Lorna Warwick â?? CEO, Lymphoma Coalition

CAR-T, which was touted as a game-changing curative treatment, has been the answer for some patients, but not all

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Lorna Warwick is CEO of the Lymphoma Coalition, a worldwide network of patient groups with a full or partial focus on providing support to patients with lymphoma. In this wide-ranging interview, Warwick highlights the progress made in lymphoma treatment in recent years and the work still to be done to better integrate authentic patient experiences and insights into the drug development, regulation, and assessment processes, especially for cutting-edge therapies such as CAR-T.

How did your entry into the world of patient advocacy come about?

When I left school, my ambition was to become a teacher. However, at the time, there were no conventional teaching jobs, so I began teaching life skills classes to seniors and at-risk groups of adults through the Salvation Army. This fostered a love of the non-profit world, which I continued to develop in other organisations, eventually in management positions.

From there, I moved to Habitat for Humanity, a poverty relief organisation, and then eventually into health. When I joined the Leukemia and Lymphoma Society in 2003, I found that this was really the best fit for me, with so much progress happening in science and a wide variety of patient experiences. I found it engaging from both the analytical/data side of things, as well as inspiring in terms of the patient stories. Iâ??ve made and lost many friends through the years working in blood cancers, but it never ceases to amaze me how people take these awful experiences and try to do something good for other people. Working with these people on ways to improve systems, care, and overall make things better for the next wave of patients has kept me motivated.

I have been CEO of the Lymphoma Coalition for about two and a half years, having originally joined as Director of Strategic Communications and Engagement. The Lymphoma Coalition had been collecting data via global patient surveys since 2008 which was being well used for planning purposes and within our member organisations but was not impacting the scientific community in the way they had hoped. I was brought in to increase the reach of the data we produce and the reports we write and have some impact within the research and medical community.

What is the mission of the Lymphoma Coalition?

The Coalition was founded in 2002 by a group of four advocates who met at the American Society of Hematology (ASH) Meeting. They found out that they had different areas of expertise and access to different layers of information, depending on their local connections with healthcare professionals. They were running very different kinds of programs for their patients and caregivers locally and realised there was a lot they could learn from each other.

Today, we now have 83 member organisations in 52 countries and one of our key premises remains best practice sharing so that our members can learn from each other.

As well, there is so much happening in lymphoma, across the many different subtypes, therefore we funnel information about these constant updates to local groups so they can stay on top of them.

In addition, we have always trained our advocates how to advocate, and how to ensure that the right policies and procedures are in place. However, since I became CEO we created a new strategic plan, and now work within the two equal pillars of information provision and advocacy to meet the organisational mission of enabling global impact by fostering a lymphoma ecosystem that ensures local change and evidence-based action. We have expanded our advocacy role And while we still train our members, we also use our own voice more than in the past, with engagement in regional and global discussions. Additionally, while we still do patient group member training, we also mentor them now walking them through the process, helping them take the knowledge they have and using it in their local contexts.

As patient advocacy has grown in stature and status over the past ten years, is it becoming easier to attract and train new generations that already have some awareness of the field?

Various things are coming into play. In lymphoma, most people become advocates due to a personal experience â?? being either a patient or the loved one of a patient â?? and a desire to make things better for others. The average age of a lymphoma diagnosis is quite high, so even though we do have younger advocates, most are more mature. They come with passion, but not necessarily the knowledge of what it is to work and volunteer within a charity organisation or how bureaucracy works when trying to initiate change with regulators. Our organisation can help them navigate these difficulties while maintaining their passion.

I often hear the assumption that working for a non-profit must be fabulous as everybody is united working together for a good cause and so it must be a happy place to work or volunteer. However, that is not always the case. While advocates do have a lot of passion, it is not always directed in the same way as their fellow advocates and sometimes this can lead to conflict. Therefore, open communication and finding commonalities when working together are very important. This communication piece â?? ensuring that messaging is clear and focused â?? is vital on both a global and local level.

How much progress has been made from a scientific perspective on lymphoma in recent years?

Lymphoma survival rates are still rising, which is hugely positive. A significant milestone was rituximabâ??s approval for medical use back in 1997, which precipitated a dramatic change in the survival curve for B cell-based lymphoma patients. Since then we have seen incremental changes, mainly focused on patients in a relapsed refractory situation with less activity in first-line treatments. This is positive as there was a need for better treatments for relapsed refractory patients, but there are still a lot of gaps, even within this population and with some others.

Lymphomas are generally diagnosed when patients are older, but many clinical trials are held with younger populations. Therefore, these older people do not necessarily do well with traditional treatments and there is still a gap there. Integrating learnings from the gerontology community into how we treat these patients and assess fitness for treatment without making assumptions about their treatment goal is crucial. We need to ask the older population what they are willing to tolerate and what they would like to see happen.

In terms of subtypes, we have seen a lot of activity in chronic lymphocytic leukaemia (CLL) around novel BTK inhibitors and Bcl-2s which, again, is very positive. We are helping people with poor genetic markers live longer, but the treatments available remain life-extending rather than curative. As shown in the responses to our annual global patient surveys, our patients want a cure; meaning that there is still plenty of room for improvement.

Are these treatments gaps being caused by a lack of investment from industry sponsors into what they see as a risky area or because the science is simply not there yet?

When BTKs came in, it was anticipated that they might be like Gleevec was for CML, where patients take the medication every day for the rest of their lives and their cancer stays in remission. Since Gleevec first came to market, they figured out that some patients can stop the therapy and stay in remission, which is great. BTKs did not quite live up to that expectation. We are approving these medications on Phase II data, which is still short-term (I am not saying that they should not be approved because getting effective treatment to patients as soon as possible is important) so the long-term data ends up coming from the real world. Over time, we are seeing higher rates of drug resistance and of patients stopping the drug because of side effect tolerability. Because of this, patients still need something new to help keep them living well with their cancer if we cannot offer a cure.

CAR-T, which was touted as a game-changing curative treatment, has been the answer for some patients, but not all. We still see a significant number of patients that are either not responsive or relapsing, usually within the two-year mark. The question is therefore how we do a better job of figuring out which treatment is best for which patient and what order we should be progressing through these treatments to take the best advantage of what is currently available. There is work to be done around how the state of a patientâ??s T cells impacts their response to a CAR-T therapy and whether we should be harvesting T cells earlier in the treatment paradigm in case of a relapse later. I know there are clinical trials investigating these things, but we are learning a lot from the real world.

There are many relapsed/refractory patients wondering whether there are any treatments left for them; we need to do more research to figure out how to cure them.

It seems like you are advocating for the use of more post-administration data.

For sure. Data is key. We are asking what we can learn from the data and how quickly it gets pushed back into a mechanism whereby researchers can use it to start looking at that next step. So far, we have not been very good at this. Data needs to be gathered and fed back into the system within realistic timeframes so that scientists can learn more and move forward. There are still gaps. For example, many CAR-T patients did not feel prepared for what happened to them. We prepare patients well for high-intensity side effects like CRS and neurotoxicity, but often the greater patient concerns are around smaller, lesser-known, things like weight issues, muscle cramping, and persistent ongoing fatigue. In total, we are seeing a lot of conversation among patients where they feel unprepared about how to cope.

CAR-T was first approved in 2018 amid a lot of hype. How did you work to prepare (and temper the expectations of) the lymphoma community?

In higher-income countries where CAR-T was a real possibility, there were more patient requests for knowledge. Back in 2018, we began to create patient materials, explaining the basic science behind CAR-T, the clinical trial experience for the Novartis, Kite, and Celgene/BMS products, as well as the differences in their reporting. This helped give patients a realistic expectation of how many trial participants got a positive response, educated them that not everyone that has their cells collected in a trial then has their manufactured cells reinfused and that CAR-T is in effect a manufacturing process within which errors sometimes occur.

In terms of side effects, the intensity of CRS that patients with CAR-T experienced and neurotoxicity, especially when symptoms can be so subtle, was something new. Lymphoma patients have always had a heavy reliance on their caregivers, but CAR-T patients need their caregivers to be especially alert and recognise signs of neurotoxicity so they can be treated properly. If a CAR-T patient is taken to a regular hospital that has no concept of CAR-T, it may look as if they are having a stroke, the treatments for which are very different. This placed a new level of stress on caregivers.

In countries where CAR-T was not on the agenda for the immediate future, patient groups and physician communities were reluctant to distribute information about a therapy that local patients were unable to access. However, anyone with an internet connection can access information about CAR-T; the challenge is ensuring that this information is good and credible. There has been a lot of misinformation. There have been instances where patients have been able to travel across the world and pay to obtain CAR-T therapy, whereas for many others that is far beyond their means.

Beyond the equity and patient education questions that CAR-T brings up, there is a wider question of which stakeholders should be paying for and providing the therapy and surrounding services. What is your take?

Today, many hospitals are determining what treatment to give their patients based on the service packages that private companies are offering, rather than the quality of the product. Often, physicians are recommending packages where a company provides costs for patient transportation and accommodation because that relieves the burden on the patient if no other resources are available. That has a broader impact on healthcare systems and how they are used.

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We must remember that our healthcare systems recently spent a lot of money that they were not planning to on COVID. Regulators are now making more selective decisions around approvals due to reduced budgets. Every CAR-T patient *should* have a complete multidisciplinary circle of healthcare providers around them, covering everything from the pharmacist, physician, and nurse to specialists dealing with the treatmentâ??s psychosocial impact and its effect on quality of life in terms of finances etc.

However, with constrained resources and healthcare professionals choosing to leave the field post-COVID, there is going to have to be a lot of reorganisation around how we take care of these patients. Our patients do receive some fantastic support from our partner organisations, but the burden of care cannot be left to them alone.

Ideally, when CAR-T is introduced into a hospital or facility, it should encompass this multidisciplinary approach from the beginning. However, at the same time, this may limit some hospitalsâ?? ability to adapt the therapy and offer it to patients. In some cases, cross-border may be the best answer to help patients get to the therapy because it is not realistic for it to be offered everywhere. This raises questions about how this is implemented and ensuring it is a much easier and clearer process than it is today.

Industry sponsors argue that CAR-T should be moved up into a first-line therapy. If such a move is to happen, the use of patient and scientific data will be crucial. Is the Lymphoma Coalition working with that data, if so how, and which stakeholders will need to ensure that patients share their data?

We now see more analysis of the data, a lot of which comes from the willingness of pharmaceutical companies to share both clinical trial and real-world data. I am hoping that these companies remain willing to share data, at least with the doctors participating in their clinical trials, so that we can incorporate that data and then make better choices about trials in the future.

As we are looking at earlier lines of therapy, are we learning something about the patients that have responded well? Have they all had similar prior therapies? Do they have some other common characteristics? Would the therapy work better in a particular group if given earlier, or would it perhaps never work for that group? It is about figuring out what makes a particular patient a great candidate compared to others. The sharing of data â?? which pharma companies have traditionally been somewhat reticent to do â?? will have a giant impact.

As a patient advocate, what would be your advice to industry sponsors on things that could be done better or differently?

I must admit that a couple of companies have been engaging with us a lot more recently in very early-stage trial development. With our input, these trials can better match patient preference, include more patients who might stand to benefit, have their results measured more accurately, and include a greater consideration of quality of life impact.

For example, we often suggest not only measuring the grade of toxicity but also the length of time. Sometimes, a Grade 2 adverse event that persists over many months has a bigger impact on a patient than a Grade Four managed within a very short timeframe with medication in a hospital.

We do community advisory boards, including some with a specific focus on CAR-T, where â?? rather than the pharma company organising an advisory board with their hand-selected advocates of choice â?? we bring together well-trained advocates â?? including patients, caregivers and members of the medical community â?? to co-write an agenda. We hear both the problems from a pharma company and a patient perspective. These boards are focused on outcomes and what we do with our learnings, identifying areas where the community lacked information or support and filling those gaps. Sometimes those go back into our member organisations to effect change at a local level, while sometimes the changes can be made at a regional or even global level.

At the end of the day, pharmaceutical companies are creating most of the therapies coming out and there are far fewer investigator-led trials happening. We need to work together to find commonalities, improve patient outcomes, as well as improve systems themselves.

Do you feel that regulatory bodies are changing at a swift enough pace and taking metrics beyond safety and efficacy into account broadly enough?

There is still plenty of room for improvement in terms of how regulators work as many of these organisations have a lot of embedded bureaucracy. While we do see more engagement with patients, how that impacts decisions remains hit and miss. Not only do regulators sometimes have strange expectations of what patient input can be, but they are also not equipping the patients well enough to participate in a way that makes sense.

For example, when we talk to regulators, we bring in data from our global patient survey of 12,000 lymphoma patients and caregivers. This data can be broken down by subtype, from stages of the patient experience to geography etc. While we understand that regulators look primarily at drugsâ?? safety and efficacy, they also need to be aware of patient experience data pre- and post-treatment and how drugs may resolve certain issues but remain problematic in others.

Unlike many other non-profits, we have the scale to employ epidemiologists who analyse the data we collect. Data analysis is very normal for us, meaning that we can speak the same language around cost-economic and efficacy as regulators and therefore have a better dialogue. This is another key skill that patient advocacy groups increasingly need as they begin to engage more deeply in decision-making processes. More needs to be invested into finding the right people to participate in this way.

The mission of drug companies tends to be to find cures for specific diseases, whereas patient groups look to improve quality of life. What are your thoughts on the compatibility of these two missions?

Our surveys show that the number one thing that patients and caregivers look for is a cure. Number two is quality of life. If we are not curing patients, then we really need to focus on that quality of life. At the end of the day, if a drug extends a patientâ??s life for a certain number of years but has made them so sick that they are unable to enjoy that life, then there was no benefit.

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