Real-World Treatment Patterns and Outcomes Among Patients With Newly Diagnosed *NPM1*-Mutated Acute Myeloid Leukemia in the United States

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- Although there are large datasets focused on real-world outcomes in newly diagnosed *NPM1*m AML, real-world evidence that captures academic and community sites and longitudinally reports on relapse is limited[1]
- *NPM1* mutations occur in ~30% of adult AML cases[2]
  - Patients with *NPM1*m AML without *FLT3*-ITD comutations are assigned to the favorable-risk cohort,[3] but outcomes in R/R *NPM1*m AML are poor[4]
  - Less is known regarding long-term treatment outcomes among patients with newly diagnosed *NPM1*m AML treated in community and academic centers

The objective of this study is to describe treatment patterns and outcomes among patients with newly diagnosed *NPM1*m AML in the United States

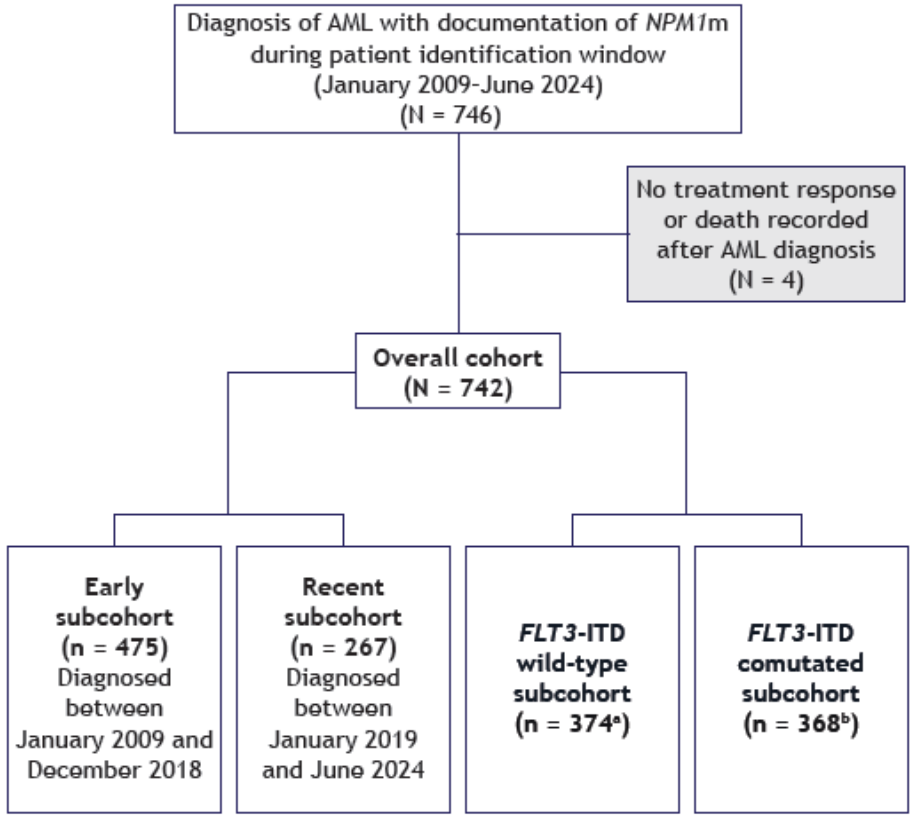
FLT3-ITD, fms-like receptor tyrosine kinase 3 internal tandem duplication.

1. Othman J, et al. *Blood*. 2024;144(7):714–728. 2. Papaemmanuil E, et al. *N Engl J Med*. 2016;374(23):2209–2221. 3. Döhner H, et al. *Blood*. 2022;140(12):1345–1377. 4. Issa GC, et al. *Blood Adv*. 2023;7(6):933–942.

Study design

- This retrospective study used real-world data from COTA Healthcare collected from adults with an initial AML diagnosis between January 2009 and June 2024 and had documented *NPM1*m status
- Patients were grouped into subcohorts by diagnosis year to evaluate the impact of venetoclax approval in November 2018
  - Early: diagnosed between January 2009 and December 2018
  - Recent: diagnosed between January 2019 and June 2024
- Patients were also grouped into subcohorts by *FLT3*-ITD comutation status

Figure 1. Patient selection

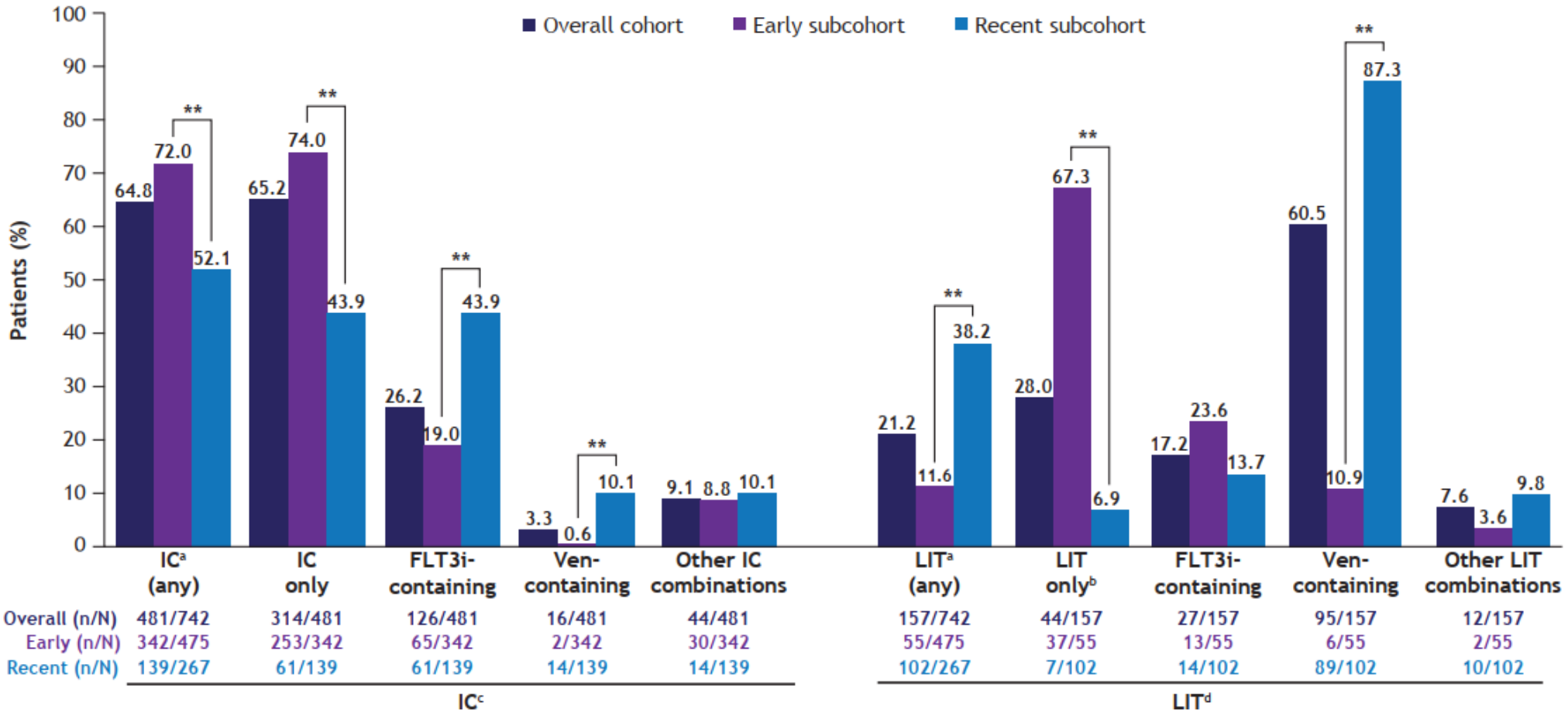


[a]Without FLT3-ITD comutation at any time during follow-up or unknown. [b]With FLT3-ITD comutation at any time during follow-up. ITD, internal tandem duplication.

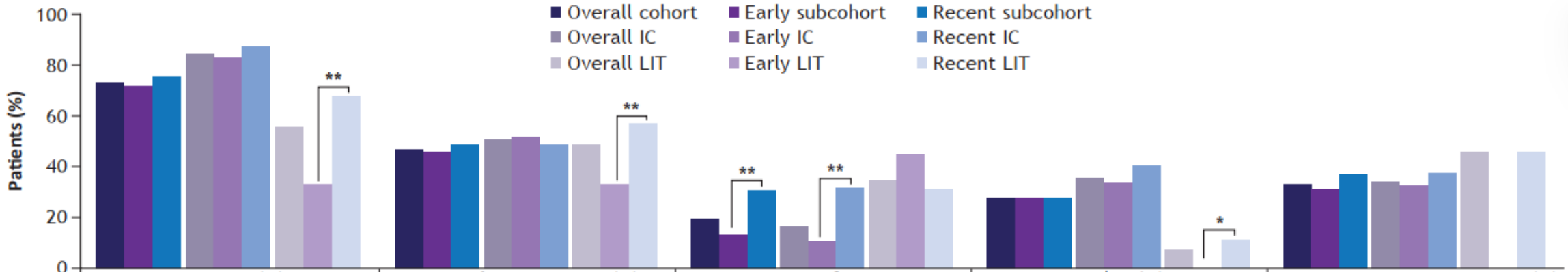
Table1. Demographic and baseline characteristics[a]

	Overall cohort (N = 742)	Early subcohort (N = 475)	Recent subcohort (N = 267)	*FLT3* -ITD wild-type subcohort[b] (N = 374)	*FLT3*-ITD commutated subcohort (N = 368)
Age at initial AML diagnosis, median (IQR), y	62.0 (51.0-71.0)	60.0 (50.0-69.5)	66.0** (56.0-73.0)	63.0 (52.0-72.0)	61.0 (50.0-70.0)
Age group , n (%)**					
19-59 y	317 (42.7)	227 (47.8)	90 (33.7)	149 (39.8)	168 (45.7)
≥60 y	425 (57.3)	248 (52.2)	177 (66.3)	225 (60.2)	200 (54.3)
Male, n (%)	322 (43.4)	205 (43.2)	117 (43.8)	176 (47.1)	146 (39.7)†
Race, n (%)					
White	570 (76.8)	376 (79.2)	194 (72.7)	281 (75.1)	289 (78.5)
Black or African American	34 (4.6)	24 (5.1)	10 (3.7)	15 (4.0)	19 (5.2)
Asian	30 (4.0)	17 (3.6)	13 (4.9)	17 (4.5)	13 (3.5)
Other/multiple/missing	108 (14.6)	58 (12.2)	50 (18.7)	61 (16.3)	47 (12.8)
Clinician practice setting at start of AML treatment, n (%)					
Academic	452 (60.9)	287 (60.4)	165 (61.8)	227 (60.7)	225 (61.1)
Community	290 (39.1)	188 (39.6)	102 (38.2)	147 (39.3)	143 (38.9)
Presence of positive comutations, n (%)	581 (78.3)	350 (73.7)	231 (86.5)**	213 (57.0)	368 (100)‡
FLT3-ITD	368 (49.6)	243 (51.2)	125 (46.8)	0	368 (100)‡
FLT3-TKD	110 (14.8)	70 (14.7)	40 (15)	57 (15.2)	53 (14.4)
DNMT3A	214 (28.8)	113 (23.8)	101 (37.8)**	97 (25.9)	117 (31.8)
IDH2	118 (15.9)	61 (12.8)	57 (21.3)**	69 (18.4)	49 (13.3)
IDH1	103 (13.9)	56 (11.8)	47 (17.6)*	69 (18.4)	34 (9.2)‡
NRAS	75 (10.1)	38 (8)	37 (13.9)*	46 (12.3)	29 (7.9)†
Duration of follow-up from AML diagnosis to death or end of study period, median (IQR), mo	23.8 (9.5-60.2)	29.0 (11.6-78.8)	17.4 (7.9-39.2)	32.7 (12.2-65.1)	19.7 (8.3-55.4)

*P <0.05 between Early and Recent subcohorts. **P <0.01 between Early and Recent subcohorts. †P <0.05 between *FLT3*-ITD wild-type and comutated subcohorts. ‡P <0.01 between *FLT3*-ITD wild-type and comutated subcohorts.
[a]At initial AML diagnosis. [b]Documented negative or unknown, or undocumented testing.
IQR, interquartile range; TKD, tyrosine kinase domain.

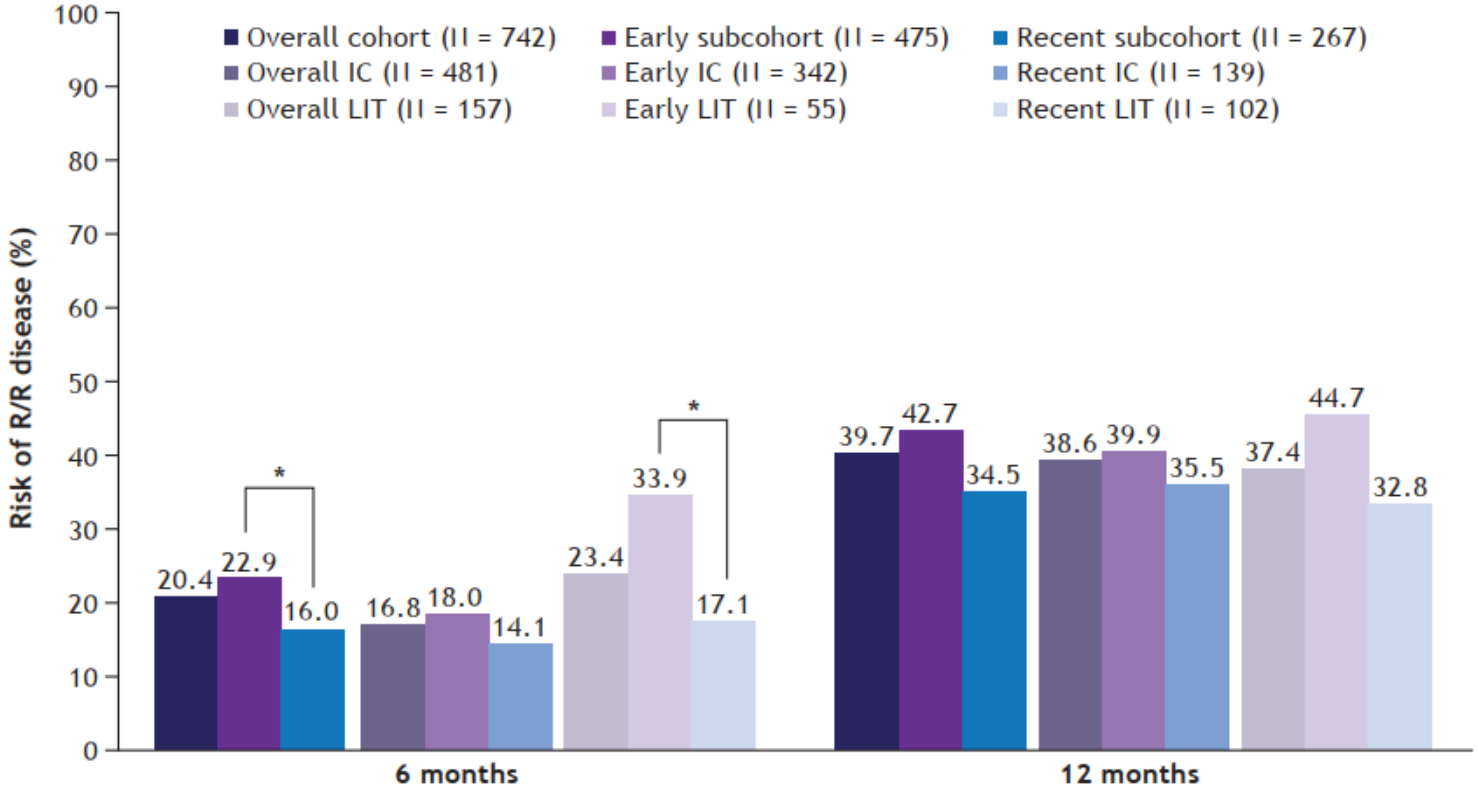


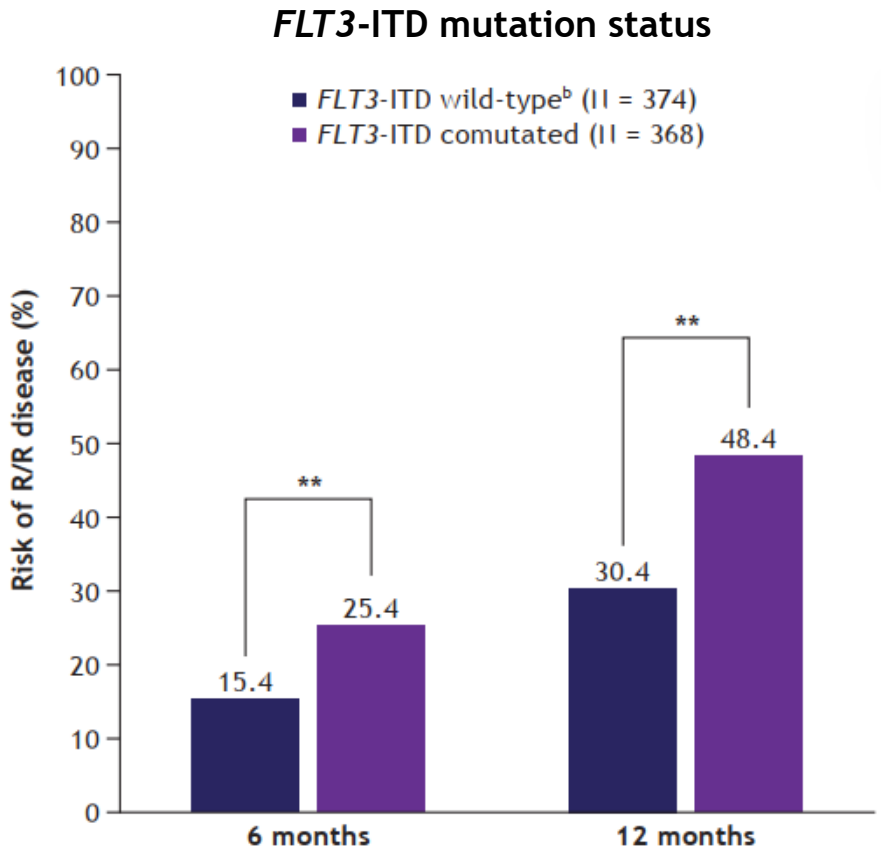
**P <0.01 between Early and Recent subcohorts.
[a]Subcategories are not mutually exclusive (eg, patients could have received both an FLT3i and venetoclax). [b]LIT only contains hypomethylating agent, gemtuzumab, or LDAC. [c]IC included HiDAC, fludarabine + cytarabine + granulocyte colony-stimulating factor ± idarubicin, and mitoxantrone + etoposide + cytarabine. [d]LIT included venetoclax-based regimens, targeted and hypomethylating agents, and LDAC.
HiDAC, high-dose cytarabine; LDAC, low-dose cytarabine; ven, venetoclax.



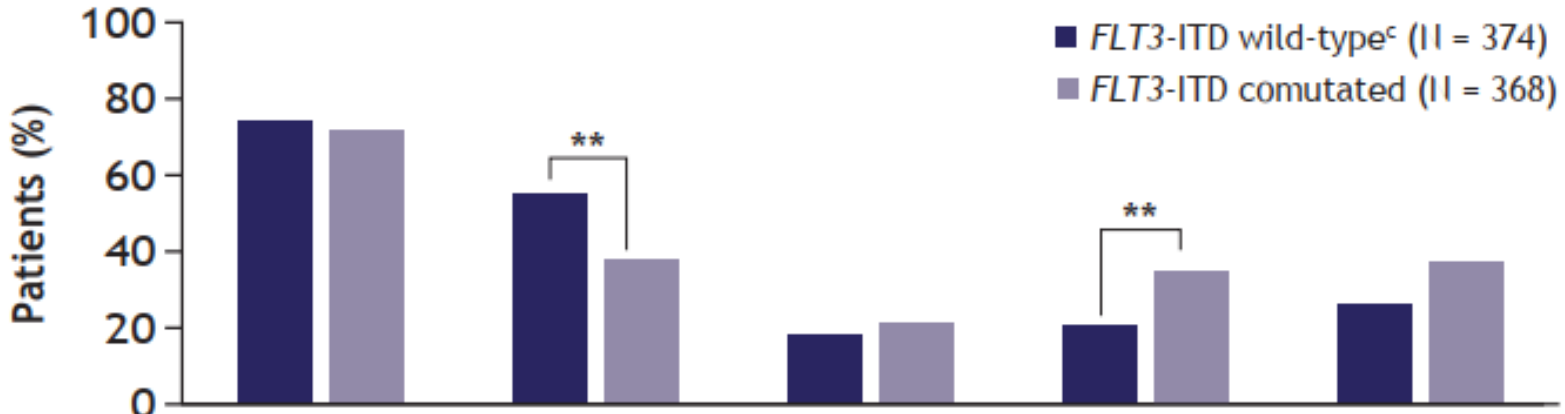
	CRc, n (%)	CRc without HSCT, n (%)	Maintenance for patients with CRc without HSCT, n (%)	HSCT,[b] n (%)	Post-HSCT maintenance, n (%)
Overall (II = 742)	541 (**72.9**)	345/541 (**63.8**)	67/345 (**19.4**)	203 (**27.4**)	67/203 (**33.0**)
Early (II = 475)	340 (**71.6**)	216/340 (**63.5**)	28/216 (**13.0**)	130 (**27.4**)	40/130 (**30.8**)
Recent (II = 267)	201 (**75.2**)	129/201 (**64.2**)	39/129 (**30.2**)**	73 (**27.3**)	27/73 (**37.0**)
Overall IC (II = 481)	405 (**84.2**)	242/405 (**59.8**)	39/242 (**16.1**)	170 (**35.3**)	58/170 (**34.1**)
Early IC (II = 342)	283 (**82.7**)	175/283 (**61.8**)	18/175 (**10.3**)	114 (**33.3**)	37/114 (**32.5**)
Recent IC (II = 139)	122 (**87.8**)	67/122 (**54.9**)	21/67 (**31.3**)**	56 (**40.3**)	21/56 (**37.5**)
Overall LIT (II = 157)	87 (**55.4**)	76/87 (**87.4**)	26/76 (**34.2**)	11 (**7.0**)	5/11 (**45.5**)
Early LIT (II = 55)	18 (**32.7**)	18/18 (**100**)	8/18 (**44.4**)	0	II/A
Recent LIT (II = 102)	69 (**67.6**)**	58/69 (**84.1**)	18/58 (**31.0**)	11 (**10.8**)*	5/11 (**45.5**)

**P* <0.05 between Early and Recent subcohorts. ***P* <0.01 between Early and Recent subcohorts.
[a]Percentages calculated among the total patient numbers for each subgroup shown, unless otherwise specified. [b]Seven patients (6 in Early subcohort and 1 in Recent subcohort) had HSCT without CRc.
CRc, composite complete remission.



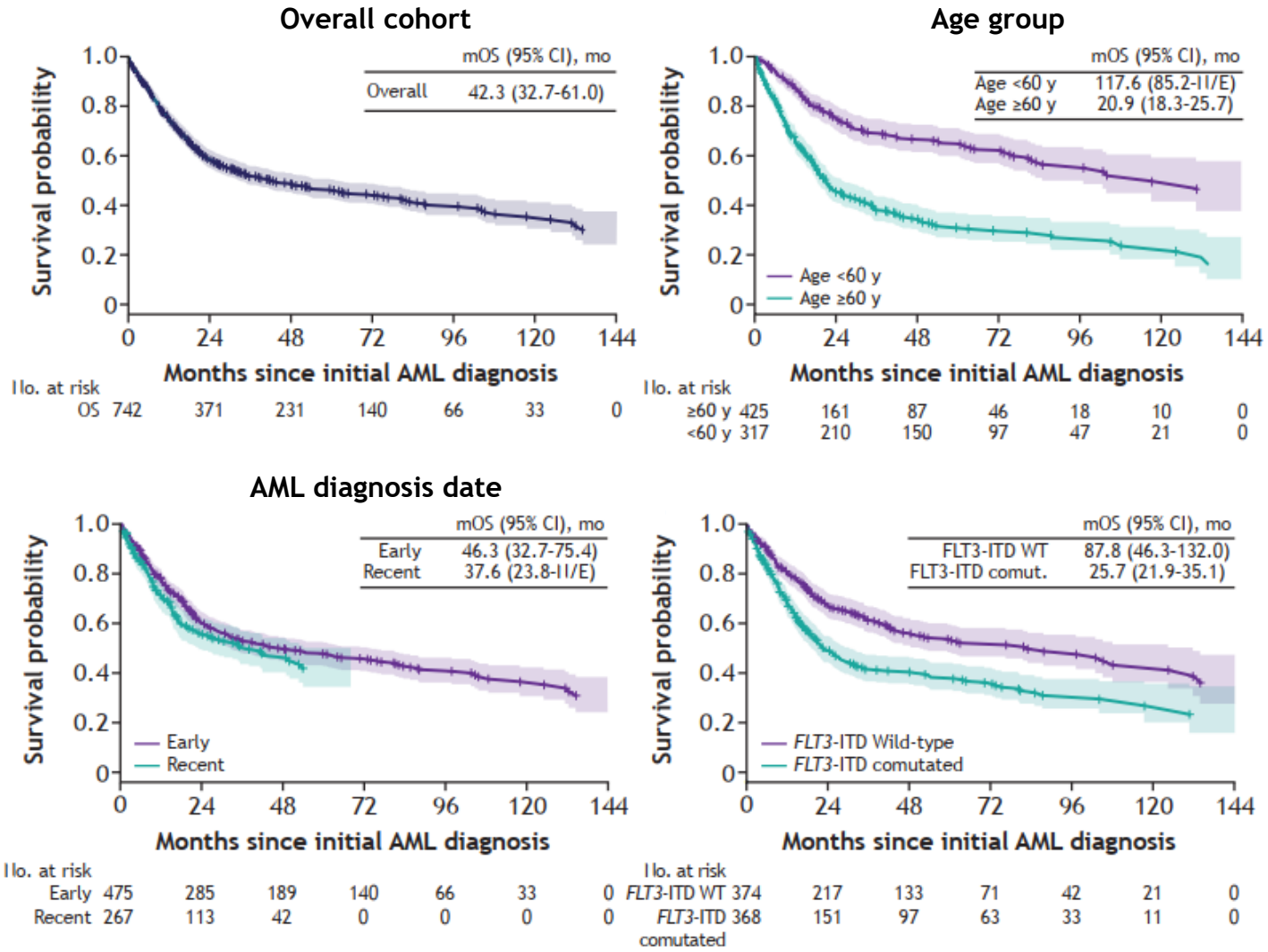


*P <0.05 between Early and Recent subcohorts. **P <0.01 between Early and Recent subcohorts.
[a]From date of AML diagnosis and includes time to frontline treatment and first assessment. [b]Includes patients with documented negative testing and undocumented testing.

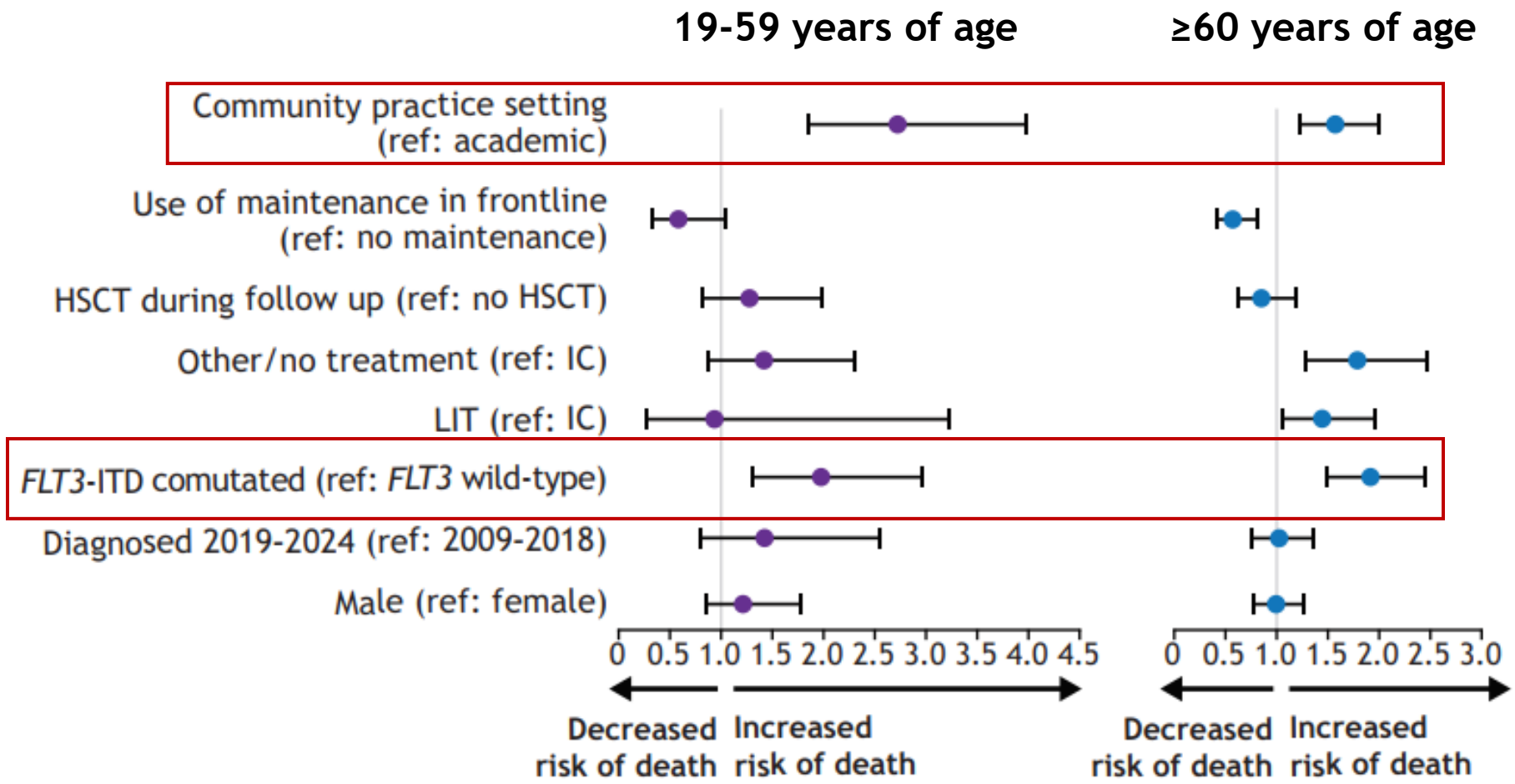


	CRc, n (%)	CRc without HSCT, n (%)	Maintenance for patients with CRc without HSCT, n (%)	HSCT,[b] n (%)	Post-HSCT maintenance, n (%)
FLT3-ITD wild type	278 (**74.3**)	205 (**54.8**)	37/205 (**18.0**)	76 (**20.3**)	20/76 (**26.3**)
FLT3-ITD comutated	263 (**71.5**)	140 (**38.0**)**	30/140 (**21.4**)	127 (**34.5**)**	47/127 (**37.0**)

**P <0.01 between *FLT3*-ITD wild-type and comutated subcohorts.
[a]Percentages calculated among the total patient numbers for each subgroup shown, unless otherwise specified. [b]Seven patients (3 in *FLT3*-ITD wild-type subcohort and 4 in *FLT3*-ITD comutated subcohort) had HSCT without CRc.
[c]Includes patients with documented negative testing and undocumented testing.



Comut, comutated; ITD, internal tandem duplication mo, months; mOS, median overall survival; N/E, not evaluable; WT, wild-type.



ITD, internal tandem duplication; ref, reference population.

Limitations

- Electronic health record data may be incomplete or inaccurate due to missing fields, inconsistent documentation, and variation in coding and recording practices across providers
- Analyses were limited to variables available in the COTA database, which may not include all relevant patient characteristics and outcomes of interest
- Identification of comutations may be impacted by testing patterns over time, with more testing in the Recent subcohort resulting in higher percentages of patients with comutations
- Risk of R/R may be underestimated, as it includes time between diagnosis and treatment and time between treatment and first response
- The study population may not be representative of all adults with *NPM1*m AML in the United States

Conclusions

- The study showed less use of IC and more use of LIT, primarily with venetoclax, in patients with newly diagnosed *NPM1*m AML in 2019 to 2024 compared with 2009 to 2018
- Among those treated with LIT, risk of R/R at 6 months decreased between the 2 time periods; however, risk of R/R is still unacceptably high, with ~1/3 of patients at 12 months reaching the same rate of R/R as those treated with IC
- No statistically significant differences were detected in OS between the 2 time periods
- Outcomes with frontline therapies remain suboptimal despite recent treatment advances, such as venetoclax, highlighting the need for novel therapeutic approaches, including targeted therapies

Acknowledgments

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