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ORAL ABSTRACTS

903.HEALTH SERVICES AND QUALITY IMPROVEMENT -MYELOID MALIGNANCIES

Risk of Therapy-Related Acute Myeloid Leukemia (t-AML) in Adolescent and Young Adults Cancer Patients Treated with Chemotherapy with or without Radiotherapy: A National Population-Based Cohort Study Using SEER Registry

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INTRODUCTION
The risk of treatment-related acute myeloid leukemia (t-AML) in adolescents and young adults (AYA) with first cancers treated with chemotherapy with or without radiation is not well characterized. We analyzed Surveillance, Epidemiology and End Result (SEER) data for the past 45-years (1975-2020) to identify the overall risk of t-AML in treated AYA cancer patients (pts) and by index cancer sites as well as latency periods.

METHOD
We analyzed NCI's SEER-8 registries. ICD-O-3/WHO-2008 codes were used to identify pts with index cancer types between the ages of 15-39 years (AYA), treated with either chemotherapy or radiotherapy, and with a subsequent diagnosis of acute myeloid leukemia (AML) at least one year after index cancer, between January 1975 and December 2020. The risk of t-AML was estimated by standardized incidence ratio (SIR), defined as the ratio of observed t-AML-cases in the AYA-with-cancer, to the expected number of AML-cases in the matched general US population. A reference rate file for AML incidence in age, gender, race and calendar-year matched US population is available in SEERStat software. A Poisson distribution of observed t-AML was assumed for the calculation of 95% confidence intervals (CIs). A *P*-value <.05 was considered statistically significant. We stratified the risk of t-AML for index cancer types with ten or more pts, by attained-calendar-years, and latency at multiple time intervals (Table-1) from index cancer diagnosis.

RESULT
Among 102,879 AYA cancer pts eligible for analysis, 236 pts developed t-AML with SIR of 6.19 (95%CI: 5.43-7.04, *P* <.05) with excess risk of 1.46 per-10000 person-years (pyrs). (Table-1). We stratified risk for index cancer types with at least ten patients developing t-AML, these included breast, Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), testicular, thyroid, bone and joint, and soft tissue including heart. As a general trend, risk of t-AML was highest during 1-3 years after index cancer diagnosis compared to subsequent latency periods. However, risk for t-AML was significantly greater than the matched-general US population even after 20-40 years of breast cancer, HL, and NHL (Table-1).
When stratified by attained calendar-year periods (1975-1985, 1986-1995, 1996-2005, 2006-2015, 2016-2020), risk for t-AML was higher than general population in all time periods. However, overall SIR was comparatively lower for recent time periods, particularly lowest during 2016-2020 [SIR: 3.49 (2.51-4.72, *P* <.05)]. Notably, the highest risk for t-AML in 2016-2020 was observed with index cancer of soft tissue including heart [SIR: 10.12 (1.23-36.57), *P* <.05].

CONCLUSION
In this study spanning between 1975-2020, we observed the risk of t-AML trending down among AYA in recent years, albeit higher than the age matched general population. The risk of t-AML remained significantly elevated even after 20-40 from diagnosis of breast cancer, HL and NHL. Since these pts likely received radiation and older (higher intensity) chemotherapy based-regimens, it is essential to analyze the long-term impact of newer therapies for these cancers and assess the risk of t-AML in future studies.

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Table 1: Risk of acute myeloid leukemia among adolescent young adults with cancer, compared to general US population, stratified by site of index cancer

	SIR stratified by time-period												SIR stratified by latency (years) after index cancer						
	Overall		1975-1985		1986-1995		1996-2005		2006-2015		2016-2020								
Site	N	SIR	N	SIR	N	SIR	N	SIR	N	SIR	N	SIR	1-3	3-5	5-10	10-15	15-20	20-40	40+
All	236	6.19* (5.43-7.04)	13	20.42* (10.87-34.93)	33	12.28* (8.45-17.25)	54	7.50* (5.63-9.78)	94	6.05* (4.89-7.4)	42	3.49* (2.51-4.72)	32.66* (25.98-40.55)	14.39* (9.91-20.21)	9.65* (7.21-12.66)	4.74* (3.07-7)	1.91 (0.91-3.51)	1.88* (1.28-2.67)	3.26 (0.67-9.53)
Breast	58	6.32* (4.8-8.17)	1	8.71 (0.22-48.54)	10	15.96* (7.65-29.34)	14	7.95* (4.34-13.33)	21	5.61* (3.47-8.57)	12	4.10* (2.12-7.17)	41.35* (27.69-59.38)	9.33* (3.42-20.31)	4.79* (1.93-9.87)	3.59* (1.17-8.38)	1.5 (0.18-5.42)	2.54* (1.16-4.82)	0 (0-37.5)
HL	47	9.12* (6.7-12.13)	5	41.73* (13.55-97.39)	11	25.56* (12.76-45.73)	11	10.42* (5.2-18.64)	16	7.75* (4.43-12.59)	4	2.7 (0.74-6.91)	42.61* (22.02-74.43)	18.09* (5.88-42.23)	20.57* (11.25-34.52)	10.07* (4.05-20.75)	1.4 (0.04-7.77)	3.37* (1.45-6.64)	0 (0-28.97)
NHL	37	10.78* (7.59-14.86)	1	17.94 (0.45-99.97)	2	8.74* (1.06-31.58)	10	15.92* (7.63-29.28)	15	10.65* (5.96-17.57)	9	8.10* (3.7-15.38)	61.80* (32.9-105.67)	25.24* (8.2-58.91)	14.60* (5.87-30.09)	10.59* (3.44-24.7)	4.21 (0.51-15.2)	3.33* (1.08-7.76)	0 (0-39.77)
Testis	16	2.43* (1.39-3.95)	2	21.00* (2.54-75.87)	2	4.97 (0.6-17.95)	2	1.72 (0.21-6.22)	7	2.57* (1.03-5.3)	3	1.36 (0.28-3.98)	11.89* (2.45-34.74)	7.83 (0.95-28.29)	5.87* (1.6-15.03)	2.62 (0.32-9.45)	1.16 (0.03-6.45)	1.14 (0.31-2.92)	0 (0-14.57)
Thyroid	14	3.15* (1.72-5.28)	0	0 (0-114.41)	1	5.23 (0.13-29.15)	2	2.83 (0.34-10.22)	5	2.62 (0.85-6.11)	6	3.74* (1.37-8.13)	12.16* (3.31-31.13)	12.21* (3.33-31.26)	3.82 (0.79-11.16)	1.41 (0.04-7.85)	3.2 (0.39-11.55)	0 (0-2.32)	0 (0-46.4)
Bones and Joints	11	33.42* (16.68-59.8)	0	0 (0-541.23)	0	0 (0-141.76)	2	28.91* (3.5-104.42)	8	61.67* (26.63-121.52)	1	10.27 (0.26-57.21)	105.30* (21.72-307.73)	178.11* (48.53-456.03)	63.45* (13.09-185.43)	0 (0-85.86)	0 (0-87.21)	7.5 (0.19-41.79)	0 (0-299.92)
Soft Tissue (with Heart)	10	16.00* (7.67-29.42)	0	0 (0-339.18)	1	22.7 (0.57-126.5)	4	33.55* (9.14-85.9)	3	11.84* (2.44-34.6)	2	10.12* (1.23-36.57)	64.64* (13.33-188.92)	78.03* (16.09-228.04)	35.09* (7.24-102.56)	0 (0-45.01)	0 (0-45)	0 (0-13.52)	55.51* (1.41-309.27)

* p value < 0.05; SIR: standardized incidence ratio, expressed with 95%CI. SIR is stratified for Index cancer sites with at least 10 patients developing AML during 1975-2020. HL= Hodgkin lymphoma, NHL= non-Hodgkin lymphoma

Figure 1