Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Alliance

Meeting of the SWAG Network Cancer of Unknown Primary (CUP) Clinical Advisory Group (CAG)

Tuesday 2nd November 2021, 12:00-13:00, via MS Teams

Chair: Dr Tania Tillett (TT)

NOTES (To be agreed at the next CAG Meeting)	**ACTIONS**

1. Review of Last Meeting Report and Work Programme

As there were no amendments or comments following distribution of the report from the meeting held on Wednesday 18th November 2020, the report was accepted as accurate and finalised.

The meeting today is slightly abridged due to workload pressures, but felt important to convene as the previous meeting had to be cancelled due to the COVID-19 pandemic.

Work Programme:

012/15: Identification of Poor Prognostic Support Groups:

Groups have been established in UHBW and RUH, but not yet in SFT or GRH.

SFT have a meeting next week to discuss how to develop the CUP service and this could be added to the agenda.

Action: Details of the support group in UHBW will be shared with SFT — **H Dunderdale**

Due to COVID-19, the face to face wellbeing days have stopped, with some continuing virtually.

It is hoped to make the Living With Advanced Cancer Day available again as soon as possible, as it is of particular value for this group of patients to meet for supportive purposes.

In UHBW, the First Steps, Next Steps and Advanced Cancer events have been recorded into bite-size sessions that are now available on the website. Cancer Support Workers are referring patients via the usual channels - by letter and follow up telephone call.

The number of CUP patients that would be able to attend was thought to be quite low; however quite a few did attend when this was first established.

017/15: Patient Experience Surveys

It is a sensitive, difficult subject to obtain patient experience feedback from CUP patients due to the most commonly unfavourable nature of the diagnosis. Survey cards in patient packs did not work well, and it is felt that more real time individual feedback would be the best approach with this patient group.

Cancer Support Workers routinely call patients to offer support after the initial appointment.

Action: All sites to contact Cancer Support Workers to request informal feedback on the patient experience when calling post first appointment — **CAG members to coordinate**

009/16: Genomic Medicine Biopsy Sampling:

There is no standard genomic testing for CUP patients at present.

The genomic guidelines that were developed after conclusion of the 100,000 genomes project have prioritised mainstreaming Whole Genome Sequencing (WGS) to all Sarcoma, some Haematological Malignancies and all Paediatric Malignancies. It is not known when this will roll out to other cancer sites.

Next Generation Sequencing (NGS) for NTRK gene fusions is available as it is a tumour agnostic test funded by NHS England.

Action: CUP MDTs are to commence reflex testing for NTRK gene fusions — **AGREED**

A Foundation Medicine pathway has been set up in Taunton for detection of circulating tumour cells in blood.

RUH currently don't have access to NGS outside the confines of clinical trials.

Roche have just set up access in SFT. RUH did have 50 free tests from Roche but these have all been used within a short time frame.

010/16: An invitation is to be sent to Chief Investigator (CI) of CUP 1:

Multiple attempts had been made to invite the CI of CUP 1, but the trial data had now become dated, and this will be removed from the Work Programme.

Action: CUPISCO CI Dr Kai-Kean will be invited to a future meeting — **H Dunderdale**

005/17: Straw poll of confirmed CUP definitions:

This can be removed from the Work Programme as it has been replaced by the CUPISCO guidelines.

006/17: Reformation of an Acute Oncology Group:

This should be under the remit of the Cancer Alliance. It is not possible for H Dunderdale to provide support to an additional group, which will most likely involve a lot of work pulling together regional standard operating procedures and guidelines.

Action: T Tillett will liaise with Cancer Alliance Clinical Director Helen Winter about the need for a group — **T Tillett**

003/18: Use of Cancer Research UK Consent Forms:

These are now used as standard and the action can be removed from the Work Programme.

Working groups have been established to try and move to online signatures.

005/18: Review of Serial Responders:

This agenda item will be revisited in 1-2 years, when services have recovered to a new normal following the pandemic.

001/19: Implementation of the Royal College of Pathologists' (RCP) CUP datasets:

The RCP algorithm was considered useful to use as a check list, but completing the actual dataset itself was not helpful, as it was not possible to complete until all further tests have been reported. It was therefore agreed that completion of the dataset should not be mandatory. **AGREED**

004/19: Patient Experience Staff Training:

Since the pandemic began, there had been no further conversations about developing an education programme for staff from Primary and Secondary care on delivering diagnoses, and having appropriate and realistic discussions about patients' wants and needs when considering ongoing treatment. It was recommended that this should be linked with the development of Rapid Diagnostic Services due to the link across Primary and Secondary care, plus Palliative Medicine and Community Services: To remain a rolling agenda item.

007/19: Network audit of prospective cases:

The pathway timeframes were very concerning at present, with many patients presenting with late end stage disease. The audit will be revisited at the next meeting in May, when it is hoped that services may have returned to a new normal.

008/19: Rapid Diagnostic Service:

On the agenda.

Action: A presentation on the different RDS models will be requested at a future meeting in approximately 6-12 months **H Dunderdale**

004/20: Somerset PCN/RDS to resolve inequity in GP access to direct CT requests:

H Dunderdale has contacted Somerset CCG representative A Beattie about GP access to CT and awaits a response; to remain a rolling agenda item.

006/20: Enhanced Supportive Care Service (ESC) Provision:

Somerset and Gloucestershire have functioning ESC services which are working very well. They provide support to any patient well enough to come for an outpatient appointment, and direct those who can't attend to community

services.

Bristol and Bath do not have an ESC service at present; development of a pilot service was planned in UHBW but stalled due to the pandemic, when funding options changed and there were no longer the staff to provide the service.

Action: To encourage adoption of ESC services across the network — **H Dunderdale / CUP CAG Recommendation**

2. Clinical Opinion on Network Issues

2.1 MDT / Service Changes

RUH: There have been no changes to the service since the last meeting. Delayed referrals due to the COVID-19 pandemic remain concerning, as do the delays in most steps of the patient pathway, notably with scan reports, biopsy results and delays to surgery.

UHBW: The combined Bristol and Weston MDT service, together with NBT, appears to be working well. The service has good quoracy and excellent coverage from both pathology and radiology services. There are service challenges at Weston with delivering urgent biopsies due to coordinating getting a COVID test result prior to arranging the biopsy.

SFT: There have been no changes or issues with the MDT continuing to link with the UGI MDT. In the future, linking with the YDH service is being considered.

YDH: It would be helpful for the YDH team to link with SFT, as the dedicated CUP Consultant has left the service, which then moved from the UGI to the Lung MDT, and now has had to move again to join the Breast MDT, as this is the only place where oncologist cover could be provided.

A new specialty Doctor C Miller has been recruited and starts in post next week.

It was considered to be beneficial for both services to link, as SFT often have to cancel approximately 3-4 meetings a year due to no cover during annual leave. The challenge will be coordinating the times as the SFT MDT is held directly after the UGI MDT.

Action: Linking the Somerset Services will be considered further — **E Cattell / A Evenett**

GLOS: The Clinical Team are not available to attend the meeting today.

3. Clinical Guidelines

T Tillett has reviewed the SWAG Clinical Guidelines and made a few amendments. These will be circulated to CUP leads for agreement in the near future.

T Tillett

Action: T Tillett to circulate CUP Clinical Guidelines to E Cattell and T Wells

4. Coordination of Patient Care Pathways

4.1 Changes / concerns due to COVID-19

All services have concerns about the effects of the COVID-19 pandemic on patient referrals and patient treatment pathways. However, all services are learning to adapt to the situation and resume activities under 'new normal' conditions.

5. Research update

Please see the presentation uploaded to the SWAG website

Presented by T Tillett

There are currently 2 clinical trials available in RUH which are so important for CUP patients as survival curves (available within the presentation) show that the median survival rate for CUP treated outside a clinical trial, is 9 months, with a very poor long term prognosis.

CUPISCO (a first line trial) initially had very good recruitment, but this has dropped as patients need to have a Performance Status of 0-1 and, in part, due to difficulties getting repeat biopsies and scans performed in a timely manner.

Inclusion criteria:

- Adenocarcinomas only
- Histologically confirmed CUP
- PS 0-1
- Sufficient tissue for NGS carried out on tumour and blood.

Exclusion criteria:

- Favourable prognostic sub groups
- Central nervous system metastases
- Within 4 weeks of major surgery / radiotherapy
- Non-adeno sub-types
- Previous malignancy within the last 5 years that could be in keeping with a recurrence of that malignancy
- Primary declared by the investigators
- Neuroendocrine tumours – either poorly or well differentiated
- Women with peritoneal carcinomatosis with a serous papillary sub-type (treated as an ovarian cancer)
- Women or men with isolated axillary nodal metastases particularly carrying hormone receptors (treated radically as breast cancers)
- Squamous cell carcinomas of cervical lymph nodes (treated radically as head and neck cancers)
- Patient with metastatic disease in keeping with a pattern of metastatic colorectal cancer who is CK20 positive, CDX2 positive but CK7 negative in keeping with a colorectal sub-type is now considered a favourable sub-type and treated as metastatic colorectal cancer
- Solitary deposits (treated radically as single metastatic sites)

- Bone metastases with PSA expression (treated as prostate cancer).

These definitions were all felt to be reasonable.

The following definitions of lung primary cause some controversy and lots of screening failures:

- Anybody who has an adenocarcinoma that is CK7 positive and TTF1 positive, if they have any lung mass, can't enter CUPISCO and are treated as a lung primary.
- Those with TTF1 negative (although we know there are a proportion of lung cancers that don't carry TTF 1), if there is a lung mass with hilar lymph nodes, are treated as lung.
- If TTF1 negative with no lung mass but mediastinal lymph nodes and other metastatic sites in keeping with lung cancer, such as bone, adrenal, are treated as lung.

Anybody with TTF1 negative with no lung mass, no mediastinal lymph nodes, and a metastatic pattern not in keeping with lung can try to enrol.

Anybody who carries TTN1 positivity who has no lung mass or thoracic disease can try to enrol.

Another definition that causes controversy and screening failures is cholangiocarcinomas if they are CK7 positive and their profile is compatible with an Upper GI or pancreato-biliary with liver only disease; or if they have 1 or 2 predominant lesions within the liver or coalescing lesions within the liver, plus or minus satellite lesions with in the liver and other metastatic sites; or f there are other metastatic sites apart from very small pulmonary metastases, then they consider that to be in keeping with a cholangiocarcinoma.

Multiple liver metastases with non-pulmonary metastases can try to enrol.

The CUP algorithm was considered very useful.

CUP-COMP is an observational trial through which CUP patients can access NGS.

Inclusion criteria:

- PS 0-2
- MDT diagnosis of confirmed CUP (it doesn't have to go through CUPISCO stringent criteria)
- Neuroendocrine and squamous cell carcinomas are included
- Repeat biopsy and fresh frozen tissue sent to the trial unit.

The Foundation 1 results are released immediately for review by Tumour Board whereas in CUPISCO, Foundation 1 results are only released if you get randomised to the treatment arms. If randomised to the control arm, they are only released on progression, which can cause upset to patients who then have to wait for them.

Patients can be treated in their local centre, but need to come to the RUH for 3 blood tests.

At present, it is only possible to open CUP-COMP if you have CUPISCO open as it is just a small trial team working off the back of CUPISCO, but it may expand to other sites in the future.

CUP-M is open in University College London, and they have opened a second cohort for first line chemotherapy naïve CUP patients for pembrolizumab, looking at response rates and toxicity. This is planned to close in March 2022. Otherwise this is also open as a second line treatment for patients who have progressed after platinum chemotherapy.

Action: The slides will be added to the website **H Dunderdale**

6. Service Development

6.1 Rapid Diagnostic Service / Innovation due to COVID-19

Rapid Diagnostic Service pilots continue to develop across the region.

The RUH referral pilot is established and working well.

The Somerset pilot went live at the end of July, run by the CNS team L Page and A Evenett. This is open to all PCNs in Somerset.

UHBW have been working with the SWAG Cancer Alliance and have recently appointed a CNS.

7. Any Other Business

There were no other items to raise at this meeting.

Date of next meeting: Wednesday 11 May 2022, 10:00-14:00, venue to be confirmed.

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