

ALK-Positive Lung Cancer.

Do Not Resuscitate (DNR) Decisions.

A Guide for Doctors, Patients and Families.



Patients may wish to share this leaflet with any doctor or other health professional who may not be familiar with ALK-Positive lung cancer.

Oncology experts in ALK-Positive Lung Cancer have reasonable hope that this cancer will be seen as a long-term chronic disease within the lifetime of existing patients.

ALK-Positive Lung Cancer (LC) is rare and many doctors will be unfamiliar with it. Doctors have a responsibility to be fully informed about any serious disease affecting a patient in their care and especially so if considering a Do Not Resuscitate (DNR) decision.

This leaflet covers key points about ALK-Positive LC, information about Cardiopulmonary Resuscitation (CPR) and the medicolegal aspects of DNR decisions. It is intended to help inform doctors, patients and families, to facilitate discussions between them and to guide the doctor's decision about whether or not to sign a DNR order for a patient with ALK-Positive LC.

ALK-POSITIVE LUNG CANCER:

- **Patients have typically never smoked and are often younger**
- **87% are at stage 4 (metastatic spread to another body organ) at diagnosis**
- **Oral targeted therapy is effective in stage 4 metastatic disease**
- **Drug resistance is likely in time but there is a next generation targeted therapy as well as other treatment for this situation**
- **Current therapies successfully manage this condition and median survival in the UK for stage 4 ALK-Positive LC is 6.2 years and increasing.**

ALK-Positive Lung Cancer (LC) is a rare type of non-small cell lung cancer (NSCLC) in which there is an abnormal fusion of the anaplastic lymphoma kinase (ALK) gene and another gene. This rearrangement is present in only about 4% of all people with NSCLC and is acquired, not inherited. The trigger for the abnormal fusion is currently unknown. The abnormal gene fusion means an anomalous hybrid ('mutant') protein is produced that is responsible for uncontrolled cell division, resulting in the cancer and its spread.

**First identified in 2007, few doctors will have looked after
a patient with ALK-Positive LC.**

Facts about ALK-Positive LC based on analysis of the UK population and current NICE Treatment and Management Guidelines are presented here:

- **ALK-Positive LC patients have typically never smoked and are often younger¹**
 - **69%** have never smoked (or smoked very little).
 - Median age of **53 years** at diagnosis.
 - **54%** are female.
- **87% are at stage 4 (metastatic spread to another body organ) at diagnosis¹**
 - **30%** have brain metastases at diagnosis².
 - Other common metastatic sites:
 - bone
 - intra-abdominal
 - malignant pleural effusion
 - lymph nodes

-
- **Oral targeted therapy is effective in stage 4 metastatic disease³**
 - Tyrosine Kinase Inhibitors (TKIs) are used for targeted therapy of ALK-Positive LC.
 - 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 as the first line in treatment of ALK-Positive LC.
 - 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 time³**
 - Regular surveillance with 3-monthly CT scanning (and in many cases brain MRI) is required.
 - The next step is usually the 3rd generation TKI, Lorlatinib.
 - Significant numbers of patients have resolution of the progression and generally have further years of stable disease.
 - Localised progression may be treated by radiotherapy in combination with current TKI.
 - Clinical trials of a 4th generation TKI are already running in the UK.
 - Further progression or TKI intolerance may be treated with chemotherapy and immunotherapy.

 - **Median survival in the UK for the stage 4 ALK-Positive LC is 6.2 years¹**
 - Although median survival is 6.2 years, over half of patients survive longer than this.
 - 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.

CPR AND DNR

Cardiopulmonary Resuscitation (CPR) is a treatment that can be given when a person's breathing stops (respiratory arrest) or their heart stops beating (cardiac arrest). CPR is a term which embraces all the procedures from basic first aid to advanced medical interventions (including defibrillation)⁴. The aim is to restart the breathing and heart when they have stopped.

- Actions used in CPR, such as chest compressions, can cause bruising, break ribs and puncture lungs.
- CPR restarts the heart and/or breathing for between 1 and 2 people in 10.
- Of those resuscitated some are left with permanent heart and/or brain damage.
- The best chance of CPR restarting the heart and breathing is in those people with heart, lungs and other organs that are healthy and working well before a cardiac or respiratory arrest.
- Chances of successful CPR are lower if a person has previous organ damage (eg heart disease), current severe illness (eg sepsis with multi organ failure), is frail or approaching the end of life.

DO NOT RESUSCITATE (DNR)⁵ ORDERS

- ONLY specify whether a person will receive CPR or not.
- are signed to allow dignity and a peaceful death.
- permit the healthcare team not to try to restart a patient's heart or breathing.
- are recorded on a special form. Doctors and hospitals may use different forms. Examples include a DNACPR form, a treatment escalation plan or a summary plan for emergency care and treatment (ReSPECT⁶ form).
- can be reviewed and revoked if circumstances change (eg after recovery from an episode of severe illness).

DNR is a medical decision made by the doctor. Patients and families must be told if a DNR order will be/has been completed. An explanation about DNR orders and why the doctor thinks resuscitation would not be in the best interests of the individual patient must be given. Patients should have the opportunity to express their wishes and preferences, but the doctor makes the final decision even if the patient does not agree.

DNR is only about CPR: patients will still receive appropriate care, treatment, symptom control and support.

A DNR order applies only to CPR and so having a DNR order should not affect what other treatment a patient receives. Research however, has suggested this has been an area of confusion for some healthcare professionals, and patients should discuss any concerns with their doctor so they are clear about the full treatment plan being proposed and what role the DNR order plays within that plan⁷.

OBLIGATIONS OF DOCTORS

Doctors in the UK are regulated by the General Medical Council (GMC)⁸. This means all doctors have a duty of care to:

- act in the best interest of the patient.
- offer treatment options based on up-to-date clinical evidence.
- be fully informed about the patient's condition, the nature of the disease(s) affecting the patient and the likely risk of cardiac or respiratory arrest and response to CPR.
- discount their personal views of the patient's quality of life.
- act on the presumption to prolong life but are under no absolute obligation to prolong life irrespective of consequences.

Doctors also have an obligation⁸ to seek advice or a second opinion from a colleague with relevant experience (who may be from another specialty, such as oncology or palliative care) if:

- the doctor and the healthcare team have limited experience of the condition.
- they are in doubt about the benefits, burdens and risks of a DNR decision for the individual patient.
- there is a significant difference of opinion between the doctor and patient.

REFERENCES

1. Gomes F, Yip K, Tokaca N, Greystoke A, Escriu C, Conibear J, et al. *The ALK project: a real-world national network and database. Lung Cancer.* 2019;127:S31-S2.
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> (last accessed May 23, 2023).
4. Resuscitation Council UK www.resus.org.uk (last accessed May 23, 2023).
5. DNR may also be referred to as DNAR (Do Not Attempt Resuscitation) or DNACPR (Do Not Attempt Cardiopulmonary Resuscitation). For the purposes of this leaflet we use the term DNR.
6. *Recommended Summary Plan for Emergency Care and Treatment,* www.respectprocess.org.uk (last accessed May 23, 2023).
7. Leigh Day Solicitors *Do Not Resuscitate (DNR) Decisions: A guide for patients and families.* www.alkpositive.org.uk (last accessed May 23, 2023).
8. *General Medical Council Guidance: Treatment and care towards the end of life.* www.gmc-uk.org (last accessed May 23, 2023).

This leaflet has been produced by the Medical & Scientific Panel of ALK Positive Lung Cancer UK (registered charity number 1181171) May 2023