

**Title: Experiences of Care of Patients with Cancer of Unknown Primary (CUP): Analysis of the 2010, 2011-12 & 2013 Cancer Patient Experience Survey (CPES) England**

Wagland R,<sup>1</sup> Bracher M,<sup>1</sup> Ibanez Equeda A,<sup>1</sup> Schofield P,<sup>2</sup> Richardson A.<sup>3</sup>

1. University of Southampton, UK
2. Swinburne University of Technology, Melbourne, Australia
3. University of Southampton & University Hospital Southampton NHS Foundation Trust, UK

**Background:** The limited evidence on quality of life (QoL) issues facing patients with cancer of unknown primary (CUP) indicates they are often poorly supported over their illness trajectory. The national Cancer Patient Surveys (CPES) invite all patients with a cancer diagnosis in active treatment to complete questionnaires on care quality experienced. The survey contains a free-text box that asks patients to provide comments on their care.

**Aim:** To analyse experiences of patients with CUP as they have reported them within the free-text question of three CPES periods of observation: 2010; 2012; 2013.

**Methods:** Thematic content analysis, informed by a three-stage coding process: sorting of data into categories of interest; exploration of specific content of comments; identification of crosscutting latent themes.

**Results:** In total 9242 patients with CUP (67% of those who returned questionnaires) provided comments over the three periods of observation. Almost two-thirds (63.5%, n=5866) respondents were women, with majorities within 51-65 and 66-75 year age groups. Of 17 coded themes: positive comments were predominant for eight and negative for nine. Proportions of patients providing comments for each theme remained consistent over three time-points, with similar positive-to-negative ratios. Dominant crosscutting themes identified a lack of coordination and continuity of care, with poor communication between health sectors, Trusts and clinical teams; a lack of person-centred care; and a need for clinical nurse specialists (CNSs).

**Conclusion:** This is the largest study thus far of experiences of patients with CUP. Findings provide clear support for the recommendations of the CUP NICE Guideline, in particularly for the development of a specialist CUP team within each trust.

## **Variation in recommended diagnostic and treatment strategies among guidelines for Carcinoma Unknown Primary.**

M. Kok<sup>1</sup>, H. van Laarhoven<sup>2</sup>, V.E.P.P. Lemmens<sup>1</sup>, C. Schroten<sup>1</sup>

1. Comprehensive Cancer Organization the Netherlands, Department of Research, Utrecht, The Netherlands
2. Academic Medical Center, Department of Medical Oncology, Amsterdam, the Netherlands

**Background:** Guidelines intend to provide the medical professional with a set of recommendations for the best standards of cancer care. For carcinoma of unknown primary, a heterogeneous group of metastatic malignancies for which the site of origin is not detected, several guidelines are available. Because each guideline is developed by a different committee with their own point of view, these guidelines might advise differently regarding diagnostics and treatment strategies for patients with a malignancy of unknown origin. Different diagnostics also implicate different definitions of carcinoma unknown primary (CUP) and vice versa.

**Methods:** Via an internet search, using the terms “guideline(s)”, “CUP” and “carcinoma unknown primary”, four guidelines were identified. These consisted of: the NCCN guideline from the USA, the SEOM guideline from Spain, the NICE guideline from the United Kingdom and the European guideline (ESMO), based in Switzerland. These guidelines and the guideline used in The Netherlands, were compared and an overview was made of the differences and consistencies of the advised diagnostic, treatment and follow-up strategies.

**Results:** Of the five compared guidelines, the guideline of NICE mainly focuses on the logistics with regard to patient care while other guidelines focus more on the diagnostics to identify the primary tumor site. The described diagnostics, by guideline and metastatic site, sometimes show overlap but frequently differ on the various recommended diagnostic tools to identify the site of tumor origin such as PET,CT,MRI, IHC markers, ultrasound and endo-, colo-, colposcopy. For the treatment of patients with CUP the guidelines often refer to the guideline of the suspected primary tumor site. The NICE guideline generally refers to a multidisciplinary team to discuss the best possible treatment for the patient.

**Conclusion:** Besides an overlap between the studied guidelines, also numerous differences were observed. These differences in diagnostic strategies, and the different diagnostic tools used, implicate divergent perceptions regarding the definition of the term “carcinoma unknown primary” and makes comparison of incidence rates, survival times and treatment strategies challenging. Yet, medical professionals and their patients could benefit from alternative diagnostic/treatment strategies described by other guidelines in case the followed guideline does not result in the primary tumor site identification or treatment effects.

## **The workload and impact of a dedicated CUP service on patients with imaging suggestive of metastatic disease.**

Authors: The Royal Free Hospital CUP team: Drs Roopinder Gillmore and Grant Stewart (oncology), Jackie Marshall (CUP CNS), Drs James Bell and Katie Planche (radiology), Drs Jennifer Watkins, TuVinh Luong, Ian Clarke (histopathology), Dr Rachel Craig (palliative care) and Silvia DeVanna (MDT co-coordinator)

### **Background**

In response to the NICE guidelines (2010) “Diagnosis and Management of Metastatic Malignant Disease of Unknown Primary Origin (MUO)” the Royal Free Hospital, London established a Cancer of Unknown primary (CUP) service whose role is to review all patients with suspected metastatic disease on the basis of abnormal imaging.

### **Aims**

The aims of this service are to ensure patients have **(A)** consultant led oncology input to determine the appropriateness of and streamlining of investigations, **(B)** access to psychological support and information from a dedicated CNS during the patient’s journey from when cancer is considered a possibility rather than only with histological confirmation, **(C)** earlier input from palliative care facilitated by the CUP team, **(D)** expedited time to diagnoses and treatment decisions and **(E)** access to clinical trials.

### **Methods**

The initial Royal Free Hospital London CUP multi-disciplinary team (MDT) meeting took place on 6<sup>th</sup> April 2011 and has continued to meet on a weekly basis with consultant input from radiology, histopathology, medical oncology, clinical oncology, nuclear medicine and palliative care.

The Royal Free CUP team has established “fast-track” pathways with radiology, histopathology, endoscopy and nuclear medicine to ensure those patients fit for treatment are diagnosed rapidly. Furthermore, closer working relationships with palliative care have been forged to ensure patients are reviewed immediately by the palliative care team.

### **Results**

For the time period covering 1<sup>st</sup> April 2013 – 31<sup>st</sup> March 2015: 303 patients were referred to the service.

Rapid time to consultant / CNS reviews **(A, B)**: 161 of 164 (98%) of all inpatients were seen within one working day and 129 of 137 (94%) of all outpatients were seen within 2 working weeks

#### **Expediting Time to diagnosis (D): Median from Date of referral to Date of Diagnosis was 5 days**

Final diagnosis (n=303): Primary tumour identified 157 (52%), MUO 57 (19%), pCUP 7 (2.3%), cCUP 17 (5.6%), benign: 56 / 303 (18.5%) and outstanding 9 (3%).

Input from palliative care **(C)**: Earlier input from palliative care ensured that terminally ill inpatient referrals were more likely to be safely discharged from hospital to their preferred place of death compared to before the establishment of the CUP service (7% vs 67%).

Clinical trials **(E)**: the Royal Free Hospital CUP team enrolled 106 patients into the translational aspect of the NCRN-badged CUP-ONE trial.

### **Conclusions**

The establishment of a multi-disciplinary CUP team allows patients with imaging suggestive of metastatic disease access to expert input from oncology, diagnostics and palliative care expediting decisions regarding the appropriateness of further investigations and treatment.

## **THE CARCINOMA OF UNKNOWN PRIMARY MULTIDISCIPLINARY MEETING : EXPERIENCES OF THE FIRST YEAR.**

Dr Anna Green, Dr Fiona Kyle, Rachel Ingham, Dr Nick Maisey, Dr Michael Green, Dr Sarah Ngan, Dr Giuseppe Culora

Guys and St Thomas' Hospital Foundation Trust

### **ABSTRACT**

#### **Background**

Cancer of unknown primary, the majority of which are carcinomas (CUP) accounts for 3- 5% of cancer diagnoses, has a poor prognosis with a median survival of less than 10 months and is the 4<sup>th</sup> most common cause of cancer related death in the UK. In accordance with NICE guidance, GSTT established a CUP MDM in April 2013. This review evaluates the first year of the service, focusing on the pathological aspects of the cases discussed.

#### **Methods**

A retrospective review of all cases referred to the GSTT MDM between April 2013 and April 2014, with collation of data with respect to patient demographics, diagnosis, histology and cytology, radiology and, where relevant, tumour markers. Both local and cancer network cases were reviewed.

#### **Results**

55 patients were discussed during the review period, of whom 27 were diagnosed with confirmed-CUP (cCUP), median age 69 years and 63% female. Adenocarcinoma was the most common diagnosis (n=11), followed by poorly/undifferentiated carcinoma (n=8). The median number of immunohistochemical stains used in diagnosis was 9, with CK7 and CK20 used most commonly (n=21). 4 cases were diagnosed on the basis of a cytology specimen alone.

#### **Conclusions**

The demographics and tumour profile was similar to that reported in the literature. With the increasing role of molecular diagnostics, preservation of tissue is becoming imperative. The GSTT CUP MDM provides a streamlined service for patients, enabling in depth case discussion, and guiding appropriate management.

## **An audit of The Carcinoma of Unknown Primary Service at Barnet Hospital.**

Kellie O’Riordan, Tanya Ahmad, Daniel Krell and Ursula McGovern.  
Department of Oncology, Barnet Hospital, Hertfordshire, UK.

In 2010 NICE introduced guidelines covering the treatment and care of adults with suspected or diagnosed carcinoma of unknown primary (CUP). As a result, all Hospital Trusts were expected to develop a service to deal with the needs of this complex set of patients, aiming to improve care and involving a multi-disciplinary approach to ensure better outcomes.

A CUP Service and MDT was established in Barnet Hospital in August 2013, involving a core team consisting of oncologists, a radiologist, a histopathologist, a palliative care physician and clinical nurse specialist and in total 39 patients to date have been discussed at the MDT. Patients are initially identified usually through inpatient acute oncology referrals and increasingly from primary care via GP referrals.

Of the 39 patients discussed at the MDT, 23 primaries (Upper and Lower GI, Sarcoma, Breast, Renal Gynecological, Skin, Lung, Hematology and two patients were found to have no cancer) were identified following review of the images by the CUP team and patients subsequently were referred to the appropriate site specific MDT. All of these patients went on to have systemic treatment. 6 patients had imaging consistent with malignancy but were deemed too unwell for further investigations (all had received inpatient review by the CUP team) and best supportive care was advised by the MDT. All of these patients died within a short number of days (average 14 days).

The remaining 10 patients were identified as “true CUP” patients. Out of these a total of 8 patients went on to have treatment with either chemotherapy or radiotherapy. The remaining 2 patients deteriorated quickly and subsequently died. Of the 8 patients who received treatment, 5 are still currently alive.

The Barnet CUP MDT has played an essential role in improving and expediting the management of patients presenting with unknown malignancy. By ensuring multidisciplinary review, often primary tumour sites are subsequently identified which avoids diagnostic delay for patients and ensures patients are rapidly referred to appropriate site specific specialists. Equally, with early review by the MDT, inappropriate invasive investigations in patients who are clearly too unwell for systemic treatment are avoided, allowing the early involvement of the palliative care team and improving end of life care for patients with poor prognosis who present with advanced malignancy.

# **A review of establishing a Cancer of unknown primary two-week wait GP referral service at University Hospitals Bristol NHS Foundation Trust**

Jo Ocen, Oncology Fellow at the Bristol Cancer Institute

## **Introduction**

Cancer of unknown primary (CUP) is where a patient has a malignancy without an identified primary source. Following National Institute of Health and Care Excellence guidance, many hospital trusts have established a CUP service to coordinate care for these patients. University Hospitals Bristol NHS Foundation Trust (UHB) and North Bristol NHS Trust run a joint CUP service accepting internal referrals and, since July 2014, a GP two-week wait service. Currently the clinic is staffed by 1 consultant and 3 clinical nurse specialists.

## **Methods**

Data for this project was collated from a database of GP referrals made to the CUP service at UHB from July 2014 to January 2015, compiled by the CUP specialist team. It included details of dates of referrals, when they were seen in clinic, when cases were discussed at the CUP multi-disciplinary team (MDT) meeting and their outcomes. Clinic letters/discharge summaries were used collect details on management and outcomes. Details on initial CT imaging requests were collected from Sunquest online system.

## **Results**

44 GP referrals were made to the CUP service. Full body CT scans were requested by the GPs with 24 of the referrals. 19 patients were seen in clinic from July to January, 79% within 2 weeks. 5 were admitted to hospital before being seen. 29 cases were referred directly to the CUP MDT for discussion. 20% of the referrals were inappropriate.

10 patients were found to have had confirmed CUP, 8 were for best supportive care and later died. 5 patients had no cancer. 13 of the referrals had site-specific cancers.

## **Conclusion**

This project has shown this service to be an effective 2-week wait referral system with the majority of patients being seen within 2 weeks. It highlights the importance of early CT imaging and MDT involvement when assessing and managing these patients.

## **The role of HPV in neck lymph node metastases from unknown primary**

Authors: L. Schroeder<sup>1</sup>, D. Holzinger<sup>1</sup>, L. Baboci<sup>1</sup>, G. Dyckhoff<sup>2</sup>, C. Herold-Mende<sup>2</sup>, J. Hess<sup>1,2</sup>, C. Lucena Porcel<sup>2,3</sup>, P. Boscolo-Rizzo<sup>4</sup>, L. Alemany<sup>5</sup>, M. Pawlita<sup>1</sup>

### Institutions:

<sup>1</sup>German Cancer Research Center (DKFZ), Heidelberg, Germany

<sup>2</sup>University Hospital Heidelberg, Heidelberg, Germany

<sup>3</sup>NCT Tissue Bank of the National Center of Tumor Diseases (NCT), Heidelberg, Germany

<sup>4</sup>University of Padua, Treviso Regional Hospital, Treviso, Italy

<sup>5</sup>Catalan Institute of Oncology, Barcelona, Spain

Human papillomavirus (HPV) infection is a risk factor for head and neck squamous cell carcinoma (HNSCC). HPV-positive HNSCC show a better survival compared to HPV-negative HNSCC despite their frequent early metastatic spread to lymph nodes. Patients initially presenting only with a neck lymph node metastasis (NLNM) are frequently diagnosed with HNSCC. In some NLNM cases no primary tumor is detected. Aggressive treatment of these squamous cell carcinomas from unknown primary (SCCUP) often leads to substantial side effects and severely reduced quality of life.

Recent studies provide evidence that the HPV status may have a prognostic value in SCCUP and may serve as a predictor for oropharyngeal localization of the primary tumor. In a multinational retrospective study (Germany, Spain, Italy) we determined the prevalence of HPV-driven lymph node metastases in SCCUP patients. Presence of 51 mucosal HPV types was analyzed in fresh-frozen and/or formalin-fixed paraffin-embedded tissue from 185 SCCUP. To identify truly HPV-driven cases additional markers including viral load, E6\*1 oncogene mRNA and expression levels of the cellular protein p16INK4a were determined. 16% of SCCUP were HPV-driven (10% in Barcelona, 18% in Northern Italy, 21% in Heidelberg).

HPV prevalence increased over sampling time 1988 – 2014 (8% – 23%). Analysis of additional molecular markers for HPV transformation is ongoing. Preliminary data analysis indicates that HPV-driven SCCUP appear to have a better overall and progression-free survival. HPV status might help to guide individualized treatment decisions. The study is open for additional clinical collaborators.

## **Vertebral Biopsy: Establishing Diagnosis in Cancer of Unknown Primary.**

Dr Sarah Scobie, Edinburgh Cancer Centre, Dr Sally Clive, consultant med onc, Edinburgh Cancer Centre

### **Background:**

Establishing pathological diagnosis in a timely manner is paramount in patients with advanced malignancy, in whom the treatment window for initiating systemic therapies can be relatively narrow. Bone biopsy of suspicious lesions may be the most technically accessible site but histological diagnosis takes longer than from visceral sites because of decalcification. An inconclusive result delays treatment.

### **Aims:**

- Determine proportion of diagnostic vertebral bone biopsies in suspected malignant lesions.
- Assess if patient demographics, lesion site, radiological features, biopsy technique or cancer history predict for diagnostic outcomes.
- Is vertebral bone biopsy time-effective manner to establish definitive diagnosis?

### **Methods:**

A retrospective analysis of 116 consecutive vertebral bone biopsies performed in South East Scotland from Jan 2008 to June 2014; the mean age was 61 (22-87). 60 were male, 56 female. Analysis included all bone lesions and those with paravertebral involvement with significant bone invasion. Patient demographics, biopsy method, lesion location, radiological appearance and suggested radiological diagnoses were collated. Initial biopsy was classified as diagnostic or indeterminate. Malignant pathological subgroup and likely primary site was recorded. Timescales assessed the efficiency of our current service, including time from biopsy to result and to date of death.

### **Results:**

Most commonly biopsied sites were lower thoracic and lumbar, with 50% of biopsies from the lumbar spine. Location of lesion did not affect biopsy success rate. The majority had CT guided biopsies (85%), 11% were fluoroscopic guided and 4% open biopsy. All open biopsies were diagnostic. Malignancy was diagnosed in 78 patients (67%), infection in 25% and 8% were non-diagnostic. None of those with radiologically suspected infection were subsequently found to have malignancy on biopsy. 90% of patients biopsied because of suspected cancer had diagnostic first biopsies. In the 78 patients with diagnostic biopsies, 61 out of 68 with radiologically malignant looking lesions had cancer confirmed, giving a PPV of  $61/68 = 90\%$ , and a NPV of  $8/10 = 80\%$ . 17% of biopsies of lytic lesions were non-diagnostic. Only 2 of the non-diagnostic biopsies carried out were associated with a crush fracture. In the 30 patients with a cancer history, 27 (90%) had diagnostic vertebral biopsies. In 18 (67%), biopsy was consistent with previously diagnosed malignancy, 4 (15%) diagnosed a new primary and 2 (7%) concluded metastatic cancer of unknown primary (mCUP); the remaining 3 were benign. It took a median of 9.6 days from biopsy to result, those non-diagnostic resulted 2 days sooner. Haematological diagnoses took longest (10.5 days), with greatest range (2-15 days), reflecting the subgroup heterogeneity. Those with a large soft tissue component averaged 8.5 days. Death from date of malignant biopsy ranged from 2 days to 43 months (median 10 weeks). 73% died within 6 months of biopsy, 22% of whom died within 6 weeks. 31 out of 34 biopsies (91%) performed in mCUP were diagnostic. 77% provided immunohistochemistry that helped indicate a likely primary site (16 lung adeno or squamous, 6 haematological, 1 cordoma and 2 upper GI adenocarcinoma). 7 remained mCUP, mostly poorly differentiated carcinoma.

### **Conclusion:**

- 90% initial biopsy success rate in those with radiological suspicion of cancer.
- Radiological appearance is a good predictor of malignancy.
- Biopsy of lytic lesions are least likely to give diagnostic results, though 84% success rate is not unreasonable. Crush fractures do not impact chance of biopsy success.
- It took a median of 9.6 days from biopsy to histology result.
- In mCUP patients, there was a reassuringly good initial biopsy success rate and enough tissue to indicate likely primary cancer site in most.