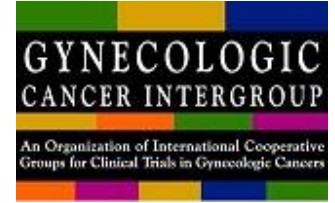




Ongoing Trials – status update

**ENGOT-EN5/SIENDO Selinexor
maintenance in advanced or recurrent
endometrial cancer**



ENGOT-EN5/SIENDO

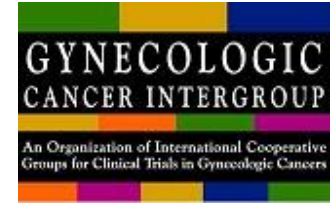
**A randomized phase III trial of maintenance
with **S**elinexor/placebo after **c**ombination
chemotherapy **I**n patients with advanced or
recurrent **ENDO**metrial cancer**

Sponsor: BGOG

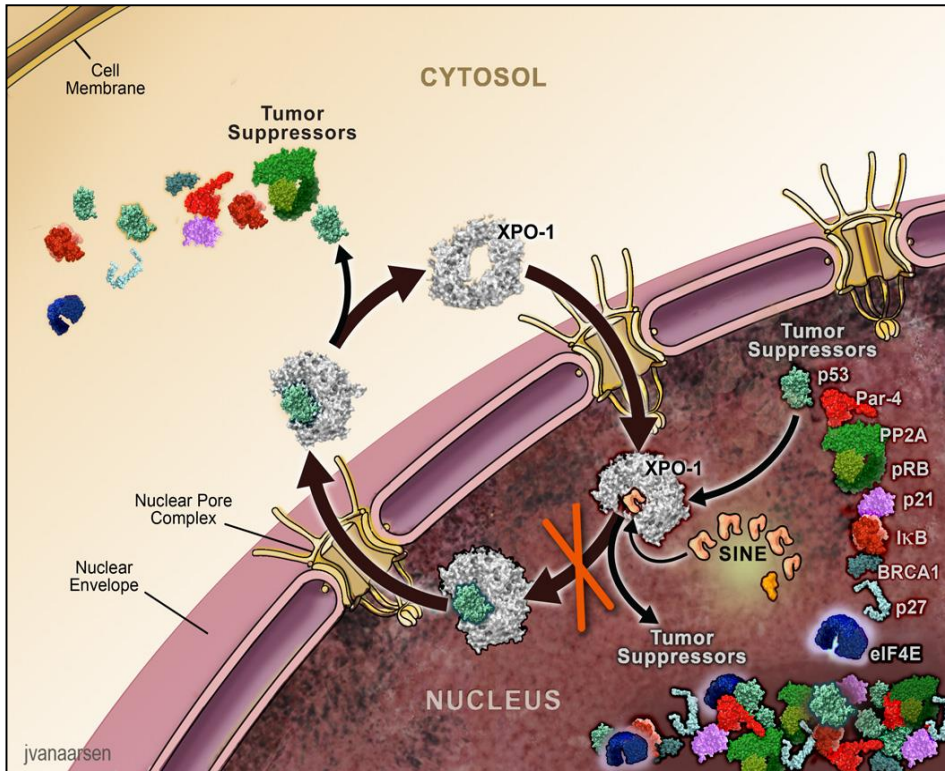


Ongoing Trials – status update

ENGOT-EN5/SIENDO Selinexor maintenance in advanced or recurrent endometrial cancer



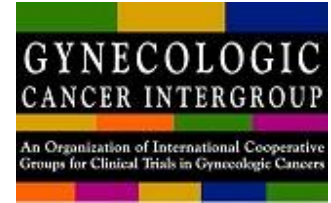
SELINEXOR – Mechanism of action



- **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**



SIGN study



Primary endpoint – Disease Control Rate (CR + PR + SD≥12 Weeks)

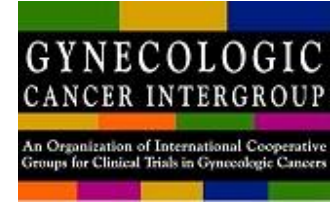
Cancer Type	Dose	N	DCR (%)	PR (%)
Ovarian	35 mg/m ² (BIW)	18	11 (61%)	2 (11%)
	50 mg/m ² (BIW)	22	10 (45%)	3 (14%)
	50 mg/m ² (QW)	19	8 (42%)	3 (16%)
	All Doses	59	29 (49%)	8 (14%)
Endometrial	50 mg/m ² (BIW)	20	9 (45%)	3 (15%)
Cervical	50 mg/m ² (BIW)	23	6 (26%)	1 (4%)

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≥12)



Ongoing Trials – status update

ENGOT-EN5/SIENDO Selinexor maintenance in advanced or recurrent endometrial cancer

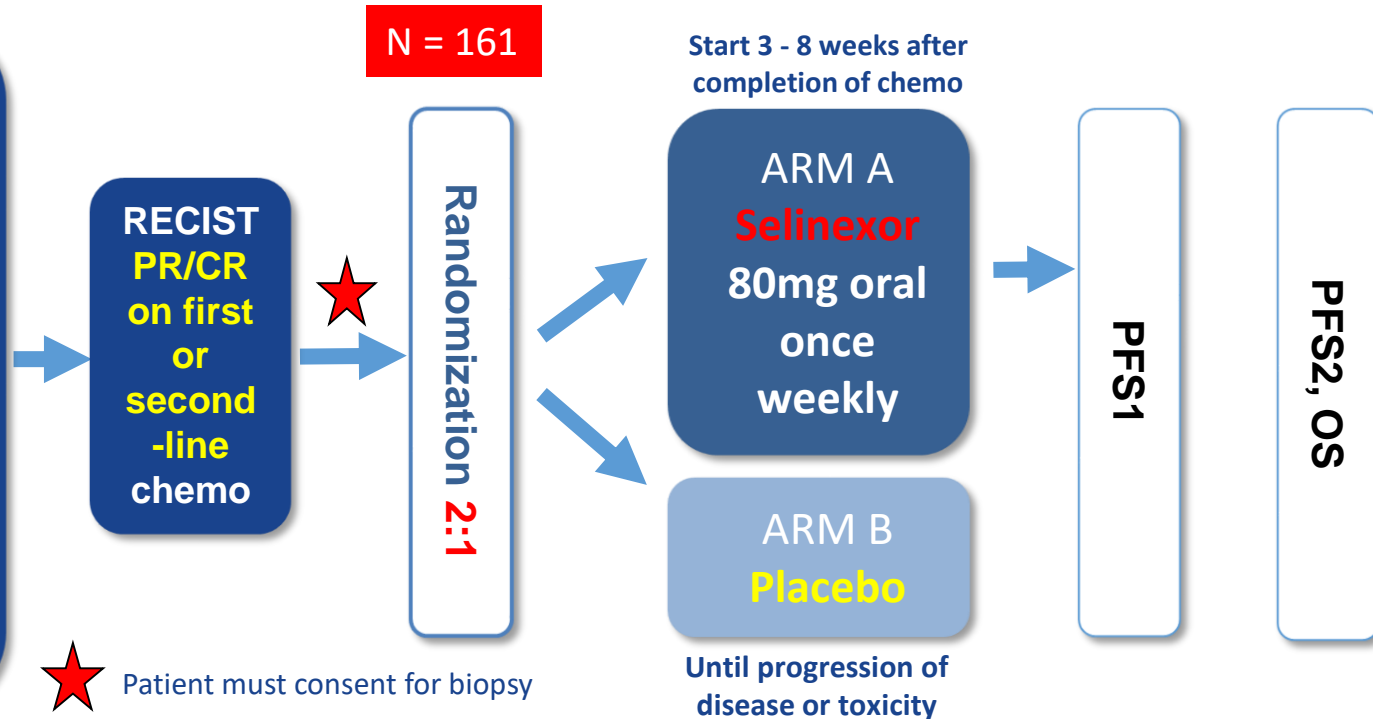


Advanced stage IV, or first/second relapse of endometrial cancer

Endometrioid, Serous, Undifferentiated or Carcinosarcoma

- Earlier (neo)adjuvant or first-line metastatic **Taxane-Carboplatin***, or
- If second line metastatic: again **Taxane-Carbo** or **Anthracycline-based***
- Prior adjuvant for stage I-III is **not counted** as a line of chemotherapy (except if relapse within 6 months after last adjuvant chemo course)
- Prior surgery, radiotherapy, or hormonal therapy allowed

* Chemo for at least 12 weeks



FPI: **expected Dec 2017** ; LPI: Q3 2018

Primary endpoint: **PFS** Secondary endpoint: OS, QOL, TTP, TFST, TSST, PFS2, TUDD, ORR, DOR, Toxicity

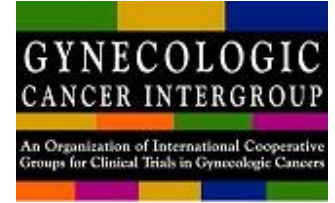
Stratification: a. 1 vs 2 prior lines b. PR vs CR

Capping: 2 prior lines will be capped at 50%



Ongoing Trials – status update

ENGOT-EN5/SIENDO Selinexor maintenance in advanced or recurrent endometrial cancer



STATISTICS

- Median PFS on standard treatment of **4.5 months**
- To be able to detect
 - an absolute difference of **3 months**,
 - **HR=0.60**,
 - with 80% power
 - at the two-sided 5% level,
- **129** events
- Accrual period 18 months followed by another 12 months of follow-up, then **153** eligible patients needed.
- Assuming a 5% drop-out rate the total accrual is **161**