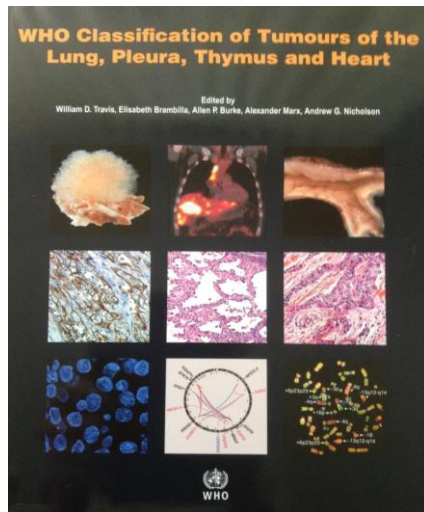


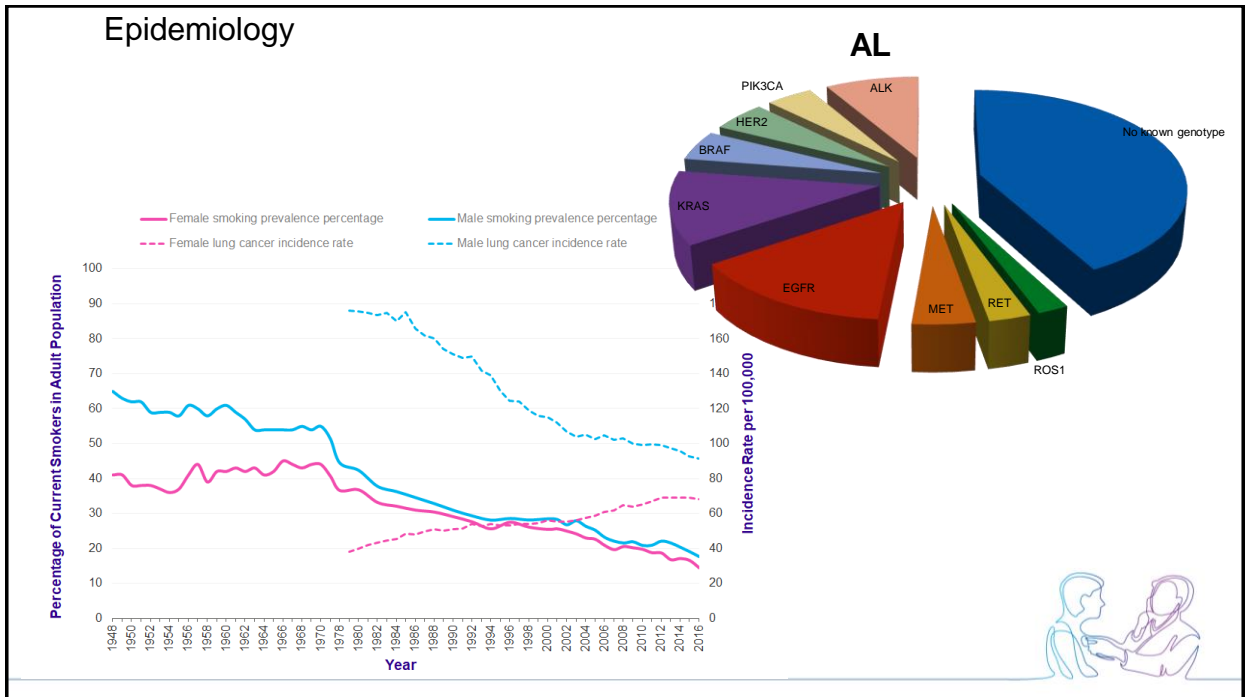
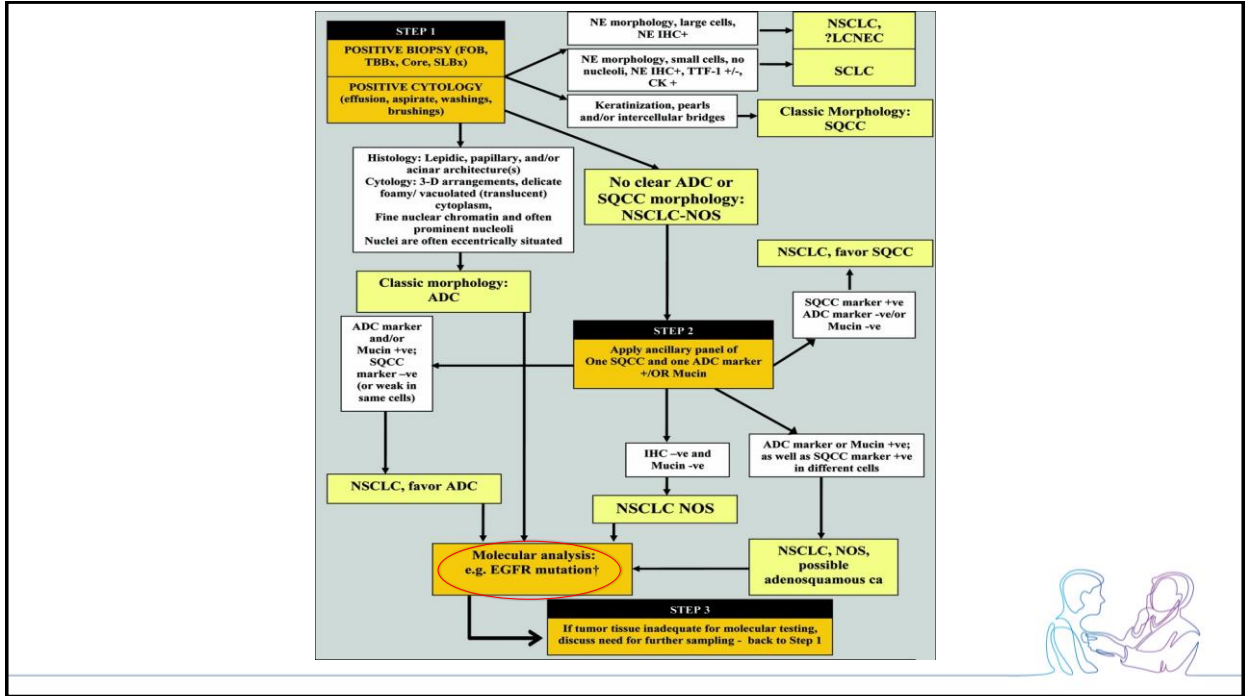
Роль ALK тестирования при раке легкого и особенности его интерпретации

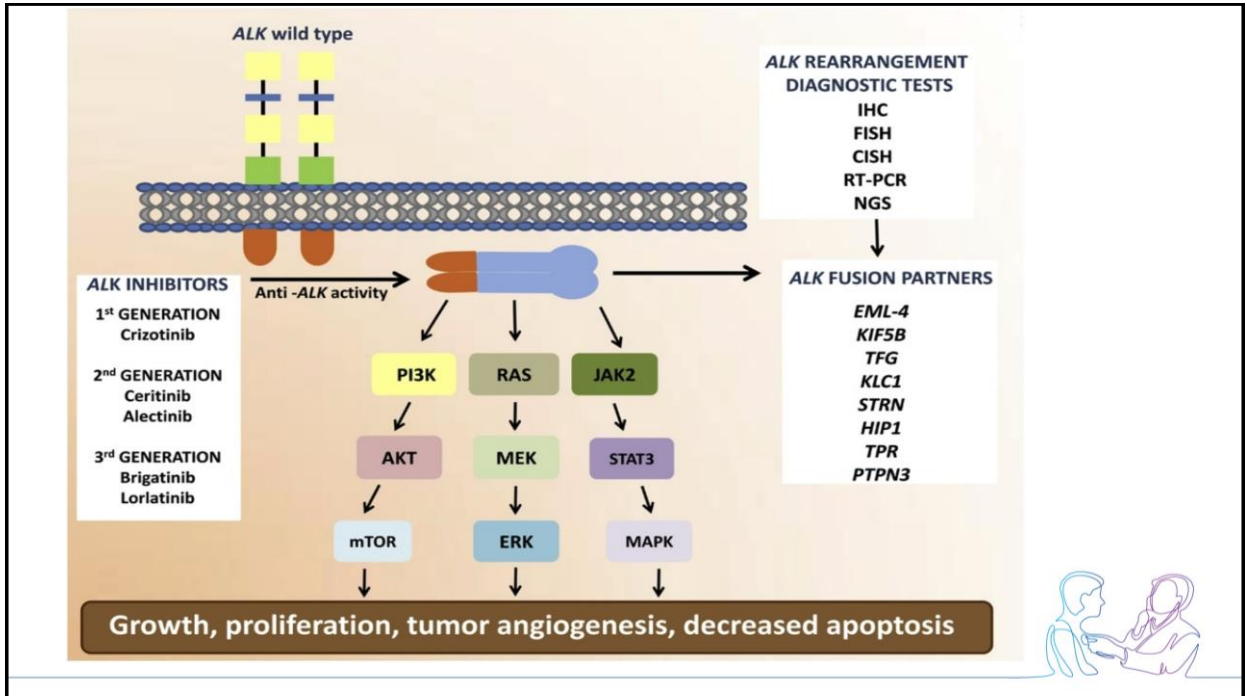


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WHO classification 2015





**Table 2**

Incidence of *ALK* rearrangements in NSCLC in populations from different countries.

Country of origin	N	n (%)	Reference
Latin-America	188	19 (10.1)	(Corrales-Rodríguez et al., 2017)
Latin-America	7600	487 (6.4)	(Martín et al., 2018)
Mexico	200	18 (9)	(Cruz-Rico et al., 2017)
Argentina	131	8 (6.11)	(Verzura et al., 2018)
Brazil	62	2 (3.23)	(Lopes and Bacchi, 2012)
Chile	49	3 (6.12)	(Fernandez-Bussy et al., 2017)
Italy	96	1 (1.04)	(Lee et al., 2018)
Spain	97	2 (2.06)	
Germany	97	2 (2.06)	
Australia	92	4 (4.35)	
Japan	100	2 (2.00)	
Korea	94	9 (9.57)	
Taiwan	80	3 (3.75)	
China	1387	71 (5.12)	(Tian et al., 2017)
China	1160	94 (8.10)	(Hong et al., 2014)
USA	1387	49 (3.53)	(Dai et al., 2012)
Australia	296	25 (8.45)	(Tan et al., 2018)
Korea	3767	270 (7.17)	(Lee et al., 2016)

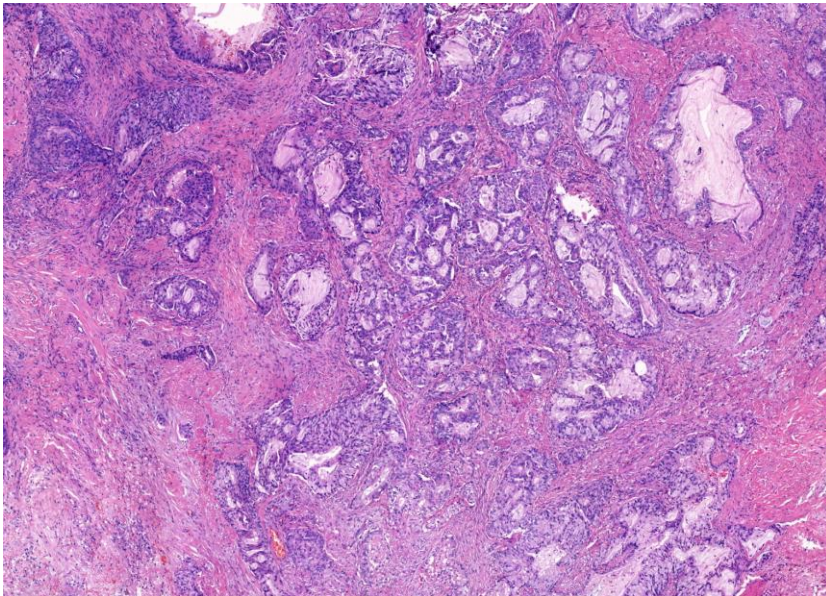
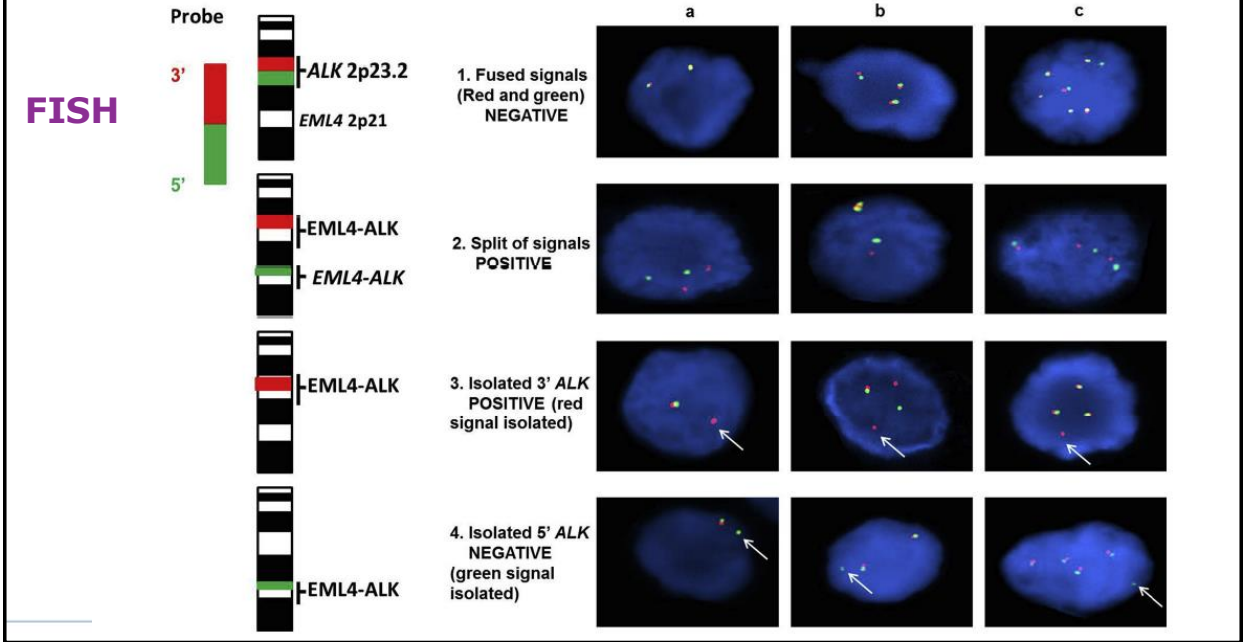
Table 1
ALK fusion partners in NSCLC.

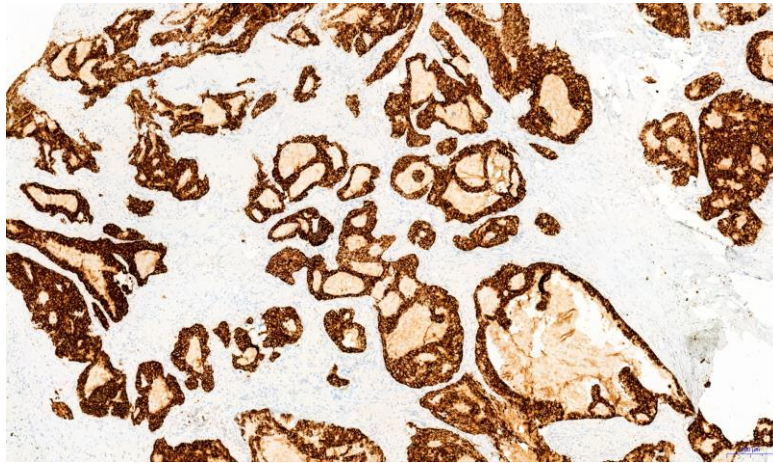
ALK cr.2	FUSION PARTNER	LOCALIZATION	REARRANGEMENT	BREAKPOINT
exon 20	<i>EML4</i> (Echinoderm microtubule associated protein like 4)	cr.2	inv(2)(p21p23)	exon 2 exon 6 exon 13 exon 14 exon 15 exon 18 exon 20
	<i>KIF5B</i> (Kinesin family member 5B)	cr.10	t(2;10)(p23;p11)	exon 15 exon 17 exon 24
	<i>TFG</i> (TRK-fused gene)	cr.3	t(2;3)(p23;q21)	exon 3 exon 4 exon 5
	<i>KLC1</i> (Kinesin light chain 1)	cr.14	t(2;14)(p23;q32)	exon 9
	<i>STRN</i> (Striatin, calmodulin binding protein)	cr.2	del(2)(p22p23)	exon 3
	<i>TPR</i> (Translocated promoter region)	cr.1	t(1;2)(q31.1;p23)	exon 15
	<i>HIP1</i> (Huntingtin Interacting Protein 1)	cr.7	t(2;7)(p23;q11.23)	exon 21 exon 28
	<i>GCC2</i> (GRIP and coiled-coil domain containing 2)	cr.2	t(2;2)(p23;q12)	exon 12
	<i>DCTN1</i> (Dynactin subunit 1)	cr.2	t(2;2)(p13;p23)	exon 26
	<i>SQSTM1</i> (Sequestosome 1)	cr. 5	t(2;5)(p23;q35)	exon 5
	<i>LMO7</i> (LIM domain 7)	cr. 13	t(2;13)(p23;q22)	exon 15
	<i>BIRC6</i> (Baculoviral IAP repeat-containing 6)	cr. 2	t(2;2)(p22;p23)	exon 10
	<i>PHACTR1</i> (Phosphatase and Actin Regulator 1)	cr. 6	t(2;6)(p23;p24)	exon 7
	exon 10 or 11	<i>PTPN3</i> (Protein tyrosine phosphatase, non-receptor type 3)	cr.9	t(2;9)(p23;q31)

Методы детекции

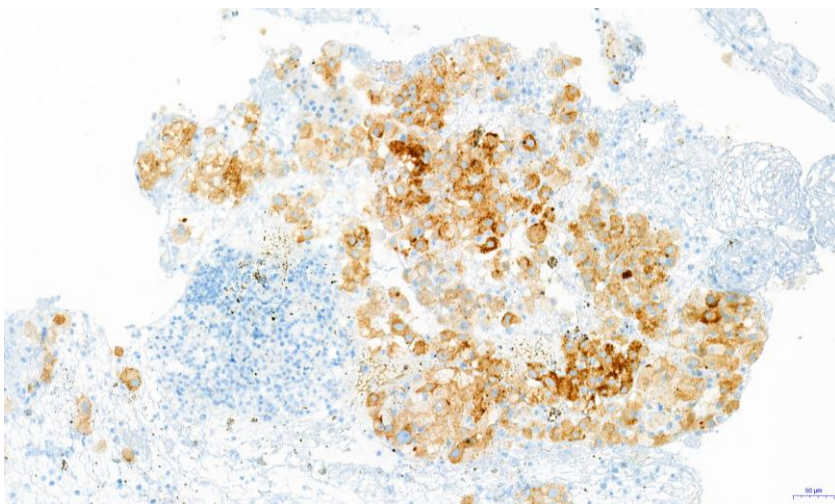
- ИГХ
- FISH
- CISH
- RT-PCR
- NGS





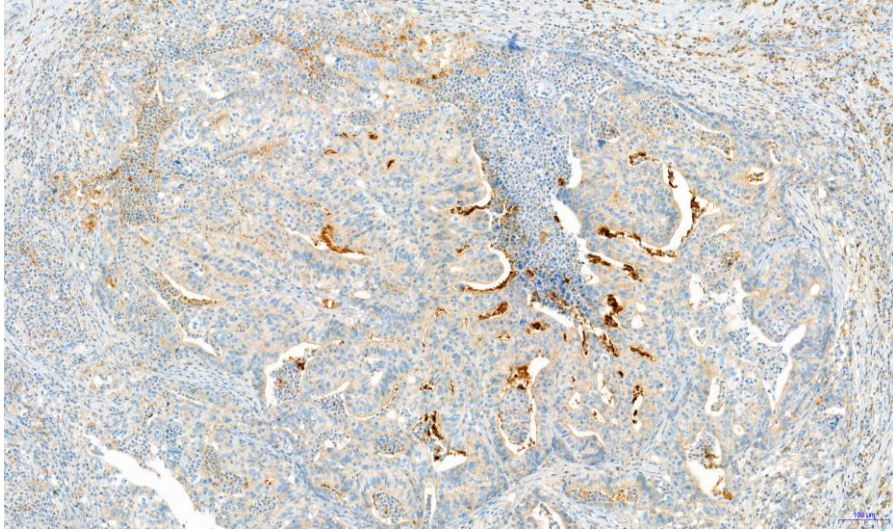


ALK D5F3

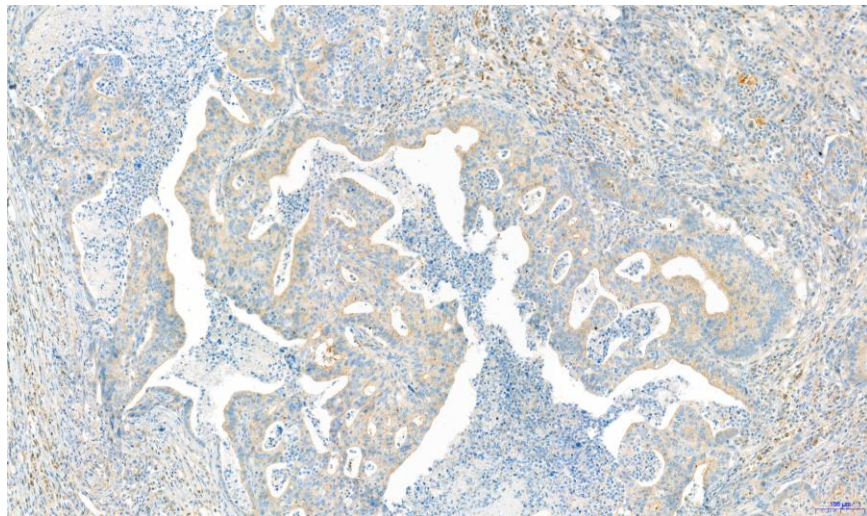


ALK D5F3





ALK D5F3

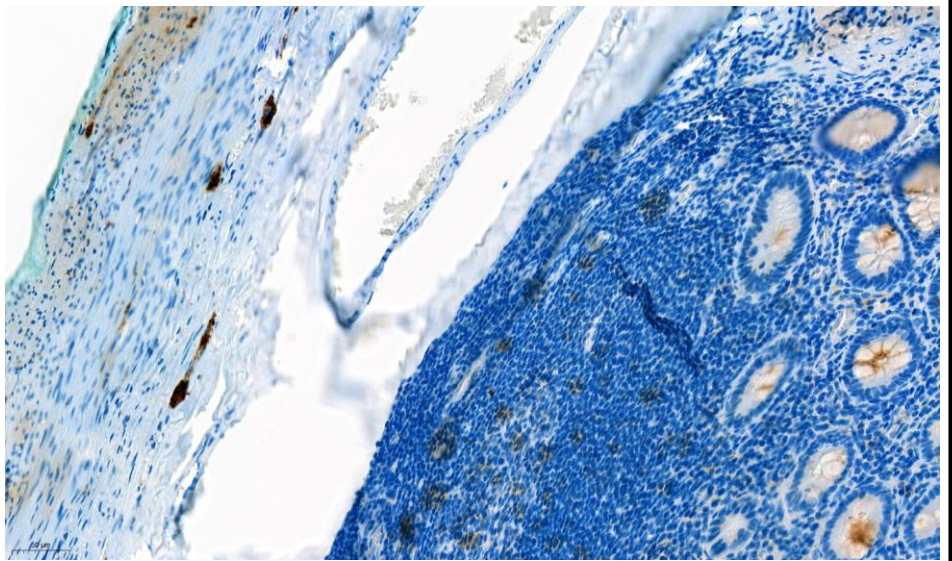


ALK D5F3



контроль

Аппендикс



Позитивная реакция

Цитоплазматическое

Гранулярное

Интенсивное / яркое

Всех или части опухолевых клеток



Негативная реакция

Мембранное

Слабой интенсивности

Неспецифическое диффузное окрашивание

Окрашивание муцина

Окрашивание нормальных клеток и структур (лимфо-макрофагального ряда, нервных)

Некротизированные ткани и детрит

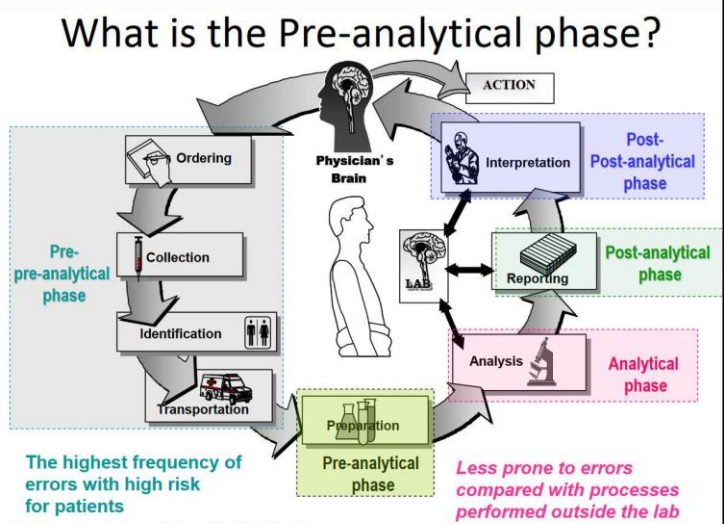


Факторы, влияющие на результат

Фиксатор

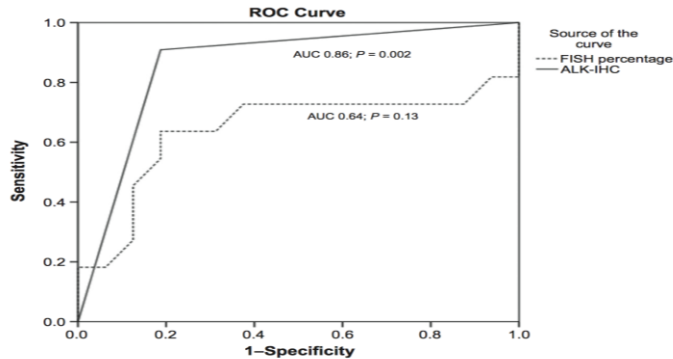
Время фиксации

Время и условия хранения срезов



Dichotomous ALK-IHC Is a Better Predictor for ALK Inhibition Outcome than Traditional ALK-FISH in Advanced Non-Small Cell Lung Cancer

A.J. van der Wekken¹, R. Pelgrim², N. 't Hart², N. Werner², M.F. Mastik², L. Hendriks³, E.H.F.M. van der Heijden⁴, M. Looijen-Salamon⁵, A.J. de Langen⁶, J. Staal-van den Brekel⁷, S. Riemersma⁸, B.E. van den Borne⁹, E.J.M. Speel¹⁰, A-M.C. Dingemans³, T.J.N. Hiltermann¹,



COLLEGE of AMERICAN
PATHOLOGISTS

Template for Reporting Results of Biomarker Testing of Specimens From Patients With Non-Small Cell Carcinoma of the Lung

Version: Lungbiomarker 1.3.0.2

Protocol Posting Date: June 2016

+ ALK by Immunohistochemistry

+ ___ Negative[#]

+ ___ Positive^{##}

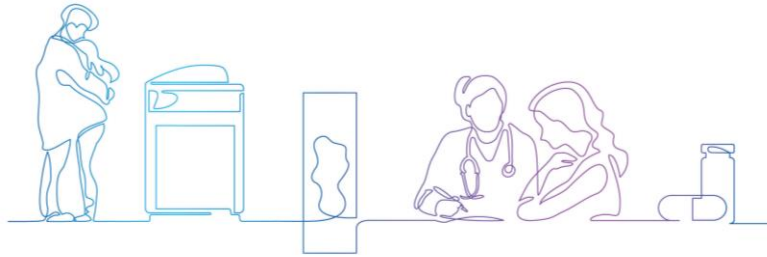
+ ___ Equivocal^{###} (explain): _____

[#] Absence of ALK protein expression in cancer cells suggests that this tumor is unlikely to harbor ALK rearrangement and to respond to treatment with a targeted inhibitor, such as crizotinib and ceritinib.

^{##} ALK protein expression in cancer cells (based on platform criteria) predicts the presence of ALK rearrangement and response to therapy with a targeted inhibitor, such as crizotinib and ceritinib.

^{###} Tumors with faint cytoplasmic labeling should be designated as equivocal. This result can rarely occur both with and without mutation.

Approximately 5% of lung adenocarcinomas have a chromosomal rearrangement involving the *ALK* gene, most commonly in the form of an intrachromosomal inversion leading to the EML4-*ALK* fusion product associated with ALK protein overexpression.¹⁵ Patients with this tumor type are responsive to therapy with ALK tyrosine kinase inhibitors, such as crizotinib.¹⁶ Fluorescence in situ hybridization (FISH) using break-apart probes is currently considered the “gold standard” for detection of *ALK* rearrangement, which may manifest as separation of the 5' and 3' FISH probes or as deletion of 5' probe. Although both types of alterations are associated with response to ALK-targeted therapies, some studies suggest that 5' probe deletion can rarely represent a false positive FISH result.^{17,18} Detection of ALK protein overexpression by IHC using the 5A4 or D5F3 clones is highly sensitive and specific for an *ALK* gene rearrangement in lung adenocarcinoma,¹⁹ and the FDA has approved the use of the Ventana ALK (D5F3) CDx Assay as a companion diagnostic for crizotinib.²⁰ According to the current guidelines, other carefully-validated, but non-FDA approved, ALK immunohistochemistry assays may also be used to screen for *ALK* rearrangement with confirmation by FISH before initiating ALK-targeted therapy.²



Спасибо за внимание!