

Cancer Center Amsterdam



Annual Review 2018

Amsterdam UMC Cancer Center Amsterdam

Cancer Center Amsterdam houses one of the largest oncology research centers in the Netherlands, joining cancer researchers from the Academic Medical Center and the VU University Medical Center Amsterdam. Our mission is to improve treatment, life expectancy and quality of life for patients with cancer and to reduce the impact of cancer on health care and society. With an integrated, multidisciplinary approach we bring findings from the laboratory into clinical practice. We believe that a better understanding of the underlying pathophysiology, combined with technical advances and patient-tailored novel combination therapies, is key to improve outcome for our patients.

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Preface

Complex care, multifaceted research

2018 was an eventful year for the Dutch healthcare sector with the bankruptcies of MC Slotervaart hospital and the IJsselmeer hospitals, and – at a different level – for our own hospitals with the administrative merger of AMC and VUmc to become **Amsterdam UMC**. The two developments have had and are still having an enormous impact on both staff and patients. Organizations that are in flux create uncertainty. Fortunately, they also offer opportunities.

Against this mixed background, we have been able to continue doing a lot of good work together, and this Annual Review is proof of it. We are a changing organization. This also applies to our oncological care and research. Oncological care at our hospitals will be gradually merged in the coming years, and move to the VUmc location. For the research, in anticipation of the administrative merger the oncological research institutes of AMC and VUmc already merged in 2016 into the joint **research institute Cancer Center Amsterdam**, and the institutes have been successfully working together.

Our research institute has over 1100 oncological researchers who jointly account for more than 1000 scientific publications. Within our three research programmes, researchers collaborate from a variety of disciplines. In 2018 too, this led to interesting insights that have been published in high-impact scientific journals, the obtainment of subsidies to finance our research, and ideas for new, innovative research. In this Annual Review, you can find highlights of the results we attained in the last year.

In all these activities and developments, it is our people who make the difference. They dedicate themselves day and night to our patients, at their bedside or in the lab. Together, we work towards a better standard of (early) diagnoses, personalized treatments and innovative medications, aiming to improve the quality of life of patients with cancer and lessen the impact of the disease.

We achieved a lot in 2018, and in the coming years we will keep up our efforts to improve prospects for our patients!

Prof. dr. Jan Paul Medema & Prof. dr. Henk Verheul

Co-directors research institute Cancer Center Amsterdam



Cancer Center Amsterdam a bird's-eye view

Patient care, research and training

Cancer is a disease that touches everyone. One in three people will get a cancer diagnosis at some point.

At Amsterdam UMC Cancer Center Amsterdam we work hard to provide around-the-clock care for our patients, who often face complex oncological issues. Our academic centre hosts patient care, research and training, all under one roof. This is a deliberate choice which ensures that our specialized doctors, nurses and researchers can work closely together. And our patients notice that: they receive good and professional care, and are treated according to the latest advances.



1128
researchers

596 scientific associates
512 PhD students
20 guest researchers

Mission and Vision

We want to deliver the very best care for patients with cancer, combined with innovative research and education by our physicians and researchers. In the process, we improve the quality of life of patients with cancer and reduce the impact of the disease on the healthcare system and society.

Patient care



Professional and complex care by specialized doctors and nurses



State-of-the-art treatment, participation in experimental treatments



Expertise centre for various types of cancer, second opinion, quick diagnoses



Supportive care such as psychological help, physiotherapy, diet and lifestyle consult



Amsterdam UMC's rating at www.zorgkaartnederland.nl

Research



Fundamental scientific research and clinical trials



More than 1100 researchers, about half of them doctoral candidates



145 principal investigators and 100 professors



Over 1000 scientific publications per year



About 80 dissertations per year

Training



Oncology Graduate School; all of the 500+ doctoral students are members



Annual CCA Retreat for all our researchers and physician-researchers



Oncology Course for doctoral candidates and clinical fellows



Patient care

Amsterdam UMC Cancer Center Amsterdam has expertise in the care of patients with cancer, including those who suffer from an additional condition, such as diabetes, cardiovascular disease, osteoarthritis and osteoporosis. We not only look at the disease of cancer, but at the whole person, because treatment of one condition can in fact influence treatment of a different disease. At Amsterdam UMC, all medical specialisms are represented on-site 24/7.

Expertise centre and second opinions

Patients can come to Amsterdam UMC Cancer Center Amsterdam for the treatment of virtually any type of cancer. For certain cancers, we are the expertise centre – the only or one of the few centres in the Netherlands offering treatment for a specific type of cancer. Patients can also come to our center for a second opinion. This is independent advice from a different medical specialist than the patient's own doctor. Hundreds of patients take advantage of this option every year.



Multidisciplinary teams

At our hospital, we work in multidisciplinary teams. This means that patients are discussed in a team of several physicians from different specialisms. In this way, diagnoses can be carefully established. We discuss which treatment is the most effective, and together with the patient we examine what fits with someone's personal situation and preferences. Cancer Center Amsterdam, together with collaborating partners, has a wide range of services and facilities available to make patients' lives as tolerable and as pleasant as possible – before, during and after treatment.



Deciding together

Increasing numbers of patients extensively consult the internet in advance, have a proactive disposition during the diagnosis and treatment process, and want to be intensively involved during the treatment trajectory. This makes the patient part of the care team, as it were. Physicians at Amsterdam UMC Cancer Center Amsterdam present the possibilities, and together with the patient decide on the preferred option. All facilities, the treatment process and our staff are set up to follow this approach to patients.



Quick diagnoses

Cancer Center Amsterdam offers quick diagnoses for certain types of cancer. This means that a diagnosis and treatment plan are available within 48 hours of the first appointment. In this short period of time, the results of the scans and the blood and tissue samples are known, the results are discussed with the involved physicians, and a plan is drawn up for the best way to treat the cancer.



Care in the region

Amsterdam UMC Cancer Center Amsterdam works together intensively with other care providers in the region. With these collaborating partners, we look at the best way to organize the care, in order to ensure that patients can count on the best-possible treatment, regardless of which hospital they choose. Collaborating partners of Amsterdam UMC Cancer Center Amsterdam include:



Since 2015, Amsterdam UMC Cancer Center Amsterdam has been actively involved in the programme 'Naar regionale oncologienetwerken' ('Towards regional oncology networking'), financed by the Citrien Fund (ZonMw). Details about this programme can be found on page 14 of this Annual Review.

Tumor workgroups and care pathways

For purposes of diagnosis and treatment, different specialisms collaborate in tumor workgroups, also known as care pathways. These workgroups organize multidisciplinary consultations (where agreements and treatment plans are defined), and every three months discuss healthcare and research developments with each other. Amsterdam UMC has the following tumor workgroups:

- Pulmonary oncology
- Neuro-oncology
- Breast cancer
- Urological oncology
- Gynaecological oncology
- Endocrine/thyroid cancer
- Sarcoma (bone and soft-tissue tumors)
- Dermatological oncology (especially melanoma)
- Head-neck oncology
- Haematology
- Retinoblastoma
- Upper GI (stomach/esophagus cancer)*
- Lower GI (colorectal carcinoma)*
- HPB (liver-pancreas-gallbladder carcinoma)*



* Gastro-Intestinal Oncological Center Amsterdam (GIOCA)



In 2018, we worked hard to improve patient information at the neuro-oncology nursing ward and the outpatient clinic of the Amsterdam Brain Tumor Center. Neuro care nurse **Myrthe Pelt** and neurology resident **Hinke van Thuijl** tell us about the new developments.



Hinke: 'Oncological care keeps increasing in scope as well as in complexity, and so do care-related questions. We notice this every day at the ward and at the outpatient clinic.'

Myrthe: 'Patients admitted to the ward have to deal with so much that we want to assist them during the entire care trajectory. Diligently informing patients is very important in this context. To offer more customized information we revised our brochures. These can also be used for communication between nurses and physicians. In this way, we optimize intermural and extramural bridges.'



Hinke: 'Patients receive much information during appointments, often from several physicians on the same day. It is likely that not all information is adequately absorbed. A patient information record, personalized to their trajectory which also includes contact information gives the patient a sense of control.'

Myrthe: 'At this point, patients receive information on paper, but we have started a pilot to offer digital data through the MediMapp app, which is used in other hospitals with great success. The improvement is that patients receive relevant information at the right moment in their disease course, and have this information readily available all the time. We are now adjusting the app to make it operational for our patients at the Brain Tumor Center Amsterdam.'



Hinke: 'The app also provides a solution for patients care-takers since it offers a convenient and user-friendly way to obtain information. We have started with glioblastoma, the most aggressive subtype with the most intense trajectory. In the future, we will expand this app for other types of brain tumors. Eventually, we hope to provide information for patients in all stages of the disease course, including the palliative phase.'



KNAW Bob Pinedo Cancer Care Award

On 22 November, Prof. dr. Martine Piccart, scientific director of the Institut Jules Bordet in Brussels, received the KNAW Bob Pinedo Cancer Care Award 2018 for her leading scientific contributions to the treatment of breast cancer. This prize is given biannually for excellent research by an international cancer researcher or research team. The prize is named after Prof. dr. Bob Pinedo, founder of Cancer Center Amsterdam. Before the awards ceremony, a symposium titled 'Think BIG: advances in breast cancer treatments' was organized with speakers Prof. dr. Liesbeth de Vries (UMCG), Prof. dr. René Bernards (NKI/AVL) and dr. Laurien Buffart (Amsterdam UMC), concluding with Prof. dr. Martine Piccart (Institut Jules Bordet). In her presentation, she stressed the importance of teamwork for future research.

AYA: 'Normal questions in abnormal situations'

Since late October 2018, Amsterdam UMC has an Adolescent & Young Adult (AYA) lounge at its AMC and VUmc locations. This is a spot where young adults (ages 18-35) with cancer can meet and share experiences, and where during a special AYA session there is the opportunity for one-on-one contact with an AYA nurse. Every year, 2700 young adults in the Netherlands get the news that they have cancer. During the treatment, as well as during the follow-up trajectory, they may have age- and life-phase-specific questions. According to Lobke Börger, haematology and oncology nurse at Amsterdam UMC, the impact of cancer and its treatments on this age group is large: 'A lot changes when you turn 18. You're probably finishing secondary school and may be planning to go live on your own and start a professional education. But there's also the period right after that, when you're about to join the job market, enter into a relationship and start a family – these are important milestones. Being sick can lead to a delay in your future plans and to social isolation, financial insecurity and a changed

self-image. These are issues that you could be dealing with when you come to AYA, so the support and guidance we offer can be of real benefit to these patients.' In spring 2018, nurses Lobke Börger and Lisanne van Harten received the Nursing Prize for founding the AYA lounge.



World Cancer Day 2018


Every year on February 4, cancer gets special attention worldwide. On and around World Cancer Day, organizations make joint efforts towards increasing awareness of cancer and informing people about options for treatment, prevention, early diagnosis and psychosocial care. In 2018 too, staff of the Cancer Center Amsterdam commemorated this date. To show support for our patients, we treated them to tasty macaroons.



 www.wereldkankerdag.nl

Skin Cancer Day 2018

Saturday 2 June 2018 was National Skin Cancer Day. Just like in previous years, dermatologists of Amsterdam UMC examined the skin of visitors who had registered via the Skin Cancer Day website. Every year we witness a rise in the number of patients who get a first diagnosis of skin cancer, which by now makes it one of the three most common types of cancer. One of the research focuses at Amsterdam UMC Cancer Center Amsterdam is melanoma, an aggressive form of skin cancer that can develop from benign and changing moles or from normal skin that did not originally contain a mole. Melanomas appear mostly between ages 45 and 60 and can metastasize, which is why timely detection and treatment is extremely important.

 www.huidkankerdag.nl



For the seventh consecutive year, on 21 October, Cancer Center Amsterdam was the good cause of the TCS Amsterdam Marathon. Throughout the years, the marathon has collected over €1 million for our cancer research. In 2018, the total amount was €167,982. This will be used, among other things, to investigate the impact of strength and endurance training on chemotherapy. With her research, dr. Laurien Buffart,

researcher at the Departments of Epidemiology & Biostatistics as well as Medical Oncology at Amsterdam UMC Cancer Center Amsterdam, hopes to answer the question of whether physical training during a chemotherapy cure contributes to better survival chances of patients with metastasized colon cancer. The results of this study can hopefully offer better supportive care to these patients in the future.

Interview with dr. Laurien Buffart:

Your research received a lot of attention in the run-up to the marathon – what was that like?

‘Of course, it’s really nice when the research you’re conducting receives attention, and to get the opportunity to tell people about it in lay terms on several occasions. The reactions were positive. It was also a really intensive period in which I sometimes had to get out of my “comfort zone”, for instance during recorded interviews and at the press conference. All of a sudden, you’re in the spotlight, with a large camera in front of you. It also meant that I regularly had to change my schedule around in order to be available at certain times. But all in all, it was fun and instructive to be a part of it.’

Have you already started with your research? When do you expect the first results?

‘Before we can start with the inclusion of patients we must get official authorization from the medical ethical testing committee. We hope to get the green light soon. The setup will be a multicentre study, so we will also be talking to oncologists from other hospitals to start including patients simultaneously. Each patient will be followed during primary care for 16-18 weeks (in connection with the treatment scheme). Partly depending on when we can actually start following up patients and the inflow tempo, I expect the first results after two or three years.’

Why are you focusing specifically on patients with metastasized colon cancer?

‘Previous studies show that nutrition and exercise can play a role in colon cancer. Previous observational studies on patients with colon cancer have shown that there is a connection between increased movement and better survival. Observational research of our Medical Oncology department has also shown that patients with metastasized colorectal cancer lose part of their muscle mass during three months of chemotherapy, and that loss of muscle mass is related to poorer survival chances. We cannot demonstrate a causal connection from this type of observational studies, though – which makes it unclear whether interventions aimed at maintaining muscle mass and endurance, such as strength and endurance training, can actually influence progression-free survival. This is why we want to study that.’

... and finally: Will you be participating again next year?

‘Yes, I’d love to! This year, I ran the 8k, but next year I hope to run the half marathon or perhaps even the full marathon, although that might have to wait another year. I’ve never run a marathon, but it’s definitely on my bucket list.’

Care in the region: towards regional oncology networks

The goal of the Citrien Fund, founded by VWS, is to improve care and make it more sustainable. The fund consists of five different programmes with more than 100 projects. The programme 'Towards regional oncology networks' works specifically on oncological care, focusing on improvement of care in the region through better collaboration. In the context of this programme, in recent years Amsterdam UMC Cancer Center Amsterdam has set up projects with several hospitals in the region with an emphasis on improving the consultation possibilities between specialists from different hospitals.

Interactive network meeting North-Holland/Flevoland

'Working in a network'. This was the central theme in the network meeting of Oncology Network North Holland/Flevoland that took place on 22 May 2018 in Amsterdam. Several presentations provided interesting insights as well as questions, including the following: What does the oncological network of the future look like? The preliminary conclusion: 'The network has to be a well-oiled machine, and together with the physician the patient determines the further design and pace of the care trajectory'.



Regional expert panels: 100th patient treatment recommendation released

In the online expert panel for metastasized colorectal cancer, imaging material is digitally presented to various specialists in the region, who then advise about the technical feasibility of local treatment of the metastases in the liver. This recommendation is included in the local multidisciplinary consultations, after which a definitive treatment plan is set up together with the patient. Project Manager drs. Tessa Hellingman: 'Being able to count on the expertise of multiple specialists during the local multidisciplinary consultations without them having to sit through the meeting physically or by phone constitutes great progress compared to how things used to be. We are proud of the fact that with these expert panels we have now been able to release our 100th recommendation, and are working hard at further improving the process and expanding the network.'

Project Coordinator drs. Eefje van Kessel MBA: 'It is wonderful to now be able to see the concrete, tangible results of our efforts. In recent years, our network has really expanded in the region. When we started in 2015, there were mainly one-on-one relationships between AMC, VUmc and surrounding hospitals in the North Holland and Flevoland provinces. Now there's much more of a unified network of hospitals. Our initiatives have intensified the various contacts between the hospitals in the region. The expert panel for metastasized colorectal cancer is a great example of that.'



Research

In 2016, anticipating the administrative merger of the hospitals in June 2018, the oncological research institutes of Academic Medical Center (AMC) and VU Medical Center (VUmc) joined forces as the allied research institute Cancer Center Amsterdam, which has since become one of the largest research institutes in the Netherlands.

At the Center, more than 1100 physicians and physician-researchers from various disciplines, including 500 doctoral candidates, work together in the field of cancer research. This includes fundamental scientific research that investigates the biological properties of cancer as a disease as well as clinically applied research whose focus lies on diagnosis/early diagnosis, treatment possibilities and issues related to quality of life.

Core facilities

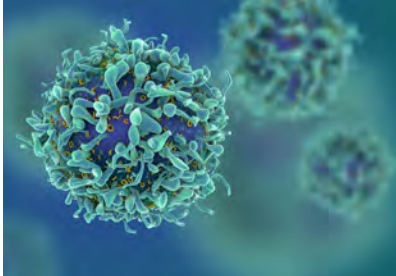
The research institute Cancer Center Amsterdam offers easy access to core facilities. These facilities are located close to the research units, to promote their individual and joint use. In addition to the availability of these facilities, the collaboration with the clinic and the teamwork within the multidisciplinary care pathways (see also page 9 of this Annual Review) are essential to our translational research.

Three research programmes

The goal of the eight allied research institutes within Amsterdam UMC Cancer Center Amsterdam being one of them – is threefold: 1. to improve the quality of scientific research; 2. to increase the possibilities of exchange, and 3. clinical studies for/by more patients. Within these goals, the focus at Cancer Center Amsterdam lies on early diagnosis, personalized therapy and improving the quality of life of patients with cancer. This focus translates into three research programmes, each with its own theme structure:

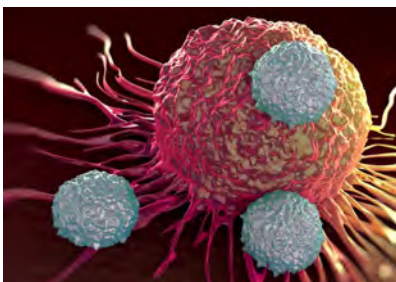
Programme 1: Cancer biology and immunology

Within this programme, basic cancer research is conducted in the field of cancer biology and immunology to better understand the physiology/pathophysiology of the disease of cancer and the immune system.



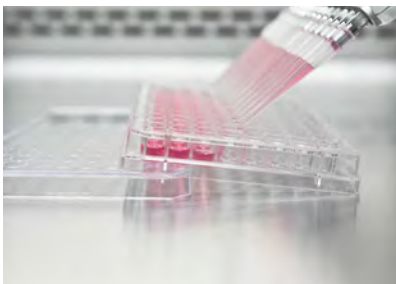
Programme leaders Cancer Biology

- Prof. dr. E. Eldering
- Dr. R.D.M. Steenbergen
- Prof.dr. L. Vermeulen
- Dr. R. Wolthuis



Programme leaders Cancer Immunology

- Prof. dr. M. van Egmond
- Prof. dr. T.D. de Gruijl
- Prof. dr. A.P. Kater
- Prof. dr. R.M. Luiten



Programme leaders Target Discovery & Pre-clinical Therapy Development

- Prof. dr. V.W. van Beusechem
- Prof. dr. R.H. Brakenhoff
- Prof. dr. K.K. Krishnadath
- Dr. M. Spaargaren

Programme 2: Imaging and biomarkers

The focus within this programme lies on potential diagnostic and predictive biomarkers and imaging techniques in order to detect cancer at early/earlier stages and offer personalized treatments.



Programme leaders Imaging

- Prof. dr. G.A.M.S. van Dongen
- Prof. dr. H.W.M. van Laarhoven
- Prof. dr. A.G.J.M. van Leeuwen
- Dr. J.M. Zijlstra



Programme leaders Biomarkers

- Dr. M.F. Bijlsma
- Prof. dr. E. Dekker
- Prof. dr. C.R. Jimenez
- Dr. D.M. Pegtel

Programme 3: Treatment and quality of life

The research within this programme focuses on the clinical implementation and evaluation of possible new treatment methods and the improvement of patients' quality of life.



Programme leaders Clinical Therapy Development

- Prof. dr. M.I. van Berge-Henegouwen
- Prof. dr. A.A. van de Loosdrecht
- Prof. dr. S. Senan
- Prof. dr. L.J.A. Stalpers



Programme leaders Evaluation of Cancer Care

- Dr. L.M. Buffart
- Dr. H. Klümpen
- Dr. M.G.H. van Oijen



Programme leaders Quality-of-life*

- Prof. dr. M.A. Grootenhuys
- Prof. dr. J.C. Reijneveld
- Prof. dr. M.A.G. Sprangers
- Prof. dr. L.M. Verdonck-de Leeuw

* On 1st of January 2018



Liquid biopsies

One year after the opening of the Liquid Biopsy Center of Amsterdam UMC Cancer Center Amsterdam in October 2017, bodily fluids (such as blood and urine) of over 500 patients from the AMC and VUmc locations have been taken and stored. These 'liquid biopsies' are used for cancer-research purposes. By collecting the bodily fluids of cancer patients, the appearance and growth of cancer cells in the body can be studied in a structured setting. In the long term, this can help develop better diagnostic tests and treatment plans for cancer patients.

At the Amsterdam UMC Liquid Biopsy Center (LBC), the bodily fluids of patients and healthy controls undergo standard storage procedures. 'What's unique about the LBC is that it's easier to exchange and compare data between study groups in the Netherlands and abroad', says dr. Michiel Pegtel, who heads the LBC

project. 'This increases the reliability of findings, and these can be implemented in practice, i.e. on the patient, sooner.' CCA researchers search in different ways for cancer in the blood, for example by examining small tumor vesicles (exosomes) and blood platelets, and now also circulating tumor DNA. For questions or to request blood for research, please visit www.liquidbiopsycenter.nl



In November 2018, LBC researcher dr. Florent Moulière was on the cover of the authoritative journal *Science Translational Medicine* with his article about a new method to detect tumor DNA in the blood of cancer patients. Read a brief interview with him on the right-side page.

Three questions for dr. Daniël Warmerdam (CRISPR-Cas expert)

1. What is CRISPR?

'CRISPR stands for Clustered Regulatory Interspersed Short Palindromic Repeats, and is a method used to modify DNA and RNA. CRISPR was discovered in bacteria, where it works as a sort of immune system to offer protection against viral infections. The properties of the CRISPR system enable us as scientists to edit the genome of any organism.'

2. How does this technology work?

'CRISPR makes recognition of specific DNA and RNA sequences by Cas proteins possible. After recognition, Cas cuts the corresponding DNA/RNA. The subsequent repair of the broken DNA/RNA sequence allows for very accurate modification around the cut location. So CRISPR can actually be seen as a toolkit that scientists

use to process DNA and RNA sequences very precisely and selectively by cutting and pasting.'

3. What possibilities does this technology offer?

'CRISPR offers many new possibilities for biomedical research and could be deployed in the future for clinical applications. To optimally benefit from the applications of CRISPR, our center has initiated the CRISPR platform and appointed me as CRISPR consultant. Via the CRISPR platform our researchers can find relevant information and request materials and protocols. Additionally, introductory and user meetings are being organised and I give advice and help with new applications.'

For more information about CRISPR:

<https://crispr.amsterdamumc.nl>

Interview with dr. Florent Moulière:

What are the results of your research?

'In our research, which was largely conducted in Cambridge, we examined what is known as "circulating DNA" – small broken pieces of DNA that come from dead cells roaming in the blood. It now appears that these small pieces of waste DNA can also predict whether cancer is present somewhere. We have investigated to what degree the size of these loose DNA molecules are relevant to the detection of cancer. To our great surprise, the length of the DNA pieces turned out to be very important, thanks to which we can now predict with greater certainty whether someone has cancer just by looking at their blood.'

What is the next step in your research?

'Examining the properties of circulating tumor DNA seems to be a promising route. We hope that in the future this will lead us to early detection of even small stacks of cancer cells by using relatively simple tools. And perhaps clinical applications can be devised, so that we can also treat cancer in the future with our technology. At our Liquid Biopsy Center, we are looking at different application possibilities.'

Being on the cover of a renowned medical journal is a rare feat; what reactions did you get from your professional environment?

'I got many nice, positive reactions from my peers, both at Cancer Center Amsterdam and abroad. Because of the publication, I am now in contact with many research groups at Amsterdam UMC for follow-up studies to see how we can apply this promising technique at the clinic. I suspect that they would have found the article anyway had it not been on the cover, but it's still quite an honour.'

Clinical trials

A lot of medical-scientific research can only be conducted when patients want to participate. It goes without saying that patients are extensively informed about the pros and cons of participating. For clinical trials that test medications, during the research it is closely monitored whether the treatment meets the expectations and whether there are any side effects. Patients do not always benefit from the study, but with their participation they help future patients. At Amsterdam UMC Cancer Center Amsterdam there are 350 clinical trials on average every year.

In May 2018, Carin Miedema was appointed to chart the clinical trials, and where necessary support physicians and researchers with the preparations to set up the trials. Carin works in the 'High-quality Trial Accelerating Program (TAP)' to improve the infrastructure surrounding clinical trials, aiming to further stimulate our translational research.



CCA-APP

In 2018, Cancer Center Amsterdam allocated financing to the CCA Ambulatory Patient Outcome Assessment Platform (CCA-APP project). The primary goal of this project is to realize a better embedding of supportive care (such as exercise, nutritional and psychosocial interventions) for inpatients and outpatients with cancer at Amsterdam UMC. Within the CCA-APP project, a digital platform will be developed to monitor physical and psychosocial problems of patients with cancer. In the long term, this platform can be deployed for further referrals to available supportive care interventions within Amsterdam UMC and in the region.

GLASS-NL: Research into the disease trajectory of mutated brain tumors

Every year, about 1000 people in the Netherlands are diagnosed with a brain tumor (glioma). Especially in young patients around age 40, this tumor is often defined as an 'IDH-mutant astrocytoma'. These IDH-mutant gliomas often start out as nonaggressive tumors that do not necessitate therapy yet, but later on they develop into aggressive tumors that require aggressive treatment. So far, it remains difficult to determine when treatment should start. In April 2018, the Glioma Longitudinal AnalySiS (GLASS-NL) study got started. GLASS-NL is part of a large international consortium that brings together experts in the assessment and treatment of gliomas. It received a subsidy of €1.2 million from the Dutch Cancer Society (KWF). On behalf of the Brain Tumor Center Amsterdam, part of Amsterdam UMC Cancer Center Amsterdam, Prof. Pieter Wesseling, dr. Mathilde Kouwenhoven, dr. Bart Westerman and Prof. dr. Mark van de Wiel participated in the GLASS-NL study. You can find more information about GLASS-NL at:

www.glass-consortium.nl

The first patient in the ADVANCE-II was administered the cancer drug DCP-001

In late 2018, the first patient in the ADVANCE-II study was administered the orphan drug DCP-001. A total of 20 patients with acute myeloid leukaemia (AML), a rare form of leukaemia, are participating in this phase-2 study. Haematologist Prof. dr. Arjan van de Loosdrecht: 'We are very pleased that the first patient in the ADVANCE-II study is being treated with the DCP-001 vaccine. This is an important study, in which we want to demonstrate the potential effectiveness of this cancer vaccine on patients who after previous treatment are still at risk of recurrence of this rare disease.' The ADVANCE-II study is a European collaboration between several hospitals, including Amsterdam UMC's VUmc location as central coordinator and various businesses (together the AML-VACcIN consortium), and is supported by a European Horizon subsidy. The results of the phase-1 study with DCP-001 were published in 2018 in the scientific journal *Cancer Immunology Immunotherapy*.

PERFECT study: Add immunotherapy to the treatment of patients with colorectal cancer

The standard treatment for patients with colorectal cancer without distant metastases consists of chemoradiotherapy followed by surgery. Despite this intensive treatment, about half of the patients still die of colorectal cancer within five years. Recently, 'checkpoint inhibitors' have been deployed for different types of cancer. This form of immunotherapy restores the ability of the immune system to recognize the tumor as foreign to the body. The nonrandomized PERFECT study investigates whether this form of immunotherapy (atezolizumab; PD-L1 inhibitor) also works for patients with colorectal adenocarcinoma without metastases in combination with preoperative chemoradiotherapy. Since 2017, 38 patients are participating in this phase-2 study at Amsterdam UMC's AMC location and at UMC Utrecht. A total of 40 patients will participate in this study. The clinical data will be analysed in 2018. Biomarkers in blood, tissue and stools will also be examined. Researchers are hopeful that this will lead to greater knowledge about possible predictors of response to therapy. This study was set up by oncologist Prof. dr. Hanneke van Laarhoven of the AMC location of Amsterdam UMC. Oncologist dr. Nadia Haj Mohammad is involved at UMC Utrecht.

LEOPARD studies: minimally invasive pancreatic surgery in the Netherlands

In 2013, a national training programme (LAELAPS) was started for minimally invasive pancreatic surgery. All the hospitals of the Dutch Pancreatic Cancer Group (www.dpcg.nl) participated in it. After the training programme, laparoscopic pancreatic tail resection was performed seven times more often, with improved results. Next, the national randomized LEOPARD trial compared minimally invasive pancreatic tail resections with the open approach. Results show that minimally invasive resection shortened the time to functional recovery by two days. After this successful introduction, there was increased interest in performing the more complex pancreatic head resections as minimally invasive procedures. A new training programme was developed (LAELAPS-2), followed again by a national randomized trial (LEOPARD-2). In this trial, laparoscopic pancreatic head resection was compared with the open approach. The trial was ended prematurely due to complications in the laparoscopic group, without patient gains. The results of the LEOPARD-2 trial led to worldwide discussions about the learning curve and the minimal annual volume of laparoscopic pancreatic head resections. At present, this procedure is not being performed in the Netherlands, but the DPCG has started the LAELAPS-3 training programme for robot-assisted pancreatic head resections.

External subsidies

External subsidies from subsidy sources like the Netherlands Organisation for Scientific Research (NWO), ZonMw, the Dutch Cancer Society (KWF) and the European Commission are crucial to making scientific research possible. Every year, our researchers apply for subsidies and financing from external organizations and institutes towards research and diagnostic equipment. Subsidy desks at Amsterdam UMC offer support to search for fitting subsidy options and prepare competitive applications. In 2018, multiple subsidies were once again granted to researchers of Amsterdam UMC Cancer Center Amsterdam.

Some of them are:

1

Pathologist Prof. dr. Daphne de Jong, of the prestigious European TRANSCAN programme, together with teams from Germany, France and Austria, received almost €1.7 million for their research into a rare form of lymphatic cancer. Of this amount, €400,000 will go to the Amsterdam UMC group via the Dutch Cancer Society.

Prof. dr. De Jong: 'It remains difficult to find out why T-cell lymphoma goes away or returns despite treatment. No biomarkers are known that can predict the disease either, so there are no new medications or better treatments on the horizon. With our research, we want to bring about changes in this respect.'

2

The Dutch Oncology Research Platform (DORP) is a facilitating infrastructure for researcher-initiated multicentre clinical cancer research financed by the Dutch Cancer Society for over €6.5 million. It strives for more, better-quality studies for more patients that are completed in time. The four cornerstones of DORP are statistical support, monitoring, project management and patient involvement.

Prof. dr. Punt (principal investigator of DORP): 'In the first six months of this project, Jacolien Coes was appointed as director, the work packages of the four cornerstones were set up, the basis was established for a governance structure in consultation with the national research groups, and several studies have already been selected for DORP support. In 2019, the formation will be expanded, and there will be a second call for studies that wish to make use of DORP.'

3

The submitted project, led by Prof. dr. Irma Verdonck-de Leeuw and titled 'Effectiveness and cost-utility of tailored psychological treatment targeting cancer patients with an adjustment disorder' received a subsidy from ZonMw in 2018.

Prof. dr. Verdonck-de Leeuw: 'In this study, together with our partners VU (dr. Femke Jansen), Radboud UMC (Prof. dr. Judith Prins), and IKNL (dr. Chantal Lammens), we will examine the clinical and cost effectiveness of personalized psychological care for adjustment disorders in patients with cancer. We also want to get a better understanding of how often these disorders affect patients with cancer.'

4 At the AMC location, Prof. dr. Marc van de Vijver has started an infrastructural study titled 'Bouwen in archipel van onderzoek naar ovariumkanker in Nederland', on ovarian cancer in the Netherlands. To this end, he received more than €1.2 million from the Dutch Cancer Society.

Prof. dr. Van de Vijver: 'We are very happy with the granting of this subsidy. It allows us to establish a national platform to research ovarian cancer in which several disciplines involved in the diagnosis and treatment of these tumors are represented.'

Publications

Amsterdam UMC Cancer Center Amsterdam publishes more than 1000 scientific articles in renowned journals every year. Below we highlight a few:

- Stem Cell Functionality is Microenvironmentally Defined During Tumor Expansion and Therapy Response in Colon Cancer. Lenos et al. in *Nature Cell Biology*, 2018
- Loss of Chromosome 18q11.2-q12.1 is Predictive for Survival in Patients with Metastatic Colorectal Cancer Treated with Bevacizumab. Van Dijk et al. in *Journal of Clinical Oncology*, 2018
- Consensus Statement on Mandatory Measurements in Pancreatic Cancer Trials (COMM-PACT) for Systemic Treatment of Unresectable Disease. Ter Veer et al. in *Lancet Oncology*, 2018
- Fixed Duration of Venetoclax-Rituximab in Relapsed/Refractory Chronic Lymphocytic Leukemia Eradicates Minimal Residual Disease and Prolongs Survival: Post-Treatment Follow-Up of the MU-RANO Phase III Study. Kater et al. in *Journal of Clinical Oncology*, 2018
- Phase I Dose-Escalation Study of Once Weekly or Once Every Two Weeks Administration of High-Dose Sunitinib in Patients with Refractory Solid Tumors. Rovithi et al. in *Journal of Clinical Oncology*, 2018
- MicroRNA 125a Regulates MHC-I Expression on Esophageal Adenocarcinoma Cells, Associated With Suppression of Antitumor Immune Response and Poor Outcomes of Patients. Mari et al. in *Gastroenterology*, 2018
- Robot-assisted Laparoscopic Implantation of Brachytherapy Catheters in Bladder Cancer. Boschieter et al. in *European Urology*, 2018
- Value of an Immediate Intravesical Instillation of Mitomycin C in Patients with Non-muscle-invasive Bladder Cancer: A Prospective Multicentre Randomised Study in 2243 patients. Boschieter et al. in *European Urology*, 2018
- Breast implants and the risk of anaplastic large-cell lymphoma in the breast. De Boer et al. in *JAMA Oncology*, 2018

Meet our new professors

Prof. dr. Knoop
Medical Psychology



Prof. dr. Van Berge Henegouwen
Gastrointestinal Surgery



Prof. Dr. Nederveen
Radiology and Nuclear
Medicine

Prof. dr. Sonke
Adaptive Radiotherapy



Prof. dr. Amant
Gynecological Oncology



Prof. Dr. Besselink
Pancreatic and
HepatoBiliary Surgery



Dissertations

Every year about 80 PhD students take their degree at Amsterdam UMC Cancer Center Amsterdam. The image above is made up of the covers of last years' dissertations.



Nieuwsuur, 4 January 2018 **Daphne de Jong**



Nieuwsuur, 19 January 2018 **Tom Würdinger**



Zorgvisie, 22 January 2018 **Hans Knoop**



De Volkskrant, 5 February 2018 **Jorine de Haan**



AT5, 14 March 2018 **Idris Bahce & Michiel Pegtel**



NRC, 6 April 2018 **Arnon Kater**



De Volkskrant, 24 April 2018 **Hanneke van Laarhoven**



Elsevier, 1 May 2018 **Geert Kazemier**



Het Financieele Dagblad, 23 May 2018 **Hans van der Vliet**



AVRO/TROS, 4 June 2018 **Evelien Dekker & Marcel Spaargaren**



RTL.nl, 17 June 2018 **Arjan Griffioen**



NU.nl, 25 July 2018 **Arjan Griffioen**



Editie.nl, 19 September 2018 **Simone Eerenstein**



AD.nl, 18 September 2018 **Geert Kazemier**



Radar+, 1 October 2018 **Irma Verdonck**



Vraag Vandaag, 5 October 2018 **Tom Würdinger**



Algemeen Dagblad, 11 December 2018 **Sarah Derks**



Noordhollands Dagblad, 12 December 2018 **Tessa Hellingman**



Research in national media

PICTURE

Awards: Picture Project wins two SpinAwards

During the SpinAwards ceremony on 25 April 2018, the neurosurgical team of Amsterdam UMC Brain Tumor Center Amsterdam was honoured twice. The development of the technically complex PICTURE tool (in collaboration with digital design and development agency 'Active Collective') earned a silver and a gold award. Neurosurgeon dr. Philip de Witt Hamer: 'Thanks to our tool, specialists all over the world can easily share treatment information on brain-tumor patients. We can send each other the available imaging material, making it possible to share surgical results with each other. This creates a standard with which we can improve the treatment of brain tumors.'

But many more awards have been won in 2018. Below are a few examples:

Lianne Vriend won the FARF Tank Award at the Fanconi Anemia Research Fund symposium in Newport Beach (USA).

Remco Molenaar won the CCA PhD thesis award

Bas Koster won the CCA Publication award

Geert Kazemier won the '2 handen op 1 buik' award of the Maag Lever Darm Foundation

Jisce Puik received the Nijbakker-Morra award and the AACR-Warner Fund Scholar-in-Training award

Jony van Hilst received two awards during the International Pancreas Club conference in Washington

Connie Jimenez was nominated for the VIVA400

Jens Voortman won the 2017 PCF Challenge Award together with Otto Hoekstra and Gem Kramer

Tommy Solinge received the Professor Chris Gips Student Award



Training & Education

Amsterdam UMC, in collaboration with the University of Amsterdam (UvA) and Vrije Universiteit Amsterdam (VU Amsterdam), offers training education for students, physicians and scientists.

The UvA, via the Biomedical Sciences Master's programme, offers an oncology trajectory that includes topics such as elementary cell and molecular biology, genetics, and development of new strategies for the diagnosis and treatment of cancer. The VUmc School of Medical Sciences offers Bachelor's and Master's programmes and the Zigma graduate entry programme, as well as a Master's in Oncology, a Master's in Cardiovascular Research and the post-initial Master's programme in Epidemiology. Students are trained and an investment is made in the further professionalization of teachers and educators in medical education and specialization programmes.

The Master's in Oncology aims at understanding molecular mechanisms involved in the growth of cancer cells and the effect of this disease on patients' lives, morbidity and risk factors. During this Master's programme, students learn about the emergence and development of cancer and about treatment possibilities, and are trained in state-of-the-art techniques used in assessment and therapy.

Oncology Graduate School Amsterdam

The Oncology Graduate School (OGS), which all of our 500+ doctoral candidates are member of, plays an important role in the training and educational programmes for our doctoral candidates. The OGS is a joint research school of the VUmc and AMC locations of Amsterdam UMC and the Dutch Cancer Institute - Antonie van Leeuwenhoek Hospital (NKI-AVL). The OGS has been accredited since 1993 by the Royal Netherlands Academy of Arts and Sciences (KNAW) and has a long tradition of offering solid educational programmes. The three-day annual retreat for doctoral candidates is one of the OGS activities that contribute to maintain and build on an active network of oncological researchers.

In addition to the activities of the OGS, during the year various seminars and symposia are organized by Cancer Center Amsterdam post-doc researchers (Post-doc Alliance Initiative) and doctoral candidates (CCA Next and CCA Seminars).

Event: Retreat 2018

On 15 and 16 February 2018, more than 400 AMC and VUmc basal and clinical researchers participated in the annual Cancer Center Amsterdam retreat at Conference Centre Leeuwenhorst in Noordwijkerhout. For two days, they updated each other on the latest ins and outs of cancer research. Internationally renowned top researchers gave talks, and 54 doctoral candidates and postdocs presented their work during the various parallel sessions.



Visiting Prof. dr. Cornelis Murre

Invited by researchers Bart Westerman (Amsterdam UMC, location VUmc), Nicolas Leveille and Louis Vermeulen (both at Amsterdam UMC, location AMC), in spring 2018 Prof. dr. Cornelis Murre began a two-year association with Amsterdam UMC Cancer Center Amsterdam. In summer 2018, Dutch-born Prof. dr. Murre came for two months from his current home base, the University of California San Diego, to lecture and teach. This included a well-attended course on functional genomics, which will be repeated in 2019, and a very inspiring CCA seminar. In the two years that Prof. dr. Murre is appointed as visiting professor, together with CCA researchers he will study intercellular heterogeneity in gliomas and intestinal tumors.



Oncology Course

On 9 July, 50 doctoral candidates and clinical fellows gathered to participate in the first Oncology course of the CCA. During a five-day intensive programme, all eight CCA research topics were discussed. The goal of these five days was to establish a solid basis, from basal cancer biology to oncological care.



Quote of an Oncology course participant:

'Because of my studies, I already knew a lot about the topic, but it was very useful to refresh this knowledge and hear about new developments in the field of oncology.'

Internal subsidies: CCA Travel Grant

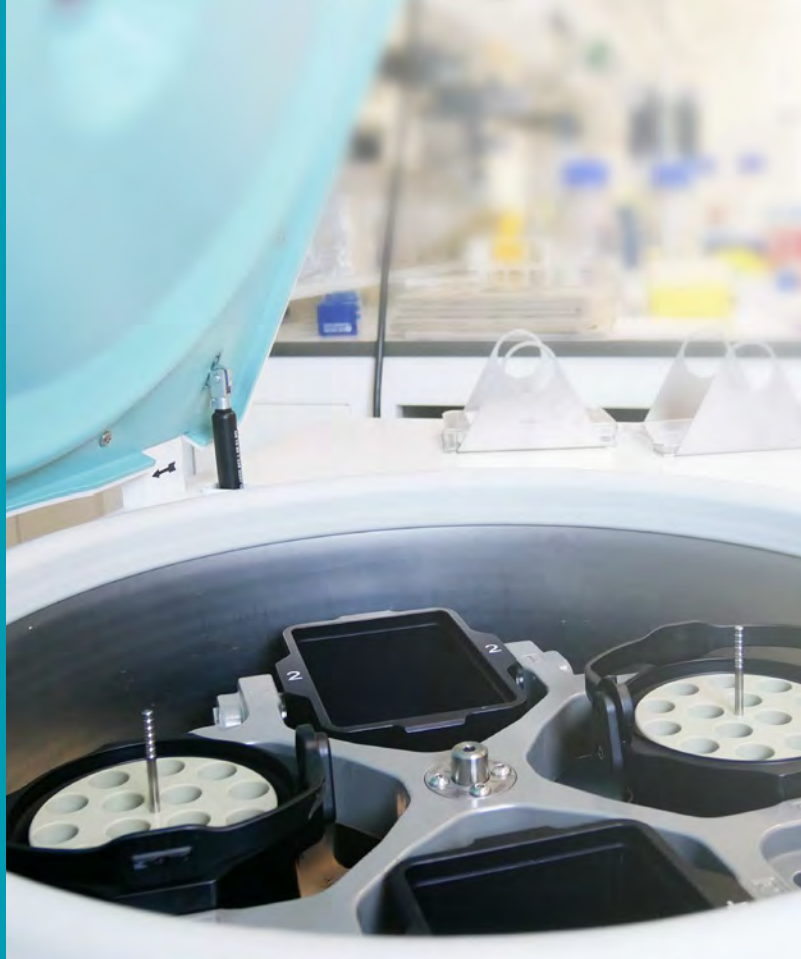
In July 2018, ten doctoral candidates and postdocs of Amsterdam UMC Cancer Center Amsterdam received a travel grant from the Center for a total amount of **€25,000**. Thanks to this grant, they have been able to learn new research techniques abroad and develop them further. The researchers have travelled to various institutes, including the University of Michigan Hospitals and Health Centers (USA), the Norwegian University of Science and Technology (Norway) and the University of Liverpool (UK).



PhD student MDL oncology group
Sanne Hoefnagel:

"I visited the lab of Professor Stoecklein, at the Heinrich-Heine-University in Düsseldorf Germany. His lab is specialized in single cell isolation and analysis. Lab members showed me various techniques for cell selection, such as the DEParray, CELLSEARCH for circulating tumor cells from the blood and FACS.

It was a very interesting work visit, I learnt a lot, techniques that I can teach my CCA colleagues. I will certainly continue our collaboration with Prof. Stoecklein and his colleagues."



Fundraising Foundation

For more than 30 years, VUmc Cancer Center Amsterdam has been involved in research to make early detection and better treatment methods possible for people with cancer. Throughout the years, thanks to gifts from donors and special fundraising activities at Cancer Center Amsterdam, the Foundation has been able to financially support cancer research and purchase diagnostic equipment.



We are very thankful for the trust and the financial support we have received from the Foundation VUmc Cancer Center Amsterdam. Do you want to help us reach our goals? Please contact Foundation VUmc Cancer Center Amsterdam via +31 (0)20 444 1058 or cca@vumc.nl



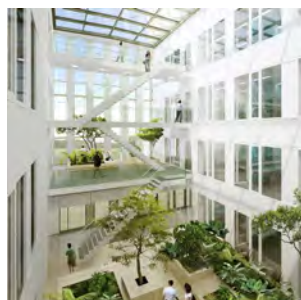
Prof. dr. Geert Kazemier, oncological surgeon and director of the Foundation VUmc Cancer Center Amsterdam:

'At the moment, we are recruiting funds for a new initiative, the ADORE project. In this project, we bring together the research fields of oncology and neurology. ADORE stands for Amsterdam Oncology and Neuroscience Research. Together with neurologist Prof. dr. Philip Scheltens and our colleagues, we are convinced we can learn from each other to further innovate our research. We are using the same techniques and conduct research in the same way into invasive, mostly complex and prolonged diseases. By bundling our brainpower and sharing our techniques, we can challenge each other to look at things differently. That is very exciting.'



With the support of our donors, we are able to conduct groundbreaking research into cancer, thus making a real contribution to the well-being of our current and future patients.

Design for the future-proof accommodation of the ADORE project



working at Amsterdam UMC

Do you want to join us to make a difference?



Our people make the difference. Together, we strive to give patients with cancer the very best care and conduct innovative research. We want to improve the quality of life of patients with cancer, and hope to reduce the impact of this disease on the healthcare system and society.

Are you interested in a career at Amsterdam UMC Cancer Center Amsterdam? Take the first step and visit one of our websites, which contain extensive information about working in patient care or research.



Patient care: www.werkenbijvumc.nl



Research: www.amsterdamresearch.org

Colophon

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