Q&A with Prof Bjørn-Tore Gjertsen

Professor Bjørn Tore Gjertsen, MD PhD, has studied Mendus' lead product vididencel in acute myeloid leukemia as part of the ADVANCE II trial. He will also be the principal investigator for the first trial with vididencel in chronic myeloid leukemia.

Professor Gjertsen, can you describe your research background?

BTG: As a Professor of Hematology at the University of Bergen and Senior Consultant Hematologist at Haukeland University Hospital in Bergen, Norway, my general interest is to combine the treatment of myeloid malignancies with research studying the molecular pathways causing the disease. In the Phase I clinical trials unit at Haukeland University Hospital, we focus on clinical trials in CML and AML, combined with biomarker programs, disease profiling and response evaluation. This approach allows us to investigate potential new treatments and obtain a deeper understanding of their potential efficacy at an early stage of development. Collaboration is an essential part of innovation, and we have established multiple organizations to facilitate the exchange of information and expertise, such as the Centre for Cancer Biomarkers (CCBIO). I am currently Director at K.G. Jebsen Centre of Myeloid Blood Cancer, which focuses on gathering basic, translational, and clinical researchers to develop novel concepts for future clinical trials. I am also a founding member and chair of the Norwegian AML Group and the Nordic AML Group, and member of the Nordic CML Study Group. International collaborations are important, illustrated by our collaboration with the Dutch HOVON group in late phase trials in AML. We enrolled our first patients in a HOVON trial in 2009, and we are now as the Nordic AML Group participating in an outstanding trial program through the academic-industry partnership of HOVON.

What do you see as major developments in the treatment of AML?

BTG: AML is a very aggressive disease, which upon diagnosis is treated with chemotherapy to suppress the tumor cells to the level of complete remission. Unfortunately, the morphological assessment of the bone marrow does not mean the disease is gone. Residual cancer cells put patients at a very high risk of disease relapse, which is often fatal. The only curative method available to treat residual disease is to consolidate the therapy with an allogeneic hematopoietic stem cell transplantation (HSCT). Relapses are seen in a quarter of the transplanted AML patients, again resulting in a very difficult disease to cure. Also, HSCT is a procedure associated with severe side effect, including transplant-related mortality and chronic graft-versus-host disease, a serious condition in which the new immune system attacks the tissues of the patient it sees as "foreign". Two main developments have changed the treatment landscape of AML in recent years. First, we are learning to better manage the risks associated with HSCT, mak-

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Professor Bjørn Tore Gjertsen, MD PhD

ing the procedure more accessible for patients. Secondly, we are increasingly finding molecules that target specific mutations associated with AML and they are allowing us to define more optimal first-line treatments. Particularly, this is the case for venetoclax, a highly effective drug which in combination with another drug, azacitidine, is now used increasingly as an alternative for high-intensity chemotherapy in the first-line treatment of AML. However, we do not know if these targeted therapies can cure patients without HSCT as consolidation.

What has been your experience with vididencel in AML?

BTG: Our center participated in the ADVANCE II trial, in which we treated AML patients who were in a complete remission following chemotherapy but diagnosed with measurable residual disease (MRD), which is associated with a high risk of disease relapse. Vididencel was administered as six intradermal injections, which is a relatively straight-forward route of administration for blood cancer patients who are used to regular monitoring of their blood and bone marrow samples. Interestingly, we saw signs of potential efficacy already early in the trial because several patients experienced a strong reduction of their MRD levels following vididencel treatment. It became even more interesting when we realized that the patients who responded to the therapy early, based on disease monitoring and immunological analyses, had a good chance of long-term disease-free survival. This prospect makes vididencel an interesting product to examine more broadly as a novel post-remission treatment in AML.

How does CML fit into this picture?

BTG: Unlike AML, CML can be effectively suppressed over a long period of time by currently available medication with tyrosine kinase inhibitors (TKIs). Because these treatments are effective and overall survival of CML patients is very close to that of the general population, the attention has shifted from acute disease control to quality of life. The main struggle for CML patients is the burden of life-long medication and the side effects associated with TKIs. Unfortunately, when treatment is stopped many patients face rising disease levels and have to go back to their earlier or novel TKI treatment. The low success rate of treatment-free remissions, with overall only in one of five patients successfully stopping TKI, may improve if the immune system is able to control residual disease. Therefore, immunotherapy has always been a field of interest in CML. Current available immunotherapies include interferon-alpha and HSCT. However, the clinical benefit of combining TKI with interferon-alpha is unfortunately still unclear and HSCT is an intensive therapy that is a last resort in patients with overt TKI resistance and the aggressive blast crisis. Vididencel could provide an alternative, based on the durable clinical remissions observed in AML combined with a strong safety profile. We first plan to study the effect of vididencel in patients with stable persistent disease levels, establishing safety and initial signs of efficacy. As a next step, we will more broadly explore the use of vididencel to allow more patients to stop TKI treatment safely and successfully.

What is the ultimate goal in treating myeloid blood cancers?

BTG: Ultimately, we strive to effectively control disease to a point where patients can be considered cured, without the need for further treatment. So far, this has been very difficult in myeloid blood cancers. We are putting a lot of effort into better understanding how we can better predict the response to available treatments, to adjust treatments quickly and effectively to result in better outcomes for patients. It will be most rewarding if therapies become so successful that patients can experience long periods free of treatment, in which they can live healthy lives without the imminent risk of recurrence of their disease. Although a lot more research is needed, immunotherapy has the potential to deliver that prospect.