Prevalence and characteristics of lung cancer in families harboring pathogenic germline variants in cancer predisposing genes

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Poster N#138

BACKGROUND

- Emerging evidence indicates that lung cancer can be associated with certain hereditary cancer syndromes caused by pathogenic germline variants (PGVs) [1-3]
- However, this population is not currently studied in Genetic Counseling Units (GCU) and their role in patients (pts) with lung cancer remains unknown

OBJECTIVE:

To describe the prevalence and characteristics of lung cancer cases in families harboring PGVs in cancer predisposing genes

METHODS

- Retrospective study of the personal & family history of lung cancer in families studied in the GCU
- Centre: Hospital Clinic of Barcelona (Spain)
- Period: January 2001 to December 2021
- PGVs studied are included in the Catalan Consensus on Genetic Studies
- We collect from medical records the personal and family history of cancer in three-generation pedigree, clinical characteristics of the patients and molecular data of the tumors

RESULTS

Study population

In **2.521 families studied**, a total of **702 families were PGV-carriers**. Among them, we identified 121 families (17%) with at least one case of lung cancer (n=147 pts) (**Figure 1**).

Clinical characteristics		N=147
Age	Median, range	63 (27-88)
Gender	Male	122 (82%)
	Female	25 (17%)
Smoking status	Current/former	41 (27%)
	Non-smokers	4 (3%)
	Unknown	102 (69%)
Histology	Adenocarcinoma	4 (3%)
	Squamous	3 (2%)
	Unknown	140 (95%)
PGV carrier	Yes	13 (9%)
	No	2 (1%)
	No studied/Not available	132 (90%)

Table 1. Baseline characteristics of patients with lung cancer in families harboring PGV.

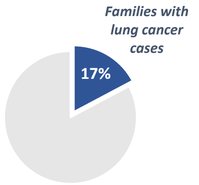

Figure 1. Prevalence of families with patients with lung cancer

Patients with Lung cancer: PGV-carriers

Out of **147 cases with lung cancer**, only **13 (9%) had confirmatory** germline study

	Baseline characteristics					Homologous recombination		Mismatch repair Pathway			CDKN2A Pathway
	Age	**Gender**	**Smoker**	**Histo**	**Molecular profile**	***BRCA2***	***PALB2***	***MLH1***	***MSH2***	***MSH6***	***CDKN2A***
N#1	69	Male	Yes	Squam	Unk						
N#2	57	Male	Yes	Unk	Unk						
N#3	67	Female	No	Adeno	***EGFR* ex20 ins**						
N#4	69	Female	Yes	Adeno	***KRAS* G12V**						
N#5	Unk	Male	Unk	Unk	Unk						
N#6	55	Male	Unk	Unk	Unk						
N#7	52	Male	Yes	Adeno	***KRAS* G12A**						
N#8	80	Male	Unk	Unk	Unk						
N#9	76	Male	Unk	Unk	Unk						
N#10	40	Male	Unk	Unk	Unk						
N#11	81	Male	Yes	Unk	Unk						
N#12	54	Male	Yes	Squam	Unk						
N#13	42	Female	Unk	Unk	Unk						

Table 2. Baseline characteristics of patients with lung cancer who harbor a PGV.

Pathogenic Germline Variants & Hereditary Syndromes

The PGV detected in the families of the patients with lung cancer (n=121), were mainly in genes related to **DNA repair pathways**, followed by **Mismatch Repair System** and in ***CDKN2A***

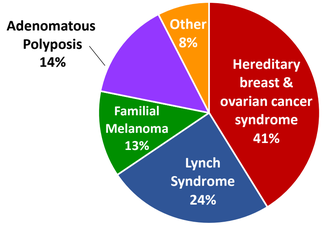

Figure 2. Hereditary Syndromes in the families of patients with lung cancer

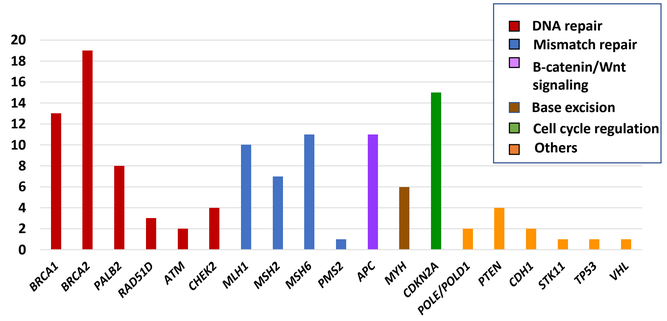

Figure 3. Distribution of PGV by pathway

CONCLUSIONS

- **Lung cancer** is one of the tumors observed in families harboring PGVs in cancer predisposing genes
- PGV detected in families with patient with lung cancer were mainly related to **DNA repair pathways**
- **Clinical and molecular characteristics of patients** with lung cancer should be registered in more detail in GCU in order to establish common patterns associated with PGV

REFERENCES:

1. *Mezquita L, Jove M, et al J Thorac Oncol 2020*
2. *Mezquita L et al, AACR 2021,*
3. *Lincoln SE et al, JAMA Netw Open. 2020*

DISCLOSURES: JC Laguna have nothing to declare.