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Professor Stéphane De Wit, head of the Department of Infectious Diseases at St Pierre University Hospital outlines Belgium's approach to tackling HIV treatment, how academia-industry collaboration is progressing in the country, and the potential of innovative new treatment nodes such as CAR-T.

You are at the forefront of HIV treatment in Belgium as head of the infectious disease unit in Brussels St Pierre University Hospital. As such you have been at the forefront of the Kick and Kill strategy to try and defeat this terrible disease. Can you tell us more about this strategy?

First and foremost, I want to indicate that the solution to HIV will be multiple, and it will be a combination of solution approaches. Kick and kill is one of the solutions we are working on, but we are not pretending that it is the only one.

Current existing treatments kill the virus as it multiplies. Our approach is to target the "reservoir" of dormant HIV cells, that we know can survive for years without replicating, but have a very strong memory. Our goal is to "activate" -kick- those sleeping cells, by removing the locks that keep them dormant. It is when they get activated that we kill them. The idea is then to replicate the process until we have emptied the reservoir. We have been working on that approach for years now, and

have a good understanding of the process. We are looking at the right combination to activate and kill those cells.

But, once again, it is very important to understand that the kick and kill approach is only one of the avenues and possibilities, and there are many more options being developed out there. We should not neglect any, whether the kick and kill approach or whether immune activation or CAR-T.

The problem with HIV is that it is an extremely complex virus. The main reason behind this complexity is that it not only attacks the immune system, but it is also integrated. Unlike a disease like hepatitis, the fact is that it is integrated in cells that have a very long memory. This means that you always have cells that are ready to be reactivated by any antigenic exposition.

Overall, how do you judge your collaboration with the pharmaceutical industry throughout the years?

In general, it has been very good. But one of the main unfortunate changes I have observed across the years is the number of companies that have dropped out from the HIV field. In the past, we used to collaborate with five or six companies and today we are left with only two main partners: Gilead and ViiV Healthcare. Janssen and MSD are still present to a certain extent, but they hardly do clinical research projects anymore.

Generally speaking, I would say that collaboration with pharma companies has always been very good. We are happy to see that despite Belgium being a rather small country and market, big multinational companies still consider us as a serious partner. I have to say that this is mainly because of the top quality of clinical research conducted in Belgium in general, and this is very positive. We are considered as very serious partners because of the output and the quality of data that we produce out of those researches.

We are however starting to collaborate with generic companies too, as some of the latest treatments are coming to market in their generic forms. This is obviously a completely new setting, where we try to understand how to increase the usage of generics and control the costs. Nevertheless, this remains something very important. It may present much less clinical interest, but it is perfectly sound in a universal healthcare environment.

Today, treatments have dramatically improved. But beyond finding a cure for the disease, do you think that failing to find a vaccine to prevent it after more than 30 years is really worrisome, and how hopeful are you that this happens in a short horizon?

That is indeed one of the most unfortunate stories. It is really a terrible situation and an incredible challenge. The worst part being that today, in 2020, we still have no realistic signals of a potential vaccine coming to market in the foreseeable future.

This is not for lack of trying. In fact, there have already been many trials which have unfortunately not shown any benefits. That includes large scale trials with no results. To make the matter worse, you even had trials where vaccines had the opposite effect. The harm was worse than the benefits, with an increase of the patient susceptibility to the virus.

As far as our Institute is concerned, we have been integrated in several projects, but these trials are mainly concentrated in large scale institutes in the US or in France, which have the resources and scale to conduct them. Furthermore, testing vaccines does not quite enter in the scope and mission of our Institute, as we treat patients. If there were vaccines that would play a double role, prevention and treatment, we would then certainly be very interested.

But today, there is no such lead. And once again it is not a question of lack of investment, lack of efforts or even lack of technology. It has just proven very difficult and unfortunate to find such a vaccine.

You initially mentioned CAR-T, a technology mainly associated with oncology, as one of the avenues to fight HIV. How realistic is this considering not only the cost but also the implementation difficulties associated with this technology?

Let me first clarify, that I am absolutely not a specialist in the CAR-T area and that I have no experience in this technology. That being said, CAR-T is really one of the new fields that has opened in the last 2-3 years with regards to HIV.

There are trials on the way, and we will probably be cooperating with some of them in the near future. The goal here is to find a cure. But it is only one of the avenues, one of the strategies that we need to explore. I am a firm believer that the solution will come from a global approach and through a combination of different solutions.

If CAR-T was the absolute and ultimate solution it would probably already have been shown. I do believe CAR-T will be part of the solution within a multistep process, with different points of action and very precise sequences of intervention. Maybe the first could be the kick and kill strategy, and then you could use different approaches such as CAR-T.

But as you mentioned this is a very complex technology that you cannot obtain simply as a medication. This does raise serious questions of feasibility, accessibility and cost. At this stage, we don’t know what the frame will be. We are at the very beginning of the process. Despite all these questions it remains one of the new approaches with extremely promising perspectives in HIV, for the simple reason that when talking about HIV, we are talking about T-Cells. Since the disease is directly present in T Cells, CAR-T seems very promising.

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