**PRESS RELEASE**

**Early Genetic Analysis of Advanced and Metastatic Biliary Tract Cancer to Optimize Second-Line Therapy**

**New recommendations on current best treatment options favor targeted therapies for specific genetic alterations in tumor cells**

**Krems (Austria), 21. September, 2023: Experts from Austria have now published new recommendations on the current best treatment options for advanced or metastatic biliary tract cancer. The new consensus favors personalized second-line therapies that target specific genetic alterations of tumor cells. For first-line therapies, the addition of modern immunotherapeutics (checkpoint inhibitors) to standard chemotherapy is recommended under certain circumstances. These recommendations are made in light of new therapeutic options and study results that have become available in recent years.**

Locally advanced or metastatic biliary tract cancer is an aggressive cancer which is challenging to treat. For more than ten years, chemotherapeutic combination therapy with cisplatin and gemcitabine has been the standard of care for first-line therapy. The combined use of both chemotherapeutic agents was established after a study in 2010 demonstrated the significant mortality reduction (-36%) compared to treatment with gemcitabine alone. Recent results and studies have now been evaluated by experts from several Austrian medical universities and hospitals, and a consensus on the resulting best treatment options has been published. First author of the consensus paper is Dr. Hossein Taghizadeh, PhD, MSc, from Karl Landsteiner University of Health Sciences (KL Krems).

**Molecular testing: right at the start!**

"One important recommendation we make," explains Hossein Taghizadeh, PhD, MSc at the Clinical Division of Internal Medicine 1 at St. Pölten University Hospital, one of the teaching and research sites of KL Krems, "is that early genetic analysis of the tumor has to be performed. If certain genetic alterations are present, a modern and personalized second-line therapy can be started immediately if the first-line therapy fails." In fact, there are already some cancer drugs that target cancer cells with certain genetic abnormalities. For biliary tract cancer, these alterations include the following genes: *IDH1*, *FGFR2*, *BRAF V600E*, *HER2*, and *KRAS G12C*.

The panel recommends that in the presence of these genetic variations, targeted cancer therapeutics should be used in second-line therapy in preference to nonspecific chemotherapeutics. However, the latter should continue to be used if none of the above-mentioned alterations can be detected.

**Immunochemotherapy in the first line**

For first-line therapy, the experts evaluated in particular the results of the clinical phase III of the so-called TOPAZ-1 study. In this trial, the addition of an immunotherapeutic agent known as durvalumab (a monoclonal antibody that acts as a checkpoint inhibitor) to standard first-line therapy (cisplatin + gemcitabine) was evaluated. This form of therapy is now recommended for those affected individuals whose physical condition and well-being are good (ECOG 0 -1) and who have no known intolerance to immunotherapeutic agents such as the anti-PD-L1 antibody. Additional recommendations for first-line therapy include administration of durvalumab as a maintenance treatment when prior stabilization has been achieved with combination therapy (cisplatin + gemcitabine + durvalumab).

"We believe," Dr. Taghizadeh, PhD, MSc sums up the joint deliberation with his colleagues, "that targeted therapies already offer great opportunities in the field of oncology and their potential will continue to grow in the future. We are pleased that there are already proven successful therapies of this type for biliary tract cancer and that there is a willingness in clinics to perform the necessary genetic analyses." The consensus paper on the treatment of advanced or metastatic biliary tract carcinoma, which has now been published in *Frontiers in Oncology*, was compiled with the involvement of experts from the main treatment centers in Austria, including KL Krems, the Medical Universities of Vienna, Innsbruck, Graz, Klagenfurt Hospital, Landesklinikum Wiener Neustadt, Klinik Favoriten, the Ordensklinikum Linz, Paracelsus Medical University, Hospital Feldkirchen and St. Vincent Hospital Zams.

**Original publication**: Systemic treatment of patients with locally advanced or metastatic cholangiocarcinoma – an Austrian expert consensus statement. H. Taghizadeh, A. Djanani, W. Eisterer, A. Gerger, B. Gruenberger, T. Gruenberger, H. Rumpold, L. Weiss, T. Winder,E. Wöll & G. W. Prager. 2023, Front. Oncol. 13:1225154. doi: 10.3389/fonc.2023.1225154

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At Karl Landsteiner University of Health Sciences (KL) in Krems, the comprehensive approach to health and disease is a fundamental objective for research and teaching. With its Europe-wide recognized bachelor-master system, KL is a flexible educational institution that is tailored to the needs of students, the requirements of the labor market as well as the scientific challenges. Currently KL hosts about 700 students in the fields of medicine and psychology. The three university hospitals in Krems, St. Poelten and Tulln as well as ion beam therapy and research centre MedAustron in Wiener Neustadt and the Psychosomatisches Zentrum Waldviertel in Eggenburg ensure clinical teaching and research at the highest quality level. In research, KL focuses on interdisciplinary fields with high relevance to health policy - including medical technology, molecular oncology, mental health and neuroscience, as well as water quality and related health aspects. KL was founded in 2013 and accredited by the Austrian Agency for Quality Assurance and Accreditation (AQ Austria). [www.kl.ac.at/en](http://www.kl.ac.at/en)

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