Expert Consensus on Diagnosis, Risk Stratification, and Treatment of Smoldering Multiple Myeloma: Results From a Multinational Delphi Panel Study

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Key Takeaway

While stratified models have been developed, their use is varied. Thus, there is a need for a uniform use

Conclusions

- Using a standardized risk stratification model for SMM is needed
- Early intervention testing for HR SMM is required
- Treatment of patients with HR SMM may lead to better outcomes
- Evidence-based treatment guidelines and approved treatments could improve consistency in SMM treatment approaches and delay progression

Background

- Smoldering multiple myeloma (SMM) is an asymptomatic plasma cell disorder[1]
- It is estimated that 51% of patients with SMM will progress to multiple myeloma (MM) within 5 years of diagnosis (66% within 10 years)[2]
- Some patients with SMM progress more rapidly to MM than others[3]; therefore, the identification of those high-risk (HR) patients is necessary for disease management
- Data on the diagnosis, risk stratification, and treatment of SMM by risk level for progression to active MM are needed to clarify burden of illness and unmet needs in these patients
- Real-world practices for SMM are not well understood because retrospective databases do not capture data in this setting due to lack of SMM-specific coding
- A Delphi panel was conducted to assess expert consensus on diagnosis, risk stratification, treatment practices, and their impact on SMM outcomes

Methods

Delphi panel

- Hematologists/oncologists were identified via expert associations and/or specialized treatment centers to participate in a Delphi panel
- Each panel member had expertise in diagnosis, management, and treatment of MM and SMM
- A total of 24 experts from France, Germany, Italy, Spain, and the US participated, with 4 from France and 5 from each other country

N=4   N=5   N=5   N=5   N=5

- 3 rounds of Delphi surveys were conducted (Figure 1)

Figure 1: Rounds of Delphi panel

Round 1	Round 2	Round 3
Survey on • Diagnosis • Risk stratification • Treatment approach	Verify responses after reviewing country-level summary outputs from round 1 responses	Expert-rated consensus statements based on survey outputs from rounds 1 and 2

- Results are described based on average responses received within the survey
- Consensus statements are described based on expert agreement

Figure 2: Definition of consensus by ≥75% of experts per country
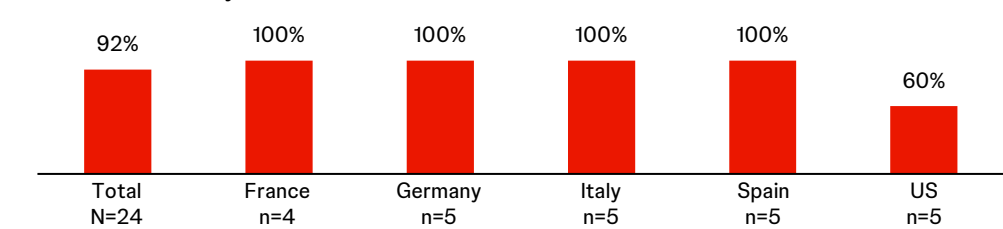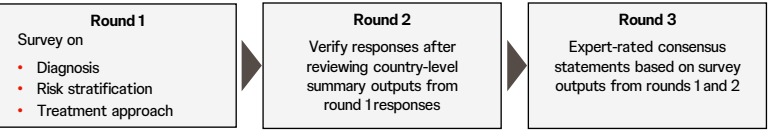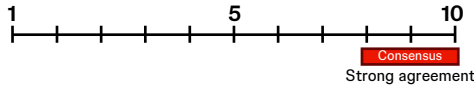

Results

Expert responses on diagnosis and risk of SMM

- France and Germany were consistent in their average age at diagnosis, with the US being slightly younger and Italy and Spain being slightly older (Table 1)

Table 1: Survey results - Average age of patients at SMM diagnosis across countries

	France	Germany	Italy	Spain	US
Average age at SMM diagnosis in years (range)	58.8 (50–65)	60 (55–65)	63.6 (58–65)	63.8 (60–65)	56 (50–70)

- Experts strongly agreed (92%) that risk stratification is necessary at initial diagnosis of SMM (data not shown)
- The most common risk stratification criteria were International Myeloma Working Group (IMWG) 2020[4] (cat 4) and Mayo 2018[5] (cat 3), although many criteria were used by all who were surveyed
- A strong consensus on the diagnostic criteria for SMM was reached across Europe (Figure 3)

Figure 3: Results of consensus statement – "To diagnose patients with SMM, I refer to the IMWG 2014/IMWG 2020/Mayo 2018 criteria"

Expert responses on HR SMM diagnosis and progression (Table 2)

- The proportion of patients with SMM diagnosed as HR was consistent across most markets, with France and Spain suggesting a relatively higher rate of HR diagnosis
- Experts indicated a longer time frame to progress from low to intermediate risk than from intermediate risk to HR across countries that stratify this way

Table 2: Survey results - HR SMM incidence and progression

	France	Germany	Italy	Spain	US
Proportion of SMM patients diagnosed as HR [average (range)]					
Proportion diagnosed as HR	28% (25–30%)[a]	22% (20–30%)	22% (15–30%)	28% (20–35%)	19% (10–30%)
SMM time to progression in months [average (range)]					
Low to intermediate risk	[b]	72 (36–120)	53 (24–90)	80 (40–120)	98 (60–200)
Intermediate to HR	[b]	41 (24–60)	35 (24–50)	65 (30–100)	45 (36–60)
Low to HR	80 (60–120)	36 (36–36)	54 (48–60)	66 (60–72)	[c]

[a]Excludes 1 expert who entered 60%. [b]Only stratifies between low and HR. [c]Only stratifies between low, intermediate, and HR.

Expert responses on the treatment of SMM

- A higher proportion of patients appears to be treated in France, Spain, and the US compared with Germany and Italy (inclusive of clinical trials) (Table 3)
- Survey results suggest that the proportion of those who progress to MM is lower in patients with HR SMM receiving treatment (Table 3), which was consistent with consensus results (data not shown)

Table 3: Survey results – Proportion of patients with HR SMM who are prescribed treatment and the percentage of patients (not treated or treated) who progress from HR SMM to MM in 1 year

	France	Germany	Italy	Spain	US
Proportion of patients with HR SMM prescribed treatment					
Average (range)	46% (0–100%)	8% (0–25%)	13% (0–50%)	46% (15–95%)	51% (5–100%)
Percentage of patients who progress from HR SMM to MM in 1 year					
Not treated	48% (10–80%)	37% (19–70%)	35% (20–60%)	32% (1–60%)	31% (10–50%)
Treated	3% (0–10%)	1% (0–5%)	10% (0–50%)	16% (1–40%)	10% (0–35%)

- Consensus was that the time to progression to MM was longer in patients with HR SMM receiving treatment and was most consistent among Germany, Spain, and the US (Figure 4), which was consistent with survey results (data not shown)

Figure 4: Results of consensus statement – "HR patients who are being treated progress more slowly to MM than HR patients who are NOT being treated"
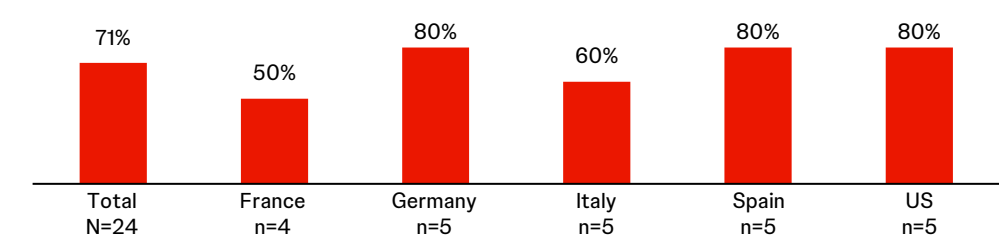
- A higher proportion of patients was prescribed treatment outside of clinical trials for HR SMM in Spain, whereas both France and the US have more patients with HR SMM treated in clinical trials (Table 4)

Table 4: Survey results - Percentage of patients with HR SMM undergoing treatments

	France	Germany	Italy	Spain	US
In clinical trials	75%	5%	4%	13%	45%
Not in clinical trials	0%	3%	0%	79%	1%

- Survey results showed that the average treatment duration for HR SMM was consistent at 6 months (range, 1.3–9.8) across most countries (data not shown)

References
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