Clonal Hematopoiesis of Indeterminate Potential (CHIP) Clinic: The Cleveland Clinic Experience

Sindhusha Veeraballi*, Teodora Kuzmanovic*, Donna Horvath, Natalya Karasik, David Bosler, Jame Abraham, Halle Moore, Jessica Geiger, Aaron T. Gerds, Anjali S. Advani, Sudipto Mukherjee, John Molina, Sophia Balderman, Moaath Mustafa Ali, Brian Bolwell, Jaroslaw P. Maciejewski, Hetty E. Carraway, Bhumika J. Patel, Abhay Singh
*denotes co-first author status
Taussig cancer Center, Leukemia Department, Cleveland Clinic, Cleveland, Ohio

soho2023 ELEVENTH ANNUAL MEETING

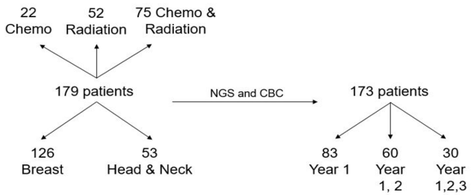
Cleveland Clinic

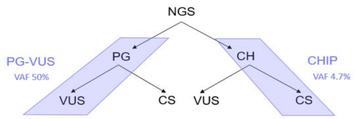
INTRODUCTION

Clonal hematopoiesis of indeterminate potential (CHIP) is the presence of a clonally expanded hematopoietic stem cell caused by a leukemogenic mutation in individuals without evidence of hematologic malignancy, dysplasia, or cytopenia[1][2]. CHIP is associated with a 0.5-1.0% risk per year of leukemia and is a novel cardiovascular risk factor[1][2]. There is currently paucity of data on the demographics, management and clinical outcomes of CHIP patients seen in the survivorship setting. Our CHIP clinic model addresses this issue following cancer survivors for potential long-term CHIP related issues.

METHODS

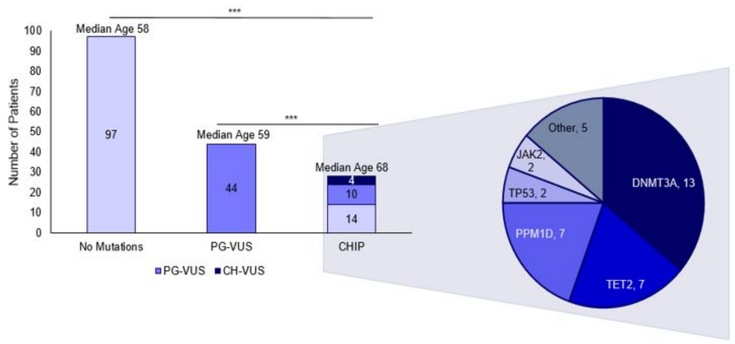
Patients from our survivorship Clinic at CCF with prior diagnosis of Breast (BC) and Head and Neck cancer (HNC) were screened and enrolled into this study if eligible/agreeable between 2020 and 2023. Patients are being followed at our clinic with annual next generation sequencing (NGS) and complete blood count.



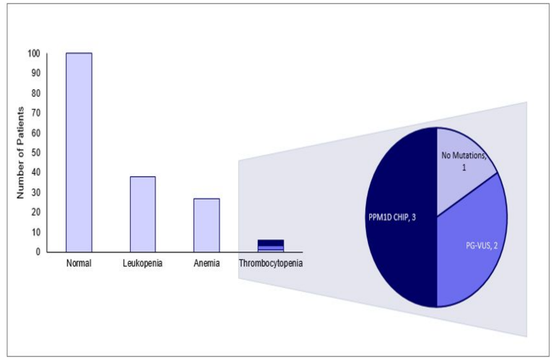


PG, potentially germline; **VUS**, variant of uncertain significance; **CS**, clinically significant; **CH**, clonal hematopoiesis; **VAF**, variant allele frequency

RESULTS



CHIP found in 16% of patients. CHIP patients were older, and half co-occurred with VUS. *DNMT3A*, *TET2*, *PPM1D are* most frequently mutated.



Most patients had normal CBC (58%), some mild stable leukopenia (22%) and anemia (15%). Thrombocytopenia seen in 6 patients, half with *PPM1D* CHIP

Patient	Cardiology Visit	CVD Comorbidities	CVD Medication	NGS Classification	PG Mutations	CH and CHIP Mutations	Serial NGS Status
1	Yes	HTN, HLD	Yes	CHIP		***DNMT3A***	Stable
2	Yes	T2D, HTN, HLD	Yes	CHIP + CH-VUS		***PPM1D***, *SUZ12*	Stable
3	Yes	HTN, HLD	Yes	CHIP + PG-VUS	*CUX1*	***TET2, TP53, PPM1D****	Worse, Better (Overall Stable)
4	Yes	HTN	Yes	CHIP + PG-VUS	*GATA2*	***TP53****	Better
5	Yes	T2D, HTN, HLD	Yes	CH-VUS + PG-VUS	*KMT2A*	*CUX1*****, ***JAK2*****	Worse; Better (Overall Better)
6	No	HTN	Yes	CHIP		***DNMT3A***	Stable
7	No	None	No	CHIP + CH-VUS + PG-CS	*TET2*	***PPM1D***, *DNMT3A, RAD21*	Stable
8	No	HTN, HLD	Lifestyle Modification	CHIP and CH+VUS		***GNAS***, *ZRSR2*	Stable

CHIP and Preventive Cardiology. Genes in bold, CHIP mutations. HTN, hypertension, HLD, hyperlipidemia, T2D, type 2 diabetes. **PPM1D* appeared in year 2 and disappeared in year 3. ***TP53* appeared in year 1 and disappeared in years 2 and 3. **** *CUX1* appeared in year 1 and disappeared in years 2 and 3.***** *JAK2* appeared in year 2 and disappeared in year 3

CONCLUSION

This ongoing prospective cohort study is one of the largest to report characteristics and clinical outcomes of patients referred to a CHIP clinic with anticipated further expansion. Collaborative efforts between hematologists and cardiologists have led to improved cardiac management in numerous patients. The study results will contribute to the development of better risk predictors for therapy-related myeloid neoplasms (tMN) and identification of targeted mechanisms to prevent morbidities and fatal complications.

Future Directions:

1. Expansion of the study to other cancer cohorts.
2. Impact of CVD risk reduction strategies and their role in promoting clonal stability.
3. Facilitate confirmatory germline testing and genetic counselling in relevant patients.

REFERENCES

1. Marnell, Christopher S et al. "Clonal hematopoiesis of indeterminate potential (CHIP): Linking somatic mutations, hematopoiesis, chronic inflammation and cardiovascular disease." *Journal of molecular and cellular cardiology* vol. 161 (2021): 98-105. doi:10.1016/j.yjmcc.2021.07.004
2. Gumuser, Esra D et al. "Clonal Hematopoiesis of Indeterminate Potential Predicts Adverse Outcomes in Patients With Atherosclerotic Cardiovascular Disease." *Journal of the American College of Cardiology* vol. 81,20 (2023): 1996-2009. doi:10.1016/j.jacc.2023.03.401.

CONTACT

Dr. Sindhusha Veeraballi, Clinical and Research fellow- Experimental Therapy in Hematology and Oncology , Taussig Cancer Center, Cleveland Clinic, Ohio.
veerabs@ccf.org