ELSEVIER

Blood 142 (2023) 912–914

The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

902.HEALTH SERVICES AND QUALITY IMPROVEMENT - LYMPHOID MALIGNANCIES

Incidence of Second Primary Malignancies in Medicare-Insured Patients in the US with Triple-Class Exposed Relapsed/Refractory Multiple Myeloma

Sikander Ailawadhi[1], Thomas Delea[2], Aaron Moynahan[2], Wenzhen Ge[3], Christian Hampp[4], Alexi Archambault[5], Ning Wu[3], Karen Rodriguez Lorenc[3], Irene Noguera-Troise[3], Glenn S. Kroog[3], Yariv Houvras[3], Qiufei Ma[3]

[1] Mayo Clinic, Jacksonville, FL
[2] Policy Analysis Inc., Boston, MA
[3] Regeneron Pharmaceuticals, Inc., Tarrytown, NY
[4] Regeneron Pharmaceuticals Inc., Tarrytown, NY
[5] Regeneron Pharmaceuticals, Inc., Tarrytown

Background
As therapeutic advances have increased life expectancy for patients (pts) with relapsed/refractory (RR) multiple myeloma (MM), second primary malignancies (SPMs) have become an increasingly important safety consideration. Prior studies have demonstrated that treatment with alkylators, autologous stem cell transplantation, and immunomodulatory drugs (IMiDs), specifically lenalidomide, are associated with increased risk of SPM. Pts who are triple-class exposed (TCE), defined as prior exposure to an IMiD, a proteasome inhibitor (PI), and an anti-CD38 monoclonal antibody (mAb), represent an increasingly large subgroup of RRMM pts. The objective of this study was to describe the incidence and characteristics of SPMs in Medicare-insured pts with TCE RRMM initiating a new line of therapy (LOT).
Methods
Adult pts with an incident diagnosis (Dx) of MM (≥2 outpatient Dx 30-365 days apart OR ≥1 inpatient Dx AND 6 months of continuous eligibility prior to initial Dx) during the study period (Nov 14, 2006-Dec 31, 2020) who were TCE (≥1 claim each for an IMiD, a PI, and an anti-CD38 mAb) were selected from the Center for Medicare and Medicaid Services Chronic Conditions Data Warehouse (TCE pts were assumed to have RRMM based on exposure). The first LOT after TCE was defined as the index LOT and the associated date of initiation was defined as the index date. Pts with SPMs prior to the index date were excluded. SPMs were identified based on having ≥2 outpatient Dx of SPM (of the same cancer type) 30-365 days apart OR ≥1 inpatient Dx of SPM. Dx of SPM included Dx of invasive malignancies or myelodysplastic syndromes (MDS), excluding MM, Waldenström macroglobulinemia, plasma cell leukemia, non-melanoma skin cancers, or primary bone malignancies that were preceded by a Dx of bone metastases. The incidence of SPM was calculated per 100 person years (PY) of follow-up, considering only the first SPM for each pt. Cumulative incidence of SPM (with death as a competing risk) was also calculated. For pts who experienced SPM, overall survival (OS) and measures of healthcare resource utilization (HRU) and costs (in 2021 USD, on a per patient per month [PPPM] basis) were calculated.
Results
A total of 3,088 TCE RRMM pts were identified, of whom 989 had no evidence of SPM prior to the index date (Table). These 989 pts had a mean age of 75.2 years, a mean of 2.9 prior LOTs and a mean of 3.1 years since MM Dx. Over a median follow-up of 7.1 months, 166 pts (19.3 per 100 PY) experienced an SPM, including 93 (10.8 per 100 PY) with a solid tumor and 73 (8.5 per 100 PY) with a hematologic malignancy. The latter included 27 (3.1 per 100 PY) with acute myeloid leukemia (AML) and 18 (2.1 per 100 PY) with MDS. The cumulative incidence of SPM (95% confidence interval [CI]) at 12, 24, and 36 months was 15.2% (12.8-17.9%), 19.7% (16.8-22.8%), and 23.8% (20.2-27.6%), respectively (Figure). Median (95% CI) OS from SPM Dx was 7.9 months (5.4-10.9). Kaplan-Meier estimated probability of survival (95% CI) at 12, 24, and 36 months following SPM Dx was 40.3% (31.6-48.9%), 27.6% (18.6-37.4%), and 9.5% (2.1-23.8%), respectively. Mean (95% CI) total costs after SPM were $22,514 ($19,105-$26,404) PPPM.
Conclusions
The incidence of SPM in Medicare-insured TCE RRMM pts is high. Many SPMs in these pts, such as AML, are life-threatening and may interfere with or prevent MM treatment. Pts with SPMs have poor survival and high HRU and costs. With increasing

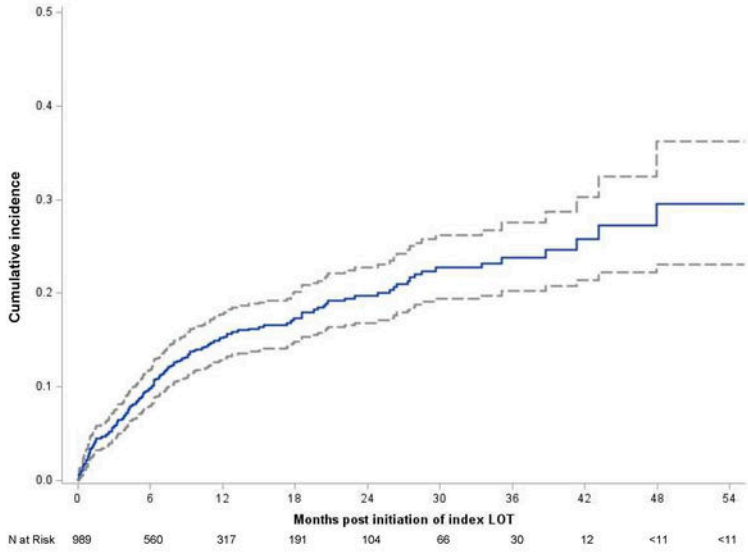
OS for RRMM pts due to therapeutic advancements, there is a need for effective treatments that are not associated with increased risk of SPMs.

Disclosures Ailawadhi: *AbbVie, Amgen, Ascentage, BMS, Cellectar, GSK, Janssen, Pharmacyclics, Sanofi:* Research Funding; *Beigene, BMS, Cellectar, GSK, Janssen, Pfizer, Regeneron, Sanofi, Takeda:* Consultancy. **Delea:** *Merck:* Research Funding; *Novartis:* Research Funding; *Pfizer:* Research Funding; *Celgene:* Research Funding; *Bristol-Myers Squibb:* Research Funding; *Amgen:* Research Funding; *AbbVie:* Research Funding; *Regeneron:* Research Funding; *Sanofi:* Research Funding; *Takeda:* Research Funding. **Moynahan:** *Bristol-Myers Squibb:* Research Funding; *Celgene:* Research Funding; *Merck:* Research Funding; *Takeda:* Research Funding; *Sanofi:* Research Funding; *Regeneron:* Research Funding; *Pfizer:* Research Funding; *Novartis:* Research Funding; *Amgen:* Research Funding; *Abbvie:* Research Funding. **Ge:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Hampp:** *Regeneron:* Current Employment, Current equity holder in publicly-traded company. **Archambault:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Wu:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Rodriguez Lorenc:** *Regeneron:* Current Employment, Current holder of *stock options* in a privately-held company. **Noguera-Troise:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Kroog:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Houvras:** *Regeneron:* Current Employment. **Ma:** *Regeneron:* Current Employment, Current equity holder in publicly-traded company.

Table. Baseline characteristics, incidence of SPMs, and HRU and costs post-SPM

	(N=989)
Baseline characteristics	
Age, years, mean (SD)	75.2 (7.0)
Age ≥65 years, n (%)	935 (94.5)
Female, n (%)	535 (54.1)
Race, n (%)	
Asian	15 (1.5)
Black	110 (11.1)
Hispanic	12 (1.2)
White	821 (83.0)
Other	31 (3.1)
NCI Charlson comorbidity index, mean (SD)	1.7 (1.8)
Years since initial MM Dx, mean (SD)	3.1 (2.0)
Number of previous LOTs, mean (SD)	2.9 (1.2)
Prior ASCT, n (%)	190 (19.2)
Prior alkylator therapy, n (%)	373 (37.7)
Length of prior IMiD therapy months, mean (SD)	13.8 (12.9)
Outcomes	
Follow-up, months, mean (SD)	10.4 (10.0)
Incidence of SPM post-index, n (per 100 PY)	
Any	166 (19.3)
Hematologic malignancies	73 (8.5)
AML	27 (3.1)
MDS	18 (2.1)
Solid tumors	93 (10.8)
HRU and costs post-SPM	N=166
PPPM HRU, mean (95% CI)	
Outpatient visits	7.35 (6.71, 8.09)
Hospitalizations	0.18 (0.14, 0.22)
PPPM Costs, 2021 USD, mean (95% CI)	
MM medications and administration	14,349 (11,767, 17,291)
Other MM-related	6,371 (5,318, 7,635)
Non-MM-related	1,795 (1,261, 2,465)
Total all-cause	22,514 (19,105, 26,404)

Figure. Cumulative incidence of SPMs



Dashed gray lines are 95% CIs.
AML, acute myeloid leukemia; ASCT, autologous stem cell transplantation; CI, confidence interval; Dx, diagnosis; HRU, healthcare resource utilization; IMiD, immunomodulatory drug; LOT, line of therapy; MDS, myelodysplastic syndromes; MM, multiple myeloma; NCI, National Cancer Institute; PPPM, per patient per month; PY, person years; SD, standard deviation; SPM, second primary malignancy.

Figure 1

https://doi.org/10.1182/blood-2023-188562