PM1183-B-002-11 Study

Lurbinectedin (PM01183) activity in platinum-resistant/refractory ovarian cancer. Preliminary results of an ongoing Phase II study

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No Conflicts of Interest to declare

Ovarian Cancer
Platinum resistant/refractory disease (OPRRD)

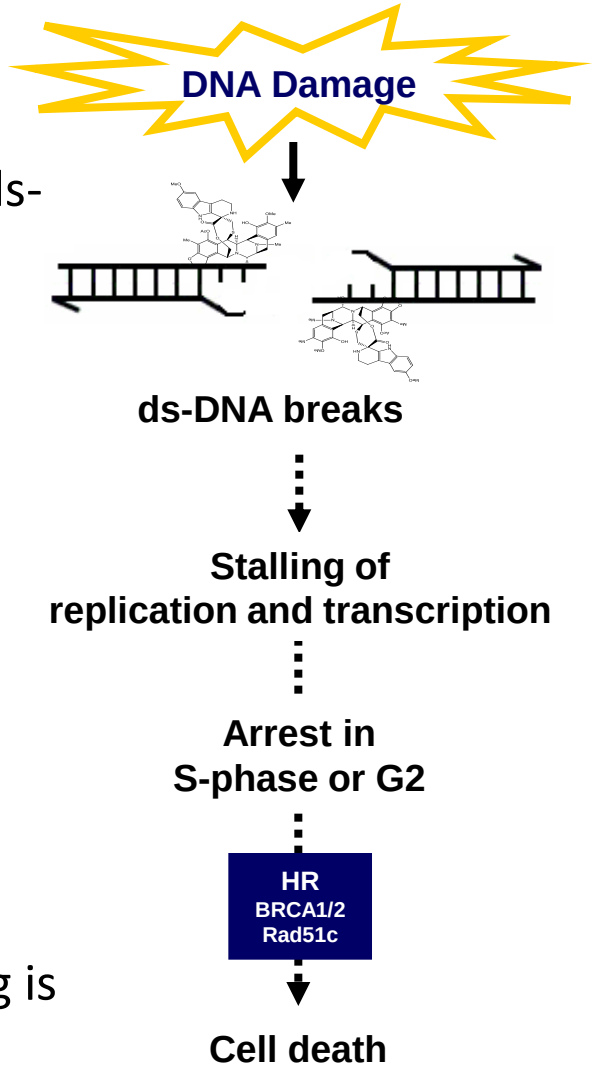
- At first relapse, ~30% of patients have OPRRD; though almost all recurrent ovarian cancer patients (pts) will ultimately develop platinum resistance

- Paclitaxel, PLD and topotecan are approved agents used in OPRRD
  - 10-15% of response
  - Progression-Free Survival (PFS) < 4 months (mo)
  - Median overall survival (OS) is usually < 12 mo

- Results combining any of these agents and an anti-VEGF have recently shown a significant PFS and response rate improvement (though OS data still immature)

Background

- PM01183 (lurbinectedin) is a new synthetic entity, belonging to the tetrahydroisoquinoline family
- It binds to the DNA minor groove inducing primarily ds-DNA breaks and transcription blockade
- Deficient homologous recombination system favors PM01183-induced apoptosis
- Broad antiproliferative activity *in vitro and in vivo* (orthotopic cisplatin resistant EOC*)
- Extensive liver microsomal metabolism
- PK in humans showed :
  - Linearity across the dose-range explored
  - Clearance did not correlate with BSA thus flat dosing is used



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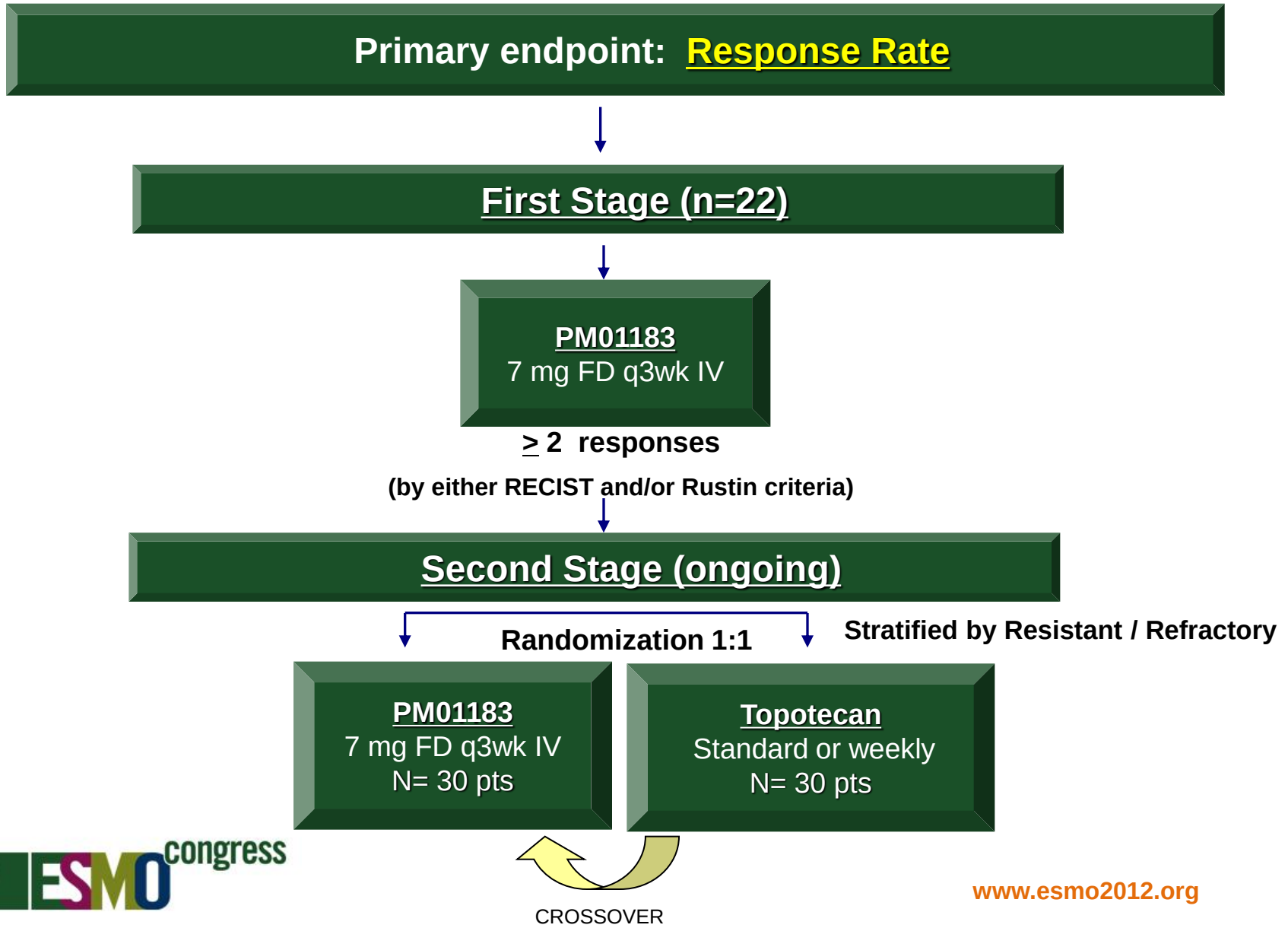
PM1183-B-002-11 - Study Design



PM1183-B-002-11
Main eligibility criteria

- Epithelial ovarian, fallopian tube or primary peritoneal cancer
- Locally advanced or metastatic
- Measurable disease (either RECIST v1.1 or GCIG)
- Platinum-resistant/refractory disease
  - Resistant: relapse < 6 mo after last platinum-containing chemotherapy
  - Refractory: did not respond during last platinum-containing chemotherapy
- Less than 3 prior lines of chemotherapy for advanced disease
- ECOG-PS 0-2
- No prior topotecan

First Stage: Patient Characteristics

PM01183 treated patients		**22**
Median Age (range)		**59 (35-77)**
ECOG PS	0/ 1/ 2	**9 (41%) / 12 (55%) / 1 (4%)**
Main primary site/Histology	Ovarian / Serous	**17 (77%) / 16 (73%)**
# prior lines in adv disease	1 / 2	**12 (55%) / 10 (45%)**
Platinum Status	Resistant Refractory	**16 (73%)** **6 (27%)**
Median Platinum Free Interval (mo) **- PFI < 3 mo** **- PFI 3-6 mo**		**3.8** **32%** **68%**
RECIST v1.1 measurable		**18 (82%)**
Median CA-125 at study entry (U/ml) **Range**		**326** **13-3860**

First Stage: Efficacy (n=22)

Median administered cycles (range)*	**5 (1-10+)**
Overall Response Rate RECIST v1.1 **and/or Rustin**	**6 (27%)** **95%CI (11-50%)**
Evaluable pts as per RECIST v1.1 ** (n=18)	4 (22%)
Disease Control Rate (PR / SD)	**16 (73%)** **95%CI (50-89%)**
Median PFS (mo)	**4.0** **95%CI (1.4-5.1)**

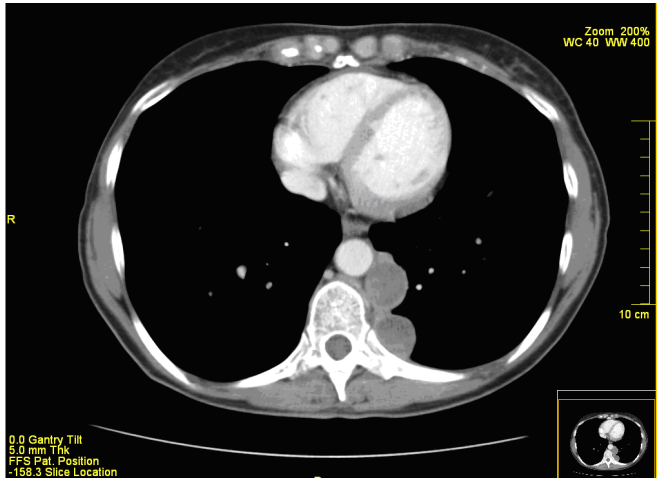
*2 pts still ongoing
** One complete radiological response

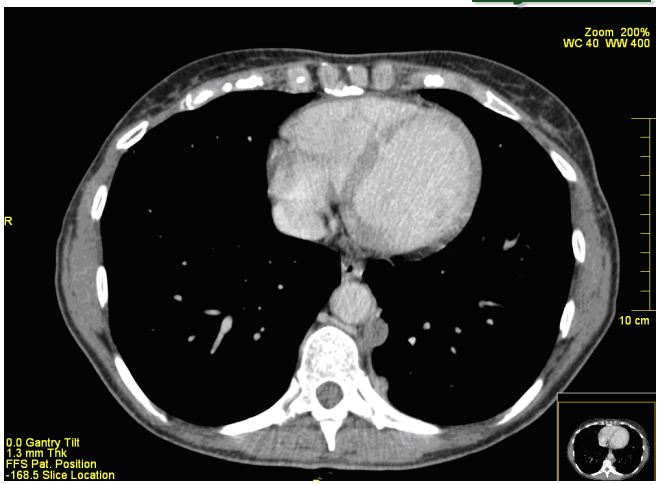
First Stage: Efficacy

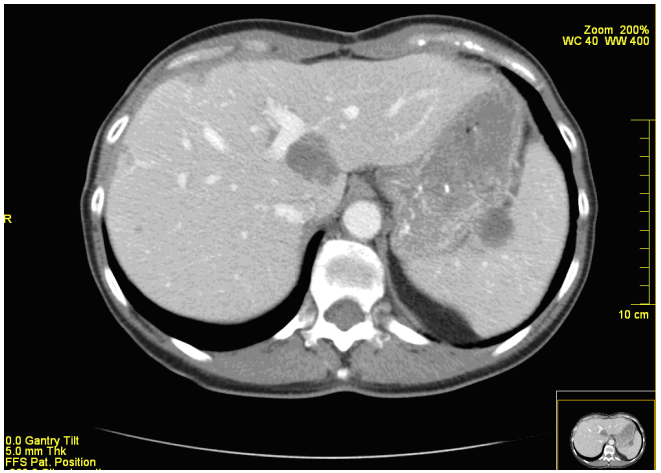
58 y old, locally advanced endometrioid ovarian cancer, multiple visceral and serosal metastases.
After relapse (PFI: 3.3 mo) received paclitaxel, best response PD.
Completed 7 cycles with PM01183, best response PR.

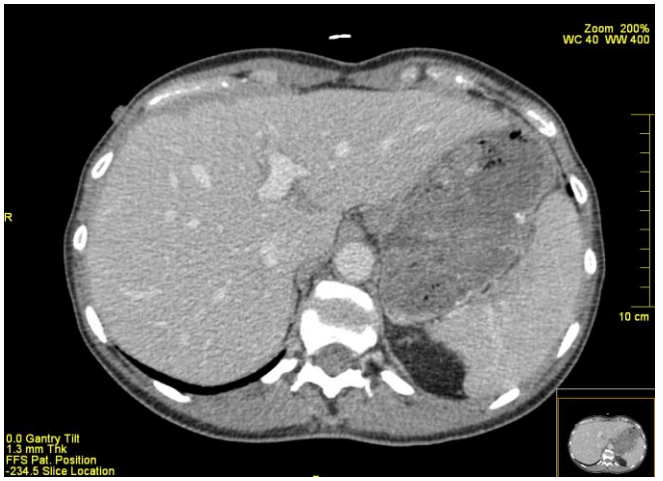
Baseline

Cycle 4









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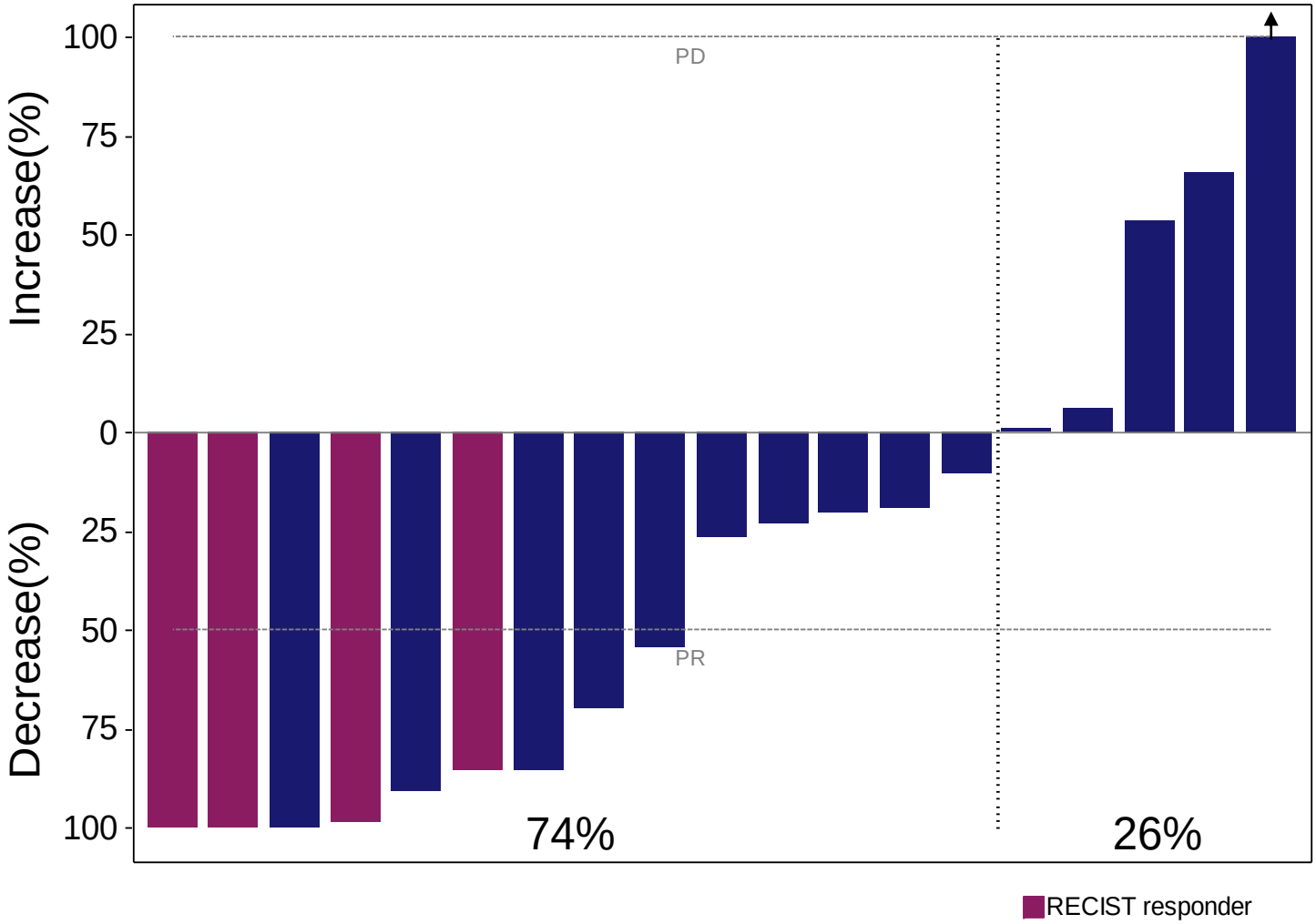
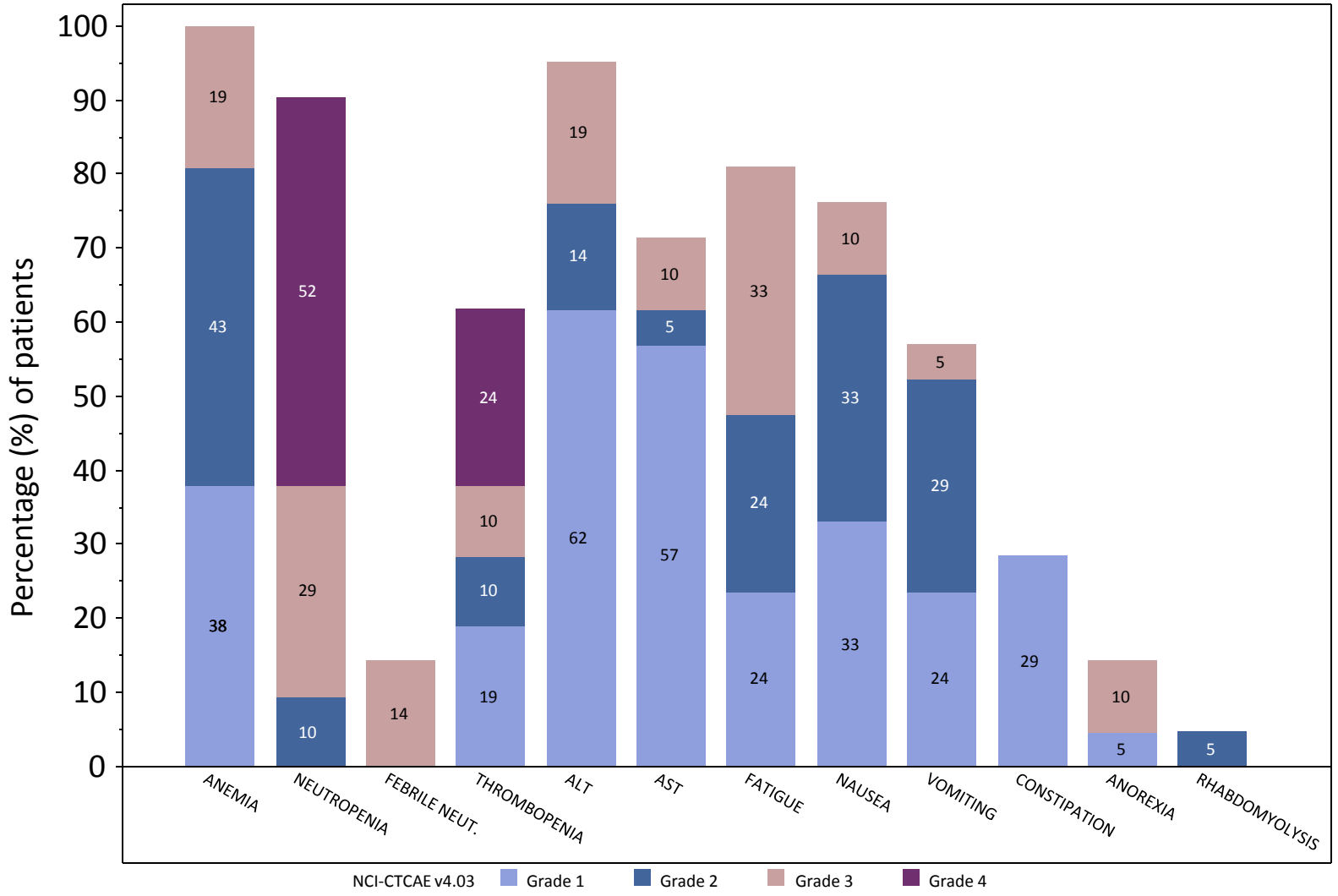
Maximum variation of CA-125 (N=19)*



*Patients with abnormally elevated CA-125 levels at baseline. Patients with value normalized (<35 UI/ml) in treatment, imputed as 100% decrease

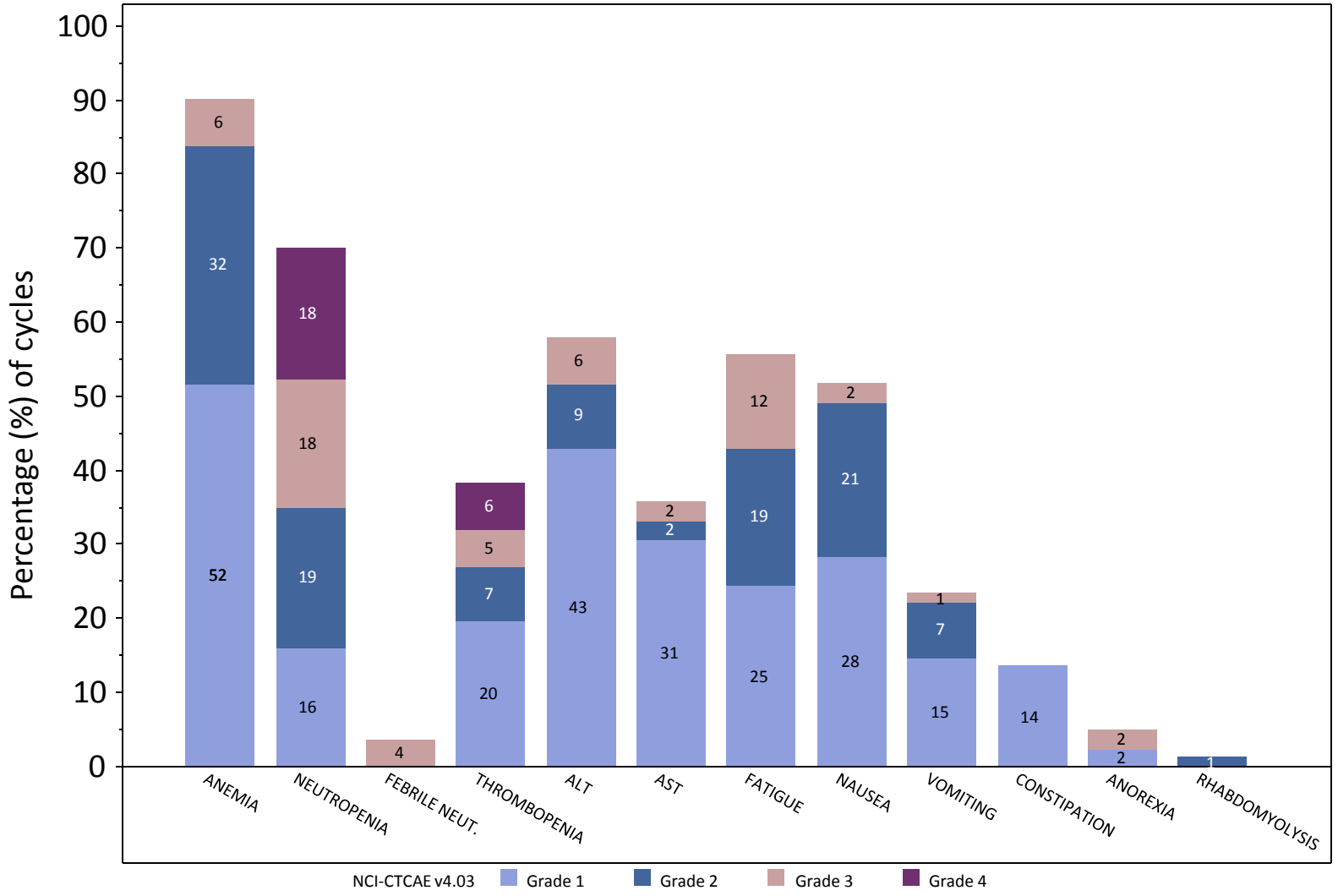
First stage safety

worst grade per patient (n=21)



First stage safety

worst grade per cycle (n=81)



Second Stage (ongoing)
Patient Characteristics
n=22 (60 are planned)

Characteristic		PM01183 (n=11)	Topotecan (n=11)
Median Age (range)		58 (40-80)	58 (37-73)
ECOG PS 0-1		11	11
Main primary site/Histology	Ovarian/serous	10/10	7/7
# prior lines in advanced disease	1 2	9 2	10 0
Platinum Status	Resistant Refractory	6 5	7 4
Median Platinum Free Interval (mo)		3.2	2.8
RECIST v1.1 measurable		10	9
Median CA-125 at study entry (U/ml) Range		229 10-657	157 11-2002

Summary

- PM01183, in resistant/refractory OC pts is active
- The toxicity is manageable
  - non cumulative hematological toxicity is the most common feature
- The randomized 2nd stage is ongoing to confirm these promising results
- PGx evaluations are being performed to identify potential biomarkers

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