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IDH-1 somatic mutations are more commonly observed among patients with concomitant Myelodysplastic syndromes and connective tissue disease.

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INTRODUCTION

- We previously reported that autoimmune diseases (AID) are commonly observed in MDS patients (pts) (28%) including autoimmune rheumatic diseases (AIRD).
- There is increase recognition of the association of certain acquired somatic mutations and inflammation.
- Recent study reported enrichment of AIRD among chronic myeloid neoplasms (MN) pts with high prevalence of *IDH* mutations suggestive causative association particularly between *IDH* mutations and seronegative rheumatoid arthritis (Hong et al, Blood 2024).
- Here, we compare the genomic landscape of MDS pts with concomitant defined AIRD to those without.

METHOD

- We identified MDS pts with concomitant AIRD.
- We selected Rheumatoid arthritis (RA) and systemic lupus (SLE) as AIRD given more objective diagnostic criteria and accurate data capturing.
- We compared those MDS pts with AIRD to MDS pts without.

RESULTS

- We compared 79 MDS pts with AIRD to 2469 MDS pts without in our database.
- AIRD were more observed among female MDS pts compared to non-AIRD MDS pts (59% vs 32%, p < 0.0005). There was no difference in age, race, t-MDS, WHO 2022 classification, IPSS-M risk stratification. There was no difference in baseline myeloblasts% or blood counts.
- Among 21 common somatic mutation tested, *IDH-1* somatic mutation was the only mutation observed more among AIRD MDS pts compared to non-AIRD MDS pts (11% vs 3%, p <0.0005).
- Among male AIRD MDS pts rate of *IDH-1* was 15% vs 3% and 8% vs 3% among females AIRD MDS pts compared to non-AIRD MDS pts. (p <.0005)
- There was no difference among AIRD- MDS pts and non-AIRD MDS pts in median overall survival or AML transformation rate.
- There was a non-statistically significant trend for worse median OS among AIRD MDS pts with *IDH-1* mutation (30 mo vs 40 mo).

CONCLUSIONS

- Our data confirm recently reported observation that *IDH-1* somatic mutations are enriched among myeloid neoplasms patients with AIRD.
- Further studies to explore the underlying mechanism, and potential therapeutic implications with targeted *IDH-1* inhibitors are warranted.

CONTACT INFORMATION

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TABLE-1 BASELINE CHARACTERISTICS
TABLE-2 COMPARISON OF SOMATIC MUTATIONS

	AIRD-MDS	NON-AIRDS	P Value
Age (mean, year)	69.17	69.65	0.6
Sex (male)	46 (41%)	1648 (68%)	< .005
Race (white)	2189 (91%)	102 (92%)	0.4
t-MDS	469 (19%)	16 (14%)	0.2
WHO 2022 (MDS-IB)	17 (17%)	535 (25%)	0.2
IPSS-M Lower risk Higher risk	 46 (44%) 59 (56%)	 920 (42%) 1266 (58%)	0.3
LGL clone	12/44 (27%)	213/898 (24%)	.75

	AIRD-MDS	Non AIRD MDS	P Value
TET-2	29 (26%)	528 (22%)	0.5
DNMT3A	17 (15%)	361 (15%)	0.2
ASXL-1	23 (21%)	536 (22%)	0.8
IDH-1	**12 (11%)**	**67 (3%)**	**< .005**
IDH-2	7 (6%)	114 (5%)	0.45
SF3B1	22 (20%)	448 (18%)	0.9
SRSF2	20 (18%)	282 (12%)	0.13
U2AF1	8 (7%)	261 (11%)	0.44
ZRSR2	6 (5%)	144 (6%)	0.9
EZH-2	5 (5%)	150 (6%)	0.8
TP53	20 (18%)	503 (21%)	0.8
RUNX-1	16 (14%)	264 (11%)	0.5
SETBP1	2 (2%)	111 (5%)	0.4
ETV-6	3 (3%)	81 (3%)	0.8
PHF6	5 (5%)	40 (2%)	0.05
CBL	4 (4%)	64 (3%)	0.8
NRAS	2 (2%)	69 (3%)	0.75
JAK-2	9 (8%)	112 (5%)	0.2
NPM-1	2 (2%)	30 (1%)	0.4