Concurrent Clonal Hematopoiesis Mutations in advanced solid tumors prior to chemotherapy exposure: A Retrospective Study

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Introduction

Clonal Hematopoiesis of Indeterminate Potential (CHIP) involves somatic mutations in hematopoietic stem cells, which can predispose to myeloid neoplasms. While common in patients with solid tumors, most studies detect CHIP after cytotoxic therapy. Its prevalence at diagnosis, prior to treatment, remains underexplored in non-hematologic malignancies.

Objectives

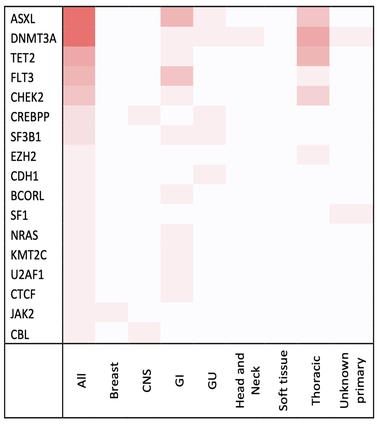
To determine the prevalence of CHIP at cancer diagnosis before therapy, using next-generation sequencing (NGS) on tissue and blood samples.

Methods

This retrospective single-institution study included 130 patients diagnosed with non-hematologic cancers between 2022-2023. Samples were analyzed via FoundationOne NGS platform. Baseline characters in Table 1

Characteristic	Value
No. of Patients	130
Age (years) Median	66
Body-Mass Index Median	26.95
Smoking	24
Type of cancer	
Gastrointestinal	45 (34.6)
Breast	15 (11.5)
Central Nervous System	4 (3.1)
Genitourinary	18 (13.8)
Head and Neck	3 (2.3)
Sarcoma	1 (0.8)
Soft Tissue	3 (2.3)
Thoracic	38 (29.2)
Thyroid	1 (0.8)
Unknown Primary	2 (1.5)

Figure 1. Frequency of samples with genetic mutations by cancer type



Results

27% (36/130) had CHIP mutations; 21% (28/130) at diagnosis before treatment. Among these, 52.7% had liquid biopsies, and 47.2% had tissue analysis. Specifically, 25 patients had blood testing, with 19 (76%) positive for CHIP. Of 105 tissue samples, 17 (16%) tested positive. The leading cancer types were lung (44%) and colon (27%). CHIP-positive patients were mostly smokers (66.7%) with a mean age of 66.8 years. Common mutations included DNMT3A (n=10), ASXL1 (n=10), TET2 (n=6), and CHEK2 (n=4). Other mutations were in CREBBP, SF3B1, KMT2C, NRAS, CBL, EZH2, CTCF, SF1, BCORL1, CDH1, JAK2, and U2AF1 in figure 1 and Figure 2 for frequency and distribution of mutations in across different cancers. No significant correlation between CHIP and tumor type was observed, likely due to limited sample size.

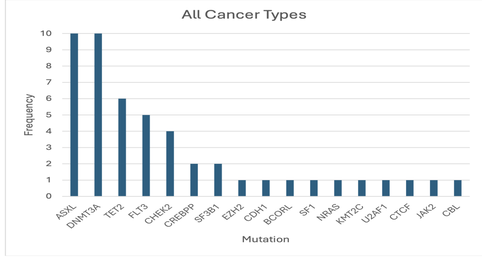


Figure 2 shows mutation frequencies by gene across all cancer types.

Discussion

This is the first study to evaluate the prevalence of CHIP at diagnosis in non-hematologic cancers. Our findings indicate that CHIP is already present at initial diagnosis, with approximately 76% of the blood samples tested demonstrating CHIP mutations. This raises important questions regarding the value of combining blood and tissue analyses for more comprehensive detection. About one-fifth of patients had CHIP detected before any treatment, underscoring the need for further investigation into clonal dynamics, the potential impact of chemotherapy, and clinical outcomes. We are currently expanding our cohort to better understand the associations between CHIP and tumor types, the influence of cytotoxic therapy on CHIP development, and the broader implications for patient prognosis.