



Three Year Research Strategy 2017-2020

Filling the Research Gap

Three year research strategy

This document is designed to lay out Oracle Cancer Trust (Oracle's) Research Strategy for the three years between 2017-2020.

At the time of writing (March 2017), Oracle is funding ten pioneering head and neck cancer research projects on a range of exciting topics. The Charity aims to increase this number to 18 by the end of the three years to December 2019.

Produced by Oracle's Research Innovation and Advisory Committee¹, this Research Strategy outlines what research Oracle is seeking to fund and why as it aims to meet its ambitious goal. This Research Strategy has been approved by Oracle's Board².



Oracle's vision



Over the past five years, Oracle has invested over £2million in world class research programmes. As a direct result of Oracle's pioneering research work, more head and neck cancer patients are now receiving successful treatment and are suffering with significantly fewer immediate and long-term side-effects.

Moreover, Oracle's work is vital. By focussing on funding early stage research and proof-of-concept projects, Oracle is laying the scientific foundations for larger-scale clinical trials and commercial research. Oracle is filling a 'research gap'. Despite this, Oracle receives no government funding and relies entirely on charitable donations to carry out its vital work.

About head and neck cancer



Head and neck cancer refers to cancers originating in the tissues of the head and neck region (between the base of the brain and the collar bones). Head and neck cancer refers not to one single cancer type but to several distinct sub-types.

The variety of tumour types reflects the diverse tissues in the head and neck region and includes oral cavity, oropharyngeal, laryngeal, hypopharyngeal, sinus, salivary gland and thyroid cancers.



4% of all cases of cancer nationally³ and 6% globally⁴



Third fastest growing type of cancer in the UK⁵



Incidence of oral cancer has increased by 90% since the 1970s⁶



31 people are diagnosed with head and neck cancer every day in the UK⁷

Head and neck cancers are as complex as other cancers but also present some particular issues. The head and neck area has many critically important and delicate organs in close proximity; treating a tumour in one area will often have serious effects on other surrounding organs.

These cancers affect a very visible part of the body where many of the vital senses (smell, taste, sight, hearing) are located and the cancers and current treatments can affect some of the most important functions such as speaking, swallowing and even breathing.

There is an urgent need to develop better and kinder treatments for patients.

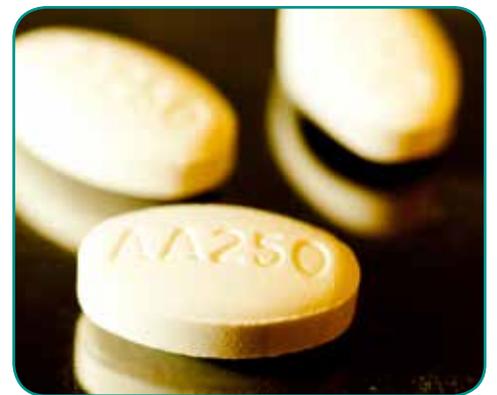
Oracle's Research Strategy

Oracle Cancer Trust's strategy is to provide full or joint funding for research projects that help improve outcomes for patients. This includes projects focussed on the detection and treatment of head and neck cancers and those focussed on preserving the senses and improving quality of life of those affected.

Oracle understands that it is unlikely to be able to take a potential project from inception to full regulatory approval given the considerable sums involved in large-scale clinical trials. However, there is a clear gap in research funding for proof-of-concept, early stage work. The large funders of research are unwilling to support work at this early stage in the research process.

For a research concept to reach a level where it can be taken up by one of the large grant-funding bodies it needs 'pump priming' or 'piloting' and that is where Oracle can add the most value. Additionally some research projects, because they focus on areas that cannot be commercialised or in the modern NHS are deemed unprofitable, are not of interest to pharmaceutical companies or other major funders of research; here too Oracle can fill a research funding gap.

Oracle will support projects at hospitals and research institutes in the United Kingdom that can demonstrate a commitment to research in head and neck cancers. The Institute of Cancer Research, given its leading role in the sector, provides the vast majority of current projects Oracle supports. However Oracle is also supporting a project at Addenbrooke's Hospital (part of the Cambridge University Hospitals). Oracle is keen to widen the localities for its research grants and is actively seeking high quality projects from other head and neck centres in the UK.



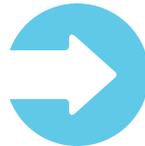
“Oracle’s funding helps fill the gap that exists between a scientist or a head and neck cancer specialist seeing the need for a particular area of research and the point at which larger research funding bodies or pharma companies can get involved.”

Tom Bland – Deputy Director,
The Institute of Cancer Research

Oracle's Research Pillars

Oracle's research funding is based on four key pillars in relation to head and neck cancers

Radiotherapy



Cure More, damage less
Real-time adaptive therapies
Modulating dose - minimising side-effects

Immunotherapy



Virus therapies
Gene-Directed Enzyme Prodrug Therapies
Combining therapies to improve efficacy
Immune checkpoint inhibitors

Surgery



Robotic techniques
Patient Selection
Real-time analysis

Detection, prediction,
monitoring, selection and
analysis



Imaging methods
Biomarker test development
Improving diagnosis

Radiotherapy

Radiotherapy is a key treatment for head and neck tumours, either alone or in combination with chemotherapy. But current radiotherapy techniques can cause serious side-effects for patients.

Oracle is looking to support research projects that either increase the effectiveness of radiotherapy or reduce the damage caused to patients by its use, particularly where such damage affects functionality.

Cure more, damage less

Oracle would be excited to fund projects developing methods for determining patient suitability for radiotherapy treatments; looking at the impact of combining radiotherapies with chemotherapy or drugs; and looking to combat tumour resistance to radiotherapy.

Example Oracle Project

Oracle is currently funding PhD student Elise Lepicard of the ICR to examine novel agents to increase sensitivity of tumours to radiotherapy

Real-time adaptive therapies

Oracle is passionate about funding the most innovative projects. The development of pioneering real-time adaptive therapies which can precisely locate tumours, tailor the shape of X-ray beams in real-time, and accurately deliver doses of radiation even to moving tumours, has hailed an exciting new era for radiotherapy as has the development of novel proton beam therapies.

Oracle is excited to fund projects in this domain and is already funding one project at the new MR Linac facility.

Modulating dose - minimising side-effects

By modulating the dose of radiation applied to and around a tumour, radiotherapy can be targeted and surrounding normal tissues spared. This can reduce the burdensome side-effects incurred by patients such as dry mouth, swallowing difficulties, speech loss and osteoradionecrosis.

Example Oracle Project

Oracle is currently funding Clinical Research Fellow, Dr Imran Petkar, on a first-of-its-kind Swallowing Project; under the guidance of Professor Chris Nutting, Imran is examining how modulating radiotherapy dosage can preserve swallowing function.



Example Oracle Project

MR Linac - revolutionising radiotherapy

Oracle is currently funding a PhD student to undertake a cutting-edge computational project at the ICR's Division of Radiotherapy and Imaging.

Under the guidance of Professor Uwe Oelfke (pictured), Jennifer Kieselmann is designing software that will allow clinicians to automatically define the boundaries between normal head and neck tissues and cancerous tumours on MRI images.

It is hoped that the work will help to support the development of real-time adaptive radiation therapies such as those that will be delivered by The Royal Marsden Hospital's revolutionary new MR Linac machine.

Immunotherapy

The ability of immunotherapies to specifically target tumour cells without conferring toxicity to surrounding cells has made the therapies a promising prospect for researchers, particularly in head and neck cancers in which the side-effects to surrounding tissues can be so damaging.

While researchers have been exploring the potential benefits of such therapies since the 1970s, recent developments have provided cause for real excitement and Oracle is excited to support novel research in the sphere over the coming months.

Virus therapies

Therapies which take advantage of oncolytic viruses- those which preferentially infect and kill cancer cells- have been a promising area of research over recent years. Oracle has already invested funding in a number of these projects, including Dr Martin McLaughlin's project (see right).

Gene-directed enzyme prodrug therapies

Another type of targeted therapy which has shown marked promise and in which Oracle is keen to invest funding is that of Gene-Directed Enzyme Prodrug Therapies.

Example Oracle Project

Guided by ICR team leader, Professor Caroline Springer, Oracle is funding the costs of a postdoctoral scientist to engineer a virus to deliver a cancer-killing therapy straight to cancer cells, using a technique known as Gene-directed enzyme prodrug therapy (GDEPT).

Combining therapies to improve efficacy

By using immunotherapies in combination with traditional treatments such as chemotherapy and radiotherapy, it is hoped that cancer cells can be targeted more effectively, increasing the efficacy of combination therapies as compared to monotherapies and in effect providing in-situ vaccination against cancer recurrence.

Example Oracle Project

Oracle is funding PhD student Victoria Roulstone of the ICR to combine oncolytic viruses - viruses that preferentially infect and kill cancer cells- with a number of conventional therapies to test the efficacy of over 80 combination therapies for head and neck cancer.



Example Oracle Project

Reovirus Study

Oracle has agreed funding for a project studying the ability of viruses to induce cancer cell death.

The pioneering study at the ICR, led by Professor Harrington and conducted by post-doctoral researcher Dr Martin McLaughlin, will specifically investigate the ability of a particular class of virus - reovirus - to kill cancers cells by increasing the cancer cells' visibility to the body's own immune system.

The ability of immune therapies to specifically target tumour cells without causing toxicity to surrounding cells has made these therapies a promising prospect for researchers.

Surgery

For a number of years, surgery, although a key part of the treatment of head and neck cancers, has not received proportionate support, either in funding or research.

Surgery is generally considered the gold standard for head and neck cancer treatment. This makes investment in more precise and efficient forms of surgery even more important and a key research priority for Oracle.

Robotic techniques

Surgical advances are rarely commercializable and therefore not regarded as a 'profit centre' for the public or private sectors. However, advances in robotic surgery provide a compelling opportunity for collaboration between traditional clinicians and technologists and a potential source of interest for commercialization.

Oracle is keen to investigate opportunities to fund new research in the field and Founder and eminent ENT surgeon, Peter Rhys Evans, has personally begun to explore opportunities (see right).

Patient selection

Stratifying patients to provide personalised therapies minimises the risk of adverse or unnecessary treatments or side-effects.

Oracle are looking to fund projects looking to develop new methods for determining how to best select patients for the most appropriate surgical techniques.

Real-time analysis

Real-time analysis aiding surgical accuracy is a growing area of interest.

For example, methods such as biomarking or histochemical staining of tumours can serve to provide a visual guide to the location of the interface between tumour and healthy tissue.

Oracle are keen to fund research developing similar or novel techniques to help improve surgical outcomes for patients.



Peter Rhys Evans, Oracle Chairman and Founder

Peter Rhys Evans is one of Europe's most eminent Cancer ENT Surgeons and was an early pioneer in new techniques of laser conservation surgery and reconstruction of the voice mechanism in the early 1980s.

Peter and his team have developed many innovative techniques over the years and was formerly Chief of ENT/Head and Neck Surgery at The Royal Marsden Hospital in London.

Currently he is involved in developing new robotic surgical techniques for tumours of the throat and is working on a training project for the Oracle Cancer Trust named "Karsten Schubert Robotic Surgery Research Fellowship."

Detection, prediction, monitoring, selection and analysis

Early detection of cancer or of metastasis is one of the largest components in the successful treatment of head and neck cancers.

Work that allows prediction of whether and how a cancer may spread allows clinicians to target treatment both in terms of location and intensity. Similarly, projects developing methods to support clinicians in selecting the most effective and least invasive treatments for patients are crucial to improving outcomes.

Imaging methods

Innovative imaging techniques such as MRI, fMRI, PET and CT scanning have provided scientists and clinicians with the opportunity to visualise cancers in entirely new ways.

Oracle is currently funding a number of projects pioneering the use of imaging to visualise tumours and biomarkers in order to analyse the effect of treatments and tumour behaviour. One such Oracle project is being carried out by Dr Gabriela Kramer-Marek of the ICR (see right).

Biomarker test development

The development of biomarker tests and analyses to allow clinicians to detect head and neck cancers before and during treatment and to predict the efficacy of treatment regimes is vital to the early detection and management of cancers.

Example Oracle Project:

Dr Furrat Amen of Addenbrooke's Hospital in Cambridge is currently undertaking an Oracle-funded study to look at whether we can identify biomarkers which differ in patients with metastatic tongue cancer to those whose cancers do not metastasise.

Improving diagnosis

Finally, projects focused on increased, quicker and more precise analysis of cancers can help to overcome issues associated with misdiagnoses or the prescription of inappropriate treatment regimes.



Imaging Biomarkers of Resistance in head and neck cancer

Drug resistance is one of the main problems in cancer research today.

Despite the fact that we use standard chemotherapies or targeted therapy drugs, the responses of tumours are highly variable. Therefore, developing ways of predicting which patients will respond to which treatment is a key aim in current research.

Dr Kramer-Marek is building on groundbreaking work she has undertaken in other cancer types to use imaging to measure the presence of key molecules of interest (or 'biomarkers') in cancer cells and assess how we can use the levels of these biomarkers in a tumour to predict the likelihood a tumour will or won't be resistant to treatment.

Conclusion

The developments in cancer research move at an incredible pace and, whilst it is important to lay out our research pillars on a tri-annual basis, the Charity cannot hope to cover every potential research opportunity.

Oracle are already supporting worthy projects that do not fall within our research pillars such as Dr Amanda Swain's work on Adenoid Cystic Carcinoma, a rare cancer of the salivary glands (see right) and will continue to review all research projects submitted.

Oracle also encourage applications from all suitable UK institutions as part of our current outreach programme.

2017 has already been a fantastic year for Oracle Cancer Trust funded research with a number of projects being published in medical and scientific journals and proof-of-concept work funded on the CHK1 Inhibitor being taken forward to a potential treatment that can improve outcomes for patients of head and neck cancers.

In summary, Oracle hopes that this document will give guidance to research applicants on the Charity's focus, and also demonstrate to donors, and potential donors, the commitment and passion in funding high quality research that can lead to a real difference to patients' lives.



Analysing new therapeutic options for adenoid cystic carcinoma (ACC) of the salivary glands.

Oracle is currently funding a PhD researcher, working for Dr Amanda Swain (pictured), in determining whether existing targeted therapies may be effective in treating ACC of the salivary glands.

Adenoid cystic carcinoma is a cancer of the salivary glands and is not a research area that has been previously funded by Oracle.

There is no curative or palliative treatment and patients will eventually succumb to the disease. This is a first-of-its-kind project into a cancer type about which little research has previously been undertaken.

¹Oracle's Research Innovation and Advisory Committee comprises of Professor Kevin Harrington, Professor Chris Nutting, Dr John Glaholm and Peter Rhys Evans

²Oracle's Board comprises of Peter Rhys Evans, Keith Jones, Sir Michael Lockett, Nicola Ridges-Jones and Jamie Newall

³2014 England figures - calculated from ONS and Cancer Research UK data

⁴2012 figures - calculated from American Cancer Society and WCRF data

⁵2001-2014 England figures - calculated from ONS, Cancer Research UK and NHS England data

⁶Cancer Research UK, Cancer Statistics by Cancer Type - Oral Cancer: <http://www.cancer-researchuk.org/health-professional/cancer-statistics/statistics/statistics-by-cancer-type/oral-cancer> (October 2016)

⁷This compares to an incidence of 55,000 cases/year of breast cancer and 2,300 cases/year of testicular cancer; <http://www.macmillan.org.uk/documents/aboutus/research/rich-pictures/update/rp-people-with-head-and-neck-cancer.pdf>

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Professor Kevin Harrington



Oracle Cancer Trust,
32-36 Loman Street
London SE1 0EH