Jon Amund Kyte – Head, Department of Experimental Cancer Treatment, OUH Comprehensive Cancer Center, Oslo University Hospital, Norway

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Oncologist Jon Amund Kyte shares some of the groundbreaking immunotherapy research that he and his team is conducting at Oslo University Hospital. Kyte also explores how Norway can better develop its clinical footprint and what his hopes for the future of experimental cancer treatment in the country are.

Photo: Sofia Linden / Oslo Cancer Cluster

Can you begin by introducing yourself and the work you are undertaking as head of the Department of Experimental Cancer Treatment at Oslo University Hospital?

I am an oncologist and immunotherapy researcher and head of experimental cancer treatment at Oslo University Hospital. I also lead a research group at the department of cancer immunology, Institute of Cancer Research, at the same institution. My main interest, in terms of research, is making major advances in cancer therapy. I am particularly interested in applicable preclinical research and carrying out clinical trials with new drugs, especially in immunotherapy.

The department I now head is made up of three separate units and has around 50 employees. The first unit is the Phase 1-2 Trial unit, which consists of nurses and doctors that specialize in doing early phase trials which require special expertise as they are testing new drugs for the first time. This is the largest early phase unit in Norway and recruits patients from all over the country.

The second unit is the study nurse unit, which supports clinical trials across the hospital. This means that the late stage trials, typically Phase 3 trials, are handled by doctors that are specialized in specific tumour forms. For example, a lung cancer phase 3 trial should be handled by a lung cancer expert, who will then be supported by our study nurses. This same model is used across the different tumour entities.

The third unit is what we are building now, which will be a clinical trial office within our department. We already have that to some extent, but we are expanding it. This is for the project coordinators and the project managers who will help the doctors and nurses to conduct the trials, by, for instance, applying to regulatory authorities, carrying out procedures for storage of data, reporting adverse events and so on. This is also the entry point for pharma. Any new trial will go through the project managers, who go through the planning and paperwork.

I also do research myself, through my research group of 13 members at the cancer immunology department. We have two scientific focuses, both of which are in immunotherapy. One is on CAR-T cell research – developing new CAR-T cells for cancer therapy with a focus on solid tumours – and the other is combining immune checkpoint inhibitors with standard therapies. Our research group runs clinical trials with the clinical trial unit, which is the connection between my two roles.

As for my own background, I have a PhD in cancer vaccines, and I also specialized in oncology. In terms of experience, I had a stay at the clinical trials unit, which was very valuable for me as I gained a lot of experience in clinical trials. I was then a researcher at the cell therapy department, and thereafter breast cancer oncologist. I also had a research stay at University College London, under Dr Martin Pule, where I learned about CAR-T cells. Autolus Therapeutics, Europe’s only major commercial CAR-T therapy company, was spun-off from this group.

To what extent do immunotherapies represent a paradigm shift in terms of cancer treatment?

Immunotherapy drugs are the most important and exciting breakthrough in cancer therapy in the past 30 years. Before immunotherapies, the three pillars of cancer treatments were chemotherapy,

radiotherapy, and surgery. One should not underestimate the importance of any of those three pillars as most patients that are cured of cancer are cured by surgery. However, immunotherapies, as the new kid on the block, have really established themselves as a separate fourth pillar.

The most important potential of immunotherapy may be the possibility of curing cancers which, despite all other advances, remain incurable. This is still the case for nearly all solid cancers once they have metastasised beyond regional lymph nodes. That, of course, is very serious and the main source of anxiety for patients. Many patients are anxious about the potential for a relapse. If we get to a position where we can cure other forms of cancers as well, or at least offer very long term survival, then that will not only increase the number of people who are cured, but it will also help those who fear a relapse.

Immunotherapies can be used to cure some metastatic patients, or at least give them really long-term survival, without many side effects. We have melanoma patients now that have lived for nearly 20 years, who had a life expectancy of nine months before they got this treatment. Immunotherapy can give really sustained effects that chemotherapy and most targeted drugs cannot.

What are your thoughts on cancer vaccines?

Cancer vaccines are still not proven, and they are not yet important for treating cancer patients. Even though I have a PhD in cancer vaccines, that is just reality! Of course, that does not include prophylactic cancer vaccines against viruses. For instance, in cervical cancer you can prevent the cancer by vaccinating against the virus that causes the cancer but that is a special case. Most cancers are not caused by a virus.

However, this does not mean that cancer vaccines cannot become important, and there are possibilities in combination therapies. It is possible to make new vaccines based on tumour-specific neoantigens and to test the more interesting candidates with checkpoint inhibitors. However, it is too early to say whether that will actually produce something.

What are Norway’s key selling points in terms of attracting clinical trials?

One of the most important factors is our ability to do long-term follow-ups. If you start a trial in the US, you have to recruit considerably more patients than you are actually aiming to get the data

from. In Norway, you will get the data and the follow up for almost all participants. The reason for that is the strong national healthcare system with no private alternative. Even if people move around Norway, they will still be within the national healthcare system, so we do not lose patients. Our registries, including the Norwegian cancer registry, could also be useful for companies looking to extract real world data on patients.

Here in Norway, we can enrol patients from across the country in clinical trials, because the government pays travel expenses for patients to visit study sites. Yesterday, I got an email about a patient living in a town on the Russian border. I will probably get this patient into my clinical trial, even though they live the same distance from Oslo as Oslo is from southern Italy. They connect with three flights, paid for by the regional government.

Another key factor is Norway's highly educated population that speaks well English, which is useful for international studies, as they are able to understand and closely follow instructions, including the reporting of side effects etc.

At our site we are strong in some very specific areas, one of which is immuno-oncology, and we also have the largest academic cell therapy facility in northern Europe, meaning that we have strong milieus for CAR-T cell research, checkpoint inhibitor research, and other aspects of oncology.

In summary, even though Norway is a very small country, our hospital is actually a very big cancer hospital. In two years, we will also get a proton therapy centre thanks to a very big investment from the government. Our centre is also accredited by the Organisation of European Cancer Institutes (OECI) as a Comprehensive Cancer Centre due to the fact we carry out both translational and basic cancer research activities, as well as clinical activity. I, for example, spend 50 percent of my time in the research lab, and the other part of my time in the hospital seeing patients and doing clinical trials. I can carry out both tasks in the same location because the Cancer Research Institute is co-localized with the hospital. That co-localization is extremely valuable because it means people like me can have direct contact with researchers.

Norway, as a small country, is increasingly looking to collaborate with its neighbours to provide a larger patient pool for clinical trials. The Nordic Nect project, for example, draws on patient pools from across Sweden, Finland, Denmark and Norway, to create access to a potential 25 million patients rather than just 5 million in Norway alone. How successful has this project been?

There are a lot of improvements to be made. The potential is there for really good Nordic collaboration, partly because the healthcare systems are so similar, as well as the fact that in all the Scandinavian countries, apart from Finland, we understand each other. I would have no problem going to Sweden or Denmark and talking to people in their language, and if someone were to speak in a regional dialect, we could switch to English. Therefore, the aim should be for the Nordics to become one region for clinical trials, so that Norwegian patients can go to Sweden and Swedish patients can come to Norway, for example. That would help us a lot, but it would also be advantageous for patients because they would then have much more choice about which trials to enter.

Nordic Nect has helped us connect better, but at the same time, there are some important hurdles. The Nordic region is not working well in terms of clinical trials, with the main problem the question of who covers travel expenses not covered by the trial itself. In some cases, the pharmaceutical companies cover everything, but in most cases, the hospital in either Sweden or Norway would have to cover some costs. Then there is also the problem of insurance, as insurance only covers patients in their own country. All of these questions are unanswered, and what usually happens is the patients never go to Sweden for that trial, because neither the doctor nor the patient has the time or energy to work out a special solution.

Norway is not known globally as a medical research destination. Its expertise has traditionally lain more in energy and fishing. With cutting-edge research groups such as yours, do you feel the tides are changing? What more needs to be done to support medical research in Norway?

At our hospital, we are actually very good at bringing ideas through to clinical testing, partly because we have a co-localised cancer research institute. When I do my research in my lab, the cell therapy lab is just one floor below me, and my other job is to actually run the Phase 1 trial unit. So, in some ways, we are very well positioned to bring something from an idea to clinical testing.

What’s not so strong in Norway is bringing new biotech inventions into companies, and letting those companies grow. We lack a big milieu that could actually take these ideas and bring them to markets. Norway does not have this milieu because it does not have a big biotech or pharmaceutical company.

However, there is great potential in this field, thanks to our aforementioned well-educated population and comprehensive national healthcare system. We should stop thinking that we should

only be the best in the world at oil and gas. We should do as they have done in Houston and use the oil money to invest in other areas. Houston was built on oil, but nowadays, patients from all over the world go to the MD Anderson Cancer Center. Cancer treatment has become a cornerstone of their economy, which is something we could replicate.

CAR-T therapies are just as much in the news for their revolutionary therapeutic nature as for their eye-watering price tags, with Novartis' Kymriah drug being sold for hundreds of thousands of dollars for a single course of treatment. What is your take on this and how much do these debates influence your work?

Production of CAR-T cells is highly resource-intensive, so CAR-T cells will only be applied as a treatment when they are clearly better than every other cheaper alternative. At the same time, CAR-T cells have in some cases proven a potency and efficacy that is far beyond what you get with alternatives. The best example is with the breakthrough we had in child leukaemia. We were able to cure patients with very aggressive forms of cancer – patients who had a life expectancy of weeks, or at best a few months – who had been very heavily treated for years with chemotherapy. It is akin to stopping a fire, long after it looks impossible.

CAR-T cells have huge potential if they can cure aggressive forms of cancer. That comes back to what I see as the main problem for oncology, which is the inability to treat metastatic disease. CAR-T cells potentially represent an approach that changes that. If we can make it work on solid tumours, we could achieve something impossible by other means.

If we manage to develop CAR-T cells that are really efficient, which can kill metastatic cancers, they will be used even if they are costly. A good example is bone marrow transplants, which are even more costly than CAR-T cells, and are a standard therapy all over the world for haematological cancers because there is no better alternative. Bone marrow transplants are extremely toxic – a lot of patients die from the treatment – and extremely costly. Yet they are used as a treatment and have been used for 30 years. So, if the results are good enough, the cost is not going to stop it being used.

What are your hopes for the future of experimental cancer treatment in Norway?

This kind of work is very hard. It takes a lot of work to combine the roles of clinician and researcher, but it is also very motivating to work in such an important field

We are now focusing on investigator-initiated trials, where we get free drugs from companies. Through collaborating with companies, we allow them to test their drugs in promising patient populations, and in return we are able to carry out important research. The added benefit of these trials is that we put Norway on the map for clinical research.

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