X. LELEU, MD[1], B. GORSH, PHARMD[2], A. BESSOU, MSC[3], P. PAKA, PHARMD[2], J. DE NASCIMENTO, MSC[3], X. COLIN, MSC[4], S. LANDI, PHD[5], P. FENG WANG, PHD[2]

[1]Department of Hematology, Centre Hospitalier Universitaire, Université de Poitiers, Poitiers, France | [2]GlaxoSmithKline, Upper Providence, PA, USA | [3]IQVIA, Paris, France | [4]GlaxoSmithKline, Rueil-Malmaison, France | [5]GlaxoSmithKline, Research Triangle Park, NC, USA

INTRODUCTION

- The global incidence of multiple myeloma (MM) has increased by 126% from 1990 to 2016 and is highest in Australia, Western Europe, and the United States.[1]
- France has the second-highest incidence of MM in the European Union-27, with an estimate of 10 cases per 100,000 population.[2]
- The Système National des Données de Santé (SNDS) database is a French database which includes anonymised information based on health insurance reimbursement claims including patient demographic data, health care encounters, hospital visits, diagnoses, medicines, medical devices, and date of death, among other data.[3]
- Up-to-date real-world data and comprehensive analyses on MM survival in France are limited.

OBJECTIVE

- To examine the overall survival (OS) of patients with MM at various stages of treatment in France. This aim was achieved by describing the OS of patients with MM from:
  - Time of diagnosis
  - Start of lines of treatment (line of therapy [LOT]1 to LOT4), stratified by current standard of care regimens
  - Start of triple-class exposure (TCE)
  - Start of subsequent treatment/end of last treatment if no subsequent treatment
  - Subsequent treatment/no treatment following TCE and LOT5+

Additionally, other patient outcome measures were also examined, including duration of therapy (DoT), time to next line of treatment (TTNT), and duration of treatment gap.

METHODS

Study Design and Setting

- This was a retrospective, observational cohort study using claims data collected from the SNDS, which includes approximately 99% of French residents (Figure 1).
  - The SNDS consists of anonymised data of reimbursed claims for patients affiliated with one of the compulsory health insurance providers.[3]
  - Diagnoses are coded in the database according to the International Classification of Diseases version 10 (ICD-10).

Study Population (Participants)

- The analysis included patients (aged ≥18 years) who had ≥2 records of an MM diagnosis (ICD-10 codes C90/C90.0), and/or long-term disease during the study period; ≥1 dispensation/administration of MM drug treatment and date of death available during the time between 1 January 2013 and 31 December 2019 (index date).
- Using the criteria established by Palmaro et al[4] LOT was algorithmically defined based on drug regimen, time since administration, and gap between regimens.
- OS was analysed from 5 time points.
- Patient OS was assessed by Kaplan–Meier, method and death rates were calculated.
- LOT duration was calculated using Kaplan-Meier analysis; the end of a LOT was the event and patients were censored at the end of follow-up.
- Time to next treatment (TTNT) was calculated from the start of the LOT until the start of the subsequent LOT.
- For OS analysis following TCE, patients were analysed from start of subsequent treatment following TCE and from last treatment for patients with no subsequent treatment.
- All patient demographic and clinical characteristics at index date (baseline) were summarised using the most recent record prior to index date.

Figure 1. Study Design
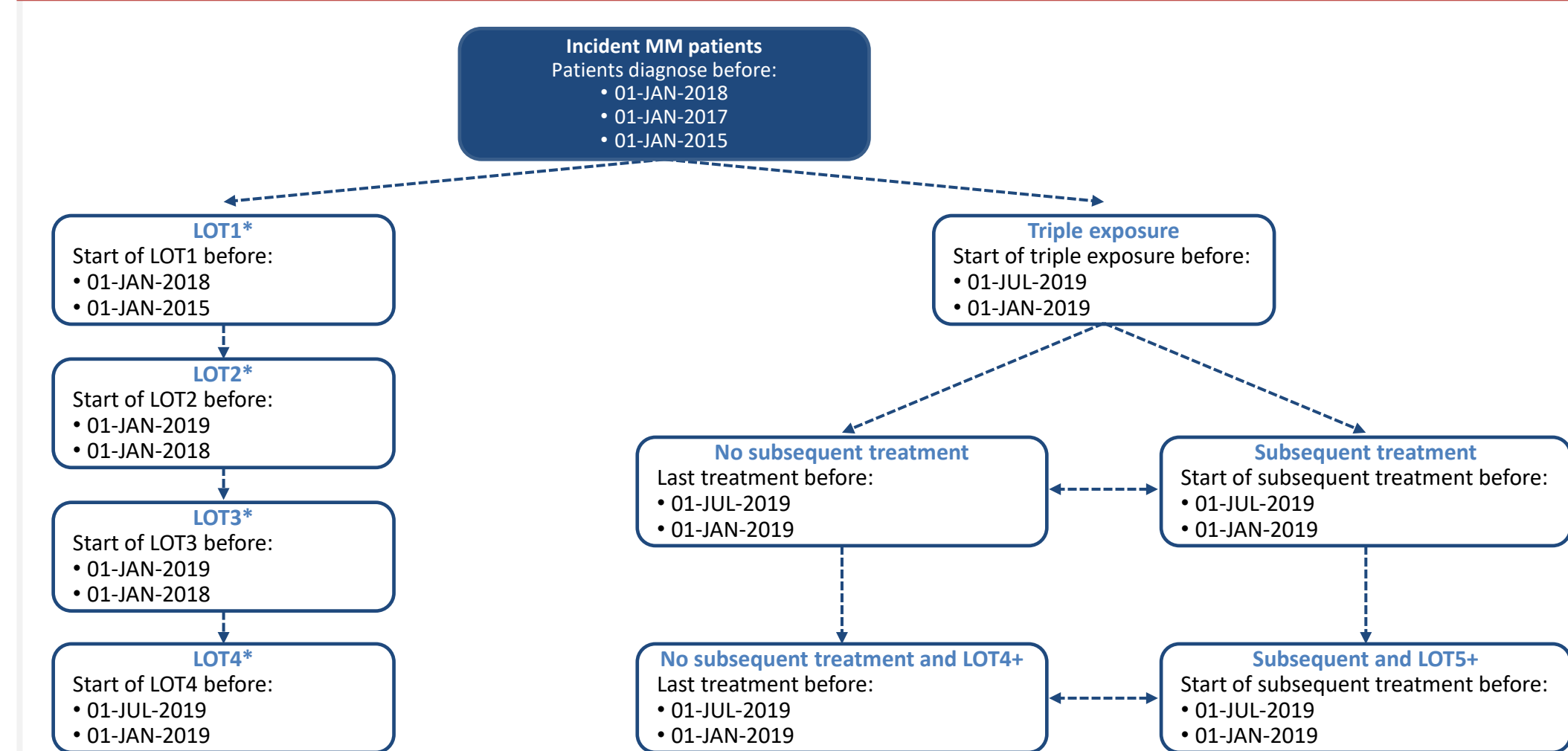
LOT, line of therapy; MM, multiple myeloma. *Line of therapy (LOT) was defined as the first dispensation of any drugs of interest; all drugs dispensed within 28 days following the treatment initiation date were considered the 1st LOT. A LOT was defined as continuing until a regimen switch (eg, addition of another MM drug), or the discontinuation of all drugs in the LOT. Subsequent LOTs (LOT2, LOT3, LOT4) were defined as a new regimen prescribed before the previous LOT was completed or beginning after a gap of at least 90 days.

RESULTS

Patient Population

- Of the 33,397 patients with a diagnosis of MM identified in the SNDS database, a final sample of 14,309 patients who were diagnosed with MM between 2013 and 2017 were included in the analysis.
- Patient demographic and clinical characteristics are presented in Table 1.
  - Median age was 71 years at index.
  - Most patients (59%) were between 65 and 84 years.
  - 51% of patients were male.
  - A total of 66% of patients had a Charlson score of 1-2 and by the index date 29% of patients had received stem-cell transplant (SCT).

### Table 1. Patient Demographics and Clinical Characteristics

Characteristics	Total patients (N=14,309)
Age at index date, median	71
Age at index date, n (%)	
0–54	1,455 (10)
55–64	2,821 (20)
65–74	4,322 (30)
75–84	4,190 (29)
85+	1,521 (11)
Sex, n (%)	
Male	7,238 (51)
SCT status, n (%)	
Yes	4,111 (29)
No	10,198 (71)
Year of index date, n (%)	
2013	2,976 (21)
2014	2,961 (21)
2015	2,842 (20)
2016	2,835 (20)
2017	2,695 (19)
Charlson score at index, n (%)	
1-2	9,446 (66)
3-4	3,241 (23)
5+	1,622 (11)

*SCT was determined during follow-up by the presence of a hospitalization with a related drug and/or a medical procedure code

Death Rates and OS From Time of Diagnosis

- Death rates gradually increased from time of diagnosis from 1% at 1 month to 24% at 24 months (Figure 2).
- Median OS gradually decreased across age groups, ranging from 87.2 months in the younger age group (18–54 years), to 69.7 months in patients between 65–74 years, and to 24.6 months among patients aged ≥85 years.
- Median OS for the full population was 63.8 months.

Figure 2. Death Rates Increased Over Time (A), and OS Decreased by Age From Time of Diagnosis (B)
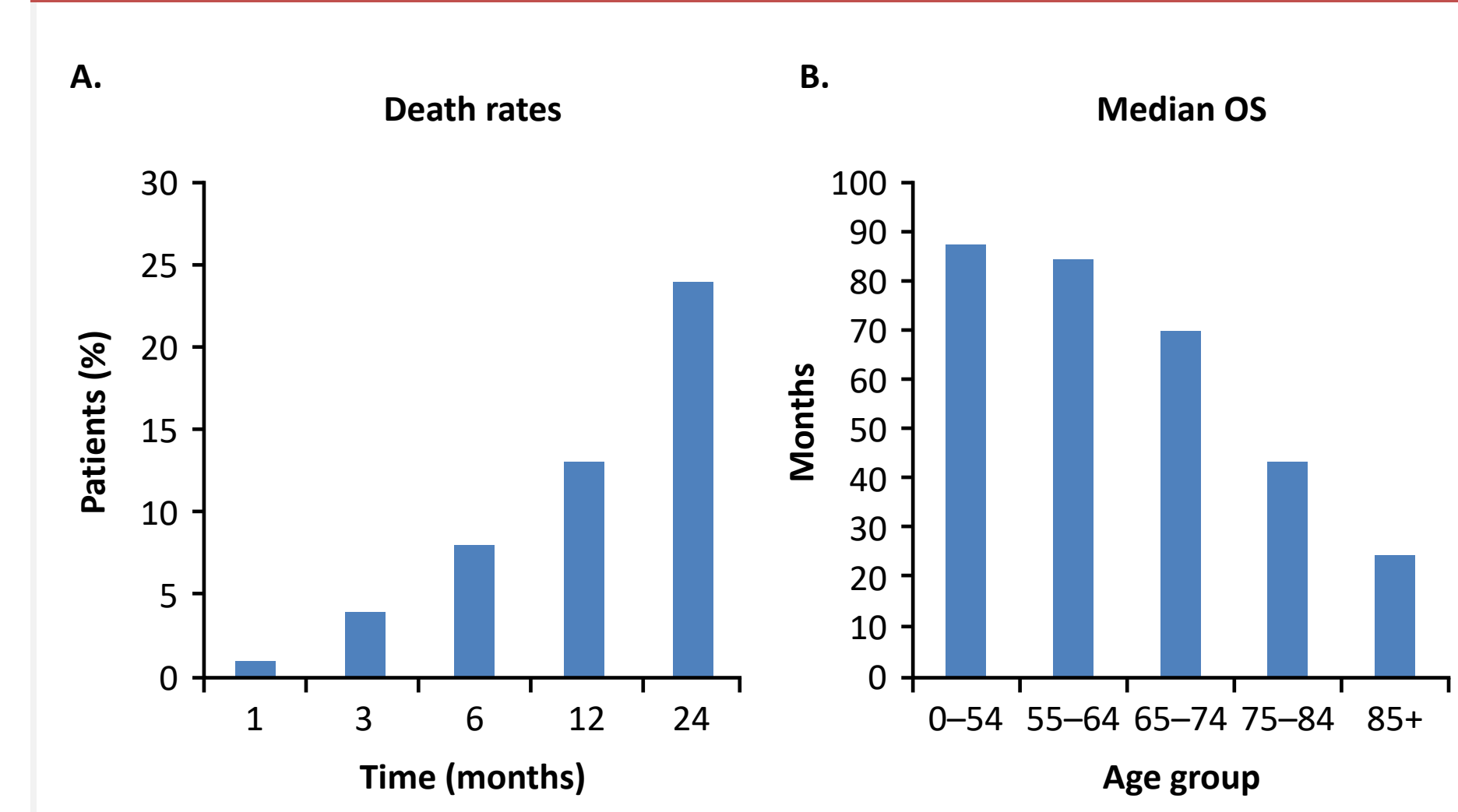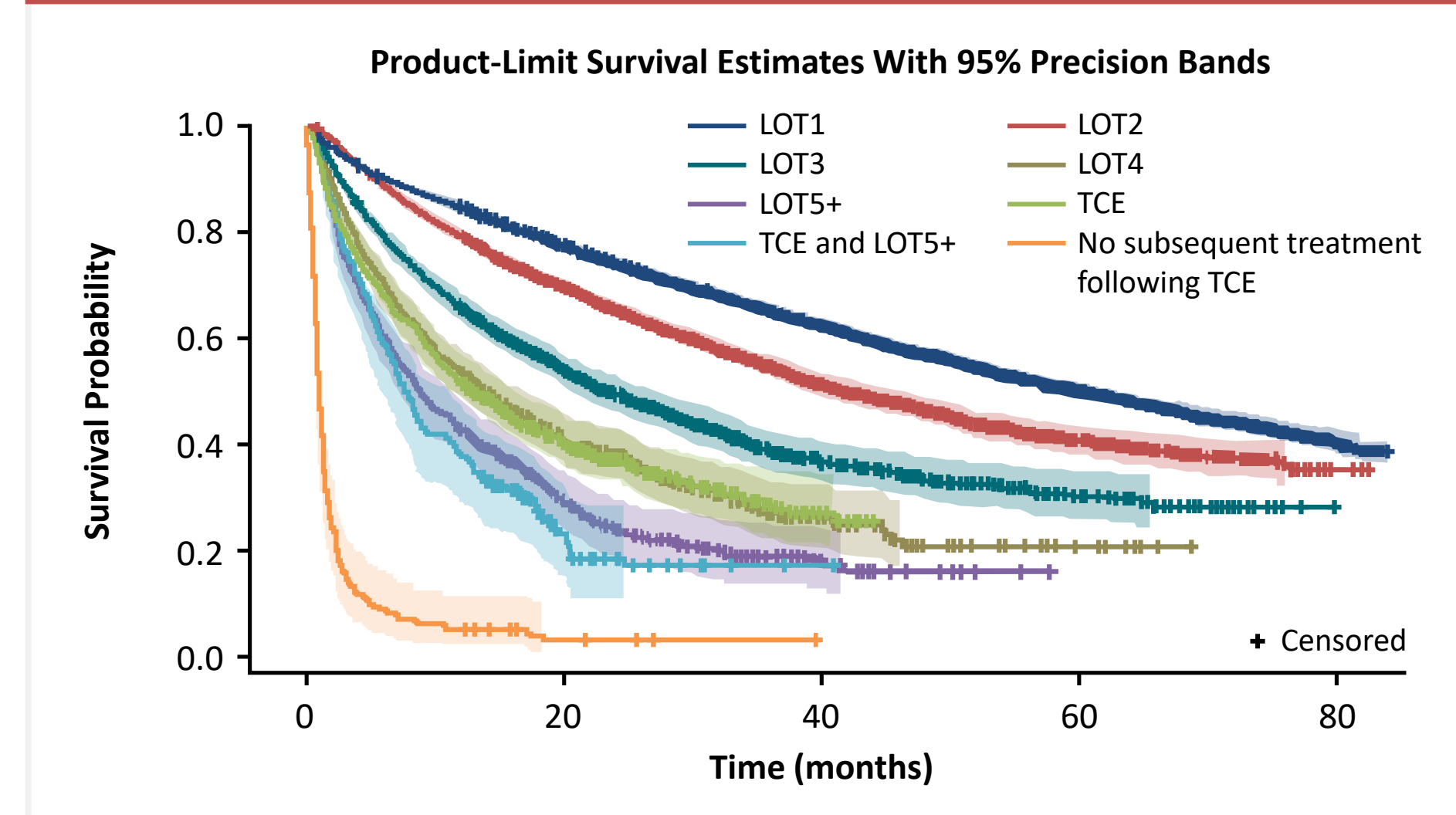

SCT/Non-SCT Death Rates

- The median age at index was 60 years for SCT patients vs 76 years for non-SCT patients.
- Patients who received an SCT had a lower 24-month death rate compared to non-SCT patients (6%, 262/4,111 patients vs 31%, 3,166/10198 patients).

OS of MM Patients From Start of LOT

- The number of patients at the start of each line decreased from LOT1 to LOT 4.
- Patient initiation by LOT was as follows:
  - LOT1 (n=12,901)
  - LOT2 (n=6,658)
  - LOT3 (n=2,880)
  - LOT4 (n=1,545)
- The death rate at 6 months by LOT was as follows:
  - LOT1: 10% (1,255/12,901)
  - LOT2: 11% (752/6,658)
  - LOT3: 21% (598/2,880)
  - LOT4: 28% (439/1,545)
- Survival probability decreased over time following each subsequent LOT (Figure 3).
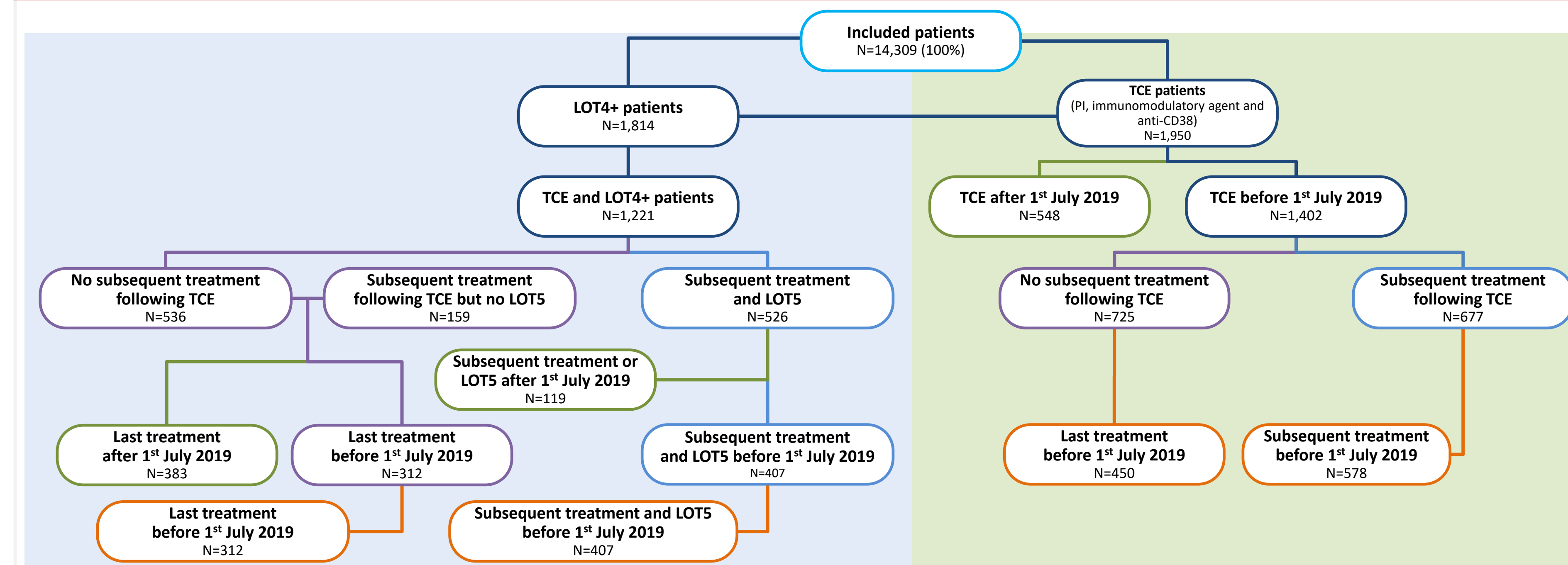- Median OS decreased from 61.0 to 14.8 months from LOT1 to LOT4, or about 30% to 50% with each additional LOT.

Figure 3. Kaplan–Meier Survival Probability Curve of Patients with MM Who Started Each LOT

OS From the Start of TCE

- Among the 14,309 patients included in the study as shown in Figure 4.
  - 1,402 patients (72%) started treatment with a proteasome inhibitor, immunomodulatory agent, and anti-CD38 monoclonal antibody before 1st of July 2019, meeting the requirements for TCE.

- Among LOT4+ patients, 1,221 (63%) also had TCE to a proteasome inhibitor, immunomodulatory agent, and anti-CD38 monoclonal antibody.
- The median OS of TCE patients was 14.7 months.
- Lowest median OS of 11.4 months was found in patients older than 85 years.

OS of TCE Patients From the Subsequent Treatment/No Treatment Following TCE

- The OS of TCE patients according to the presence of any subsequent treatment was also evaluated, and the following 3 groups of patients were considered:
  - TCE patients with any subsequent treatment received before the 1st of July 2019 (at least 6 months of potential follow-up).
  - TCE patients without any subsequent treatment, with last treatment received before the 1st of July 2019 (at least 6 months of potential follow-up).
  - TCE patients with or without any subsequent treatment, with subsequent or last treatment received before the 1st of July 2019 (at least 6 months of potential follow-up).
- TCE patients with any subsequent treatment had better survival outcomes with a lower 6-month death rate of 35% (n=200) compared to TCE patients without any subsequent treatment of 87% (n=393) (Table 2).

OS of MM Patients From the Subsequent Treatment/No Treatment Following TCE and LOT5+

- The following 2 groups of patients were considered:
  - TCE patients with at least 5 LOTs and any subsequent treatment received before the 1st of July 2019 (at least 6 months of potential follow-up).
  - TCE patients with at least 4 LOTs and without any subsequent treatment or with any subsequent treatment (e.g. LOT2, 3, or 4) but no LOT5 , with last treatment received before the 1st of July 2019 (at least 6 months of potential follow-up).
- The median OS for TCE patients with at least 5 LOTs and a subsequent treatment following TCE (n=407) was 8.2 months, and the 6-month death rate was 39% (n=157).
- The median OS for TCE patients with at least LOT4 and without any subsequent treatment or with any subsequent treatment but no LOT5 (n=312) was 1 month, and the 6-month death rate was 88% (n=274) (Table 2).

Figure 4. Attrition Flowchart for TCE Patients

*All patients had at least 6 months of potential follow-up after the start of TCE

Table 2. Death Rates and OS of TCE Patients Based on Defined Criteria

	TCE with any subsequent treatment[a] N=578	TCE without any subsequent treatment[b] N=450	TCE with or without any subsequent treatment[b] N=1,028	TCE with LOT5+ and any subsequent treatment[a] N=407	TCE with LOT4 and without subsequent treatment, or subsequent treatment but no LOT5[b] N=312
Death rate, n (%)					
1 month	20 (3)	257 (57)	277 (27)	13 (3)	160 (51)
3 months	113 (20)	369 (82)	482 (47)	86 (21)	255 (82)
6 months	200 (35)	393 (87)	593 (58)	157 (39)	274 (88)
OS, median (months)[c]	9.4	0.9	3.8	8.2	1.0

[a]Subsequent treatment before 1-JUL-2019 and at least 6 months of potential follow-up, [b]Last treatment before 1-JUL-2019 and at least 6 months of potential follow-up, [c]Median OS was calculated using Kaplan–Meier product limit estimates and is measured in months since the start of subsequent treatment or end of last treatment to death, or end of follow-up

CONCLUSIONS

- Patients with MM experience worsening survival outcomes with increasing time from diagnosis and with subsequent line of therapies (LOT).
- Median OS was better among TCE patients with subsequent treatment (9.4 mos) or patients with TCE with LOT5+ (8.2 mos) but worse in TCE patients without subsequent treatment (0.9 mos) and TCE patients with LOT4 without subsequent treatment (1.0 mos)
- Increased age, presence of comorbidities, and non-SCT status, shorter time between LOTs, and earlier onset of TCE status were associated with worse survival outcomes and may be associated with more aggressive disease.
- Overall, this study provides evidence of unmet needs in the management of patients with MM in France, which may be addressed by updating real-world practice with regimens shown to improve patients' overall survival in clinical trials.
- Despite therapeutic advances an unmet need for improved access to novel therapies with unique mechanisms of action remains, especially in those TCE patients.

DISCLOSURES

ACKNOWLEDGEMENTS

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CONTACT INFORMATION

Hold and email: xavier.leleu@chu-poitiers.fr