ABSTRACT/ POSTER 1605215

IMPACT OF A BEST PRACTICES PROGRAM IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA RECEIVING SELINEXOR

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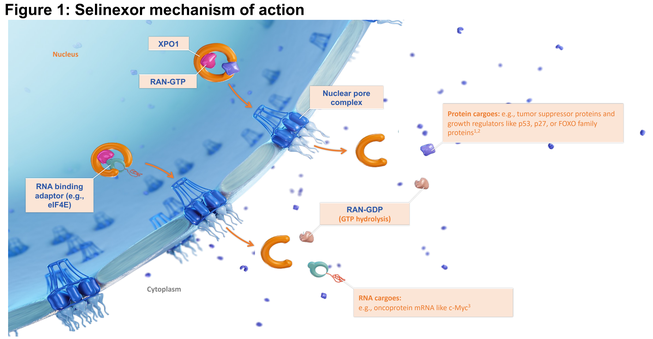
INTRODUCTION

- Selinexor, an oral exportin 1 (XPO1) inhibitor, prevents the XPO1-mediated export of several tumor suppressor proteins (TSPs), leading to the accumulation of TSPs in the nuclei of malignant cells, and blocks protein translation of oncogenes that drive cell proliferation, ultimately causing cell cycle arrest and apoptosis.[1]

Figure 1: Selinexor mechanism of action



- Best practices (BP) programs are health practices, methods, interventions, procedures or techniques based on high-quality evidence that aim to improve patient and health outcomes.[2]
- Florida Cancer Specialists & Research Institute, LLC. (FCS) implemented a BP program on March 1, 2022 supporting selinexor for patients with relapsed/refractory multiple myeloma (RRMM).
- The BP program involved:
  1. Proactively prescribing antiemetic therapy such as ondansetron, olanzapine, and/or rolapitant.
  2. Initiating selinexor at doses ≤ 80 mg once weekly.
- This study investigated the impact of the BP program in patients with RRMM receiving a selinexor-based regimen.

METHODS

- This retrospective, observational study evaluated patients with RRMM treated with a selinexor-based regimen pre- and post-implementation of the BP program at FCS.
- Study endpoints included time to treatment failure (TTF), duration of therapy, frequency of dose-limiting toxicities (DLTs) and overall survival.
  - TTF was defined as the time from the start of selinexor to disease progression, discontinuation because of drug toxicity or death.
- Multivariate cox proportional hazard regression was implemented to measure the impact of patient clinical characteristics on TTF.

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REFERENCES: 1. Tai YT, et al. CRM1 inhibition induces tumor cell cytotoxicity and impairs osteoclastogenesis in multiple myeloma: molecular mechanisms and therapeutic implications. *Leukemia*. 2014, 28, 155-65. **2.** Makic MB, et al. Putting evidence into nursing practice: four traditional practices not supported by the evidence. *Crit Care Nurse*. 2013;33(2):28-42. doi:10.4037/ccn2013787

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RESULTS

Table 1. Demographic and clinical characteristics of patients prior to the start of selinexor during the pre- and post-best practices implementation period.

Parameter	Pre-implementation (n=68)	Post-implementation (n=41)
Median age at MM diagnosis (range)	64.0 (33–80)	67.0 (40–80)
Median age at the start of selinexor (range)	69.5 (37–85)	71 (45–85)
Female sex	55.9% (38)	56.1% (23)
ECOG Performance Status		
0 or 1	79.4% (54)	75.6% (31)
≥ 2	14.7% (10)	14.6% (6)
Not documented	5.9% (4)	9.8% (4)
Median time from diagnosis to the start of selinexor (years; range)	5.5 (1.5–23.1)	5.3 (1–21.5)
Cytogenetics		
t(4;14)	8.8% (6)	9.8% (4)
t(14;16)	2.9% (2)	0.0% (0)
del(17p)	19.1% (13)	9.8% (4)
gain/amp[1q21]	30.9% (21)	26.8% (11)
Prior drug exposure		
Lenalidomide	100% (68)	100% (41)
Pomalidomide	95.6% (65)	95.1% (39)
Bortezomib	97.1% (66)	97.6% (40)
Carfilzomib	91.2% (62)	70.7% (29)
Daratumumab	97.1% (66)	97.6% (40)
Isatuximab	11.8% (8)	7.3% (3)

Abbreviations: MM = multiple myeloma, ECOG: Eastern Oncology Cooperative Group

- Median follow-up time for disease progression or death was 24.0 and 6.7 months in the pre- and post-periods, respectively.
- Patients in both periods were similar in age, gender, performance status, and prior exposure to lenalidomide, pomalidomide, bortezomib and daratumumab **(Table 1).**
- Use of selinexor as a doublet therapy declined from 42.7% to 14.6% in the pre- and post-implementation period, respectively, with a concurrent increase in the utilization of triplet therapy from 54.4% to 85.4% **(Table 2).**
- More patients initiated selinexor at doses ≤ 80 mg once weekly in the post-implementation period compared to the pre-period (78.0% vs. 48.5%) **(Table 2)**.
- Median TTF was 2.3 months (IQR: 1.2-4.4) vs. 7.1 months (IQR: 1.2-NR) in the pre- and post-periods, respectively (HR = 0.50 (0.27-0.92)) **(Table 3; Figure 2).**

Table 3. Multivariate Cox regression analysis on time to treatment failure.

Parameter[1]	Hazard Ratio[2]	95% Confidence Interval
Post- vs. pre- best practices implementation	0.50	(0.27–0.92)
Dose modification	0.44	(0.25–0.77)
Dosing schedule change	0.26	(0.10–0.64)
Selinexor start dose (ref = ≤ 60 mg)		
80 mg dose	1.41	(0.66–3.00)
100 mg dose	2.52	(1.12–5.65)
≥ 120 mg dose	5.43	(2.25–13.08)

[1]These are the final variables that were retained following the application of the Likelihood ratio test (p < 0.05 to retain) in a backwards elimination process. The best practices implementation variable was the primary independent variable and was kept in the model notwithstanding.
[2]An HR of less than one indicates a lower risk and greater than one an increased risk of treatment failure.

Table 2: Characteristics of selinexor therapy during the pre- and post-best practices implementation period.

Parameter	Pre-implementation (n=68)	Post-implementation (n=41)
Selinexor regimen		
Xd	42.7% (29)	14.6% (6)
XVd	30.9% (21)	48.8% (20)
XKd	10.3% (7)	22.0% (9)
XPd	11.8% (8)	9.8% (4)
XDd	1.5% (1)	4.9% (2)
Other[1]	2.9 (2)	0.0% (0)
Line of therapy		
Third	2.9% (2)	4.9% (2)
Fourth	10.3% (7)	9.8% (4)
≥ Fifth	86.8% (59)	85.4% (35)
Selinexor starting dose		
≤ 60 mg	17.7% (12)	14.6% (6)
80 mg	30.9% (21)	63.4% (26)
100 mg	25.0% (17)	9.8% (4)
≥ 120 mg	26.5% (18)	12.2% (5)
Dose modifications	44.1% (30)	43.9% (18)
Dosing schedule change	17.7% (12)	14.6% (6)
Dose delays	16.2% (11)	19.5% (8)
Treatment interruptions	36.8% (25)	48.8% (20)
Other treatment modifications	2.9% (2)	2.4% (1)
Treatment discontinuation	66.2% (45)	29.3% (12)
Reason for discontinuation[2]		
Disease progression	45.6% (31)	12.2% (5)
Adverse events	44.1% (30)	19.5% (8)
Lost to follow up	11.8% (8)	4.9% (2)
Death	5.9% (4)	7.3% (3)
Enrollment into clinical trial	1.5% (1)	0.0% (0)
Other	23.5% (16)	36.6% (15)
Median treatment duration (IQR)[3]	2.5 (1.2–4.4)	4.4 (1.1–9.4)
Patients alive at 6 months from the start of selinexor[4] (95%CI)	57.0% (44.3–67.8%)	73.6% (55.1–85.4%)
Patients alive at 12 months from the start of selinexor[4] (95%CI)	38.2% (26.6–50.0%)	51.6% (24.8–73.0%)

Abbreviations: CI = confidence interval, X = Selinexor, D = Daratumumab, d = dexamethasone, K = Carfilzomib, P = Pomalidomide, V = Bortezomib, IQR = interquartile range
[1]Includes selinexor monotherapy (X only) and quadruplet (XPd + isatuximab)
[2]In some patients, there were concomitant reasons that led to treatment discontinuations.
[3]P=0.037, as determined by the Log-rank test.
[4]Estimated using the Kaplan-Meier estimator method.

Figure 2. Time to treatment failure during the pre- and post-BP implementation.

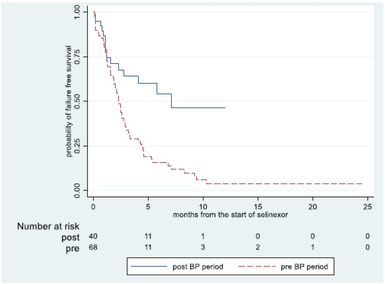

Table 4. Treatment limiting toxicities during selinexor therapy.

Parameter	Pre-implementation (n=68)	Post-implementation (n=41)
Drug discontinuation due to AEs	44.1% (30)	19.5% (8)
AEs contributing to discontinuations[1]		
Nausea	22.1% (15)	9.8% (4)
Vomiting	8.8% (6)	2.4% (1)
Weight loss	5.9% (4)	7.3% (3)
Diarrhea	4.4% (3)	9.8% (4)
Fatigue	17.7% (12)	7.3% (3)
Decreased appetite	11.8% (8)	9.8% (4)
Asthenia	7.4% (5)	4.9% (2)
Dizziness	4.4% (3)	2.4% (1)
Thrombocytopenia	13.2% (9)	4.9% (2)
Other[2]	17.6% (12)	19.5% (8)

Abbreviations: AEs = adverse events.
[1]In some patients, there were concomitant AEs that led to treatment discontinuations.
[2]Includes but not limited to constipation, dyspnea, insomnia, anemia, neutropenia, leukopenia, and pneumonia

LIMITATIONS

- Longer median follow-up time in the pre-period compared to the post-period.
- Risk of temporal bias due to pre- vs. post- study design.
- Presence of both measured and unmeasured confounding variables.
- Selection bias: patients included in the pre-BP period may have had specific unmeasured characteristics that differed from the post-BP patients.

CONCLUSIONS

- The implementation of a BP program tailored to selinexor where patients initiated selinexor at doses ≤ 80 mg once weekly and in combination with standardized antiemetic therapy was associated with reduced likelihood of treatment failure, increased treatment duration, and lower incidence of DLTs.
- These findings support the hypothesis that a BP program designed around specific anticancer drugs can optimize prescribing practices, potentially leading to better disease control and improvements in a patient's cancer care journey.

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