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Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

IASLC HIGHLIGHTS

7-10 DE SEPTIEMBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

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BARCELONA

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Patología II

Dra. Lara Pijuan

Hospital del Mar de Barcelona

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

P2.09-34 - Next-Generation Sequencing Implementation in Non-Small Cell Lung Cancer Molecular Diagnosis

NEXT-GENERATION SEQUENCING IMPLEMENTATION IN NON-SMALL CELL LUNG CANCER MOLECULAR DIAGNOSIS

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BACKGROUND

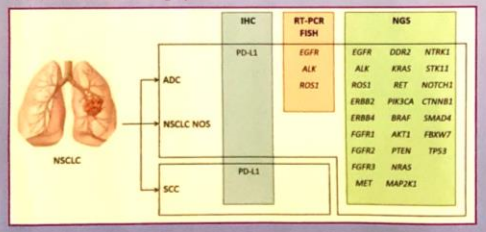
- Currently, all patients with advanced non-small cell lung cancer (NSCLC) require *EGFR*, *ALK*, *ROS1* and *BRAF* molecular characterization.
- Next-generation sequencing (NGS) allows the simultaneous analysis of these biomarkers optimizing both the sample and the economic cost.
- The purpose of this study was to compare NGS results with those obtained using single gene analysis in a prospective clinical setting.

METHODS

During 12 months, 50 paraffin-embedded samples from patients with advanced NSCLC (46 adenocarcinomas and four NSCLC-NOS) were prospectively analyzed in our Institution.

Molecular characterization was carried out using the NGS Oncomine Solid Tumor DNA and Fusion Transcript Kits for hotspot mutations and gene fusions (Thermo Fisher) and results were compared with Therascreen *EGFR* RGQ PCR Kit (Qiagen), and Vysis *ALK* and *ROS1* Break Apart FISH Probe Kits (Abbott Molecular, ZytoVision) (Figure 1).

FIGURE 1. Molecular testing algorithm. Both tissue biopsies and cytologies preserved as FFPE cell blocks are diagnosed by the same pulmonary pathologist. Once classified according to the histological subtype, tissue sections are prepared to perform all molecular tests in parallel. Molecular workflow is completed for all tests in less than 10 working days.



RESULTS

All samples studied by NGS for hotspot mutations were assessable and we detected pathogenic alterations in 90% (n= 45) (Figure 2).

Regarding targetable alterations, we identified nine patients harboring *EGFR* mutations (18%), in agreement with real-time PCR (except for one case which had an exon 20 insertion not interrogated by Therascreen), and one patient with a *BRAF* mutation (2%) (Figure 3).

We highlight the presence of *TP53* mutations in 27 cases (54%), *KRAS* in 16 cases (32%) and *STK11* in three cases (6%). *TP53* mutations were concomitant with other alterations in 70% of the cases (n= 19), without being significantly associated with any of them.

Gene fusion analysis by NGS was assessable in 80% of the samples (n= 40): six samples had insufficient RNA quality and four had not enough material. We detected only one case with an *ALK* rearrangement (2%), confirmed by FISH (Figure 4).

FIGURE 2. Molecular alterations identified by NGS. *TP53* is the most frequent pathogenic alteration in our series and was found in 70% of cases concurrent with another mutation. Half of the patients presenting *EGFR* sensitizing alterations also harbored *TP53* mutations. Only five patients in our cohort (10%) did not present any molecular alteration.

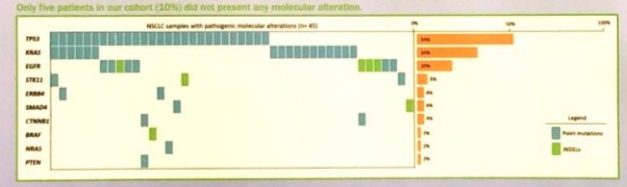


FIGURE 3. Targetable alterations. With the use of a single NGS test, 22% of patients (n= 11) may be eligible for targeted treatment with tyrosine kinase inhibitors.

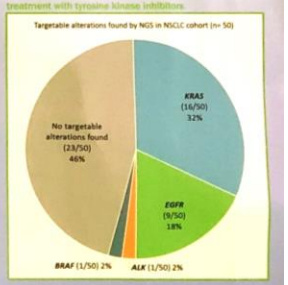
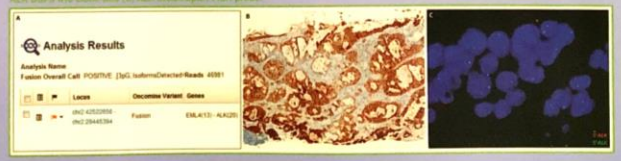


FIGURE 4. *ALK*-rearranged case tested using NGS, IHC and FISH. (A) EML4(13)-ALK(20) positive case was tested orthogonally by (B) anti-ALK D5F3 IHC clone and (C) *ALK* break-apart FISH probe.



CONCLUSION

- NGS technology for NSCLC molecular diagnosis could be considered as the initial screening test although the success rate in gene fusion assessment is closely related to RNA paraffin-embedded evaluation.
- NGS also detected other genomic alterations not tested routinely in gene-by-gene approach that may be useful for referral of patients to clinical trials.

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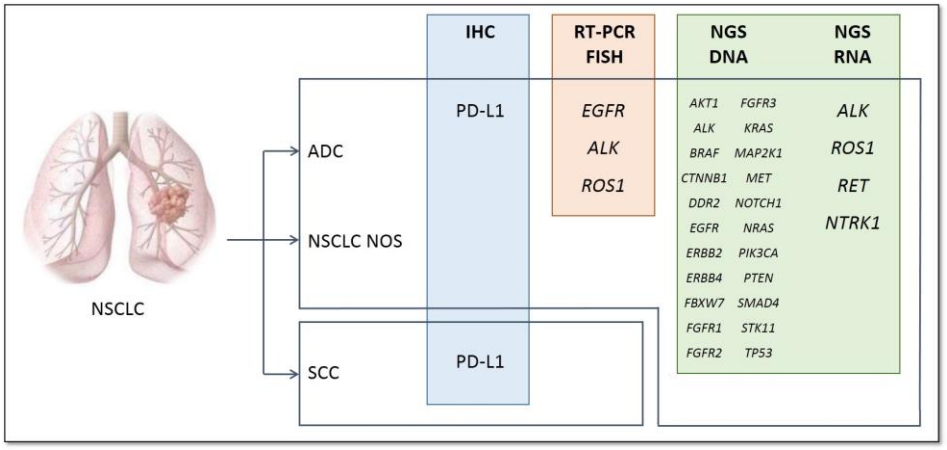

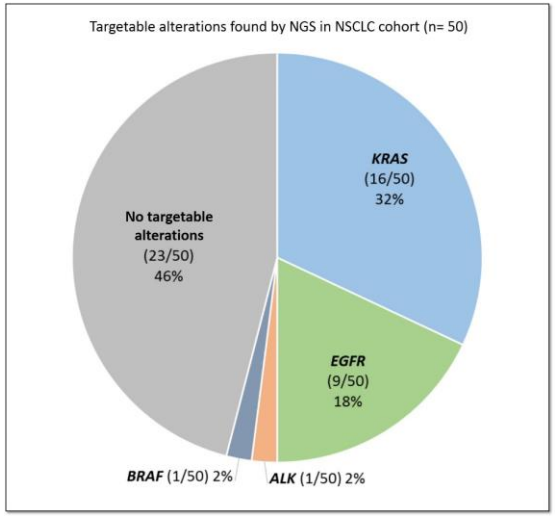

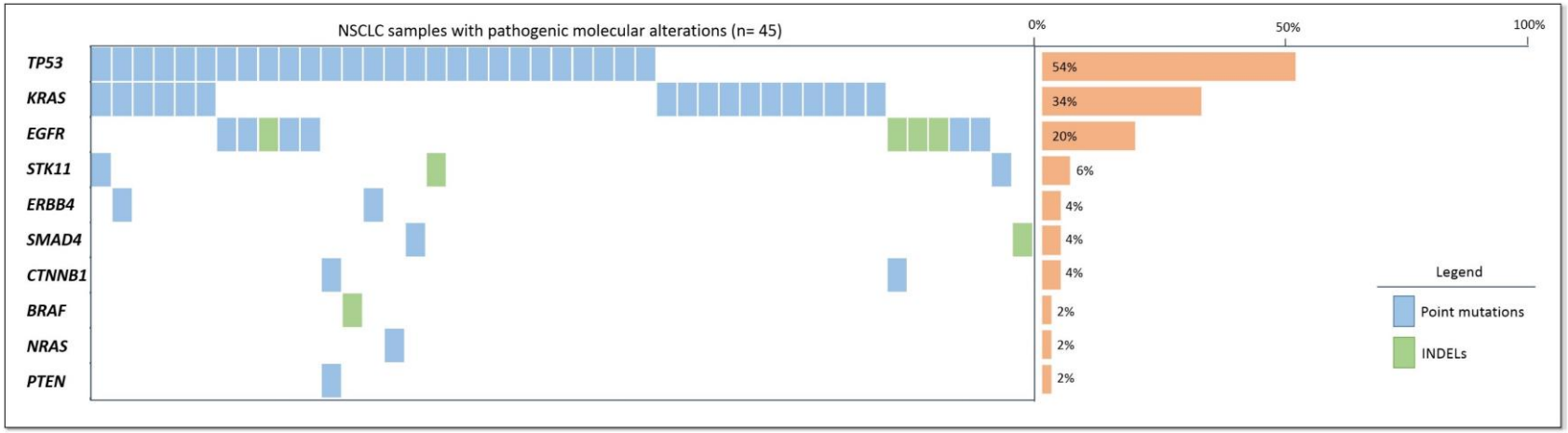

Iniciativa científica de:

GECP lung cancer research

EP1.14-29 - Mutational Landscape in Lung Cancer Patients by Targeted Next-Generation Sequencing and Differences by Gender in Spanish Population

LUNG CANCER UPDATES
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MUTATIONAL LANDSCAPE IN LUNG CANCER PATIENTS BY TARGETED NEXT-GENERATION SEQUENCING AND DIFFERENCES BY GENDER IN SPANISH POPULATION

CENTRO INTEGRAL ONCOLÓGICO hm CIOCC HOSPITALES

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[1]Oncology Department, [2]Internal Medicine Department, [3]Pathology-Laboratorio de Dianas Terapéuticas, [4]Thoracic Surgery Department, [5]Radiology Department. CIOCC, HM Sanchinarro Norte, Madrid. [6]Oncology Department. HM Delfos, Barcelona. Spain.

BACKGROUND

Personalized treatment with targeted therapies according to genomic alterations improves treatment outcome in advanced NSCLC and some genomic alterations are linked to sex. Next Generation Sequencing (NGS) is a reliable tool for genomic profiling. We aim to search clinical and pathological differences by sex in NSCLC patients with a comprehensive genomic profile by NGS.

METHODS

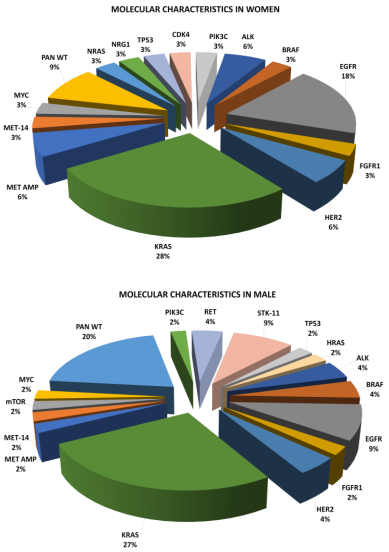
We retrospective assessed clinical-pathological and molecular characteristics of 73 stage I-IV lung cancer patients and NGS at baseline. NGS was performed in 67% by Oncomine ™, 30% by OCA v3 and 2% by Foundation One

RESULTS

The cohort included: 49% of females (F), the mean age was 63 years (40-85), 90% stage IV, 91% adenocarcinoma, followed by squamous cell carcinoma (9.5%) and small cell (2%). Former smoker were reported in 74% and 80% of male (M) and females, respectively. Primary tumor lung biopsy was the main source of sample for NGS in 90% of cases.

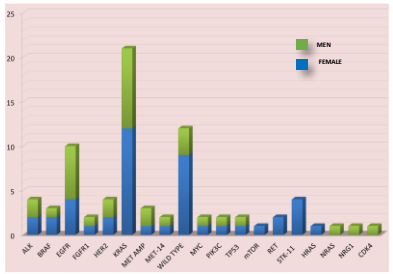
RESULTS

Figure 1. Mutational landscape by gender.



The majority of somatic genomic alterations were mutations (64% M *vs*. 78% F), followed by CNV (19% M *vs*. 11% F) and rearrangements (17% M *vs*. 11% F). In both genders KRAS mutation (mut) was the most common (M vs. F) (27% vs. 28%), and wild-type tumors were reported in 20% and 9%, respectively.

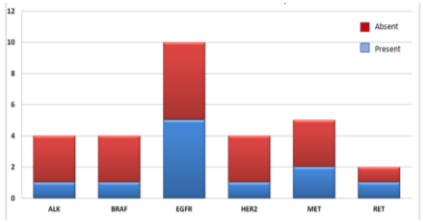
Figure 2. Association by gender for genomic alterations



Regarding actionable drivers, there was a higher incidence of *EGFR* mut (18% *vs*. 9%), *ALK* rearrangements (6% *vs*. 4%) and *HER 2* mut (6% vs 4%) in F vs M, respectively. On the other side, *BRAF* mut (4% *vs*. 3%), and *RET* rearrangements (4% *vs*. 0%) were more frequent in M (***Figure 1 and 2***)

Baseline brain metastases in patients with *EGFR and BRAF* mut were similar regardless of sex (50% and 0%), whereas in *ALK* and *HER2* they were more frequent in F (50% F vs. 0% M). Twenty-nine percent of patients received personalized treatment according to these results.

Figure 3. Baseline brain metastases by targeted therapies.



CONCLUSIONS

NGS identifies an important proportion of therapeutically relevant driver alterations in LC. This has lead to individualized treatment in LC patients. Some clinical features were found by gender in our population probably related to genomic differences linked to sex.

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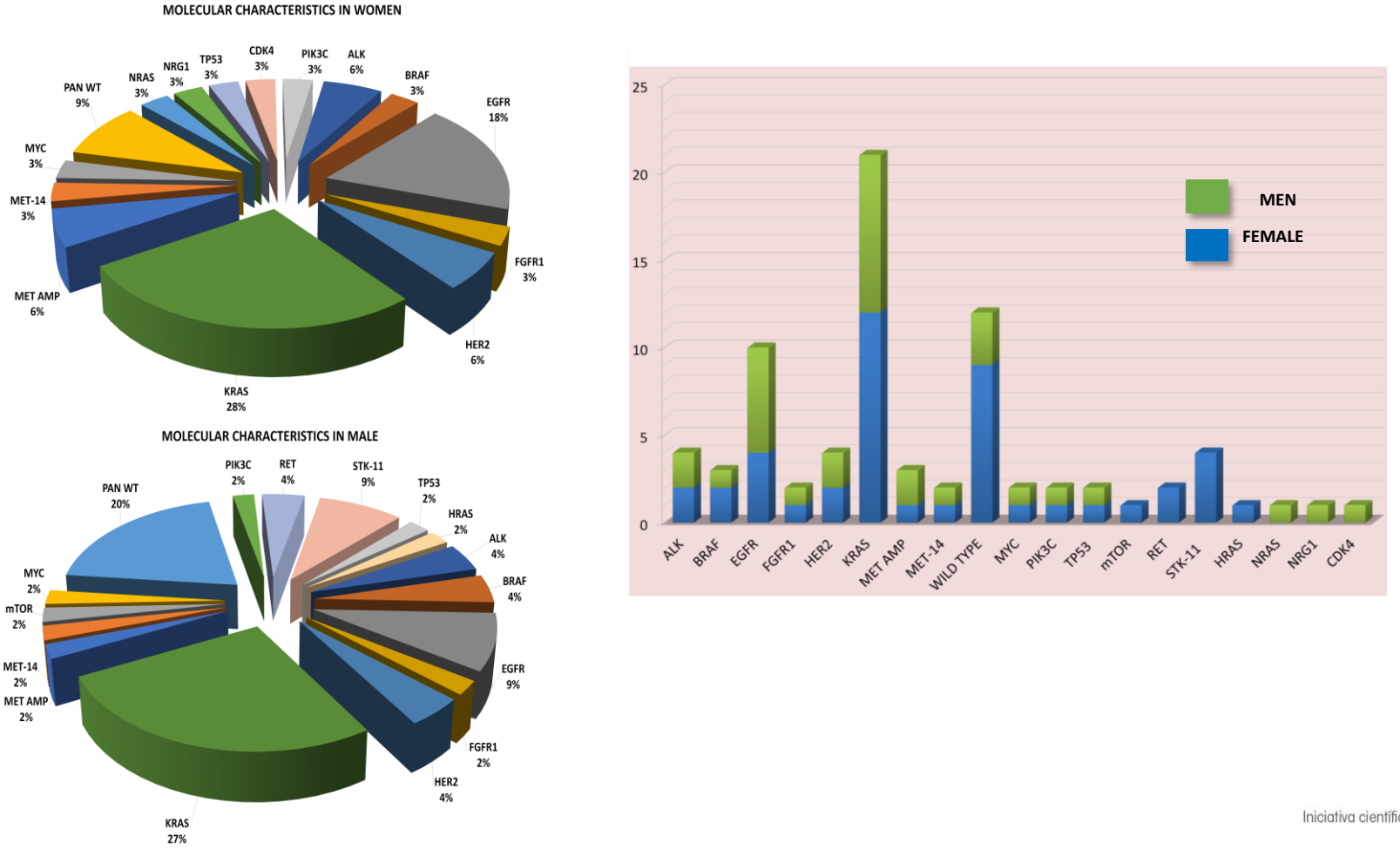

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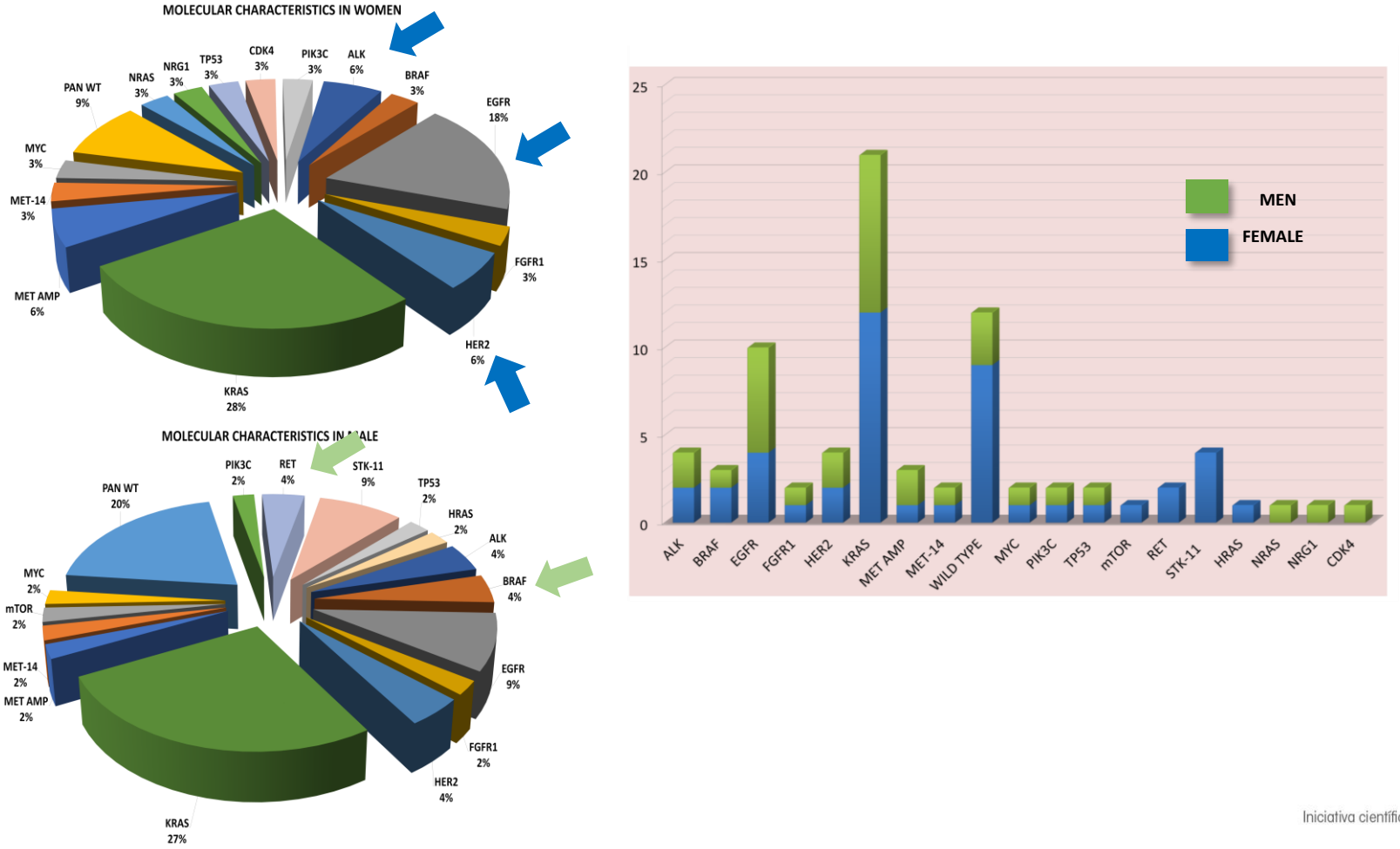

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