

The 2020 GIST award goes to Dr. rer. medic. Thomas Mühlenberg D- Essen

November 20, 2020 – The GIST Group Switzerland has awarded its GIST prize for the eleventh time. This year's recipient is Dr. rer. medic. Thomas Mühlenberg, D-Essen

The laudatio was held by Dr. med. Michael Montemurro, member of the GIST Group Award Committee and medical advisor of the GIST- Group Switzerland.

The GIST Group Switzerland, the support group for patients with gastrointestinal stromal tumor (GIST), has awarded its science prize for the eleventh time. The 2020 GIST prize, worth CHF 10,000, was awarded to Dr. Thomas Mühlenberg for this publication on:

„KIT -Dependent and KIT-Independent Genomic Heterogeneity of Resistance in Gastrointestinal Stromal Tumors - TORC1/2 Inhibition as Salvage Strategy,,

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Overview of the study

The majority of patients with gastrointestinal stromal tumors (GIST) respond to treatment with specific KIT-inhibitors (e.g. imatinib), but develop resistance in the course of treatment. The development of effective salvage therapies hampered by the heterogeneity of the secondary mutations in KIT.

To obtain an updated overview of the (secondary-) mutation spectrum in KIT, we analyzed the databases of routine diagnostics of our pathology and those of our national and international collaborators. Since next generation sequencing is meanwhile employed in routine pathological diagnostics in many cancer centers, mutations in other genes that can activate KIT-dependent signaling pathways independently of mutations in KIT have been identified in pretreated patients. These data illustrate the complexity of the resistance mechanisms in GIST.

In order to better understand these mechanisms and, if necessary, to be able to overcome them, we have applied CRISPR / Cas9 technologies to generate a cell line panel in which recapitulates the mutations identified in patients in KIT, PTEN, KRAS, NF1 and TSC2. This panel was then examined for sensitivity to approved GIST therapies. Furthermore, the novel mTOR kinase inhibitor sapanisertib (MLN-0128) was evaluated alone and in multiple dose combinations (isobolograms) with established inhibitors from KIT and MEK.

We found that the modeled mutations indeed lead to resistance against KIT inhibition, which is overcome effectively by the synergistic combination of sapanisertib and the MEK inhibitor trametinib. Our work shows that despite (or possibly because of) the constant improvement of KIT inhibitors, in the future, inhibition of KIT-dependent signaling pathways may be necessary in GIST.

The award ceremony took place on 20. November 2020 at the SAKK Award Session at the virtual Swiss Oncology & Hematology Congress (SOHC) 2020.

GISTs are very rare cancers of the gastrointestinal tract that are classified as sarcomas, a group of malignant tumors that affect connective tissue, bone and muscle. They occur in 10-15 people per one million population per year. SAKK, a non-profit organization, also conducts studies on such rare forms of cancer.

Background information

Gastrointestinal stromal tumors (GISTs)

Gastrointestinal stromal tumors are rare malignancies of the gastrointestinal tract. They are classified as sarcomas, a group of malignant tumors that affect connective tissue, bone and muscle. Some 40-70% of primary GISTs occur in the stomach, 20-40% in the small intestine and 5-15% in the colon and rectum. GISTs must not be confused with the much more common cancers of the gastrointestinal tract that are classified as carcinomas. GISTs account for only about 2% of all gastrointestinal tract cancers. Carcinoma may occur at the same sites as GISTs, but their origins and treatment are completely different.

GIST Group Switzerland

The GIST Group Switzerland is an organization for the support of those affected by gastrointestinal stromal tumors. It supports every effort to improve the treatment of GISTs. To this end, the GIST Group awards an annual prize to organizations or individuals committed to achieving this goal. The prize is awarded for lectures, publications, panel discussions, scientific or socially relevant projects. The award of CHF 10,000 is donated by the GIST Group Switzerland.

Further information: www.gist.ch, gist@gist.ch

SAKK

The Swiss Group for Clinical Cancer Research (SAKK) is a non-profit organization, which has been conducting clinical trials in oncology since 1965. Its primary objective is to research new cancer therapies, to develop existing treatments further and to improve the chances of a cure for patients with cancer. This takes place through cooperative projects within Switzerland and in collaboration with centers and study groups abroad. The SAKK is supported by a service level agreement with the State Secretariat for Education, Research and Innovation (SERI) and also by partners such as the Swiss Cancer League and Swiss Cancer Research. For more information, go to www.sakk.ch, info@sakk.ch

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