



The Answer to Cancer

Immunotherapies are the scientific answer to cancer, how important is marketing?

This paper is a critical review of multiple evidence sources, examining the evolution of how oncologists make treatment decisions and whether non-clinical influences have become more important over recent years. Together it is a 10-12 minute read, however each section is designed to be a stand-alone short 1-2 minute read should the reader be short on time.



Click on the image to see each section, the home icon will return you to this page.



Why is a drug the market leader in an indication in which it doesn't have a license?

1-2 min read

What is happening in Oncology at a macro level, are certain molecules bucking the accepted wisdom that "oncology is special" and clinical is king.

The rise and rise of immunotherapy

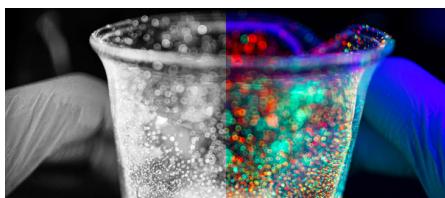
1 min read

Dr Michael Gaschler from Cerner Enviza gives a primer on the evolving scientific marketplace in Oncology.

Oncologists are people too

3 min read

Examines factors that drive decision making and includes highlights from interviews conducted with oncologists.



Branding is here

3 min read

The emergence of branding in oncology and how brands are starting to dominate the therapy area, especially in immuno-oncology.

The 500lb gorilla in the room, Keytruda – is it an anomaly or the new norm?

3 min read

An in-depth look into the oncology brand that changed everything, how oncologists talk about it and how Merck leverages both science and marketing in positioning it.

It's Science AND Marketing, not OR

2 min read

How should we as the people defining the future of oncology brands start to make decisions, understanding our situation and harnessing available data and approaches.



Why is a drug the market leader in an indication in which it doesn't have a license?

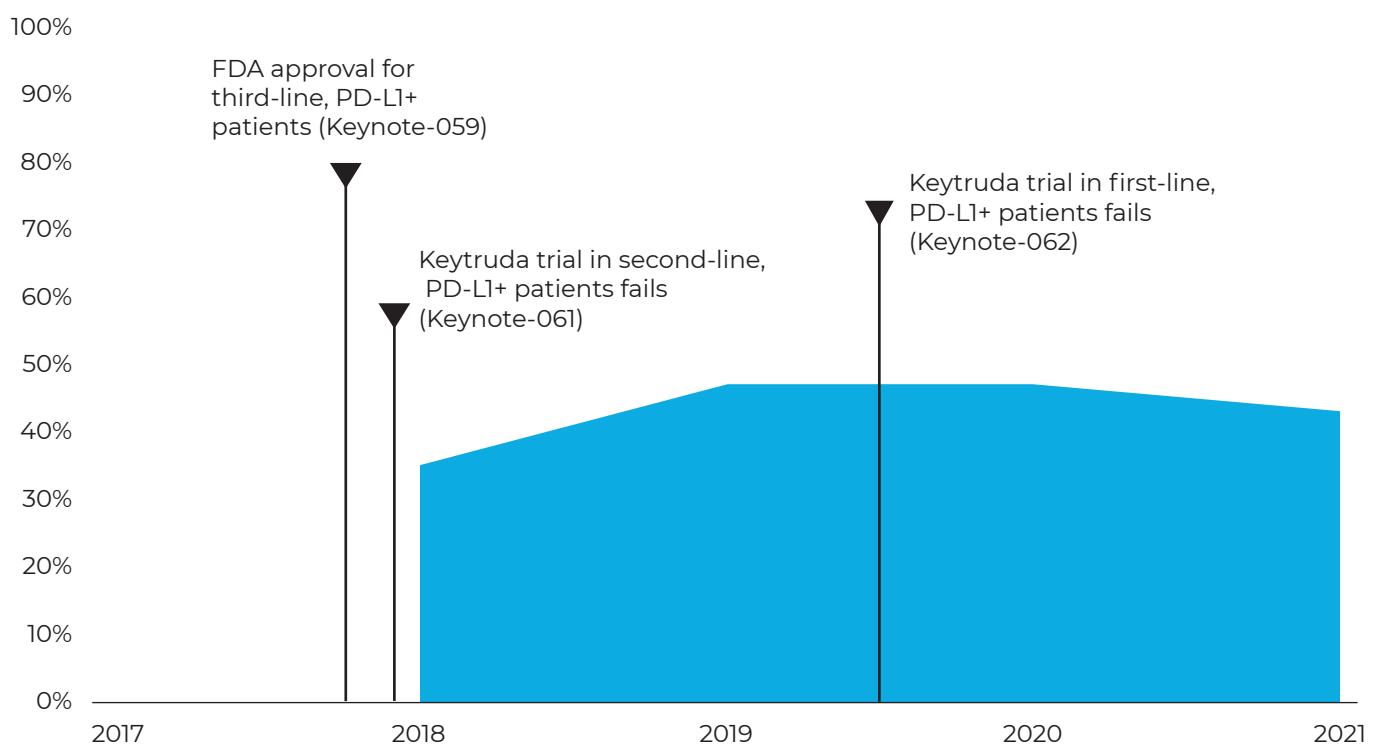
People with metastatic gastric cancer that progresses despite initial chemotherapy have poor outcomes.

Even with existing second-line treatment, the majority of patients can expect to live for only a few more months. This significant unmet need is what motivated Merck to run KEYNOTE-61, a two-year, 30-country, 148-centre phase 3 trial that pitted Keytruda (pembrolizumab) against chemotherapy drug, Taxol (paclitaxel).

Sadly, after two years, KEYNOTE-61 became yet another entry on the very long list of disappointing trials, delivering a terrible blow for patients and their families. Or did it?

In 2021, respondents to a syndicated Cerner Enviza survey reported that nearly 50% of eligible patients are being prescribed Keytruda in second line gastric cancer. This raises a simple question, what is going on in oncology, an area of medicine famous for being so data-driven and rational?

Keytruda Use among Second-Line, PD-L1 Positive Metastatic Gastric Cancer Patients (% of patients), USA



This white paper seeks to answer that question. It also proposes a new approach to oncology, asking whether the time has come for pharma to accept that oncology may be changing and that success may be driven by a wider range of factors than simply the strength of a product's trial data.

Oncology is special, of course. What other field of medicine has had such a profound impact on tens of millions of people? And the pipeline for new treatments is fuller than ever before. But as the number of available therapies increases, as more pathways and genetic variations are mapped and as the science grows ever more complex, how will oncologists be able to differentiate them all?

Branding and marketing are gaining pace within immuno-oncology and oncology in general. Ask oncologists what they think about when you say "Keytruda" and they won't just mention the data, their answers will also reflect the influence of feelings, trust, brand personality and salience. Even if companies were not actively marketing and differentiating their brands – and they are – your customers will do it for you.

Oncology is unique and clinical evidence will remain central, but just as in other therapeutic areas, successful brand strategy will need to be informed by both clinical data and marketing efforts

"The only time you can use clinical only to differentiate is if you have no competition and there is no competition within 4-5 years" - Senior Oncology Leader

Underpinning the arguments in this white paper are a wide range of new insights. We have interviewed oncologists on three continents, as well as oncology scientists and senior oncology leaders in life science companies, to trace the most cutting-edge trends. We've media-scraped from oncology brands, used semiotic expertise to analyse imagery and consulted with behavioural science experts to map how oncologists and other stakeholders perceive existing brands.

And, finally, we have leveraged the best expertise in branding to ensure the approach we propose strikes the right balance between science and marketing in oncology.

"The only time you can use clinical only to differentiate is if you have no competition, and there is no competition within 4-5 years"

Senior Oncology Leader





The rise and rise of immunotherapy

How the rise (and rise) of immunotherapy has shifted the science and marketing paradigm by Dr Michael Gaschler, Engagement Manager at Cerner Enviza

“We live in a golden age of oncology. The long-dreamed-of goal of harnessing the body’s own immune system to treat cancer has become a reality, and we have seen the extension in the tail of the survival curve which has given patients and their clinicians disease relief, time, hope and in some cases cures”

Dr. M. Gaschler - Cerner Enviza

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As with all transformational science, success took time. Early immunotherapies were often difficult to administer and only effective in specific treatment settings. But then came the checkpoint inhibitors; therapies like PD-1 and PD-L1 inhibitors revolutionised the way cancer was treated, garnering armfuls of accolades including a Nobel Prize in 2018.

Their significance is also evident in the commercial landscape. Seven PD-L1 inhibitors have been approved in the US with approved indications growing by 83% year-on-year from first approvals in 2014 through 2020.

Data supporting meaningful improvements in survival have driven physicians to favour regimens containing immunotherapy. However, clinical data alone cannot explain every prescribing choice, especially when they fly in the face of clinical trial outcomes.

Keytruda as a therapy for second-line metastatic gastric cancer is a case in point. Following accelerated FDA approval in third-line cancer, KEYNOTE-061 evaluated single-agent Keytruda versus conventional chemotherapy in a second-line metastatic gastric cancer.

Keytruda missed its endpoint in 2018 : yet, in 2019 and 2020, US respondents to Cerner Enviza Treatment Architecture surveys reported prescribing single-agent Keytruda to about 47% of their second-line PD-L1 positive patients.

Clearly, when it comes to physician prescribing, the decision has a number of contributing factors, we see this especially in the context of IOs. These factors will vary by tumour type and setting, of course, but the truth is out and life science companies seeking to launch new medicines in immuno-oncology would be wise to look more closely at evidence around what motivates oncologists when they reach for the prescription pad.

So, what's going on in the mind of oncologists?





Oncologists are people too

"I am a human dealing with humans; often there are times when you know there is a truth behind the need to go with your gut and feelings – as long as you are in touch with your own emotions and feelings."

- US oncologist

As humans we like to believe we are rational beings. In fact, traditional economic theory insists on it. These theories have more recently been challenged by behavioural scientists who demonstrated that many factors come into play when making the myriad of decisions we make every day; indeed, behavioural science tells us that up to 95% of our decisions are based on mental shortcuts, instinctive response, intuition and context.

Human behaviour is simply not the result of perfect logic and careful deliberation. When we think about the big decisions we make in our personal lives; getting married, moving house, having children, we can readily acknowledge many more factors affecting decision-making than can be captured in a cost/benefit analysis!

Our professional lives are no different and we see this often in research when stated intent does not match behaviour, prescribing patterns do not appear to be logical and respondents are unable to provide a clear explanation for the things they do. Studies have, in fact, demonstrated clinical decision makers are also at risk of error¹ due to bias and a lack of insight into one's own biases is common² which may result in significant cognitive biases.^{3,4}

Data is important no doubt, but oncologists are human too and there are many layers to their decision-making. To ignore them does us and them a disservice.

"I am a human dealing with humans; often there are times when you know there is a truth behind the need to go with your gut and feelings – as long as you are in touch with your own emotions and feelings." - US oncologist

To understand deep motivators to behaviour, we cannot rely solely on standard Q&A based approaches. The purely rational route will generate justifications and post rationalisations. We also need to understand context, socio-cultural and environmental factors as well as emotion, instinctive response and values.

How oncologists make decisions

In interviews with oncologists, we explored in a variety of different ways, the factors that drive decision-making in the context of IOs and NSCLC. Of course, all the key performance parameters such as guidelines, efficacy, safety and toxicity sit high on the list when oncologists are asked about key decision influencers.

However, conversations around 'FOMO' (fear of missing out) and comparisons with Coca Cola in terms of brand presence and reach, might not have been so easily anticipated; nonetheless, those topics are included in the discussion and articulated by oncologists in our interview sample, as factors that may indirectly come into play.

Key decision influencers that oncologists readily acknowledge

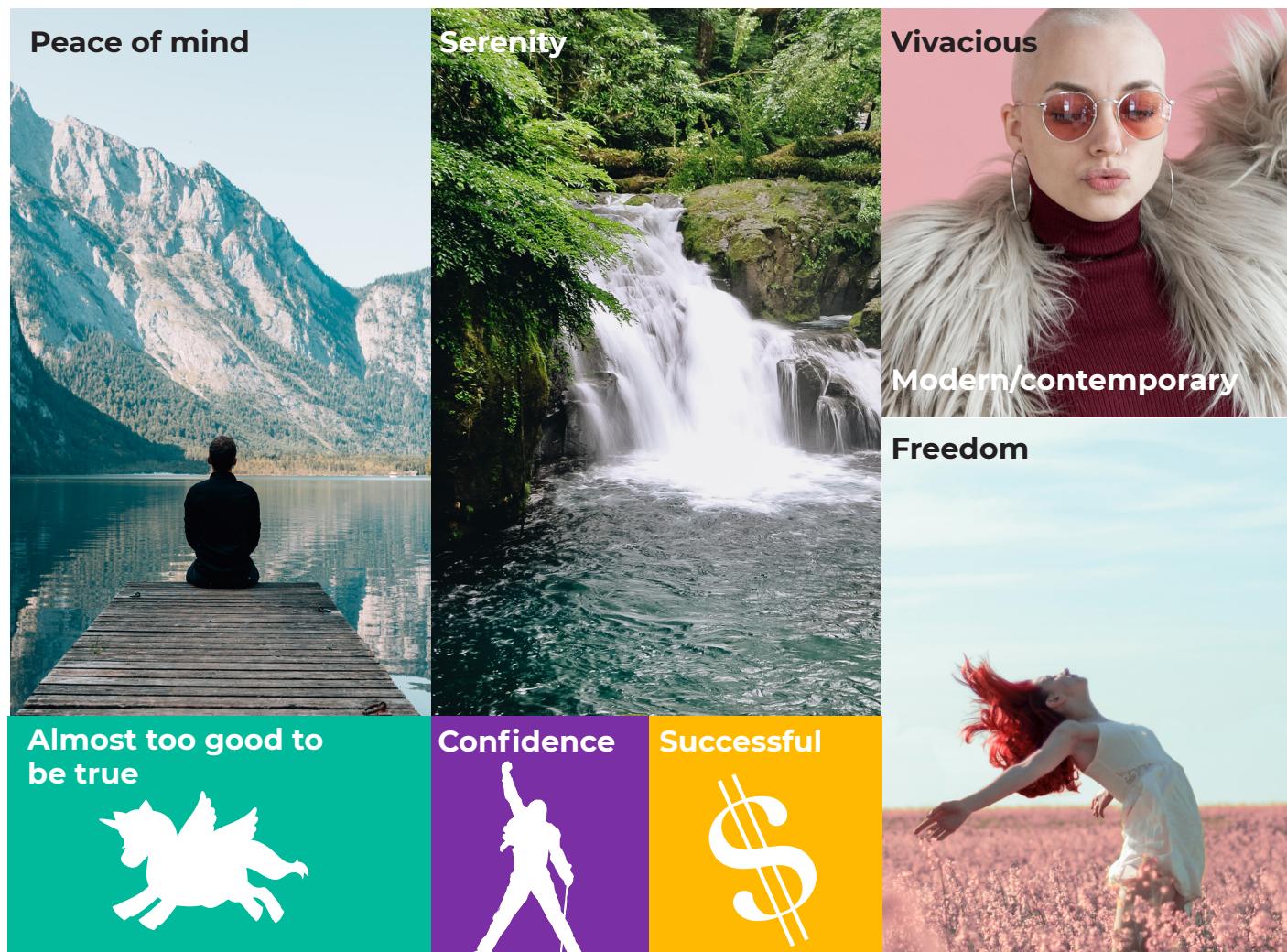
Avoiding peer judgement	Regimen burden	Patient medical IQ
I want to make the 'right choice' in the eyes of my colleagues as much as the patient and family in front of me "I'm not worried about litigation, oncology is a 'dying business'. But I do think about what my partners say... you know, 'we wouldn't have done this so why did you?'" – US oncologist	How do I minimise the burden of regimen and volume of hospital visits "Longer dosing frequency helps the fantasy of patients that they don't have cancer. I'm pleased to let them have their fantasy, let them feel normal. Why should they be reminded every week that they have a terrible disease that's trying to kill them?" - UK oncologist	Can the patient fully engage with the treatment and all implications? "Some patients are plain clueless. You give them an IO therapy, they get sick and wait it out to their next appointment. You have to ask them why they didn't call when they got sick. That's the kind of patient you don't want to give a stick of dynamite to and say 'here you go'. You put them on a treatment where you can watch them closely." - US oncologist
Anticipated regret	Brand salience	Trust and comfort
After years of limited options, I now find choosing between drugs overwhelming; I'm torn between what I know and an underlying desire to not miss out on 'shiny and new' "When I try something new, I think maybe I'm missing out on an opportunity to give a patient what I know they will get with Keytruda. I don't necessarily feel bad that I've gone for something shiny and new, it's more that I've neglected to just stick with what's old and tried." - US oncologist	As more indications are obtained for a drug, I'm aware of brand discussions. if it works in one indication and then another... you hear about it more and more. Of course, the reverse is true, bad news travels fast around the oncology community and poor performance in one indication can lead to 'guilt by association' "Keytruda has its own momentum, just being everywhere. It's the Coca-Cola of IOs. Coca-Cola is on every billboard, in every store; because it's everywhere, you assume it must be good, even if it isn't." – US oncologist	For me, trust is essential. Clinical data is foundational which is enhanced by stories, case studies and experiences. These are the factors that lead me to feel familiar and comfortable with the decisions I'm making "If all IOs were the same – same indication, same cost, dosing regimen, side effects...I would basically go with the drug I am most familiar with." – Singapore oncologist

Oncologists build connections with brands

In response to an alternative line of questioning, oncologists are clearly able to articulate a deep-seated association with brands and provide us with insights into more subliminal drivers influencing treatment decisions, as the section below illustrates.

Clear differentiators are apparent when we compare positive and negative associations across brands; the term 'copycat brand' appearing on one image board.

Brand X is...



The problem

In this paper so far, we've highlighted an issue: while clinical data is incredibly important in oncology, a highly complex web of factors underpin oncologists' prescribing decisions. Some of these are highly rational, but there are also other, often subconscious, influences which are less easily explained. In fact, it is clear from our own work that oncologists have highly evolved relationships with the brands they prescribe.

Yet, the conventional wisdom for pharma brands entering the immuno-oncology space is that strategy must be driven solely by the data. Success can be found through this strategy, no doubt, but it ignores the very powerful forces bubbling away under the surface.

The alternative is to recognise and harness the power of these forces and the best way to do that is a process everyone is already very familiar with – marketing and branding.

This leads us to a fundamental question

Should we focus on

science
or

marketing?





**Branding is the natural next
step for oncology**

In 2000, Harvard Business Review published an article⁵, that stated: *"It may sound paradoxical, but adopting a marketing-led strategy is likely to improve rather than weaken the quality of a company's science."* - Harvard Business Review, Managing Pills to Managing Brands.

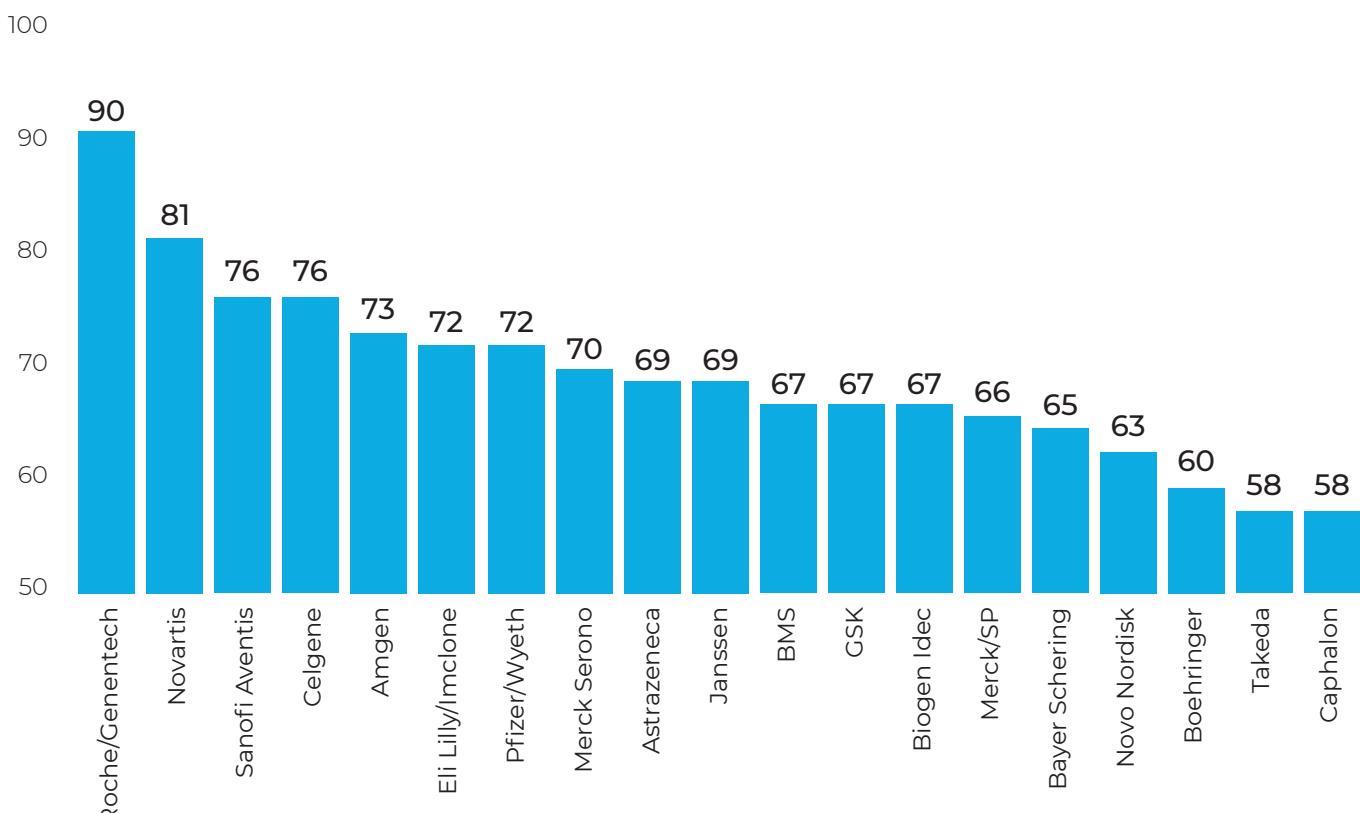
The article postulates that Science and Marketing together were stronger than either alone in building a brand and/or franchise to attract scientific talent and strong foothold in the market. This approach is now common, with organisations such as Novartis' "category captainship" to only play in markets where it could be dominant.

Soon after the HBR article, in the early 2000s, many life science companies began to gravitate towards oncology, especially after Roche took what was perceived as a huge gamble in acquiring biotech firm, Genentech. With the purchase came Avastin, Herceptin and Rituxan, and Roche's oncology portfolio was bursting at the seams.

Avastin changed the oncology world. The Roche molecule was hitting endpoints all over the place and was proving that great clinical outcomes were blockbuster material, but what the company also appeared to do, was understand the wider needs of the oncologist. This is shown clearly by the chart below showing how oncologists scored Roche way-ahead of the competition in terms of customer experience, creating apostles for Avastin as a brand, not just for its clinical data.

"It may sound paradoxical, but adopting a marketing-led strategy is likely to improve rather than weaken the quality of a company's science." - Harvard Business Review

If we want to engage physicians on other than purely rational levels, we must go beyond features and proof points to leverage the meaning of these by communicating benefits aligned with oncologists' values at a rational and non-rational level.

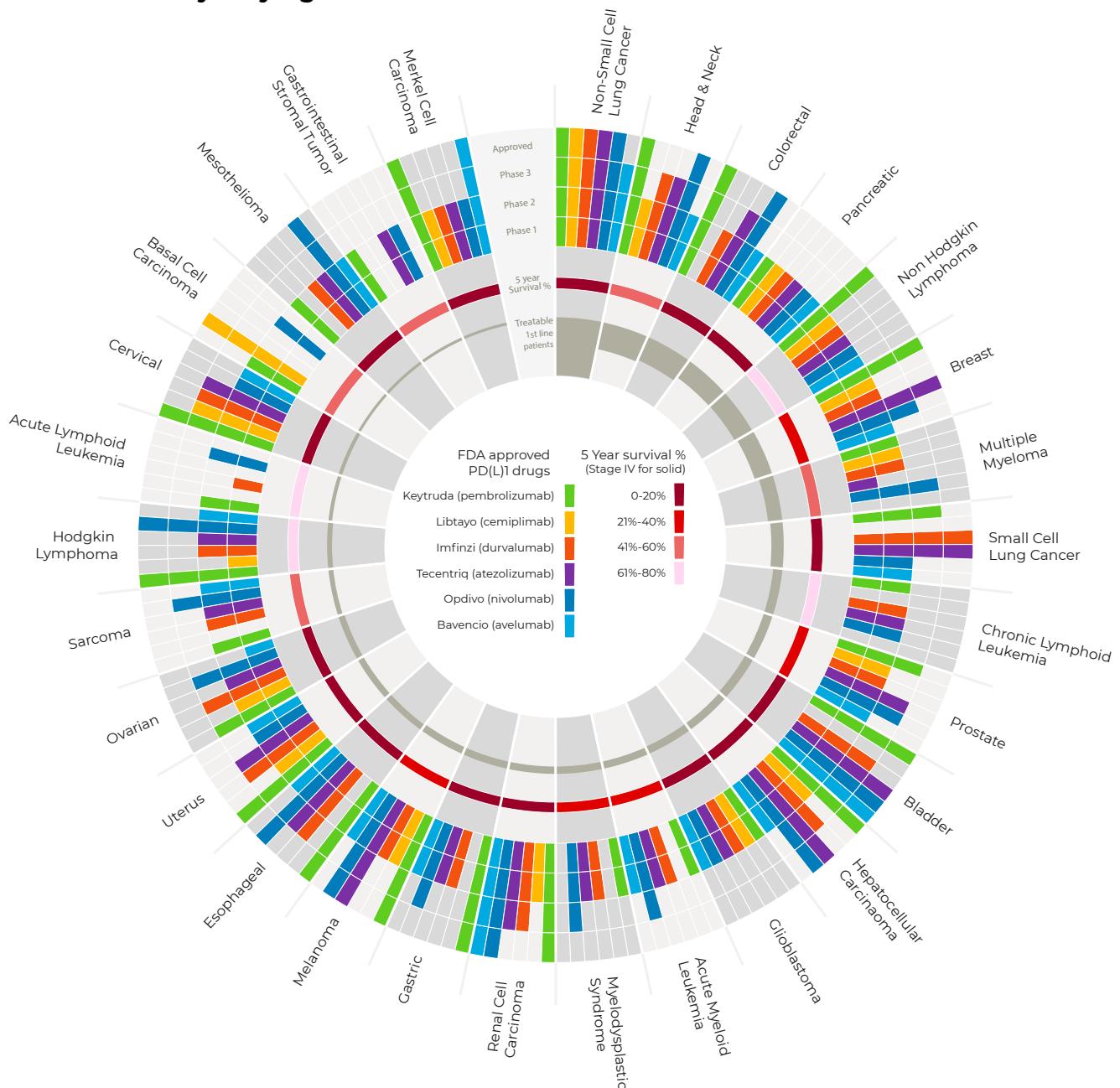


TRI*M Index (customer experience score) of HCPs with Oncology specialists.
Source: Cerner Enviza Customer Experience Study 2010

The Breadth of PD(L)1 Development in 2021

Immuno-oncology is where the building of brands, alongside great clinical data, is starting to dominate. The wheel below shows the sheer volume of clinical activity driven by a small number of molecules. These are no longer just referred to by their molecule names by physicians, (which in itself is an interesting phenomenon in this cohort), we see brand names starting to dominate in every day conversation.

Data from CancerMPact® highlights the extent of PD(L)1 development across tumors of widely varying unmet need



Development of immuno-oncology drugs has risen dramatically over the last decade. With 6 PD(L)1 agents now FDA approved, development now extends across numerous tumor types. In particular, tumors with poor prognoses (based on 5-year survival) and large patient populations (based on treatable 1st-line patients), such as Non-Small Cell Lung Cancer and Bladder Cancer, have seen significant success. Yet in others, like Pancreatic Cancer and Glioblastoma, development and/or successful outcomes have been limited.

A Case Study outside of PD-(L)1 therapies

In this paper so far, we've highlighted that the dynamics between science and marketing have started to merge in the context of PD-(L)1 agents, but similar dynamics are at play in other drug classes indicated for other tumor types.

Relapsed/refractory DLBCL has seen significant development of new targeted agents with different technological approaches. First to market in the US were chimeric antigen receptor- T cell (CAR-T) therapies, a treatment that transforms a patients own immune cells to engineer a bespoke cellular therapy that targets cancer. Soon after, another class of therapies began to receive US approvals. These so-called antibody-drug conjugates (ADCs) link an antibody that targets cancer cells specifically to a potent chemotherapy payload, allowing the drug to kill cancer cells with high specificity.

Importantly, none of these therapies have been compared directly to the other, limiting the ability of clinical science to definitively conclude which therapy offers superior outcomes for patients. The decision of which therapy to use is further complicated by the fact that some therapies in each class use the same CD-19 protein present on cancer cells to recognize and target cancer cells. Collectively, the differences between these therapies is highly nuanced, and physician decisions of which therapy to prescribe are likely driven by how they perceive value and utility in the product overall – a decision that marketing is well-suited to inform.

We expect that the complexity of these decisions will increase in the future as yet another therapeutic technology class called bi-specific antibodies comes onto market, creating an increasing need for a marketing approach that communicates the differentiated value of each product.

	CAR-T Therapies		ADCs	
Brand Name	Breyanzi	Yescarta	Polivy	Zynlonta
Generic Name	lisocabtagene maraleuce	axicabtagene ciloleucel	polatuzumab vedotin	loncastuximab tesirine
Indication (USA)	3L+ DLBCL	3L+ DLBCL	3L+ DLBCL (+ bendamustine & rituximab)	3L+ DLBCL
Target	CD-19	CD-19	CD-79b	CD-19
Developer	BMS	Gilead	Genentech / Roche	ADC Therapeutics
Registrational trial	TRANSCEND-NHL-001	ZUMA-1	GO29365	LOTIS-2
Registrational trial comparator arm	None [single-arm]	None [single-arm]	bendamustine & rituximab	None [single-arm]

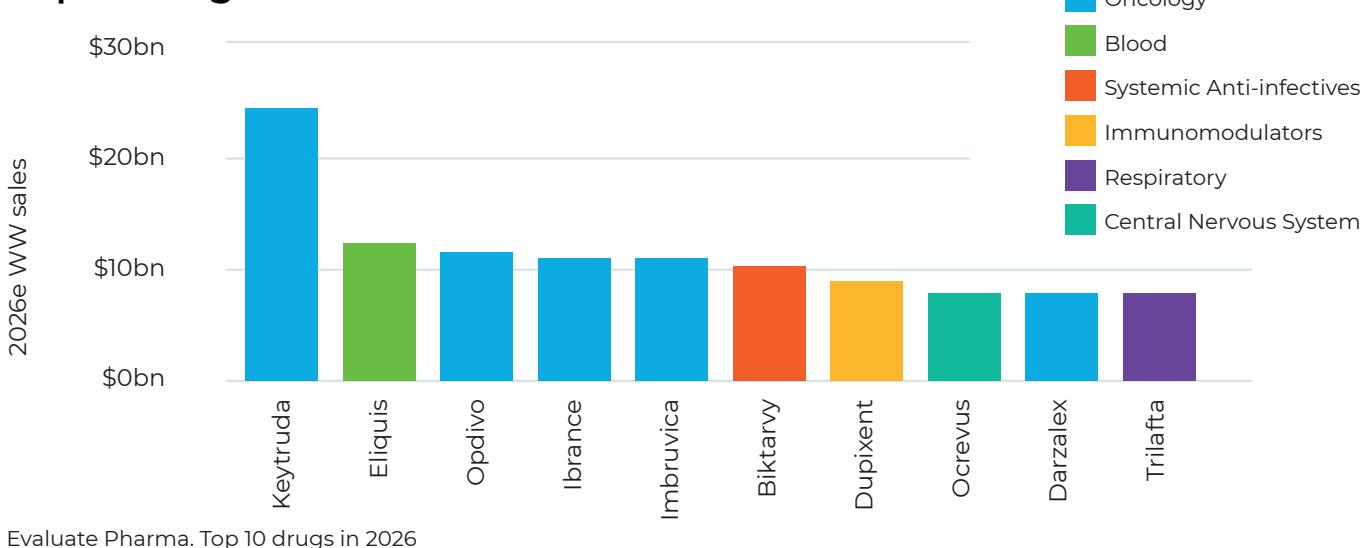




The 500lb gorilla in the room, Keytruda – is it an anomaly or the new norm?

We all know about Keytruda and the fact that it is the second largest selling drug on the planet, still growing revenues at 30% year-on-year, and projected to dominate not only oncology but the whole pharmaceutical market through to at least 2026 (pre covid vaccine sales data – Comirnaty \$36bn in 2021).

Top 10 drugs in 2026



Evaluate Pharma. Top 10 drugs in 2026



It's not by accident that Keytruda is in the position it currently is. Merck has worked hard at balancing phenomenal clinical data, (as we saw in the indication wheel above), and with building what may be the strongest life sciences brand ever.

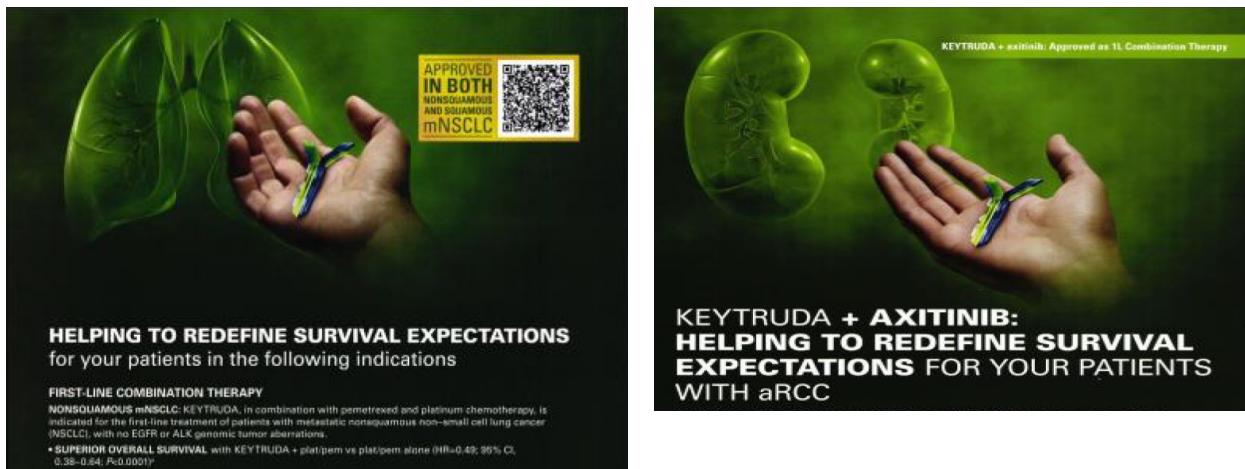
It comes as no surprise that Merck is the company behind this success; a company steeped in experience of playing in me-too markets for example, Cozaar in hypertension and Januvia in a very crowded diabetes market. Merck always builds equity and the following sales by making good molecules great, through marketing.

Keytruda may be their greatest success, and they went in early, in 2017 spending tens of millions on TV ads in the US, when it was not necessarily considered appropriate to talk about cancer treatments on TV. In 2019 the brand team had over \$150m in ad spend⁶



The "Tru" campaign, not only broke that mould but introduced stand out iconography which has become recognisable as the brand, even when seen in isolation.

We applied the science of semiotics to Keytruda's most recent campaign and analysed the visuals to reveal some interesting insights.



Clearly, the image is patient centric – literally at the heart of the concept.

Weaving together the rational and emotional

The composition effectively highlights Keytruda's scientific credentials whilst simultaneously evoking emotional touch points suggestive of a caring approach to cancer. The open hand imagery draws the viewer in, creating a personal connection and primes the idea that the 'solution is in your hands', as well as clearly alluding to the structure of anti-bodies. Neatly embedded in the hand is the 'Y' of Keytruda, the key to the door opening onto a solution.

Reality vs aspiration

The realistic depiction of the hand anchors the promise in reality rather than aspiration. The less naturalistic representation of the organs, depicted in green, signals vitality and health as the goal - in this case, an aspiration.

Promise of a bright outcome

The contrast of the dark background with the neon-coloured organs emphasizes the difference between old and new, suggestive of a new and bright future.

The success Keytruda has achieved is driven by a fine balance between clinical data and brilliant marketing.

"Keytruda has its own momentum, just being everywhere. It's the Coca-Cola of IOs. Coca-Cola is on every billboard, in every store; because it's everywhere, you assume it must be good, even if it isn't." – US oncologist

"Keytruda is the answer to Cancer." - US Oncologist

Social media and a focus on marketing in an industry not used to it can be unforgiving though, and when you are a brand as big as Keytruda, there can be problems.

This level of prominence also attracts negative press: The brand received criticism from a prominent tech co-founder who claimed to have experienced over 74 targeted connections from Keytruda following a simple Google search on the drug.

Activist group IMAKglobal have also criticised Merck for 'over patenting' Keytruda to push the price up - individuals connected to the group tried to amplify this through Twitter posts.





**It's Science AND
Marketing, not OR**

It is absolutely clear and correct that clinical efficacy and scientific differentiation are at the core of decisions about how a disease is treated. But the effect of marketing is also very evident: we may never have thought we would hear the words "me-too brand" in relation to oncology, or that a physician would compare an oncology product to Coca-Cola, but that is the situation we now find ourselves in.

So both science and marketing are influential. The question is how to understand the impact that each is having and make decisions about how marketing strategies can best complement, communicate and increase the impact of the science that underpins a product.

We are as an industry in a fortunate place, in that we do not have to make those decisions without rigour and process. There are data available, whether through quantitative or qualitative primary research, Electronic Health Records and, increasingly, Real World Evidence data in the commercial world.

In this situation, the concept of brand or treatment equity can be very helpful. Equity describes the strength of the attraction of a physician to a particular brand, a combination of their awareness and understanding of the science and data that underpin a brand, together with their feelings and associations with that brand, alongside their ability to access and prescribe it. It is a summary of the impact of both science and marketing.

Building brand/ treatment equity



It is only by laddering up a higher level like equity that we can understand the relative contributions of science and marketing and make resourcing decisions to drive ROI. Each of these pillars will also have tactics associated with them, like clinical congresses or a channel strategy, and again a measure like equity can help prioritize where to play.

We must also think about the human brain, and the oncologist's brain specifically. Clearly, when it comes to physician prescribing, more factors are at play than just clinical data. The challenge is to look at the balance of rational and subliminal triggers to better understand what is it that influences actual behaviour change. These factors will vary by tumour type and setting, of course, but life science companies seeking to launch new medicines would be wise to look more closely at what motivates oncologists up to the point at which they enter their prescription decisions into their systems.

As a leader in one of the top five oncology companies commented:

"Except for rare extreme exceptions, I think that it is a myth of the medical and medical Pharma community that brands could sell just based on their clinical data."

Huge strides have been made in oncology in recent years, with many more exciting developments still to come. As the market becomes ever more complex, a combination of science and marketing will be needed for a brand to establish its position, differentiate itself and achieve its true potential.



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About Cerner Enviza

Cerner Enviza aims to accelerate the discovery, development and delivery of extraordinary insights and therapies to improve everyday health for all people globally. By combining decades of innovation, life sciences knowledge and collaborative research, Cerner Enviza provides data-driven solutions and expertise that helps bring remarkable clarity to healthcare's most important decisions. For more information on Cerner Enviza, visit www.cernerenviza.com.

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