NDRS Lynch syndrome webinar
30.04.2021

Q&A that took place in the chat box throughout the session
If you have any more questions for the molecular & genomics team, please email: steven.hardy@phe.gov.uk or more general questions for the NDRS, email: NDRSengagement@phe.gov.uk

Q: Is there a link to the Implementation document just mentioned

A: Its currently just on the Cancer Alliance Workspace but we will be publishing formally soon. I am happy to send the handbook to anyone that would like it (E.Watts, NHS). Email NDRSengagement@phe.gov.uk and we will put you in touch with her.
Resources & Materials - Cancer Alliances Workspace - FutureNHS Collaboration Platform

Q: Are the terms "Lynch syndrome" and "MSI-H/dMMR" directly synonymous?

I.e. do 100% of lynch syndrome patients necessarily have MSI-H/dMMR tumours, and can 100% of patients with MSI-H/dMMR tumours be described as having Lynch syndrome?

A: Not all dMMR tumours are associated with Lynch.

A: No. dMMR simply indicates a tumour that has deficient MMR, some of which are sporadic, some of which are due to Lynch. Most dMMR cancers have MSI(-H), but not all.

See Cerretelli, G., Ager, A., Arends, M. J., & Frayling, I. M. (2020). Molecular pathology of Lynch syndrome. *The Journal of pathology*, *250*(5), 518-531.

BRAF V600E test only applies to COLON cancers. Because sporadic dMMR colon cancers generally arise from sporadic right-sided serrated lesions. Rectal cancers with dMMR are 3:1 on due to Lynch, whereas dMMR colon cancers are 3:1 on sporadic.

Q: Are there other genes involved with Lynch syndrome which have been identified through research but not tested for currently in NHS genetic testing and/or are there other candidate genes for inherited colorectal cancers?

A: There don't appear to be any other genes involved in Lynch, and we seem to have identified most if not all genes causing all the various other bowel cancer-predisposing conditions. The one remaining condition that we can't get far with is Serrated Polyposis Syndrome, where a gene called RNF43 is involved in a tiny fraction of families, but the rest are a mystery. That said, much research is being carried out.

Q: I was diagnosed in 2010 - can I request a test now? There is a family history. If I can who do I ask - GP or consultant?

A: Ask your GP to refer you to your Regional Genetics Service. There's a list of them at https://www.bsgm.org.uk/healthcare-professionals/list-of-genetic-clinics/

There are Lynch Syndrome patient groups in UK https://www.lynch-syndrome-uk.org/ and Ireland https://lynchsyndromeireland.com/ Highly recommended if you are a patient.

Q: What % records do you have ethnicity on?

A: We hold ethnicity data for 94.2% of diagnoses (this is based on 2018 data)

Comment: Such brilliant work, thanks, will be very helpful in managing services and pathways to improve patient care

Comment: Agree - important that the NHSE PLCM data is also integrated in this work

Comment: InSiGHT is the International Society for Gastrointestinal Hereditary Tumours. We help clinicians and patients with all aspects of hereditary bowel and related tumours. You can find out about syndromes, genes, variants etc at https://www.insight-group.org/

Q: What percentage of patients with dMMR tumours are associated with Lynch vs sporadic?

A: About 1/30 bowel and endometrial cancers in the developed world are due to Lynch.

Comment: Www.lynch-syndrome-uk.org
Great support here and a wealth of personal experience with the added bonus of having Ian, Sir John and many other LS experts on board.

Q: Are you also collecting/linking to data on biallelic MMRD syndrome in young people with lymphoma/leukaemia/CNS tumour but not (yet) colon cancer?

A: The linkage to the cancer registry includes paediatric patients, so we can correlate biallelic MMR mutations with any tumours. As we're right in the early stages of our work, we've only looked at colorectal and endometrial so far, but there is definitely the potential there to look at CMMRD.

Comment: I still look at those lines on the aspirin graph with amazement. And even more amazement with non-CRC effect of resistant starch!

Q: Presumably from the test data you can see geographical variation in test activity? Do you have suitable reference demographics to determine testing rate?

A: We do have demographics so could assess geographical variation in test activity - we can assess by other factors too e.g. ethnicity. We'll be looking at the demographics over the next few months - watch this space...! In terms of NHSE PLCM, we have had several discussions with NHSE Genomics and NDRS are extremely keen to bring in this data to see what value we can derive by

linking PLCM to wider registry data and outcomes - assessing equity of access would be a good starter for 10 - any other suggestions extremely welcome

Q: Most data suggests NSAID effect is maximal anti-cancer effect in first 3 years and reduces there after. what is the evidence from your work that longer treatment is beneficial?

A: We're only just getting the long-term data, but the concept back then of longer treatment falls into the category of "it seemed like a good idea at the time."