Guillermo Chantada â?? Incoming President Elect, International Society of Paediatric Oncology (SIOP)

> We could accelerate knowledge, save more children, and position drugs for more indications if we were able to conduct research [in Latin America]

06.09.2021

Tags:

Argentina, SIOP, Patients, Patient Association, Association, Oncology

Dr Guillermo Chantada, incoming president-elect of the International Society of Paediatric Oncology (SIOP) highlights the progress of paediatric oncology in Latin America and gives a call to arms to the global pharmaceutical industry to situate more research in this field in his continent.

Could you start by introducing yourself to our international audience?

I trained in Argentina at the University of Buenos Aires and practised for most of my career at the Garrahan Hospital, a referral hospital for paediatric cancer in the same city. Over the past 15 years, I have begun to work more internationally, collaborating with the St. Jude Hospital in Memphis, Tennessee in the US on the international outreach program. I also joined the paediatric haematology and oncology department at Sant Joan Hospital in Barcelona, Spain, where I spent about three months per year prior to the COVID pandemic. Last year, I left my position as chair of precision medicine at Garrahan and moved to Montevideo, Uruguay, where I am now the scientific director of the Pereira Rossell Hospital and the PÃ©rez Scremini Foundation. I am currently the Latin America president for the International Society of Paediatric Oncology (SIOP) and from October this year, I will be president-elect.

My major interests are in global medicine. I am an MD and PhD and therefore I also do some work in the lab, primarily in retinoblastoma tumour research. I am the co-chair of GALOP, the Latin American group for paediatric oncology, where we work on clinical research protocols. In recent years I have been doing more work in neuroblastoma, the most common solid tumour, and we have developed a very interesting protocol repurposing an innovative treatment based on immunotherapy. It was meant to be used in adult lung cancer and melanoma and we repurposed it in neuroblastoma. The Phase II trial for Latin America was completed very recently. There is a lot of promise in repurposing existing drugs and discovering paediatric applications.

What is your take on the overall situation of paediatric oncology in your region?

It is a very exciting time to be a paediatric oncologist. The WHO is now prioritizing paediatric oncology in their global childhood health agenda on our continent through the Global Initiative on Childhood Cancer, which is based on two major pillars. The first pillar is SIOP, of which I will become president in a few months, and the second is the St. Jude Global Alliance. St. Jude Childrenâ??s Hospital in Memphis, has a very active Global Alliance, which was launched a few years ago and has transformed childrenâ??s access to treatment around the world. They are bringing paediatric oncology to places where it previously did not exist; countries that did not have paediatric oncologists are now able to treat cancer in children. Countries that *did* had paediatric oncologists are now working in better environments with support for clinical trials and comparative groups. It was amazing to be a paediatric oncologist in the 1980s in the US and in Europe because things were changing and improving dramatically in terms of survival rates, etc. But now it is the turn of the developing world, and finally, we are acting in the best interests of the public, big institutions are supporting our work, and we are able to produce results that are applicable in a global setting.

WHOâ??s Global Initiative on Childhood Cancer aims to reach at least a 60 percent survival rate for children with cancer by 2030 and focuses on six common cancers. Why were these cancers specifically chosen?

It was a smart decision, because it was decided that all of these six tumours represent one or two different features of paediatric oncology. For example, one of them is acute lymphoblastic leukaemia (ALL), the most common paediatric cancer. Therefore, every change that we make there will have an impact on many children.

The second type of cancer selected is brain tumours. Improving the results in patients with brain tumours has been difficult all over the world because they are difficult to treat. They are not so chemo-sensitive, you need sophisticated treatment units and well-trained surgeons.

The third one is retinoblastoma, which in developed countries has a cure rate of 95 percent but in low- and middle-income countries is sometimes not cured at all due to late diagnosis. Having a tumour where we could achieve good results only by diagnosing it in a timely manner is a major goal because it involves the entire social and health care system in the country.

Then there are two lymphomas: Burkitt lymphoma and Hodgkinâ??s lymphoma. The first is very common in low- and middle-income countries. Hodgkinâ??s lymphoma is a highly curable tumour, with a relatively simple treatment with which very good results can be achieved.

Finally, the sixth most common type of cancer in children is Wilms tumour, a kidney tumour that has a very good prognosis as well and needs input from paediatric surgeons.

In developed countries, the cure rate without relapse is quite high. What is the situation in Latin American countries?

In Latin America, there is a lot of inequality. There are centres with expertise in big cities like Sao Paulo, Buenos Aires, Santiago, Montevideo, and Mexico City, but also many other centres in the same countries without the same knowledge or access.

Overall, there have been great improvements over the decades. In Central America for example, home to some of the most vulnerable countries on the continent, St. Jude has been working for a long time supporting the cooperative group AHOPCA and now has prospective protocols and data. Survival rates are still lower than in Europe and the US, but a roadmap is in place and progress is being made.

Countries like Argentina, Chile, Uruguay, Brazil are relatively developed and have a comparative group called GALOP which is achieving great results. Taking retinoblastoma as an example, Europe has a 95 percent survival rate, and we are at 93 percent.

It is an exciting time because we are seeing many developments. We have realized that problems are different in every country, and we have come up with a response to those problems. We understand now that solutions to our problems are not going to come only by experience in developed countries, we must learn from our own results and make improvements.

It is no secret that big pharma companies do not conduct a significant amount of R&D in Latin America. What do you see as the role of clinicians in paediatric oncology when it comes to R&D?

We have a history here in Latin America of clinicians working in clinical trials, but we do not have enough access to new experimental drugs despite the fact that there are many children with cancer living here and many centres with the requisite capabilities. For instance, I am personally involved in two or three protocols in Latin America for new drug filing.

One of the reasons for this lack of access is that 80 percent of our children are treated in public hospitals sponsored by the government, and it is not a priority for any government to develop new drugs. While governments are not willing to invest in this, they are still interested in improving their results on evidence-based treatments or randomized treatments with therapy intensification or therapy reduction, and that is what is being done for the most part in Latin America.

Can you outline the goals of your project to repurpose existing drugs intended for other indications?

I wanted to do a study in retinoblastoma and was interested in a ganglioside; a molecule present in the cell of malignant tumours. I was looking for teams that were experts in that field in Argentina, and I found a team that was studying a different type of cancer in adults. After realizing they were not studying the same type of cancer, I could have left it there, but I remained interested in what they were doing. There was a lung cancer drug related to their research and even though I was not looking for a new treatment but a new diagnostic tool I asked them â??are you interested in looking for targets in paediatric tumours?â?•

We did several studies looking for the target in our paediatric cancers and then we identified one of them, which was neuroblastoma, the most common paediatric cancer. We were able to prove that the drug was not toxic to children and was well tolerated. We have now finished Phase II trials and do not know if the drug will ever be commercialized.

Regardless, this process was extremely helpful in raising the standards of how children are diagnosed here because we had to do the Phase II study to the same level as we would in the US or in Europe. We had to improve the diagnosis procedure for all the patients in the country. Because we were able to get more specific drugs, we sent people abroad, they were trained, they came back, they implemented what they had learned, and now the diagnosis is world-class. We have also learned how to go from the bench to the bedside. I hope that the drug will be commercialized and pique the interest of the pharma industry, but even if not, many children have benefited from our work.

Do you believe Latin America can bring competitiveness and diversity to paediatric oncology?

Absolutely, that is something we are trying to achieve with SIOP; there is a great opportunity for Latin American countries. Interestingly, most patients are treated in a small number of institutions, so we have centralized care, good access, and many children.

One of the problems is funding, but SIOP has a great role as a catalyst to bring the attention of several stakeholders that are going to accelerate knowledge growth not only in the countries in which we are doing the studies but in many countries in the region and worldwide.

What is your take on CAR-T compared to typically used oncology treatments? What was your first impression when the therapy came to the market?

The introduction of CAR-T was like a dream come true to me. The results, not just in ALL â?? the disease that has FDA has approved for use in children â?? but also with second-generation CAR-T cells for other tumours, have been striking. We are even trying injecting CAR-T cells intraocularly for retinoblastoma, so it is a great way forward.

Still, there are some pieces missing, I strongly believe that medical evidence is very context-sensitive. If something has proven to be cost-effective, or it has improved results in one setting, that will not necessarily be the case in other settings. In Latin American countries we do not have the same favourable access conditions as in Europe or the US. Without the labs or clinical facilities to support the children, results are not going to be the same. Under these circumstances, other treatments could be more effective.

I am convinced that in our countries we do not have to apply the regulations or the approvals exactly as in the high-income countries; we must do those studies here and check how well they perform. CAR-T is a perfect example of a therapy that has to be studied here. My dream is that the pharma industry starts supporting research initiatives in our region just as they do it in high-income countries, and then adapt that treatment to our reality comparing it to the standard treatments and see how well CAR-T performs. We might get information that otherwise would not be available.

It seems like the position of patient advocacy groups is that because the real-world evidence from 15 years down the line does not exist, they struggle to support CAR-T as a first line of treatment. What is your take on that?

I can give you the example of immunotherapy for neuroblastoma. We have an FDA approved treatment for patients that have undergone a transplant procedure that improves results. However, we have many centres here that are not equipped to do transplants but could access the drug. It might be that the drug itself can give good results even if a patient did not have a transplant, but we do not know that yet, so what should we do? Should we use the drug the same way it is used in the US or Europe even when our reality is different? Or should we generate our own evidence to see how the drug can benefit children here?

That is where these partnerships between pharma and different groups should take place as they do in high-income countries. It would be easier to assume that any result would be the same as in Europe or the US, but that is not necessarily the case.

Do you think that regulators in Latin America have the capacity and skills needed when it comes to approving new therapies?

I know the situation in Argentina, Uruguay, Brazil, and to some extent Chile very well, but I can tell you that the regulatory offices are very good, and the studies that we are doing in Phase II are being audited by the regulatory office. I would say it is world-class. When it comes to research and approving new treatments it is not something that cannot be done because of the regulators; it is more a matter of infrastructure settings and perhaps monetary resources and organization.

What message would you like to send from Latin America and as the upcoming president-elect of SIOP?

We need our voices to be heard. It is starting to happen, but we still need to generate data. Pharma should consider that, especially in paediatric cancer, supporting research in the region is vital. What we constantly get is a treatment being approved in the US and Europe and two years later being brought here with the intention of using it the same way it is being used in these other countries. But what ends up happening is that only a small number of patients get the drug, we do not get any results, do not know if the drug is useful or not, and lose the opportunity of saving more children.

We could accelerate knowledge, save more children, and position drugs for more indications if we were able to conduct research here as well.

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