

A Phase 2 Trial of Voreloxin (SNS-595) in Platinum - Resistant Epithelial Ovarian Cancer

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Voreloxin: First-In-Class Anti-Cancer Agent

A validated mechanism of action (MOA) with distinct advantages over older compounds

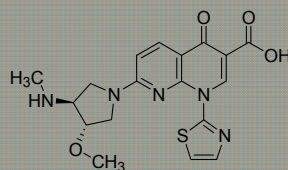
Proven MOA

- DNA intercalator
- Topoisomerase II inhibitor
- Treatment standards in both solid and liquid tumors
- Approved drugs include etoposide, doxorubicin, and daunorubicin

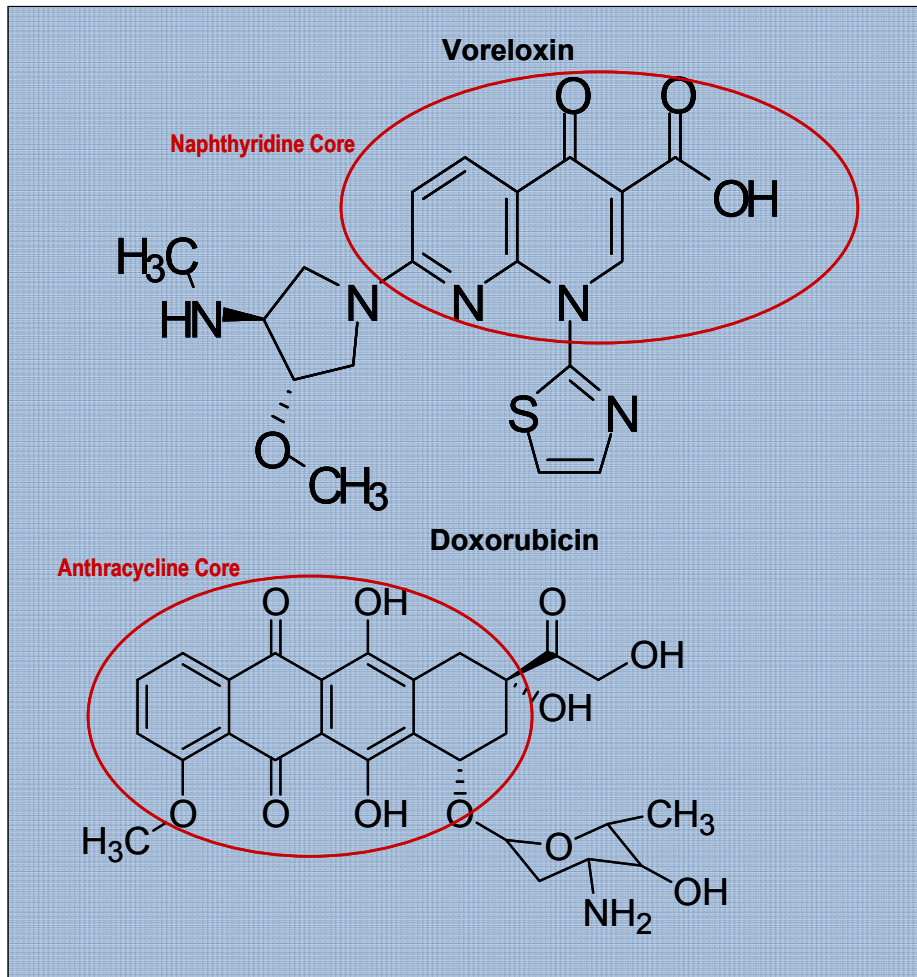
New Class Anti-Cancer Agent

- Broad therapeutic index due to limited distribution to normal tissues
- Evades common drug resistance pathways
- Lower potential for organ toxicity, including cardiotoxicity
- New USAN stem

VORELOXIN



Voreloxin has a Validated Mechanism of Action With Distinct Advantages Over Anthracyclines



Voreloxin: Novel topoisomerase II inhibitor and DNA intercalator

- **Active in anthracycline-resistant settings**
 - Not a P-glycoprotein substrate
 - Unaffected by p53, p63 or p73 status
- **Not a CYP450 inhibitor or inducer**
 - Low potential for drug-drug interaction
- **Lower potential for cardiotoxicity than anthracyclines**
 - Anthracyclines generate substantial Reactive Oxygen Species (implicated in cardiotoxicity), unlike voreloxin

Phase 2 Platinum-Resistant Ovarian Cancer Study Design

Population: Platinum-resistant ovarian cancer	<ul style="list-style-type: none">• Progression while on or within six months of completing 1-3 platinum-based chemotherapy• Patient could have failed an additional non-platinum based cytotoxic
Voreloxin Regimens	48 mg/m ² q3wk N=65 (37% Doxil failure)
	60 mg/m ² q4wk N=35 (20% Doxil failure)
	75 mg/m ² q4wk N=24 treated of 30 to be enrolled in 2008
Objectives	<ul style="list-style-type: none">• Objective response by GOG-RECIST• Duration of response• Median PFS• Safety

Safety Profile Allowed Increased Dose Intensity



Step 1

- Extended cycle length to 4 weeks to allow for marrow recovery
- Raised dose to maintain dose intensity of ~15 mg/m²/week
- Decreased ANC criterion for repeat doses to standard practice (1,000/μL)
- Observation
 - Proportionally fewer dose delays/reductions
 - 40% at 48 mg/m² vs. 14% at 60 mg/m²

Step 2

- Raised dose to increase dose intensity 25% to ~19 mg/m²/week

Patient Demographics - Histology

Histology	48 mg/m ² N=65	60 mg/m ² N=35
Serous Cystadenocarcinoma	63%	54%
Papillary serous	8%	17%
Clear cell	11%	14%
Endometrioid	5%	9%
Adenocarcinoma, NOS	12%	3%
Other	1%	3%

Patient Demographics – Treatment History

Prior Tx	48 mg/m ² N=65	60 mg/m ² N=35	Number Prior Tx	48 mg/m ² N=65	60 mg/m ² N=35
1 ^o platinum resistant/refractory	48%	63%	1	20%	31%
2 ^o platinum resistant	52%	37%	2	43%	37%
Doxil [®] (Caelyx [®])	38%	20%	3	22%	23%
Gemcitabine	25%	17%	≥ 4	14%	9%
Bevacizumab	6%	6%			
Topotecan	9%	6%			

- Increase in 1^o platinum resistant/refractory patients in 60 mg/m² cohort (63%) compared to 48 mg/m² (48%) may decrease ORR

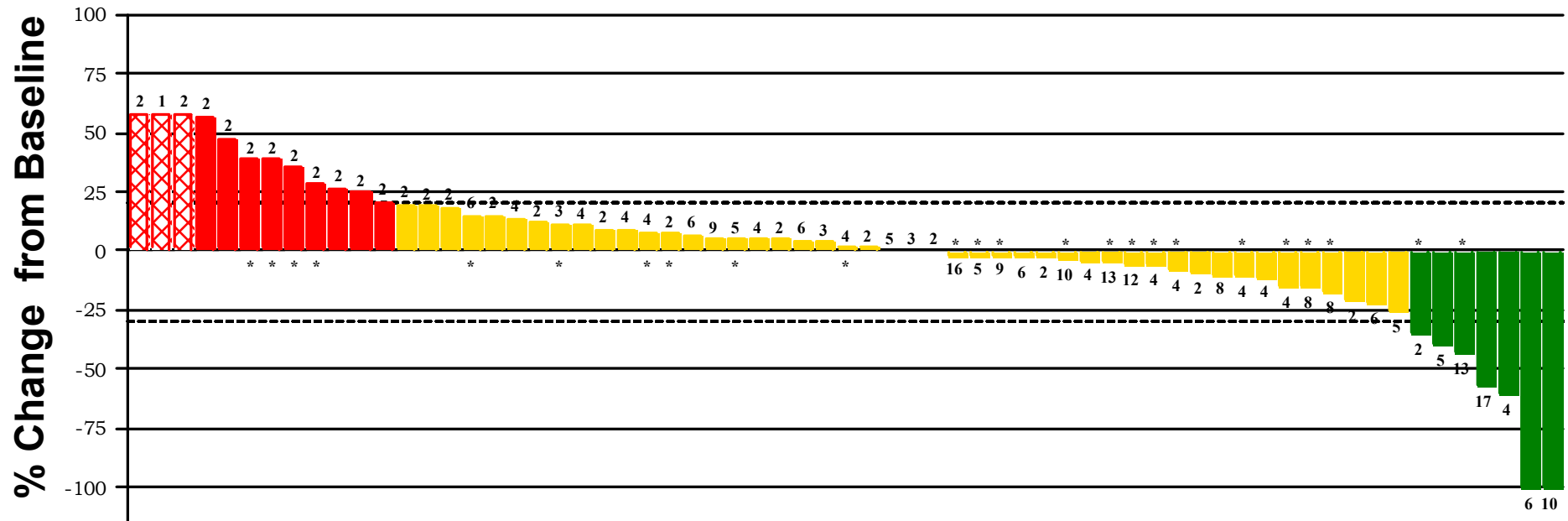
Voreloxin is Generally Well-Tolerated: All Grade 3 or Grade 4 AEs ($\geq 5\%$)

	48 mg/m ² N=65	60 mg/m ² N=35
Patients with \geq Grade 3 AE	34 (52%)	15 (43%)
Febrile Neutropenia	5 (8%)	2 (6%)
Neutropenia	49 (75%)	27 (77%)
Anemia	5 (8%)	3 (9%)
Vomiting	4 (6%)	0
Fatigue	9 (14%)	4 (11%)
Hypokalemia	1 (1.5%)	3 (9%)
Infections	5 (8%)	1 (3%)

- **Asymptomatic neutropenia is the most frequent toxicity**

Voreloxin Demonstrates Single Agent Activity in Advanced Platinum-Resistant Ovarian Patients – 48 mg/m²

Waterfall Plot of Best Response (RECIST) at 48 mg/m² q3weeks N=65



■ Progression
 ■ Stable Disease
 ■ Complete or Partial Response
 * Doxil[®] failure

- 2 CR and 5 PR observed for an ORR of 11%
- Disease control (CR + PR + SD for ≥ 90 days) achieved in 46%
- Preliminary median PFS of 82 days (95% confidence interval 52 – 98 days)
- Most (5 of 7) objective responses occurred at Cycle 4 or later (range 2-10)
- Median cycles received is 4 (range 2-17)

Responder Characteristics at 48 mg/m²

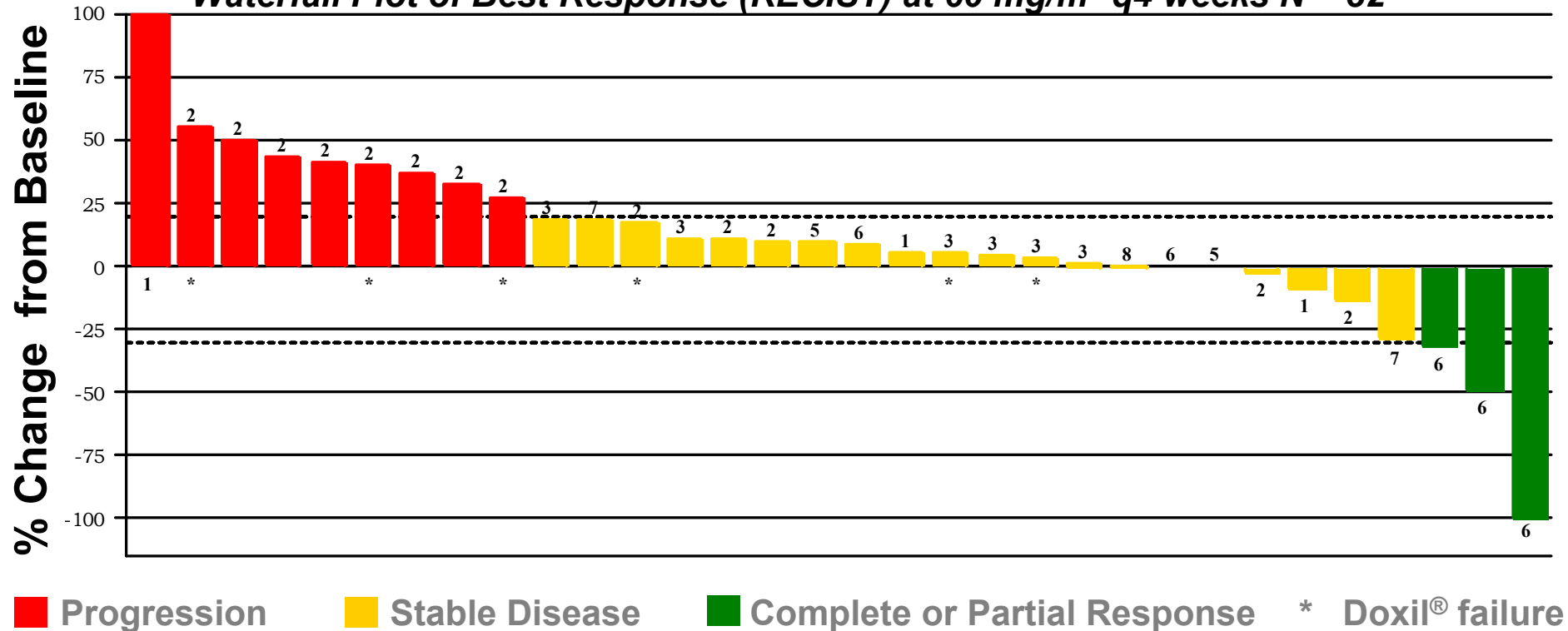
Responder Characteristics	1° or 2° Platinum-Resistant	Best Response	Cycle At Which PR or CR First Observed	Cycles
1 st line: Carbo/Gemcitabine – Carbo/Taxol® 2 nd line: Carbo/Gemcitabine 3 rd line: Doxil BRCA-1 mutation	2°	PR	4	13
1 st line: Carbo/Taxol 2 nd line: Doxil off-study due to AE (bowel obstruction)	2°	PR	2	2
1 st line: Carbo/Taxol/Avastin®	1°	PR	10	17+
1 st line: Carbo/Taxol 2 nd line: Carbo/Gemcitabine BRCA-2 mutation, off chemo with CR at 9+ mo	2°	CR**	6	6
1 st line: Cis/Topotecan Carbo/Taxol 2 nd line: Carbo/Gemcitabine	2°	CR	8	10+
1 st line: Carbo/Taxol (Clear cell)	1°	PR	2	4
1 st line: Carbo 2 nd line: Carbo	2°	PR	4	5+

** CR as of 15Feb08 after 6 cycles of voreloxin; remains in CR as of 6Aug08.

+ Indicates patient remains on study receiving voreloxin.

Preliminary Efficacy at 60 mg/m²

Waterfall Plot of Best Response (RECIST) at 60 mg/m² q4 weeks N = 32



- Data are not yet mature enough to assess ORR or PFS
- 13 of 35 patients remain on study

Responder Characteristics at 60 mg/m²

Responder Characteristics	1° or 2° Platinum Resistant	Best Response	Cycle At Which CR or PR first Observed	Cycles
1 st line: Carbo/Taxol 2 nd line: Carbo/Taxol	2°	CR	2	6+
1 st line: Carbo/Taxol	1°	PR	4	6+
1 st line: Carbo/Taxol – Cis/Taxol	1°	PR	2	6+

+ Indicates patient remains on study receiving voreloxin.

Conclusions

- **Voreloxin has single agent activity in advanced platinum-resistant ovarian cancer patients**
 - **Activity at 48 mg/m² q3weeks is similar to commonly used therapies**
 - **ORR 11% with preliminary median PFS of 82 days**
 - **Preliminary response rate data at 60 mg/m² q4weeks appear comparable**
 - **Responses, including CRs, have occurred late, after 4 or more cycles**
- **Voreloxin is generally well-tolerated**
 - **Asymptomatic neutropenia (~75%) is the most frequent toxicity**
- **Low incidence of febrile neutropenia (< 10%) supported dose escalation to 75 mg/m² q4weeks**
 - **24 of 30 patients enrolled at this dose level**
 - **Early efficacy readout anticipated first half of 2009**

Thank You

- **To all study investigators and site study personnel**
- **Special thanks to all the patients who have participated in this clinical study**