MM-348

Fluorescence in situ hybridization (FISH) t(11;14) testing practices over time in patients with newly diagnosed multiple myeloma (MM) in the USA in the Flatiron Health database

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Summary

This analysis of a real-world database investigates testing practices in patients with MM in the USA

FISH testing at diagnosis has increased over time alongside changes in MM management guidelines

The results presented here contrast with other studies, which have shown imbalances in real-world survival, highlighting the need to address disparities pre- and post-MM diagnosis

17.8% of FISH-tested patients with MM tested positive for t(11;14), of which 44.0% also had at least one secondary high-risk abnormality

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Background

- Multiple myeloma (MM) is a hematologic malignancy, with an incidence of approximately 34,470 new cases diagnosed in 2022 across the United States (US).[1]
- As MM management evolves with emerging targeted therapies and risk-stratification measures, there has been an increasing need in fluorescence in situ hybridization (FISH) testing for t(11;14)
  - t(11;14) and t(11;14)(q13;q32) CCND1:IGH are important biomarkers of MM prognosis and response to therapy
  - Potential therapies such as the BCL-2 inhibitor venetoclax are being investigated for patients with t(11;14) positive (+) MM.[2]
- We assessed testing practices in MM to understand biomarker testing trends over time and equitable practices in the US using a real-world database.

Methods

- This retrospective study used the nationwide Flatiron Health electronic health-record derived, longitudinal database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction[3,4]
  - During the study period, the de-identified data originated from ~280 US cancer clinics and 800 sites of care.
- Patients aged ≥18 years, diagnosed with MM as their only malignancy, between January 2011–July 2022, with ≥2 clinic encounters 6 months after diagnosis were included and clinical trial participants were excluded.
- FISH testing rates at diagnosis (≤30 days prior to or 90 days post diagnosis) were evaluated yearly and across three timeframes:
  - Start of study period to Revised International Staging System (R-ISS) publication (January 2011–August 2015)[5]
  - R-ISS to updated NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), which include venetoclax/dexamethasone as a treatment option for t(11;14)+ MM (September 2015–May 2020)[6]
  - Updated NCCN Guidelines® to the end of study period (June 2020–July 2022).
- Time to FISH test from MM diagnosis, t(11;14)+ rate, and rate of high-risk secondary abnormalities were also assessed.

Results

Baseline characteristics

- Overall, 12,284 patients were eligible for inclusion with a median age of 70 years at diagnosis.
- Among those who were eligible, 9,157 patients had ≥1 FISH test ≤30 days prior to or any time after MM diagnosis.
- Demographic data for all patients and patients with ≥1 FISH test are described in **Table 1.**

Table 1. Patient demographics.

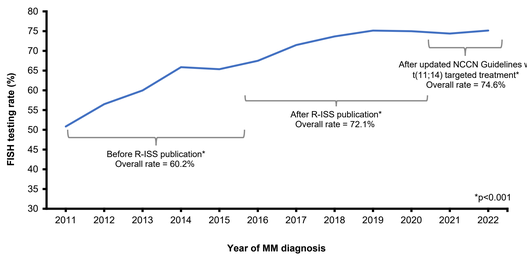
	All patients N=12,284	Patients with ≥1 FISH test N=9,157
Age at diagnosis, median (IQR)	70 (61–77)	69 (60–76)
Age group, n (%)		
<65 years	4,351 (35)	3,484 (38)
65–75 years	4,088 (33)	3,123 (34)
>75 years	3,845 (31)	2,550 (28)
Sex, n (%)		
Female	5,666 (46)	4,181 (46)
Male	6,618 (54)	4,976 (54)
Practice type, n (%)		
Academic	2,458 (20)	1,768 (19)
Community	9,446 (77)	7,099 (78)
Both	380 (3)	290 (3)
Race/ethnicity, n (%)		
Asian	219 (2)	170 (2)
Black or African American	2,152 (18)	1,612 (18)
Hispanic or Latino	876 (7)	662 (7)
White	7,041 (57)	5,245 (57)
Other	935 (8)	698 (8)
Unknown	1,061 (9)	770 (8)
Insurance type, n (%)		
Commercial health plan	4,019 (33)	3,143 (34)
Medicaid	269 (2)	190 (2)
Medicare	4,197 (34)	2,982 (33)
Other	636 (5)	482 (5)
Unknown	3,163 (26)	2,360 (26)
SES index, n (%)		
1 – lowest SES	1,791 (15)	1,303 (14)
2	1,999 (16)	1,481 (16)
3	2,242 (18)	1,703 (19)
4	2,528 (21)	1,944 (21)
5 – highest SES	2,505 (20)	1,856 (20)
Unknown	1,219 (10)	861 (9)

FISH, fluorescence in situ hybridization; IQR, interquartile range; SES, social economic status.

FISH testing rates at diagnosis and patterns over time

- Testing rates at diagnosis increased yearly, from 50.8% in 2011 to 75.2% in 2022 (**Figure 1**).
- There was a significant difference in FISH testing rates between the three timeframes (p<0.001):
  - From the start of study period to R-ISS publication (January 2011–August 2015), FISH testing rate was 60.2%
  - From R-ISS publication to updated NCCN Guidelines, which include venetoclax/dexamethasone as a treatment option for t(11;14)+ MM (September 2015–May 2020), FISH testing rate was 72.1%.
  - From updated NCCN Guidelines to the end of study period (June 2020–July 2022), FISH testing rate was 74.6%.

Figure 1. Yearly FISH testing rates among all patients with MM.



FISH, fluorescence in situ hybridization; MM, multiple myeloma; NCCN, National Comprehensive Cancer Network® (NCCN®); NCCN Guidelines, NCCN Clinical Practice Guidelines in Oncology; R-ISS, Revised International Staging System.

Time to FISH test from MM diagnosis

- Time to FISH test from MM diagnosis decreased with age but was similar regardless of other patient characteristics.
- All subgroups had a median time to FISH test of <30 days (**Table 2**).

Table 2. Time to FISH test from MM diagnosis; N=9,157.

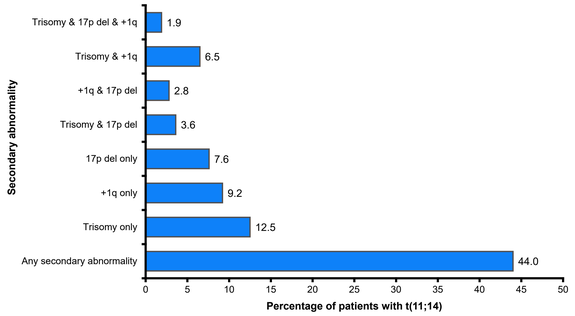
	Median days (IQR)
Age group	
<65 years	15 (5–26)
65–75 years	14 (4–24)
>75 years	11 (2–21)
Sex	
Female	13 (4–24)
Male	14 (4–24)
Practice type	
Academic	16 (5–27)
Community	13 (4–23)
Both	15 (7–26)
Race/ethnicity	
Asian	12 (6–22)
Black or African American	13 (4–23)
Hispanic or Latino	14 (4–26)
White	13 (4–24)
Other	13 (3–23)
Unknown	12 (3–21)
Insurance type	
Commercial health plan	13 (4, 23)
Medicaid	13 (4, 23)
Medicare	12 (3, 23)
Other	12 (4, 22)
Unknown	16 (5, 26)
SES index	
1 – lowest SES	13 (4–23)
2	13 (4–23)
3	14 (4–24)
4	14 (5–24)
5 – highest SES	13 (3–24)
Unknown	13 (5–24)

FISH, fluorescence in situ hybridization; IQR, interquartile range; MM, multiple myeloma; SES, social economic status.

t(11;14) positivity and other secondary abnormalities

- Overall, 17.8% (1,627/9,157) of patients tested positive for t(11;14), of which 715 (44.0%) were diagnosed with at least one secondary abnormality.
- The percentage of patients with either a single secondary abnormality or a combination of secondary abnormalities in addition to t(11;14) are presented in **Figure 2**.

Figure 2. Secondary abnormalities in addition to t(11;14).



del, deletion.

First treatment regimen used after MM diagnosis

- t(11;14) status did not appear to impact transplant status or choice of first treatment regimen, with similar first-line regimens reported for patients with and without t(11;14)+ MM (**Table 3**).

Table 3. Top 5 first treatment regimens used after MM diagnosis.

Regimen*, n (%)	Patients with t(11;14) N=1,627	Patients without t(11;14) N=7,530
Bortezomib, dexamethasone, lenalidomide	546 (33.6)	2,796 (37.1)
Dexamethasone, lenalidomide	217 (13.3)	1,188 (15.8)
Bortezomib, cyclophosphamide, dexamethasone	144 (8.9)	727 (9.7)
Bortezomib, dexamethasone	122 (7.5)	750 (10.0)
No therapy	108 (6.6)	398 (5.3)

*Table displays top 5 treatment regimens used and is not inclusive of all patients with MM.

MM, multiple myeloma.

Transplant status

- Among patients with t(11;14)+ MM, 469 (28.8%) had a transplant after MM diagnosis and 503 (31.0%) had a transplant at any time.
- Among patients without t(11;14)+ MM, 2,898 (27.2%) had a transplant after MM diagnosis and 2,900 (27.2%) had a transplant at any time.

Conclusions

- FISH testing at diagnosis has increased over the past decade alongside changes in MM management guidelines, indicating positive improvements in standardizing cytogenetic testing.
- While there is little divergence in testing rates and time to FISH test at diagnosis across patients in the Flatiron Health database, other studies have shown imbalances in real-world survival across race and socioeconomic status, highlighting the need to identify and address disparities pre- and post-MM diagnosis.[7,8]

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Disclosures

LBB and SKK: employees of Mayo Clinic.
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AG: employee of AbbVie, Inc.