Pan-Tumor Real-World Liquid Biopsy (LB) in Molecular Tumor Boards (MTB): Clinical Impact of Systematic Clonal Hematopoiesis (CH) Filtering - PRECISO Program

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INTRODUCTION

LB enables minimally invasive genomic profiling, but CH may contribute variants unrelated to the tumor. Although increasingly recognized, its prevalence and clinical impact in pan-tumor real-world practice remain unclear. The PRECISO program prospectively integrates LB into a multidisciplinary MTB with systematic CH filtering.

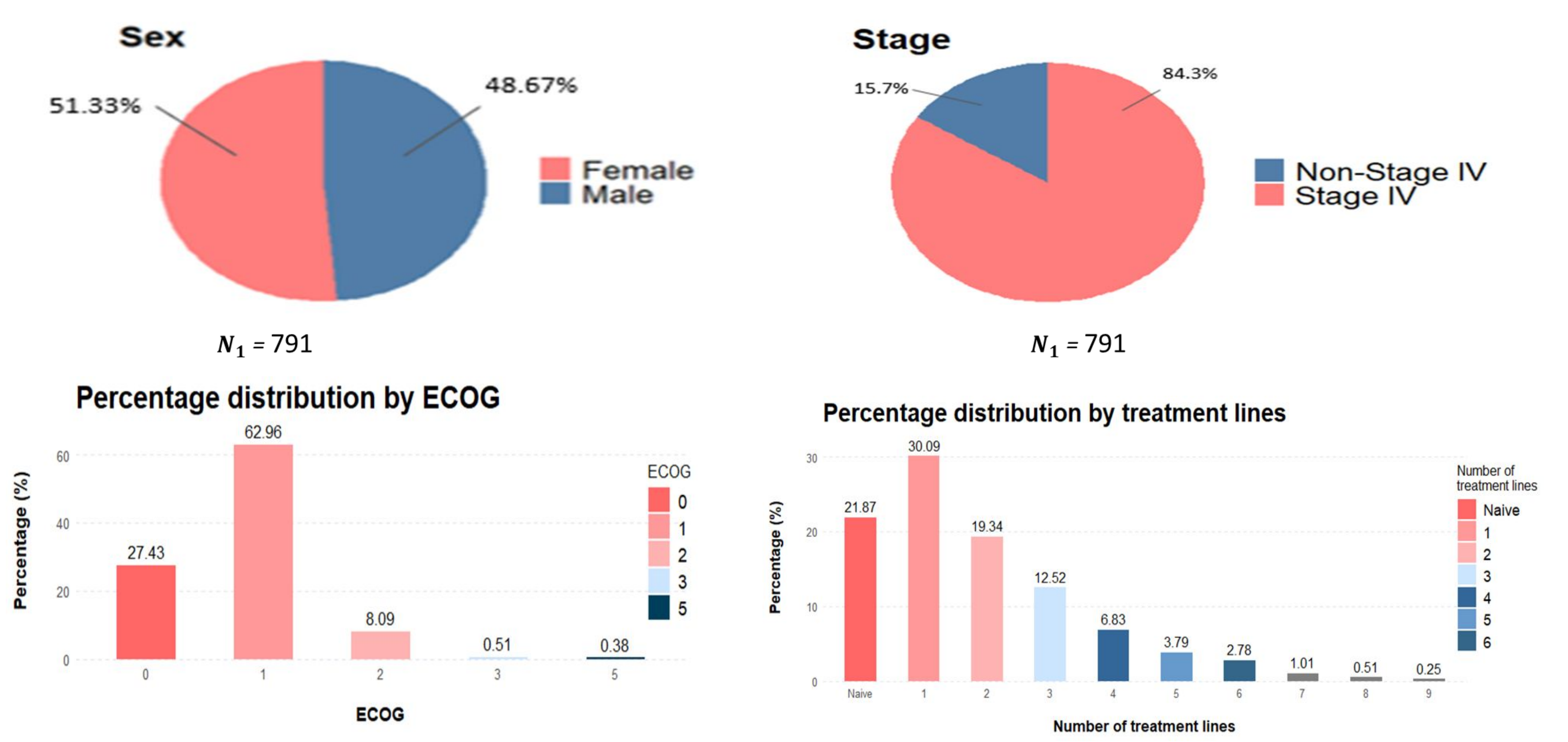
This study assessed the implementation and clinical utility of blood-based NGS within a real-world MTB

METHODS

Patients with advanced solid tumors undergoing LB (FoundationOne® Liquid CDx, Feb 2024–Sept 2025) at Hospital 12 de Octubre were prospectively analyzed. Clinical variables, LB results, and MTB recommendations were recorded. CH was identified using Foundation Medicine's Variant Origin Prediction (VOP) algorithm, classified as CH with probability >0.5. All results were reviewed in an MTB that applied ESCAT ranking and issued treatment recommendations. Informativeness was defined as tumor-derived reportable variants (pathogenic/likely pathogenic) after exclusion of CH.

RESULTS

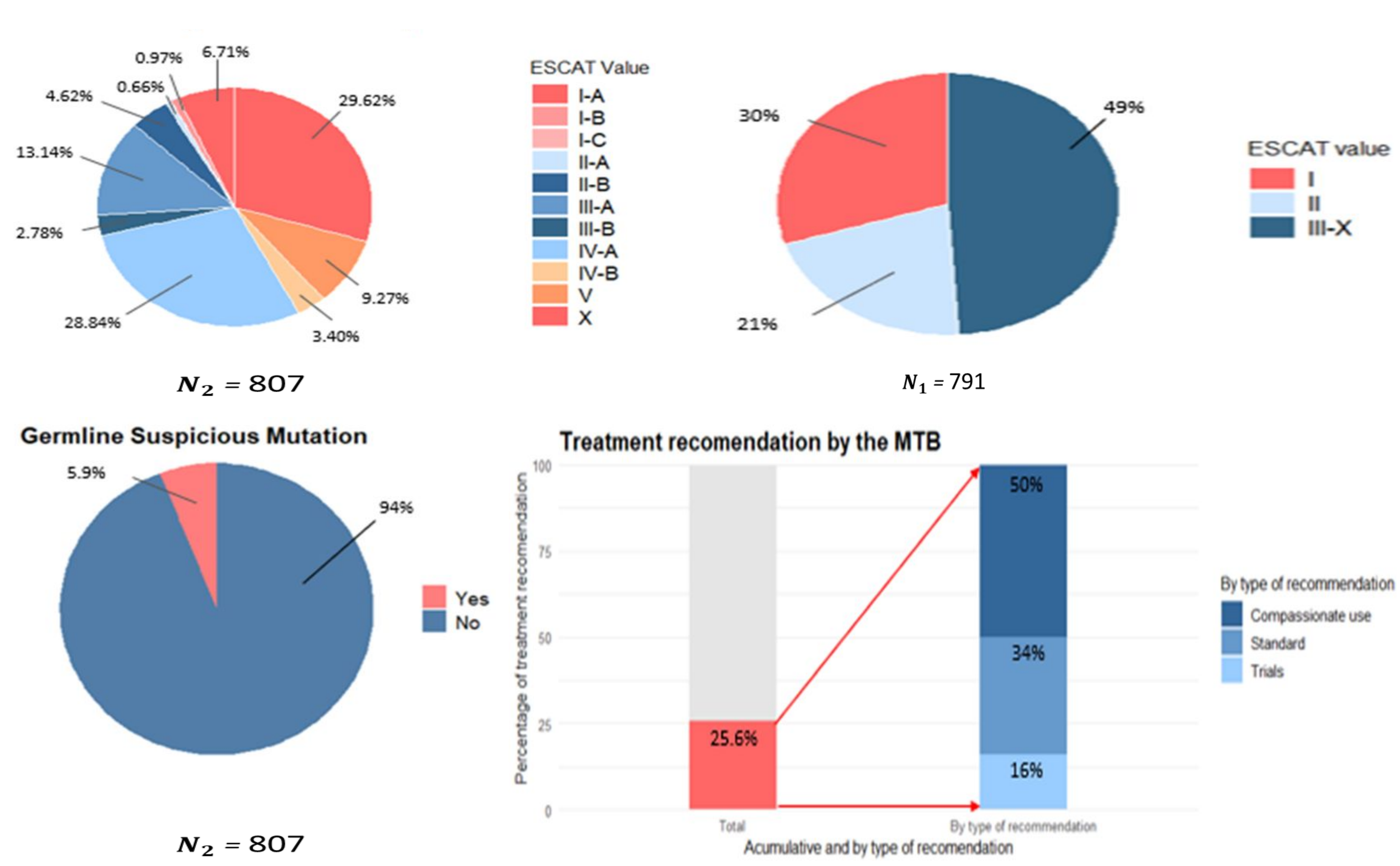
Figure 1. Patients characteristics



Abbreviations: ECOG, ECOG performance status. Stage IV: Metastasis.
N_1 = Total number of patients.

- A total of 807 LBs were performed in 791 patients (51.3% female; median age 63.5; ECOG ≤1 90.4%; stage IV 84.3%).
- Tumor types included thoracic (46%), gastrointestinal (19%), breast (10%), gynecologic (7%), and others. Overall, 67.3% of LBs were informative, with a median turnaround of 11 days.
- Informativeness was higher in metastatic vs non-metastatic disease (71% vs 47%, p<0.001) and in progressive vs non-progressive patients (70% vs 39%, p<0.001)
- ESCAT I/II alterations were found in 37%, including 30.8% of those progressing without prior molecular findings (16.4% ESCAT I). MTB recommended targeted therapy in 25.6% (50% trials, 34% standard, 16% compassionate use)
- CH variants were detected in 91.5% of patients, most frequently in DNMT3A (69.76%), TP53 (34.94%), CHEK2 (29.98%), ATM (25%), TET2 (16.60%), and ASXL1 (10%).
- After CH exclusion, 81.7% (646 patients) remained informative, with actionable findings remaining at 37%.
- Suspected germline variants were identified in 5.9% overall.

Figure 2. NGS performance



Abbreviations: ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; MTB, Molecular tumor board; NGS, next generation sequencing. N_2 = Total number of NGS.

Figure 3. Informative vs Non-informative by NGS context

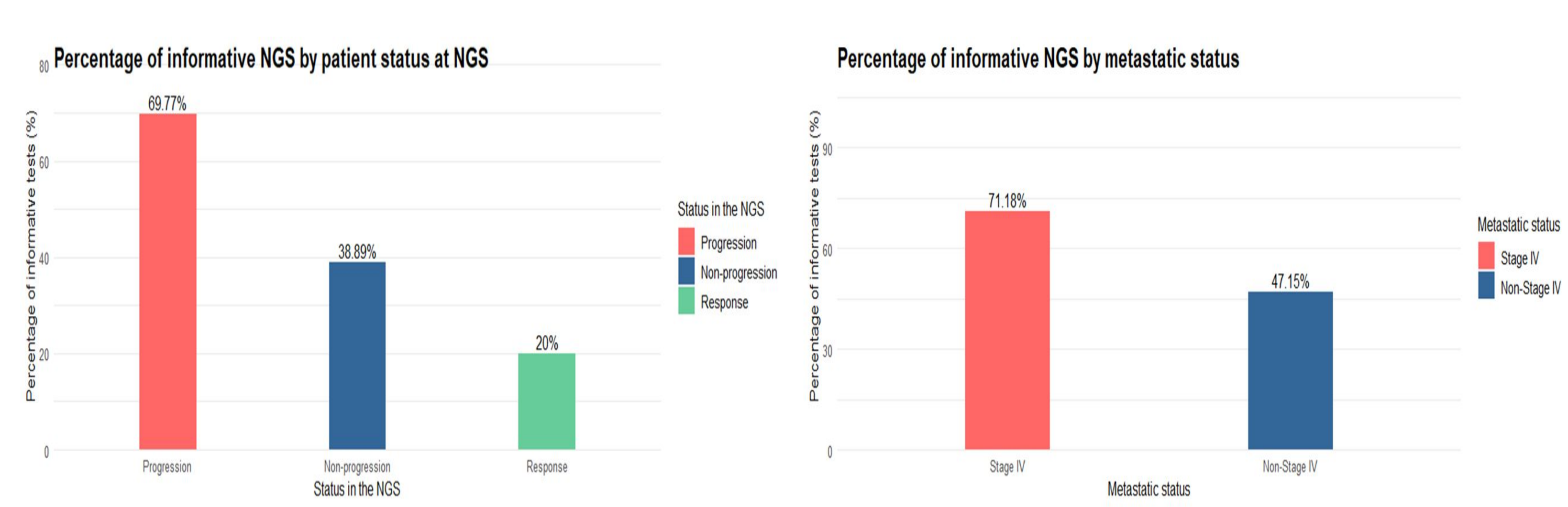


Figure 4. CH Gene type and frequency by VOP

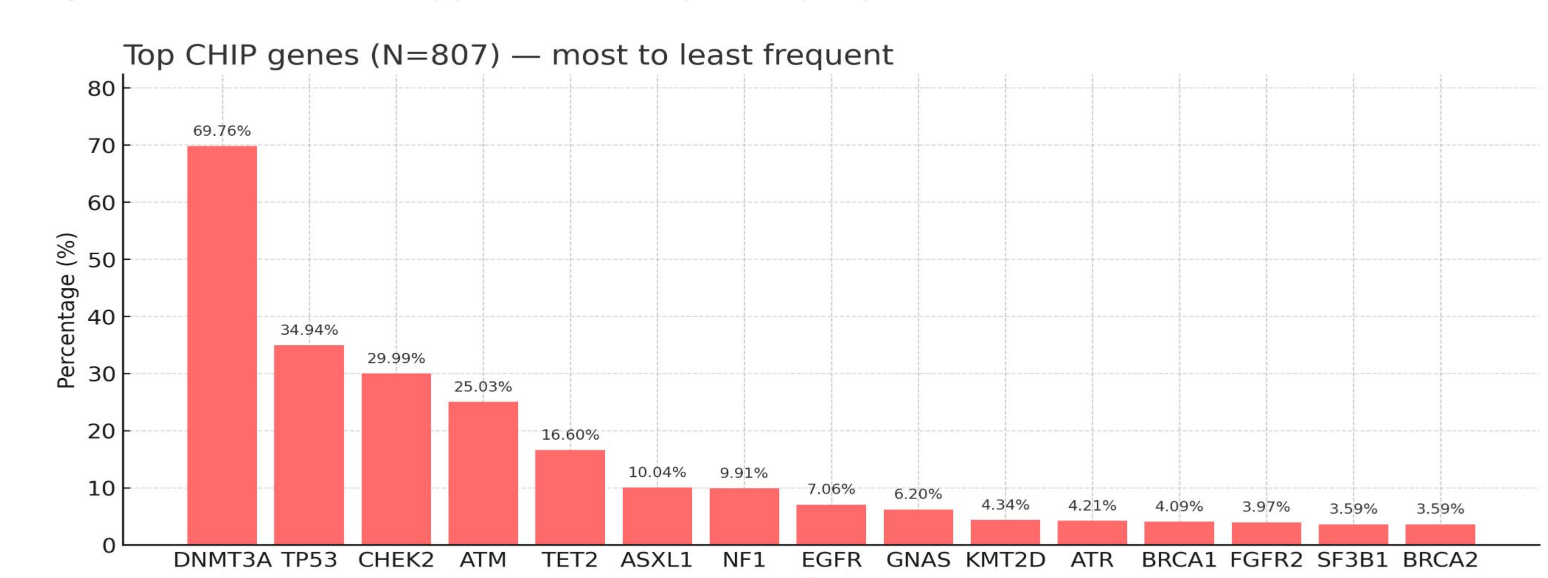


Figure 5. Patients characteristics by tumor subtype

	All patients (n=791)	Thoracic (n=368)	Upper GI tract (n=90)	Breast (n=81)	Lower GI tract (n=57)	Gynecologic (n=55)	Head & Neck (n=43)	Urinary tract (n=30)	Cutaneous (n=23)	Prostate (n=6)	Others (n=38)
Median age (years)	63.5	64.9	61.6	60.0	61.9	56.7	61.9	58.7	61.3	70.0	58.4
Sex (Male/Female)	51.3% / 48.7%	53.8% / 46.2%	64.4% / 35.6%	0.0% / 100.0%	64.9% / 35.1%	0.0% / 100.0%	55.8% / 44.2%	83.3% / 16.7%	73.9% / 26.1%	100.0% / 0.0%	52.6% / 47.4%
ECOG 0–1	90.4%	88.9%	91.1%	87.7%	93.0%	98.2%	97.7%	96.7%	78.3%	100.0%	86.8%
Stage IV	91.2%	91.8%	93.3%	11.1%	100.0%	92.7%	83.7%	100.0%	100.0%	100.0%	86.8%
Brain metastases	21.5%	27.7%	0.0%	9.9%	0.0%	1.8%	4.7%	3.3%	39.1%	0.0%	7.9%
Prior Radiotherapy	38.0%	35.9%	13.3%	76.5%	29.8%	30.9%	69.8%	36.7%	56.5%	50.0%	15.8%
Treatment line											
* Naive	27.8%	33.7%	22.2%	16.0%	8.8%	0.0%	9.3%	0.0%	0.0%	0.0%	18.4%
* 1L	29.4%	23.1%	42.2%	38.3%	36.8%	29.1%	48.8%	23.3%	34.8%	0.0%	28.9%
* 2L	20.4%	18.8%	15.6%	13.6%	21.1%	27.3%	16.3%	26.7%	26.1%	16.7%	26.3%
* 3L	22.4%	23.4%	20.0%	32.1%	31.6%	43.6%	20.9%	50.0%	39.1%	83.3%	23.7%
NGS											
*at diagnosis	21.4%	31.5%	32.2%	0.0%	12.3%	3.6%	2.3%	6.7%	4.3%	0.0%	31.6%
*at PD	65.3%	61.1%	47.8%	96.3%	73.7%	83.6%	67.4%	66.7%	82.6%	100.0%	47.4%
*at Other situations	13.3%	7.3%	20.0%	3.7%	14.0%	12.7%	30.2%	26.7%	13.0%	0.0%	21.1%
Informative NGS	67.3%	76.6%	51.1%	50.6%	66.7%	78.2%	44.2%	73.3%	91.3%	100.0%	65.8%
ESCAT I/II	37.0%	50.8%	20.0%	33.3%	28.1%	25.5%	2.3%	16.7%	65.2%	66.7%	15.8%
Suspected germline mutation	5.9%	6.8%	5.6%	3.7%	5.3%	7.3%	2.3%	6.7%	0.0%	33.3%	5.3%

Thoracic tumors included: Non-small cell lung (n=359; 276 Adenocarcinoma; 83 Others); Malignant pleural mesothelioma (n=6); Thymic malignancy (n=3). **Upper GI tract included:** Stomach (n=25); Esophagus (n=4); Gastroesophageal junction (n=5); Pancreas (n=40); Biliary tract (n=16). **Lower GI tract included:** Colon (n=45); Rectum (n=11); Anus (n=1). **Head & Neck tumors included:** Squamous head & neck (n=29); Thyroid (n=13); Salivary gland (n=1). **Gynecologic tumors included:** Ovarian/peritoneal (n=38); Cervix (n=9); Endometrium (n=5); Fallopian tube (n=1); Other gynecologic neoplasms (n=2). **Urinary tract included:** Kidney (n=27); Muscle-invasive bladder (n=3). **Cutaneous neoplasms included:** Melanoma (n=22); Non-melanoma skin (n=1). **Others included:** Cancer of unknown primary (n=18); Neuroendocrine neoplasm (n=13); Soft tissue sarcoma (n=3); Central nervous system (n=2); Pheochromocytoma (n=1); Paraganglioma (n=1).

CONCLUSIONS

- PRECISO delivers a comprehensive, real-world LB program integrated with an MTB and systematic CH filtering.
- CH is highly prevalent and, without filtering, may drive false-positive signals (e.g., DNMT3A/TET2/ASXL1/TP53).
- A CH-aware pipeline increases the clinical specificity of LB, concentrates actionability in high VOP/ESCAT tiers, and supports context-dependent recommendations across tumor types and treatment lines.

Fundación OncoSur

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