Phase 2 Study of NKTR-102 in Women with Platinum-Resistant/ Refractory Ovarian Cancer

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Disclosure

None of the authors have any commercial relationships to disclose in relationship to this study except D. Maslyar who was employed by Nektar Therapeutics

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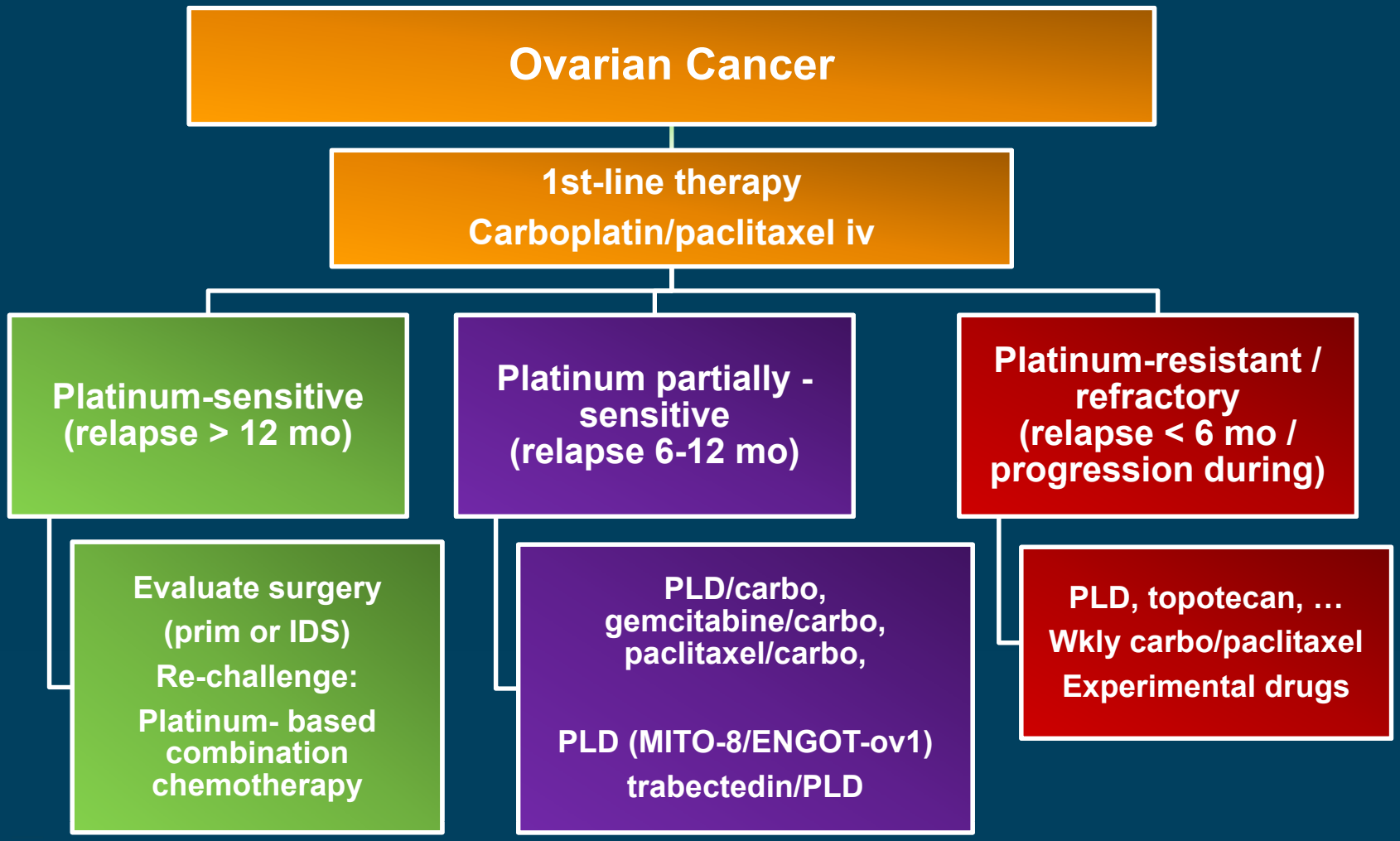
Ovarian Cancer Treatment Algorithm



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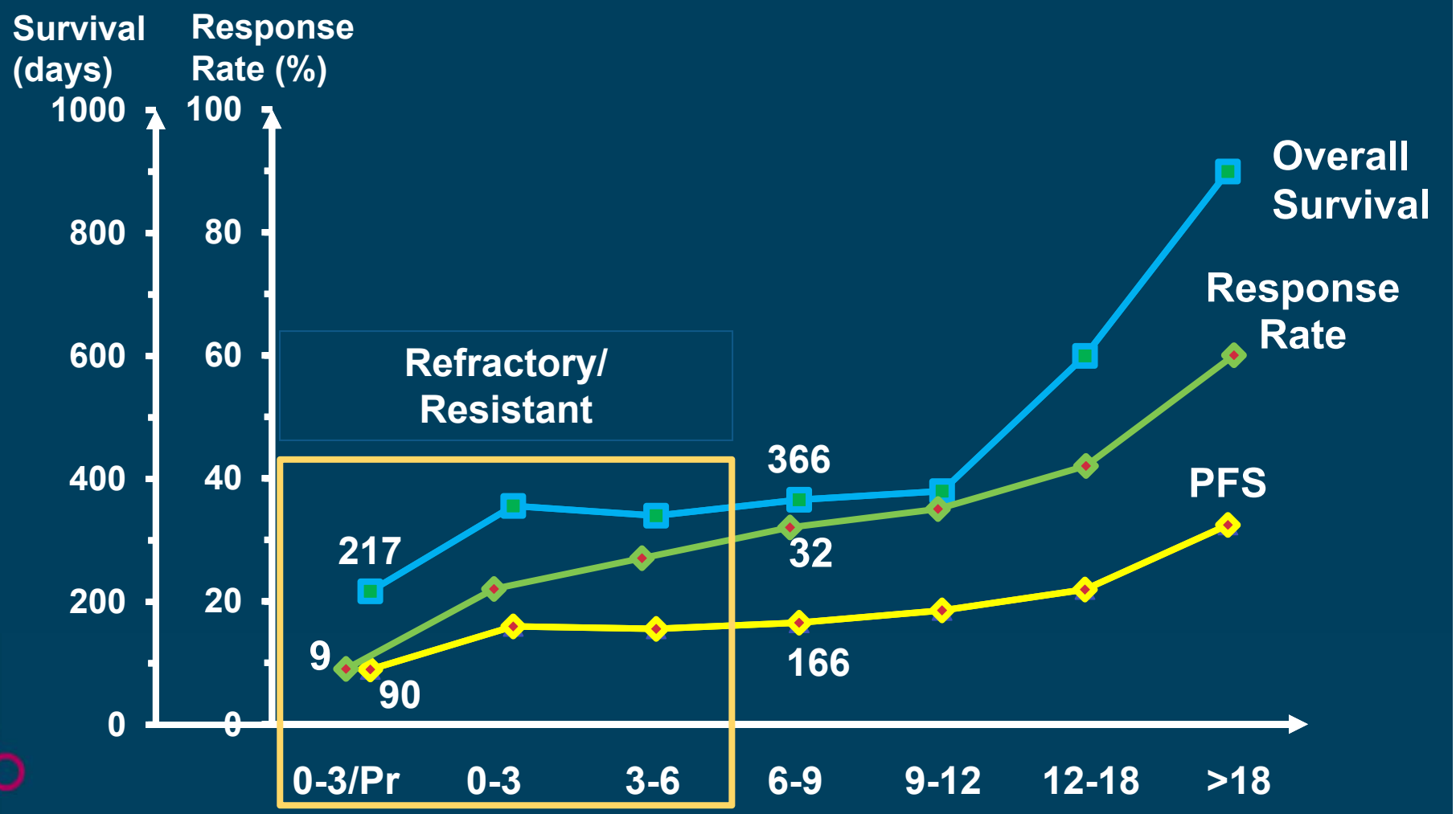
Vergote I , 2009, adapted from the NICE Guidelines

Analysis of GINECO Studies

Therapy-Free Interval and Efficacy



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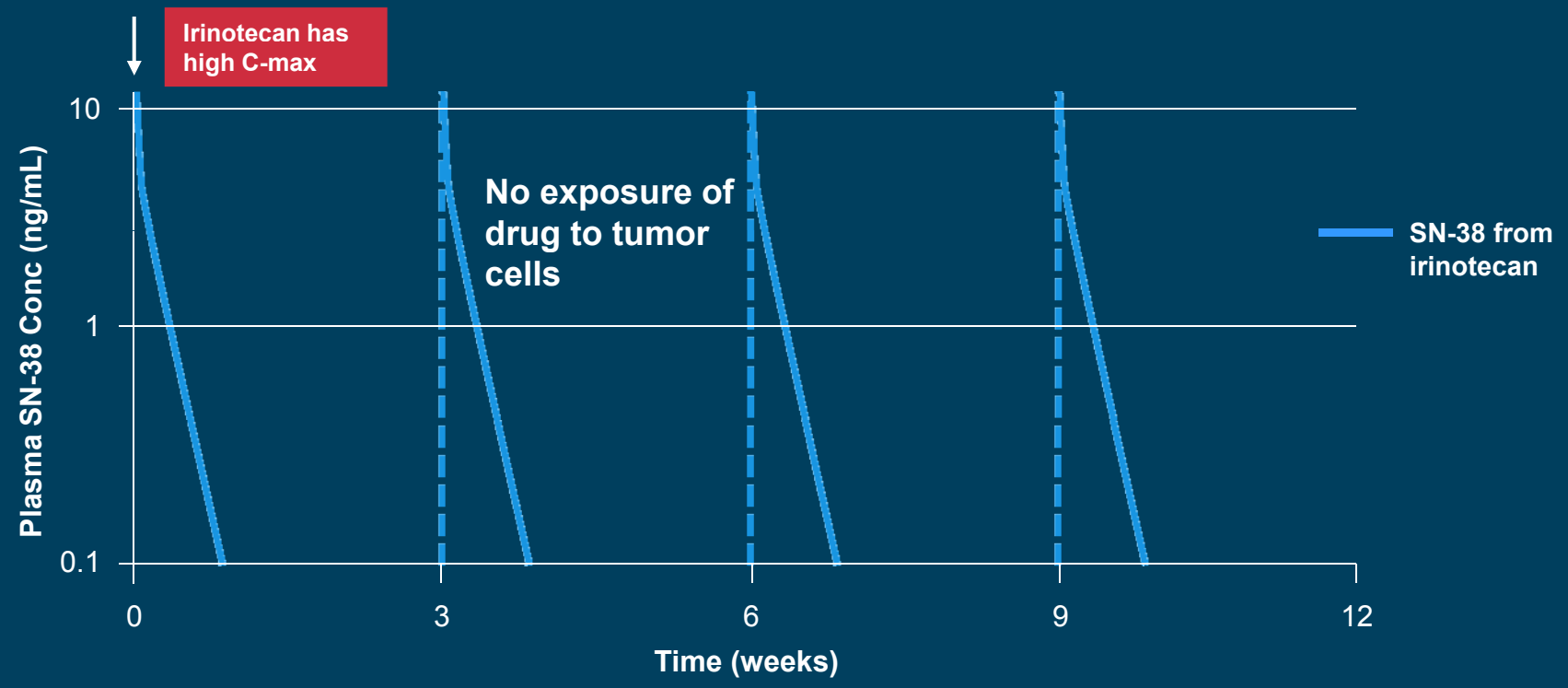
Pujade-Lauraine E, et al. *Proc Am Soc Clin Oncol.* 2002;21: Abstract 829.

NKTR-102: Topoisomerase I inhibitor (irinotecan)-polymer conjugate



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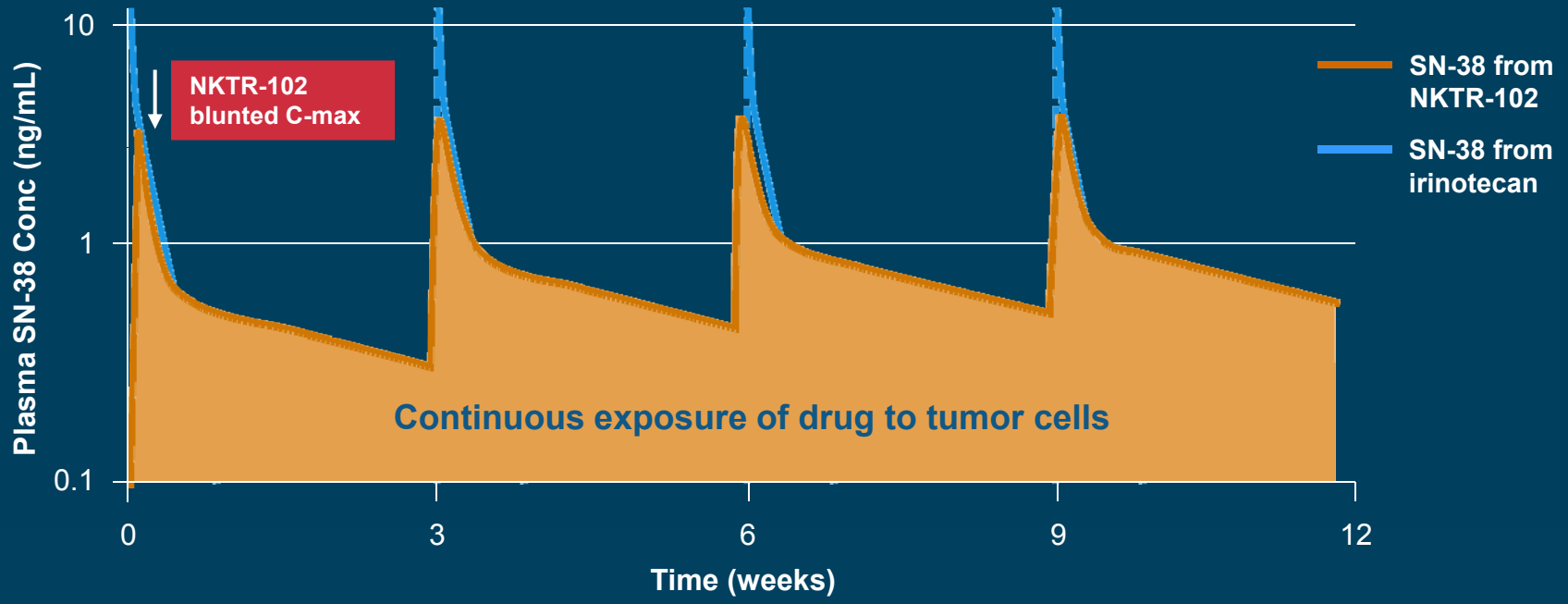
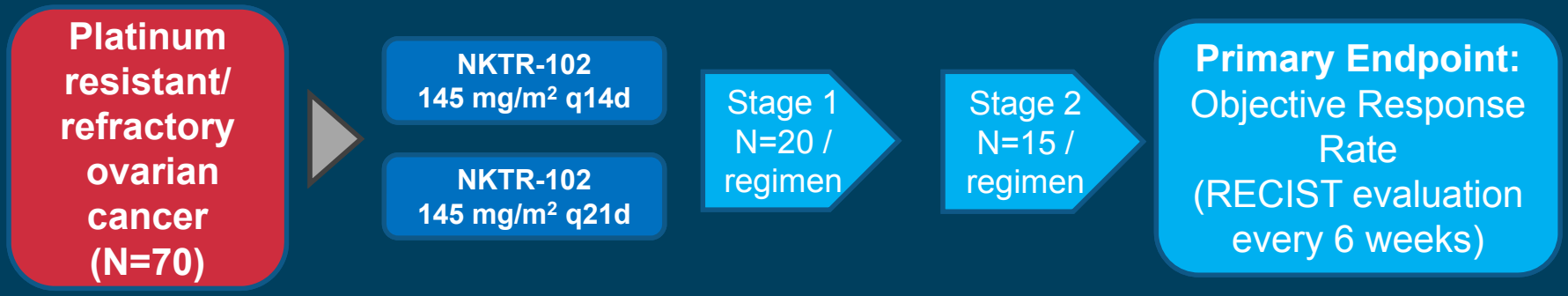
NKTR-102: Topoisomerase I inhibitor (irinotecan)-polymer conjugate

- NKTR-102 extends half-life of active metabolite to ~50 days (normally ~2 days)
- Continuous long-term exposure with markedly reduced peak concentration



Phase 1 data demonstrated significant anti-tumor activity in patients with refractory solid tumors (RECIST confirmed response rate 11%)

Study 08-PIR-04 Design: Two-Stage



Statistical Hypotheses: 2-stage design (with power of 0.85 for a RR of 20% and with alpha of 0.03 for RR of 5%

Stage 1: If ≥ 1 patient responds, that treatment regimen proceeds to the next stage

Stage 2: An additional 15 are patients enrolled

If ≥ 5 patients respond out of 35 patients (Stage 1 and Stage 2 combined), the drug has met the efficacy threshold.

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Inclusion Criteria and Objectives

Key Inclusion / Exclusion Criteria

- Ovarian, fallopian, or primary peritoneal carcinoma
- Platinum resistant or refractory disease to any line of platinum-based chemotherapy (platinum-free interval less than 6 months)
- Evaluable disease by RECIST or CA-125
- No prior treatment with topotecan or irinotecan

Key Objectives

- Objective Response Rate (RECIST and GCIG response criteria [i.e., combines RECIST and CA-125])
- Safety

Demographics (1)

	NKTR-102 145 mg/m^2 q14d (N = 36)	NKTR-102 145 mg/m^2 q21d (N = 35)	Total (N = 71)
Age			
Median (range)	60 (42,83)	63 (26,80)	61 (26,83)
≥ 65	33%	46%	39%
ECOG PS			
0	50%	54%	52%
1	50%	46%	48%
Measurable disease	97%	91%	94%
CA125 evaluable	86%	83%	85%
Histological Subtype			
Serous	89%	83%	86%
Clear Cell	6%	0	3%
Mucinous	0	6%	3%
Endometrioid	0	6%	3%
Other	6%	6%	6%

All data presented herein from the May 15, 2010 data capture

Demographics (2)

	NKTR-102 145 mg/m^2 q14d (N = 36)	NKTR-102 145 mg/m^2 q21d (N = 35)	Total (N = 71)
Platinum-Free Interval*			
<1 month (refractory)	39%	57%	48%
1-3 months (resistant)	17%	23%	20%
3-6 months (resistant)	39%	17%	28%
> 6 months (platinum sensitive)**	6%*	3%*	4%*
Previous Platinum Regimens			
1	33%	31%	32%
2	44%	40%	42%
3	17%	14%	16%
4+	6%	14%	10%
Prior Lines of Therapy (median)	3	3	3
Prior PLD	44%	49%	47%
Prior bevacizumab	11%	14%	13%
Prior gemcitabine	39%	46%	42%
Prior taxane	97%	94%	96%

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* From date of last dose of platinum to progression

**These patients not included in following efficacy tables

Objective Response Rates
(Platinum Resistant / Refractory Patients)

	NKTR-102 145 mg/m^2 q14d	NKTR-102 145 mg/m^2 q21d
RECIST		
N (evaluable)	33	31
Confirmed + Unconfirmed	8 (24%)	9 (29%)
Confirmed	7 (21%)	7 (23%)
GCIG		
N (evaluable)	34	34
Confirmed + Unconfirmed	14 (41%)	14 (41%)
Confirmed	10 (29%)	13 (38%)
CA-125		
N (evaluable)	29	29
Confirmed	11 (38%)	11 (38%)
Clinical Benefit (CR+PR+[SD≥3 months])		
N (evaluable)	33	31
Confirmed RECIST	17 (52%)	14 (45%)

ORR by Platinum Free-Interval
(From date of last dose of platinum to progression)

	NKTR-102 145 mg/m^2 q14d			NKTR-102 145 mg/m^2 q21d		
	PFI ≤ 1 month (refractory)	PFI ≤ 3 months	PFI 1-6 months	PFI ≤ 1 month (refractory)	PFI ≤ 3 months	PFI 1-6 months
RECIST						
N (evaluable)	14	19	19	18	25	13
Conf + Unconf	0	4(21%)	8 (42%)	4 (22%)	5 (20%)	5 (39%)
Confirmed	0	3 (16%)	7 (37%)	3 (17%)	4 (16%)	4 (31%)
GCIG						
N (evaluable)	14	20	20	20	28	14
Conf + Unconf	4 (29%)	8 (40%)	10 (50%)	7 (35%)	10 (36%)	7 (50%)
Confirmed	1 (7%)	5 (25%)	9 (45%)	7 (35%)	10 (36%)	6(43%)

ORR by Prior Lines of Platinum
(Platinum Resistant / Refractory Patients)

Prior Platinum Lines		NKTR-102 145 mg/m^2 q14d	NKTR-102 145 mg/m^2 q21d
1	RECIST N (evaluable) Confirmed + Unconfirmed Confirmed	 11 2 (18%) 1 (9%)	 10 3 (30%) 2 (20%)
2	RECIST N (evaluable) Confirmed + Unconfirmed Confirmed	 16 4 (25%) 4 (25%)	 12 3 (25%) 3 (25%)
3+	RECIST N (evaluable) Confirmed + Unconfirmed Confirmed	 6 2 (33%) 2 (33%)	 9 3 (33%) 2 (22%)

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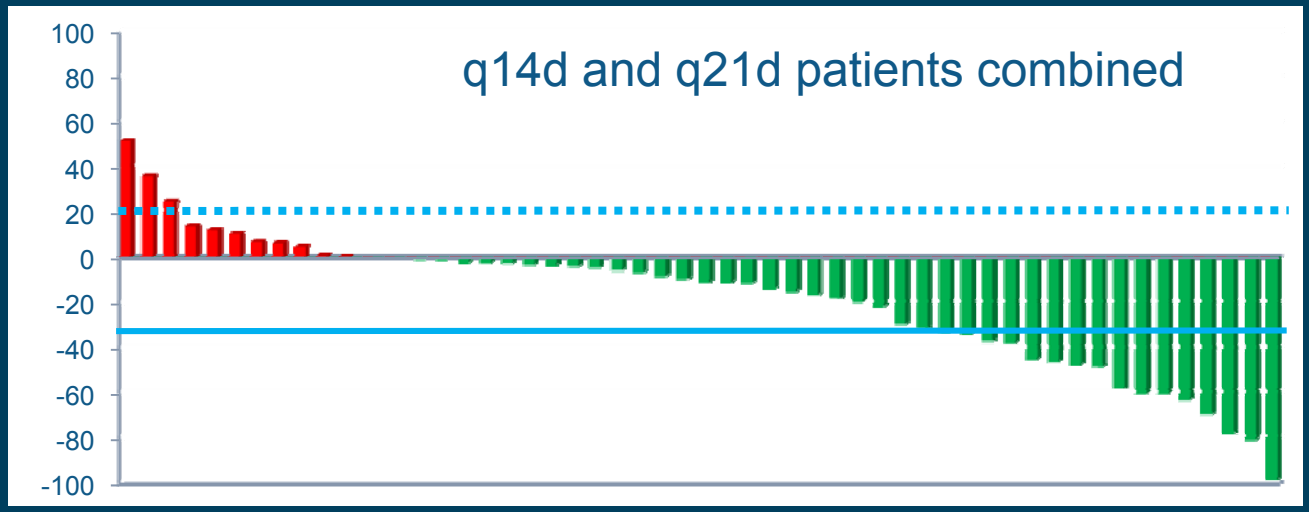
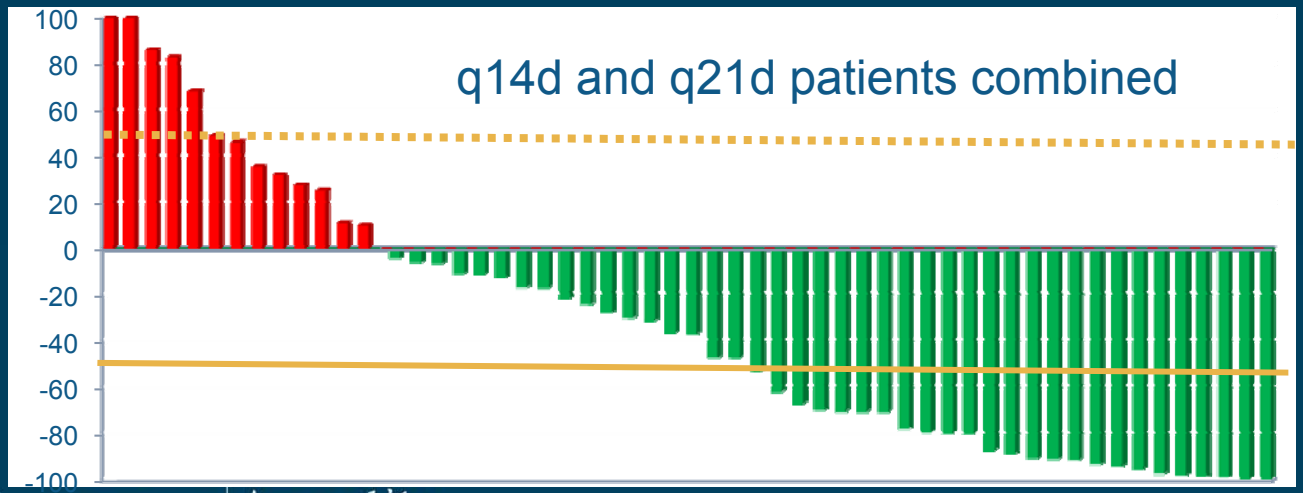
ORR by Prior PLD
(Platinum Resistant / Refractory Patients)

		NKTR-102 145 mg/m^2 q14d	NKTR-102 145 mg/m^2 q21d
Prior PLD	RECIST		
	N (evaluable)	15	14
	Confirmed + Unconfirmed	4 (27%)	6 (43%)
	Confirmed	3 (20%)	4 (29%)
No Prior PLD	RECIST		
	N (evaluable)	18	17
	Confirmed + Unconfirmed	4 (22%)	3 (18%)
	Confirmed	4 (22%)	3 (18%)

Maximum Decline by RECIST or CA-125





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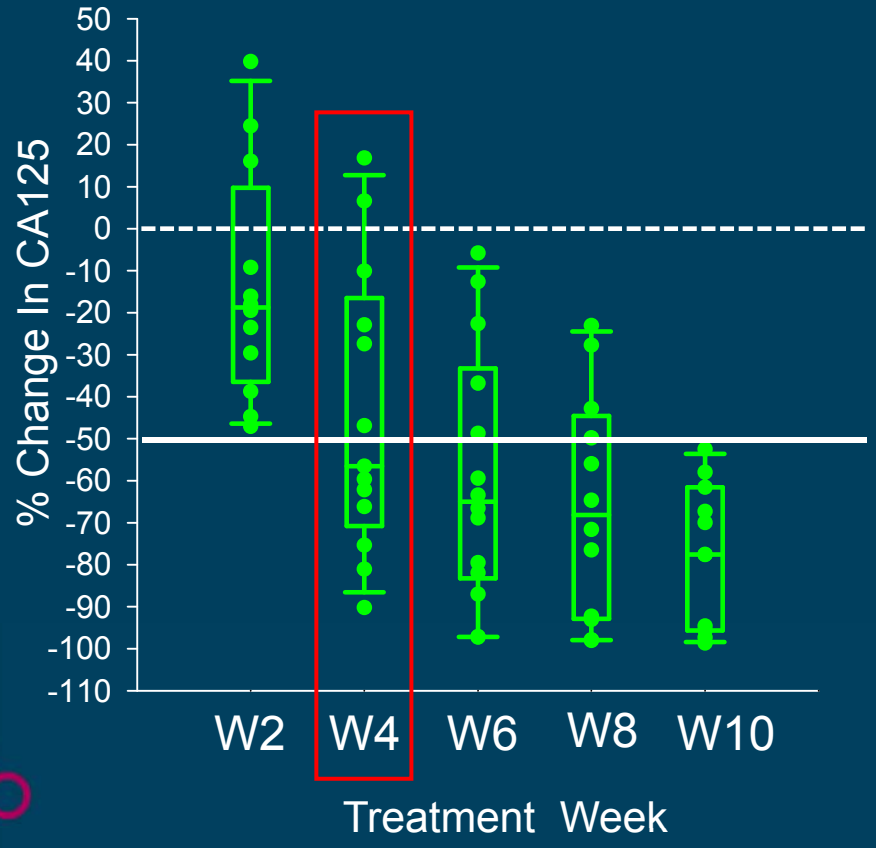
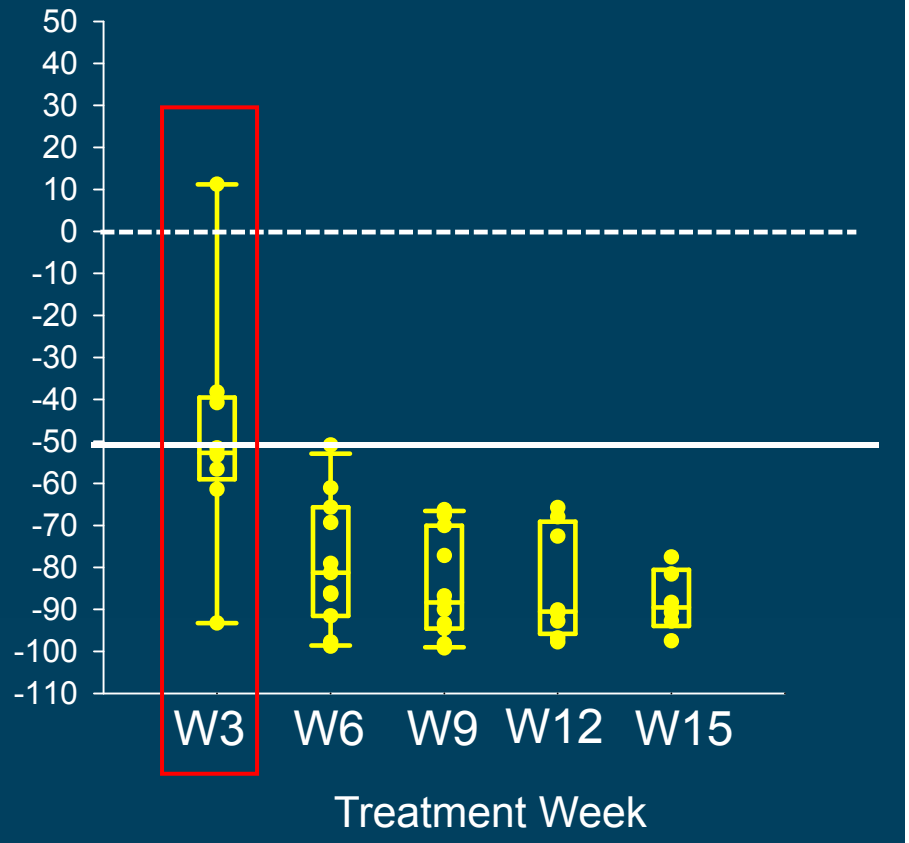
Platinum Resistant / Refractory Patients

Rapid Decline for CA-125 Responders
(Platinum Resistant / Refractory Patients)

145 mg/m² q14d Schedule



145 mg/m² q21d Schedule



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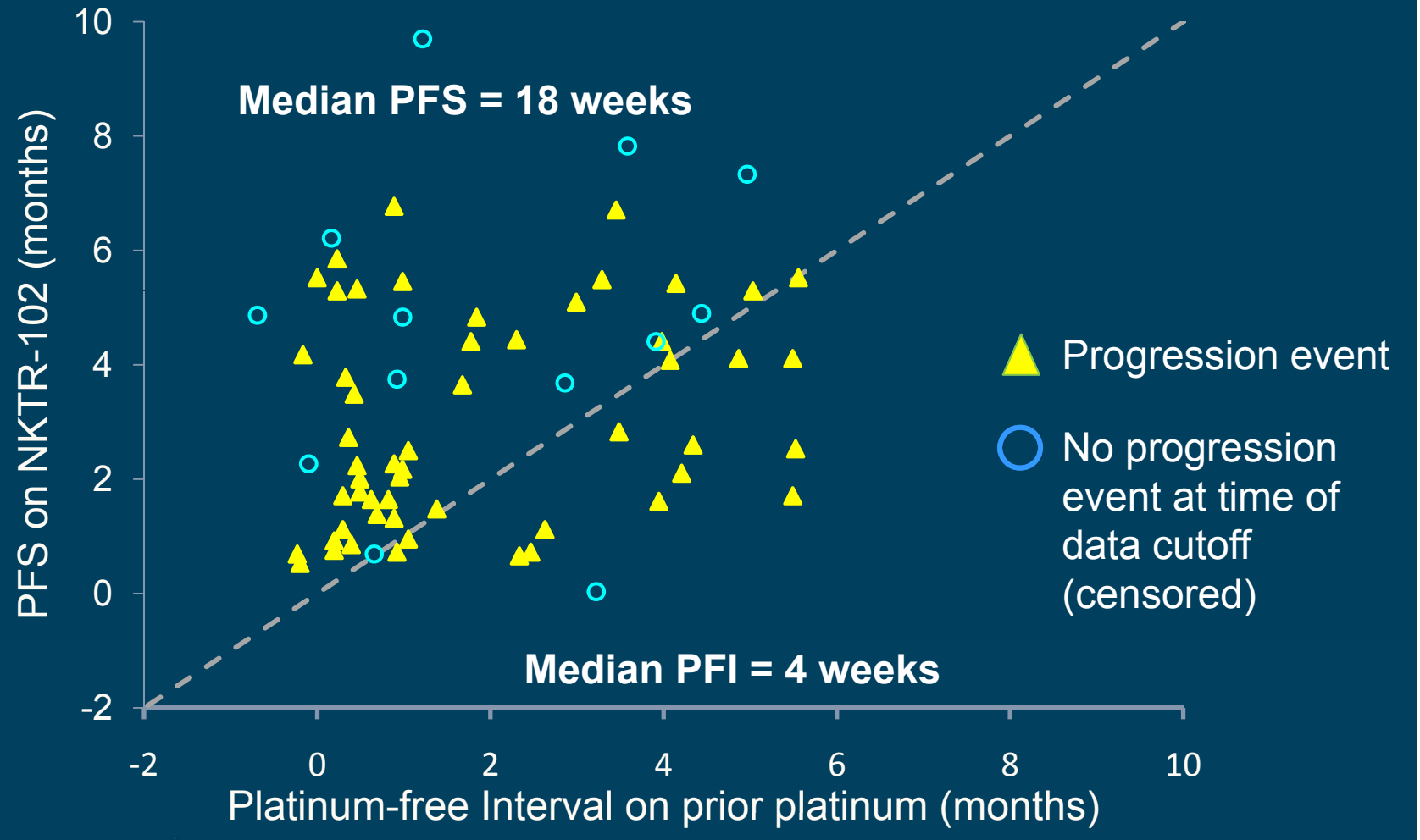
PFS on NKTR-102 versus Prior PFI
(All Platinum Resistant / Refractory Patients)



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NKTR-102 Safety Profile: All Patients

Most Common* Drug-related Grade 3 and 4 AEs *>5% overall	NKTR-102 145 mg/m^2 q14d (N = 36)		NKTR-102 145 mg/m^2 q21d (N = 35)	
	Grade 3	Grade 4	Grade 3	Grade 4
Diarrhea	25%	0%	14%	0%
Dehydration	22%	0%	6%	0%
Hypokalemia	17%	3%	9%	0%
Fatigue	6%	0%	14%	0%
Nausea	14%	0%	3%	0%
Vomiting	11%	0%	3%	0%
Abdominal pain	6%	0%	6%	0%
Hyponatremia	8%	0%	3%	0%
Neutropenia	6%	0%	6%	3%

Two NKTR-102 related deaths:
q14d: acute renal failure
q21d: neutropenic sepsis

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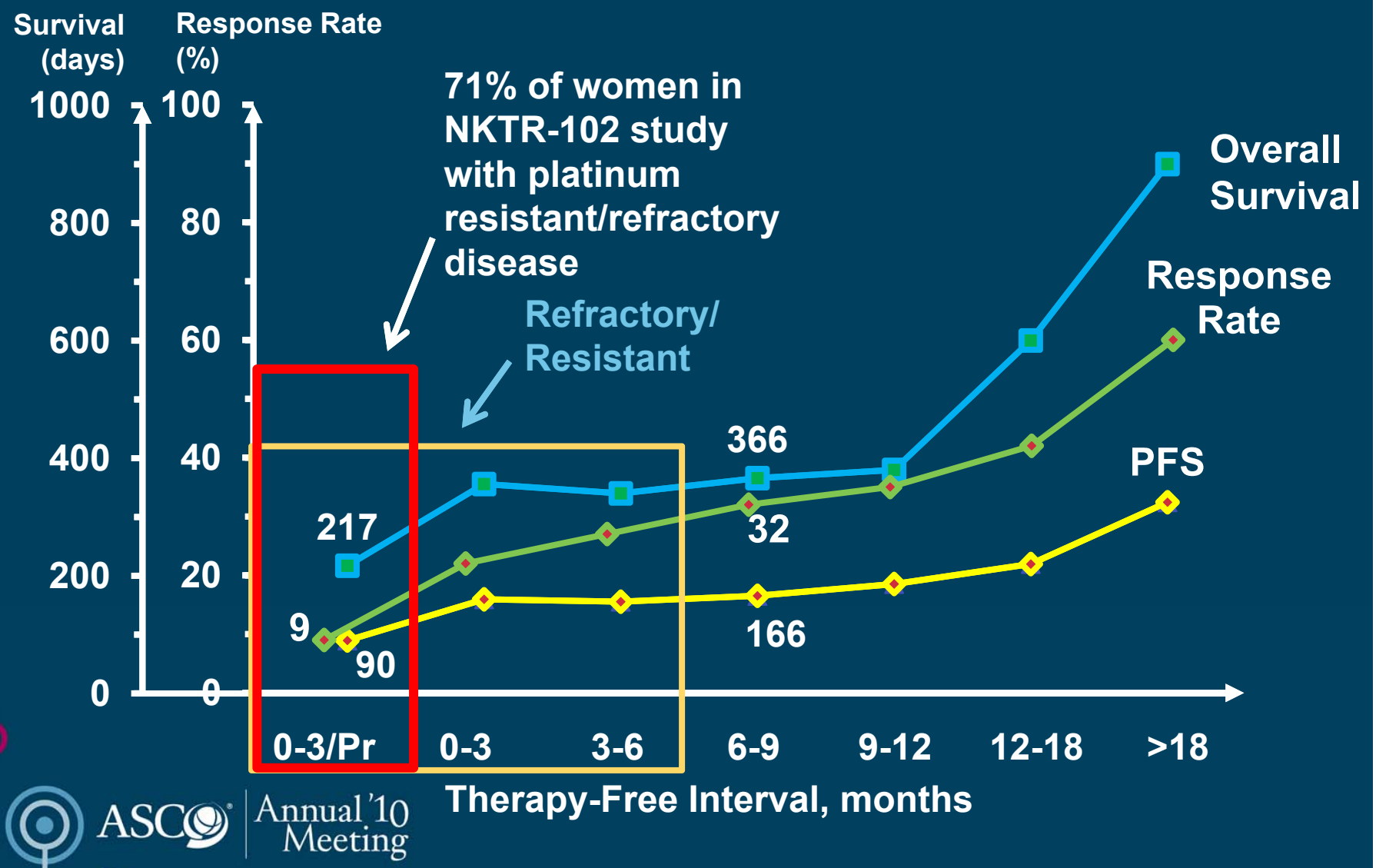
Conclusions



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Pujade-Lauraine E, et al. *Proc Am Soc Clin Oncol.* 2002;21: Abstract 829.

Conclusions

- NKTR-102 is well tolerated, especially with the q21d regimen
  - Due to a better toxicity profile, q21d is the preferred regimen for Phase 3
- NKTR-102 has a notably higher than expected objective response rate in this group of heavily pretreated platinum resistant / refractory ovarian cancer patients
  - Median 4th line treatment
  - 57% platinum refractory in q21d regimen
  - Confirmed RECIST/GCIG response rates of 23%/38%, respectively, in the q21d regimen
- Phase 3 Study planning underway