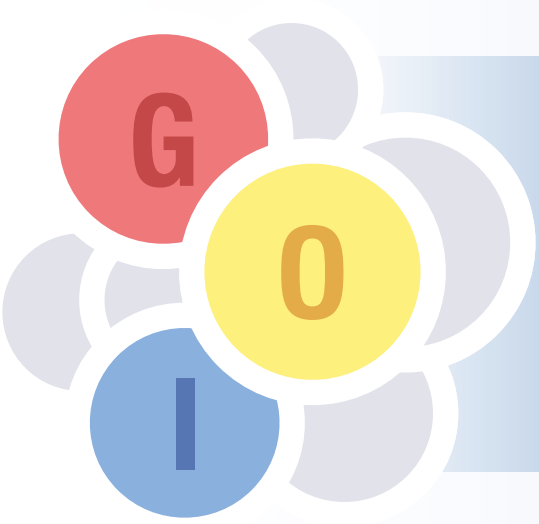

Grant for Oncology Innovation Awards

Friday 26 September 2014
19:00 - 20:00

Auditorium of the Chamber of Physicians
of Madrid
Colegio de Medicos de Madrid
Calle Santa Isabel 51
Madrid, Spain

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Contents

The Grant for Oncology Innovation

Welcome to the first annual award presentation of the Grant for Oncology Innovation (GOI), a Merck Serono-sponsored initiative. The GOI was launched at the joint European CanCer Organization (ECCO) and European Society for Medical Oncology (ESMO) meeting in Amsterdam in 2013, and 143 proposals were received from around the world for the inaugural award. The top five countries by number of applications were Spain (24), China (20), USA (20), Italy (16) and Portugal (11). The Scientific Committee reviewed the proposals and invited a shortlist of six applicants whose proposals were considered worthy of progressing to the second round. These investigators were requested to submit a more detailed proposal for further evaluation by the Scientific Committee. Each proposal was assessed against a set of five specific criteria (relevance to patient care, innovative approach, scientific impact, feasibility, relevance for the personalization of treatment), and discussed in detail by the GOI Scientific Committee. Finally, the Scientific Committee identified three outstanding projects this year to receive a GOI award.

Each year, researchers from around the world will be invited to submit proposals for promising projects, and the GOI will fund successful applicants.

It has been a privilege for the Scientific Committee to have had the opportunity to review the many high-quality applications from across the globe for research in the field of oncology.

On behalf of the GOI Scientific Committee, I would like to extend my warmest congratulations to this year's winners. The Scientific Committee and I also look forward to reviewing many more applications for the 2015 GOI award.

Yours sincerely

Professor Rolf Stahel

GOI Scientific Committee Chair
Clinic of Oncology, University Hospital Zürich, Zürich, Switzerland

Winners of the GOI Award 2014

Ulrich Güller

Kantonsspital St Gallen, St Gallen, Switzerland

Professor Ulrich Güller performed his training in general surgery at the University of Basel, Switzerland. During his residency he spent a 2-year research fellowship at Duke University, North Carolina, USA, where he received a master's degree in clinical epidemiology and statistics and collaborated with the American College of Surgeons Oncology Group (ACOSOG). Professor Güller underwent further fellowship training in surgical oncology (Society for Surgical Oncology programme) and minimally invasive surgery at the University of Toronto, Canada. He has authored and co-authored more than 140 articles and book chapters and became full Professor of Surgery at the age of 37. He is currently Head of Gastrointestinal Oncology at the Kantonsspital St Gallen, St Gallen, Switzerland. Professor Güller is married and has three children.

Markus Jörger

Kantonsspital, St Gallen, St Gallen, Switzerland

Dr Markus Joerger is an attending oncologist at Kantonsspital St Gallen, St Gallen, Switzerland, and Assistant Professor of Clinical Pharmacology at the University of Basel, Switzerland. He graduated from medical school at the University of Basel in 1996, completed a PhD entitled 'Pharmacogenetics and pharmacokinetics in solid tumor patients' at the Netherlands Cancer Institute, Amsterdam, Netherlands, and received his 'habilitation' in January 2012 under the supervision of Professor Krähenbühl, head of the Department of Clinical Pharmacology and Toxicology at the University Hospital of Basel. Dr Joerger is co-President of the Swiss Group for Clinical Cancer Research (SAKK) New Drugs Development Group and chair of the Working Group Phase III Studies of the CESAR study group.

Prospective, double-blinded, placebo-controlled, Phase III randomized trial of adjuvant aspirin treatment in PIK3CA mutated colon cancer patients

Despite curative intention, up to 50% of patients with colon cancer have disease that recurs after resection and adjuvant chemotherapy. To date, molecularly-targeted treatment has failed to improve the prognosis of patients with stage II and III colon cancer. However, new evidence has arisen that patients with PIK3CA-mutated colon cancer may derive a very substantial benefit from daily oral aspirin (Liao et al., *N Engl J Med* 2012;367:1596; Domingo E et al., *J Clin Oncol* 2013;31:4297). Both studies were retrospective, but showed about 85% risk reduction in tumour relapse in patients who received aspirin compared with patients who did not receive aspirin.

The objective of the present proposal is to confirm these results in a prospective randomized trial.

Tumours from consenting patients with stage II–III colon cancer after potentially curative resection will be screened for PIK3CA mutations. Patients with confirmed PIK3CA mutations will be randomized 2:1 to either daily aspirin or placebo over 3 years. With an expected proportion of 17% for positive PIK3CA-mutations, 1088 patients will be screened, and 185 patients will be included into the study. The primary objective is to show an improvement in 3-year disease-free survival from 70% to 85%, corresponding to a conservative hazard-ratio estimate of 0.5. Tumour tissue and blood samples will be stored centrally for future translational studies (e.g. evaluation of other predictive and prognostic markers).

The proposed Phase III randomized trial is expected to demonstrate a protective effect of aspirin in patients with PIK3CA-mutated colon cancer and to confirm the data from retrospective studies. The use of daily aspirin represents a simple and safe intervention. If the proposed Phase III randomized trial confirms the positive results from the above-mentioned studies, it would be a breakthrough in treating one of the most prevalent malignancies, resulting in a change of current clinical practice and would lead to tremendous patient benefit.

Winner of the GOI Award 2014

Clara Montagut

Hospital del Mar, Barcelona, Spain

Dr Clara Montagut, oncologist, is coordinator of the Gastrointestinal Cancer Unit in the Medical Oncology Department at Hospital del Mar, Barcelona, Spain. She specializes in colorectal cancer and, together with her team, she has achieved clinically relevant advances in the field of biomarkers for personalized medicine.

Dr Montagut graduated in medicine from the Universitat Autònoma de Barcelona in 1999 and completed her residency in Medical Oncology at the Hospital Clínic de Barcelona. She obtained her doctorate cum laude from the Universitat Autònoma de Barcelona in the field of personalized therapies. In 2007 she moved to the USA to complete a postdoctoral fellowship in the laboratory directed by Professor Jeff Settleman at the Harvard School of Medicine's Massachusetts General Hospital Cancer Center. She returned to Barcelona where she combines her clinical practice at Hospital del Mar with translational research on personalized medicine in colorectal cancer at Institut Hospital del Mar d'Investigacions Mèdiques (IMIM). Dr Montagut is the author of numerous research papers in leading journals such as *Journal of Clinical Oncology* and *Nature Medicine*, and she has conducted lectures and presentations at several national and international conferences.

Ultra-selection and molecular monitoring of colorectal cancer patients treated with anti-EGFR therapy using NGS platforms and serial liquid biopsies

The use of markers in the tumour or plasma of cancer patients that predict response to a specific drug has meant a major improvement in the treatment of cancer. RAS is a clinically established biomarker to select patients with metastatic colorectal cancer (mCRC) that may benefit from anti-epidermal growth factor receptor (EGFR)-based treatment with cetuximab or panitumumab. Unfortunately, not all RAS wild-type tumours respond to anti-EGFR therapy and all responding patients eventually develop resistance.

The Colorectal Cancer Translational Research Group at Hospital del Mar has been working on potential strategies to improve selection of anti-EGFR therapies. This is done by: a) improving selection of responding patients by using highly sensitive next-generation sequencing (NGS) platforms and validating other predictive biomarkers beyond RAS; and b) monitoring molecular resistance on serial liquid biopsies for the early identification of resistant mutations that arise during treatment. Such strategies may help to individualize further therapeutic decisions. We have recently identified mutations in the ectodomain of EGFR that cause acquired resistance to cetuximab.

The general objective of this project is to assess the clinical relevance of ultra-selection and molecular monitoring of colorectal cancer patients treated with anti-EGFR therapy with the use of NGS platforms and liquid biopsies. Specific aims of the study will be firstly to assess the sensitivity and clinical relevance of using NGS platforms in tissue samples from 500 patients with mCRC to establish a clinically relevant threshold for predicting efficacy to anti-EGFR therapies; and secondly to assess the sensitivity and clinical relevance of using plasma samples in patients with colorectal cancer treated with anti-EGFR therapy.

Winner of the GOI Award 2014

Stefan Sleijfer

Erasmus MC Cancer Institute, Rotterdam, Netherlands

Professor Stefan Sleijfer obtained his PhD from the State University of Groningen, Netherlands, in 1997. He is head of the Department of Oncology at the Erasmus MC Cancer Institute in Rotterdam, Netherlands, where he has worked since 2004. He has also been a research coordinator in Cancer Genomics and Proteomics in the same department since 2008. He has been full Professor in Translational Medical Oncology since 2011.

Professor Sleijfer is a board member of the Erasmus Trustfonds and a former chairman of the Translational Research Advisory Committee of the European Organisation for Research and Treatment of Cancer (EORTC). At present he is a member of the Scientific Council of the Dutch Cancer Society (Koningin Wilhelmina Fonds). Together with Professor John Foekens he coordinates the research line 'Translational Cancer Genomics and Proteomics'. His main research activities focus on soft tissue sarcomas, prognostic and predictive factors, biomarker-circulating endothelial cells and circulating tumour cells. He has published more than 150 papers.

Non-invasive monitoring of breast cancer therapy using cell-free tumour DNA in blood

Endocrine treatment is the cornerstone of treatment for patients with ERα-positive metastatic breast cancer (MBC). However, resistance inevitably occurs, probably due to emerging mutations in genes affecting endocrine sensitivity such as ESR1 (the gene encoding ERα) and genes of the PI3K-Akt-mTOR pathway.

Early detection of resistance and identification of the underlying mechanisms is essential to allow an early treatment switch to another treatment in an individual MBC patient. Preferably, such a treatment consists of an endocrine agent combined with a compound targeting the mechanism responsible for resistance. This requires constant monitoring of the molecular characteristics of metastatic cancer cells during treatment. But repetitively taking biopsies from metastatic lesions is a cumbersome procedure for patients and frequently not possible due to inaccessibility of lesions.

Circulating cell-free tumour DNA (ctDNA) in blood bears great promise as a non-invasive means to obtain 'liquid biopsies' from solid tumours. Such liquid biopsies can in principle provide the genetic landscape of all metastatic lesions at a certain point.

This project aims to obtain detailed molecular information on mutations of genes putatively involved in endocrine resistance by targeted next-generation sequencing of ctDNA in plasma of MBC patients before and during therapy with aromatase inhibitor–based treatment. The ultimate aim of this project is to determine which of the collected genetic information will be maximally informative to predict and monitor disease progression to eventually guide the choice of therapies, thereby further contributing to a more individualized treatment of MBC patients.

Chair of the Scientific Committee

Rolf A Stahel, MD

Clinic of Oncology, University Hospital Zürich, Zürich, Switzerland

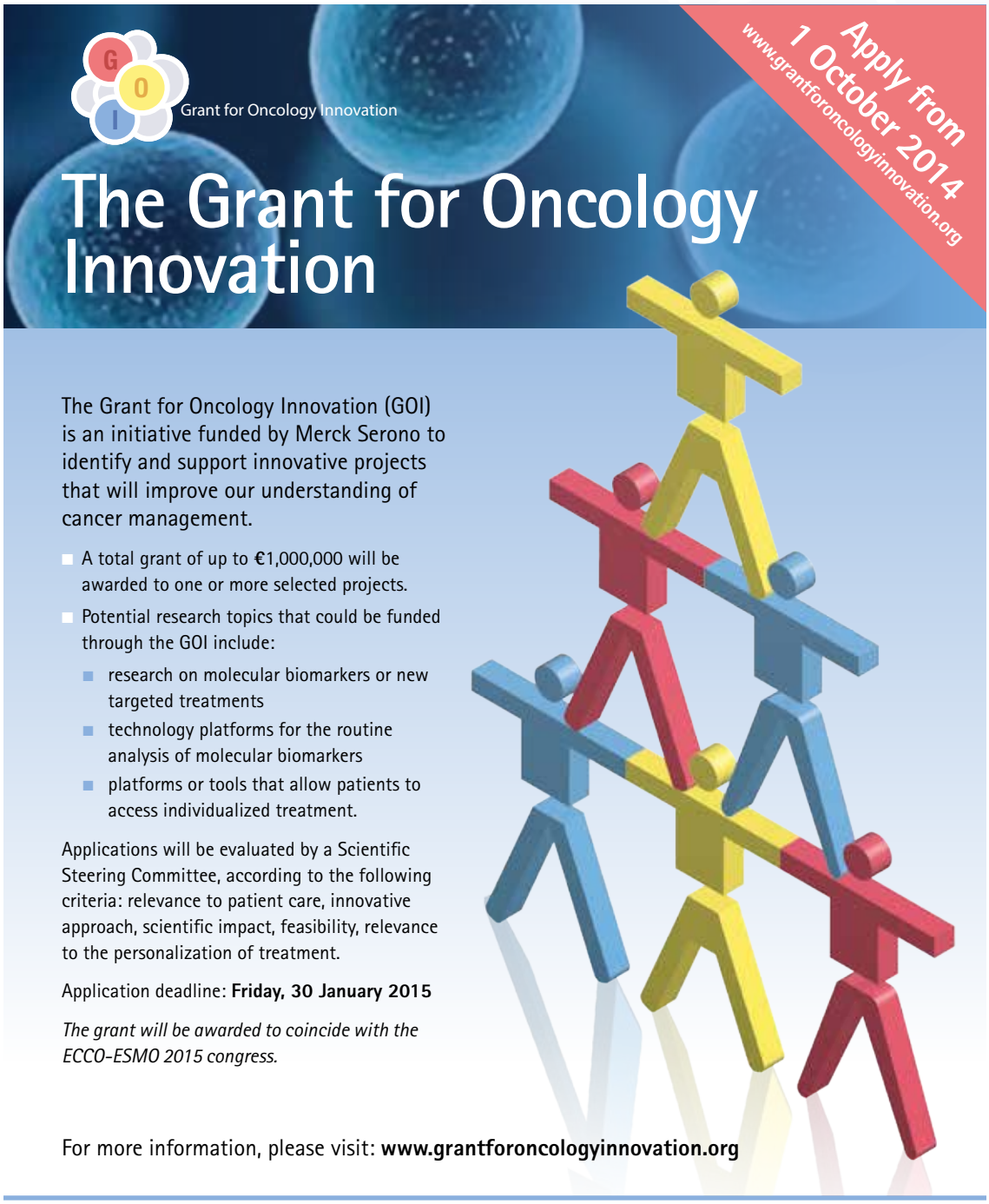
Professor Rolf A Stahel, MD, is head of the Center for Lung and Thoracic Oncology and Senior Staff Physician at the Clinic of Oncology at the University Hospital of Zürich, as well as Titular Professor of Medicine at the University of Zürich, Switzerland. He is certified in internal medicine and medical oncology by both the American and Swiss Boards. His major interest is thoracic oncology, including multidisciplinary treatment approaches, translational research and targeted therapy.

Professor Stahel was a founding member and the first president of the Swiss Society for Medical Oncology. He served as President of the Swiss Institute for Applied Cancer Research from 1999 to 2005. He is a member of the International Association for the Study of Lung Cancer (IASLC), where he served as chair of the fellowship committee and was a member of the board of directors until 2013. He served as National Representative of ESMO from 1998 to 2004 and chaired the ESMO Task Force on Guidelines from 1999 to 2005. He has also been a member of the ESMO board of directors and member of the Executive Committee since 2003, was the chair of the Educational Committee from 2006 to 2011, was President-elect from 2012 to 2013, and is currently the President of the Society (2014/2015).

In addition, Professor Stahel has been President of the Foundation Council of the International Breast Cancer Study Group (IBCSG) since 2008 and President of the European Thoracic Oncology Platform (ETOP), a foundation with the aim to bring together European collaborative groups and institutions focusing on research on thoracic malignancies, since 2009.

Professor Stahel is Editor-in-Chief of *Lung Cancer* and Editor of *Cancer Treatment Reviews*.

GOI 2015



The Grant for Oncology Innovation (GOI) is an initiative funded by Merck Serono to identify and support innovative projects that will improve our understanding of cancer management.

- A total grant of up to €1,000,000 will be awarded to one or more selected projects.
- Potential research topics that could be funded through the GOI include:
  - research on molecular biomarkers or new targeted treatments
  - technology platforms for the routine analysis of molecular biomarkers
  - platforms or tools that allow patients to access individualized treatment.

Applications will be evaluated by a Scientific Steering Committee, according to the following criteria: relevance to patient care, innovative approach, scientific impact, feasibility, relevance to the personalization of treatment.

Application deadline: **Friday, 30 January 2015**

The grant will be awarded to coincide with the ECCO-ESMO 2015 congress.

For more information, please visit: **www.grantforoncologyinnovation.org**

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Notes

GOI questionnaire

How did you first find out about the GOI award?

- ❑ Word of mouth/colleague (please give details in the space below)
- ❑ Journal/newsletter advert
- ❑ At ECCO 2013 – Amsterdam
- ❑ At ESMO 2014 – Madrid
- ❑ Via a Merck Serono contact
- ❑ Via another Merck Serono event
- ❑ At another non-Merck Serono event
- ❑ On a website

I first learned about the GOI award via...

_____

_____

Do you think the chosen studies will advance our understanding of the field of oncology?

❑ Yes ❑ No ❑ Don't know ❑ I don't have enough information to provide an opinion

How can Merck Serono improve the grant programme?

_____

_____

Would you like to receive more information about the grant, including the opportunity to apply?

Please write your email address in BLOCK LETTERS*:

_____@_____

* By giving Merck Serono your email address you agree to receive periodic emails from the GOI team about the grant. Your details will not be passed to anyone outside the GOI team.

Merck Serono's interest in Oncology

Merck Serono, a biopharmaceutical division of Merck KGaA, offers leading brands in 150 countries to help patients with cancer, multiple sclerosis, infertility, endocrine and metabolic disorders, and cardiovascular diseases. It focusses its oncology research on the development of therapies that target the tumour cell directly, the tumour environment and/or the immune system. These include a monoclonal antibody and an investigational hypoxia-activated prodrug.

Merck Serono has an enduring commitment to deliver novel therapies in our core focus areas of neurology, oncology, immuno-oncology and immunology.

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