Imperial College London

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

ASCARA

Multinational Anal Squamous Cell Carcinoma: Registry and Audit

Information for Researchers

Chief Investigator

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IRAS: 249488

Introduction

Anal Squamous Cell Carcinoma (ASCC) is an uncommon cancer with an incidence rate between 1 and 2 per 100,000 per year. The incidence of ASCC is increasing rapidly, with an overall 63% increase in incidence rate of ASCC in the UK since the 1990's. However, there is much discrepancy in best surgical practice for the treatment and prevention of ASCC.

As ASCC is a rare cancer it is difficult to gain sufficient patient numbers with enough statistical power to be able to provide evidence-based conclusions on best practice. Regional guidelines differ considerably and there is widespread variance in practice between different clinical centres.

Although generic cancer databases such as Cancer Outcomes and Services Dataset (COSD) in the UK and the National Cancer Database (NCDB) in the USA exist they are limited to the data streams that are available to them. Both cannot link, for example, to HIV status or outcomes related to Anal Intraepithelial Neoplasia (the precursor to ASCC). Neither can they report treatment regimes and recurrence rates. It is likely that the increasing incidence is related to, at least in part, the increasing prevalence of HIV therefore not including this data is a significant confounding factor.

In order to provide a suitable platform to allow further dedicated study into ASCC, we have developed an international Anal Squamous Cell Carcinoma registry; mASCARA.

What is mASCARA?

mASCARA is a secure web-based platform that will be available to use from May 2019. It has been designed to be GDPR compliant and has gained ethical approval from a specialist GDPR database Research and Ethics Committee in the UK. Data will be pseudo-anonymised to submitting direct care teams (to allow outcomes such as survival and recurrence to be updated by the direct care team over time) but will be fully anonymised to the study group.

We will roll out the platform out to clinical centres who wish to include their retrospective and prospective data voluntarily over the next year. Our aim however would be, similar to other schemes like the National Bower Cancer Audit in the UK, to gain endorsement from regional Colorectal associations for international mandatory adoption.

Method

We are requesting the submission of retrospective ASCC or high-grade AIN patients as well as the prospective recruitment of patients with newly diagnosed with ASCC or high-grade AIN.

Any patients that are diagnosed with ASCC/high-grade AIN before 1st January 2019 will be defined as a retrospective patient and will not need to be consented to be included in mASCARA.

However, prospective patients will need to give their informed consent prior to their inclusion in mASCARA. A prospective patient will be defined as any person diagnosed with ASCC or high-grade AIN after 1st January 2019. An example consent form and patient information leaflet has been provided within the study documents.

High-grade AIN will be defined as patients with histology specimens classified as:

- AIN2
- AIN3
- Moderate Anal Intraepithelial Neoplasia.
- Severe Anal Intraepithelial Neoplasia
- HSIL (High grade squamous intraepithelial lesion)

Once registered to take part, local Research and information governance approval will need to be completed at the new clinical site please see Figure 1

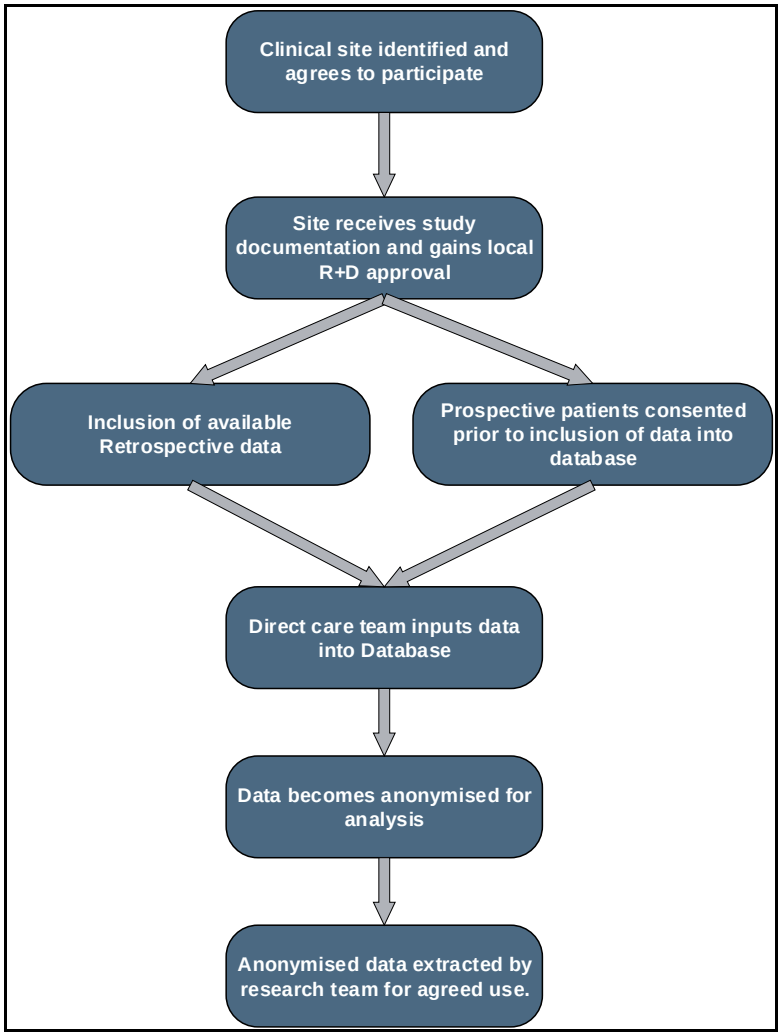

Figure 1: Data flow after identification of participating clinical site.

Inclusion Criteria

- Any patient (male or female) over 18 years old, with or without HIV, with a histologically confirmed diagnosis of high grade Anal Intraepithelial Neoplasia or Anal Squamous Cell Carcinoma.

Exclusion Criteria

- Patient under the age of 18 years
- Prospective patient (diagnosed after 1st January 2019) that refuses informed consent.
- Prospective patient (diagnosed after 1st January 2019) that does not have the capacity to consent to be take part.
- Patients with histology other than Squamous Cell Carcinoma

Primary Objectives

- Investigate demographic risk factors of patients with ASCC
- Determine risk factors for AIN progression to ASCC.
- Investigate best treatment for patients with multifocal low-grade disease.
- Compare end outcomes of different ASCC and AIN management guidelines from different centres.

We expect there to be many more potential objectives and have gained generic approval from the Research and Ethics committee to use the data collected for any relevant scientific research related to ASCC.

We also have prior ethical approval to share the anonymised dataset for research with collaborators that can provide a retrospective dataset of greater than 100 patients within the first 6 months of mASCARA being launched.

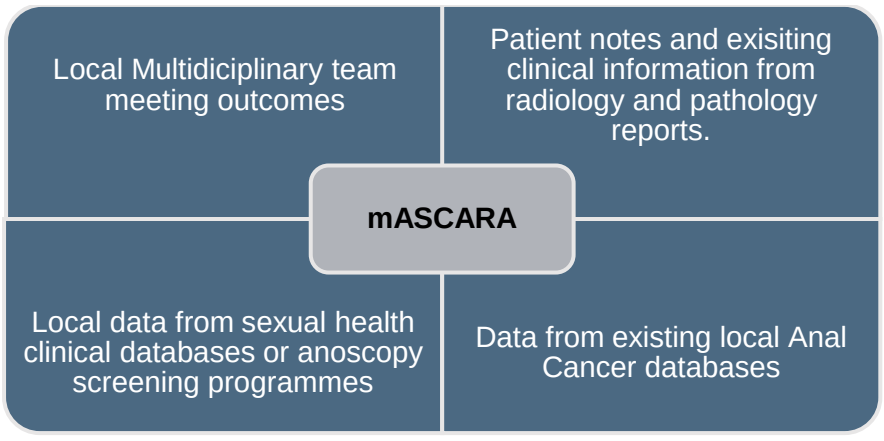

Figure 2: Potential Data Sources

Demographics	HIV	Sexual Health	Surveillance	Pathology	Oncological Treatment	Recurr-ence	Survival
Age	Date of Diagnosis	Anal warts	Previous AIN diagnosis	Staging	Chemotherapy	Date	5 year survival
Sex	AIDS	Receptive anal intercourse	AIN grade at first diagnosis	Tumour differentiation	Radiotherapy	Local vs. distant	Disease free
Co-morbidities	Viral load	Hepatitis C/ B	Method of AIN diagnosis	Surgical treatment	Staging after treatment	Salvage surgery	Date of death
ASA grade/ performance status	CD4 count	Illicit drug use	Participation in screening		Reason for unsuitability for CRT.	R0/R1 resection outcomes	Cause of death
Smoking	Antiretrovirals used	Other HPV dysplasia or malignancy	Number of anoscopies		Last date of follow up	Reason for not having further treatment	
Immunosuppression	Compliance	HPV cytology	Date of high grade AIN diagnosis				

Figure 3: Outcomes to be included in Database

Access to mASCARA

After successful registration and local research and Information governance approval. A password protected account will be provided to registered members of the direct care team. If you have a large dataset already available electronically, contact the study coordinator (dannibrogden@mascararegistry.com) as it may be possible to upload the dataset directly.

Role in Study	Name and Qualifications	Experience
Chief Investigator and Data Controller	Professor Paris Tekkis BMedSci, BM BS, MD, FRCS	Professor of Colorectal Surgery Imperial College London, Royal Marsden NHS Foundation Trust and Chelsea and Westminster Hospital NHS Foundation Trust
Principal Investigator	Professor Mark Bower MA MB Bchir PhD FRCP FRCPath	Professor of Oncology at Imperial College London and Chelsea and Westminster Hospital NHS Foundation Trust specialising in HIV related malignancies
Principal Investigator	Miss Sarah Mills BSc (Hons) BMCCh MD (Res) FRCS	Consultant Colorectal Surgeon Chelsea and Westminster Hospital NHS Foundation Trust and Honorary Clinical Senior Lecturer Imperial College London
Co -Investigator	Mr Christos Kontovounisios MD PhD FRCS	Consultant Colorectal Surgeon Chelsea and Westminster Hospital NHS Foundation Trust and Honorary Clinical Senior Lecturer Imperial College London
Co-investigator and Study Co-ordinator	Ms Danielle Brogden BSc (Hons) MBChB (Hons) MRCS	Colorectal Registrar Chelsea and Westminster Hospitals NHS Foundation Trust and Research Fellow Imperial College London.
Collaborator	Dr Irene Chong BSc MBBS MRCP FRCR PhD	Consultant Clinical Oncologist Royal Marsden NHS Foundation Trust and Clinical Scientist at The Institute of Cancer Research
Data Custodian	Professor Paul Elliot	Head of Department of Epidemiology and Biostatistics Imperial College London.

Figure 4: Study Management Group

Study Co-ordination

The day-to-day management of mASCARA will be co-ordinated through Danielle Brogden

Withdrawal Criteria

Patients with their data included after informed consent can request to be removed at any point in the study and, if possible, their data will be discarded.

If a patient asks to be withdrawn the direct care team will be informed and asked to identify the randomly allocated patient identification number from their pseudo-anonymisation list. The patient data can then be deleted by an administrator.

However, as analysis will be randomised, it will be impossible to delete data from previous downloaded versions of the data and previous analyses. The patient information leaflet will clearly explain that depending of the time of the request we will be able to delete the patients record from the database but may not be able to prevent their data being used in analysis.

Adverse Events

Due to the nature of this study, adverse events are unlikely. However, should any occur they will be referred immediately to the Chief Investigator and Imperial College London's Standard Operating Procedures would apply.

Funding

mASCARA is being supported by the Red Trouser Day Charity.