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ELEVENTH ANNUAL MEETING

Risk Factors Beyond Chemotherapy Exposure for Therapy-Related Myelodysplastic Syndrome (t-MDS) and Acute Myeloid Leukemia (t-AML) Development in Lymphoma Survivors: A 15-year SEER-Medicare Analysis

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INTRODUCTION

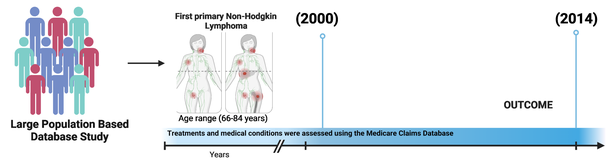
- T-AML/MDS constitute 20-30% of newly diagnosed myeloid neoplasms and have a poor prognosis.
- T-AML/MDS develop in a small percentage of patients who receive chemoradiotherapy (CRT), thereby suggesting role of additional factors that may facilitate leukemic transformation.
- Clonal hematopoiesis (CH) represents a precursor state to overt myeloid neoplasm, and those surviving CRT/genotoxic stress may give rise to T-AML/MDS.

AIM

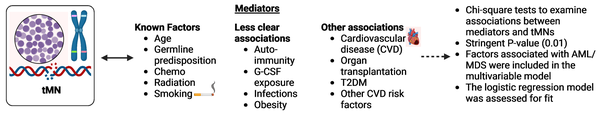
To assess if clonal hematopoiesis-related comorbidities (cardiovascular disease, infections, autoimmunity, etc.) are associated with t-AML/MDS, beyond chemoradiotherapy.

METHOD

SEER-Medicare Database



Associations between MN and proposed mediators examined



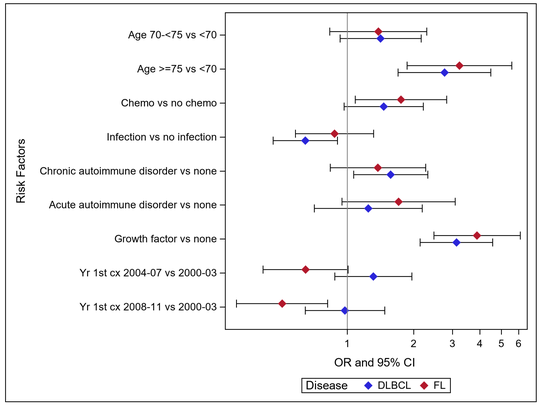
RESULTS

Table 1: Risk of t-AML/MDS after first primary DLBCL or FL diagnosed 2000-2011 using SEER-Medicare

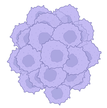
	DLBCL			FL		
	OR	95% CI	p-value	OR	95% CI	p-value
Age at first primary cancer			0.0002			<.0001
<70 years	ref			ref		
70-<75 years	1.42	(0.93 , 2.17)		1.37	(0.83 , 2.28)	
≥75 years	2.77	(1.71 , 4.49)		3.19	(1.85 , 5.52)	
Initial chemotherapy			0.055			0.015
no chemotherapy	ref			ref		
chemotherapy	1.51	(0.99 , 2.30)		1.82	(1.12 , 2.96)	
Cardiovascular disease			0.283			0.193
no cardiovascular disease	ref			ref		
cardiovascular disease	0.79	(0.51 , 1.22)		0.72	(0.44 , 1.18)	
Infections			0.024			0.765
no infection	ref			ref		
infection	0.67	(0.48 , 0.95)		0.94	(0.61 , 1.44)	
Long autoimmune conditions			0.019			0.181
no autoimmune conditions	ref			ref		
autoimmune conditions	1.60	(1.08 , 2.36)		1.41	(0.85 , 2.32)	
Short Autoimmune conditions			0.428			0.067
no autoimmune conditions	ref			ref		
autoimmune conditions	1.26	(0.71 , 2.21)		1.74	(0.96 , 3.14)	
Growth factor			<.0001			<.0001
no growth factor	ref			ref		
growth factor	3.12	(2.14 , 4.55)		3.90	(2.48 , 6.14)	
Year of NHL			0.247			0.016
2000-2003	ref			ref		
2004-2007	1.33	(0.89 , 1.99)		0.65	(0.42 , 1.02)	
2008-2011	0.99	(0.65 , 1.50)		0.51	(0.32 , 0.83)	

*Models controlled for months of Medicare coverage and were statistically significant for an interaction between infection and growth factor.

Among 24,425 DLBCL and FL patients, 274 t-AML/MDS cases were identified

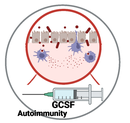


CONCLUSIONS

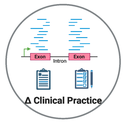




Large-scale population-based database study
- Re-demonstrated well-established and known risk of excess MDS/AML risk following chemotherapy exposure



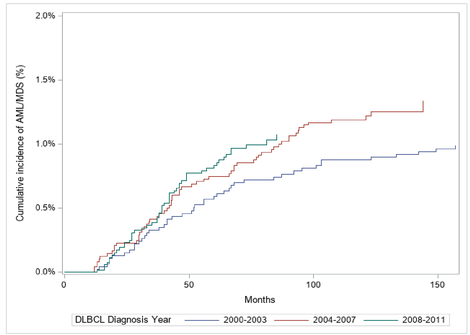
Other clinical factors (mediators)
- Are involved in the evolution to MDS/AML (tMN) after chemotherapy exposure



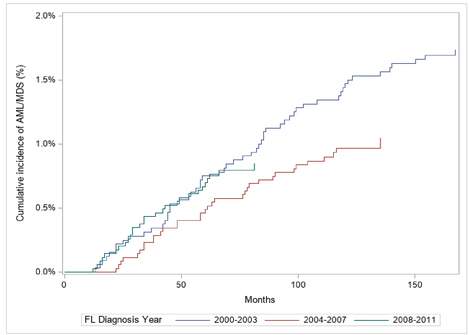
Next Steps
- Reconsideration of common clinical practices such as routine use of G-CSF as primary prophylaxis to limit neutropenia
- Understand role of pre-existing molecular aberrations leading to progression to tMN
- Avoid exposure in patients with underlying pre-malignant aberrations to prevent future MDS/AML (tMN) development

RESULTS

First primary DLBCL – Cumulative incidence of t-AML/MDS adjusting for the competing risk of death



First primary FL – Cumulative incidence of t-AML/MDS adjusting for the competing risk of death



Cumulative incidence

First primary DLBCL: The cumulative incidence of t-AML/MDS for DLBCL patients diagnosed in 2000-2003 was lower than more recent years. This increase in t-AML/MDS could be due to the increase in auto transplant in the recent cohorts. Alternatively, this increase could be due to the survival effect of rituximab.

First primary FL: 2000-2003 cumulative incidence of AML/MDS for FL patients is higher than that of 2004-07. This difference could be due to the change in therapy from more intensive to less intensive regimens

CONTACT INFORMATION

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