ALK Positive Lung Cancer (UK)

2024 Conference Report

Our 3rd national weekend conference for patients and a family member was held in September at the Radisson Red Hotel, London. Attendance at the conferences has increased from 100 in 2022, to 140 in 2023, and 170 in 2024. The conference opened with a dinner at which Professor Sanjay Popat delivered the keynote address.

The Chair of the Charity, Debra Montague, welcomed Professor Sanjay Popat, medical oncologist at The Royal Marsden Hospital and also the Charity's Clinical Advisor. He had flown in from addressing a conference in South Korea and had come directly to the conference. He said that there have been amazing improvements in the treatment of ALK-positive lung cancer in recent years and he was confident that this would continue. The world of drug development is changing so quickly and exciting research is being carried out in China. He ended with a quote from Nelson Mandela "It always seems impossible until it is done."

The first speaker on Saturday morning was Dr Fabio Gomes, medical oncologist at The Christie Hospital, Manchester, and he gave an update on **The ALK Education Project** which aims to

- Produce and promote educational material about Alk-positive lung cancer
- Develop a collaborative web platform to facilitate interaction and learning
- Utilise expertise from healthcare professionals and patients

The interactive website will have three modules –

- Lung cancer healthcare professionals
- Primary and secondary healthcare professionals with no specific experience in lung cancer
- ALK positive patients and their families

Debra said that the Charity fully supports this project which will be a valuable source of information not only for patients but also for primary healthcare providers so that they can consider lung cancer in younger non-smokers and bring about earlier diagnosis.

Dr Riyaz Shah, medical oncologist, Kent Oncology, spoke about circulating tumour DNA (**ctDNA**). He explained how cancer cells shed DNA into the blood stream so that a blood sample can be subjected to analysis and results can be available quicker than when a solid biopsy is done. However, oncologists should but reply solely on ctDNA testing and should also carry out a solid tumour biopsy.

England is a leader with national Genomic Hubs and ctDNA testing is now available throughout the NHS. Dr Shah ended by asking whether ctDNA could be used to

- Monitor the effectiveness of a TKI treatment
- Ascertain why a treatment has stopped working
- Detect of lung cancer at an early stage
- Determine whether a TKI should be prescribe following surgery and chemotherapy in an early-stage cancer.

Dr Anna Minchom, medical oncologist and lead investigator of the Nuvalent Trial at The Royal Marsden Hospital and Clinical Scientist, Institute of Cancer Research, closed the morning session with an informative presentation about the clinical trials that are available in the UK. She gave details of world-wide trials as

- 4th generation TKI (Nuvalent)
- Antibody Drug Conjugates
- Immunotherapy
- Vaccines
- Tumour Infiltrating Lymphocytes (a type of immunotherapy)
- Radiotherapy (oligo-progression)

Dr Minchom said that the range of trials is bewildering, access will be limited and many trials do not produce successful outcomes. Normally, patients will only consider a trial when their cancer progresses and there are no other options.

Question of the Conference goes to AiChoo Bennett. Dr Minchom had said that immunotherapy was effective in smokers but not so effective in non-smokers. AiChoo's question, "Should I start smoking?" created a loud reaction in the audience.

Dr Shobhit Baijal, Medical Oncologist, Universal Hospital, Birmingham, bravely led an open Question and Answer session. We had asked members who were unable to attend to let us have questions that they would like us to ask. However, there was no shortage of questions from delegates and we were able to include only a few extra ones. Dr Baijal dealt with questions that covered a wide range of topics. It isn't possible to list all these in this report but the video of this sessions is well worth viewing.

Professor Alastair Greystoke, Medical Oncologist, Northern Centre for Cancer discussed Local Consolidative Therapy. He explained that LCT is targeted treatment, usually by radiotherapy or surgery, for Limited number of sites to where the cancer has spread. Oligometastatic refers to a small number of sites where the cancer has spread. There is discussion as to what is meant by "small" – originally referred to not more that three sites but some oncologists now think that it could include may more.

Professor Greystoke discussed the situation where a TKI had produced a partial response, e.g. the primary tumour had reduced by 70% and the number of metastases had reduced from 6 to 3 and this condition remained stable for some time. The argument for treating the small number of metastases with LCT is

▪ Prevent local symptoms	▪ Kill off residual clones

▪ Reduce disease burden
  ▪ Emerging mutations
  ▪ Systemic impact
	▪ Extend time on therapy/life

Metastasis is to the brain will usually be treated with LCT (radiotherapy) but this is not general practice with metastases in the body.

So, if LCT to the body might be effective, why shouldn't we do it?

▪ Impact on organ reserve/quality of life	▪ Kill off residual clones
▪ Prevent/reduce options for future local treatment, including trials	▪ Extend time on therapy/life

▪ Impact on cancer biology
  o Release of growth factors (surgery)
  o Lymphocytes (radiotherapy)
	▪ Impact on delivery of systemic treatment
	  o Pneumonitis
	  o Radionecrosis

There have been many studies into the effectiveness of LCT, often with conflicting results. The 5-year HALT study which opened in 2017 is due to report next year. The aims of the trial are to

- Find out if targeting the areas of cancer growth with SBRT helps TKIs work for longer
- Find out more about quality of life after having SBRT and TKI
- Learn more about the side effects of SBRT and TKI when used together

Karen Clayton is a Macmillan Lung/Palliative Clinical Nurse Specialist (CNS) in Cheshire and Chair of Lung Cancer Nurses UK. She explained what patients can expect from their CNS. Their role is to provide specialist guidance, support and a point of contact at all stages of care and treatment. Originally, the standard of provision was one full-time CNS per 80 but with new drugs extending live expectancy the workload has considerably increased. The CNS is an important member of the Multidisciplinary Team which considers the treatment plans for patients. The current national target is for 85% of patients to be seen by a CNS at diagnosis but, currently, only 72% are seen. Some ALK positive patients will have routine meetings with their CNS instead of an oncologist when the treatment is going well. In reply to a question, Karen said not every patient may have a named nurse but should have a Named Team with a contact number that will always be answered.

Professor Ben Solomon, Medical Oncologist, Melbourne, was unable to attend in person but delegates were able to receive his prerecorded presentation. He gave a brief history of the discovery of the rearranged ALK gene and the development of targeted drugs. He emphasised the importance of biomarker testing, so that an accurate diagnosis can be made and also brain MRIs, as about 30% of patients will have brain mets at diagnosis.

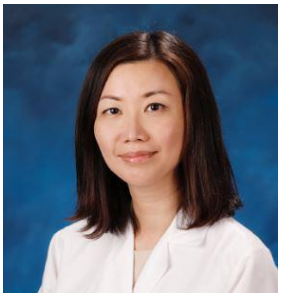
Dr Solomon spoke at length about Lorlatinib, a 3rd generation TKI and about how it could deal with some mutations that 2nd generation couldn't. He spoke about the latest Crown Study report on the effectiveness of Lorlatinib as 1st line treatment. He said that the results were remarkable and the best results for any targeted therapy to date, with sustained benefit. After 5 years, 60% of patients had no progression. He also referred to the effectiveness of Lorlatinib dealing with brain mets. The side effects of Lorlatinib are very different to other TKIs and dose reduction is often needed.

Dr Solomon concluded by looking at what the future holds –

- Newer more effective remedies, including 4th generation TKI
- Targeting at an earlier stage
- Striving for cure – chronic myeloid leukaemia as an example.

Dr Sharmistra Ghosh, Medical Oncologist, Guy's & St Thomas' Hospital, interrupted her Sunday morning hospital round to join the conference by Zoom and to answer questions arising from Dr Solomon's presentation. In answer to questions, she said

- There are unlikely to be trials that compare Lorlatinib with a 2nd generation TKI but it is likely that a 4th generation TKI in trial will be compared with a 2nd generation TKI.
- Lorlatinib has very different side effects to other TKIs and these will need to be monitored closely if Lorlatinib is used as 1st line over many years.
- In the USA, the FDA approves the safety of drugs but does not consider value for money or whether prescribers will be reimbursed. In the UK, NICE considers value for money and whether a drug should be made available in the NHS.
- Toxicity can often be well manged by dose reduction.
- Combining TKIs is not likely to be effective but using a TKI with, for example, immunotherapy is being looked at.



Dr Viola Zhu, Vice-President of Medical Development at Nuvalent Inc, presented information about the ALKove-1 trial. NVL-655 is a 4th generation TKI with good brain penetration. It is designed to remain active in tumours that have developed resistance to first, second, and third generation ALK inhibitors. Side effects of other ALK TKIs including cognitive impairment, mood disorders, sleep disorders, dizziness, ataxia (poor muscle control) and weight gain, among others, are hoped to be minimised.

Phase 1 of the trial with 133 patients started in June 2022 to determine the safety of the drug and determine the dose to be used in Phase 2. Phase 1 was completed in February 2024 and Phase 2 started in May 2024. 229 patients have been recruited worldwide and this may increase to 400. The trial will end in March 2026.

Phase 2 will determine the objective response rate (ORR). Secondary objectives will include the duration of response (DOR), time to response (TTR), progression-free survival (PFS) and overall survival (OS)

Phase 3 will have more patients and will compare NVL-655 with Alectinib.

In answer to questions, Dr Zhu said -

Stable is good.

There are two trial sites in the UK, The Royal Marsden and The Christies but if you are doing well on Alectinib then stay on it.

Phase 2 is open to all ALK+ patients, including those who have previously been prescribed a TKI and Phase 3 will be for patients who have not previously been prescribed a TKI.

Debra Montague, Founder and chair of ALK Positive Lung Cancer (UK), explained the structure of the charity and introduced two recently appointed trustees, Andy McKay, a patient who will chair the Audit Committee, and Kathy Redmond who will lead on Strategy and Performance. She also introduced Rebecca (Becs) Welsh, our recently appointed Charity Manager. Deb elaborated on

- the charity's vision and our long-term strategic objectives
- social media campaigns on raising the profile of non-smoking lung cancer
- our publications, including the latest Impact report
- accreditation as a Trusted Information Creator
- life coaching service

Debra concluded by thanking all those volunteers who have contributed to the work of the charity and the amazing fundraisers who enable us to support, empower, advocate and campaign.

Following the conference, delegates were asked to complete an online feedback survey. The response was overwhelmingly positive and many members said that it was the best conference yet. We will take into consideration all the constructive comments received when planning next year's conference

From a patient, *"Thank you for the incedible and informative conference and for the invaluable organisation. I feel so lucky to have been there and, even though I was meeting everyone for the first time, we felt very much like a community."*

From a lung cancer nurse, *"I just wanted to let you know that I saw a patient in clinic last week and he couldn't compliment the ALK Positive conference highly enough.*

"He was so enthusiastic about it – as was his wife. It was amazing to see and hear the passion that they both had and the positivity that they came away with.

"I just wanted to let you know what a fantastic job you're doing."

It is not possible in this report to capture the depth and breadth of all the matters discussed at the conference but videos of all presentations, discussions and what the delegates thought can be viewed at

Videos | ALK Positive UK | Supporting patients of ALK+ lung cancer