Thein *et al.*
Experimental Hematology & Oncology (2021) 10:59
https://doi.org/10.1186/s40164-021-00251-0

Experimental Hematology & Oncology

LETTER TO THE EDITOR

Open Access

Selinexor in combination with standard chemotherapy in patients with advanced or metastatic solid tumors

Kyaw Z. Thein[1,2*], Sarina A. Piha-Paul[1], Apostolia Tsimberidou[1], Daniel D. Karp[1], Filip Janku[1], Siqing Fu[1], Vivek Subbiah[1], David S. Hong[1], Timothy A. Yap[1], Jatin Shah[3], Denái R. Milton[4], Lacey McQuinn[1], Jing Gong[1], Yanyan Tran[1], Brett W. Carter[5], Rivka Colen[6], Funda Meric-Bernstam[1] and Aung Naing[1]

Abstract

Selinexor, an oral selective inhibitor of nuclear export (SINE), was demonstrated to hinder the DNA damage repair (DDR) system by reducing DDR proteins while enhancing the killing of cancer cells by DDR-based therapeutics in vivo studies. In this single-center, multi-arm phase 1b study, selinexor with carboplatin, doxorubicin and cyclophosphamide (DC), irinotecan with fluorouracil and folinic acid (FOLFIRI), irinotecan, and capecitabine and oxaliplatin (XELOX), were employed as separate parallel arms. Eligible patients have relapsed/ metastatic refractory solid tumors following standard therapy or addition of selinexor to systemic therapy was appropriate. Nineteen patients were treated in the 5 arms. Tumor types included were colorectal (n = 3), breast (n = 3), neuroendocrine (n = 2), ovarian (n = 2), and pancreas cancers (n = 2). All patients developed one treatment-related adverse events (TRAE). The most prevalent TRAE were thrombocytopenia (84%), nausea (68%), leukopenia (68%), neutropenia (63%), and fatigue (58%). The common grade 3/4 TRAE were neutropenia (42%), leukopenia (26%), and hyponatremia (21%). Three patients had dose-limiting toxicities (DLT) in 3 separate arms. Fourteen patients were evaluable for response. Although no patients achieved complete or partial response (CR or PR), seven patients attained stable disease (SD). Disease control rate (DCR) was 14%. The combination of oral selinexor with different standard chemotherapies showed limited clinical activity despite toxicity and DLT prevented further dose escalation. Optimizing supportive care, the utility of growth factors, and aggressive measures on antiemetics strategies remain tangible.

Trial registration ClinicalTrials.gov Identifier: NCT02419495. Registered 14 April 2015, https://clinicaltrials.gov/ct2/show/NCT02419495). Sponsor(s): Karyopharm Therapeutics

Keywords: Selinexor (KPT 330), Carboplatin, Irinotecan, FOLFIRI, Doxorubicin and cyclophosphamide, Capecitabine and oxaliplatin (XELOX)

To the editor,

Selinexor (KPT-330) is an oral selective inhibitor of nuclear export (SINE) and was shown to hinder the DNA damage repair (DDR) system by diminishing DDR proteins expression while enhancing the killing of cancer cells by DDR-based therapeutics in vivo preclinical models [1–3]. Previous early phase studies demonstrated the modest activity of single agent selinexor in patients with

*Correspondence: theink@ohsu.edu
[2] Division of Hematology and Medical Oncology, Oregon Health and Science University/Knight Cancer Institute, 3181 SW Sam Jackson Park Rd, Mail Code: OC14HO, Portland, OR 97239, USA
Full list of author information is available at the end of the article

Table 1 Patients baseline demographics and disease characteristics

Characteristic	Selinexor 60 mg QW/BIW + carboplatin 6 AUC Q3W (*N* = 6)	Selinexor 60 mg QW/BIW + doxorubicin 60 mg/m^2 + cyclophosphamide 600 mg/m^2 Q3W (*N* = 4)	Selinexor 40 mg QW + FOLFIRI[a] (*N* = 3)	Selinexor 60 mg QW + irinotecan 125 mg/m^2 D1 and 8 Q3W (*N* = 3)	Selinexor 40 mg QW + XELOX[b] (*N* = 3)	All patients (*N* = 19)
Age at consent (years)						
Median range	56.1 (31.2–76.1)	61.7 (23.6–64.9)	49.9 (38.1–70.7)	67.8 (57.9–72.3)	65.9 (51.8–72.8)	60.6 (23.6–76.1)
Gender, *N* (%)						
Male	1 (17)	2 (50)	1 (33)	1 (33)	2 (67)	7 (37)
Female	5 (83)	2 (50)	2 (67)	2 (67)	1 (33)	12 (63)
Race/ethnicity, *N* (%)						
White	4 (67)	4 (100)	3 (100)	1 (33)	3 (100)	15 (79)
Hispanic	0	0	0	0	0	0
Black	1 (17)	0	0	1 (33)	0	2 (11)
Asian	1 (17)	0	0	1 (33)	0	2 (11)
ECOG performance status, *N* (%)						
0	1 (17)	0	1 (33)	2 (67)	1 (33)	5 (26)
1	5 (83)	4 (100)	2 (67)	1 (33)	2 (67)	14 (74)
Primary tumor, *N* (%)						
Ovarian	0	2 (50)	0	0	0	2 (11)
Breast	3 (50)	0	0	0	0	3 (16)
Colorectal cancer	0	0	1 (33)	1 (33)	1 (33)	3 (16)
Endometrial/fallopian	0	0	0	0	0	0
Lung	1 (17)	0	0	0	0	1 (5)
Neuroendocrine	0	0	1 (33)	1 (33)	0	2 (11)
Pancreas	0	0	1 (33)	0	1 (33)	2 (11)
Esophageal	0	0	0	0	0	0
Head and neck/salivary gland	1 (17)	0	0	1 (33)	0	2 (11)
Liver/cholangiocarcinoma	0	0	0	0	1 (33)	1 (5)
Sarcoma	0	1 (25)	0	0	0	1 (5)
Prostate	0	1 (25)	0	0	0	1 (5)
Others	1 (17)	0	0	0	0	1 (5)
Prior lines of systemic therapies, *N* (%)						
0–1	1 (17)	0	0	0	0	1 (5)
2–3	4 (67)	3 (75)	2 (67)	2 (67)	2 (67)	13 (68)
4–5	1 (17)	1 (25)	1 (33)	0	1 (33)	4 (21)
> 5	0	0	0	1 (33)	0	1 (5)
Median range	2.5 (1.0–4.0)	2.0 (2.0–4.0)	3.0 (3.0–5.0)	3.0 (2.0–6.0)	3.0 (2.0–4.0)	3.0 (1.0–6.0)

N number; *ECOG* Eastern Cooperative Oncology Group; *QW* once weekly; *BIW* twice weekly; *AUC* area under curve; *mg/m^2* milligrams per square meter; *D1 and 8* on days 1, and 8 of each cycle; *Q3W* every 3 week; *FOLFIRI* irinotecan with fluorouracil and folinic acid; *XELOX* capecitabine and oxaliplatin

[a] FOLFIRI—irinotecan of 180 mg/m^2, 5-FU continuous infusion of 2400 mg/m^2, 5-FU bolus of 400 mg/m^2, and leucovorin of 400 mg/m^2 on days 1, and 15

[b] XELOX—capecitabine was dosed at 900 mg/m^2 orally (PO) divided into 2 doses on days 1–14, along with oxaliplatin of 130 mg/m^2 IV Q3W

Table 2 Summary of treatment-related adverse events (TRAE) in all grades of severity

N (%)	Selinexor 60 mg QW/BIW + carboplatin 6 AUC Q3W (*N* = 6)		Selinexor 60 mg QW/BIW + doxorubicin 60 mg/m^2 + cyclophosphamide 600 mg/m^2 Q3W (*N* = 4)		Selinexor 40 mg QW + FOLFIRI[a] (*N* = 3)		Selinexor 60 mg QW + irinotecan 125 mg/m^2 D1 and 8 Q3W (*N* = 3)		Selinexor 40 mg QW + XELOX[b] (*N* = 3)		All patients (*N* = 19)	
	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4
Anemia	5 (83)	2 (33)	2 (50)	0	1 (33)	0	1 (33)	0	1 (33)	1 (33)	10 (53)	3 (16)
Leukopenia	4 (75)	1 (17)	3 (75)	3 (75)	3 (100)	0	1 (33)	0	2 (67)	1 (33)	13 (68)	5 (26)
Neutropenia	4 (75)	2 (33)	3 (75)	3 (75)	2 (67)	1 (33)	2 (67)	1 (33)	1 (33)	1 (33)	12 (63)	8 (42)
Thrombocytopenia	6 (100)	3 (50)	3 (75)	0	2 (67)	0	2 (67)	0	3 (100)	0	16 (84)	3 (16)
Constipation	0	0	0	0	0	0	0	0	0	0	0	0
Diarrhea	2 (33)	0	0	0	0	0	1 (33)	0	1 (33)	1 (33)	4 (21)	1 (5)
Nausea	4 (75)	0	4 (100)	0	1 (33)	0	1 (33)	0	3 (100)	0	13 (68)	0
Vomiting	4 (75)	0	3 (75)	0	0	0	1 (33)	0	2 (67)	0	10 (53)	0
Elevated AST/ALT	0	0	0	0	1 (33)	0	1 (33)	0	0	0	2 (11)	0
Mucositis	0	0	0	0	0	0	0	0	0	0	0	0
Fatigue	4 (75)	0	2 (50)	0	1 (33)	0	3 (100)	1 (33)	1 (33)	0	11 (58)	1 (5)
Anorexia	1 (17)	0	0	0	0	0	1 (33)	0	2 (67)	0	4 (21)	0
Hyponatremia	3 (50)	2 (33)	0	0	1 (33)	1 (33)	1 (33)	0	1 (33)	1 (33)	6 (32)	4 (21)
Hypomagnesemia	1 (17)	0	0	0	0	0	0	0	1 (33)	0	2 (11)	0
Hypoalbuminemia	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	1 (33)	0	1 (5)	0
Cough	0	0	0	0	0	0	0	0	0	0	0	0
Elevated CPK	1 (17)	0	0	0	0	0	0	0	0	0	1 (5)	0
Infection or infestation	0	0	0	0	0	0	0	0	0	0	0	0
Elevated lipase	1 (17)	1 (17)	0	0	0	0	0	0	0	0	1 (5)	1 (5)

[a] FOLFIRI—irinotecan of 180 mg/m^2, 5-FU continuous infusion of 2400 mg/m^2, 5-FU bolus of 400 mg/m^2, and leucovorin of 400 mg/m^2 on days 1, and 15

[b] XELOX—capecitabine was dosed at 900 mg/m^2 orally (PO) divided into 2 doses on days 1–14, along with oxaliplatin of 130 mg/m^2 IV Q3W

QW once weekly; *BIW* twice weekly; *AUC* area under curve; *mg/m^2* milligrams per square meter; *D1 and 8* on days 1, and 8 of each cycle; *Q3W* every 3 weeks; *ALT* alanine aminotransferase; *AST* aspartate aminotransferase; *CPK* creatine phosphokinase; *FOLFIRI* irinotecan with fluorouracil and folinic acid; *5-FU* 5-fluorouracil; *XELOX* capecitabine and oxaliplatin

solid tumors [4–6]. In vivo studies of selinexor in combination with different chemotherapeutics demonstrated synergistic activity [3, 7, 8]. An open-label, multi-arm phase 1b study utilizing selinexor in combination with different standard chemotherapies was conducted at MD Anderson Cancer Center to evaluate the safety and tolerability of the combination. Herein, we report results from 5 closed separate arms of the study.

Eligible patients were adult (age $\geq$18 years) patients with histologically documented, relapsed/metastatic refractory solid tumors following standard therapy or adding selinexor to systemic therapy was appropriate. The primary aim was to evaluate the safety and tolerability of selinexor when given in combination with different standard chemotherapies and the secondary aim was to determine the preliminary antitumor activity [DCR (CR + PR + SD $\geq$6 months), and progression-free survival (PFS)].

Nineteen patients with relapsed/refractory solid tumors were enrolled between July 2015 and January 2017. The demographic and clinical characteristics of all patients enrolled are summarized in Table 1. No patients are currently in the study where the majority of patients withdrew from the study due to progression of disease while 5 patients withdrew due to clinically intolerable treatment-emergent adverse events (TEAE). All patients experienced at least one TEAE and TRAE (Table 2 and Additional file 1: Table S2). The commonest TRAE were thrombocytopenia (84%), nausea (68%), leukopenia (68%), neutropenia (63%), fatigue (58%), vomiting (53%), and anemia (53%). The most prevalent grade 3/4 TRAE were neutropenia (42%), leukopenia (26%), hyponatremia (21%), anemia (16%), and thrombocytopenia (16%). Three patients experienced DLTs; a patient dosed at selinexor 60 mg twice weekly (BIW) with DC reported grade 3 leukopenia and grade 4 neutropenia; a patient receiving selinexor at 40 mg once weekly (QW) with FOLFIRI reported grade 3 febrile neutropenia (FN); and a patient receiving selinexor at 40 mg QW with XELOX reported grade 3 diarrhea. Four patients were reported to have serious adverse events (SAEs). One patient receiving selinexor with DC had an SAE from treatment-related grade 3 FN. Two patients in the combination of selinexor with FOLFIRI had SAEs; one patient had treatment-related grade 3 FN while the other had treatment-unrelated grade 2 pancreatitis. One patient receiving selinexor with XELOX had an SAE from treatment-related grade 3 diarrhea and treatment-unrelated grade 3 dyspnea and skin infection. No patients died during the study.

All patients enrolled had measurable disease, but 5 patients had not completed their first restaging scans due to earlier withdrawal of consent and toxicity. Fourteen patients were considered efficacy evaluable patients (Additional file 1: Figure S1). No patients had objective responses, however, 7 patients had SD. Of the 7 SD patients, 2 received selinexor with DC (ovarian cancer), 2 received selinexor with FOLFIRI [colorectal cancer (CRC); neuroendocrine carcinoma of the pancreas], 2 received selinexor with XELOX (CRC; cholangiocarcinoma), and 1 received selinexor with irinotecan (CRC). All had progressed on multiple prior lines of therapy including FOLFOX, FOLFIRI, cisplatin + gemcitabine, FOLFRINOX, temozolomide, everolimus, octreotide, capecitabine, sunitinib, and ziv-aflibercept. The median time-to-treatment failure (TTF) was 20 weeks (range, 6–29 weeks). Two patients who received selinexor with XELOX experienced disease control resulting in a DCR of 14%. A patient with CRC who progressed on prior 4 lines of therapies, had stable disease with TTF of 26 weeks. Another patient with cholangiocarcinoma who progressed on prior 3 lines of therapies including cisplatin + gemcitabine, FOLFRINOX, had stable disease with TTF of 29 weeks. The median PFS for all patients was 2.0 months (95% CI 1.2, 2.8) while the median OS for all patients was 5.2 months (95% CI 4.0, 11.2) (Additional file 1: Figure S2).

In conclusion, selinexor in combination with standard chemotherapy showed limited clinical activity with some toxicity. Although RP2D of selinexor was 40 mg QW in combination with XELOX or FOLFIRI, the study arms were not pursued for dose expansion due to toxicities and lack of response. Optimizing supportive care, proper use of growth factors, and aggressive measures on antiemetics strategies are important to mitigate TRAE.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40164-021-00251-0.

Additional file 1: Table S1. Summary of treatment-emergent adverse events in the phase I safety population. **Table S2.** Summary of treatment-emergent adverse events (TEAE) in all grades of severity. **Figure S1.** Waterfall plot of maximum change in tumor measurements (per RECIST v1.1) for evaluable patients. **Figure S2.** Kaplan-Meier plot showing progression-free survival (PFS) and overall survival (OS) for all treated patients.

Acknowledgements
We thank the patients who participated in this study, and their families for supporting them.

Authors' contributions
All the authors have contributed to the preparation of this manuscript. All authors read and approved the final manuscript.

Funding
Karyopharm Therapeutics, Clinical and Translational Sciences Award (1UL1TR003167) (NIH/NCATS), and MD Anderson Cancer Support Grant (P30CA016672) (NIH-NCI).

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability
Not applicable.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Institutional Review Board or Independent Ethics Committee at MD Anderson Cancer Center and was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice, and all local and federal regulatory guidelines (obtained).

Consent for publication
Applicable (obtained). Informed consent was obtained from all individual participants included in the study (obtained).

Competing interests
Apostolia-Maria Tsimberidou has the following financial relationships to disclose: Research Funding (Institution): Immatics, Parker Institute for Cancer Immunotherapy, Tempus, OBI Pharma, EMD Serono, Baxalta, ONYX, Bayer, Boston Biomedical, Placon Therapeutics, Karus Therapeutics, and Tvardi Therapeutics. Consulting or Advisory Role: Covance, Genentech and Tempus. Aung Naing reports research funding from NCI; EMD Serono; MedImmune; Healios Onc. Nutrition; Atterocor; Amplimmune; ARMO BioSciences; Eli Lilly; Karyopharm Therapeutics; Incyte; Novartis; Regeneron; Merck; BMS; Pfizer, CytomX Therapeutics; Neon Therapeutics; Calithera Biosciences; TopAlliance Biosciences; Kymab; PsiOxus; Arcus Biosciences; NeoimmuneTech; ImmuneOncia; Surface Oncology. On advisory board of CytomX Therapeutics; Novartis and Genome & Company; OncoSec KEYNOTE-695; STCube. Travel and accommodation expense from ARMO BioSciences. Spouse Research funding: Immune Deficiency Foundation, Jeffery Modell Foundation and chao physician-scientist, and Baxalta. Advisory board: Takeda, CSL, Behring, Horizon, and Pharming. David S. Hong reports Research/Grant Funding: AbbVie, Adaptimmune, Aldi-Norte, Amgen, Astra Zeneca, Bayer, Bristol-Myers Squibb, Daiichi-Sankyo, Eisai, Fate Therapeutics, Genentech, Genmab, GlaxoSmithKline, Ignyta, Infinity, Kite, Kyowa, Lilly, LOXO, Merck, MedImmune, Mirati, miRNA, Molecular Templates, Mologen, NCI-CTEP, Novartis, Pfizer, Seattle Genetics, Takeda, Turning Point Therapeutics. Travel, Accommodations, Expenses: Bayer, Genmab, AACR, ASCO, P.O.E.T, CCLO, SITC. Consulting or Advisory Role: Alpha Insights, Amgen, Axiom, Adaptimmune, Baxter, Bayer, eCancer, Genentech, GLG, Group H, Guidepoint, Infinity, Liberium, Medscape, Numab, Oncology Education Project Association, Pfizer, Prime Oncology, Takeda, Trieza, Therapeutics, WebMD. Other ownership interests: Molecular Match (Advisor), OncoResponse (Founder), Presagia Inc. (Advisor). Filip Janku reports Grant/Research Funding (Institutional): Novartis, Genentech, BioMed Valley Discoveries, Plexxikon, Deciphera, Piqur, Symphogen, Bayer, FujiFilm Corporation and Upsher-Smith Laboratories, Astex, Asana, Astellas, Agios, Proximagen, Bristol-Myers Squibb. Scientific Advisory Board: Deciphera, IFM Therapeutics, Synlogic, Guardant Health, Ideaya, PureTech Health. Paid Consultant: Trovagene, Immunomet, Jazz Pharmaceuticals, Sotio. Ownership Interests: Trovagene. Funda Meric-Bernstam reports Consulting: Aduro BioTech Inc., Alkermes, AstraZeneca, DebioPharm, eFFECTOR Therapeutics, F. Hoffman-La Roche Ltd., Genentech Inc., IBM Watson, Jackson Laboratory, Kolon Life Science, OrigiMed, PACT Pharma, Parexel International, Pfizer Inc., Samsung Bioepis, Seattle Genetics Inc., Tyra Biosciences, Xencor, Zymeworks. Advisory Committee: Immunomedics, Inflection Biosciences, Mersana Therapeutics, Puma Biotechnology Inc., Seattle Genetics, Silverback Therapeutics, Spectrum Pharmaceuticals, Zentalis. Sponsored Research: Aileron Therapeutics, Inc. AstraZeneca, Bayer Healthcare Pharmaceutical, Calithera Biosciences Inc., Curis Inc., CytomX Therapeutics Inc., Daiichi Sankyo Co. Ltd., Debiopharm International, eFFECTOR Therapeutics, Genentech Inc., Guardant Health Inc., Millennium Pharmaceuticals Inc., Novartis, Puma Biotechnology Inc., Taiho Pharmaceutical Co. Honoraria: Chugai Biopharmaceuticals, Mayo Clinic, Rutgers Cancer Institute of New Jersey. Other (Travel Related): Beth Israel Deaconess Medical Center. Sarina A. Piha-Paul receives Research/Grant Funding through the institution from the following sources: AbbVie, Inc.; ABM Therapeutics, Inc.; Acepodia, Inc.; Alkermes; Aminex Therapeutics; Amphivena Therapeutics, Inc.; BioMarin Pharmaceutical, Inc.; Boehringer Ingelheim; Bristol Myers Squib; Cerulean Pharma, Inc.; Chugai Pharmaceutical Co., Ltd.; Curis, Inc.; Daiichi Sankyo; Eli Lilly; ENB Therapeutics; Five Prime Therapeutics; Gene Quantum; Genmab A/S; GlaxoSmithKline; Helix BioPharma Corp.; Incyte Corp.; Jacobio Pharmaceuticals Co., Ltd.; Medimmune, LLC.; Medivation, Inc.; Merck Sharp and Dohme Corp.; Novartis Pharmaceuticals; Pieris Pharmaceuticals, Inc.; Pfizer; Principia Biopharma, Inc.; Puma Biotechnology, Inc.; Rapt Therapeutics, Inc.; Seattle Genetics; Silverback Therapeutics; Taiho Oncology; Tesaro, Inc.; TransThera Bio; NCI/NIH; P30CA016672—Core Grant (CCSG Shared Resources). Siqing Fu reports clinical trial research funding paid to the institution from Eli Lilly, during the conduct of the study; and clinical trial research funding paid to the institution from AstraZeneca, Abbisko, Anaeropharma Science, Arrien Pharmaceuticals, BeiGene, BioAtla, LLC, Boehringer Ingelheim, Eli Lilly, Hookipa Biotech GmBH, Huya Bioscience International, IMV, Inc., Innovent Biologics, Co., Ltd., Lyvgen Biopharm, Co., Ltd., MacroGenics, Medivir AB, Millennium Pharmaceuticals, Inc., Nerviano Medical Sciences, NeuPharma, Inc., NIH/NCI, Novartis, OncoMed, Parexel International, LLC, Sellas Life Sciences Group, Soricimed Biopharma, Inc., Tolero Pharmaceuticals, all outside the submitted work. Vivek Subbiah reports research funding/Grant support for clinical trials: Roche/Genentech, Novartis, Bayer, GlaxoSmithKline, Nanocarrier, Vegenics, Celgene, Northwest Biotherapeutics, Berghealth, Incyte, Fujifilm, Pharmamar, D3, Pfizer, Multivir, Amgen, Abbvie, Alfa-sigma, Agensys, Boston Biomedical, Idera Pharma, Inhibrx, Exelixis, Blueprint medicines, Loxo oncology, Medimmune, Altum, Dragonfly. therapeutics, Takeda and, National Comprehensive Cancer Network, NCI-CTEP and UT MD Anderson Cancer Center, Turning point therapeutics, Boston Pharmaceuticals; Travel: Novartis, Pharmamar, ASCO, ESMO, Helsinn, Incyte; Consultancy/Advisory board: Helsinn, LOXO Oncology/Eli Lilly, R-Pharma US, INCYTE, QED pharma, Medimmune, Novartis. Other: Medscape. Timothy A. Yap reports research support (to institution) from Artios, AstraZeneca, Bayer, Clovis, Constellation, Cyteir, Eli Lilly, EMD Serono, Forbius, F-Star, GlaxoSmithKline, Genentech, ImmuneSensor, Ipsen, Jounce, Karyopharm, Kyowa, Merck, Novartis, Pfizer, Ribon Therapeutics, Regeneron, Repare, Sanofi, Scholar Rock, Seattle Genetics, Tesaro, and Vertex Pharmaceuticals, and consultancy fees from Almac, Aduro, AstraZeneca, Atrin, Axiom, Bayer, Bristol-Myers Squibb, Calithera, Clovis, Cybrexa, EMD Serono, F-Star, Guidepoint, Ignyta, I-Mab, Janssen, Merck, Pfizer, Repare, Roche, Rubius, Schrodinger, Seattle Genetics, Varian and Zai Labs outside of the submitted work. Jatin Shah is an employee of and stockholder of Karyopharm. All remaining authors have declared no competing interests.

Research involving human participants and/or animals
This study was conducted in accordance with the US Common Rule.

Author details
[1]Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA. [2]Division of Hematology and Medical Oncology, Oregon Health and Science University/Knight Cancer Institute, 3181 SW Sam Jackson Park Rd, Mail Code: OC14HO, Portland, OR 97239, USA. [3]Karyopharm Therapeutics, Newton, MA, USA. [4]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA. [5]Department of Thoracic Imaging, Division of Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX, USA. [6]Department of Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA.

Received: 2 October 2021 Accepted: 18 December 2021
Published online: 29 December 2021

References

1. Fung HY, Chook YM. Atomic basis of CRM1-cargo recognition, release and inhibition. Semin Cancer Biol. 2014;27:52–61.
2. Senapedis WT, Baloglu E, Landesman Y. Clinical translation of nuclear export inhibitors in cancer. Semin Cancer Biol. 2014;27:74–86.
3. Kashyap T, Argueta C, Unger T, Klebanov B, Debler S, Senapedis W, et al. Selinexor reduces the expression of DNA damage repair proteins

and sensitizes cancer cells to DNA damaging agents. Oncotarget. 2018;9(56):30773–86.
4. Shafique M, Ismail-Khan R, Extermann M, Sullivan D, Goodridge D, Boulware D, et al. A phase II trial of selinexor (KPT-330) for metastatic triple-negative breast cancer. Oncologist. 2019;24(7):887-e416.
5. Vergote IB, Lund B, Peen U, Umajuridze Z, Mau-Sorensen M, Kranich A, et al. Phase 2 study of the Exportin 1 inhibitor selinexor in patients with recurrent gynecological malignancies. Gynecol Oncol. 2020;156(2):308–14.
6. Gounder MM, Zer A, Tap WD, Salah S, Dickson MA, Gupta AA, 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(26):3166–74.
7. Baek HB, Lombard AP, Libertini SJ, Fernandez-Rubio A, Vinall R, Gandour-Edwards R, et al. XPO1 inhibition by selinexor induces potent cytotoxicity against high grade bladder malignancies. Oncotarget. 2018;9(77):34567–81.
8. Arango NP, Yuca E, Zhao M, Evans KW, Scott S, Kim C, et al. Selinexor (KPT-330) demonstrates anti-tumor efficacy in preclinical models of triple-negative breast cancer. Breast Cancer Res. 2017;19(1):93.

Publisher's Note