Unexpected results from international phase III prostate cancer study

12 July 2016, by Johannes Angerer

A recently published international clinical Phase III trial of a promising drug for treating advanced prostate cancer ended with surprising results: The new therapeutic agent failed to achieve any significant improvement in the overall survival of patients compared with the established standard treatment. This and other data from the study have now been published in the leading magazine *Journal of Clinical Oncology*. Researchers from MedUni Vienna played a significant part in the study. The study was coordinated by the recently nominated "best hospital" in the USA, Massachusetts General Hospital (MGH) of Harvard Medical School.

The urological tumors working group at MedUni Vienna's Department of Medicine I in Vienna General Hospital is known to oncologists throughout the world as a research team with recognized expertise in the modern treatment of prostate cancer. In 2012, the team was therefore invited to participate in an international study for a new drug (cabozantinib) for the treatment of advanced – so-called castration-resistant – prostate cancer. Michael Krainer, Head of the Urological Tumors working group and currently working as Visiting Scholar in the USA at the invitation of MGH, had the following to say about the results: "Although, in most cases, cabozantinib increased the overall survival of the patients by one to two months, this effect was not statistically significant when compared with the current standard treatment. This surprised us, in so far as the Phase II studies had shown clear improvements for patients in many areas."

Cabozantinib is an orally administered inhibitor of certain cellular signaling pathways (such as that of receptor tyrosine kinase MET and that of Vascular Endothelial Growth Factor (VEGF), which are closely associated with the development and progression of prostate cancer. And, indeed, initial clinical studies showed that the administration of cabozantinib had a beneficial effect upon the course of the disease for prostate cancer patients: patients' progression-free survival was prolonged and their quality of life improved.

Following these very promising results, we decided to measure overall survival in the subsequent randomized Phase III study with more than 1,000 patients," explains Krainer. "It required significantly more patients and a much longer time to determine this endpoint than was necessary in the previous studies." Patients with metastasising, castration-resistant prostate cancer, who already had bone metastases, were specifically selected. The fact that no significant improvement in overall survival was observed in this group, despite the previously measured benefits, came as a surprise – particularly since the Phase III study again showed significant improvements in secondary endpoints, such as the response of the bone scan and radiographically progression-free survival. The active agent was also associated with a reduction in circulating tumor cells, an improvement in bone-related laboratory parameters and reduced occurrence of skeletal problems. Krainer: "However, there was no significant response in terms of PSA (Prostate Specific Antigen) levels."

For the MedUni Vienna researchers, this once again underscores the value of comprehensive clinical studies, which the working group is internationally respected for supporting: "Naturally, it is disappointing for patients when a promising therapeutic approach ends up being no better than the existing treatment. Nevertheless, results such as those obtained for cabozantinib teach us a lot about the challenges we still need to overcome on the way to providing better prostate cancer treatments. It is therefore extremely important to take part in such studies, not only for research centers but especially for our patients. There is no better care for cancer patients than the care they receive as participants in clinical studies."

More information: Phase 3 study of cabozantinib

in previously treated metastatic castration-resistant prostate cancer (COMET-1). Smith, M.R., et al. *Journal of Clinical Oncology*, 2016.