

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

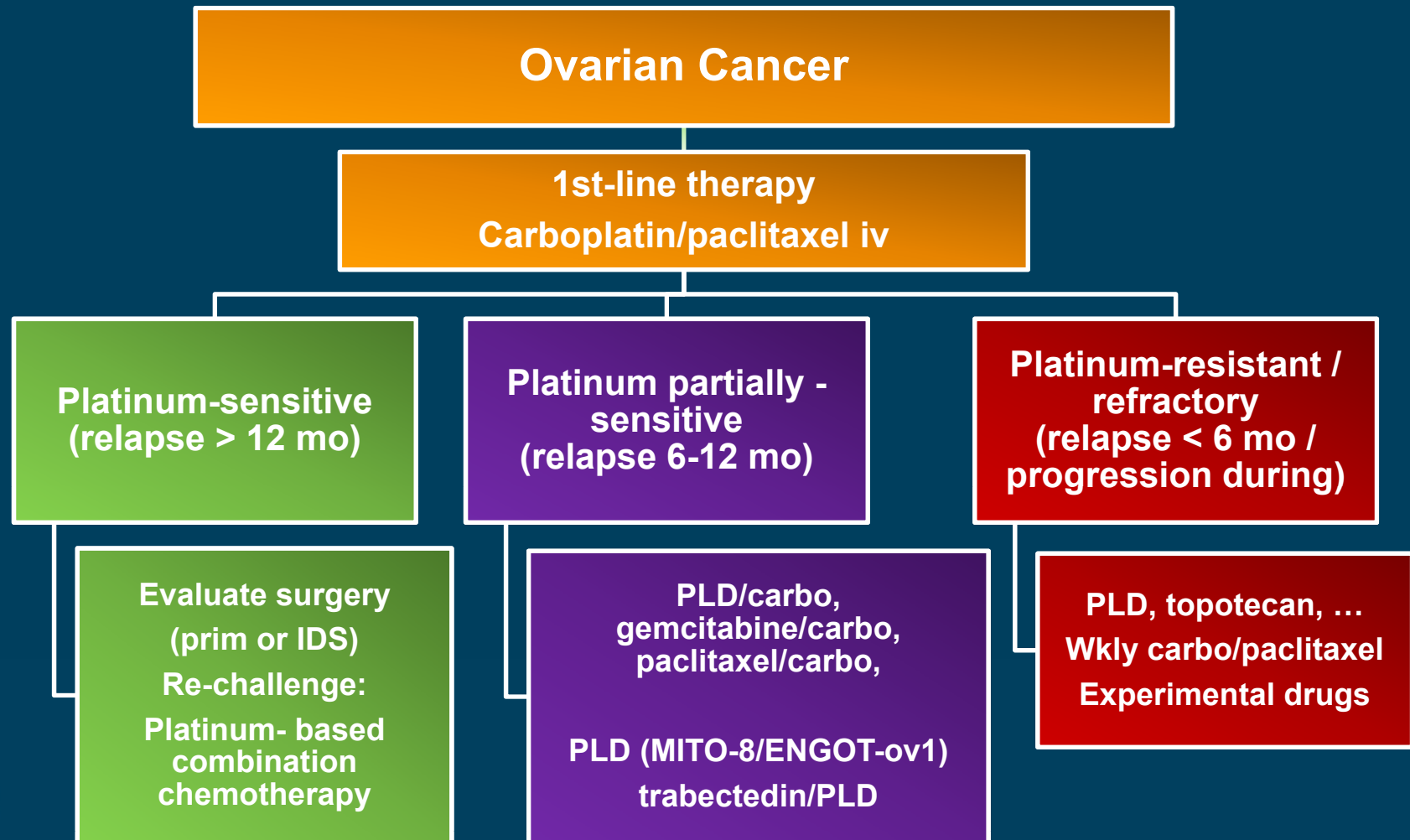
Ignace Vergote, John Micha, Charles Pippitt, Gautam Rao, Daniel Spitz, Nicholas Reed, Graham Dark, Agustin Garcia, Daniel Maslyar, Gordon Rustin

# 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

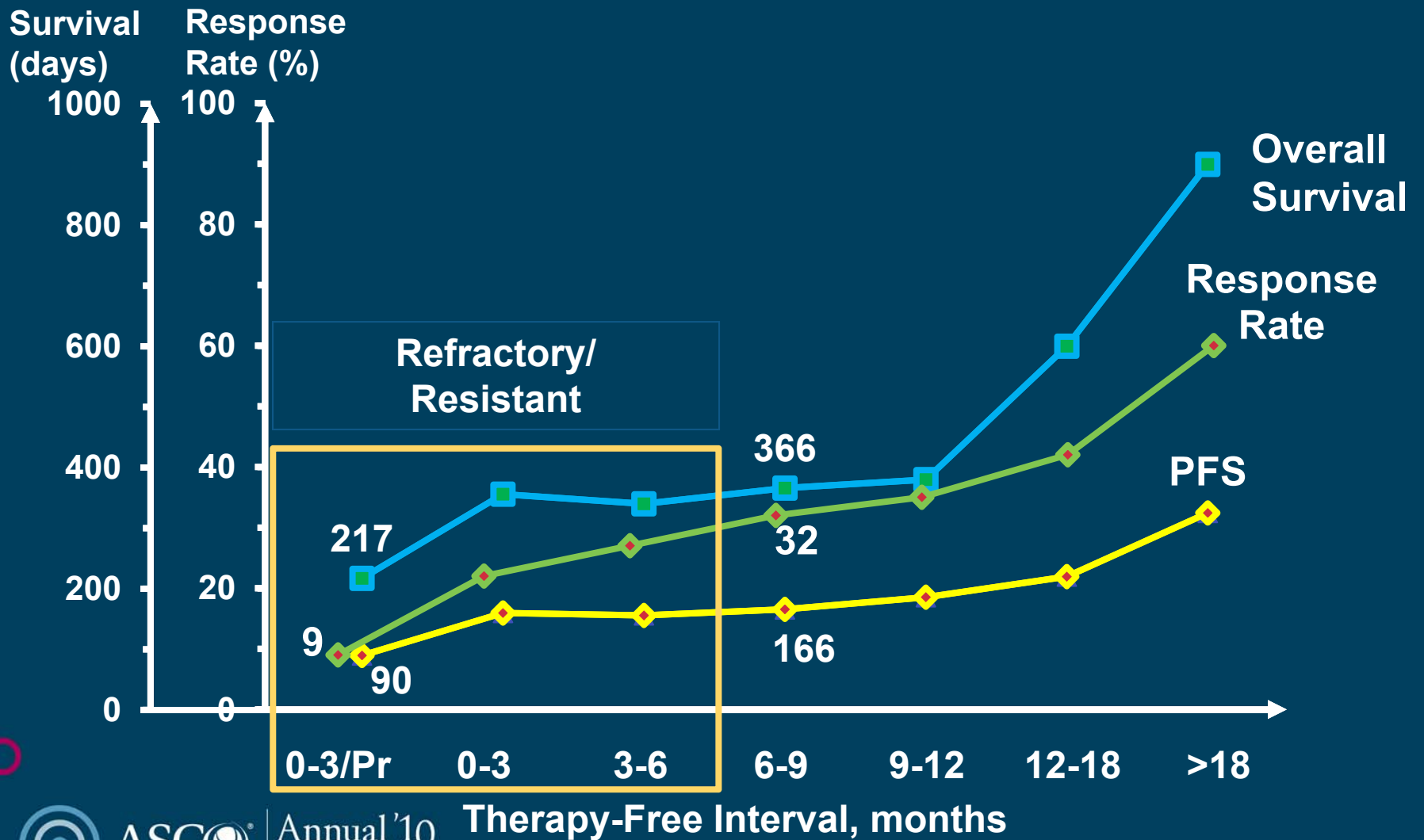
This study was supported by funding from Nektar Therapeutics

# Ovarian Cancer Treatment Algorithm

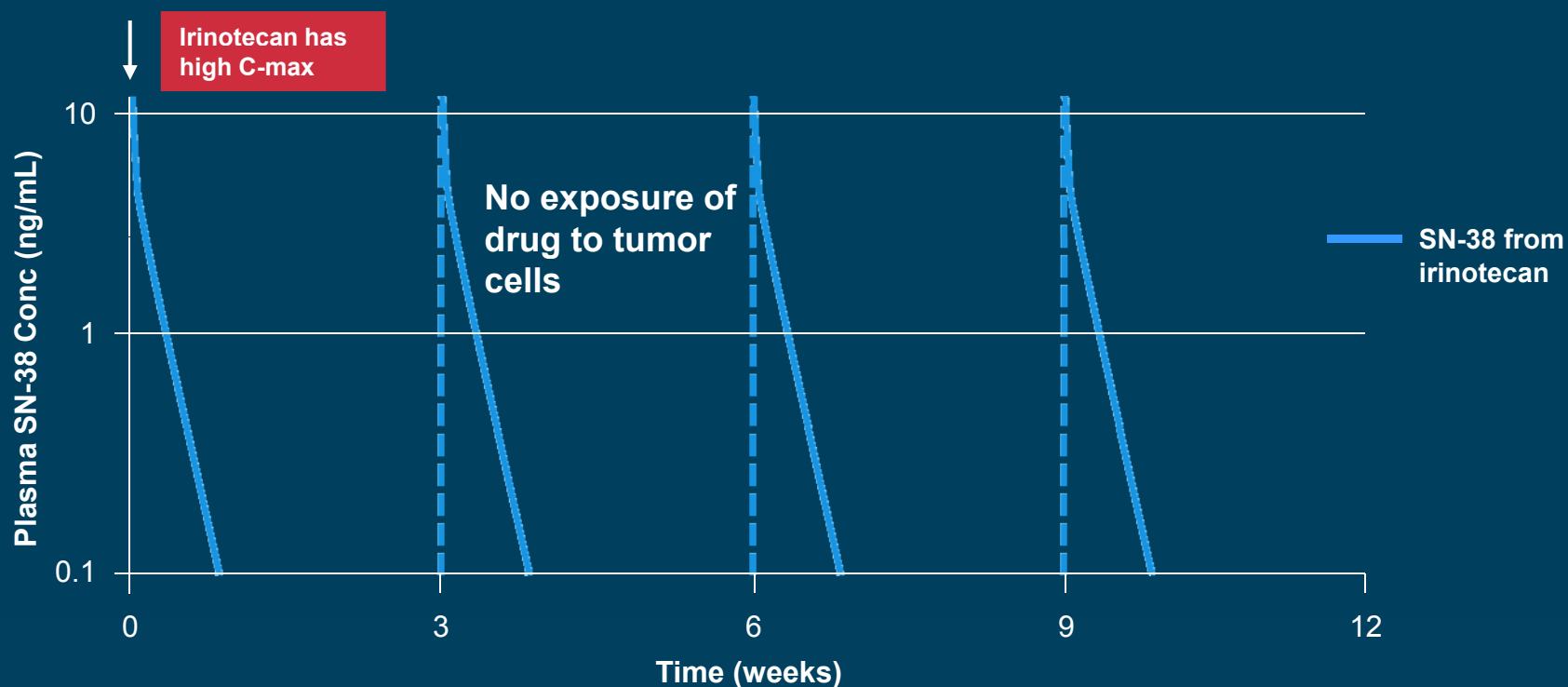


# Analysis of GINECO Studies

## Therapy-Free Interval and Efficacy

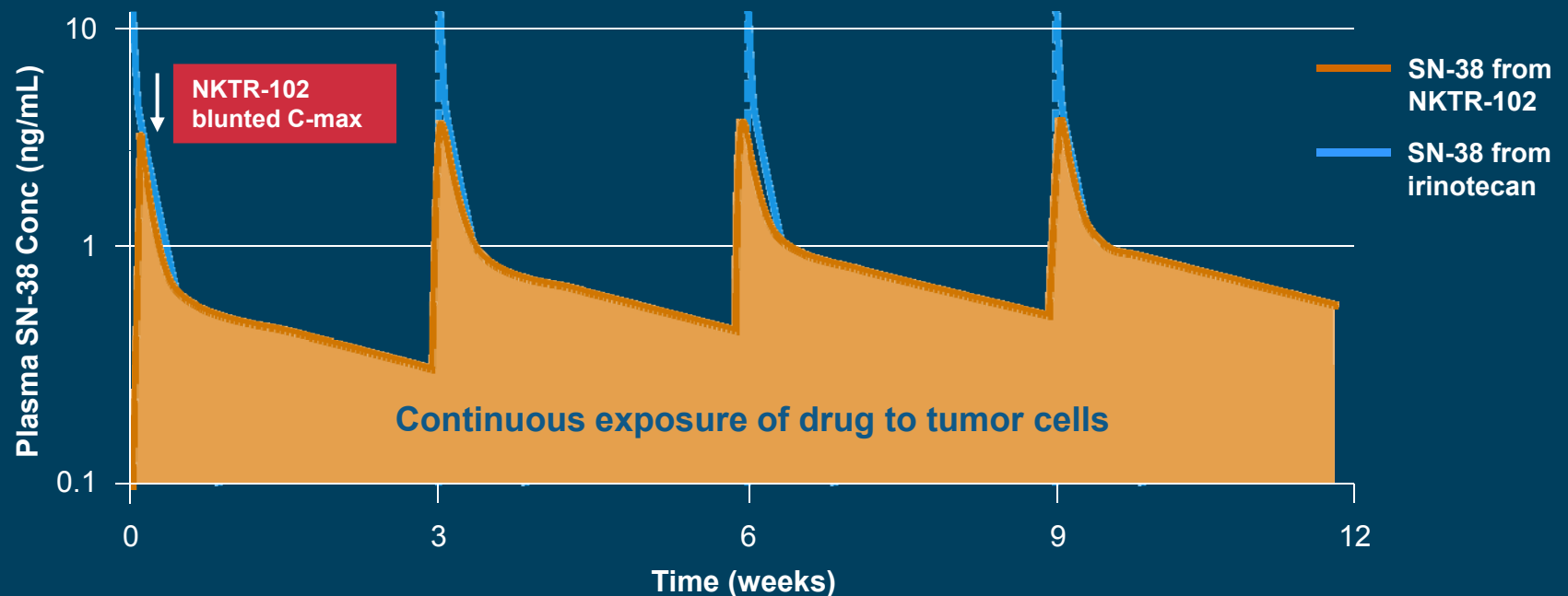


# NKTR-102: Topoisomerase I inhibitor (irinotecan)-polymer conjugate



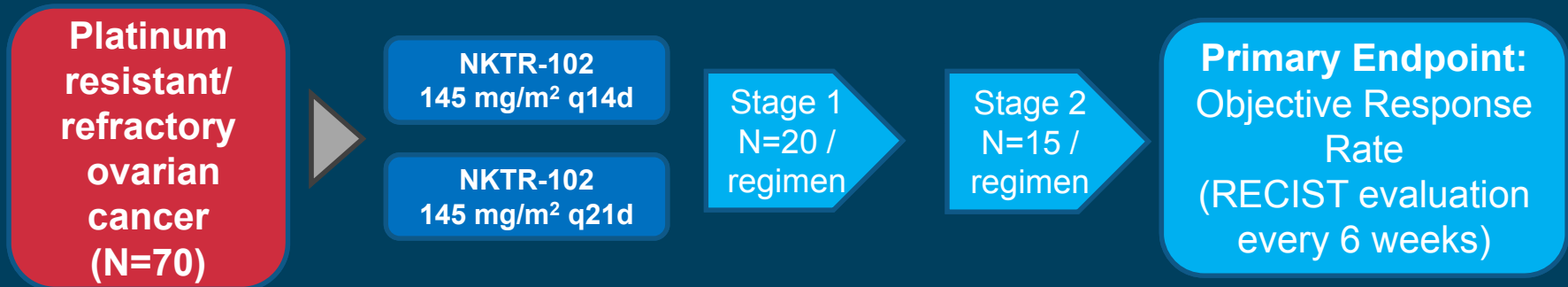
# NKTR-102: Topoisomerase I inhibitor (irinotecan)-polymer conjugate

- 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  $\geq 1$  patient responds, that treatment regimen proceeds to the next stage

**Stage 2:** An additional 15 are patients enrolled

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

# 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 <sup>2</sup> q14d (N = 36)	NKTR-102 145 mg/m <sup>2</sup> 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%

# Demographics (2)

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

# Objective Response Rates (Platinum Resistant / Refractory Patients)

		NKTR-102 145 mg/m <sup>2</sup> q14d	NKTR-102 145 mg/m <sup>2</sup> 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 <sup>2</sup> q14d			NKTR-102 145 mg/m <sup>2</sup> 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%)

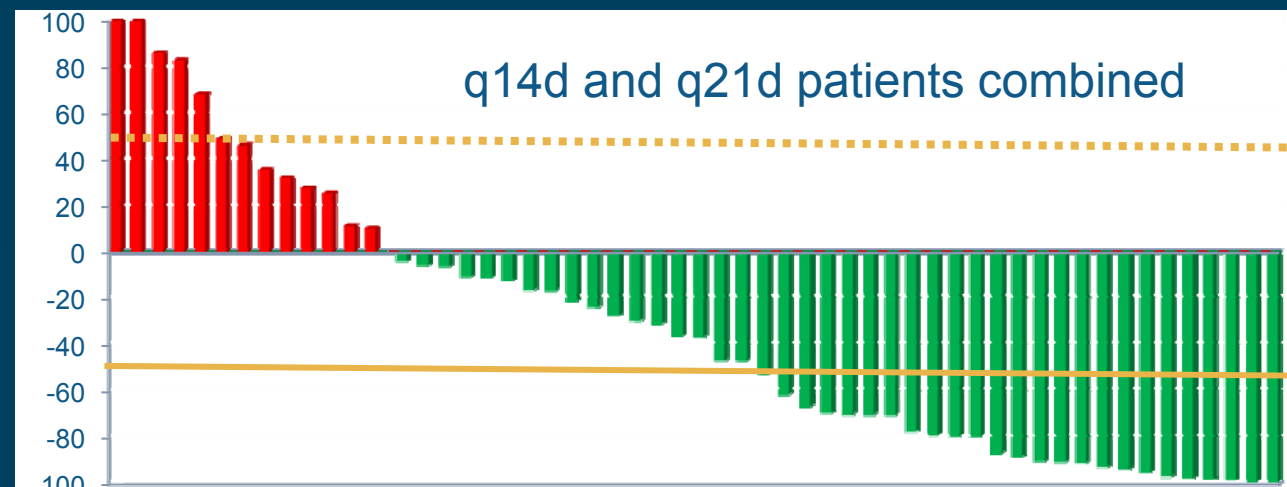
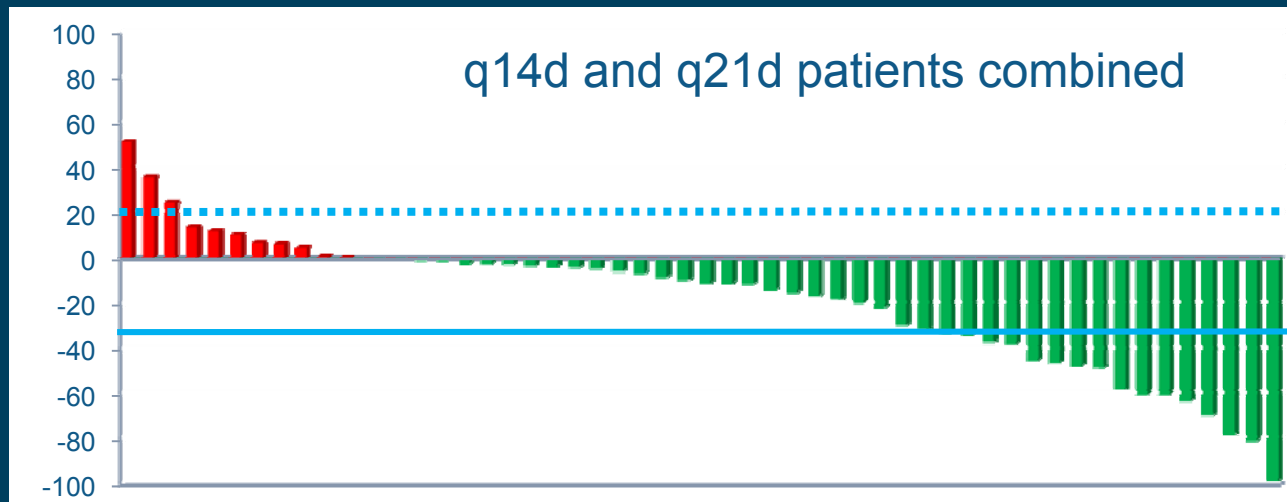
# ORR by Prior Lines of Platinum (Platinum Resistant / Refractory Patients)

Prior Platinum Lines		NKTR-102 145 mg/m <sup>2</sup> q14d	NKTR-102 145 mg/m <sup>2</sup> 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%)

# ORR by Prior PLD (Platinum Resistant / Refractory Patients)

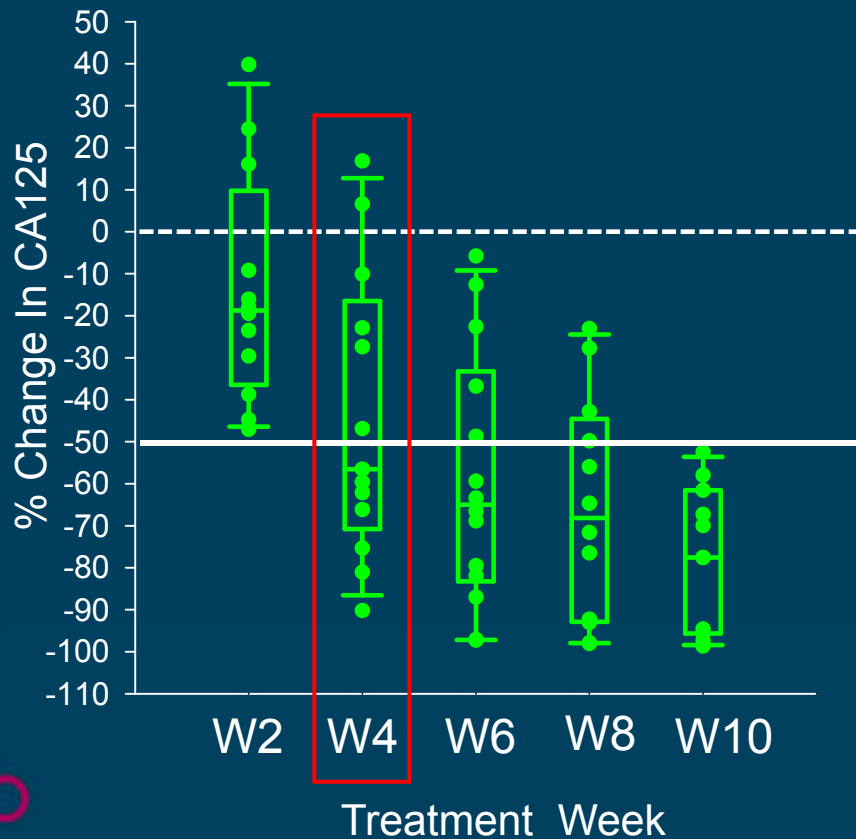
		NKTR-102 145 mg/m <sup>2</sup> q14d	NKTR-102 145 mg/m <sup>2</sup> q21d
Prior PLD	RECIST N (evaluable)	15	14
	Confirmed + Unconfirmed	4 (27%)	6 (43%)
	Confirmed	3 (20%)	4 (29%)
No Prior PLD	RECIST N (evaluable)	18	17
	Confirmed + Unconfirmed	4 (22%)	3 (18%)
	Confirmed	4 (22%)	3 (18%)

# Maximum Decline by RECIST or CA-125

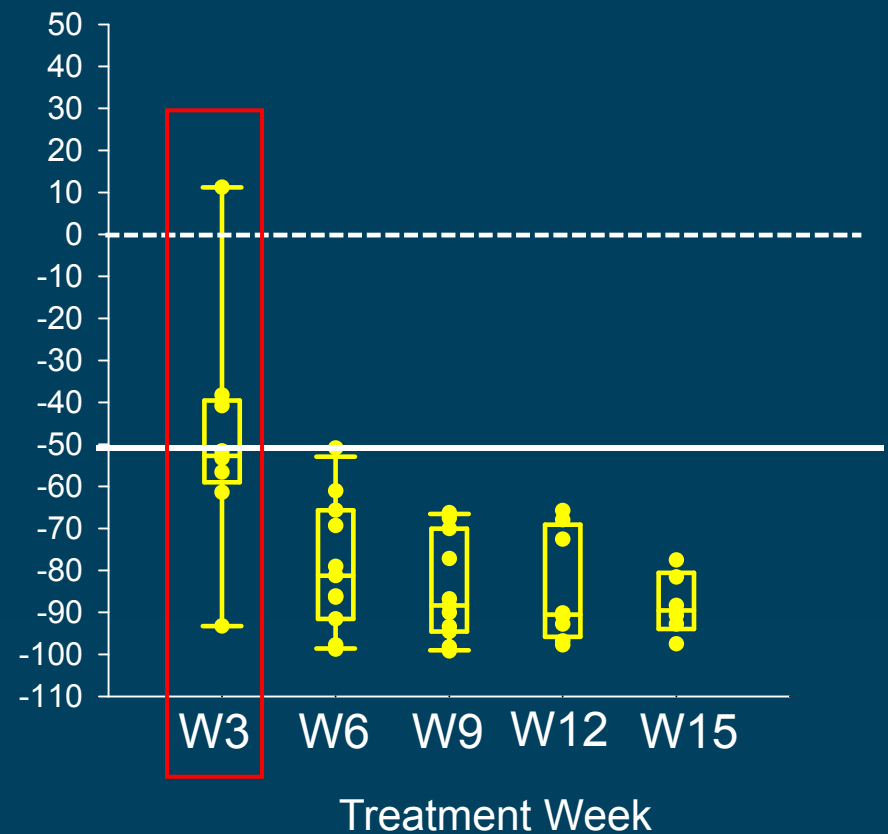


# Rapid Decline for CA-125 Responders (Platinum Resistant / Refractory Patients)

145 mg/m<sup>2</sup> q14d Schedule



145 mg/m<sup>2</sup> q21d Schedule







# NKTR-102 Safety Profile: All Patients

Most Common* Drug-related Grade 3 and 4 AEs  * >5% overall	NKTR-102 145 mg/m <sup>2</sup> q14d (N = 36)		NKTR-102 145 mg/m <sup>2</sup> 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

# Principal Investigators

## Belgium

**Ignace Vergote, MD, PhD**  
University Hospital Leuven

**Christine Gennigens, MD**  
CHU de Liege

**Luc Dirix, MD**  
AZ St. Augustinus

## United Kingdom

**Gordon Rustin, MD, MBBS**  
Mount Vernon Cancer Centre

**Nicholas Reed, MD**  
Beatson Oncology Centre

**Graham Dark, MD**  
Freeman Hospital

**Christopher Poole, MD**  
University Hospital Coventry

**Michelle Ferguson, MD**  
Ninewells Hospital

## United States

**Agustin Garcia, MD**  
USC Norris Comprehensive Cancer Center

**Gautam G. Rao, MD**  
Sarah Cannon Research Institute

**John Micha, MD**  
Gynecologic Oncology Associates

**Charles Pippitt, MD**  
Piedmont Hematology Oncology Associates

**Daniel Spitz, MD**  
Palm Beach Cancer Institute

**Emad Ibrahim, MD**  
Highland, CA

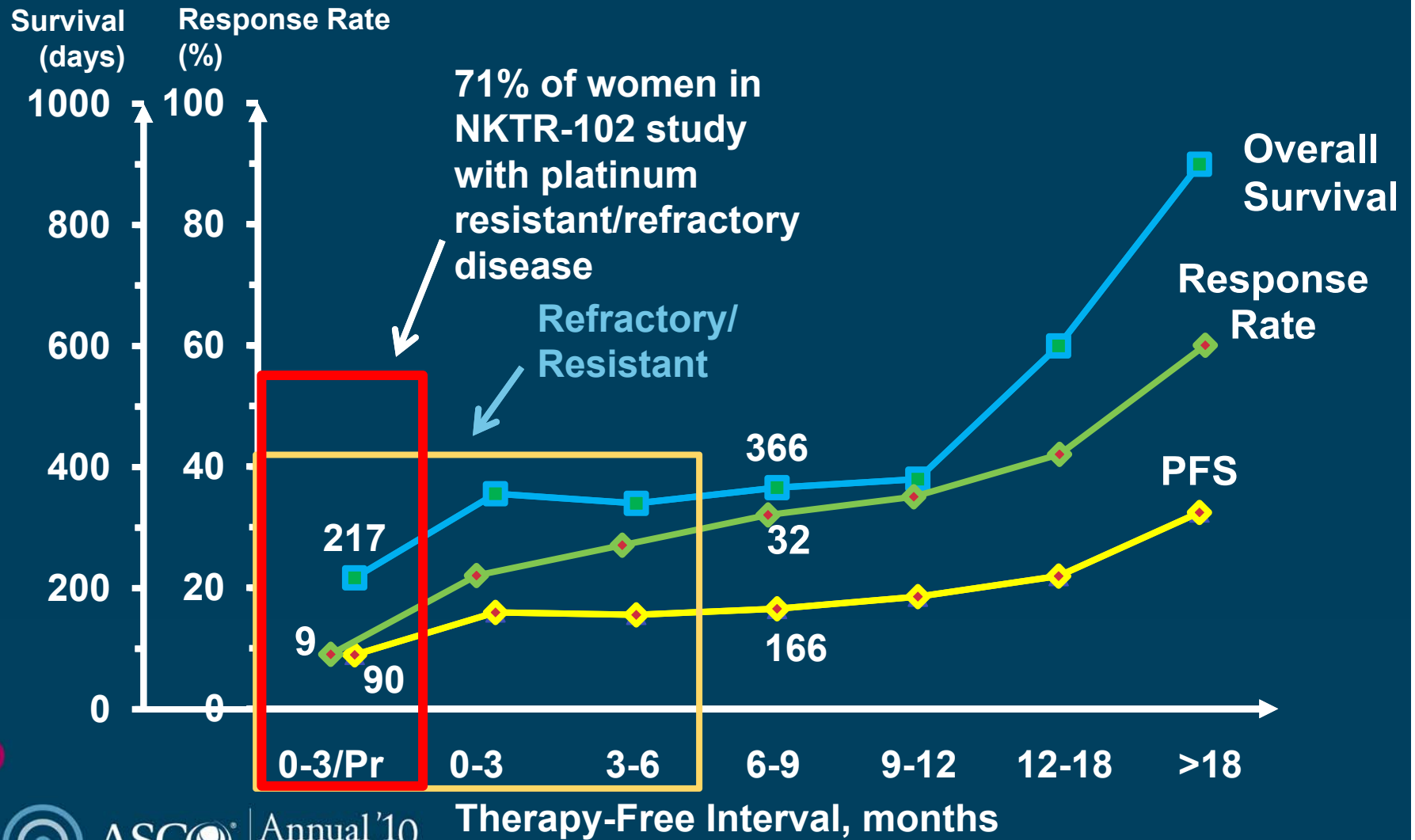
**Linda Duska, MD**  
University of Virginia

**Vincent Armenio, MD**  
Pharma Resourse

**Jeffrey Smith, MD**  
Surgical Gynecological

**Joseph Meunier, MD**  
Sparrow Regional Cancer Center

# Conclusions



# 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 4<sup>th</sup> 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