The Oncologist®

Clinical Trial Results

A Phase II Trial of Selinexor, an Oral Selective Inhibitor of Nuclear Export Compound, in Abiraterone- and/or Enzalutamide-Refractory Metastatic Castration-Resistant Prostate Cancer

Xiao X. Wei, Adam P. Siegel, Rahul Aggarwal, Amy M. Lin, Terence W. Friedlander, Lawrence Fong, Won Kim, Mirela Louttit, Emily Chang, Li Zhang, Charles J. Ryan

Division of Hematology/Oncology, University of California, San Francisco, San Francisco, California, USA

Trial Information

- **ClinicalTrials.gov Identifier**: NCT02215161
- **Sponsor(s)**: University of California, San Francisco
- **Principal Investigator**: Charles J. Ryan
- **IRB Approved**: Yes

Lessons Learned

- In abiraterone- and/or enzalutamide-refractory metastatic castration-resistant prostate cancer (mCRPC) patients, selinexor led to prostate-specific antigen and/or radiographic responses in a subset of patients, indicating clinical activity in this indication.
- Despite twice-a-week dosing and maximal symptomatic management, selinexor was associated with significant anorexia, nausea, and fatigue in mCRPC patients refractory to second-generation anti-androgen therapies, limiting further clinical development in this patient population.
- This study highlights the challenge of primary endpoint selection for phase II studies in the post-abiraterone and/or post-enzalutamide mCRPC space.

Abstract

Background. Selinexor is a first-in-class selective inhibitor of nuclear export compound that specifically inhibits the nuclear export protein Exportin-1 (XPO-1), leading to nuclear accumulation of tumor suppressor proteins.

Methods. This phase II study evaluated the efficacy and tolerability of selinexor in patients with metastatic castration-resistant prostate cancer (mCRPC) refractory to abiraterone and/or enzalutamide.

Results. Fourteen patients were enrolled. Selinexor was initially administered at 65 mg/m^2 twice a week (days 1 and 3) and was subsequently reduced to 60 mg flat dose twice a week (days 1 and 3), 3 weeks on, 1 week off, to improve tolerability. The median treatment duration was 13 weeks. At a median follow-up of 4 months, two patients (14%) had $\geq$50% prostate-specific antigen (PSA) decline, and seven patients (50%) had any PSA decline. Of eight patients with measurable disease at baseline, two (25%) had a partial response and four (50%) had stable disease as their best radiographic response. Five patients (36%) experienced serious adverse events (SAEs; all unrelated to selinexor), and five patients (36%) experienced treatment-related grade 3–4 AEs. The most common drug-related adverse events (AEs) of any severity were anorexia, nausea, weight loss, fatigue, and thrombocytopenia. Three patients (21%) came off study for unacceptable tolerability.

Conclusion. Selinexor demonstrated clinical activity and poor tolerability in mCRPC patients refractory to second-line anti-androgenic agents. ***The Oncologist*** 2018;23:656–e64

Discussion

Exportin 1 (XPO-1) is one of seven mammalian export proteins involved in the transportation of macromolecules from the nucleus to the cytoplasm, including tumor suppressor proteins p53, p73, BRCA1, p21, p27, IkB and FOXO transcription factors [1–3]. XPO-1 is overexpressed in multiple malignancies, including prostate cancer. Selinexor is a potent and selective oral XPO-1 inhibitor found to inhibit tumor growth and incidence of metastasis in preclinical models of prostate cancer [4–7].

This single-center phase II study enrolled patients with progressive mCRPC. Eligibility criteria included prior progression on

Correspondence: Xiao X. Wei, M.D., Lank Center for Genitourinary Oncology, 450 Brookline Avenue, Dana 1230, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts 02215, USA. Telephone: 617-632-4524; e-mail: xiaox_wei@dfci.harvard.edu Received November 29, 2017; accepted for publication January 2, 2018; published Online First on February 27, 2018. http://dx.doi.org/10.1634/theoncologist.2017-0624

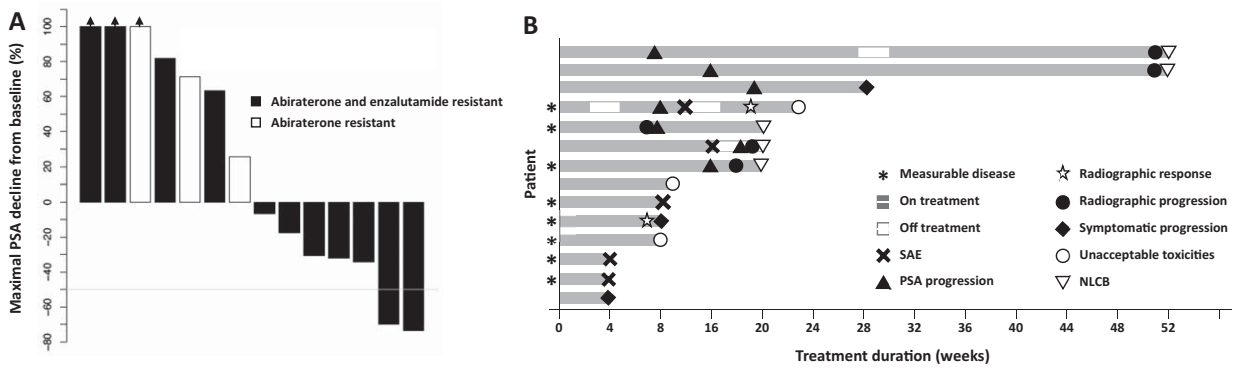

Figure 1. Selinexor treatment results. **(A)**: Waterfall plot of maximal PSA decline during selinexor treatment. Dotted line indicates the threshold for definition of PSA response (≥50% PSA decline from baseline). **(B)**: Swimmer plot of individual patient experience on selinexor. Time to PSA progression determined by PCWG2. Time to radiographic progression determined by RECIST v1.1 for soft tissue lesions and PCWG2 for bone lesions.

Abbreviations: NLCB, no longer clinically benefiting; PCWG2, Prostate Cancer Working Group 2; PSA, prostate-specific antigen; SAE, serious adverse event.

abiraterone, enzalutamide, other second-generation investigational anti-androgen/androgen receptor (AR)-targeted therapies (e.g., apalutamide), or their combination. Prior chemotherapy for mCRPC was not allowed. The primary endpoint was radiographic progression-free survival (rPFS).

A total of 14 patients were enrolled between October 2014 and October 2016. The median age was 72 years (range: 56–79). The median baseline PSA was 73.8 ng/mL (range: 12.8–686.9; Table 1). The first two patients received selinexor 65 mg/m^2 p.o. twice a week (days 1 and 3), one of whom came off study for a serious adverse event (grade 4 psychosis, related to dexamethasone prophylaxis for nausea and anorexia), and the other came off study for unacceptable treatment-related adverse events (AEs; grade 3 anorexia, nausea, vomiting, and weight loss). The study protocol was subsequently revised to reduce the selinexor dose to 60 mg flat dose twice a week (days 1 and 3), 3 weeks on, 1 week off.

The median treatment duration was 13 weeks (range: 4–48). At a median follow-up of 4 months, two patients (14%) had ≥50% PSA decline, and seven patients (50%) had any PSA decline (Fig. 1A). Only one patient (7%) had ≥50% PSA decline after 12 weeks of therapy. The median time to PSA progression was 12 weeks (range: 7–14). Of eight patients who had measurable disease at baseline; two (25%) had partial response and four (50%) had stable disease as best radiographic response. All fourteen patients had bone metastasis at baseline; four (29%) had confirmed radiographic progression on bone scan, with a median time to progression of 31 weeks (range: 7–47).

Five patients (36%) experienced SAEs (psychosis, diplopia, orthostatic hypotension, congestive heart failure, and angina), all of which were deemed unrelated to selinexor. Five patients (36%) experienced treatment-related grade 3–4 AEs (anemia, $n = 3$; nausea, $n = 2$; vomiting, $n = 2$; anorexia, fatigue, thrombocytopenia, neutropenia, hypophosphatemia, $n = 1$ each). The most common drug-related AEs of any severity were anorexia (86%), nausea (64%), weight loss (50%), fatigue (50%), and thrombocytopenia (50%). Three patients (21%) came off study for poor tolerability (Fig. 1B).

Although oral selinexor showed clinical activity, the study was terminated early due to the significant AE profile observed in the study population. The primary endpoint of rPFS is not reported because limited sample size and high rate of censoring precluded accurate estimation.

Trial Information	
Disease	Prostate cancer
Stage of Disease/Treatment	Metastatic/advanced
Prior Therapy	No designated number of regimens
Type of study - 1	Phase II
Type of study - 2	Single arm
Primary Endpoint	Progression-free survival
Secondary Endpoint	PSA decline (at least 50%) at 12 weeks
Secondary Endpoint	Time to PSA progression (PCWG2 criteria)
Secondary Endpoint	Time to confirmed radiographic progression on bone scan (PCWG2 criteria)
Secondary Endpoint	Safety
Secondary Endpoint	Pharmacodynamics
Secondary Endpoint	Pharmacokinetics

Additional Details of Endpoints or Study Design The primary endpoint of rPFS was not reported because the study was terminated early, with a limited sample size and high rate of censoring (N= 6, 43%) that precludes accurate estimation. Pharmacokinetics and pharmacodynamics studies were not performed because the study was terminated early.	
Investigator's Analysis	Clinical activity and significant toxicity profile

Drug Information for Phase II Selinexor

Drug 1	
Generic/Working Name	Selinexor
Company Name	Karyopharm Therapeutics
Drug Type	Small molecule
Dose	60 mg/m^2
Route	p.o.
Schedule of Administration First two patients: 65 mg/m^2 twice a week (days 1 and 3). Remaining patients: 60 mg flat dose twice a week (days 1 and 3), 3 weeks on, 1 week off.	

Patient Characteristics for Phase II Selinexor

Number of Patients, Male	14
Number of Patients, Female	0
Stage	Metastatic, castration resistant
Age	Median (range): 72 years (56–79 years)
Number of Prior Systemic Therapies	Median (range): 2 (1–4)
Performance Status: ECOG	0 — 9
	1 — 5
	2 — 0
	3 — 0
	Unknown — 0
Other	Cancer types or histologic subtypes: Prostate

Primary Assessment Method for Phase II Selinexor

Title	PCWG2 for bone lesions
Number of Patients Screened	19
Number of Patients Enrolled	14
Number of Patients Evaluable for Toxicity	14
Number of Patients Evaluated for Efficacy*	10
Evaluation Method	PCWG2 for bone lesions
Response Assessment CR	$n = 0$ (0%)
Response Assessment SD	$n = 9$ (64%)
Response Assessment PD	$n = 1$ (7%)
Title	Total patient population: RECIST v1.1 for soft tissue lesions
Number of Patients Evaluated for Efficacy**	6
Evaluation Method	RECIST 1.1
Response Assessment CR	$n = 0$ (0%)
Response Assessment PR	$n = 2$ (25%)
Response Assessment SD	$n = 4$ (50%)
Response Assessment PD	$n = 0$ (0%)

*4 patients were not evaluable for efficacy because of not having post-treatment radiographic evaluation ($n = 3$) or have had an unconfirmed PD ($n = 1$).

**2 patients were not evaluable for efficacy because of unconfirmed PD.

Adverse Events

	All Cycles						
Name	***NC/NA**	**1**	**2**	**3**	**4**	**5**	**All Grades**
Anorexia	14%	50%	29%	7%	0%	0%	86%
Nausea	36%	43%	7%	14%	0%	0%	64%
Weight loss	50%	29%	14%	7%	0%	0%	50%
Fatigue	50%	7%	43%	0%	0%	0%	50%
Platelet count decreased	51%	21%	21%	0%	7%	0%	49%
Vomiting	65%	14%	7%	14%	0%	0%	35%
Anemia	65%	0%	14%	21%	0%	0%	35%
Diarrhea	79%	14%	7%	0%	0%	0%	21%
Dysgeusia	79%	21%	0%	0%	0%	0%	21%
Blurred vision	79%	14%	7%	0%	0%	0%	21%
Nervous system disorders—presyncope	86%	7%	7%	0%	0%	0%	14%
Dizziness	86%	7%	7%	0%	0%	0%	14%
Neutrophil count decreased	93%	0%	0%	7%	0%	0%	7%
Hypophosphatemia	93%	0%	0%	7%	0%	0%	7%
Bruising	93%	0%	7%	0%	0%	0%	7%
Insomnia	93%	0%	7%	0%	0%	0%	7%
Hyponatremia	93%	7%	0%	0%	0%	0%	7%
Hypotension	93%	7%	0%	0%	0%	0%	7%
Cough	93%	7%	0%	0%	0%	0%	7%
Peripheral sensory neuropathy	93%	7%	0%	0%	0%	0%	7%
Flatulence	93%	7%	0%	0%	0%	0%	7%
Gastrointestinal disorders—early satiety	93%	7%	0%	0%	0%	0%	7%
Rash maculo-papular	93%	7%	0%	0%	0%	0%	7%
Skin and subcutaneous tissue disorders—lip lesion	93%	7%	0%	0%	0%	0%	7%
Watering eyes	93%	7%	0%	0%	0%	0%	7%
Gait disturbance	93%	7%	0%	0%	0%	0%	7%
General disorders and administration site conditions—craving sweets	93%	7%	0%	0%	0%	0%	7%
General disorders and administration site conditions—hypersalivation	93%	7%	0%	0%	0%	0%	7%
Night blindness	93%	7%	0%	0%	0%	0%	7%
Alopecia	93%	7%	0%	0%	0%	0%	7%
Dyspnea	93%	7%	0%	0%	0%	0%	7%

All adverse events are at least possibly related to study therapy, graded according to National Cancer Institute Common Terminology Criteria for Adverse Events v4.0.
Abbreviation: NC/NA, no change from baseline/no adverse event.

Serious Adverse Events

Name	Grade	Attribution
Psychosis	Grade 4	Unrelated
Diplopia	Grade 2	Unrelated
Orthostatic hypotension	Grade 3	Unrelated
Congestive heart failure	Grade 3	Unrelated
Angina	Grade 3	Unrelated

Psychosis was attributed to prophylactic dexamethasone, and diplopia was attributed to disease progression.

Assessment, Analysis, and Discussion	
Completion	Study terminated before completion
Terminated Reason	Toxicity
Pharmacokinetics/Pharmacodynamics	Not collected
Investigator's Assessment	Clinical activity and significant toxicity profile

In this phase II trial, selinexor was found to have clinical activity with significant nausea, anorexia, fatigue, and weight loss in abiraterone- and/or enzalutamide-refractory metastatic castration-resistant prostate cancer (mCRPC) patients. Of the 14 patients treated, 3 patients withdrew from study for treatment-unrelated SAEs, and 3 patients withdrew from study for treatment-related AEs, translating to a withdrawal rate due to selinexor of 21%. Although tolerability was improved by protocol dose reduction of selinexor from 65 mg/m^2 twice a week to 60 mg flat dose twice a week, 3 weeks on, 1 week off, 2 of the 12 patients receiving the latter dose (17%) withdrew from study for unacceptable adverse events.

The study protocol originally planned to accrue up to a total of 54 patients and specified early stopping if after the initial accrual of 18 patients, 10 or fewer patients ($\leq$56%) were classified as progression free at 16 weeks, or if more than 6 patients ($>$33%) experience unacceptable toxicity. The study was terminated early based on the assessment of tolerability and efficacy data in the first 14 patients accrued. All patients received maximal symptomatic management, including nausea prophylaxis with ondansetron and olanzapine and, if needed, dexamethasone, transfusions for cytopenias, dose reductions, and drug holidays.

The primary endpoint selected for this study was radiographic progression-free survival (rPFS), one of the coprimary endpoints in the COU-AA-302 study [8]. Of note, all seven patients with reductions in prostate-specific antigen (PSA) had mCRPC refractory to both abiraterone and enzalutamide. Two patients (of eight) with measurable disease at baseline had partial responses by RECIST criteria. Two patients (14%) remained on study for close to 48 weeks and eventually came off study for radiographic progression. It is worthwhile to note that both patients experienced a long interval of PSA progression (9–10 months) before confirmed radiographic progression on bone scan by PCWG2 criteria (Fig. 1B). One patient had an increase in PSA from 41 ng/mL at baseline to 342 ng/mL at the time of study discontinuation, without any PSA decline. The other patient had a maximal PSA decline of $-$32%. These observations raise the question of optimal primary endpoint selection for phase II studies in post-abiraterone and/or post-enzalutamide patients. Perhaps a PSA-based endpoint could improve efficacy and safety signal detection in novel drug development in this disease space; however, the best approach remains to be elucidated.

Abiraterone acetate and enzalutamide are important treatment options for men with mCRPC. However, approximately 30% of chemotherapy-naïve and 60% of postchemotherapy patients do not achieve PSA decline (i.e., primary resistance), and essentially all patients who initially benefit from treatment eventually develop progressive disease (i.e., acquired resistance) [8–11]. Furthermore, the emergence of resistant disease is often accompanied by an aggressive clinical course and poor prognosis, with a median overall survival of 12–18 months. The development of novel therapeutics for mCRPC patients after progression on abiraterone and enzalutamide should continue to be a research priority.

It is recognized that there is a significant degree of cross-resistance between abiraterone and enzalutamide, and mechanisms of resistance include constitutively active androgen receptor (AR) splice variants that effectively bypass the AR signaling pathway [12–14]. Whether targeting nuclear export with XPO-1 counteracts this and other mechanisms of resistance would be interesting to explore but is beyond the scope of this study. However, the current data do demonstrate clinical activity of XPO-1 inhibition in patients with mCRPC resistant to second-generation anti-androgen therapies, supporting further research in this area.

XPO-1 inhibition with selinexor is being actively investigated in multiple solid and hematologic malignancies and has demonstrated promising clinical activity in advanced refractory hematologic malignancies in early phase trials, with response rates ranging from 30% to 50% [15–17]. Although it is possible that differences in tissue distribution, tumor penetration, and biology across and within tumor types (i.e., differential dependence on XPO-mediated nuclear export for survival) contribute to variations in clinical activity, pharmacodynamic studies evaluating XPO-1 expression and clinical response were not performed in this study given early trial termination. It is possible that baseline fatigue and other comorbidities, bony metastases (present in all patients in this study), prior therapies, and/or other medical conditions in mCRPC patients contributed to the reduced tolerability in this population relative to other patients with solid tumors.

The adverse event profile observed in this study hinders further clinical development of twice-weekly selinexor in patients with progressive mCRPC. In contrast to this study, selinexor was found to be tolerable in patients with advanced refractory bone or soft tissue sarcoma when administered at different twice-weekly doses (30 mg/m^2, 50 mg/m^2, or 60 mg flat dose) on a continuous schedule (no break) [18]. The sarcoma patients treated were younger, with a median age of 55 years (range: 18–86), and likely had fewer comorbidities and better bone marrow reserve, which could have contributed to the differences in tolerability observed in the studies. Indeed, the overall frequency of weight loss and anorexia was higher in the current mCRPC study. Selinexor at doses of 50 mg/m^2 twice weekly, 35 mg/m^2 twice weekly, and 50 mg/m^2 weekly without break were also found to be relatively well tolerated in patients with advanced treatment-refractory gynecological cancers [19].

Second-generation selective inhibitor of nuclear export (SINE) compounds (e.g., KPT-8602) are currently being developed, which have reduced brain penetration and thereby reduced central nervous system-mediated side effects, including anorexia, fatigue, and weight loss [20, 21]. The improved adverse event profile of KPT-8602 may allow for daily

administration compared with twice-a-week dosing for selinexor, which may increase therapeutic effect. Consistent with this, early results from a phase I/II study of KPT-8602 in patients with relapsed/refractory multiple myeloma in which KPT-8602 was dosed daily (QDx5) in 28-day cycles was well tolerated [22]. The investigation of second-generation SINE compounds in advanced prostate cancer, including incorporating such agents into combination strategies, appears to be worthwhile given the clinical activity of selinexor observed in this study.

Acknowledgments

We thank all patients and their families who participated in this study. Dr. Wei is currently affiliated with the Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts. Dr. Siegel is currently affiliated with Aurora Medical Center, Summit, Wisconsin. Karyopharm Therapeutics provided financial support for this study.

Disclosures

Rahul Aggarwal: Abbvie (C/A), Illumina (H), Janssen, Novartis (RF); **Terence W. Friedlander:** Pfizer, Genentech, Clovis, Astra Zeneca (C/A), Janssen (RF); **Won Kim:** Pfizer, Genentech, Exelixis, Bayer (C/A). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

References

1. Nigg EA. Nucleocytoplasmic transport: Signals, mechanisms and regulation. Nature 1997;386:779–787.

2. Fukuda M, Asano S, Nakamura T et al. CRM1 is responsible for intracellular transport mediated by the nuclear export signal. Nature 1997;390:308–311.

3. Kau TR, Way JC, Silver PA. Nuclear transport and cancer: From mechanism to intervention. Nat Rev Cancer 2004;4:106–117.

4. Gravina GL, Mancini A, Sanita P et al. KPT-330, a potent and selective exportin-1 (XPO-1) inhibitor, shows antitumor effects modulating the expression of cyclin D1 and survivin in prostate cancer models. BMC Cancer 2015;15:941.

5. Gravina GL, Tortoreto M, Mancini A et al. XPO1/CRM1-selective inhibitors of nuclear export (SINE) reduce tumor spreading and improve overall survival in preclinical models of prostate cancer (PCa). J Hematol Oncol 2014;7:46.

6. Maity S, Wu G, Lu J et al. Preclinical efficacy of the novel, oral selective inhibitor of nuclear export (SINE) selinexor (KPT-330) on castration resistant prostate cancer. [abstract]. In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; April 5–9, 2014; San Diego, CA. Philadelphia (PA): AACR; Cancer Res 2014;74(suppl 19):3808a.

7. Mendonca J, Sharma A, Kim HS et al. Selective inhibitors of nuclear export (SINE) as novel therapeutics for prostate cancer. Oncotarget 2014;5:6102–6112.

8. Ryan CJ, Smith MR, de Bono JS et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. N Engl J Med 2013;368:138–148.

9. de Bono JS, Logothetis CJ, Molina A et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med 2011;364:1995–2005.

10. Beer TM, Armstrong AJ, Rathkopf DE et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med 2014;371:424–433.

11. Scher HI, Fizazi K, Saad F et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med 2012;367:1187–1197.

12. Antonarakis ES, Armstrong AJ, Dehm SM et al. Androgen receptor variant-driven prostate cancer: Clinical implications and therapeutic targeting. Prostate Cancer Prostatic Dis 2016;19:231–241.

13. Scher HI, Lu D, Schreiber NA et al. Association of AR-V7 on circulating tumor cells as a treatment-specific biomarker with outcomes and survival in castration-resistant prostate cancer. JAMA Oncol 2016;2:1441–1449.

14. Antonarakis ES, Lu C, Luber B et al. Androgen receptor splice variant 7 and efficacy of taxane chemotherapy in patients with metastatic castration-resistant prostate cancer. JAMA Oncol 2015;1:582–591.

15. Abdul Razak AR, Mau-Soerensen M, Gabrail NY et al. First-in-class, first-in-human phase I study of selinexor, a selective inhibitor of nuclear export, in patients with advanced solid tumors. J Clin Onocl 2016;34:4142–4150.

16. Alexander TB, Lacayo NJ, Choi JK et al. Phase I study of selinexor, a selective inhibitor of nuclear export, in combination with fludarabine and cytarabine, in pediatric relapsed or refractory acute leukemia. J Clin Oncol 2016;34:4094–4101.

17. Kuruvilla J, Savona M, Baz R et al. Selective inhibition of nuclear export with selinexor in patients with non-Hodgkin lymphoma. Blood 2017;129:3175–3183.

18. Gounder MM, Zer A, Tap WD et al. Phase IB study of selinexor, a first-in-class inhibitor of nuclear export, in patients with advanced refractory bone or soft tissue sarcoma. J Clin Oncol 2016;34:3166–3174.

19. Vergote I, Lund B, Havsteen H et al. Results of a phase 2 trial of selinexor, an oral selective inhibitor of nuclear export (SINE) in 114 patients with gynaecological cancers. Ann Oncol 2016;27:296–312.

20. Etchin J, Berezovskaya A, Conway AS et al. KPT-8602, a second-generation inhibitor of XPO1-mediated nuclear export, is well tolerated and highly active against AML blasts and leukemia-initiating cells. Leukemia 2017;31:143–150.

21. Vercruysse T, De Bie J, Neggers JE et al. The second-generation exportin-1 inhibitor KPT-8602 demonstrates potent activity against acute lymphoblastic leukemia. Clin Cancer Res 2017;23:2528–2541.

22. Cornell RF, Rossi AC, Baz R et al. A phase 1/2 study of the second generation selective inhibitor of nuclear export (SINE) compound, KPT-8602, in patients with relapsed refractory multiple myeloma. Blood 2016;128:4509.

Figures and Tables

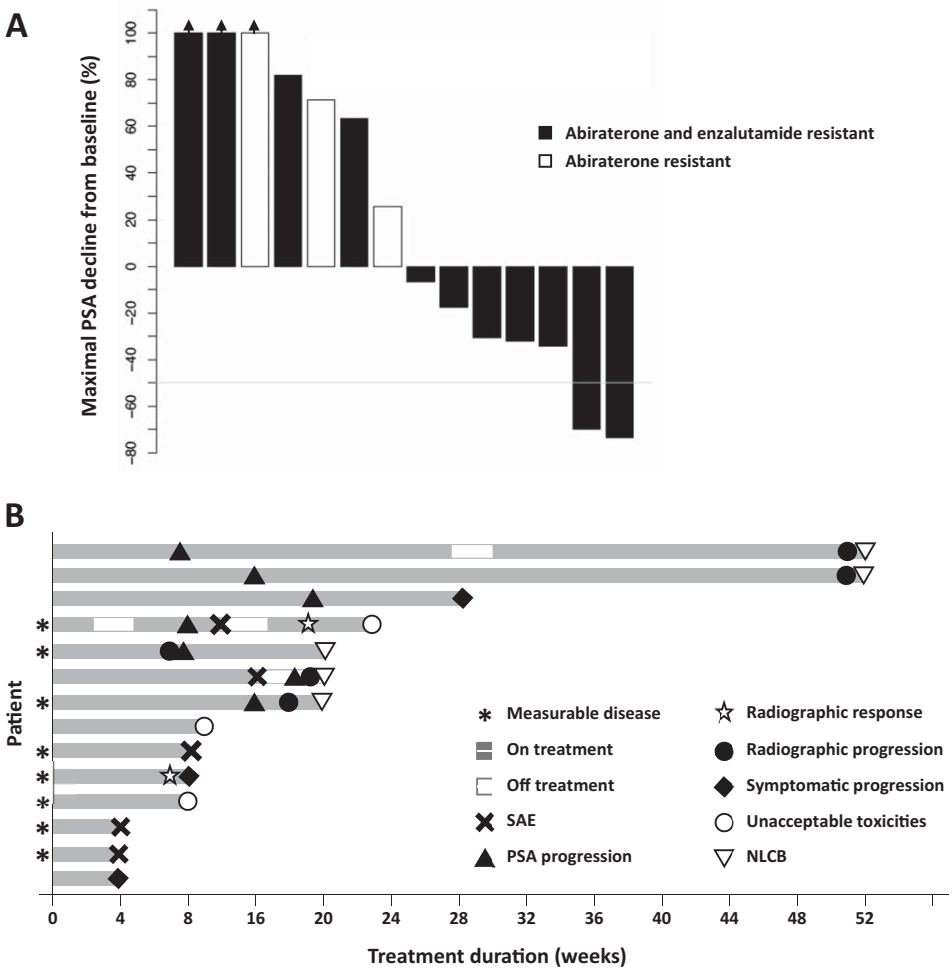

Figure 1. Selinexor treatment results. **(A)**: Waterfall plot of maximal PSA decline during selinexor treatment. Dotted line indicates the threshold for definition of PSA response (≥50% PSA decline from baseline). **(B)**: Swimmer plot of individual patient experience on selinexor. Time to PSA progression determined by PCWG2. Time to radiographic progression determined by RECIST v1.1 for soft tissue lesions and PCWG2 for bone lesions.

Abbreviations: NLCB, no longer clinically benefiting; PCWG2, Prostate Cancer Working Group 2; PSA, prostate-specific antigen; SAE, serious adverse event.

Table 1. Demographic and baseline characteristics

Characteristic	Selinexor ($n = 14$)[a]
Age, years, median (range)	72 (56–79)
Race, *n* (%)	
White	12 (86)
Asian	1 (7)
Unknown	1 (7)
ECOG performance status, *n* (%)	
0	9 (64)
1	5 (36)
Gleason score, *n* (%)	
≤ 7	5 (36)
>7	7 (50)
Unknown	2 (14)
Site of metastasis, *n* (%)	
Node only	0 (0)
Bone only	3 (21)
Bone + node	11 (79)
Visceral	0 (0)
Prior treatment for mCRPC, *n* (%)	
Aibraterone acetate[b]	14 (100)
Enzalutamide[b]	11 (79)
Sipuleucel-T	5 (36)
Radium-223	3 (21)
Chemotherapy[c]	0 (0)
PSA, ng/mL, median (range)	73.8 (12.8–686.9)
LDH, U/L, median (range)	173 (134–770)
Hematocrit, %, median (range)	36.6 (32.2–42.1)
Alkaline phosphatase, U/L, median (range)	112 (42–912)

[a]Selinexor dose: 65 mg/m^2 twice a week (days 1 and 3) for the initial two patients enrolled. Subsequently reduced to 60 mg flat dose twice a week (days 1 and 3), 3 weeks on, 1 week off, for the remaining 12 patients enrolled.
[b]Three patients had received abiraterone in the context of a phase II study of increased-dose abiraterone after progression on standard-dose abiraterone (NCT01637402). One patient had received concurrent abiraterone and enzalutamide in the context of a phase III randomized clinical trial (NCT01949337). No patient had received other second-generation investigational anti-androgen/AR-targeted therapies, including ARN-509 or Apalutamide.
[c]No patient had received prior chemotherapy for mCRPC prior to study enrollment. Two patients had received prior docetaxel for metastatic hormone-sensitive prostate cancer.
Abbreviations: AR, androgen receptor; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; mCRPC, metastatic castration-resistant prostate cancer; PSA, prostate-specific antigen.