Question and Answers from the Pathology event 12th January 2021

Introduction

1. Is the lack of engagement from Sheffield & South Yorkshire limited to pathology, or across the specialties?

Engagement varies across the specialities and across the region. Sheffield and South Yorkshire are very engaged in some of the other workstreams.

Impact of COVID

2. Do we see differences in staging at detection already?

The number of patients with outstanding diagnosis numbers are not available at the moment. We will need to monitor stage at presentation.

3. Any increase in acute presentations (obstruction etc)?

This is anticipated but we do not have stage/ presentation route breakdown information from the data that is currently available.

4. I may have missed this - but when the BCSP restarted are they picking up where they left off so everyone has a paused 6 months or are they intending to increase invites to get everyone back to their expected timeframe, so we'll get flurry of increased BCSP referrals?

The BCSP is intending to catch-up. The BCSP have been sending FIT tests out and receiving them back in. London has nearly caught up with its backlog but it has a lower rate of over 60 year olds. It will take longer to catch up in places like Yorkshire. The workload of the catch-up has not yet finished flowing through the system. This will also be impacted by endoscopy capacity.

Lynch Results from CRC Screening

5. Your 12.8% MLH1 deficient cases, presumably these were most, if not all, also PMS2 deficient. Is this correct?

This is correct. All MLH1 cases also showed PMS2 loss.

There are a small but significant number of cases showing MSH2 loss where MSH6 is partially retained. This is something to be aware of if undertaking a two stain cost-saving approach (not endorsed by NICE) as the patchy MSH6 loss may be considered as artefact e.g. due to poor fixation rather than a genuine loss. Other difficulties include mutations leading to truncation of the protein rather than complete absence therefore patchy staining making interpretation difficult. Care needs to be taken if 2 protein testing is implemented rather than 4 protein testing.

6. Is there a plan to use the MSI AI algorithm to highlight or prioritise cases that the AI programme classifies as dMMR?

We plan to validate the existing algorithm in the second programme using a prospective series across the region. If validated to 95%+ sensitivity, the plan would be to use these to identify possible dMMR cases that require confirmation via IHC or MSI. This would likely reduce the numbers needing an expensive molecular test down to 25-30%.

7. Can we reliably test suspicious biopsies, or should these be repeated on resection?

High-grade dysplasia / suspicious biopsies were excluded from the main analysis. The majority of tests on resection specimens were due to such non-diagnostic biopsies. Since the migration of testing to the NHS dMMR testing is taking place on high grade dysplasia / suspicious biopsies. dMMR occurs early in adenoma development therefore it is very rare to see it only in the invasive tumour. NW has seen only 2 cases in >4,000 reported both of which had pMMR in low grade dysplasia and dMMR in the cancer. It is therefore safe to test HGD if this is the only sample that exists, however, the advice would be to test resection specimens if one exists.

Lynch Screening of Endometrial Cancers

8. Given the subjectivity and focal nature of abnormality in some cases of G1 EM CA and interobserver variation of EIN... what are your suggestions on biopsy testing?

I would suggest the same approach as for HGD in the bowel. Where possible the sample should include definitive adenocarcinoma. Where it is suspicious or not quite invasive then it can be tested if it is the only sample and will usually show the same status as the associated invasive component. Where a second sample exists that is definitively invasive it is better to test this or subsequently test it for confirmation.

Thanks - yes I agree. However the interobserver variation is much greater in EM / EIN

9. For those who have funding, how did you secure it?

It comes from the commissioners. South Yorkshire happened first, West Yorkshire agreed some funding and the situation in North/East Yorkshire was unclear. Data on Lynch screening provided by YCR BCIP and the evidence behind the NICE guidance has been provided to the Cancer Alliances who are central to ensuring commissioned regional pathways for cancer services. Some Cancer Alliances have progressed with this quicker than others.

Following the meeting the NICE guidance on lynch testing in colorectal cancer and endometrial cancers will be circulated along with the guidance provided to Cancer Alliances by NHSE. It is important to flag the gaps in funding for pathology services for the preparation of material for molecular testing in the Genomic Laboratory Hubs and incorporation into reporting where it states that funding for this is provided by NHSE. Issues about incorporating this testing into pathways should be flagged with the clinical group Chairs in the three Cancer Alliances.

10. Once a test is fully established, should it not be incorporated into the treatment tariff rather than remaining a standalone item for funding?

Yes, this should move into the main pathway of care and incorporated into any treatment tariffs. Organisations are at various stages of being able to resolve this.