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Welcome to the 23nd edition of the Merck Young Chemists' Symposium (MYCS), formerly also known as SAYCS and MEYCS. This international conference is organized by the Young Group of Società Chimica Italiana (SCI Giovani) and the National Interuniversity Consortium of Materials Science and Technology (INSTM) with the financial support from Merck and several other sponsors, that you will meet during the conference.

The symposium covers all the disciplines of Chemistry, aiming to connect young researchers, inspire new ideas, and potentially trigger new collaborations. With the contributions of our five invited plenary speakers, and the international environment guaranteed by the presence of people coming from different countries, we truly hope that you will all enjoy this great event with us. We have worked hard to organize this meeting with 230 participants, prioritizing high-level scientific topics and other themes of crucial importance in our modern society. Thank you for the great trust shown towards SCI Giovani, Merck and all our supporters. Enjoy the conference and have a nice stay with us!

Marta Da Pian

SCI Giovani Coordinator

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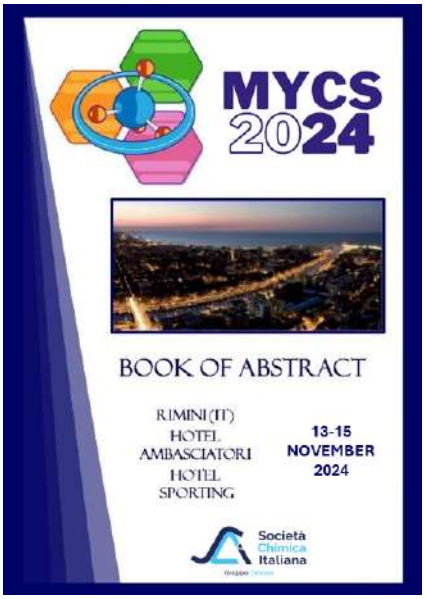	All the scientific contributions of the symposium are collected in this international volume with ISBN code. You can cite your work as follows: N. Surname, N. Surname, g and N. Surname, <Abstract title>, in Proceedings of the Merck Young Chemist's Symposium 2023, XXII Ed. I. Arduino, C. Bonfio, M. Bonomo, M. Da Pian, A. Dall'Anese, I. Fierri, A. M. Fiore, A. Marotta, M. Mendolicchio, C. M. Montone, E. Paone, F. Pizzetti, A. Polo, L. Rivoira, A. Rossetti, I. Romeo, M. Sambucci, C. Sergi, S. Tortorella, F. Vincenti. ISBN: 978-88-94952-50-6, 230, 2024, Rome.

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Optimized imidazole-thieno[3,2-c]quinolines: promising antiproliferative compounds for thyroid and NCI60 cancer cells

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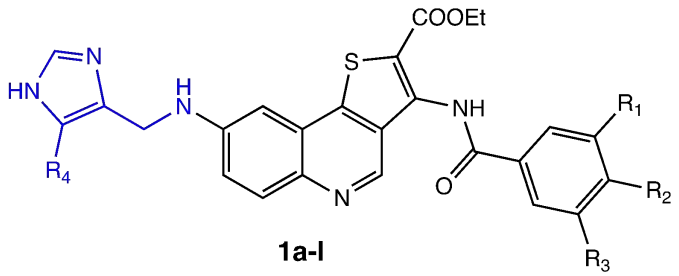
Medullary thyroid cancer (MTC), a highly aggressive endocrine malignancy, is characterized by mutations in key oncogenic targets, including RET kinase. Targeting these signaling pathways is a promising approach to improve MTC therapeutic treatment [1]. Lead optimization studies [2], allowed us to develop a new series of thieno[3,2-c]quinolines **1a-l** (Figure 1) with a hydrophilic imidazole moiety, to enhance both pharmacokinetic and pharmacodynamic profiles.



1a-l

Figure 1: general structure of antiproliferative thieno[3,2-c]quinoline compounds **1a-l**.

The thienoquinolines were successfully prepared by appropriate multistep procedures and characterized spectroscopically. *In vitro* evaluation of derivatives **1a-l** showed remarkable IC_{50} values in the 0.5-5.7 μM range against two MTC cell lines, TT(RET^{M918T}) and MZ-CRC-1(RET^{C634R}), which are known to be responsive to only a limited spectrum of anticancer drugs. Additionally, all the synthesized compounds were screened by the National Cancer Institute (NCI) under the Developmental Therapeutic Program (DTP) and tested on sixty human cell lines belonging to nine different cancer panels. Six derivatives were selected for further 5-dose assays and exhibited sub-micromolar IC_{50} values, particularly against leukemia and NSCLC panels (ranging from 0.1 to 4.9 μM). Ongoing *in vitro* biological testing will better clarify the mechanism of action (effects on cell cycle regulation, apoptotic pathways, and inhibition of key targets).

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[1] M.L. Gild, R.J. Clifton-Bligh, L.J. Wirth and B.G Robinson, *Endocr Rev* (2023) 44, 934-946.
[2] G. La Monica, G. Pizzolanti, C. Baiamonte, A. Bono, F. Alamia, F. Mingoia, A. Lauria, A. Martorana, *ACS Omega* (2023), 8, 34640-34649.