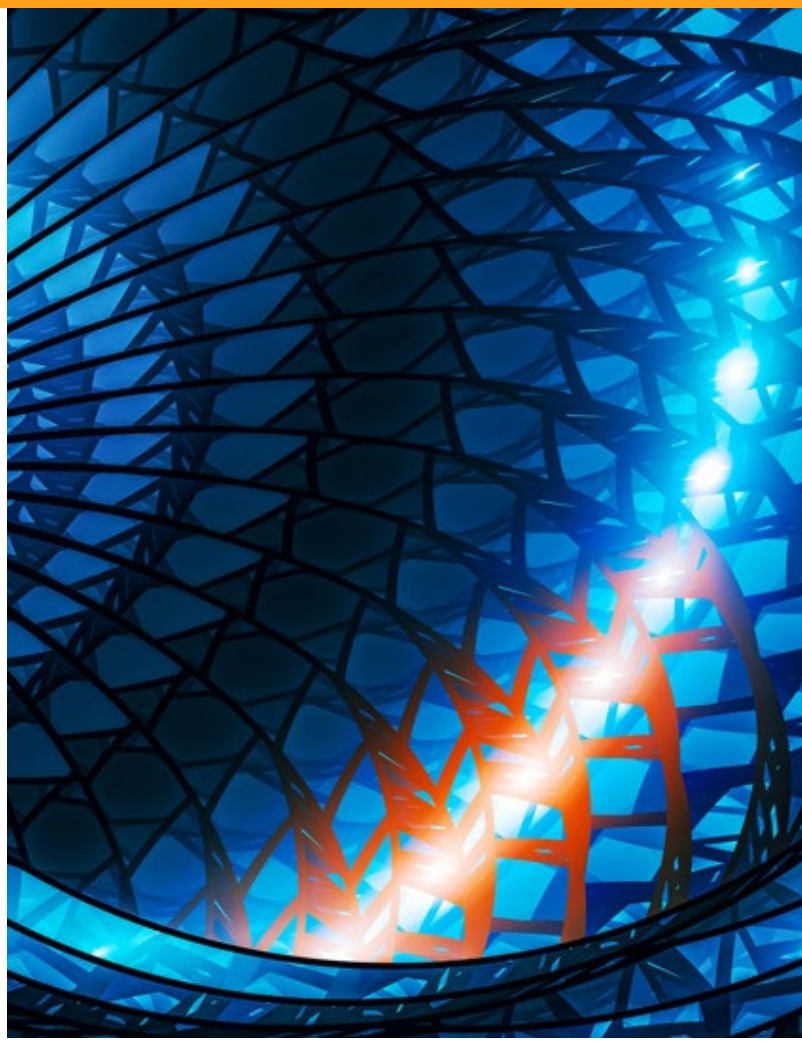
"We need to locate sites within underserved communities or at least adjacent to those communities and facilitate physical access, just like all other patients involved in the trial. We need to make sure that physicians in those communities know about studies and know how to say: 'Hey, this minority patient with breast cancer may be eligible for this study'."

However, as Drs Keith and Kenny stress, there is no one single "one-step" solution to solving health inequity in cancer trials. Establishing sustainable and meaningful change requires dedicated time and effort to earn the trust of underserved communities and develop meaningful symbiotic relationships, an element that has been missing in previous efforts to improve diversity in clinical research.

"Recently, we've seen a convergence of social awareness, social injustice, evidence generation, and rapidly evolving high priority medicines that finally have gotten to this point," explains Kenny. "It is a matter of trust and long-term investment. This has to be a grassroots effort by all of us, with all the people in our organisation, the customers we work with, and the sites we work with pulling together to achieve this goal."

Creating a multi-dimensional ecosystem

Of course, to effect change among patient communities, companies must also elevate DE&I within the healthcare and biopharma workforce. Facilitating a diverse group of stakeholders creates a complete jigsaw puzzle comprised of different experiences and backgrounds, which come together to reveal a broader understanding of the clinical trial experience.



"When we talk about community too, that includes the staff at the hospital," explains Dr Keith. "When we think about trust, people trust people who look and behave and act like them, who have a sense of community with them. That's equally true, whether it's your study nurse or your physician.

"We see institutions and foundations investing heavily in training minority investigators and nurses, as well as top-down management from institutions to promote diversity within their own staff, features that have proven extremely successful where they are implemented."

The necessity of DE&I in the trial space has not escaped the eye of regulators in the US. As Drs Keith and Kenny note, seeing key diversity and inclusion priorities for Syneos Health reflected in recent clinical trial guidance from the US Food and Drug Administration (FDA) is an encouraging sign that the industry is on the right track to ensuring that all those who want to participate in oncology trials are given the opportunity to do so.

"It was a bit eye-popping when we compare it to other guidance that we've seen because it really is the first time that the FDA has been prescriptive about what to do. The regulator has never done that before," explains Dr Keith.

"To be able to incorporate DE&I factors into our trial design and intentional efforts, and then to see different components of our strategy mirrored in the FDA draft guidance, it was a validation of we're on to something, we're on the right track," agrees Kenny.

Driving actionable change for future cancer patients

Enhancing diversity in clinical trial populations will not happen overnight. There is no switch to flip that will immediately improve inclusivity; instead, the path to diversity in the trial space is made up of dedicated and deliberate efforts to reach out to and engage underserved communities.

Recent developments, including the publication of updated FDA guidelines, are a positive sign that DE&I is moving from the fringe of healthcare to stand as a vital pillar of the drug and treatment development landscape. But to be truly realised, stakeholders across oncology must commit to challenging the accepted norms of traditional practices, using the insights provided by underserved communities to shape a system that benefits the many, not just the few.

"We need to do a better job," concludes Dr Keith. "I just hope we can sustain this enthusiasm and translate it into a permanent commitment instead of just a fashionable thing to do."

"It is a matter of trust and long-term investment, and not just around the particular individual study. You have to invest in those institutions and organisations within the community that people trust. That's our challenge."

About the authors

Nick Kenny, chief scientific officer, Syneos Health, has over 21 years of experience in clinical development and consulting. Passionate about rapidly moving compelling new science for unmet medical needs through the development process to arrive at early and innovative decisions.

Nick has been with the company since 2006. He grew and led the Oncology team until moving to the CSO role in 2018 where he now oversees the Medical Team for Syneos Health, the Consortia Models for e.g. Rare Diseases, Cell and Gene Therapy, Patient Voice. Leads our Patient Diversity in Clinical Trials initiatives and is an executive leader on the DE&I Council. Senior representative to the Forum for Collaborative Research. Early career in biomedical research in the UK, US and Canada. Faculty appointment at the University of Vermont Medical School for several years. Past experience in biopharma consulting. Nick is a Cancer survivor (Hodgkin's Lymphoma). He is also president, board of directors, Hospice of Wake County.

Stephen Keith, MD, MSPH, senior medical director, Syneos Health has over 25 years of experience in biopharma industry in vaccines development (e.g. influenza Type B, meningococcal, pneumococcal, and Group B Strep. as well as diphtheria, tetanus, pertussis, and inactivated polio vaccines). Joined Syneos Health in 2018 as medical leader and also serves leadership role with Patient Diversity initiatives.

Previously, held C-level positions at 3 biotech companies, and was a general partner in a life sciences venture capital organisation.

Prior to entering the pharmaceutical industry, served as health policy advisor to the U.S. Senate Committee on Labor and Human Resources, under Senator Edward M. Kennedy. MD Pediatrician by training /practice, and RW Johnson Clinical Scholar at UCLA with qualifications in Public Health. Faculty member at the Charles Drew Medical School & UCLA School of Medicine (Pediatrics). Fellow of the Academy of Pediatrics, and Diplomate of the American Board of Pediatrics.Board of Directors of National Medical Fellowships, and Community Health Charities.

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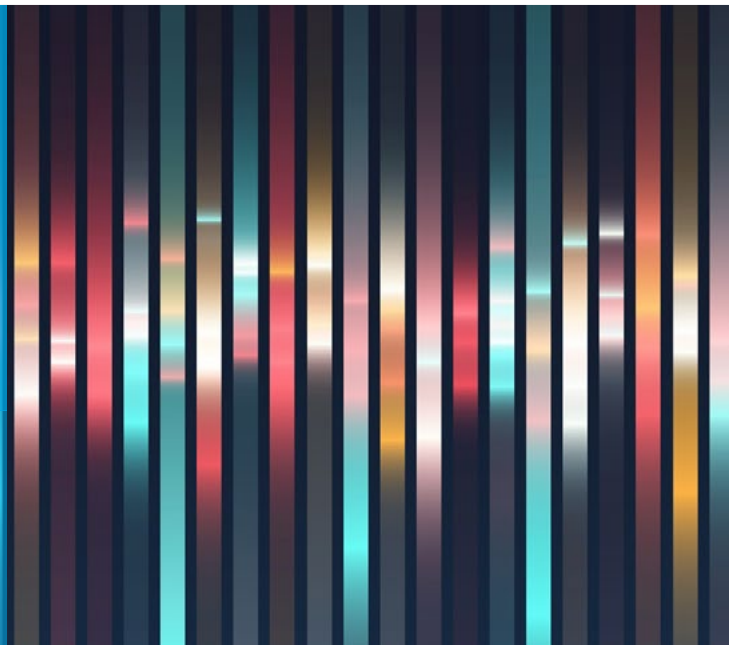
Realising the promise of genomic testing across oncology



Unlocking the secrets of the human genome has long been an ambitious pursuit for researchers around the world.

Over the past two decades, innovative research efforts, such as the Human Genome Project and 100,000 Genomes Project, have vastly expanded our understanding of the human genome and its role in driving research and development in oncology. Understandably, these ground-breaking studies have captured the attention of many across the industry, acting as a catalyst for new research into the molecular biology of cancer and revealing the biomarkers that help to diagnose and follow the course of disease and treatment outcome.

"There has been a surge in the number of biomarkers discovered through a broader understanding of the molecular pathways involved in the development of cancer, both across solid and liquid tumours," explains Orlaith Brennan, market development director, Patient & Market Access at IQVIA. "In the past few years, the testing that we can deploy to analyse the genomic profile of a tumour has expanded, and the number of therapies targeting the specific genes and proteins driving cancer cell growth has increased as a result."

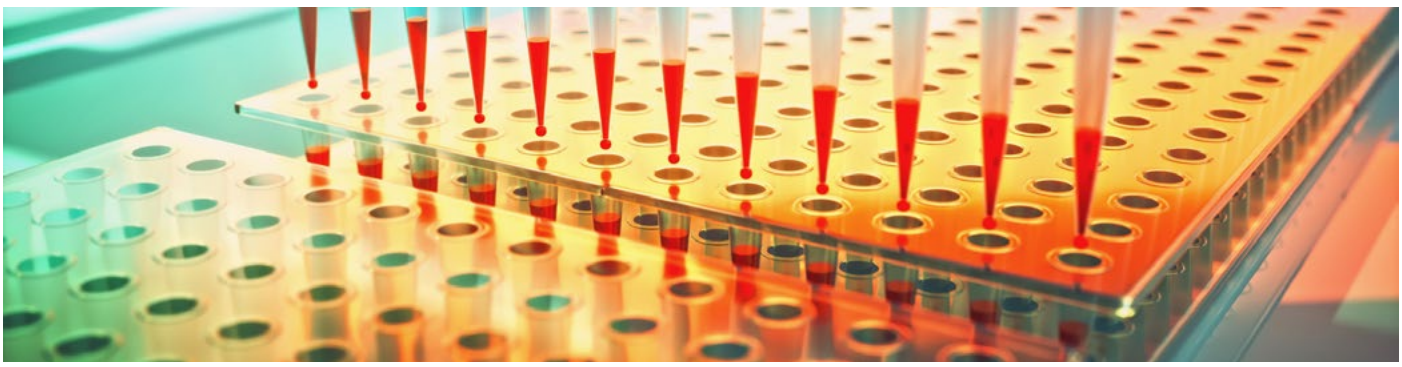
Today, the landscape of genomic testing and research is rapidly progressing, with significant scientific and technological advances driving a paradigm shift in the understanding of oncology at a molecular level. In a small but growing number of tumour types, empowered with a genomic fingerprint of the disease, practitioners can offer patients a truly personalised treatment, one that will address the specific change in the DNA of their tumour.

Optimising pathways for genomic testing in oncology

In 2020, building on the UK's long and proud history of advancing genomics, the UK Government laid out a detailed plan to embed whole genome sequencing and genomic testing as part of routine diagnostic and treatment care.

Over the past two years, stakeholders have focused on building the necessary infrastructure to support a world-leading genomics hub. In the current landscape, genomic testing in England is delivered through a network of seven Genomic Laboratory Hubs (GLHs), each responsible for coordinating services for a particular region of the country. Alongside the GLHs, seven NHS Genomic Medicine Services Alliances (GMSAs) were launched in 2020 to oversee and coordinate the embedding of genomics into mainstream clinical care and the link with personalised medicine.

"GMSAs are intended to promote education and clinical adoption," says Dr Julia Beguería, solutions specialist, Patient & Market Access at IQVIA. "There is a good structure in place. However, our analysis would tell us that the implementation and embedding of that structure is still a work in progress."



This is where Beguería sees opportunities for creative problem-solving and collaboration between stakeholders to optimise diagnostic and treatment pathways. For genomic testing in the UK and Ireland to function seamlessly, the overall vision must extend to all levels of healthcare in all regions.

"National policy is being developed at the NHSE Genomics Medicines Unit, but this needs to be cascaded all the way to local level," she explains. "What we are seeing is that the vision is perhaps not fully cascaded in terms of challenges with resourcing and ultimately standardised implementation and adoption of genomic testing.

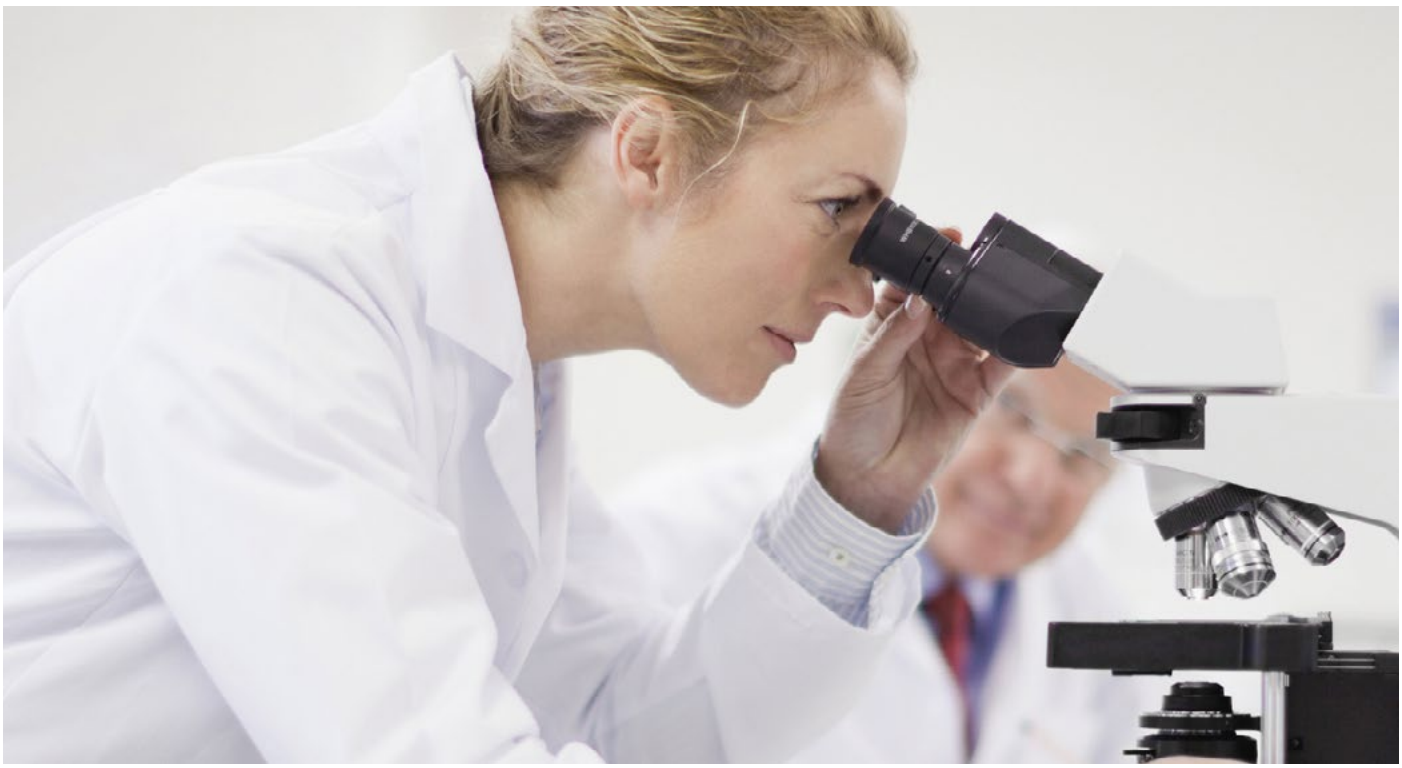
"We are seeing a huge variability because then, ultimately, it's down to the Genomic Laboratory Hub to agree on the best way that they can work with the patient population or within healthcare professional groups that they are working with depending on their local territory."

Addressing the need for education and awareness

Of course, to provide patients with the best treatment options, health professionals must first be aware of – and understand – how to use molecular testing in routine care, and what services and technologies are available to them. With each new biomarker discovery and scientific advancement, the healthcare landscape becomes significantly more complex for clinicians to navigate without having a broad understanding of the underlying tumour genomic profile.

"When launching a new targeted therapy, if companies aren't fully aware of the diagnostic landscape and understand where all the problems or challenges lie in the system, they may fail to optimise the outcome. They could conduct a perfect traditional product launch, but that's probably not going to be good enough with a targeted therapy, as access to diagnostics is an important pre-cursor to getting access to the actual treatment," says Brennan.

Given the complexity of the human genome and clinicians' busy schedules, identifying solutions to enhance education and awareness of genomic testing has become a central focus for government bodies and industry figures. This is not limited to healthcare professionals. As Dr Beguería notes, support should extend to every stakeholder in genomic testing for oncology.



"It is important to ensure that people working in the system – clinicians, pathologists, commissioners, and even policymakers – are fully up to speed with the scientific and the clinical developments relevant for oncology and that they have the tools required to confidently operate in this space," she explains.

"All stakeholders within the system have different levels of educational needs, which need to be addressed in different forms. They need to be guided and supported by industry to help them understand the best rollout of the various options for genomic testing for the different tumour types."

Healthcare professionals should also prioritise ensuring that patients have access to up-to-date information about genomic research. These patients have a unique insight into their condition and symptoms, and with accurate treatment information, they can advocate for genomic testing to be included in their treatment plans.

Building a robust and interoperable data library

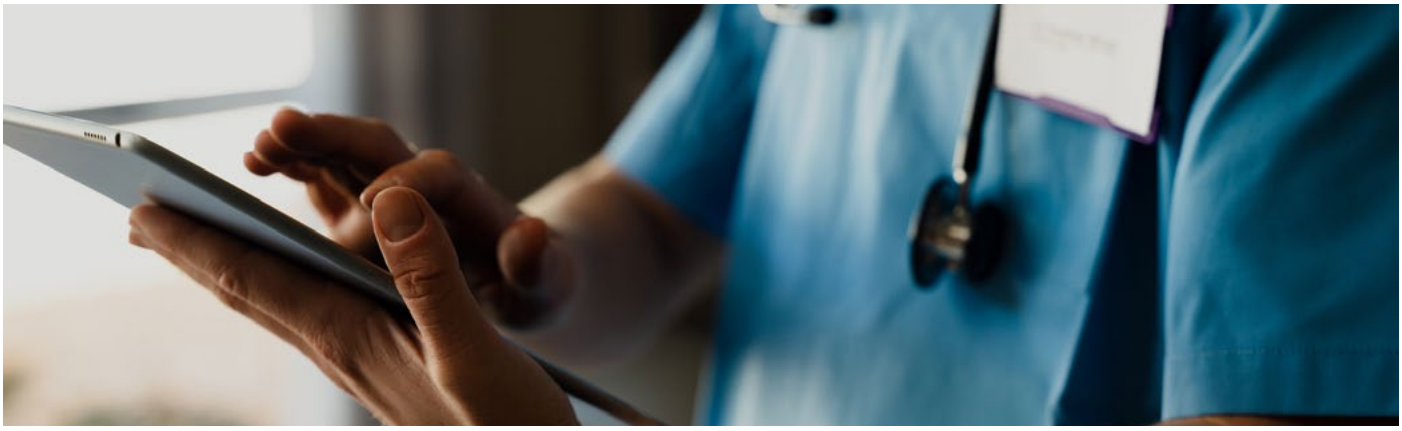
Unlocking the true promise of genomics is only achievable with an enormous wealth of data. In the UK, researchers and healthcare providers have access to a wide variety of non-identified data sources garnered from patients across the country.

IQVIA has made significant contributions to the development of such resources, including supporting Genomics England to combine clinical and genomics data to accelerate diagnosis and development of personalised medicines and attract global pharmaceutical and biotech investment to the UK.

However, in the current genomics landscape, experts must contend with the quality and interoperability of this data in order to derive actionable insights.

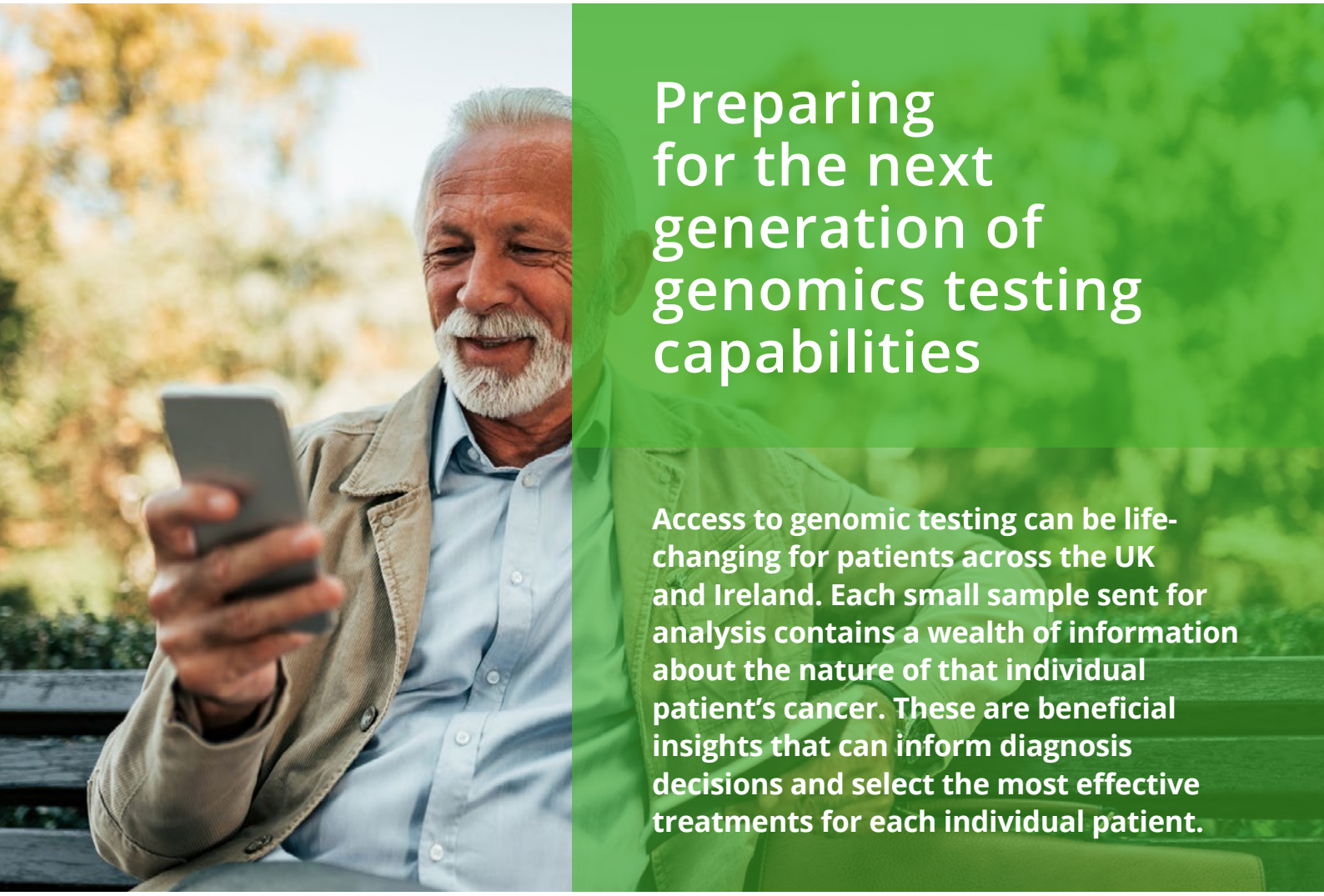
"It's important that data is standardised so that it's comparable and provides maximum societal benefit," says Dr Beguería. "This can be challenging as the amount of data collected is extensive, but that data needs to be accurate and actionable for clinicians to interpret the information correctly."

Beyond the current application of data in genomic testing, in an emerging area of research, it is also important that today's generation of clinicians continue to contribute valuable data to establish a connection between current standard of care and further clinical research.



"Information that appears to be irrelevant today could be highly relevant tomorrow," explains Brennan. "The scientific benefits of a broader data set may not add to or improve the outcome for an individual patient today, but because it goes into a repository, it has the potential to provide insights, which may become relevant and actionable in the future."

Dr Beguería agrees, "It's like creating a library of data that you still don't know how to interpret, but one day, you'll have a great data source, which will help us understand the drivers of disease across tumour types."



Preparing for the next generation of genomics testing capabilities

Access to genomic testing can be life-changing for patients across the UK and Ireland. Each small sample sent for analysis contains a wealth of information about the nature of that individual patient's cancer. These are beneficial insights that can inform diagnosis decisions and select the most effective treatments for each individual patient.

With an understanding of how a tumour is likely to react to a specific treatment, clinicians can work with patients to develop an informed treatment plan, ensuring that the optimal treatment option is used at the right time – improving the patient's quality of life.

"It's important to involve patients at all levels of genomic research," says Brennan. "Patients need to be aware of the best options for their healthcare and if there is a genomic answer to questions about their cancer diagnosis or treatment."

Beyond education, Brennan spotlights the importance of making genomics services accessible to ensure that all patients across the UK and Ireland can benefit from the promise of genomic testing as the sector evolves.

"Fundamentally, the testing structure is set up on a centralised basis across England, but equality of access to treatments will need to follow as part of that," she explains. "If the implementation isn't there on an equal basis across the country, if there are still pockets of brilliance, then all patients aren't being treated equally. It's important to have a level playing field for all patients.

About the interviewees

Dr Julia Beguería, healthcare solutions specialist, IQVIA, is medical doctor by training, also holding postgraduate studies in Health Policy. Her previous experience at IQVIA involves Market Access, Strategy & Business Planning and Account Management

Orlaith Brennan, market development director, Ireland IQVIA is a pharmacist by profession, Orlaith has over 25 years industry experience ranging from community practice to national policy development. She has worked in commercial and strategic roles in distribution and government affairs, including market access and national pricing negotiations.

About IQVIA

IQVIA is a leading global provider of advanced analytics, technology solutions and clinical research services to the life sciences industry. IQVIA creates intelligent connections to deliver powerful insights with speed and agility — enabling customers to accelerate the clinical development and commercialization of innovative medical treatments that improve healthcare outcomes for patients. With approximately 77,000 employees, IQVIA conducts operations in more than 100 countries. Learn more at www.iqvia.com

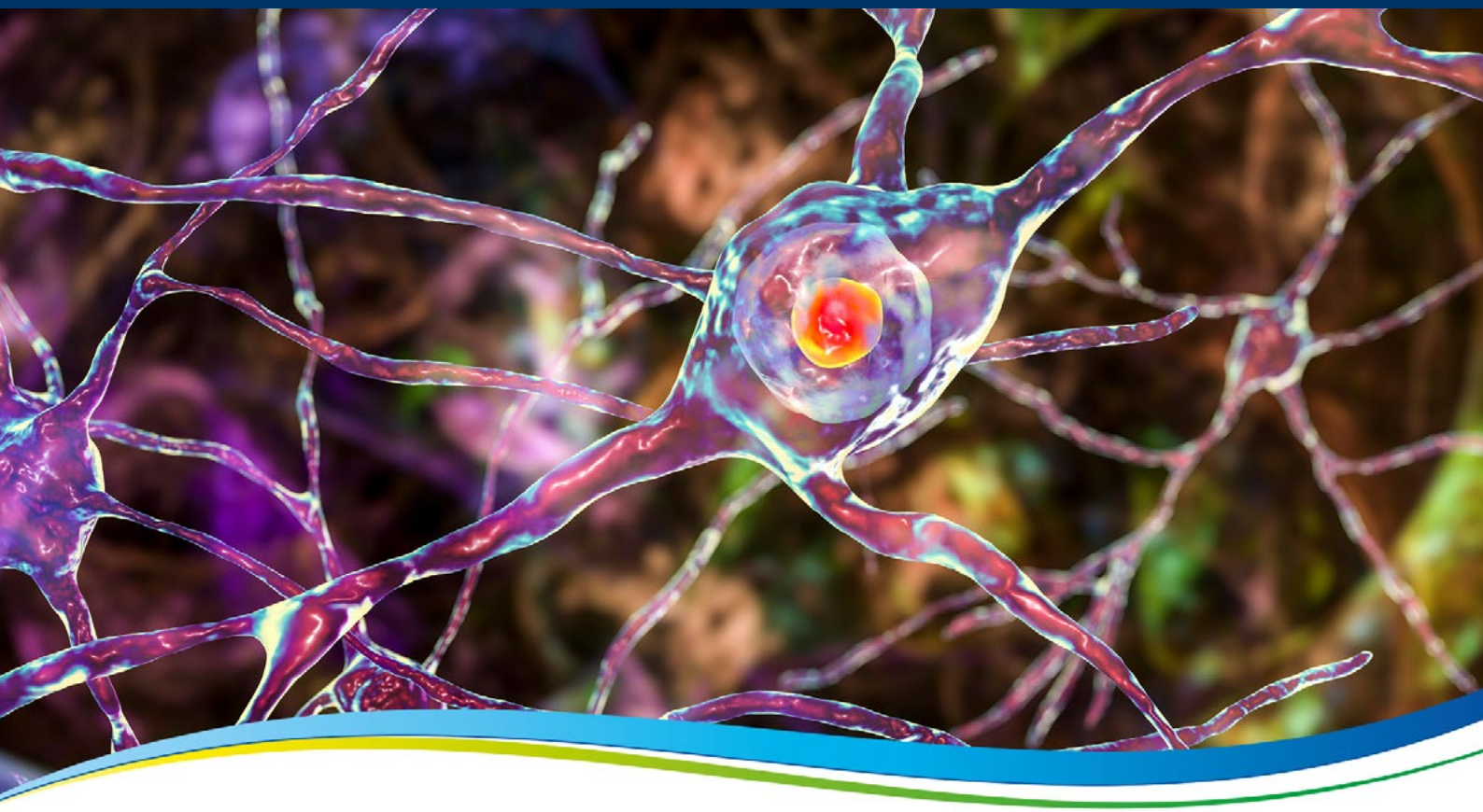
New horizons in breast cancer care

Interview with Markus Kosch, Daiichi Sankyo head of Oncology Business Division in Europe

Recent progress in immunotherapy, targeted therapies, and genetic testing has allowed physicians to target and treat breast cancer more precisely, improving outcomes and quality of life for all cancer patients. Today, more women with breast cancer are able to live longer and better than ever before. Still, there remains a vast unmet need: Breast cancer remains the third most frequent cause of death and, among cancers, has the highest morbidity. In Europe alone, over 500,000 new cases were diagnosed in 2020, and approximately 140,000 women died from the disease.

During the recent pandemic, women have been prevented from attending breast cancer screenings, and more patients are diagnosed only at a later stage. So, the progression to metastatic disease that is to be expected in about one-third of all cases will occur earlier.

With this in mind, it's important that we push to ensure that cancer care is put back on top of the priority list for societies. It deserves our full attention to collaborate as a united community to find solutions for patients. This remains one of the key visions we have – and one that I was proud to share when I joined the company back in September. We understand that no one can find a solution alone. That's why we collaborate with professional bodies and companies where we can combine our expertise and bring much-needed treatments to patients as quickly as possible.



Emerging therapies harness innovative technology to better help patients

Although there is no cure for advanced cancer, innovative advancements in oncology have the potential to change the current trajectory in breast cancer and improve outcomes for patients. This is exactly what emerging treatments, such as CAR-T cell, gene therapies, and precision medicine aim to do. Targeted therapies have also demonstrated huge potential in recent years and have become standard treatments for many types of cancers.

Such treatments aim to try and strike a balance between minimising side effects and maximising the survival benefit of an agent. But we know there is more to do to master this balance. At Daiichi Sankyo, we value cutting edge science and technology and last year invested 20% of our yearly revenue into R&D. This is how we've become one of the leading companies in oncology over the past ten years.

Such new technologies may add benefit to a multitude of therapies for other cancer types, too. Clinical trials across a range of cancers of high unmet medical need, such as lung and gastric, have shown to also benefit from this targeted form of treatment.

Keeping patients at the heart of innovation

Improving the lives of patients cannot be accomplished overnight. It requires dedication and commitment in the long term. Understanding that every breast cancer journey is a unique and personal experience helps us to conduct our science and research with a truly patient-centric focus.

One way to proactively seek this understanding is to invest in clinical trials to bring scientific information from routine clinical practice to the medical community, helping to better understand oncological diseases and improve patient care.

We know that every cancer patient may also be a mother or father who want to see their children smile. A partner, a friend, a daughter, a son who long to kiss and hug their loved ones. It is with this knowledge that we conduct our science and cancer research to see another warm embrace, another smile or touch – we know how much they matter.

A bright future

There is no doubt that this is a very exciting time in the treatment space – we've seen a number of novel medicines being approved in recent years, both for early and late stages of breast cancer. We know that tumours differ from person to person and have harnessed this knowledge to deliver more targeted therapies that aim to extend survival and reduce treatment-related side effects as much as possible.

It will also be interesting to see how we can utilise precision medicine techniques to approach detection and screening more proactively, which will be key to reversing the harsh impact the pandemic had in cancer care.

Pharma companies, regulatory bodies and reimbursement institutions need to move at the speed in which the field innovates, accelerating decision-making and increasing agility to respond to the rapid changes we see in standards of care, treatment, and diagnosis patterns. By leveraging our world-class, innovative technologies, we hope to bring more novel treatments to women with breast cancer as quickly as possible.

About the author

Prof. Dr. Markus Kosch is the head of Oncology Europe at Daiichi Sankyo. In this role, he leads the Medical Affairs, Market Access and Commercial Organisation of Daiichi Sankyo in the European countries.

Kosch has worked in oncology for his entire career. Oncology has always been his preferred field in medicine, ever since those early days as a medical student. After studies that took him to Kings College London and the UCSF in San Francisco, he obtained his medical degree at the University of Münster, Germany. Kosch is a boarded expert in internal medicine and nephrology and practiced in internal medicine, intensive care and oncology at the University Hospital Münster until 2005.

He has over 15 years' experience in the pharmaceutical industry, starting in Medical Affairs at Wyeth Pharmaceutical introducing the first mTOR inhibitor in oncology therapy and later at Pfizer leading the European teams preparing launches in hematology and in personalized therapy in lung cancer with molecular-targeted medicines as well as introducing the first CDK4,6 inhibitor in metastatic breast cancer. In addition, Kosch has published many peer-reviewed papers, reviews and book chapters and still teaches as Professor of Internal Medicine at the Medical School Münster. He is also a founding member of the "Vision Zero" cancer prevention initiative and think tank.

Kosch also has a highly personal reason for wanting to make a difference in cancer care – his father died of colon cancer when he was just 21 years old. This has always given him extra motivation, whether when treating individual cancer patients as a physician or when trying to bring them improved outcomes on a broader scale in the pharmaceutical industry.

About Daiichi Sankyo Europe

Daiichi-Sankyo

Daiichi Sankyo is dedicated to creating new modalities and innovative medicines by leveraging our world-class science and technology for our purpose "to contribute to the enrichment of quality of life around the world." In addition to our current portfolio of medicines for cancer and cardiovascular disease, Daiichi Sankyo is primarily focused on developing novel therapies for people with cancer as well as other diseases with high unmet medical needs. With more than 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation to realize our 2030 Vision to become an "Innovative Global Healthcare Company Contributing to the Sustainable Development of Society." For more information, please visit www.daiichi-sankyo.eu

Checkpoint inhibitors, Enhertu in spotlight as ASCO resumes in-person meetings

Researchers also dove into socio-economic disparities in cancer care

Last month in Chicago, Illinois the American Society of Clinical Oncology hosted its first in-person meeting since the COVID-19 pandemic began. In presentations and published abstracts, researchers shared a massive amount of data across all cancer types and treatment modalities. Below are just a few of the highlights from the show.

Many wins for checkpoint inhibitors

Checkpoint inhibitors are a growing class of immunotherapy drugs that use monoclonal antibodies to activate checkpoint proteins, thus helping reactivate parts of the patient's immune system that a cancer cell has shut down. Led by Merck's blockbuster Keytruda, these drugs have been making waves in the oncology space for some time, and this year's ASCO kept up that trend.

For instance, a small trial of GSK's Jemperli (dostarlimab-gxly) saw a rare 100% response rate in a small study of 12 patients with mismatch-repair deficient, locally advanced rectal cancer. At six months, all patients had no evidence of a tumour, allowing them to skip the chemotherapy and/or surgery that would normally be their next treatment.

"What's really remarkable is this is the first time I know of in solid tumour oncology where we've had a 100% complete response, and we've completely omitted the normal standard of care," Luis Diaz, head of the division of solid tumour oncology at Memorial Sloan Kettering and one of the doctors who designed the study, told STAT News.

As for Keytruda itself (pembrolizumab), Merck shared a number of positive results from different disease spaces, leading with the Phase 3 KEYNOTE-716 trial, which compared Keytruda to a placebo in resected stage IIB or IIC melanoma patients at a median 27.4 month follow-up. Results showed 81.2% of patients in the KEYTRUDA arm were recurrence-free at two years compared to 72.8% of patients in the placebo arm, and quality of life was comparable.

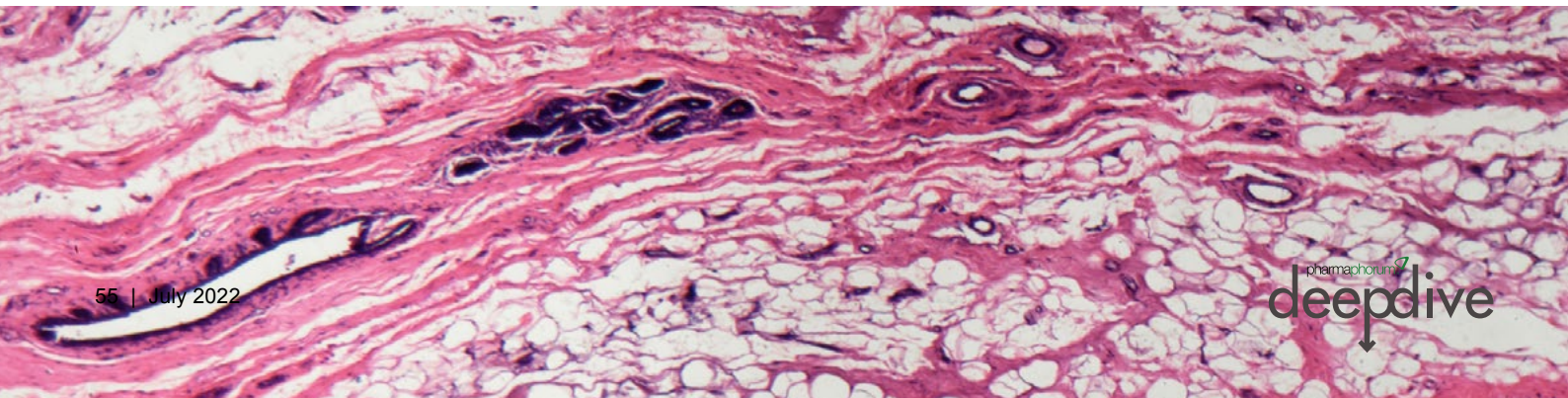
"Patients with stage IIB and IIC melanoma are at risk of seeing their cancer return and spread to distant sites," said Dr Georgina Long, co-medical director, Melanoma Institute Australia (MIA), and chair, Melanoma Medical Oncology and Translational Research at MIA and Royal North Shore Hospital, University of Sydney, said in a statement. "The latest results from KEYNOTE-716 show the potential of pembrolizumab to help reduce distant recurrence in patients with resected stage IIB and IIC melanoma, and further highlight the important role of adjuvant therapy for these patients."

Other notable checkpoint wins included promising early safety results for Adagene's SAFEbody CTLA-4-inhibitor and strong Phase 3 data for Merck KGaA's Bavencio (avelumab) PDL-1 inhibitor for kidney and bladder cancer.

Breast cancer breakthrough

The single study that seemed to receive the most buzz coming out of the show was AstraZeneca and Daichii Sankyo's DESTINY Breast-04 study of Enhertu (trastuzumab deruxtecan). The study found that Enhertu reduced the risk of disease progression or death by 49%, whilst improving overall survival by 36% compared to chemotherapy when given as third-line treatment.

What makes the study especially impressive however, is not simply the results but the fact that they essentially create a new category of addressable breast cancer patients, those who are deemed HER2 expressing, but not HER2-positive. This was teased by some data that came out of ESMO in May, when AZ's Sumil Verma talked to pharmaphorum about a predecessor study, the DAISY study.



"Traditionally, when we talk about HER2 targeted treatments, they work for HER2 positive breast cancer, accounting for about 15% to 20% of all breast cancer," Verma told pharmaphorum at the time. "But up to 50% of breast cancer has what we call HER2 expression, that is traditionally not classified as HER2 positive disease, and therefore previously was not considered to be targetable. [Our data] shows that there is potential activity in not only the traditional HER2 positive patients, but also in HER2 expressing patients."

Approval in that broader patient range could unlock $3 billion in additional sales for Enhertu, according to analysts at Credit Suisse.

For HER2 negative breast cancer patients, there was also good news from a handful of other big pharmas. A Gilead study showed that their Trodelvy (sacituzumab govitecan) could extend patient survival by 1.5 months, results that are encouraging but not necessarily clinically meaningful. Novartis's CDK4/6 inhibitor Kisqali (ribociclib), meanwhile, saw a survival extension of 5.4 months for that same group of patients.

"Kisqali is the only CDK4/6 inhibitor to have consistently demonstrated statistically significant overall survival across its entire Phase III program," Reshema Kemps-Polanco, executive vice president, US Oncology at Novartis, said in a statement. "Overall survival is the ultimate goal of oncology clinical trials and what patients hope for—to live longer, and to thrive. We are extremely proud of our quality of life data and that Kisqali has the longest median overall survival ever reported in HR+/HER2- metastatic breast cancer."

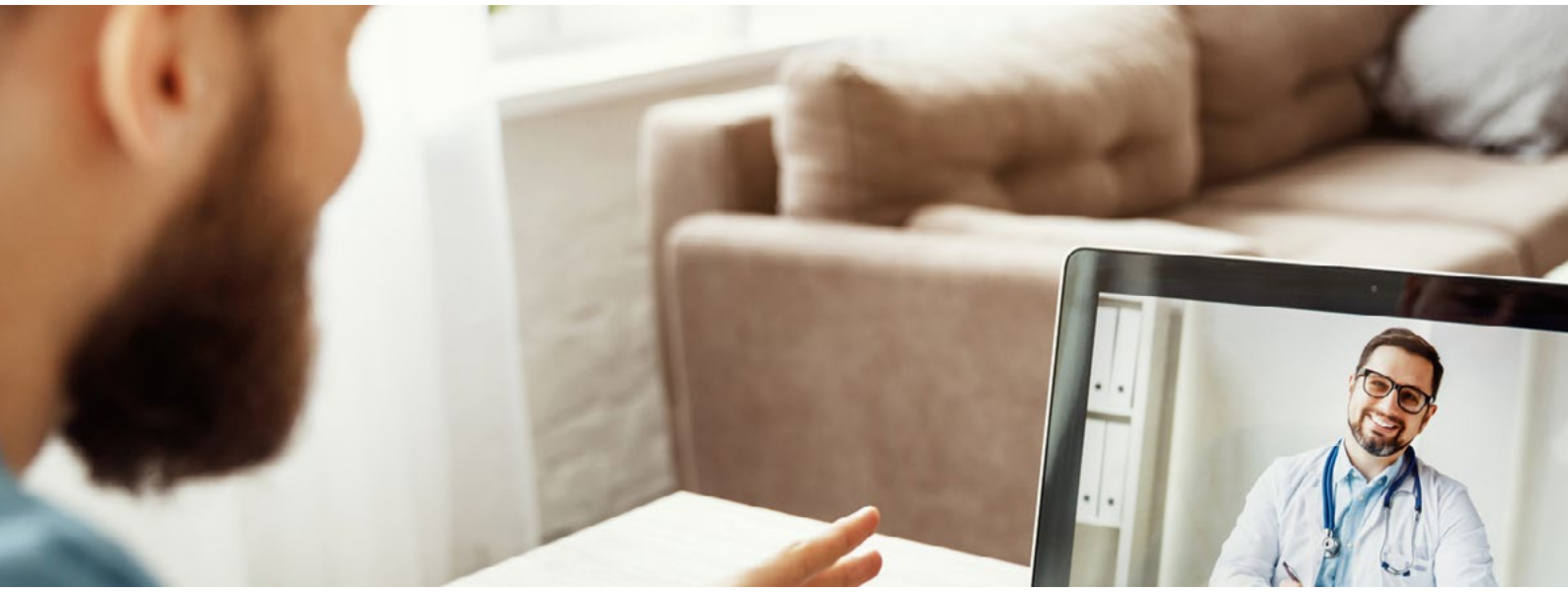
New treatment avenues for multiple myeloma

As pharmaphorum's Phil Taylor reported last month, both Janssen and Pfizer highlighted data on new BCMA-targeting bispecifics for multiple myeloma, boasting overall response rates of 63% and 60.6% respectively. Both Janssen's teclistamab and Pfizer's elranatamab were tested in populations of patients who had already tried many other treatments for the condition. The similar drugs on a similar timetable could lead to a rivalry when and if they secure regulatory approval.

Highlighting care disparities in pursuit of equity

Events like ASCO aren't just about sharing the latest clinical publications. They're also an opportunity for industry to come together for some introspection about larger trends and concerns.

The theme for ASCO this year was "Advancing Equitable Cancer Care Through Innovation" and several presentations focused on the current inequities in cancer care and clinical trials.



One study by Flatiron Health of 26,788 cancer patient records found that while telemedicine usage for cancer care increased across the board during COVID-19, its utilisation was lower for Black patients vs White patients, uninsured patients vs insured patients, rural and suburban vs urban patients, and, most dramatically, patients with lower socio-economic status, whose likelihood of using telemedicine was 10.6% vs 23.6% in the highest socio-economic groups.

Another study looked at five-year overall survival in children with neuroblastoma and found significant differences (around 10 percentage points) based on race, insurance status, and neighbourhood-level poverty.

A survey from the BECOME initiative asked 424 patients with metastatic breast cancer, 102 of whom were Black, about their feelings about clinical trials. They found that Black patients were more likely to report not having discussed clinical trials with their care teams than non-Black patients (40% vs 33%). They were also nearly twice as likely to believe unstudied treatments might be harmful.

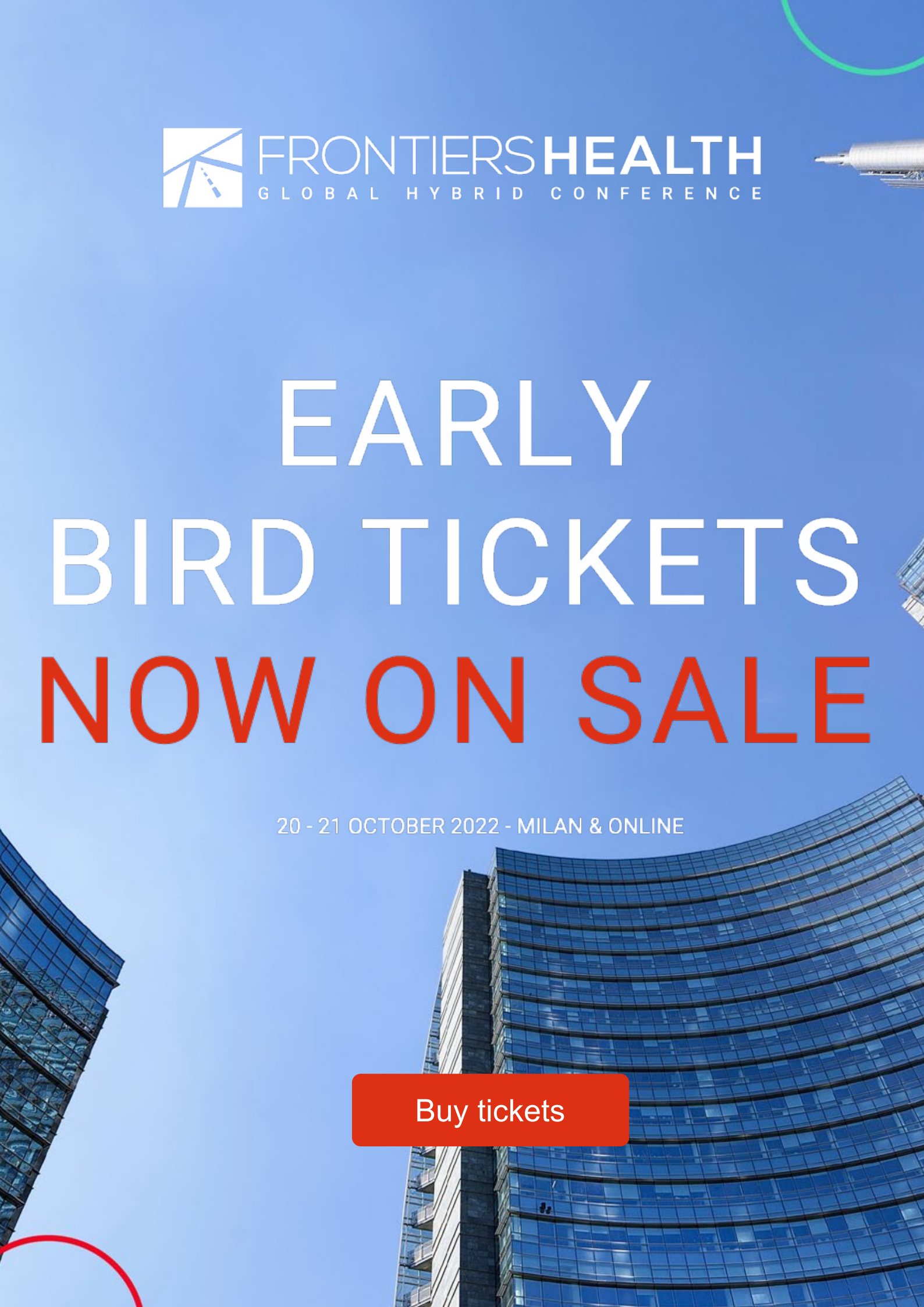
But other studies provided some hope for correcting inequities. At least two studies looked at the effect of Medicaid expansion in the United States on cancer survival rates. One found that a 10% increase in state-level social services spending improved five-year survival for non-Hispanic Black adults and narrowed the disparity between Black and non-Black patient survival rates. Another study found that the Medicaid expansion that was offered to states as part of the Affordable Care Act was associated with a threefold increase in patients using Medicaid in cancer clinical trials.

Finally, ASCO itself released a new tool, the Interactive Map of Oncology, to help clinicians explore the interaction between COVID-19, cancer, and systemic and socio-economic factors.

"The ASCO Registry is improving the understanding of the effects of COVID-19 on treatment plans and outcomes for patients with cancer," ASCO chief medical officer Dr Julie R. Gralow said in a statement. "This meticulous collection of data from practices across the country has already begun to inform us about commonalities and best practices across cancer types."

About the author

Jonah Comstock, editor-in-chief
Jonah Comstock is a veteran health tech and digital health reporter. In addition to covering the industry for nearly a decade through articles and podcasts, he is also an oft-scene face at digital health events and on digital health Twitter.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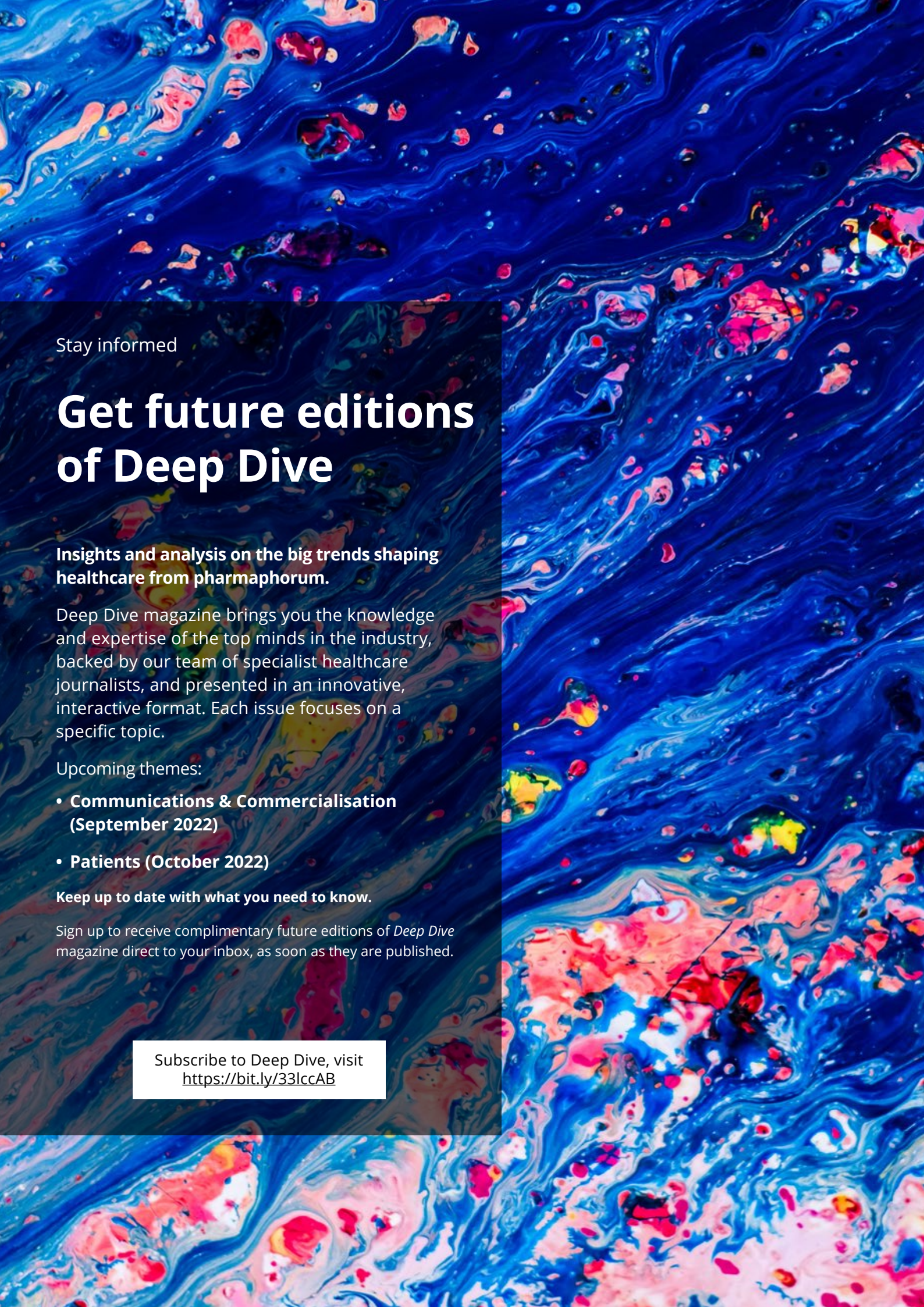

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