Annual Report 2024

ETOP·IBCSG
PARTNERS FOUNDATION

Foundation for International
Cancer Research

Annual Report 2024

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Dear Reader

While Artificial intelligence is revolutionizing and transforming some aspects of medicine, particularly in the field of pathology, development of biomarkers and imaging, clinical trials continue to be at the basis of bringing advances to patients and society.

In this year's Annual Report, we bring examples from our research activity both from the field of AI as well as from clinical trial activity.

Dr. Elisabetta Munzone and Professor Stephen Finn, on pages 24-29, discuss the significant impact of combining imaging, genomics, and clinical outcomes in better understanding tumor behavior. This comprehensive approach enhances the accuracy and efficiency of individual patient prognosis, care, and outcome.

You may find the article on our ADOPT-lung trial interesting, it is the only trial in the field which investigates the need of prolonged immunotherapy for patients with with early-stage lung cancer, as preoperative treatment of these patients with chemotherapy and immunotherapy has shown very promising results in improving survival rates and reducing the risk of cancer recurrence.

Furthermore, I am very pleased to introduce to our readers the Frontier Science Foundation-Hellas, the statistical center for all clinical trials and translational research projects in lung cancer. We have been working with Professor Urania Dafni and her agile team for over 15 years, who apply their statistical expertise to all stages of the clinical trial process.

The Foundation Board, the Scientific Committees and all our staff are immensely grateful for your interest and commitment to our mission to continue to push the boundaries of medical science and lay the foundation for future breakthroughs, bringing hope and innovative treatments to countless patients around the world.

We are delighted to provide you, our readers, with an update on our work over the past year and thank you once again for your continued trust and support.

Prof. Dr. med. Rolf A. Stahel
President of the Foundation Board

Key Figures in 2024

35

Participating countries in ongoing ETOP IBCSG trials

ETOP 12, IBCSG 33

1751

Tumor Samples in Biobank

ETOP 708, IBCSG 1043
cumulative: ETOP 14 451, IBCSG 74 472

49

Coworkers at the Coordinating Center

301

Recruited Patients

ETOP IBCSG sponsored: ETOP 94, IBCSG 184
Non-ETOP IBCSG sponsored: ETOP 0, IBCSG 23

1

Trial launched

ETOP IBCSG sponsored: ETOP 1, IBCSG 0
Non-ETOP IBCSG sponsored: ETOP 0, IBCSG 0

13

Open, recruiting trials

ETOP IBCSG sponsored: ETOP 7, IBCSG 2
Non-ETOP IBCSG sponsored: ETOP 0, IBCSG 4

14

Open trials, in follow-up

ETOP IBCSG sponsored: ETOP 3, IBCSG 4
Non-ETOP IBCSG sponsored: ETOP 1, IBCSG 6

25

Standard Operating Procedures

Finalized and put into effect

11

Publications

ETOP 3, IBCSG 8
cumulative: ETOP 40, IBCSG 431

31

Translational Research projects ongoing

ETOP 20, IBCSG 11

Promising results with immunotherapy to treat patients with early-stage non-small cell lung cancer (NSCLC)

The ADOPT-lung study investigates the optimal timing of immunotherapy in patients with early-stage non-small cell lung cancer.

In recent years, immunotherapy with immune-checkpoint inhibitors, alone or in combination with chemotherapy, has become the standard of care for locally advanced or metastatic non-small cell lung cancer (NSCLC). Following recent studies that showed good results, immune-checkpoint inhibitors are now also being used to treat patients with operable early-stage lung cancer.

Immunotherapy shows promising results in early stage

The treatment of early-stage NSCLC is evolving at an unprecedented rate. Recent studies show that immunotherapy is a promising therapeutic approach for NSCLC in earlier, resectable stages I-III. The introduction of immunotherapy into the therapeutic toolkit for these patients can improve treatment outcomes, evidenced by the increase in the time to relapse and in overall survival.

The chances of curing lung cancer depend largely on the stage at which the cancer is detected. If discovered early, a cure may be possible. However, the detection and diagnosis of early-stage NSCLC is still often a chance finding, for example on an X-ray taken for for another medical condition. Since lung cancer causes no or only minor symptoms in its early stages, work is currently being done to establish lung cancer screening for high-risk patients. In Switzerland, however, this is currently only offered in the context of pilot studies.

Immunotherapy before or after surgery, or both?

In early-stage disease, immunotherapy is given either before surgery (neoadjuvant treatment) or after surgery (adjuvant therapy). The aim of neoadjuvant therapy is on one hand to reduce the size of the tumor and make it easier for the surgeon to remove it, but, more importantly to prevent any possible metastatic spread.

The aim of adjuvant therapy is to kill any cancer cells that may have remained in the surrounding area and to reduce or delay the risk of the cancer recurring. Both types of therapy use the body's own immune system to attack and destroy cancer cells. The main difference lies in the time of the intervention: before (neoadjuvant) or after (adjuvant) surgery. In most cases, chemotherapy is also administered.

The medical community generally agrees that most patients with early-stage NSCLC should now receive neoadjuvant combined chemo-immunotherapy, i.e. immunotherapy given together with chemotherapy before surgery. The question arises as to whether anything more is needed after that - the trend is moving in that direction, but the data are still unclear.

The ADOPT-lung study is designed to answer the question of whether additional immunotherapy is needed after surgery.

In fact, several studies have examined the use of perioperative immunotherapy - that is, treatment with immunotherapy both before and after surgery. All of these studies have shown a benefit for this "total package", although it is not possible to deduce from these study results how large the additional benefit of the adjuvant therapy component ultimately is. It therefore remains unclear whether the effect is due to the treatment before or after lung surgery, or to both treatments.

The ADOPT-lung study, an international, multicenter, open-label, randomized study, is investigating this question. The study evaluates the benefit of adjuvant immunotherapy (i.e. additional immunotherapy after surgery) in patients with early-stage lung cancer.

Lung cancer screening

Lung cancer screening, i.e. the systematic examination of high-risk groups using low dose computer tomography (CT), is an important method of early detection for discovering tumors in potentially curable stages.

The development of lung cancer screening is progressing positively, albeit at different rates in different countries and also depending on whether the costs are covered by health insurance. At present, lung cancer screening is primarily aimed at high-risk groups, i.e. smokers and former smokers aged 55 to 75 with at least 30 pack-years.

In this study, all patients receive neo-adjuvant chemo-immunotherapy prior to surgery. After surgery, one group receives adjuvant immunotherapy, while the other group receives no further treatment.

The big question is whether patients who have already undergone chemo-immunotherapy before surgery will benefit from an additional year of immunotherapy every three weeks after the operation, or whether there are patients who do not need it. The aim is to determine which strategy is best suited for which patient, considering quality of life, cost-effectiveness and side effects. Because it is not just about bringing new medicines to market, it is about personalising treatment and tailoring diagnosis and therapy to the specific characteristics of each individual patient.

The ADOPT-lung study is being initiated by the ETOP IBCSG Partners Foundation, which is also the sponsor and responsible for funding and conducting the study.

The immune-checkpoint inhibitors revolution in NSCLC

The ADOPT-lung study is investigating the immune-checkpoint inhibitor durvalumab, which belongs to the group of PDL-1 inhibitors. Immune-checkpoint inhibitors, particularly PD-1 and PD-L1 inhibitors, have revolutionized the treatment of patients with NSCLC. These innovative medicines are used in immuno-oncology to activate the body's immune system to fight tumors.

PD-L1 is an important biomarker that is also used to predict the efficacy of immune-checkpoint inhibitors. A significant improvement in overall survival has been observed in patients with NSCLC whose tumors express the PD-L1 biomarker.

The ADOPT-lung study overview

The ADOPT-lung study plans to enroll 520 patients from nine countries. A total of 44 centers are participating in the study. The duration of the study will be several years because patients must be followed up for an extended period of time to analyze long-term results. The exact timeline may vary depending on the recruitment and progress of the study.

After an initial imaging assessment, the patient's medical history is discussed at a tumor board. This requires the surgeon (is the patient even operable?), the pulmonologist, who determines whether the lung function is good enough to remove a tumor surgically, and then, of course, the oncologist, who then decides on the systemic therapy. Depending on the interdisciplinary decision of the tumor board, the ADOPT-lung study may be suitable for the patient.

The importance of participating in clinical trials

In summary, the ADOPT-lung study, like all clinical trials, is of crucial importance because it not only contributes to the development of new and effective treatments for cancer patients, but also expands medical knowledge, thus offering future patients' better chances of recovery and a higher quality of life. By participating in clinical studies, patients are actively contributing to improving cancer treatment and at the same time will benefit from the latest therapeutic approaches before they are generally available.

Neoadjuvant immunotherapy:
An immunotherapy given before surgery to shrink the tumor and improve operability.

Adjuvant immunotherapy:
A complementary immunotherapy used after complete surgical removal of the tumor to combat any remaining micrometastases and reduce the risk of relapse.

Preoperative:
Before surgery

Postoperative:
After surgery

Perioperative:
Before and after surgery

We would like to thank **Dr. Sabine Schmid** for her expertise in the preparation of this article.

Dr. Schmid is a renowned specialist in medical oncology at the University Comprehensive Cancer Center Inselspital (UCI) in Berne and a private lecturer (PD) at the University of Berne, Switzerland.

Her clinical and research work focusses on thoracic oncology. She also serves as the Trial Co-Chair of the ETOP IBCSG Partners Foundation ADOPT-lung study, alongside Trial Chair Professor Solange Peters.

Newest Results from the POSITIVE Study Presented at ESMO 2024

Breastfeeding after breast cancer is both possible and safe, according to the latest results from the POSITIVE study.

The latest results from the POSITIVE study, presented at ESMO 2024 (European Society for Medical Oncology) in Barcelona, Spain, show that breastfeeding after early-stage endocrine-sensitive breast cancer is possible and does not lead to an increased risk of relapse in the short term. The data underscore the interest of young breast cancer survivors in breastfeeding and the need to include breastfeeding counselling in their individual care.

The POSITIVE study previously showed that women with hormone receptor-positive early breast cancer who have completed at least 18 months of endocrine therapy can safely interrupt therapy for up to 2 years to become pregnant without increasing their short-term risk of breast cancer.

Countries Participating in ETOP IBCSG Partners Foundation Trials

Lung Breast

	13-18 BEAT-meso	14-18 CHESS	15-19 ABC-lung	17-20 STEREO	18-21 AMAZE-lung	19-21 USZ-STRIKE	21-21 BOUNCE	22-22 ADEPPT	23-22 RAISE	25-23 ADOPT-lung	24-02 SOFT	25-02 TEXT	43-09 HOHO	48-14 POSITIVE	59-19 POLAR	67-22 PREcoopERA
Australia											x	x		x		
Austria														x	x	
Belgium	x							x			x	x		x		
Brazil											x					
Canada											x	x		x		
Chile											x					
Egypt												x				
France	x				x		x	x	x		x			x	x	
Germany			x								x	x				x
Greece														x		
Hungary											x	x			x	x
India											x	x				
Ireland								x			x			x		x
Israel											x			x		
Italy	x	x		x	x	x	x	x	x		x	x	x	x	x	x
Japan														x		
Lebanon														x		
Netherlands		x		x	x	x					x			x		
New Zealand											x	x				
Norway														x		
Peru											x	x				
Poland											x					
Portugal											x			x		
Romania									x							
Serbia											x			x		
Singapore			x	x	x											
Slovenia												x		x		
South Africa											x	x				
South Korea			x	x										x		
Spain	x	x	x	x	x		x	x	x		x			x	x	x
Sweden											x	x				x
Switzerland	x	x	x	x	x	x				x	x	x	x	x	x	x
Turkey											x					
UK	x				x	x		x			x	x				
USA											x	x		x		

A Powerful Partnership: Frontier Science Foundation-Hellas and ETOP

Frontier Science Foundation-Hellas (FSF-H) is the statistical center for all clinical lung trials and translational research projects, a highly respected academic clinical research organization, founded in 2007 in Athens, Greece, and since then led by Director Urania Dafni.

It was the materialization of a dream to create a European independent non-profit organization with a clear mission to add statistical value to medical practice. This mission was shared by the Harvard Professor Marvin Zelen, referred by many as the “Father of Biostatistics”, representing Frontier Science Foundation-US, and Professor Urania Dafni, of the University of Athens and former doctoral student at Harvard School of Public Health.

Frontier Science Foundation-Hellas provides cutting-edge science and clinical operations by designing, analyzing and reporting on Phase I, II, III clinical trials as well as observational studies. Its state-of-the-art statistical expertise follows the principles of “Good Clinical Practice”, ensuring ethical and scientific quality standards, as well as regulatory compliance. It is part of an international network of academic clinical trial expert organizations.

The non-profit status of the organization allows it to focus on the single goal of advancing scientific research and public health.

“For almost 15 years of strong partnership between ETOP and FSF-H, our commitment is conducting high-quality clinical trials and advancing statistical science in cancer research.”

Urania Dafni

Strong partnership and close collaboration

The strong partnership and collaboration between FSF-H and ETOP was initiated in 2011 by Professor Rolf A. Stahel, President of the ETOP IBCSG Partners Foundation, and Urania Dafni, the co-founder and Director of FSF-H. FSF-H and ETOP became partners from the design phase of the first lung cancer clinical study and the initiation of the Lungscape Platform. The close relationship of the two organizations, is flourishing for almost 15 years sharing the commitment of conducting high-quality clinical trials while advancing the application of statistical science in cancer research.

The partnership has grown into a significant research collaboration, with FSF-H serving as the Statistical Center for ETOP lung cancer studies and providing comprehensive biostatistical support for all of its clinical trials and translational research projects in the field of lung cancer, from conception and design to publication and dissemination of results, with almost 40 publications.

Professor Urania Dafni is a prominent figure in the field of biostatistics. She is the Director of the Frontier Science Foundation-Hellas and a member of the Board of the Frontier Science Foundation-US. She is a Biostatistics Professor at the National and Kapodistrian University of Athens, a Visiting Professor at CHUV, UNIL, as well as a founding member and past President of the Eastern Mediterranean Region of the International Biometric Society.

Urania Dafni has a rich academic background, including a Doctorate in Biostatistics from the Harvard School of Public Health, where she participated in the first Clinical Trials in HIV-AIDS. She has made significant contributions to oncology clinical trials and has served on several prestigious committees and editorial boards.

She has been a crucial contributor in the development of the ESMO Magnitude of Clinical Benefit Scale, and she still serves the ESMO as a member of the Faculty for the Principles of Clinical Trials.

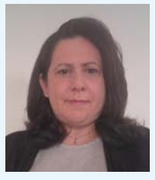
Urania Dafni is a member of the ETOP IBCSG Scientific Committee (Lung) and guest member of the ETOP IBCSG Partners Foundation Independent Data Monitoring Committees.

Dimitris Karlis,
Professor of Statistics,
Deputy Director

“Biostatistics has embraced the essence of learning from data more than any other discipline.”

Statistical science and the Clinical Trial Processes

Interaction between the FSF-H group and the ETOP scientific heads, the Principal Investigators, the Coordinating Center and the ETOP IBCSG Scientific Committees (Lung) is constant, continuous and efficient. Urania Dafni’s dual role as the head of FSF-H, and member of the ETOP IBCSG Scientific Committee (Lung) starts at the point of discussion on the concept of a new trial. The statistical expertise provided with the feedback from the subject matter experts, focuses the design to the targeted benefit and its magnitude, translating the study goal to corresponding duration and sample size while providing feasibility of reaching the set goal.



Zoi Tsourti, Senior Biostatistician,
Assistant Director

“The idea of uncovering insights from data to address complex health challenges inspires me to keep learning and growing in this field.”

Panagiota Zygoura,
Senior Biostatistician,
Assisiant Director

“I look forward to contributing to research that improves lives and advances medical understanding.”

Following the approval of the new trial concept, FSF-H contributes to all stages of the clinical trial process so as to provide the necessary tools to ensure the rigor of the trial and the validity and reliability of the results. This process is led, managed and coordinated by experienced biostatisticians, who play a crucial role in applying, analyzing and interpreting clinical and biological data to understand the effectiveness of treatments, identify risk factors and improve healthcare outcomes.

Key aspects of the statistical contribution include study design, collaboration on the synopsis and protocol document, review of eCRFs (electronic Case Report Forms) and database, data checking, SAPs (Statistical Analysis Plans) before each analysis report, data analysis at interim stages of the trial, regular reporting to the IDMC (Independent Data Monitoring Committee), final analysis and reporting, interpretation of the results, and co-writing of the publication with the main authors of the study.

Project Organization within the Data Management Process

The FSF-H team consists of more than 10 talented biostatisticians, all with postgraduate degrees. The statisticians responsible and assigned to each clinical trial, or translational research project, are organized in a “buddy system”, consisting of a primary statistician and a second statistician, who also acts as backup and tester. The role of the tester is to fully repeat the study analysis to minimize and eliminate any possibility of error.

In parallel, a younger statistician often joins the experienced project team in the project process, to learn at the same time. Continuous education is part of the every-day job, with bi-weekly seminars on diverse topics such as updates on the designs of clinical trials, regulatory environment, GCP and AI tools among others. In addition, participation in international cancer conferences and ETOP, as well as in statistics methodology, are encouraged and organized.

Key Stages explained

The process at Frontier Science Foundation-Hellas, is a comprehensive and meticulous approach designed to ensure the accuracy, integrity and compliance of clinical trial data and consists of the following (high-level) key stages:

Study Launch and Setup: At the concept stage, Urania Dafni collaborates with the ETOP office and the principal investigators to formulate the respective study’s endpoints, design and sample size. The FSF-H team further contributes to the development of protocol documents, and reviews procedure manuals, data collection instruments and study materials to meet the specific needs of the study. A dedicated database is built for each study. This is also where randomization specifications are designed to ensure unbiased allocation of participants.

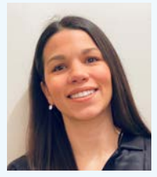
Study Conduct: During study conduct, the statisticians review data in real time to ensure that they are collected, reviewed, and delivered per study specifications and data integrity.

FSF-H tasks include writing of the Statistical Analysis Plans, periodic Independent Data Monitoring Committee (IDMC) analyses and interaction with ETOP data managers and medical reviewers, trial’s Primary Investigators and IDMC members. Pre-planned interim and final analyses (along with testing and reporting) are implemented by FSF-H for all ETOP lung trials.

Reporting and dissemination: Fully customizable reports are developed and published, which also include data visualizations and interim analyses, providing early insights into study progress. The team contributes to the interpretation and dissemination of results in major conferences and as journal articles, by collaborating in the writing and interpretation and participating as co-authors.

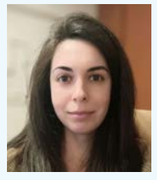
Standard Operating Procedures are active for all statistical practices.

According to Urania Dafni, the impact of the work is what makes it so exciting and fulfilling. Biostatisticians do not look only at the numbers but also at the patients in the trial and the ones out there who will benefit from a well conducted clinical trial. The responsibility of a statistician to correctly design, analyze and interpret data involves ethics as an important aspect of his/her work.



Katerina Vervita,
Biostatistician

“Being a biostatistician excites me because it combines my love for mathematics, data analysis, and making a meaningful impact on public health.”



Georgia Dimopoulou,
Biostatistician

“Biostatistics transforms raw information into meaningful insights that drive medical advancements and improve public health.”

4 Key Questions – 4 Smart Answers

Professor Stephen Finn is the distinguished Chair of the ETOP IBCSG Partners Foundation's Translational Working Group (Lung), a globally recognized consultant pathologist and Co-Director of the Cancer Molecular Diagnostics Laboratory at St. James's Hospital in Dublin, Ireland.

We were delighted to catch up with Professor Finn to ask him our 4 Key Questions.

Stephen Finn, Chair of the ETOP IBCSG Partner Foundation's Translational Working Group (Lung), holds multiple qualifications, including MB BAO BCh (medical degrees), PHD, and fellowships from the Royal College of Pathologists (FRCPath) and Faculty of Pathology (FFFPATH).

He co-directs Ireland's only fully accredited Cancer Molecular Diagnostic Laboratory at St. James's Hospital, which serves as a critical hub for advanced cancer diagnostics. He is also an associate professor of pathology at Trinity College Dublin.

His work bridges clinical practice with translational research, aiming to improve diagnostic precision and therapeutic strategies for cancer patients.

1

Your background is in Molecular Pathology. Can you tell us more about the role of the pathologist and translational researcher in clinical trials?

Clinical trials offer unique, highly controlled environments for collecting bio samples and conducting clinical research. They provide an ideal setting for high-quality translational research. In every step—from hypothesis generation and trial planning to post-trial translational studies—pathologists and translational researchers collaborate within the Translational Working Group. Their expertise ensures appropriate sample collection, storage, and management.

This collaboration facilitates biomarker identification and tissue analysis, which includes immunohistochemistry, molecular testing through Next Generation Sequencing, and gene expression profiling. These processes yield a wealth of data that enhances our understanding of tumor biology and the potential response to targeted or immunotherapies.

Molecular pathologists are critical to cancer clinical trials, offering expertise in the analysis and interpretation of molecular and genetic data related to cancer. In summary, molecular pathology and translational oncology are essential for bridging the gap between laboratory research and clinical application. They ensure that cancer clinical trials are grounded in robust molecular data, ultimately leading to personalized treatment approaches.

2

ETOP has a long and strong track record in thoracic translational research. How was that achieved?

From the outset, the strength of ETOP studies has been their multidisciplinary approach, emphasizing the importance of addressing relevant clinical questions across the spectrum of thoracic oncology while paving the way for translational studies that advance the state of the art. The ETOP ethos fosters collaboration and teamwork among various stakeholders, including clinicians, statisticians, researchers, pathologists, and industry partners. This multidisciplinary approach integrates diverse expertise and perspectives, which are essential for tackling complex challenges in thoracic oncology.

Annual in-person meetings have played a critical role in solidifying this team approach, allowing for ongoing communication and collaboration.

3

You are the Chair of the Translational Working Group (Lung). How does the working group function?

As Chair, I guide and coordinate translational research efforts within the organization, supported by the diverse expertise within the working group. This role is built on teamwork, helping coordinate efforts among group members and facilitating collaboration with other research groups and industry partners.

The Chair also helps develop the strategic direction for translational research initiatives. The working group initiates and supports specific research projects that focus on translating basic research findings into clinical applications, fostering partnerships with academic institutions and industry.

We encourage collaboration and create an environment of shared knowledge and resources essential for impactful translational research. Additionally, the working group monitors the progress of ongoing research projects, ensuring adherence to timelines and quality standards. We also provide guidance on methodologies and approaches used in translational research.

4

What excites you in terms of next steps for ETOP Translational research?

The emergence of Artificial Intelligence (AI) has the potential to rapidly transform clinical trials, offering exciting developments that enhance efficiency, accuracy, and the scope of research. There is momentum within ETOP IBCSG Partners Foundation to incorporate Digital Pathology, laying the groundwork for this transformation.

Digital pathology utilizes whole slide imaging technology, enabling remote access to pathology slides. This facilitates collaboration among our team of translational researchers and pathologists across different locations. Advanced algorithms and machine learning tools can analyze digital pathology images to identify patterns, quantify features, and detect biomarkers. This automation enhances diagnostic accuracy and speed, reduces human error, and aids in recognizing relevant histological features in trial samples.

The true power of this approach will come from integrating clinical data, allowing for a more comprehensive understanding of patient data, including imaging, genomics, and clinical outcomes. This integrated approach supports more robust analyses and correlational studies within clinical trials.

Overall, the advancements in digital pathology are paving the way for more efficient, accurate, and patient-focused clinical trials. By harnessing technology, researchers can improve data quality, enhance decision-making processes, and ultimately lead to better outcomes in cancer care and beyond.

Pioneering Breast Cancer Treatment

Sitting down with Dr. Elisabetta Munzone – Vice Chair of the ETOP IBCSG Partners Foundation's Executive Scientific Committee (Breast), a highly recognized global leader in the field of breast cancer research.

"Very early in time we knew that one treatment does not fit all patients."

Elisabetta Munzone

Elisabetta Munzone is a warm and approachable woman whose enthusiastic spirit and energy reflect her unwavering passion for her work. Her dedication to advancing breast cancer research and shaping future treatments has made her a key player in the global fight against breast cancer. Dr. Munzone is Study Chair of several clinical studies that aim to improve the treatment options for patients with early and metastatic breast cancer.

With over 30 years of experience, her research has been instrumental in advancing personalized medicine for breast cancer patients. She is deeply involved in clinical and translational research, focusing on new therapeutic approaches. Through the identification of specific cancer phenotypes and the tailoring of treatments accordingly, her research goals are to develop more effective and less toxic therapeutic options for patients with advanced and metastatic breast cancer.

Elisabetta Munzone's Decades of Contributions to the ETOP IBCSG Partners Foundation

Dr. Munzone has been involved with the Foundation since she was a very young oncologist during her residency at the IEO (Istituto Europeo di Oncologia) in Milan. It was there that she met Aron Goldhirsch, who had joined the institution as Director of the Department of Medicine, in 1997. He was a founding member, board member and Chairman of the scientific committee of the IBCSG (International Breast Cancer Study Group) and thus played a major role in advancing breast cancer research.

Together with the IBCSG they initiated the first trials for adjuvant settings for breast cancer (i.e. the provision of additional treatments after primary treatment, usually surgery, to reduce the risk of cancer recurrence), as well as the definition of biological characteristics that predict responsiveness or resistance to cancer treatments, and quality-of-life approaches. They were pioneers in the research on breast cancer subtypes with the clear motto: "There is no single treatment for all patients", or in other words, "one size doesn't fit all".

Today she is the Vice Chair of the Scientific Committee (Breast) where she supports and advises on scientific matters, including the initiation, evaluation and planning of clinical trials and translational projects. Her contributions over decades have been significant, particularly in advancing personalized treatment approaches but also with her research on metronomic chemotherapy for breast cancer.

Metronomic Chemotherapy

Dr. Munzone is world-renowned for her research into metronomic therapies, which actually originated and were developed at her institution. These regimens are designed to minimize toxicity while maintaining treatment efficacy. In this approach, lower doses of chemotherapy drugs are given more frequently than in traditional chemotherapy regimens. It is designed as an oral treatment that can be administered at home, allowing patients to reduce hospital visits to once a month instead of weekly intravenous treatments. The advantages include good tolerability of the oral regimen, minimization of side effects such as nausea and hair loss, and fewer blood tests. But it is also seen to improve quality of life due to the convenience that it can be administered at home, so that patients can lead a normal life while maintaining or even enhancing the efficacy of the treatment.

One of Elisabetta Munzone's notable studies on this was the IBCSG METEORA-II trial, which compared the efficacy of an all-oral metronomic regimen (vinorelbine, cyclophosphamide and capecitabine) with weekly intravenous paclitaxel in patients with estrogen receptor-positive (ER-positive) and HER2-negative metastatic breast cancer. The results showed that the metronomic regimen, called VEX regimen, significantly improved time to treatment failure (time from the start of treatment to earliest treatment failure and clinical progression) and progression-free survival compared to traditional intravenous chemotherapy.

Another use of metronomic chemotherapy was investigated in the randomized phase III IBCSG 22-00 trial, in which Drs. Marco Colleoni (PI) and Elisabetta Munzone (sub-investigator) studied the effects of low-dose cyclophosphamide and methotrexate in triple-negative breast cancer (TNBC), which means that the patient lacks all three receptors, estrogen (ER), progesterone (PR) and human epidermal growth factor receptor 2 (HER2). The trial was designed to see if this metronomic approach could improve outcomes for patients with this aggressive subtype of breast cancer. It was found that there was a trend for improving outcomes only in node-positive TNBC.

Today the metronomic therapy can be seen as a proof of concept and has found its way into many guidelines, such as the ABC guidelines for advanced breast cancer. Yet Elisabetta notes that there are some subgroups that do not benefit from this treatment, and therefore it is critically important to further advance and research personalized treatments to the individual subtypes of breast cancer patients.

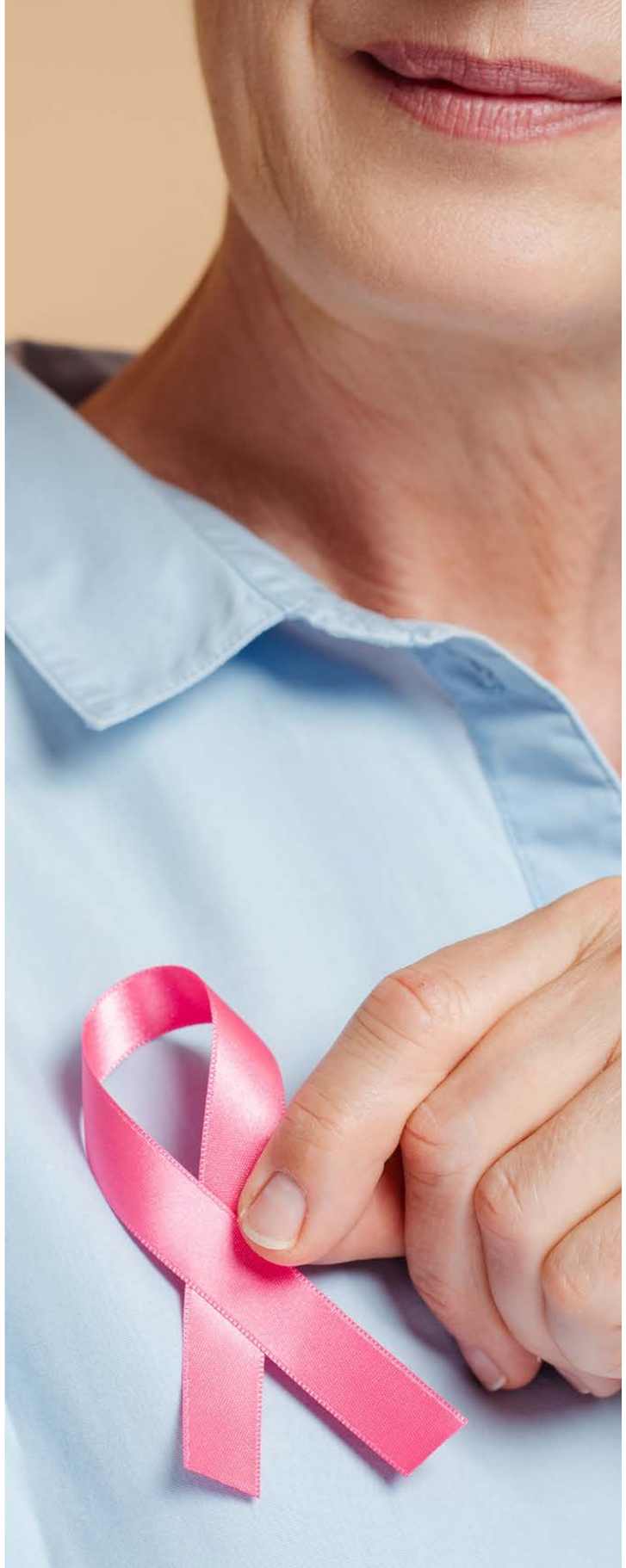
Today's challenges are the high cost and complexity of clinical trials with the available resources

According to Dr. Munzone, the ETOP IBCSG Partners Foundation has always supported and promoted investigator-initiated and academic trials to answer real-life questions about how to treat patients, with a focus on personalized medicine and individualized treatments. These trials are challenging, not only because of the high cost, but also because of the inclusion criteria and the increasing biological complexity of tumors. The pharmaceutical industry is less interested in supporting these important trials as they are more focused on designing their own trials to meet their endpoints, such as obtaining drug approval.

Pragmatic- and Window of Opportunity Trials as a new course of direction

One approach that has recently gained interest are the so-called pragmatic studies. These are studies that are closely aligned to the current clinical practice. They differ particularly in the inclusion criteria from the isolated conditions of normal clinical studies. While these are very selective in "normal" clinical studies and exclude certain patients, pragmatic studies are open to all patients who would also receive the study treatment in normal clinical practice.

The second approach mentioned by Dr. Munzone is what are called "window of opportunity" studies. These are short trials that take place in the window between diagnosis and the start of the actual treatment. Window-of-opportunity studies are most common in early-stage breast cancer, before breast surgery. They are particularly useful for testing new treatment strategies in a controlled environment. The aim of a window of opportunity trial is typically to test the biological effect of the drug, for example, on a specific biomarker on the tumor cells. This can help researchers understand how a new treatment might work in a real-world setting. A window-of-opportunity study aims to provide the basis for a subsequent clinical trial.



PREcoopERA Window of Opportunity Trial as an Example

The (IBCSG) PREcoopERA window of opportunity trial is currently being conducted for premenopausal patients with ER positive HER2 negative breast cancer in stages I-III with a Ki-67 of at least 10%. The question that is being studied is whether the patient can receive an endocrine therapy with an oral SERD* and thus avoid being given an ovarian function suppression, which often causes a lot of side effects for young patients, such as early menopause which may impair their quality of life. The goal is to enable these premenopausal women, if successful, to receive drugs without all the side effects.

Science is Data and Evidence

Dr. Munzone has recently completed a Master's degree in Artificial Intelligence and Machine Learning in Cancer Medicine, furthering her expertise in integrating AI technology into medical research, clinical practice and cancer care. She and her team at the Istituto Europeo di Oncologia (IEO) are currently developing a "clinical data platform", which can be described as a "data lake", a centralized repository of information on all patients treated at the IEO. It has also enabled a collaboration between the IEO and the Google Cloud, which significantly speeds up the analysis of clinical data, making it 300 times faster than traditional methods.

* SERD= Selective Estrogen Receptor Degrader, is a new category of drugs, coming to clinical practice now, that bind the estrogen receptor on cancer cells and causes its degradation, reducing the ability of cancer cells to grow and proliferate.

“Electronic Health Records have the potential to revolutionize healthcare.”

The data ranges from biometric and histological data to genetics, blood tests and radiological data - all going into the big data lake supported by the IT team. This enables the extraction of real-world data from electronic health records to suggest clinical trials to investigate real-world questions. The data comes mainly from their institution, and there’s a lot of it, as they operate on around 3000 patients a year. Within their database they are approaching data from 50 000 patients, which definitely gives them the opportunity to extract and analyze a lot of data and information.

The Future of Cancer Treatment

Elisabetta Munzone is convinced that, with the rapid advancement of AI tools such as radiomics, the future of cancer treatment is poised for significant improvement. Radiomics, in particular, contributes to the development of personalized medicine by extracting a large number of features from medical images and providing detailed information about the tumor and its behavior. Thanks to these technologies, it will become possible to interpret X-rays and CT scans more effectively, correlating information from these images to predict an early prognosis alongside an early diagnosis. Furthermore, when analyzing slides from pathology reports, AI tools can extract valuable information regarding a patient’s prognosis or risk of recurrence, thereby guiding and personalizing treatment decisions.

Personalized medicine is key and is quickly evolving in all directions

She adds that subgroups and niche populations of patients need to be better studied to understand how to escalate and de-escalate treatments, as there are some subgroups of patients within the same disease category who need either more or less drugs. This is important to define because it will clearly improve quality of life and outcomes. With AI tools and information from research, these patients can be identified and personalized.

In addition, a lot of information will come from the genomic side. This will help to create an individualized picture of each patient’s actual genomic situation. “We may also be able to understand which subgroups of metastatic patients could be healed”, she notes. “There is a small group of patients today which can be considered as cured, as they have been progression free for a very long time. We believe this could increase due to the new technology. So, by collecting the genetic data of these patients we try to understand their characteristics and to find the reasons for this positive outcome. Is it because of the therapy or is it individual luck?”

One other point Munzone makes is that there is a lot of research going on with antibody-drug conjugates (ADCs), a class of targeted cancer therapies that combine an antibody with a cytotoxic drug, which is working very well in many diseases, not only breast cancer. The antibodies specifically target cancer cells, delivering the cytotoxic drug directly to the tumor. This targeted approach helps to minimize damage to healthy cells and aims to improve the efficacy of the treatment while reducing side effects compared to traditional chemotherapy.

An exciting outlook from a fascinating woman and acclaimed scientist with a life-long dedication to advancing breast cancer research.

When asked about her life outside of medicine, she smiles and talks affectionately about her close family, her two children who are now studying at the university, her sporting hobbies such as tennis and skiing, which are unfortunately a little neglected these days, and how much she enjoys catching up with old friends.

Dr. Elisabetta Munzone is a distinguished medical oncologist specializing in breast cancer, based at the European Institute of Oncology in Milan, Italy.

She holds the position of Vice Chair of the Executive Scientific Committee (Breast) of ETOP IBCSG Partners Foundation. She is also the Study Chair for the IBCSG trials PRECOOPERA, POLAR and METEORA.

Munzone serves as Director of the Research Unit in Medical Senology and holds a leadership role as a senior medical officer focused on advanced therapeutic innovations for breast cancer.

Her clinical and research expertise centers on developing personalized treatments for breast cancer patients, utilizing pathological, clinical, genetic, and molecular characterization.

Additionally she is a prolific academic, with over 220 publications and 6700 citations. She has been a faculty member since 2015 in the master’s program in oncology pharmacy and pharmacology at the University of Milan. She recently completed a master’s degree in artificial intelligence and machine learning in cancer medicine.

Giuseppe Curigliano is Elected ESMO President for 2027-2028

Professor Giuseppe Curigliano, member of the Scientific Committee (Breast) of the ETOP IBCSG Partners Foundation, has been elected President of the European Society for Medical Oncology (ESMO) for the upcoming years 2027-2028. Curigliano will join the ESMO Executive Board as President-Elect from January 1st, 2025.

ESMO is the leading professional organization for medical oncology, with more than 25 000 members from around the world. ESMO was founded in 1975 and is headquartered in Lugano, Switzerland.

Curigliano states: “It is crucial for the future that ESMO continues to advance its mission of promoting excellence in the field of medical oncology and to ensure optimal care for cancer patients worldwide.”

We express our sincere congratulations to Professor Curigliano.

Giuseppe Curigliano, member of the Scientific Committee (Breast) of the ETOP IBCSG Partners Foundation, is the Head of the Early Drug Development Unit and Co-Chair of the Experimental Therapeutics Program at the European Institute of Oncology, a comprehensive cancer center in Milan, Italy.

Curigliano is a member of the Steering Committee of the Department of Oncology and Haemato-Oncology at the University of Milan. He is also a member of the Italian National Health Council and advises the Ministry of Health on cancer policy.

The Heine H. Hansen Award for 2024 Goes to Enriqueta Felip from Spain

Professor Enriqueta Felip, member of the Scientific Committee (Lung) of the ETOP IBCSG Partners Foundation, was awarded the Heine H. Hansen Prize at the ELCC 2024 (European Lung Cancer Congress).

Enriqueta Filip is honored for her outstanding contribution to thoracic oncology research. Her work focuses on accelerating more effective, personalized and targeted cancer drugs that are matched to specific molecular alterations in patients. Additionally, she is dedicated to unmasking molecular mechanisms of acquired resistance to cancer drugs. Furthermore, she optimizes immune-based strategies in advanced and early-stage non-small cell lung cancer (NSCLC).

The Heine H. Hansen (HHH) Award was established in 2015 by the International Association for the Study of Lung Cancer (IASLC) and the European Society for Medical Oncology (ESMO) in recognition of Professor Heine Hoi Hansen’s lifelong global contribution to lung cancer research and education.

The award recognizes lung oncologists who have made significant contributions to lung cancer research and education at an international level. Awardees are invited to deliver a keynote speech at the opening plenary session.

We warmly congratulate Professor Felip on this well-deserved award.

Enriqueta Felip, member of the Scientific Committee (Lung) of the ETOP IBCSG Partners Foundation. She is Head of the Medical Oncology Service at Vall d’Hebron University Hospital (HUVH), Head of the Thoracic Tumors Group at Vall d’Hebron Institute of Oncology (VHIO) and Professor of Medicine at the University Autònoma de Barcelona (UAB).

Professor Ann Partridge Honored with the 2024 ESMO Award

Professor Ann Partridge, Chair of the POSITIVE Study North America, received this year's ESMO Award during the ESMO 2024 Congress for her outstanding work in improving the care and outcomes of cancer patients, with a focus on treatment, survival and psychosocial issues for women with breast cancer.

Ann Partridge regards the POSITIVE trial to be the most important work she has contributed to and emphasizes that the study was a team effort led by Olivia Pagani from Switzerland and IBCSG, the International Breast Cancer Study Group.

The prestigious ESMO Prize was established in 1985 to honor an ESMO member who has made an outstanding contribution to the development of medical oncology.

The ESMO Congress is one of the most influential events in the field of oncology, driving progress in cancer treatment and research worldwide. The annual event serves as a hub for disseminating and sharing data from cutting-edge research, providing high-quality educational opportunities and outstanding networking opportunities in oncology.

We warmly congratulate Professor Patridge on this prestigious award.

Professor Partridge, Chair of the POSITIVE trial North America, is vice-Chair of the Division of Medical Oncology at Dana-Farber Cancer Institute in the US, where she is also director of the Adult Survivorship Program and leads the Young Women with Breast Cancer program.

She is a professor of medicine at Harvard Medical School and holds the Eric P. Winer, MD, Chair in Breast Cancer Research at Dana-Farber.

Double Honors for Professor Solange Peters

Solange Peters to be the new president of Oncosuisse

Professor Solange Peters, a member of the Foundation Board of the ETOP IBCSG Partners Foundation, was elected as the new president of Oncosuisse on September 4th, 2024.

The independent umbrella organization was founded in 1999 and unites eight Swiss cancer organizations. Its main tasks are strategic coordination, networking and political advocacy for the stakeholders in the fight against cancer in Switzerland.

The Chair plays a central role in promoting cooperation between various stakeholders in the field of cancer, with a particular focus on equity of access and high quality of care. In addition, the association aims to ensure adequate prevention and early detection of cancer, optimal care for cancer patients of all age groups, and support for people with cancer as well as cancer survivors. This is achieved through strategic and close cooperation.

Solange Peters was honored with the Giants of Cancer Care® award in the 12th Annual Class of Inductees in the lung cancer category

The **Giants of Cancer Care** is a prestigious award program created to honor individuals who have made significant contributions to the field of oncology. Presented by OncLive, a leading multimedia resource for oncologists, the initiative aims to recognize the achievements of researchers, educators and clinicians whose work has advanced cancer treatment and research.

A selection committee of more than 115 leading oncologists from around the world picks the winners for the different tumor types and specialties, awarding them for their outstanding achievements in oncology research and clinical practice. The award ceremony took place on 30 May 2024 in Chicago, Illinois.

We warmly congratulate Professor Peters on the prestigious nomination and well-deserved award.

Solange Peters, member of the Executive Committee and Chair of the Scientific Committee (Lung) of the ETOP IBCSG Partners Foundation. She is Full Professor and Chair of Medical Oncology and the Thoracic Malignant Diseases Program at the University Hospital (CHUV) of Lausanne in Switzerland. Peters is Vice President of the Swiss Cancer League and President of Oncosuisse. She is Past President of ESMO and founder of the Women for Oncology Committee.

Meetings

IBCSG Annual Meeting
- Berlin, Germany
- May 15, 2024
- Participants: 52

2nd Antibody Drug Conjugates (ADC) Workshop
- Zurich-Airport, Switzerland
- June 28–29, 2024
- Participants: 52

13th ETOP Residential Workshop
- Barcelona, Spain
- October 30–November 1, 2024
- Participants: 25 und 17 lecturers

ETOP Annual Meeting
- Barcelona, Spain
- November 1–2, 2024
- Participants: 120

ETOP Translational Research Meeting
- Nice, France
- April 20, 2024
- Participants: 35







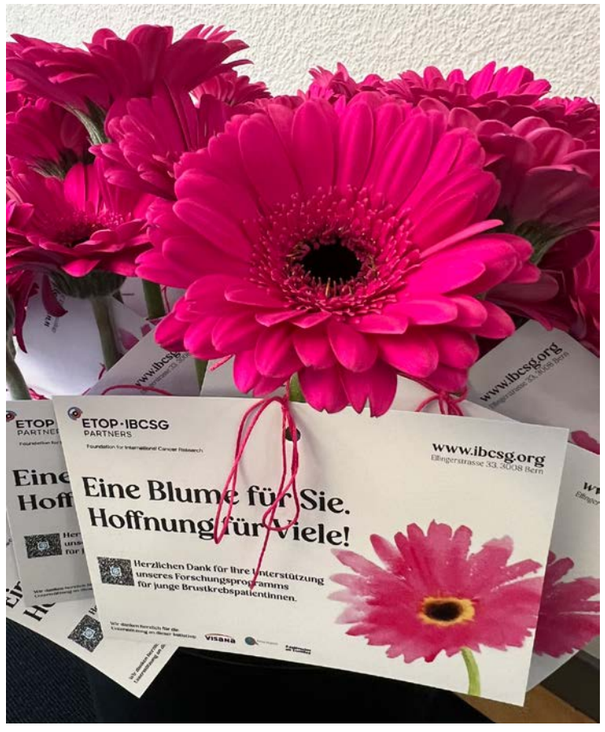


“Schweizer Frauenlauf”

On June 9th, 2024, the 38th “Schweizer Frauenlauf” took place in Berne. A run for women, a festival for all!

The “Frauenlauf”, women’s run, is an event designed to appeal to a diverse audience and to encourage widespread participation. This event is a celebration for women of all ages, from children to seniors. While athletic performance is certainly a highlight, the emphasis is equally placed on community spirit and fun. It’s more than just a run; it’s a festival that fosters connection and well-being for everyone involved.

Switzerland’s largest mass sports event for women offers a unique atmosphere to jog or walk over distances ranging from 500 meters to 10 kilometers. Around 10 000 participants and 30 000 spectators enjoyed the idyllic course along the River Aare.



Pink wigs raise awareness for the IBCSG Program for Young Patients

For the past five years, the IBCSG Pink Ladies have been at the starting line. Their mission is to raise awareness for breast cancer, the Foundation and to fundraise for “The Program for Young Patients” (PYP). The IBCSG Pink Ladies and their pink wigs are a very well-known attraction and have even been featured in the local press this year.

A flower for you. Hope for many!

This year’s group of IBCSG Pink Ladies was made up of 45 women, including coworkers, foundation members, cancer survivors and their families and friends. A beautiful and much appreciated gesture was the distribution of lovely gerbera flowers to the audience, with a mention of the POSITIVE study and how to contribute.

Pink Ribbon Golf Tour

The Pink Ribbon Golf Tour 2024 was an amazing success featuring three exclusive charity golf tournaments in Switzerland. Once again, the tour was blessed with great sunny weather, happy golfers, generous prizes and a substantial donation of 70 000 Swiss francs to the Program for Young Patients, PYP, of the ETOP IBCSG Partners Foundation.

The annual tour aims to raise funds for this important research project for young breast cancer patients, specifically the IBCSG POSITIVE trial. The trial has shown very promising results, giving hope to many young women with hormone-sensitive breast cancer who want to pause their anti-hormonal therapy to have a baby without increasing their risk of recurrence.

The Pink Ribbon Golf Tour goes beyond financial support - it symbolizes solidarity and community. The handicap-neutral tournament emphasizes team spirit, as the focus is not on performance, but simply on enjoying a wonderful day’s golf together for a good cause. The three tournaments were held at the beautiful courses of Lipperswil, Breitenloo and Winterberg.

Monica Ruggeri, Head of the ETOP IBCSG Partners Foundation’s Program for Young Patients (PYP), received a cheque for 70 000 Swiss francs, the largest donation ever raised at the Pink Ribbon Golf Tour. The cheque is presented by Nicole Zindel (center), founder of Pink Ribbon Switzerland, and Linda Fäh (left), Pink Ribbon ambassador, event host and singer.

We sincerely thank:
PINK RIBBON SWITZERLAND, Nicole Zindel, Beatrice Wegmann and Laura Schempp of 2C Communication GmbH and Anja Flückiger, all golfers, the Golfclub Lipperswil, Golfclub Breitenloo and Golfcourse Winterberg, Clarins, Julius Bär, Raffaello Rossi, Ruckstuhl Garagen, Focus Water, Spaze Studio, Massage Wiedikon and many other supporters, donors and volunteers who enabled this wonderful charity event. Special thanks to Christine Hafner and Marc Wyss for their generous donation.


Happy and engaged golf ladies at the golf course Winterberg.

Photos © PINK RIBBON SCHWEIZ

Annual Financial Statement 31.12.2024

Balance

Assets	**31.12.24**	**31.12.23**
	TCHF	TCHF
Cash	4758	3596
Financial assets short-term	5893	2974
Accounts receivable	2594	2677
Other short-term receivables	395	295
Prepaid expenses and accrued income	898	956
Current assets	**14538**	**10498**
Financial assets	11684	10853
Non-current assets	**11684**	**10853**
Total assets	**26222**	**21351**

Liabilities	**31.12.24**	**31.12.23**
	TCHF	TCHF
Accounts payable	337	1147
Advance payments short-term	13439	13501
Other short-term liabilities	103	191
Accrued expenses and deferred income	2574	1184
Short-term liabilities	**16453**	**16023**
Advance payments long-term	3720	0
Long-term liabilities	**3720**	**0**
Dedicated Fund Support Breast Cancer Clinical Research	1024	1024
Dedicated Funds	**1024**	**1024**
Foundation capital	175	175
Voluntary retained earnings		
Profit brought forward	4129	4493
Result of the year	721	-364
Equity	**5025**	**4304**
Total liabilities and equity	**26222**	**21351**

Income statement

	2024	**2023**
	TCHF	TCHF
Research contributions	11491	10292
Grants and donations/Income from other research organizations	2727	3331
Other contributions	386	267
Reimbursements from externals for services	59	53
Operating income	**14663**	**13943**
Research contributions to members/sites and suppliers	-8662	-8040
Cooperation expenses	-333	-341
Personnel expenses	-5304	-5207
Other operating expenses	-892	-767
Operating expenses	**-15191**	**-14355**
Operating result	**-528**	**-412**
Financial income	1346	463
Financial expenses	-97	-418
Extraordinary income	0	3
Result of the year	**721**	**-364**

We Express Gratitude...

...to all patients who have participated or are still participating in our trials, as well as to their families and caregivers. You are central to all of our clinical trials.

...to all investigators and their teams at participating hospitals, as well as our partner organizations, for their invaluable commitment. Their support is crucial to the success of our studies.

...to all members of our Foundation Board, the two Scientific Committees, our Study Chairs, the two Independent Data Monitoring Committees (IDMC), and the IBCSG Ethics Committee. Their vision, knowledge, and ideas lay the foundation for our research.

...to all our donors, who make a significant contribution to the funding of our projects, and to all our pharmaceutical partners, who fund the majority of many trial budgets.

...to all the staff at the ETOP IBCSG Partners Foundation Coordinating Center in Bern (Switzerland), the Statistical Centers in Boston (USA) and Athens (Greece), the Data Management Center in Amherst (USA) and the teams at the Central Laboratories in Milan (Italy) and Lausanne (Switzerland). Their expertise and commitment are vital to the success of our studies.

List of Our Donors

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- Stiftung St. Gallen Oncology Conferences (SONK)
- Swiss Cancer Foundation
- USZ Foundation
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- Supporting companies in the research-based pharmaceutical industry and many other private companies and individuals

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For reasons of legibility, the masculine form has been chosen in the text; nevertheless, the information refers to members of all genders.

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