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Real-World Outcomes in Smoldering Multiple Myeloma in Europe: Updated Results From the SPARK Study

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Key Takeaway

The findings from this large, real-world study of European patients with SMM reinforce the need for enhanced monitoring strategies and improved risk stratification to identify patients with high-risk SMM that could benefit from early treatment intervention

Conclusions

Regardless of how high-risk SMM was defined, >57% of progressions to MM were CRAB events, and >56% of progressions to MM included organ damage, most commonly bone pain, bone fractures, and anemia

Patients with high-risk SMM were monitored more frequently than non–high-risk patients, yet the incidence of organ damage at MM diagnosis remained high

These data suggest that active monitoring alone is insufficient in preventing organ damage in the majority of patients with high-risk SMM; highlighting the unmet need for early treatment intervention

https://www.congresshub.com/Oncology/IMS2026/Daratumumab/Gay

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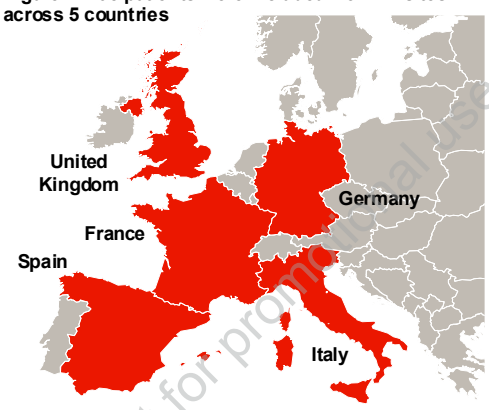
Introduction

- Smoldering multiple myeloma (SMM) is an asymptomatic precursor plasma cell disorder associated with variable risk of evolving into symptomatic multiple myeloma (MM)[1]
- The management of SMM typically relies on active monitoring to facilitate diagnosis of MM and prompt treatment initiation before organ damage develops[1,2]
  - Risk classification models are used to identify patients with SMM at high risk of progressing to MM
- Identifying patients with high-risk SMM is critical in providing proactive patient care, given their increased likelihood of progressing to active MM and developing organ damage[3,4]
- There is limited real-world evidence describing patient characteristics, disease progression, overall survival (OS), organ damage incidence, frequency of medical visits, and treatment patterns among European patients with SMM stratified by risk category
- The goal of the SPARK study is to provide a detailed description of these parameters using different risk models, including the AQUILA study criteria, Mayo 20-2-20, and the International Myeloma Working Group (IMWG) 2020 scoring system criteria incorporating cytogenetics

Methods

- SPARK is a real-world, retrospective chart review study involving hematology centers across Europe (**Figure 1**)
- Eligible patients were adults (≥18 years) diagnosed with SMM
- Data were collected from all patients who were diagnosed with SMM between January 1, 2016, and December 31, 2021, with follow-up from the date of diagnosis until December 31, 2023, death, or loss to follow-up, whichever came first
  - For patients who withdrew consent, all data entered into the electronic case report form up until withdrawal were considered for analysis
- High-risk SMM definitions per AQUILA study criteria, Mayo 20-2-20, and IMWG scoring system have been presented previously for SPARK[5]
- Here, we present updated results with extended follow-up, including all available data collected up to the cut-off date of March 2026

Figure 1: 408 patients were included from 27 sites across 5 countries



Results

Patients

- SPARK included a total of 408 patients with SMM from 27 sites across UK, Germany, Italy, Spain, and France
- Median follow-up was 59.5 months (range, 4.1–95.6)
- Patient baseline and disease characteristics are shown in **Table 1**
- SMM treatment was initiated in 8/408 (2.0%) patients (with high-risk, non–high-risk, and unclassified risk status SMM) with regimens including proteasome inhibitors, immunomodulatory drugs, corticosteroids, and monoclonal antibodies

Table 1: Baseline and disease characteristics[a]

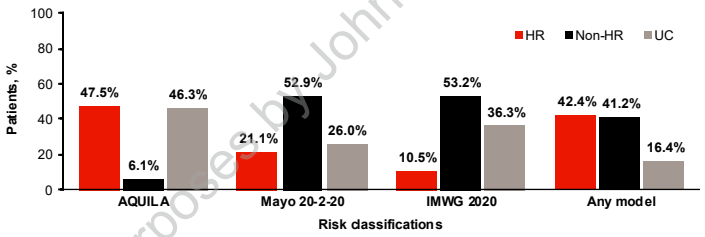
Variable	AQUILA			Mayo 20-2-20			IMWG 2020			Any model			Total
	HR (n=194)	Non-HR (n=25)	UC (n=189)	HR (n=86)	Non-HR (n=216)	UC (n=106)	HR (n=43)	Non-HR (n=217)	UC (n=148)	HR (n=173)	Non-HR (n=168)	UC (n=67)	N=408
Median age, years	66.5	69.0	68.0	68.5	65.5	68.5	64.0	68.0	68.0	68.0	65.0	68.0	68.0
Female, %	42.8	56.0	47.6	38.4	48.6	46.2	25.6	47.9	48.6	44.5	45.8	49.3	45.8
Total M protein	n=191	n=25	n=149	n=85	n=208	n=72	n=42	n=212	n=111	n=162	n=159	n=44	n=365
Median, g/dL	1.8	1.9	1.7	2.5	1.3	2.2	2.6	1.4	2.2	2.2	1.3	2.2	1.8
Involved-to-uninvolved FLCr	n=137	n=25	n=67	n=56	n=156	n=17	n=29	n=172	n=28	n=99	n=122	n=8	n=229
Median	12.4	4.0	2.7	22.1	4.1	8.6	15.3	4.5	13.9	11.6	4.0	7.6	6.5
BMPC	n=177	n=24	n=156	n=75	n=199	n=83	n=37	n=201	n=119	n=155	n=150	n=52	n=357
Median, %	19.0	14.5	14.0	29.8	14.0	15.0	30.0	14.0	19.4	18.0	15.0	20.0	15.0

[a]A patient was classified as having high-risk SMM (Any model) if they were identified as having high-risk SMM by Mayo 20-2-20, IMWG 2020, or physician assessment.
BMPC, bone marrow plasma cell; FLCr, free light chain ratio; HR, high-risk SMM; UC, unclassified risk status SMM.

Risk classification

- Distribution of patients with high-risk, non–high-risk, and unclassified risk status SMM by different risk criteria is presented in **Figure 2**

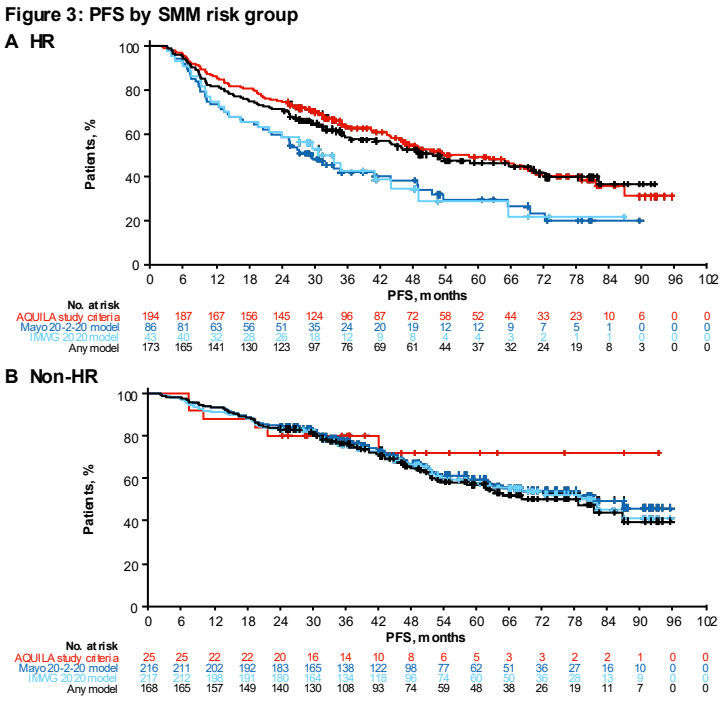
Figure 2: SPARK analysis population by SMM risk group



Outcomes

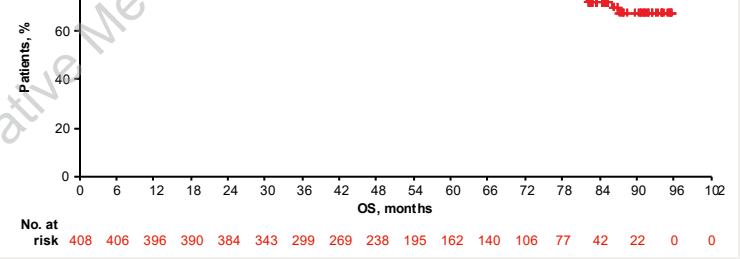
- Of 408 patients, 186 (45.6%) had a progression-free survival (PFS) event (**Figure 3**)
  - 145 (35.5%) patients progressed to MM
  - 41 (10.1%) patients died
- Median PFS was 65.0 months (95% CI, 53.0–81.7)
  - For patients with high-risk SMM, the median PFS was similar between the Mayo 20-2-20 (29.3 months) and the IMWG 2020 criteria (30.8 months); as anticipated, these results are consistent with the overall expected median PFS of 2 years
  - For patients with non–high-risk SMM, the median PFS was longer than that of patients with high-risk SMM in all 4 risk models (AQUILA, not reached [NR]; Mayo 20-2-20, 81.7 months; IMWG 2020, 81.7 months; Any model, 78.8 months)
- Kaplan-Meier plots of PFS for patients with high-risk and non–high-risk SMM by different risk criteria are presented in **Figure 3**

Figure 3: PFS by SMM risk group



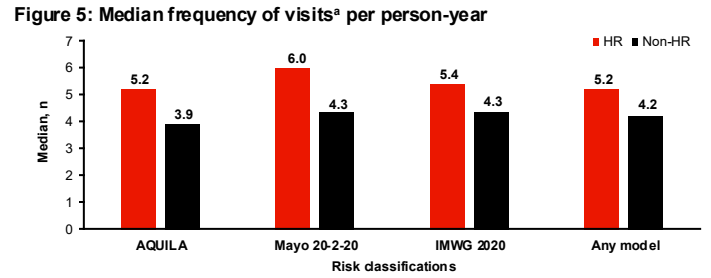
- There were 75 deaths in total (**Figure 4**)
  - The median OS was NR; the 25th percentile survival time was 78.8 months (95% CI, 68.5–NR)

Figure 4: OS (N=408, full analysis set)



- The median number of healthcare visits per person-year was higher in high-risk patients than in non–high-risk patients for all criteria; for the Mayo 20-2-20 criteria, there were 6.0 and 4.3 visits per person-year for high-risk and non–high-risk patients, respectively (**Figure 5**)

Figure 5: Median frequency of visits[a] per person-year



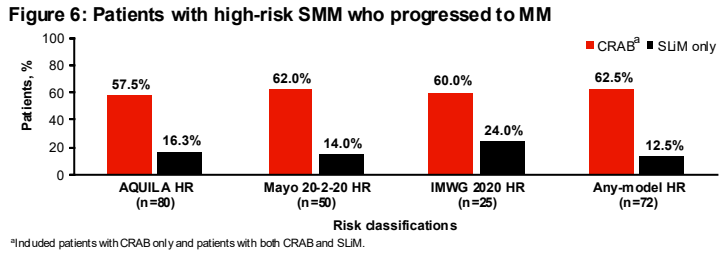
[a]Visits are the number of unique calendar dates on which a patient had documented in-person healthcare interactions.

- 145 patients progressed to MM (**Table 2**, **Figure 6**):
  - Of 114 (78.6%) patients, 71 had CRAB only, 14 had CRAB and SLiM, and 29 had SLiM only (≥60% clonal plasma cells, light-chain ratio of ≥100, magnetic resonance imaging with focal lesions)
  - 21 (14.5%) had organ damage (but no CRAB or SLiM)
- >50% of patients with high-risk SMM who progressed to MM had CRAB events

Table 2: Progressions to MM and MM-defining events (CRAB or SLiM)

	AQUILA HR (n=194)	Mayo 20-2-20 HR (n=86)	IMWG 2020 HR (n=43)	Any-model HR (n=173)	Total (N=408)
Progression to MM, n	80	50	25	72	145
CRAB or SLiM (but not CRAB and SLiM), n (%)	48 (60.0)	29 (58.0)	13 (52.0)	44 (61.1)	100 (69.0)
CRAB only	35 (43.8)	22 (44.0)	7 (28.0)	35 (48.6)	71 (49.0)
SLiM only	13 (16.3)	7 (14.0)	6 (24.0)	9 (12.5)	29 (20.0)
CRAB and SLiM in patients, n (%)	11 (13.8)	9 (18.0)	8 (32.0)	10 (13.9)	14 (9.7)
No CRAB and no SLiM, n (%)					
Organ damage	15 (18.8)	8 (16.0)	3 (12.0)	11 (15.3)	21 (14.5)
Laboratory evidence of CRAB or SLiM only	3 (3.8)	3 (6.0)	1 (4.0)	6 (8.3)	7 (4.8)
No reported MM-defining event	3 (3.8)	1 (2.0)	0	1 (1.4)	3 (2.1)

Figure 6: Patients with high-risk SMM who progressed to MM



[a]Included patients with CRAB only and patients with both CRAB and SLiM.

- The distribution pattern of organ damage was similar for patients with high-risk SMM per the AQUILA, Mayo 20-2-20, IMWG 2020, and Any-model criteria (**Table 3**)
  - >56% of patients with high-risk SMM who progressed to MM had organ damage

Table 3: Incidence of organ damage in patients who progressed to MM

Variable	AQUILA			Mayo 20-2-20			IMWG 2020			Any model			Total
	HR (n=194)	Non-HR (n=25)	UC (n=189)	HR (n=86)	Non-HR (n=216)	UC (n=106)	HR (n=43)	Non-HR (n=217)	UC (n=148)	HR (n=173)	Non-HR (n=168)	UC (n=67)	N=408
Progressed to MM, n	80	3	62	50	55	40	25	55	65	72	45	28	145
Progressed to MM and had organ damage at the time of MM, n (%)	52 (65.0)	1 (33.3)	33 (53.2)	32 (64.0)	32 (58.2)	22 (55.0)	14 (56.0)	35 (63.6)	37 (56.9)	46 (63.9)	27 (60.0)	13 (46.4)	86 (59.3)
Type of organ damage, %													
Bone pain	38.5	100	24.2	28.1	37.5	36.4	35.7	37.1	29.7	32.6	37.0	30.8	33.7
Bone fracture	25.0	0	27.3	25.0	25.0	27.3	21.4	22.9	29.7	21.7	22.2	46.2	25.6
Renal failure	5.8	0	6.1	6.3	3.1	9.1	0	2.9	10.8	8.7	0	7.7	5.8
Hypercalcemia	5.8	0	3.0	3.1	0	13.6	0	0	10.8	4.3	0	15.4	4.7
Anemia	36.5	0	51.5	40.6	37.5	50.0	50.0	37.1	43.2	43.5	33.3	53.8	41.9
Other	28.8	0	21.2	21.9	31.3	22.7	21.4	25.7	27.0	23.9	33.3	15.4	25.6

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