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Iniciativa científica de:

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7-11 DE SEPTIEMBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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Actualización de detección de biomarcadores en NSCLC

Cristina Teixidó

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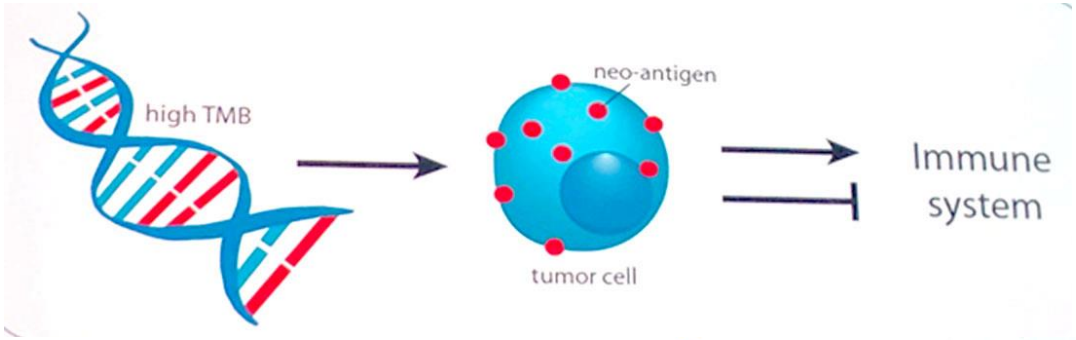
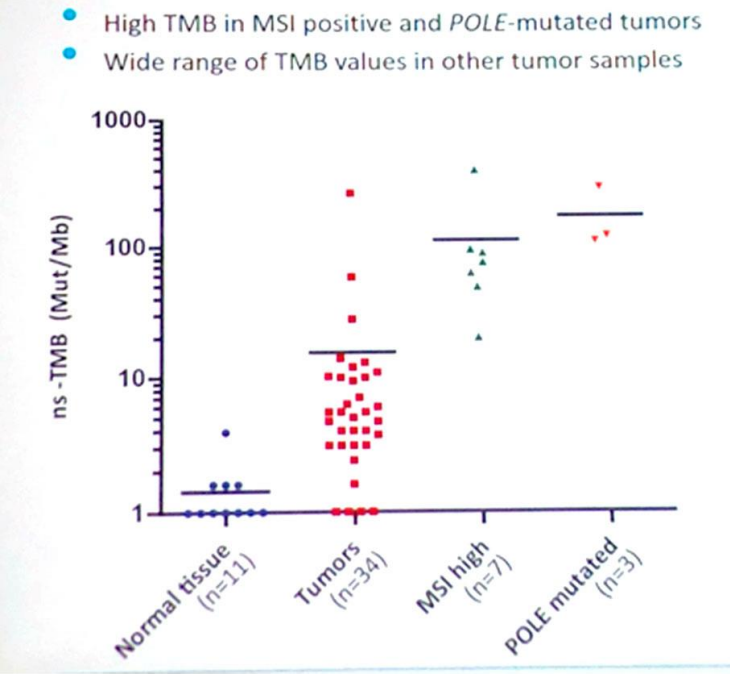
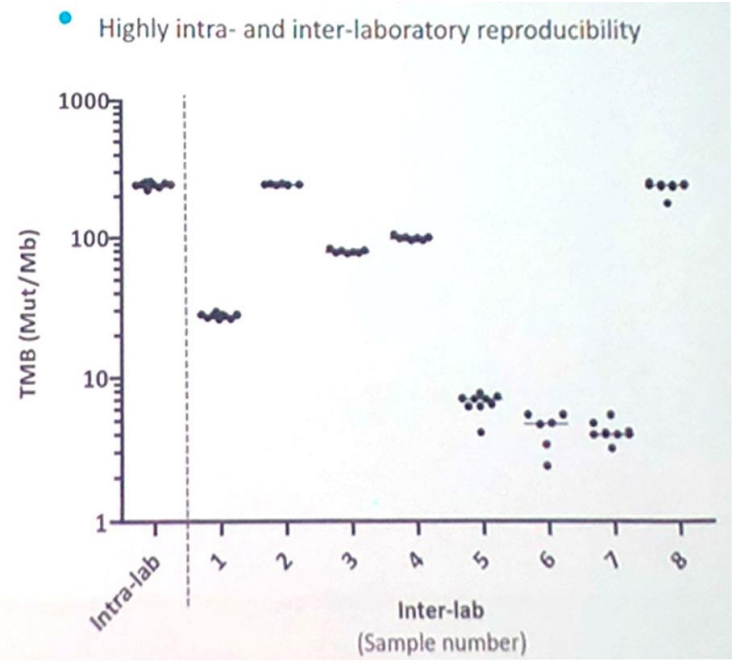
illumina
Lilly

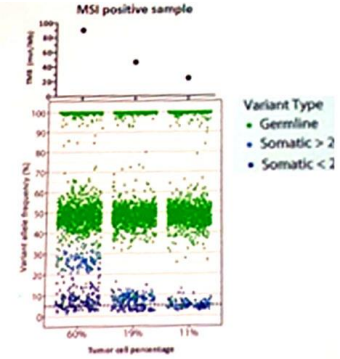
Tumor mutational burden analysis: implementation in routine diagnostics. TSO500





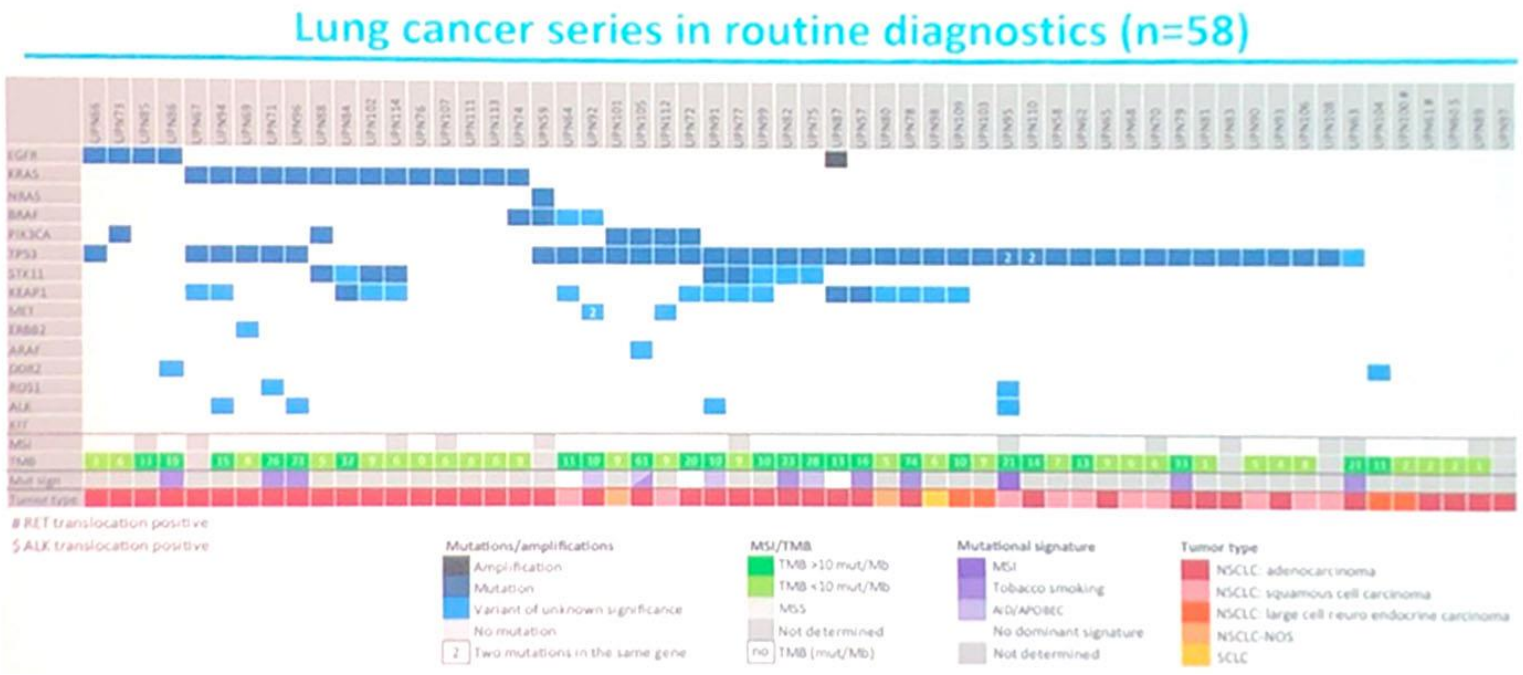


Tumor mutational burden analysis: implementation in routine diagnostics



TMB is influenced by tumor cell percentage in cases with:
- Defects in DNA repair

- TMB, MSI, CNV & mutation detection possible in 1 assay - 20 ng DNA
- TMB results are highly reproducible
- Minimum acceptance criteria for DNA quality, DNA quantity and tumor cell percentage should be defined when evaluating an assay for TMB assessment



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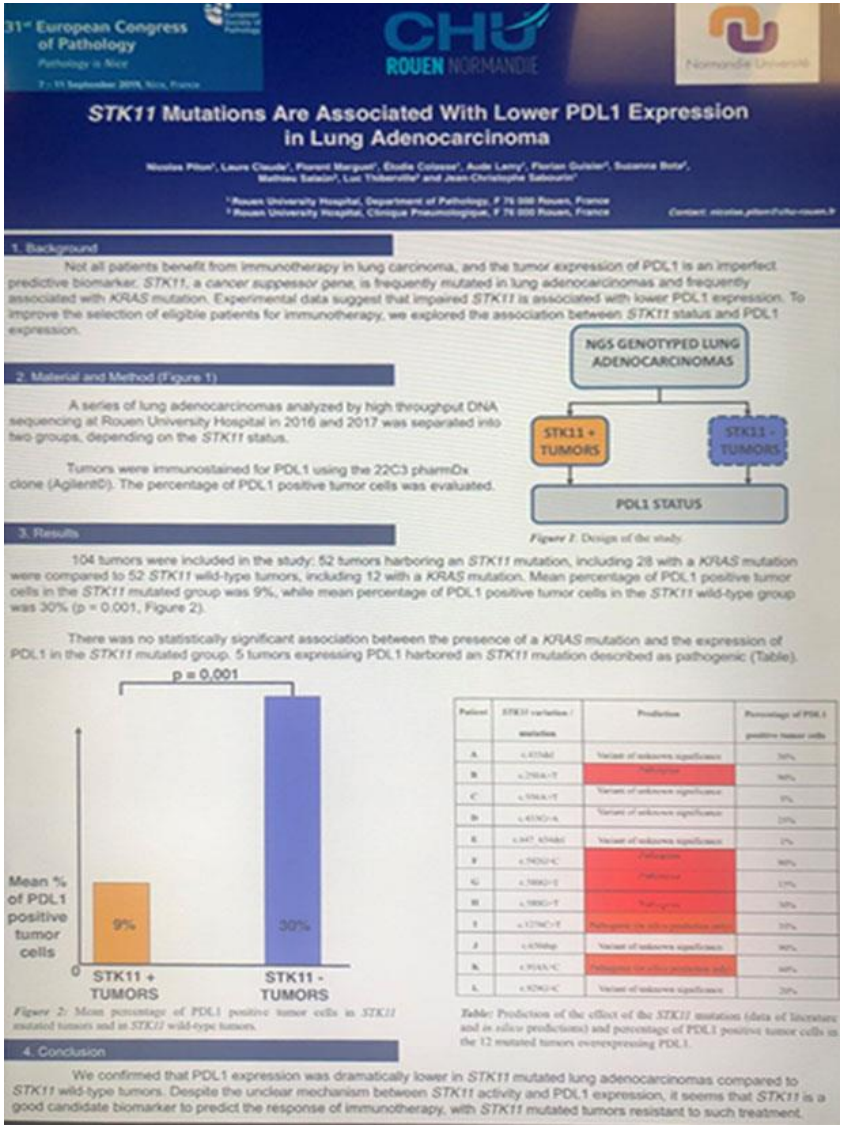
STK11 Mutations are associated with lower PDL1 expression in lung adenocarcinoma



31st European Congress of Pathology

CHU ROUEN NORMANDIE

STK11 Mutations Are Associated With Lower PDL1 Expression in Lung Adenocarcinoma

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1. Background

Not all patients benefit from immunotherapy in lung carcinoma, and the tumor expression of PDL1 is an imperfect predictive biomarker. *STK11*, a cancer suppressor gene, is frequently mutated in lung adenocarcinomas and frequently associated with *KRAS* mutation. Experimental data suggest that impaired *STK11* is associated with lower PDL1 expression. To improve the selection of eligible patients for immunotherapy, we explored the association between *STK11* status and PDL1 expression.

2. Material and Method (Figure 1)

A series of lung adenocarcinomas analyzed by high throughput DNA sequencing at Rouen University Hospital in 2016 and 2017 was separated into two groups, depending on the *STK11* status.

Tumors were immunostained for PDL1 using the 22C3 pharmDx clone (Agilent®). The percentage of PDL1 positive tumor cells was evaluated.

Figure 1: Design of the study.

3. Results

104 tumors were included in the study: 52 tumors harboring an *STK11* mutation, including 28 with a *KRAS* mutation were compared to 52 *STK11* wild-type tumors, including 12 with a *KRAS* mutation. Mean percentage of PDL1 positive tumor cells in the *STK11* mutated group was 9%, while mean percentage of PDL1 positive tumor cells in the *STK11* wild-type group was 30% (p = 0.001, Figure 2).

There was no statistically significant association between the presence of a *KRAS* mutation and the expression of PDL1 in the *STK11* mutated group. 5 tumors expressing PDL1 harbored an *STK11* mutation described as pathogenic (Table).

Figure 2: Mean percentage of PDL1 positive tumor cells in *STK11* mutated tumors and in *STK11* wild-type tumors.

Patient	*STK11* variation / mutation	Prediction	Percentage of PDL1 positive tumor cells
A		Variant of unknown significance	30%
B		Pathogenic	90%
C		Variant of unknown significance	5%
D		Variant of unknown significance	25%
E		Variant of unknown significance	1%
F		Pathogenic	90%
G		Pathogenic	15%
H		Pathogenic	30%
I		Pathogenic (in silico prediction only)	35%
J		Variant of unknown significance	90%
K		Pathogenic (in silico prediction only)	60%
L		Variant of unknown significance	20%

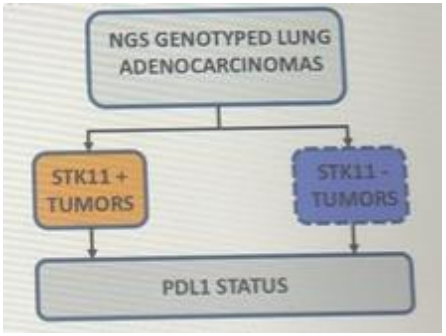
Table: Prediction of the effect of the *STK11* mutation (data of literature and *in silico* predictions) and percentage of PDL1 positive tumor cells in the 12 mutated tumors overexpressing PDL1.

4. Conclusion

We confirmed that PDL1 expression was dramatically lower in *STK11* mutated lung adenocarcinomas compared to *STK11* wild-type tumors. Despite the unclear mechanism between *STK11* activity and PDL1 expression, it seems that *STK11* is a good candidate biomarker to predict the response of immunotherapy, with *STK11* mutated tumors resistant to such treatment.

- 104 Lung ADC
- NGS + IHC PDL1

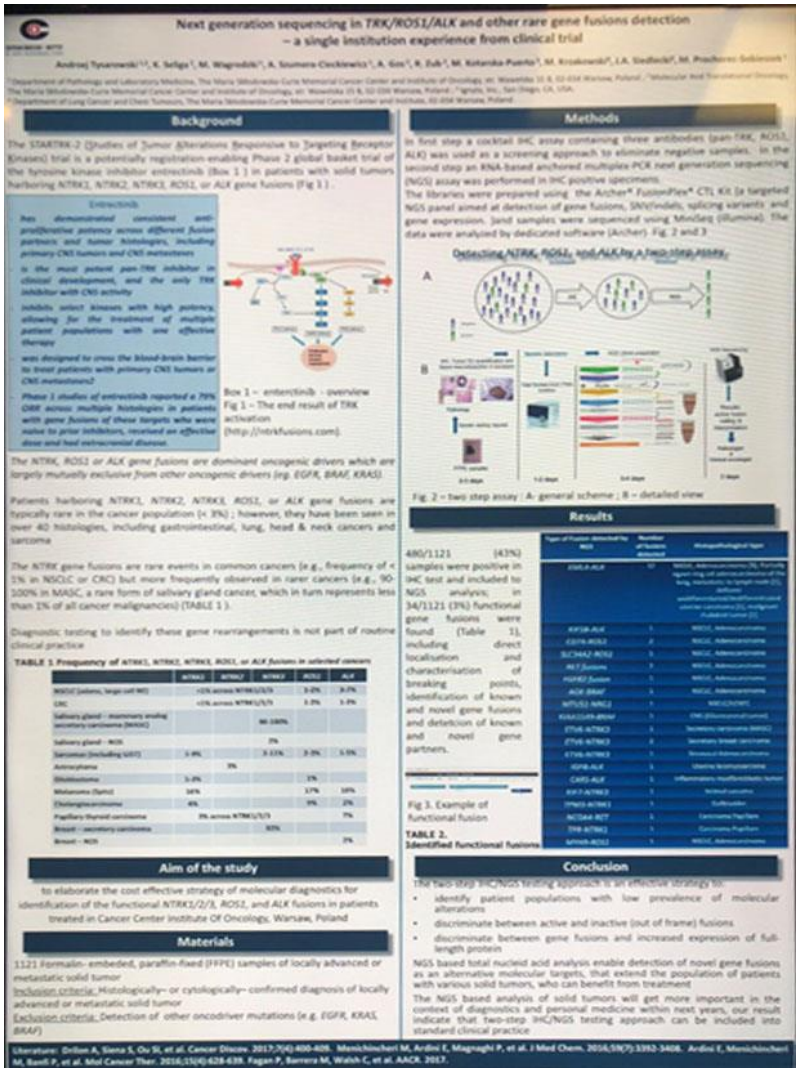
N=52



N=52

- PDL1 expression is lower in STK11 mutated lung ADK compared to STK11 WT tumors

NGS in TRK/ROS1/ALK and other rare gene fusions detection – a single institution experience from clinical trial


Next generation sequencing in *TRK/ROS1/ALK* and other rare gene fusions detection – a single institution experience from clinical trial

Background

Methods

Results

Aim of the study

Materials

Conclusion

- 1121 FFPE samples
- Excluding: EGFR, KRAS, BRAF
- Cocktail IHC assay: TRK+ ALK + ROS1

480/1121 (43%) samples were positive in IHC test and included to NGS analysis; in 34/1121 (3%) functional gene fusions were found (Table 1), including direct localisation and characterisation of breaking points, identification of known and novel gene fusions and detetcion of known and novel gene partners.

Fig 3. Example of functional fusion

TABLE 2. Identified functional fusions

Type of Fusion detected by NGS	Number of fusions detected	Histopathological type
EML4-ALK	12	NSCLC, Adenocarcinoma [9]; Partially signet-ring cel adenocarcinoma of the lung, metastatic to lymph node [1], deficent undifferentiated/dedifferenttiated uterine carcinoma [1], malignant rhabdoid tumor [1]
KIF5B-ALK	1	NSCLC, Adenocarcinoma
CD74-ROS1	2	NSCLC, Adenocarcinoma
SLC34A2-ROS1	1	NSCLC, Adenocarcinoma
RET fusions	2	NSCLC, Adenocarcinoma
FGFR2 fusion	1	NSCLC, Adenocarcinoma
AGK-BRAF	1	NSCLC, Adenocarcinoma
MTUS1-NRG1	1	NSCLC/LCNEC
KIAA1549-BRAF	1	CNS (Glioneuronal tumor)
ETV6-NTRK3	1	Secretory carcinoma (MASC)
ETV6-NTRK3	2	Secretory breast carcinoma
ETV6-NTRK3	1	Sinonasal Adenocarcinoma
IGFB-ALK	1	Uterine leiomyosarcoma
CARS-ALK	1	Inflammatory myofibroblastic tumor
KIF7-NTRK3	1	Intimal sarcoma
TPM3-NTRK1	1	Gallbladder
NCOA4-RET	1	Carcinoma Papillare
TPR-NTRK1	1	Carcinoma Papillare
MYH9-ROS1	1	NSCLC, Adenocarcinoma