

The use of results from ctDNA reports from the NHSE pilot in making initial treatment decisions for patients with advanced lung cancer.

Determine which category the blood result falls into:

- 1) **Informative result :Abnormality suggests first-line targeted treatment available**
- 2) **Informative result but no first-line targeted treatment available** (note second-line targeted or clinical trial treatments might be available such as KRAS G12C, NTRK or ERBB2)
- 3) **Result not informative to make initial treatment decision.** This may be because
 - a. There is insufficient circulating tumour DNA in the sample or
 - b. There is not an oncogenic abnormality in one of the key genes below to enable a confident treatment decision on the basis of the ctDNA alone at this time. This information may still be useful in guiding the subsequent care of the patient.

The determination of which category the result can be falls into can be made by any suitably trained person including a respiratory physician or oncologist; if there is any doubt as to which category the result falls into it should be discussed with your GMS

Action to be taken

- 1) **Informative result: Abnormality suggests first-line targeted treatment available**
Start targeted treatment immediately if radiology in keeping with stage 3 not suitable for radical treatment or stage 4 lung cancer. This is in line with NHS guidance and Blueteq criteria
- 2) **Informative result but no first-line targeted treatment available**
Once histological confirmation of NSCLC is in place start appropriate systemic treatment; there is **no requirement to await tumour molecular profiling.**
- 3) **Result not informative to make initial treatment decision**
Await histological confirmation and tumour molecular profiling if appropriate before starting treatment (as per previous practice).

The table below can be used to guide clinical management based on **pathogenic** abnormalities in the genes below and the reported **percentage** in the blood (VAF or Variant Allele Frequency

Abnormality	VAF			
	0.1-0.5%	0.5-1%	>1%	>2%
Sensitising EGFR mutations	Start targeted treatment if in keeping with clinical context. Consider GMS discussion	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context
Alk fusion	Start targeted treatment if in keeping with clinical context. Consider GMS discussion	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context
Ros 1 fusions	Start targeted treatment if in keeping with clinical context. Consider GMS discussion	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context
RET fusions	Start targeted treatment if in keeping with clinical context. Consider GMS discussion	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context
BRAF V600 mutations	Start targeted treatment if in keeping with clinical context. Consider GMS discussion	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context
Met exon 14 skip lesions	Start targeted treatment if in keeping with clinical context. Consider GMS discussion	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context	Start targeted treatment if in keeping with clinical context

KRAS G12C	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Start appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry	Informative. Book appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry	Informative. Book appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry
NTRK fusion	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Start appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry	Informative. Start appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry	Informative. Book appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry
ERBB2 mutations	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Start appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry	Informative. Start appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry	Informative. Book appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry
KRAS Non G12C	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
BRAF Non V600	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.

P53 mutation	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.
PI3K mutation	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
STK11 mutation	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
KEAP1 Mutation	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
SMARCA4	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
CDNK2a	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
PTEN	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.

FGFR1 mutations/ fusions	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
FGFR2 mutations/ fusions	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
FGFR3 mutations/ fusions	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
EGFR exon 20 mutations	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Start appropriate systemic treatment when Histology available. Result may be used to guide 2nd line treatment or trial entry	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
NF1 Mutations	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
NF2 mutations	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.

Arid1A	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	Informative. Book treatment when Histology available.	Informative. Book treatment when Histology available.
No oncogenic abnormalities in any of the above genes	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.	May not be informative. Ideally wait for histological confirmation and tumour molecular profiling.