Haematological Cancer Clinical Advisory Group

Thursday 23rd February 2023, 15:30-17:30, via MS Teams

REPORT

Chair: Sophie Otton on behalf of Richard Lush

NOTES **ACTIONS**

1. Introductions: Welcome and farewell update

Consultant Haematologist S Otton is deputising for R Lush. Future Chairmanship will be discussed once he returns.

Please see the list of attendees and apologies available on the SWAG website here.

2. Service development

2.1 South West Genomic Medicine Service Alliance (GMSA) update for Haematology

Please see the presentation uploaded on to the SWAG website

Presented by SW GMSA Head of Cancer Genomics C Wragg

Information on the following subjects is documented in the presentation:

- Haematological germline findings and cases for discussion at the Regional Acute Leukaemia Advisory Panel (MDT referrals do not need to be just for acute leukaemia): rduh.regionalacuteleukaemia@nhs.net
- Next Generation Sequencing (NGS) testing for Myeloproliferative Neoplasms (MPN), which will streamline the service and reduce turnaround times
- GMSA Turn Around Times (TATs), which will now be published on the website on a weekly basis: SWGLH Quality | North Bristol NHS Trust (nbt.nhs.uk)
- Single Nucleotide Polymorphism (SNP-A) arrays has been found to be a useful test and has been expanded for use in all adult ALL and additional pathways. An audit has been completed which has found SNP-A to be a suitable replacement for cytogenetic analysis in low risk MDS; this will be implemented locally once additional training has been completed

- Whole Genome Sequencing (WGS), which has been found to be particularly useful to focus on testing younger or fit patients with acute leukaemia (rather than all ALL patients) and sarcoma who are running out of treatment options, are able to wait for the longer analysis, and where results align with clinical trials. WGS for childhood cancers has been extended to the age of 25; to promote this, tumour agnostic guidelines will be published on the website.

Discussion:

Although results may be available in a more timely way to the laboratory, BCR-ABL1 takes a long time to be reported on the HiLIS system and, at present, Consultant Haematologists have to manually chase results.

The SIHMDS team have recently been inundated with results, which have to be manually uploaded on to HiLIS. To address this, an additional administrator will be appointed in the next few weeks.

In the long term, an automated process is being developed.

If the delays continue, Haem CAG are to flag this to C Wragg who will look for additional solutions.	**CAG Recommendation**

It is not possible to retrieve DNA from formalin fixed biopsies; samples need to be fresh frozen.

DNA extraction rate is rarely unsuccessful when using SNP-A.

3. Review of last meeting report and actions

The majority of actions from the previous meeting are on the agenda of the meeting today.

The new protocol request form is now available on the website here. Once completed, this can be sent to Network Pharmacist K Gregory: kate.gregory@uhbw.nhs.uk and copied to helen.dunderdale@uhbw.uk

The previous discussion 'CAG support discussions with CCGs to roll out Adult ALL testing in NBT' is thought to relate to MRD testing. This can now be undertaken in Severn Laboratory rather than sending to North London. Referrals need to clearly state that molecular and flow monitoring are required and should be sent with adequate samples for both.

The South West Leukaemia MDT is now up and running, chaired by T Coates.

It was not possible to continue with the Inspirata Clinical Trials AI tool pilot as the company withdrew interest.

In response to a review of the fast track referral forms, a comparison of three forms with differing data fields has been sent to Integrated Care Board (ICB) representative and GP G Beard.

H Dunderdale could send the comparison to the group to seek opinion on updating SWAG referral forms to include the data fields on the Pan-London form, for example, platelets ≤20 and actively bleeding, location of enlarged lymph nodes and additional guidance.

Referral forms are routinely received with many referral criteria not completed.

Action: Ethnicity coding needs to be included in all of the Suspected Cancer Referrals Forms to facilitate work identifying and addressing inequalities.	**G Beard/ICB Leads**

In BNSSG, further advice and guidance is available on the REMEDY website in order to keep the referral forms as succinct as possible. The guidance can be reviewed by G Beard, who can link with the other ICB Leads to ensure that this is uniform across the patch.

When referrals are received in Secondary Care, they are often imported as a 5-page document in no particular order onto the electronic notes system, with little information as to why a two week wait referral has been made. Referral information needs to be as clear and simplified as possible.

It is understood why referral quality varies at times due to current pressures in Primary Care but, in particular, the need for a para-protein rather than an IgG needs to be clarified to avoid referrals for myeloma being rejected.

The Bence-Jones criteria could also be removed and changed to provision of a serum free light-chain assay.

Action: The Advice and Guidance haematology service needs to be promoted to help redirect referrals to the most appropriate appointment.	**H Dunderdale**

The Peninsula CAG have recently revised their referral form.

Action: H Dunderdale will request access to the Peninsula referral form and share this with G Beard. **H Dunderdale**

It is possible to put frequently asked questions on REMEDY to reduce the need for repetitive queries to the Advice and Guidance service.

The action to share results from the National Quality of Life survey will be abandoned as the results have been found to be too generic to produce useful outputs.

It is hoped that results from Quality of Life studies that sit alongside research trials can be reviewed in future meetings instead. Patient Representative V Barley is a participant in a relevant study at Oxford, which included 15 QoL questionnaires.

Action: To explore if information from QoL studies would be useful to share. **H Dunderdale**

As there were no comments following distribution of the report from the meeting on Wednesday 12th January 2022, the report was accepted as finalised.

4. SIHMDS update

Presented by Consultant Haematologist S Otton on behalf of A Whiteway

A network meeting is due to convene on Friday 24th February 2023 to discuss further implementation of HiLIS, how Peer Review processes will work, and development of educational resources and tools for audit. An update will be given at the next CAG meeting.

UHBW have now moved to HiLIS. There is a need to ensure that access is granted to the enhanced user group, to ensure you can see when a report is pending or provisional.

Action: To arrange an occasional network meeting to troubleshoot any issues arising from the SIHMDS **C Wragg/ A Whiteway**

5. Research

Clinical Research Network update

Please see the presentation and Excel spreadsheet of the complete list of open studies on the SWAG website

Presented by Research Delivery Manager C Matthews

C Matthews manages the cancer portfolio for West of England CRN and combines data from Somerset so that it matches SWAG services geography.

National clinical trial recruitment from April 2022- February 2023 shows that recruitment to haematological cancer trials has decreased in comparison with 2021/22, which is most likely due to the closure of a large trial.

A comparison between national and regional recruitment figures shows the pre and post COVID comparison, as requested in the previous meeting. This reflects the sudden drop in recruitment, subsequent recovery and current status, with SWAG comparing favourably with the national data.

There are currently 69 trials open, and a further 14 in set up. In addition, there are 5 national trials open to new sites. Details of local recruitment figures are within the presentation.

The Question 58 in the National Cancer Patient Experience Survey (NCPES) 'Cancer research opportunities were discussed with the patient' scored below average across SWAG (42%) in comparison with the national average.

Haem CAG are asked to consider how to increase conversations about research.

Patient Representative feedback is to let the patient know that research trials have been considered, even if the outcome is that there is no eligible trial available.

An NIHR 6-month Associate Principal Investigator (API) role is open to any interested clinician who doesn't have research in their current role. It allows associates to work alongside current PIs on studies (as documented in the presentation) signed up to the scheme.

There are many Haematological studies included in the scheme, which has been shown to boost recruitment when an API is appointed.

Any PI interested in getting help from an API while helping their personal development is to get in touch.

NIHR website links and team contact details are available within the presentation.

Discussion:

The NCPES Survey is distributed to patients with a cancer diagnosis who have had an inpatient stay or day case stay. It will not capture those patients who have been managed as an outpatient, where the majority of haematological research discussions take place. However, work still needs to be undertaken to ensure SWAG feedback on the research question is comparable to national figures.

6. Patient experience

6.1 Consent information developed by GRH team

Presented by M Wheeler

Supportive information to facilitate consent has been developed by the GRH CNS team, and can be shared, as documented in the action from the previous meeting.

When the team converted to using CRUK SACT generic consent forms in 2019, the extra information required for lymphoma, CLL, myeloma and acute leukaemia was added using 'fill and sign'.

The information was cross-referenced with Macmillan, Myeloma UK and eMC(SPC) chemotherapy information leaflets, plus SWAG CAG and NSSG guidelines to ensure everything aligned. These were then proof read by the Consultants and made accessible to all relevant staff via a shared drive.

The generic consent form is due to be reviewed and once republished, all consent form information will be transferred to the latest version.

The practice in other centres, such as consent process for lymphoma and myeloma is of interest to the team, to see if it is possible to reduce duplication of work when updating consent forms.

The CNS team in GRH do the majority of consent work for disease areas where a protocol has been developed for this purpose, spending about 45 minutes to 1 hour with each patient. Consultant Haematologists consent to the Phase III trials.

Not all centres are using the generic forms, which are considered long and complex, and some prefer to continue completing a handwritten form.

BHOC have a generic consent form which is updated with the latest additional information. Having protocol specific consent forms could be timesaving.

It is not possible to delete the background data on the generic consent form. It is only possible to make additions.

SFT use a combination of the generic form and locally hand-written consent forms. The Consultants undertake the initial consent process, which is then run through again by the CNS. The protocols that enable GRH CNS team to undertake this work would be useful to share.

In GRH, the Consultant sees the patient for their diagnosis, who explains the treatment plan and provides the patient information leaflet. A separate appointment is then made with the CNS to go through the practicalities of how treatment is given and then through the consent process. As long as it is confirmed that the patient has good recall of the patient information given and has no specific questions for the Consultant, the CNS will take consent. This is reconfirmed by the Consultant prior to treatment commencing, and again by the SACT nurses. The CNS team have been provided with consent training, which is also now available via e-learning.

It was questioned whether the tick box of every single side effect in the CRUK form was in line with the Montgomery ruling to find out what matters to the patient.

Feedback from the Patient Representative is that a long list of side effects can sometimes be useful when a rare occurrence happens.

Patients are also given advice to contact the helpline with any symptoms of concern, and a traffic light alert card.

Consultants in GRH are allocated 40 minutes for a newly diagnosed patient; taking the detailed consent process out of this clinic session allows them more time to talk through the consequences of the diagnosis.

Linking the outputs from the original discussion at diagnosis with the consent process is recommended.

Action: Examples will be shared with the group **H Dunderdale**

7. Clinical guidelines

7.1 Review of outstanding Systemic Anti-Cancer Therapy (SACT) protocols

Presented by Network Pharmacist K Gregory

Volunteers are required to help draft the 12 outstanding new NICE TA SACT protocols.

There is a vast number of existing protocols that are past the review date, some of which are causing issues. For example, the ABVD protocol needs to be updated with dose capping recommendations and hepatic impairment details.

Although happy to produce the initial drafts, it is not possible for K Gregory to update all of the protocols in the time allocated to the role (which is for all cancer sites). Haem CAG Representatives from each tumour site are required to review and sign off that all updated information is correct.

All MPN protocols will be reviewed and updated by the MPN forum in the next two weeks.

Action: TA833 - Zanubrutinib will be completed by L Percy. **L Percy**

TA827 - Oral Azacitidine protocol has been completed and will be available on the website tomorrow.

TA813 – Asciminib will be completed by the MPN forum.

Action: TA787 – Venetoclax will be allocated to registrars with guidance from P Mehta. **P Mehta**

TA763 – Daratumumab has been drafted by B Bagnall and A Whiteway.

Action: B Bagnall and A Whiteway to send draft to K Gregory **B Bagnall/A Whiteway**

TA754 – Mogamulizumab needs to be removed from the list.

TA728 – Midostaurin will be completed by the MPN forum.

Action: TA695 - Carfilzomib with Dexamethasone and Lenalidomide for previously treated multiple myeloma will be allocated to B Bagnall and A Whiteway	**B Bagnall/A Whiteway**
Action: TA649 – Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma will be completed by S Otton	**S Otton**
Action: TA641 and TA577 – Brentuximab vedotin will be drafted and completed by N Chavda with assistance from the new clinical pharmacist	**N Chavda**

New volunteers are required to complete Triple IT.

SMILE and Idelalisib can be removed from the list.

Named authors of existing protocols will be emailed the word documents to either review themselves or delegate to a trainee.

8. Personalised care and support

8.1 Lymphoma risk stratified follow up

For discussion at a future meeting.

9. Coordination of patient care pathways

9.1 CNS Lymphoma Guidance

H Dunderdale/L Hawley

A meeting was held with representatives from Bristol Neuro-Oncology Group (BNOG) and Haem CAG on Thursday 2nd February 2023 for the purpose of optimising the CNS lymphoma pathway.

Most commonly, patients with suspected CNS Lymphoma are referred to BNOG straight from emergency departments or local general medical teams

BNOG offers a diagnostic service only for these patients; there are often uncertainties and delays in the patient pathway while the team try to establish if a biopsy is necessary/appropriate.

BNOG advise that steroids should not be started before the patient is referred for biopsy as this can make the lesion shrink and affect biopsy rates. In cases where this occurs, it is necessary to stop steroids and

wait for the lesion to reappear, and many are slow to re-emerge.

Haematology teams cannot take ownership of this patient cohort until diagnosis has been confirmed to prevent overloading clinics with other neurological conditions, but advice and guidance on appropriate management at presentation can be provided in the form of a flow chart, as can contact details in each centre.

Action: Guidelines have since been drafted by L Hawley and sent to L Percy and N Chavda to proof read from the Haematological perspective prior to further circulation to BNOG. L Percy/N Chavda

10. Clinical Guidelines continued

10.1 Lymphoma bone protection protocol

Consultant Haematologist L Lowry has drafted a lymphoma bone protection protocol which could be adopted as a SWAG wide document.

Action: To circulate to Haem CAG for comments H Dunderdale

10.2 CAR-T update

Please see the presentation uploaded on to the SWAG website

Presented by Consultant Haematologists R Alajangi and A Dayama

The following details are documented within the presentation:

- CAR-T Team – Dr Besley is returning in May 2023 and Dr D Gunasekhara is a new Associate Specialist member and it is planned to recruit an Advance Nurse Practitioner in the near future
- Data on the 2021 and 2022 referrals
- Changes to approval criteria and other updates
- Challenges for the service.

Discussion:

P53 positive disease status needs to be determined at the earliest opportunity.

The main reason for not progressing to treatment is disease progression; bridging therapies are improving.

Referrals in to the service have been smooth so far. It is helpful to know about potential patients as early on as possible.

10.3 CNS prophylaxis in High Grade Lymphoma

Presented by N Chavda and L Percy

In light of the National data gathered over the last few years, there is a waning appetite to provide CNS prophylaxis, even for some previously flagged special indications.

Giving intrathecally in the elderly population is also now mixed practice, and use of Methotrexate was much reduced.

The latest evidence from the American Society of Haematology (ASH) is to 'consider' this as a treatment option.

It has been discussed further at the South West Lymphoma meeting, where it was again noted to be increasingly difficult to justify, with no one in favour of giving it intercalated due to the delays this causes with R-CHOP delivery.

It is most appropriate for young fit patients with high-risk disease and adrenal issues. Testicular disease has definitely been flagged as an indication in several research trials.

It will be decided on a case by case basis at the end of R-CHOP after assessment of cardiac and renal function.

Action: A flow chart from the ASH team will be used to inform the updated CNS prophylaxis protocol which, once updated, will be made available on the SWAG website. **N Chavda/ L Percy**

10.4 Combined modality for Stage I/II Diffuse Large B-Cell Lymphoma (DLBCL)

Presented by Consultant Clinical Oncologists M Beasley and L Hawley

The aim of the session is to seek consensus on management of Stage I/II Diffuse Large B-Cell Lymphoma.

Historically, treatment was always combined modality treatment with 3 cycles of R-CHOP followed by radiotherapy. Following the results from recent trials, some practice has changed, and not all patients are now referred for combined modality.

The LAMIS trial showed that radiotherapy could be omitted for very low risk Stage 1 disease in young patients with a Performance Status of 0 and non-bulky disease, and that 4 cycles of R-CHOP was a safe alternative.

Discussion:

MDT discussions were noted to be increasingly nuanced and complex.

The extra option for avoiding radiotherapy is reasonable to consider if it is strictly applied only to this very low risk group. The decision may be dependent on the anatomical site of disease. **AGREED**

Combined modality should remain the norm for all other patients with DLBCL. **AGREED**

10.5 Radiotherapy for bulky DLBCL after R-CHOP

Presented by Consultant Clinical Oncologists M Beasley and L Hawley

The aim of the session is to seek consensus on management of bulky DLBCL after R-CHOP.

The results of two pre PET-CT trials show advantage in Progression Free Survival and Overall Survival when consolidated radiotherapy is given to bulky DLBCL, unless there is a significant reason not to due to RT related toxicities.

Now, a large retrospective Canadian Trial of patients with advanced bulky DLBCL has reported that patients who have a Complete Metabolic Response (CMR) on PET following R-CHOP, may be able to avoid RT – although one patient in this group did go on to have RT.

For those patients who had a Partial Metabolic Response, but still had avid disease on PET, 53% went on to have RT if deemed appropriate.

Those that were PET positive and didn't receive RT would have had extensive disease.

When looking at PFS and OS over a three year period in both the PET negative and PET positive groups, the group that received RT had comparable PFS with the PET negative group that didn't have RT.

In conclusion, it is still very relevant to give RT to patients who have had a PR to R-CHOP.

In the CMR PET negative group, there is concern that there will be a push to completely stop treating these patients with RT, as the data comes from a retrospective study, rather than a Randomised Controlled Trial (RCT), and a quarter of these patients do still relapse.

Discussion:

Haem CAG recommends that practice does not change (which does include balancing the risks of RT on a case by case basis) based on the retrospective study and should be reviewed once a prospective RCT has been undertaken. **AGREED**

The data could be useful to reassure patients who are PET negative but not appropriate for RT. **AGREED**

Date of next meeting: Tuesday 6th February 2024

-END-