

Results of a Phase II Trial of Selinexor, in Patients with Gynaecological Cancers

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Presenter Disclosures

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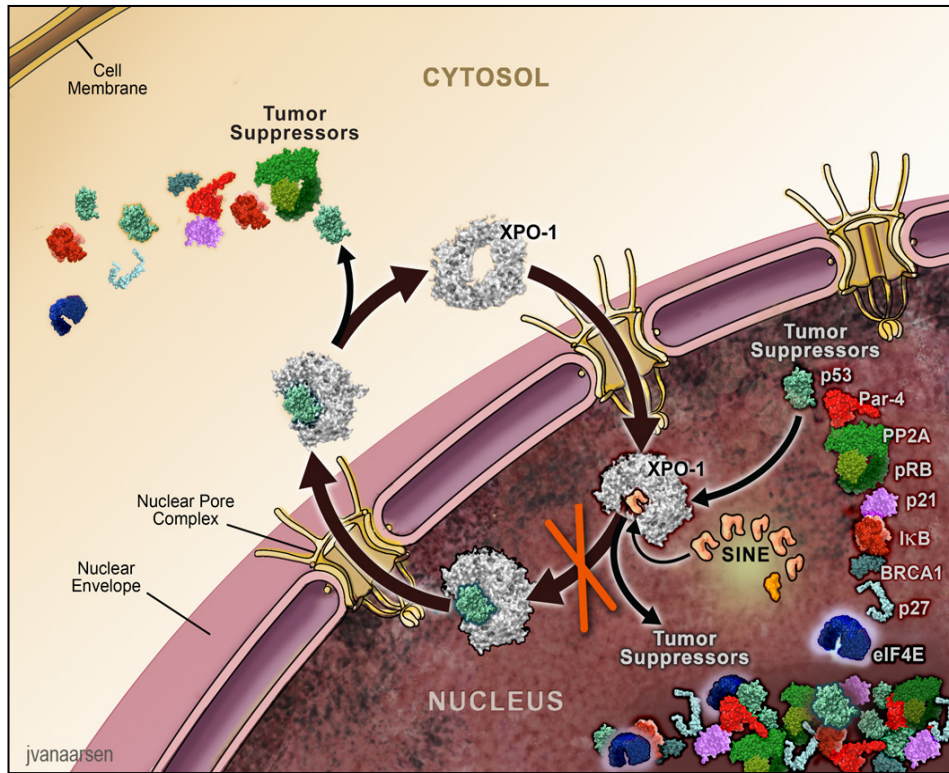
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Selinexor – Mechanism of Action



- Exportin 1 (XPO1) is the only nuclear exporter for the major tumor suppressor proteins (TSPs) including p53, p73, BRCA1 and pRB
- Selinexor, a first-in-class inhibitor of XPO1, induces nuclear retention, accumulation and activation of TSPs
- Reactivation of TSPs leads to tumor apoptosis
- Selinexor has shown preclinical activity in-vivo as well as clinical activity in a Phase I study in ovarian patients (*Razak et. al, JCO 2016*)

Selinexor In Gynecological Neoplasms (SIGN) – Phase II Study Design

- **Primary Endpoint:**
 - Disease control rate (DCR) *complete or partial response, or stable disease for at least 12 weeks (SD≥12)*
 - Looking for ≥ 8 patients in the first 21 patients enrolled per cohort to reach DCR, which will warrant Phase III exploration
- **Main Inclusion Criteria:**
 - Patients ≥18 years old, ECOG performance status 0-1, Life expectancy ≥12 weeks
 - Ovarian patients – Platinum refractory/resistant patients, ≥1 prior chemotherapy line
 - Endometrial/Cervical patients – ≥1 line of chemotherapy for relapsed or advanced disease
- **Treatment Scheme:** Twice Weekly (BIW) or Once Weekly Dosing (QW) / 28 day cycle

Ovarian Cohort

- 50 mg/m² (BIW)
- 35 mg/m² (BIW)
- 50 mg/m² (QW)

Endomet Cohort

- 50 mg/m² (BIW)

Cervical Cohort

- 50 mg/m² (BIW)



SIGN – Patient Characteristics

Characteristic	Ovarian (N=66)	Endometrial (N=23)	Cervical (N=25)
Patients Enrolled	66	23	25
Median Age (Range)	62 years (31 – 80)	67 years (53 – 75)	53 years (32 – 75)
Median Prior Treatment Regimens (Range)	6 (1 – 11)	2 (1 – 5)	3 (1 – 8)
Prior Treatments N (%)			
Platinums	66 (100%)	22 (96%)	25 (100%)
Taxanes	66 (100%)	23 (100%)	23 (92%)
Anthracyclines	55 (83%)	19 (83%)	2 (8%)



SIGN – Treatment Related Adverse Events ≥10 %

AE Term	Ovarian/Endometrial/Cervical 50 mg/m ² Twice Weekly			Ovarian – 35 mg/m ² Twice Weekly			Ovarian – 50 mg/m ² Once Weekly		
	N=73			N=21			N=20		
Gastrointestinal	Grade 2	Grade 3	Grade 4	Grade 2	Grade 3	Grade 4	Grade 2	Grade 3	Grade 4
Nausea	25 (34%)	9 (12%)	--	8 (38%)	--	--	10 (50%)	1 (5%)	--
Vomiting	16 (22%)	6 (8%)	--	3 (14%)	1 (5%)	--	6 (30%)	1 (5%)	--
Anorexia	19 (26%)	4 (6%)	--	6 (29%)	1 (5%)	--	6 (30%)	--	--
Dysgeusia	8 (11%)	--	--	--	--	--	1 (5%)	--	--
Diarrhea	7 (10%)	1 (1%)	--	2 (10%)	--	--	2 (10%)	--	--
Dehydration	--	2 (3%)	--	3 (14%)	--	--	--	--	--
Constitutional									
Fatigue	31 (43%)	11 (15%)	--	7 (33%)	5 (24%)	--	6 (30%)	1 (5%)	--
Weight Loss	15 (21%)	--	--	5 (24%)	1 (5%)	--	--	1 (5%)	--
Blood									
Thrombocytopenia	13 (18%)	17 (23%)	1 (1%)	2 (10%)	1 (5%)	--	1 (5%)	--	--
Anemia	21 (29%)	8 (11%)	--	6 (29%)	2 (10%)	--	3 (15%)	1 (5%)	--
Other									
Hyponatremia	--	6 (8%)	1 (1%)	--	1 (5%)	--	--	2 (10%)	--

- Grade 3-4 toxicities were reduced in the once weekly dosing (50 mg/m²) regimen as compared to twice weekly dosing



Primary Endpoint – Disease Control Rate ($CR + PR + SD \geq 12$ Weeks)

Cancer Type	Dose	N	DCR (%)	PR (%)
Ovarian	35 mg/m ² (BIW)	18	11 (61%)	2 (11%)
	50 mg/m ² (BIW)	22	10 (45%)	3 (14%)
	50 mg/m ² (QW)	19	8 (42%)	3 (16%)
	All Doses	59	29 (49%)	8 (14%)
Endometrial	50 mg/m ² (BIW)	20	9 (45%)	3 (15%)
Cervical	50 mg/m ² (BIW)	23	6 (26%)	1 (4%)

Responses were adjudicated according to the *Response Evaluation Criteria in Solid Tumors (RECIST v1.1)* based on interim unaudited data – DCR=Disease Control Rate (CR+PR+SD \geq 12)

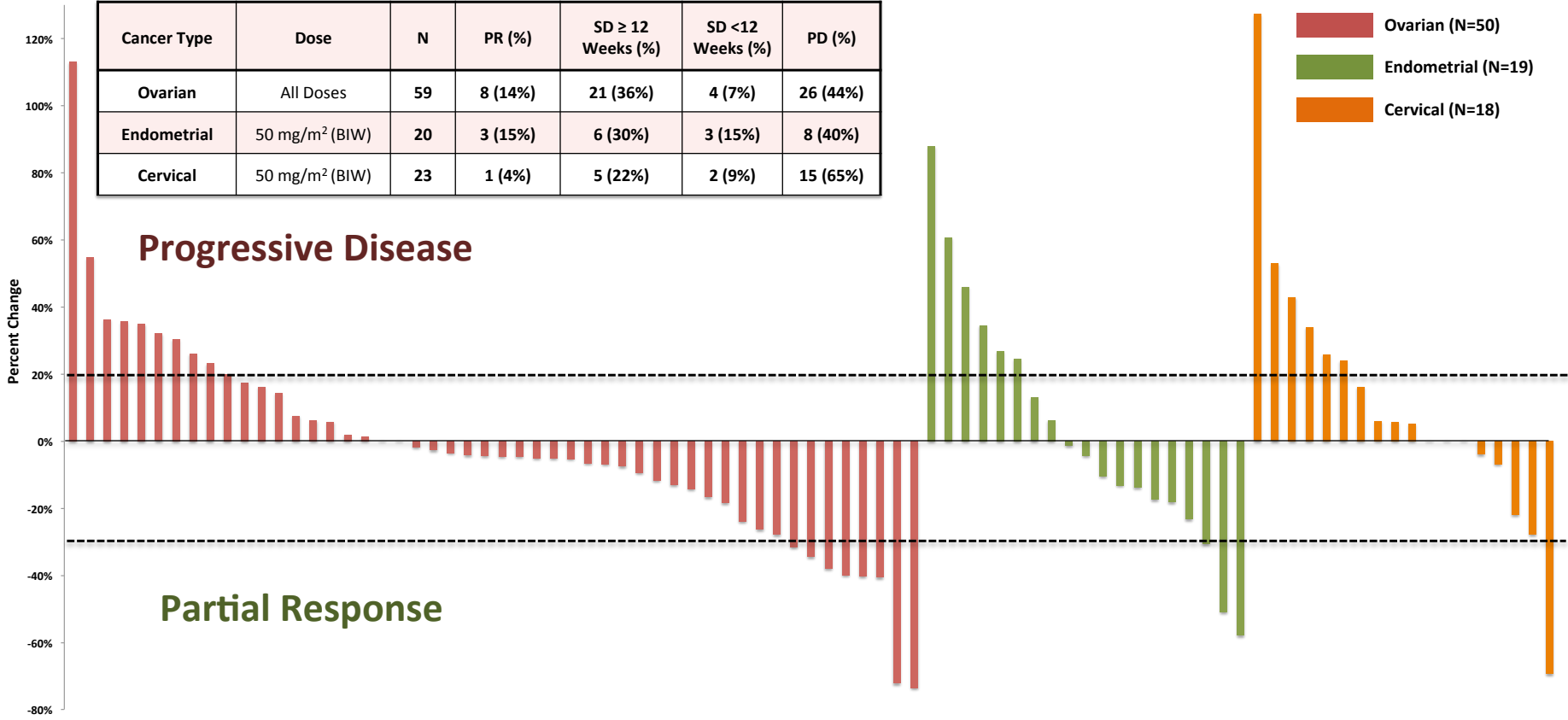


SIGN – Tumor Response

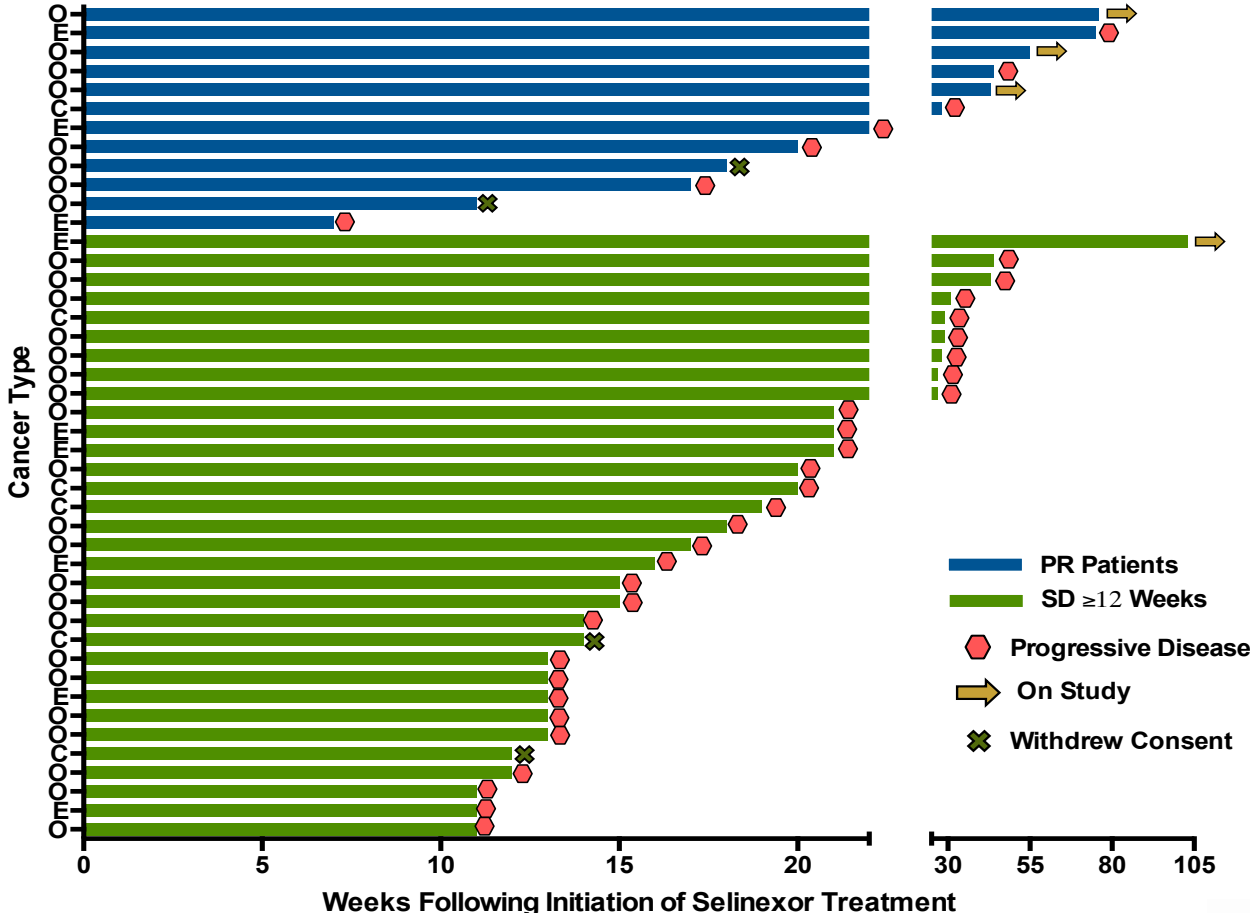
Percent Change in Target Lesions

Cancer Type	Dose	N	PR (%)	SD ≥ 12 Weeks (%)	SD <12 Weeks (%)	PD (%)
Ovarian	All Doses	59	8 (14%)	21 (36%)	4 (7%)	26 (44%)
Endometrial	50 mg/m ² (BIW)	20	3 (15%)	6 (30%)	3 (15%)	8 (40%)
Cervical	50 mg/m ² (BIW)	23	1 (4%)	5 (22%)	2 (9%)	15 (65%)

- Ovarian (N=50)
- Endometrial (N=19)
- Cervical (N=18)



DCR Patients Response & Time on Study



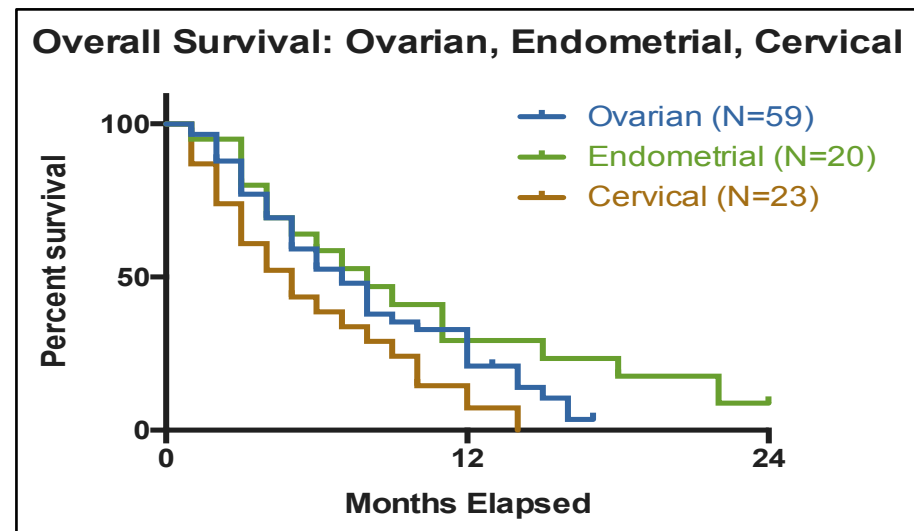
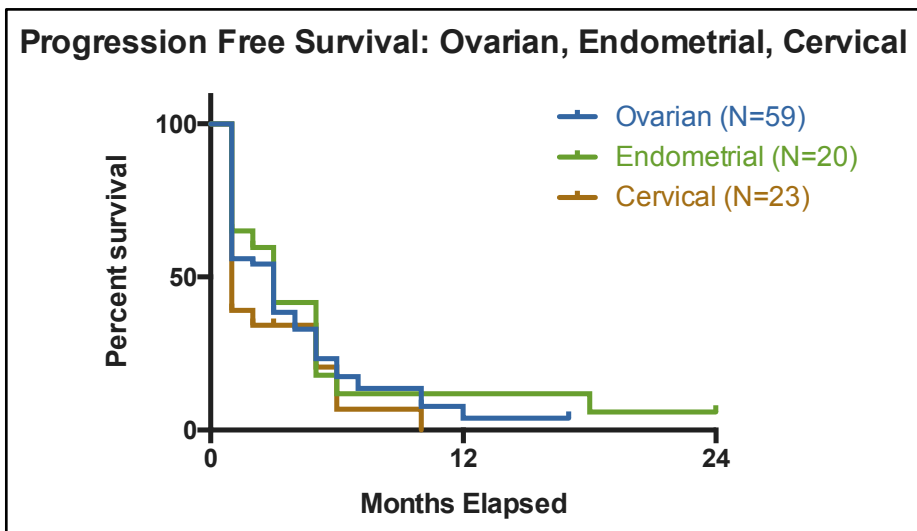
Disease Control Rate Patients – Time on Study

- For patients who met DCR (N=44), the median time on study was 20 weeks
- Four patients continue on treatment >40 weeks

PR=partial response, SD≥12 Weeks=stable disease ≥12 weeks, PD=progressive disease, WC=withdrew consent



SIGN – Progression Free Survival (PFS), Overall Survival (OS)



Median Progression Free Survival and Median Overall Survival

- Median PFS overall for the ovarian patients was **3** months, endometrial **3** months, and cervical **1** month
- Median OS overall for the ovarian patients was **7** months, endometrial **8** months, and cervical **5** months



SIGN – Conclusions

- Single agent selinexor has interesting anti-tumor activity in heavily-pretreated ovarian and endometrial cancer patients, with disease control for more than 12 weeks of 49% and 45% in the OC and EC cohort, respectively
- The main toxicities of Selinexor are nausea, anorexia, fatigue, and vomiting. These side effects are manageable with supportive care, especially in once weekly dosing (50 mg/m²)
 - Major organ toxicities are rarely observed
 - Clinically significant cumulative toxicities are uncommon
- Fifteen patients (13%) remained on single agent selinexor > 6 months, including 4 patients > 12 months
- Combination studies are ongoing & Phase III trials in OC & EC are being planned

