ALK-positive Non-Small Cell Lung Cancer (NSCLC)

Information for Doctors.

ALK-positive is a rare type of non-small cell lung cancer in which there is an abnormal fusion of the anaplastic lymphoma kinase (ALK) gene and another gene. The abnormal gene fusion results in the production of an anomalous hybrid ('mutant') protein that is responsible for uncontrolled cell division, resulting in the cancer and its spread.

- ALK-positive NSCLC was first identified in 2007
- The ALK-positive rearrangement is present in only about 4% of all people with NSCLC
- It is acquired, not inherited
- The trigger for the abnormal fusion is currently unknown.

The following key facts about ALK-positive NSCLC are based on analysis of the UK population and NICE Treatment and Management Guidelines.

ALK-positive NSCLC patients have typically never smoked and are younger

- 69% have never smoked (or smoked very little)
- Median age at diagnosis is 53 years
- 54% are female.

87% are at stage 4 (metastatic spread to another body organ) at diagnosis[1]

- 30% have brain metastases at diagnosis
- Other common metastatic sites:
  - bone
  - intra-abdominal
  - malignant pleural effusion
  - lymph nodes.

Oral targeted therapy is effective in stage 4 metastatic disease[3]

- Tyrosine Kinase Inhibitors (TKIs) are used for targeted treatment of ALK-positive NSCLC
- TKIs specifically block the abnormal ALK fusion protein thus preventing uninhibited cell division and cancer growth, reducing the size and spread of primary and metastatic lesions
- 2nd generation TKIs (Alectinib, Brigatinib) have good brain penetration; they are currently used in the UK as the first line in treatment of ALK-positive NSCLC.

- TKIs are generally well tolerated with fewer side effects than conventional chemotherapy
- Radiological resolution of primary and metastatic disease is often achieved and may last for years.

Further mutations lead to TKI resistance and progression over time[3]

- Regular surveillance with 3-monthly CT scanning (and in many cases brain MRI) is required
- Localised progression may be treated by radiotherapy or surgery in combination with continuation of the current TKI
- For more widespread progression, the next step is usually the 3rd generation TKI, Lorlatinib.

Significant numbers of patients have resolution of progression and further years of stable disease

- Clinical trials of a 4th generation TKI are already running in the UK
- Further progression or TKI intolerance

Median survival in the UK for stage 4 ALK-positive NSCLC is 6.2 years[1]

- Median survival is likely to significantly increase over time with the cohort of patients treated since diagnosis with 2nd and 3rd generation TKIs
- TKIs allow a patient to live a normal, active, progression-free life, without serious side effects, for many years.

References

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2. Wardak Z and Choy H. Improving Treatment Options for Brain Metastases From ALK-Positive Non-Small-Cell Lung Cancer. J Clin Oncol. 2016; 34:4064-5.
3. National Institute for Health and Care Excellence (NICE), Lung cancer: diagnosis and management. https://www.nice.org.uk/guidance/ng122/ chapter/Treatment (Accessed February 2025)

This leaflet has been produced by
ALK Positive Lung Cancer (UK)
1 Ethley Drive
Raglan
Monmouthshire NP15 2FD
Telephone: 07975 623515

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For further information, please visit **www.alkpositive.org.uk**

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