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BIOMARKERS IN LUNG CANCER: DESCRIPTIVE ANALYSIS OF A CENTRALISED PLATFORM IN SPAIN (LUNGPATH)

Javier Martín López, A. Brito García, E. Gallego Domínguez, J. Bautista Laforga, JL. López Hidalgo, MI. Esteban Rodríguez, MC. Saez Rodríguez, I. Sansano Valero, M. Medina Pérez, A. Benito Berlinches, F. Pérez Ochoa, F. Domínguez, A. Sánchez Espinosa, HH. Torres Rivas, N. Mancheño Franch, P. Machín Andreu, A. Lerín Martos, T. Hernández Iglesias, A. Martínez Pozo, C. Salas Antón

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Disclosure Information

I hereby declare that I have had business or personal interests in the following industrial enterprises since 1 September 2018:

Name of the enterprise / Nature of the interest

Enterprise | Interest

- Grant/Research Support: No disclosure
- Honoraria for lectures: Pfizer, Roche Farma

I have no actual or potential conflict of interest in relation to this presentation

Introduction

- Biomarkers are becoming an essential requirement to properly treat lung cancer patients, which is the leading cause of death in the world (Bray 2018). Due to their usefulness in the correct cancer management and treatment thanks to their predictive and prognostic character, they are becoming more and more important in this field.

- What is more, it is undeniable the increasing development of targeted treatments an therefore also the number of lung cancer predictive biomarkers.

- **LungPath** is an on-line tool developed by the Spanish Society of Pathological Anatomy (SEAP) which allows the Pathological Anatomy Services to monitor and trace these biomarkers in clinical practice. This allows each center to control and follow the more important predictive biomarkers in LC (EGFR, ALK, ROS1 y PD-L1) as well as to realice comparisons at a national and global level.

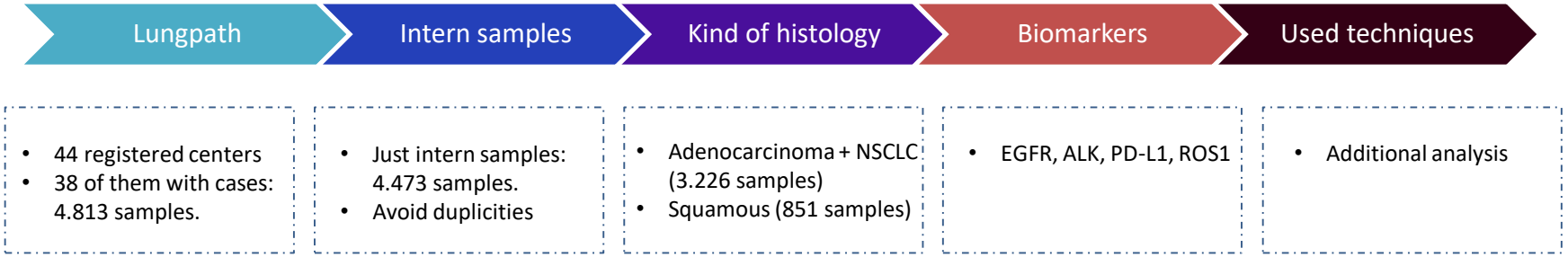
Bray F et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov;68(6):394-424. (Globocan 2018).

Materials & Methods

- The main objective was to analyze all the information recorded on LungPath from March 2018 and January 2019. Firstly a descriptive analysis of lungpath was done followed by a multivariable analysis.

- It is important to take into account that samples from the same patient but obtained in different moments of the disease where directly associated in the tool. This guarantees the possibility of knowing the whole information of the biomarkers determined in each patient with advanced or metastatic LC.

Figure 1. Flowchart followed during the analysis



* When the registry was exported, samples coming from the same patient were excluded, so each sample identifies only one patient. Thus, there is information available of 4.813 LC patients.

Results

➢ Descriptive analysis

Figure 2. Type of histology collected in the analysis **excluding external samples:**

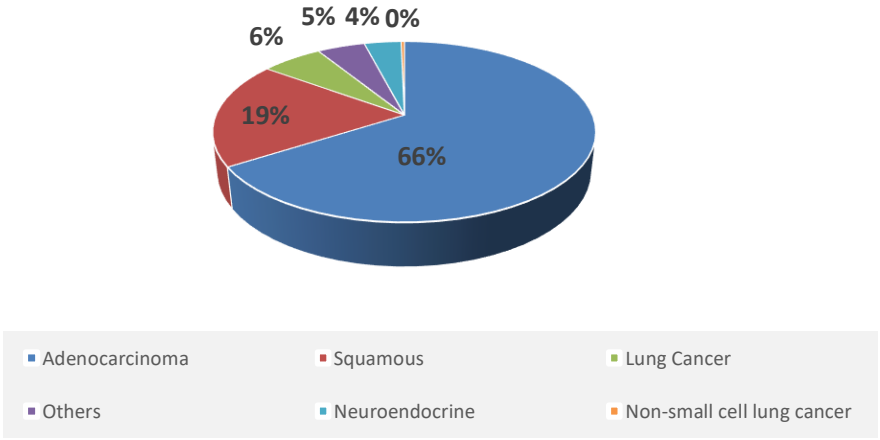
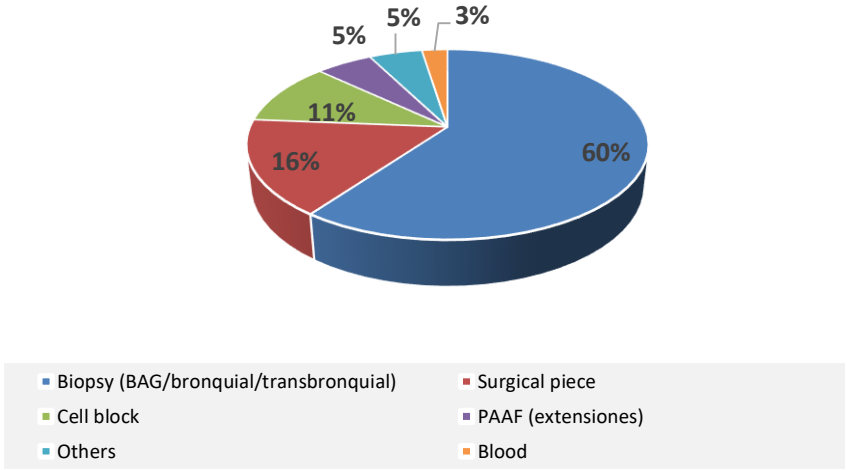


Figure 3. Type of samples collected in the analysis **excluding external samples:**



- Distincly, the adenocarcinoma was the main type of histology collected, being a total of 2.951 samples (66%), followed by squamous with 851 samples (19%) and non-small cell Lung Cancer (NSCLC), with 275 samples (6%).

- Regarding to the kind of sample obtained, biopsy was the most frequently used with 2.682 samples (60%), followed by the surgical piece with 727 samples (16%).

Results

➢ Descriptive analysis

❖ Analyzing the reasons that explain why the test was not performed we found the following:

Reasons that explain why the test was not performed	%
Not enough sample	9%
Not required/requested	42%
Not enough information	49%

❖ Take into consideration that this analysis includes all the biomarkers of LC included in the tool, internal samples and both adenocarcinoma and NSCLC histology.

❖ The analysis highlights the necessity to have professional & specialize teams to perform the biomarker test.

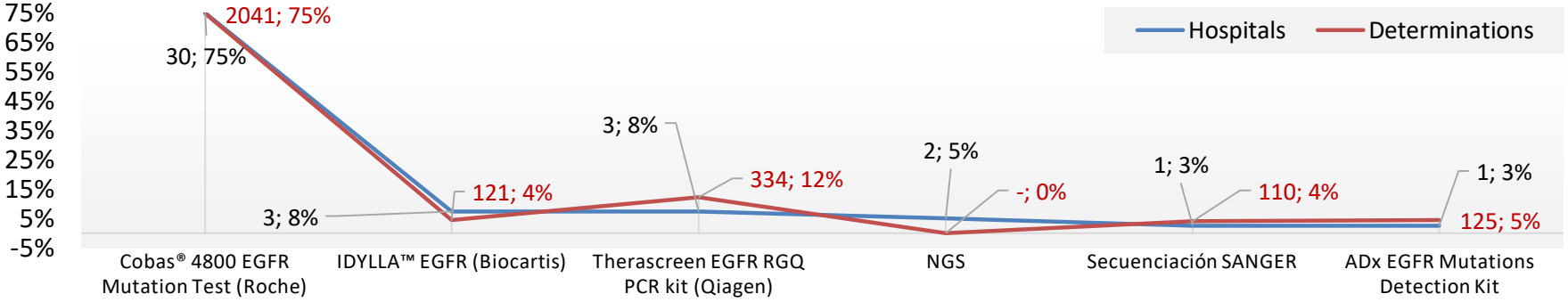
Results

➢ methods to detect the main biomarkers

Methods to define EGFR in advanced Lung Cancer

- All centers currently registered in LungPath (43) perform the EGFR test.
- All of them perform one single technique.

Figure 4. Percentage of hospitals & determinations for each technique used to determine EGFR in Lungpath



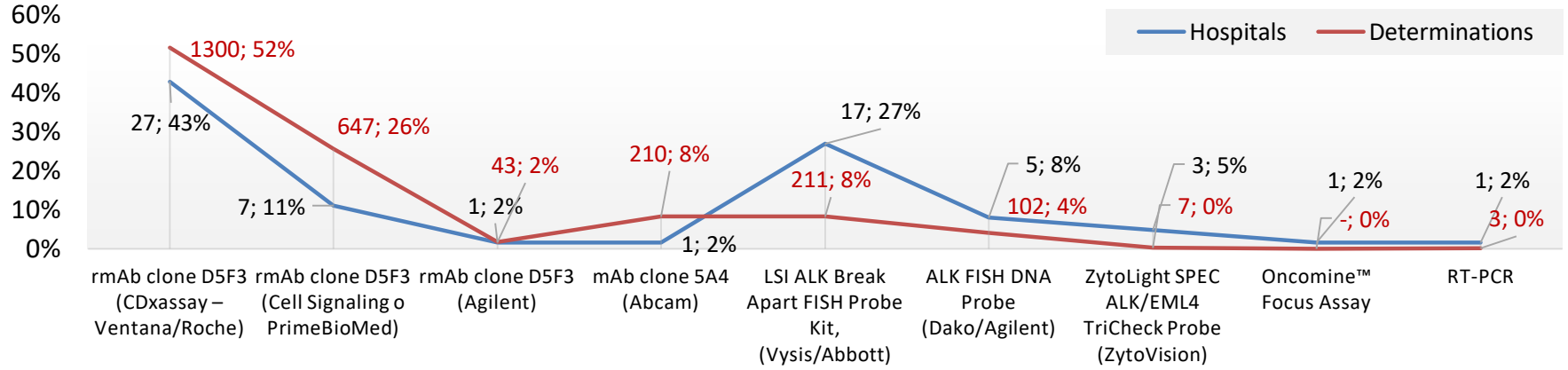
Results

➢ methods to detect the main biomarkers

Methods to define ALK in advanced Lung Cancer

- All centers currently registered in LungPath (43) perform the ALK test.
- 23 of them use just one technique and 20 of them use two techniques.

Figure 5. Percentage of hospitals & determinations for each technique used to determine ALK in Lungpath



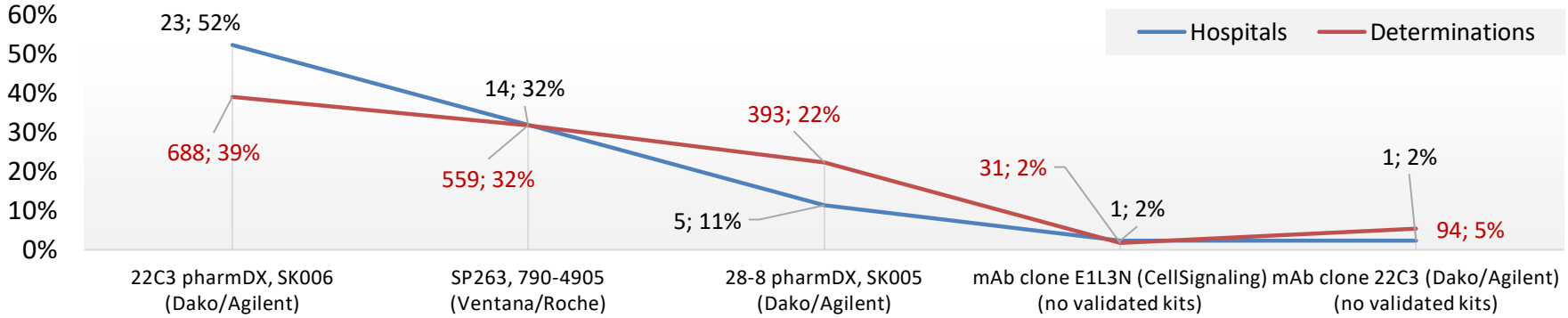
Results

➢ methods to detect the main biomarkers

Methods to define PD-L1 in advanced Lung Cancer

- All centers currently registered in LungPath (44) perform the PD-L1 test.
- All of them use the IHC technique. 42 use just one technique and 2 of them use more than one.

Figure 6. Percentage of hospitals & determinations for each technique used to determine PD-L1 in Lungpath



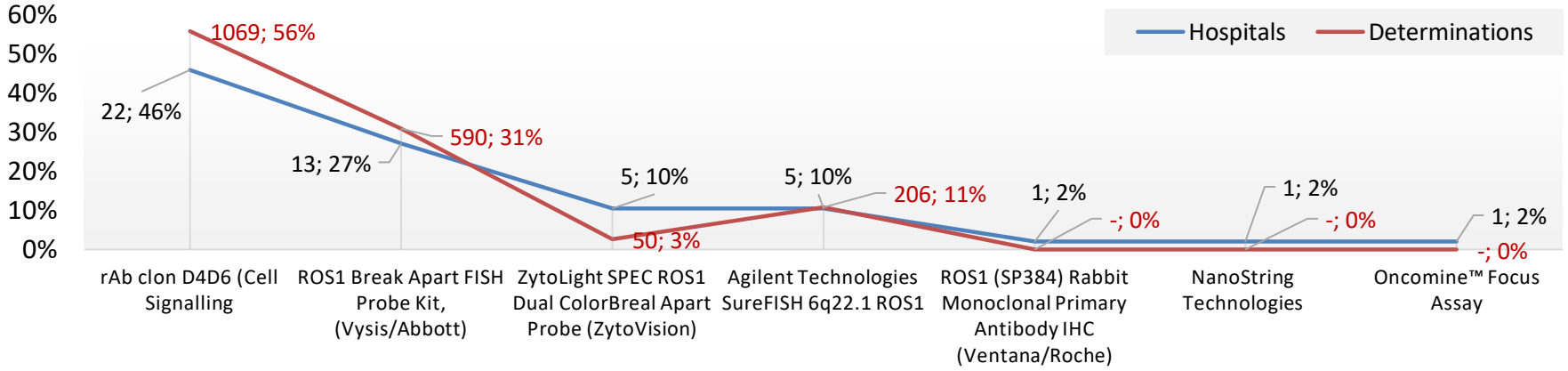
Results

➢ methods to detect the main biomarkers

Methods to define ROS1 in advanced Lung Cancer

- All centers currently registered in LungPath (38) perform the ROS1 test.
- 26 use just one technique and 12 of them use more than one.

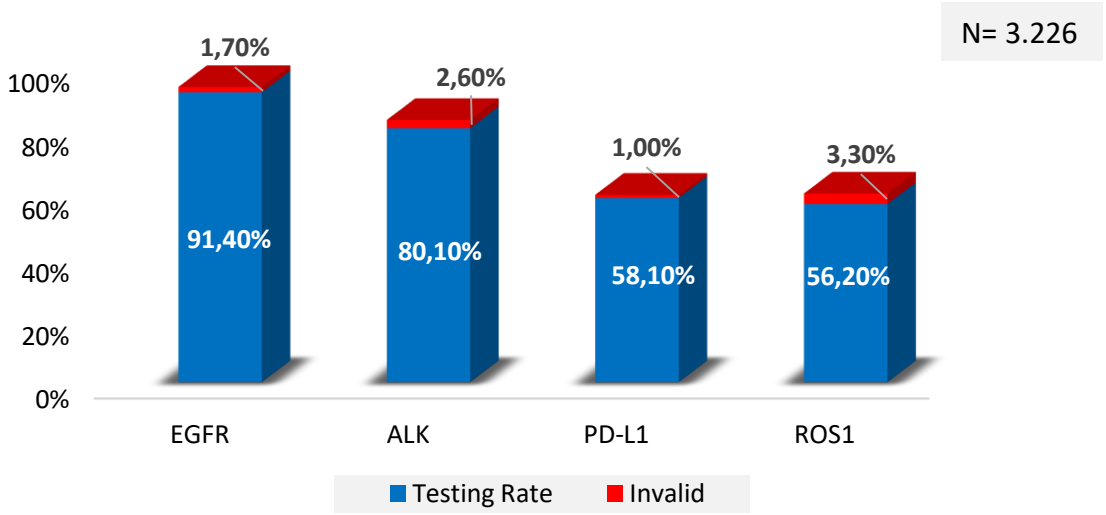
Figure 7. Percentage of hospitals & determinations for each technique used to determine ROS1 in Lungpath



Results

➢ **Primary outcomes: Testing Rate considering adenocarcinoma and NOS histology**

Figure 8. Testing rate and invalid samples in **adenocarcinoma and NOS** histology cases:

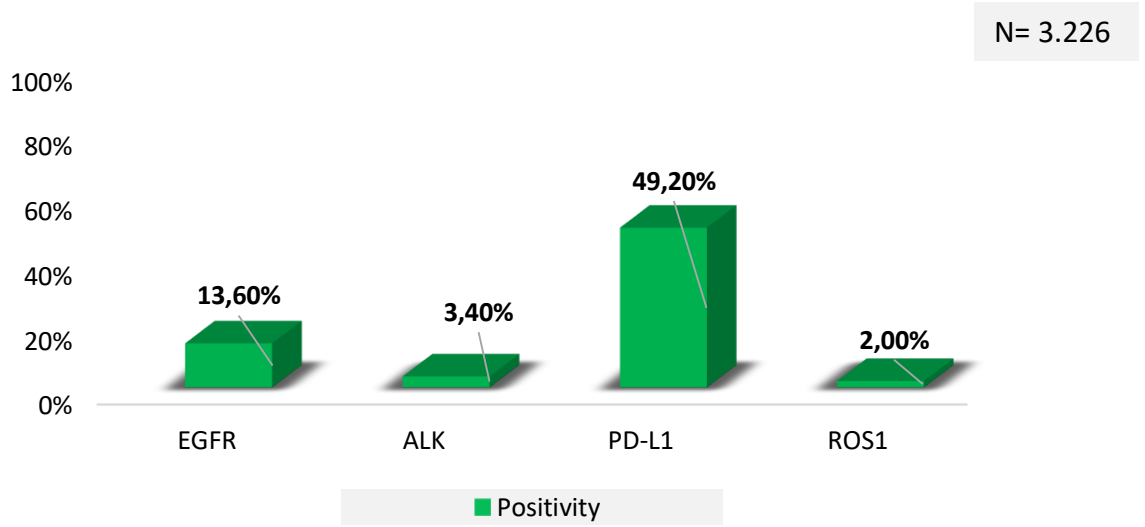


❖ Invalid cases are considered those samples which, due to different circumstances during the testing process, where not finally available to perform the biomarker test.

Results

➢ **Primary outcomes: Positivity Rate considering adenocarcinoma and NOS histology**

Figure 9. Positivity rate for the combination of both **adenocarcinoma and NOS** histology cases:



❖ The positivity rate was calculated dividing the total of positive results collected from the database by the total number of samples, either the positive or negative ones (invalid samples were not included).

Results

➢ Primary outcomes: Positivity Rate in both adenocarcinoma and NOS histology

Figure 10. Positivity rate of **both adenocarcinoma and NOS** histology cases and P value results:

Biomarker	Results	Adenocarcinoma		NOS		p-value*	Combined Adenocarcinoma+NOS	
		n	%	n	%		n	%
ALK	Positive	79	3,4%	6	2,9%	0.854	85	3,4%
	Negative	2232	96,6%	200	97,1%		2432	96,6%
EGFR	Positive	387	14,6%	7	2,8%	<0.001	394	13,6%
	Negative	2261	85,4%	244	97,2%		2505	86,4%
PD-L1	Positive	822	48,7%	91	54,2%	0.204	913	49,2%
	Negative	866	51,3%	77	45,8%		943	50,8%
ROS1	Positive	33	2,0%	2	1,5%	0.909	35	2,0%
	Negative	1585	98,0%	132	98,5%		1717	98,0%

N= 3.226

*P value was calculated by the Chi cuadrado methodology

❖ According to the P values obtained in the analysis, we could conclude that there is a statistically significant difference between the positivity rate of EGFR biomarker in Adenocarcinoma or NOS histology, where as the is not in the other biomarker determinations.

Results

➢ Primary outcomes: Testing & positivity rate squamous histology

Figure 11. Biomarkers testing rate of **squamous** histology cases:

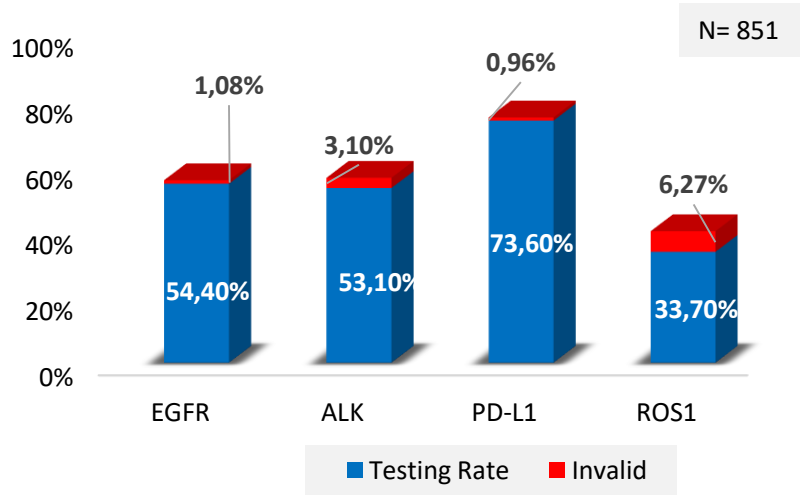
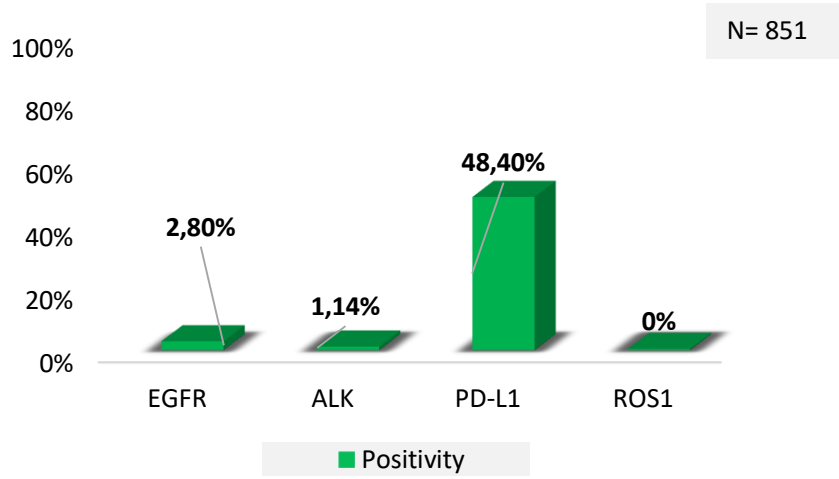


Figure 12. Positivity rate in **squamous** histology cases



- The positivity recorded of PD-L1 in in squamous tissue is distinctly superior in comparison with the other biomarkers analyzed.
- The positivity rate was calculated dividing the total positive results collected from the database by the total number of samples, either the positive or negative ones (invalid samples were not included however they are represented in Figure 3).

Results

➢ Secondary outcomes: Multivariable analysis focus on ALK biomarker

➢ Two logistic regression models with the outcome of positivity rate instead of testing rate; model 1: type of sample and histology & model 2: type of sample, histology and postivity rate

Figure 14. Logistic regression models for ALK biomarker

	Model 1		Model 2	
	OR (IC 95%)	P value	OR (IC 95%)	P value
Type of sample (ref. Biopsy)				
Block Cell	0,77 (0,31; 1,60)	0,513	0,74 (0,30; 1,56)	0,474
Fine needle puncture aspiration	1,72 (0,59; 4,04)	0,261	1,82 (0,60; 4,52)	0,237
Surgical Piece	1,13 (0,62; 1,96)	0,682	1,15 (0,63; 2,01)	0,633
Others[a]	1,48 (0,60; 3,12)	0,341	1,52 (0,62; 3,25)	0,313
Histology (ref. adenocarcinoma)				
NOS	0,85 (0,33; 1,83)	0,707	0,77 (0,29; 1,66)	0,547
Result EGFR: *Positive*	n.a.	n.a.	0,10 (0,01; 0,45)	0,022
Result EGFR: *Missing*	n.a.	n.a.	0,76 (0,18; 2,10)	0,652
Result PDL-1: *Positive*	n.a.	n.a.	1,61 (0,94; 2,83)	0,088
Result PDL-1: *Missing*	n.a.	n.a.	1,22 (0,69; 2,19)	0,501
Hosmer-Lemeshow, p value	*0,997*		*0,68*	
AUROC (IC 95%)	*0,543 (0,486 ; 0,601)*		*0,613 (0,555 – 0,672)*	

➢ Both models show the independency between the type of histology or sample with the positivity rate of ALK.

➢ The second model shows the lack of positive ALK results in a EGFR positive sample.

Conclusions

- *Until today, there were not known other registers about real diagnostic practice and performance of biomarkers test in LC in Spain.* ***Thus, Lungpath means a great progress provided by the*** **Spanish Society of Pathological Anatomy** ***(SEAP).***

- *LungPath allows to ensure the quality of the biomarkers determination and facilitates the results homogenization. Thanks to this register it has been possible to obtained and analyzed, for the first time, data from the real practice of biomarkers determinations, allowing to understand better and even compare the national diagnostic practices in LC biomarkers with other country practices.*

- *Noticing the incremental importance of predictive biomarkers in determining the future treatment of patients in this pathology, having this information is essential, specifically, for the Departments of Pathology and, generally, to the Scientific Society.*

Thank you to registred Departments

Con la colaboración de Roche

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