Peninsula and Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Services

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

Wednesday 8th November 2023, 10:00-13:00, via MS Teams

Chair: Dr Tania Tillett

REPORT **ACTIONS**

(To be agreed at the next CAG Meeting)

1. Introductions

Please find the list of attendees uploaded on to the SWAG website here.

2. Managing Staff Fatigue

Please see the presentation uploaded on to the SWAG website

Presented by Consultant Psychologist Mike Osborn

CUP CAG are invited to contact Dr Osborn with any questions that may arise following the presentation.

CAG members are encouraged to think about how to manage the potential risk of psychological fatigue caused by workload pressures, which has always been high risk, but is currently a much higher risk than usual due to the exponential increase in treatment load. Provision of intensive treatment and support to ill and distressed patients has increased 8 fold over the last decade, as demonstrated in a recent presentation by Prof Mark Beresford.

Attention should be drawn to the accumulative every day small behaviours and brief experiences that can have a critical impact on our health and immune system, rather than focusing on more profound critical incidences.

Culturally, complaining about small everyday stresses, such as car parking or problems with IT systems, can be perceived as trivial. However, recognising the impact of these issues can have the biggest return on improving your quality of life, as it is prolonged duress that makes threat defence responses dominate which, in turn, can cause fatigue. Threat defence responses also do not automatically stand down once work has finished, and it can be helpful to arrange a quiet reunion with those that you live with when you return home.

Fatigue and exhaustion differs from tiredness, as it is an indication that the brain has depleted resources to the primitive brain, which interrupts the ability to regulate your mood and find things interesting, pleasurable or amusing, which can undermine your confidence.

Because hospital staff are high functioning and used to high performance work in stressful environments, the response to fatigue is likely to be more fight than flight and result in irritation, annoyance and reduced tolerance for being critiqued.

This cognitive disruption, which is as real as the brain fog caused by chemotherapy, causes moral injury to NHS staff as you are all working very hard but also feel the need to apologise for the things that have not been possible to achieve, leading to misplaced guilt.

The talk is not presuming that everyone is feeling these pressures in the same way or at any given time but is simply to raise consciousness of the risk of cognitive fatigue.

To help mitigate or manage this risk, staff are encouraged to make deliberate and active steps to review what it is that you personally need, and to regularly incorporate these needs into your daily routine with benign self-compassion and complete moral authority.

Composure and civility should be prioritised and incivility called out. It is advised to 'strike when the iron is cold' to try to maintain your balance of composure below 4 to 5 out of 10 as once the adrenaline becomes higher than this, it can take significantly more time to dissipate. Even if anger and aggression is righteous, it is never helpful.

Fatigue management cannot be reduced to a test of will power, control or strength, but rather it is a test of flexibility and adaptability.

There is a psychological paradox of fatigue management, in that the virtues of a person working in the hospital environment exactly match fatigue risk factors.

Maintaining a healthy team culture is the most protective factor to ensure social safety.

In summary, CAG members are asked to prescribe for themselves the advice that a feisty compassionate colleague would recommend.

3. Genomic Medicine Service Alliance (GMSA) Update

Please see the presentation uploaded on to the SWAG website

Presented by Consultant Oncologist Louise Medley

The move towards personalised treatment options for patients has rapidly advanced over the past few years with the increased understanding of cancers on a genetic level.

There are limited treatment options at present, but this is likely to change in the near future.

For CUP patients, the need for speed from first presentation is paramount, which most often involved sourcing tissue from a biopsy and having several reviews of the histopathology before this is transferred to the Genomic Laboratory Hub (GLH).

An NHS England circulating tumour DNA (ctDNA) pilot has been underway for lung cancer and work is underway to try to obtain funding for CUP to do the same.

Blood samples are taken at the first two week wait clinic appointment and sent for genetic analysis, enabling reporting of the genetic signature far quicker in the patient pathway than reporting of tissue samples, reducing the time from cancer presentation to treatment.

The pilot has demonstrated the importance of this new technology.

As well as the genomic signatures, important information on the tumour mutational burden (TMB) is provided which, if high, can inform if a CUP patient may be a candidate for immunotherapy, or the gene alterations may point to a particular primary diagnosis, and/or a relevant clinical trial or drug through compassionate access.

Tumour agnostic drugs are the only accessible treatment for CUP patients when a favourable gene alteration, such as NTRK, has been identified.

The main reason for delayed diagnoses is the taking and processing of biopsies, as turnaround time from the GLH is now similar to that of taking the blood sample.

Another advance that is pending is the potential introduction of multi-cancer blood tests into the non-site specific pathway. The test looks for 50 different gene signals to try and guide the patient's initial management. This may increase the number of referrals made to CUP MDTs.

The South West GMSA's main aim is to ensure equity of access to genomic medicine to the patient population by providing the tests via Next Generation Sequencing (NGS) listed in the national genomic test directory: NHS England » National genomic test directory. Clinicians are able to apply for additional gene alterations to be included and teams are lobbying for comprehensive DNA and RNA panels for CUP patients, which it is hoped will be included in the next iteration.

Information on how to send samples to the GLH can be found on the website: South West Genomic Laboratory Hub | North Bristol NHS Trust (nbt.nhs.uk)

When requesting NTRK, additional actionable gene alterations are automatically included in the NGS report. These may result in access to therapies via the DETERMINE trial, which has recently opened in Bristol. It is hoped that it will also open at a centre in the Peninsula.

The failure rate of samples sent to the GLH has reduced and turnaround time has improved to approximately 12 days.

Action: CUP will be added to the indications on the GLH referral form **L Medley**

Patient expectations need to be managed with care as, even if an actionable mutation is found and a targeted therapy is accessible, most of the current

treatments do not have a lasting response. This further emphasises the importance of recruiting as many patients as possible to the DETERMINE trial.
It was recognised that a true confirmed CUP diagnosis is very rare and can be bewildering and stressful for patients. It can be helpful to emphasise that this is a disease that effects thousands every year, but also most important to try and identify the primary site wherever possible.

Action: To undertake a regional prospective audit of positive NTRK results and subsequent management: a proforma will be circulated. **CUP CAG**

4. CUPISCO update

Presented by Consultant Oncologist Tania Tillett

Results show that 2-5% of all malignancies are cancers of unknown primary; 80-85% of these are the unfavourable sub-set, and the mean overall survival is still less than 1 year.

CUPISCO survival data, which includes patients with a Performance Status of 0 and well enough to progress to treatment, was also very low.

Potential targeted gene alterations were seen in approximately one third of patients, with the majority defined as high TMB, who were then randomised into the immunotherapy arm.

The study design included adenocarcinomas of poor prognostic sub-type. The screening process for the trial was rigorous and a lot was learned about defining the diagnosis of TTF-1 negative lung cancer and cholangiocarcinoma's and, as a result, a lot less true cCUP patients are being found as the diagnostic tools improve.

All patients had 3 cycles of standard platinum doublet chemotherapy followed by a response assessment. Any patient who progressed at this point went to the investigator arm. Patients who responded or had stable disease were randomised three to one to the investigator arm.

The tumour molecular board were pivotal in interpreting the results.

Patients who were stratified to the molecular guided therapy versus the control arm showed a statistically significant progression free survival of 6.1 months versus 4.4 months, which is unfortunately too small for some of the Trusts to consider accessing these agents for compassionate use and reflects how this is the poorest survival sub-set.

The cohort of patients with a driver mutation treated with targeted therapy did have improved progression free survival.

The importance of providing some hope for these patients while carefully managing the expectations of finding a mutation and having access to a drug for a small chance of improvement was recognised.

Many patients choose not to have NGS as they currently have to pay for it; funding is being requested from the Cancer Alliance.

For those who do decide to pay for the test, it is made clear that this may not lead to accessing a treatment.

Data is pending on those patients who had a TMB over 15 that shows positive outcomes following treatment with immunotherapy.

The GMSA hope to routinely add TMB to reports in the future. This would be beneficial as several patients across the region have had compassionate access to atezolizumab based on this information and have responded well.

Target National is a trial that allows free access to ctDNA tests following first line treatment if the patient has progressed beyond standard care and is well enough to travel to recruiting centres; Cardiff, Birmingham and Oxford are closest.

Once consented to Target National, patients are automatically eligible for DETERMINE.

5. Work Programme review

MDT Membership update:

- Dr Abi Gee, RUH
- Dr Juliette Hamilton, RDUH
- Dr Cleo Solomon, RDUH North
- SAS Piotr Zlotkowiski, Torbay
- Radiologist Rachelle Meyer, Torbay
- Pathologist John Chapman, Torbay
  Dr Sam Guglani, GRH
- Dr Vishal Bhalla, GRH
- Dr Charlie Candish, GRH
- Dr Sean Elyan, GRH
- Dr Emily Darvill, GRH
- Lead ANP Amy Skelton, GRH.

Poor prognostic support groups to be identified: These had been paused during the pandemic but are restarting again.

Patient Experience Surveys: The CNS team will consider setting up a real time patient experience survey using a QR code. The Non-Site Specific team in SFT have done this and found it very useful, in particular for getting feedback on virtual appointments.

Action: A CNS session will be added to the agenda of a future meeting on an annual basis to provide feedback from the survey and the learning gained from poor prognostic support groups. **CNS Team**

To encourage reformation of an acute oncology group: GP Representative Joe Mays had emailed the Urgent and Emergency Care (UEC) Group to see if this could be provided as part of the new service specification; there has been no response to date.

As management of Malignancies of Unknown Origin overlap with the AO and CUP services, this will be kept on the CUP Work Programme as a recommendation and further attempts will be made with the UEC Board and Cancer Alliance for this to be resolved.

Network audit: As above, NTRK results and subsequent management.

Somerset GP direct access to CT requests: This has been raised again with the Somerset Integrated Care Board (ICB). A response has been received that the ICB will review GP direct access at a meeting in the near future.

Provision of Enhanced Supportive Care (ESC) and Palliative Medicine Services:

ESC is particularly important to the cohort of younger CUP patients who are not ready to be referred straight to palliative services.

A regional service evaluation has shown that the service provision is very variable across the region, with the majority being non-compliant with the NICE recommendation for palliative medicine representatives to attend the MDT and having less than ideal cover.

The Cheltenham team have members who are trained in both oncology and palliative practices which to an extent mitigates the risk of staff shortages, and have strong links with community services.

RUH has a Palliative Medicine Consultant in a clinic that runs parallel to the CUP clinic on Tuesday, but no other input; all patients are referred to community palliative services.

The Bristol team Palliative Medicine Consultant can no longer attend the MDT due to workforce pressures. There are no oncology or acute care areas available in Weston. Patients are assessed over the phone using validated triage tools and are seen in Same Day Emergency Care Clinic or A&E.

Community palliative care referrals are made for those who are symptomatic with a prognosis <1 year.

North Devon do have a Palliative Medicine Consultant and can access ESC via RD&E, although the equivalent service is not available further north.

Somerset also have an ESC service.

Action: As there is still no parity across the region, this will be raised again with the Cancer Operational Group and Cancer Alliance in a combined statement with other relevant Cancer Clinical Advisory Groups. H Dunderdale

It was noted that ESC and palliative care need to work seamlessly together as rapid deterioration often occurs in CUP cases.

Action: Lead Cancer Nurse R Hendy will continue to highlight the gap in provision of ESC in longer term service provision. R Hendy

The team in Gloucestershire have a different model, with the AOS, MUO and CUP nursing team working as one service, managing patients until they are handed on to community palliative care, which works well.

The nursing teams across the region also supply an excellent amount of support prior to referral to community services despite the reduced availability of Consultant Palliative Medicine support.

ESC is defined as an initiative to improve quality of life for those on active treatment with symptoms of incurable cancer and a life limiting prognosis as early on as possible; there is significant cross-over between this and transition to palliative care.

Action: To invite an ESC Consultant from RD&E or Somerset to present at a future meeting and assess if there is an unmet need in other centres. H Dunderdale

SFT and YDH merger:

The two Trusts have now merged into one, and there is now one CUP MDT meeting, with Radiology and Pathology joining from YDH. YDH lost the Consultant Oncologist in March 2023, and have yet to appoint a replacement. In the interim, Dr Cattell has been providing the service for both centres, so it has only been possible to be reactive rather than proactive at present when seeking the further development of the service. Fortunately, the CUP and AOS CNS teams provide excellent support to ensure that all patients are supported.

6. Network Audits

6.1 CUP MDT referrals analysis

Please see the presentation uploaded on to the SWAG website

Presented by Consultant Medical Oncologist Helen Winter

An analysis of CUP referrals in UHBW from 2019 to 2021 was undertaken with assistance from the South Central and West Commissioning Support Unit, for the purpose of assessing if the correct patients were being referred to the service.

The majority of referrals- 237- were received from inpatient sources and there were 195 GP referrals, 29 MDT referrals, and 22 from outpatient clinics. Direct MDT referrals have increased over the last few months.

Although the CUP referral protocol includes a CT Chest/Abdomen/Pelvis with evidence of a malignancy of unknown origin, this is often not available.

The majority of patients were referred without a biopsy. Over 20% of these had a previous cancer. 75% were diagnosed with a site-specific cancer in 2021, and only 1% were diagnosed with a confirmed CUP.

GPs should refer patients with a past medical history (PMH) of a site-specific cancer to the relevant MDT to avoid delays in the patient pathway. The CUP team are frequently referred patients who have a PMH of breast cancer or melanoma with metastatic recurrences.

With the roll out of Patient Initiated Follow Up (PIFU), patients and GPs should have clear information to gain access back to their treating MDT, who could then request the biopsy. A referral could be made to CUP in parallel if this is felt to be appropriate.

Now that Consultant Oncologist Kate Faulkner is in post, the CNS team have organised a clinic that immediately follows the MDT to assess the patient's fitness to undergo a biopsy, and book it where appropriate, which has streamlined the pathway.

As many MDTs are protocolised and surgically led, the biopsy pathway for oncological treatment is unfamiliar and may take some time to embed.

The particular skills of the CUP team, in terms of looking for signs of any cancer, plus the difficult conversations managed by the CUP CNSs, make it challenging to hand these patients back to the site-specific MDTs to arrange a biopsy, and it often seems more pertinent to book it and avoid the delays that this may cause.

Referrals where no biopsy was completed prior to referral waited an average of 21 days before the biopsy was completed.

Radiologists have been asked to add the ideal location of a biopsy to the CT report. Completion varies as some centres outsource reporting to the independent sector.

Work will continue to optimise the biopsy pathway for malignancies of unknown origin.

Action: To liaise with the site-specific teams to optimise the biopsy pathway for malignancies of unknown origin. **H Dunderdale/CUP representative**

7. Personalised Care and Support

7.1 Treatment Summaries

Trusts are being increasingly monitored on the completion of Treatment Summaries. These are essentially the documents already produced to assist transition to palliative care. Once this has been communicated to GPs and community services, the summary can be documented as complete in a specific field in the Somerset Cancer Register.

R Hendy

Action: The parameters in Treatment Summaries will be shared to ensure that regional palliative care documentation complies with these requirements.

Relevant documents could be renamed Discharge/Treatment Summary.

8. Regional opinion on network issues

8.1 Workforce Monitoring

It was proposed to track the CUP workforce including posts that were currently vacant. A spreadsheet has been produced for this purpose which should include any formal member of the MDT. **H Dunderdale**

Action: The Workforce Spreadsheet will be circulated to the MDT Leads.

9. Any other business **MDT Leads**

Action: To re-review details of long-term survivors at a future meeting.

Date of next meeting: Wednesday 8th May 2024, 12:00-13:00 via MS Teams

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