2024 ASCO® ANNUAL MEETING

Dendrimer-enhanced (DEP) SN38 (DEP irinotecan) in patients with advanced solid tumors: a Phase 1/2 trial

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Study sponsored by Starpharma Pty Ltd

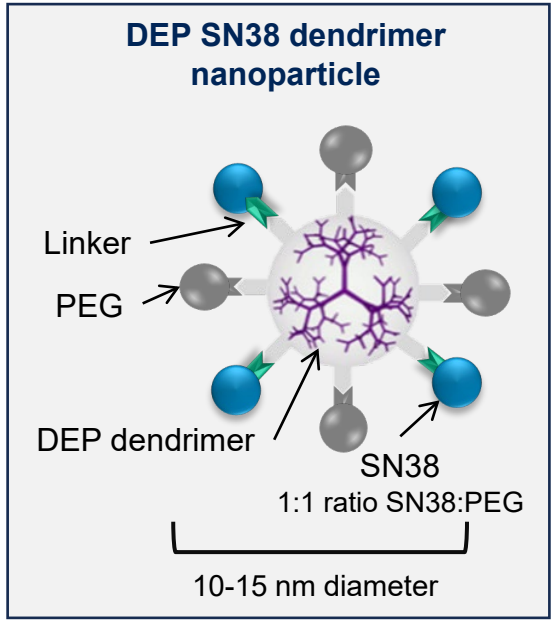
Summary

Results from DEP SN38 Phase 1/2 clinical trial in 114 patients with advanced solid tumors:

1. **Dendrimer technology has potential to deliver a range of payloads with improved safety / efficacy**

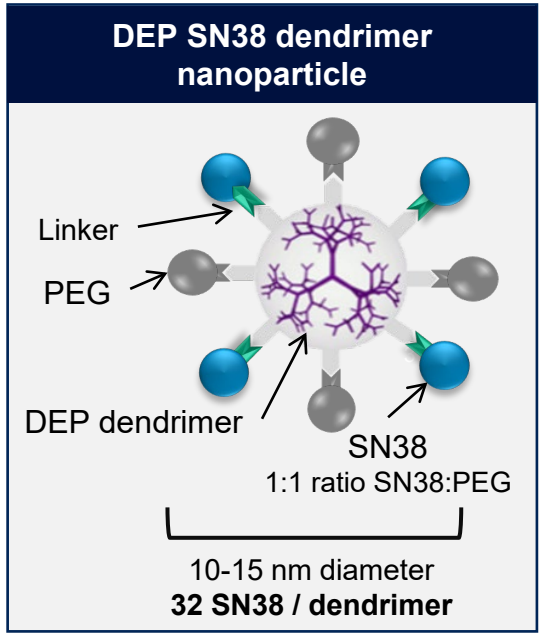
2. **DEP SN38 (12.5 mg/m^2) well-tolerated, with mostly mild/moderate gastrointestinal and no cholinergic toxicity**

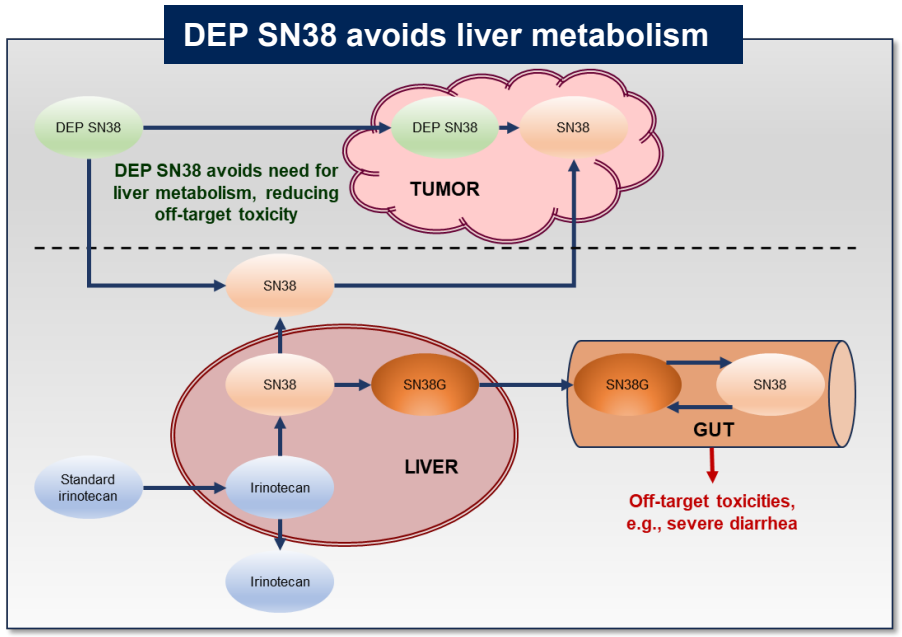
3. **Promising efficacy in irinotecan-treated CRC and platinum-resistant/refractory ovarian cancer**

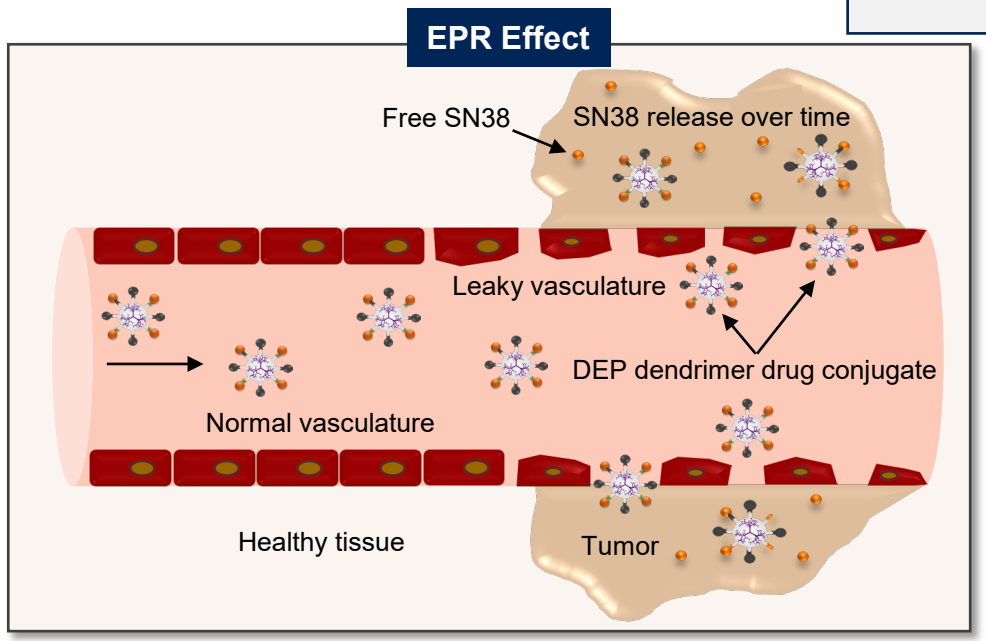


DEP SN38 Dendrimer Nanoparticle Mechanism

- 3D-poly-lysine dendrimers act as scaffold for delivery of a range of payloads, including cytotoxics[1]
- DEP SN38 does not require liver metabolism for conversion into active SN38 metabolite → reducing off-target toxicity
- DEP SN38 retained in tumor microenvironment via enhanced permeability and retention (EPR[1,2]) → improved efficacy







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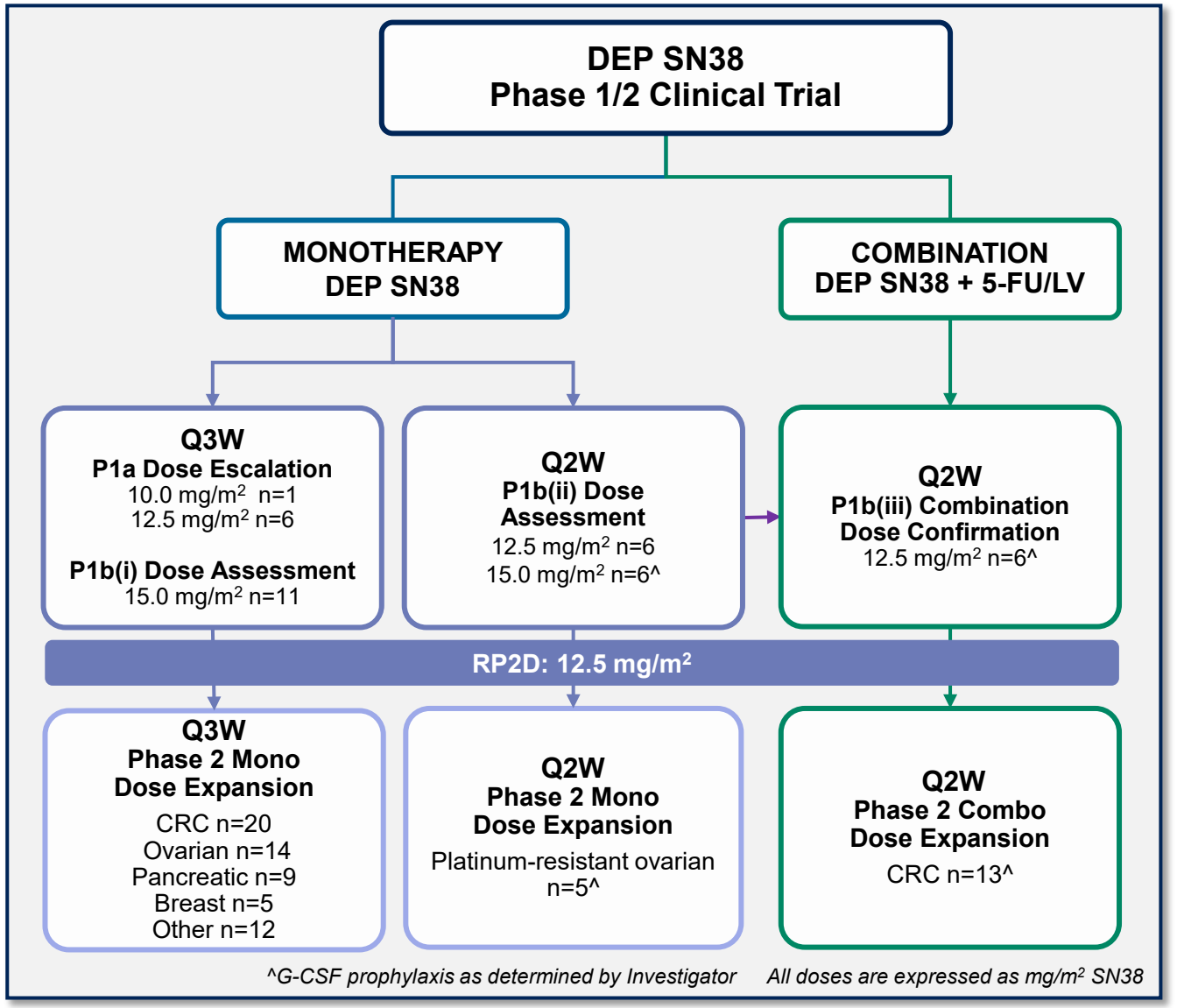
1. Kaminskas et al, *Nanomedicine* 2011, 6(6):1063-1084
2. Iyer et al, DrugDiscToday 2006, 11(17-18):812-818

Study Design

- Multicenter first-in-human open-label trial[1,2]
- DEP SN38 administered IV q3wkly or q2wkly infusion without corticosteroid/atropine pre-medication
- Dose expansion cohorts: colorectal, platinum-resistant ovarian
- Primary objective: safety profile and RP2D
- Secondary objectives: preliminary anti-tumor activity, tolerability, PK



1. EudraCT: 2019-001318-40
2. Liu et al, *Mol Cancer Ther* 2023, 22(12_Supplement):B039

Patient Characteristics – All Treated Patients

BASELINE CHARACTERISTICS		COLORECTAL	OVARIAN	PANCREATIC	BREAST	OTHER[1]	TOTAL
Subjects enrolled (n, %)		55 (48%)	23 (20%)	15 (13%)	8 (7%)	13 (11%)	114 (100%)
Subjects ongoing (n, %)		4 (7%)	2 (9%)	0 (0%)	0 (0%)	0 (0%)	6 (5%)
Age (years)	Median (range)	59 (31-78)	64 (42-74)	65 (48-76)	53 (42-66)	60 (38-73)	61 (31-78)
Sex (n, %)	Male	24 (44%)	0	8 (53%)	0	9 (69%)	41 (36%)
	Female	31 (56%)	23 (100%)	7 (47%)	8 (100%)	4 (31%)	73 (64%)
ECOG PS	0	23 (42%)	6 (26%)	6 (40%)	2 (25%)	-	40 (35%)
	1	32 (58%)	17 (74%)	9 (60%)	6 (75%)	2	74 (65%)
Stage at diagnosis	III	2 (4%)	4 (17%)	0 (0%)	0 (0%)	2 (15%)	8 (7%)
	IV	53 (96%)	19 (83%)	15 (100%)	8 (100%)	11 (85%)	106 (93%)
Prior systemic therapy (n, %)	Irinotecan	54 (98%)	0 (0%)	11 (73%)	0 (0%)	3 (23%)	68 (60%)
	Platinum	29 (53%)	23 (100%)	9 (60%)	0 (0%)	12 (92%)	73 (64%)
	Taxanes	0 (0%)	23 (100%)	2 (13%)	7 (88%)	9 (69%)	41 (36%)
Prior lines of therapy	Median (range)	4 (2-9)	6 (3 to 9)	2 (2 to 5)	7 (3 to 12)	3 (1 to 6)	4 (1 to 12)

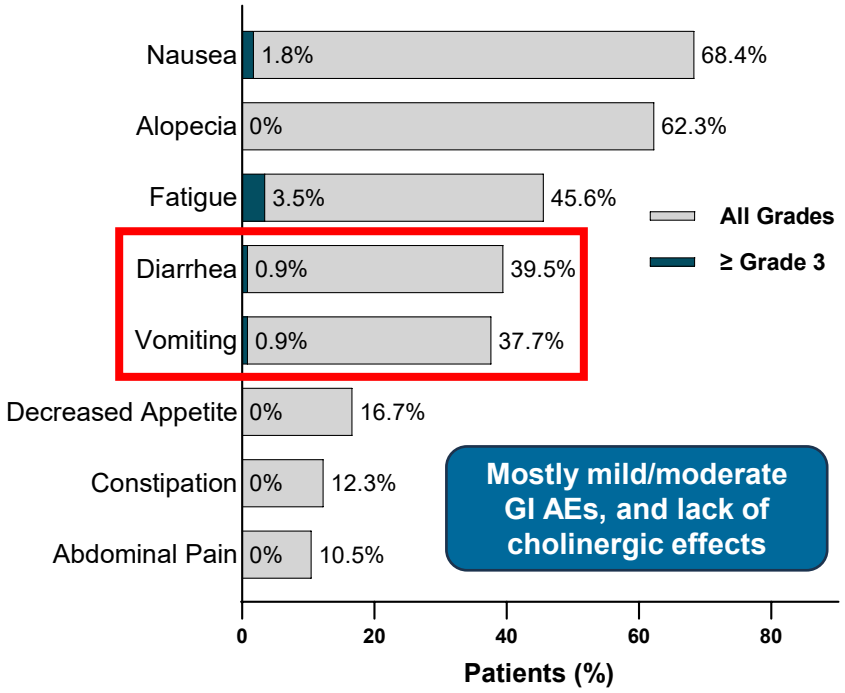
[1]*Other cancer types included lung, upper gastrointestinal, and kidney.*

DEP SN38 Safety and Tolerability

DEP SN38 is well-tolerated with a notable lack of severe GI toxicity and mostly mild/moderate AEs

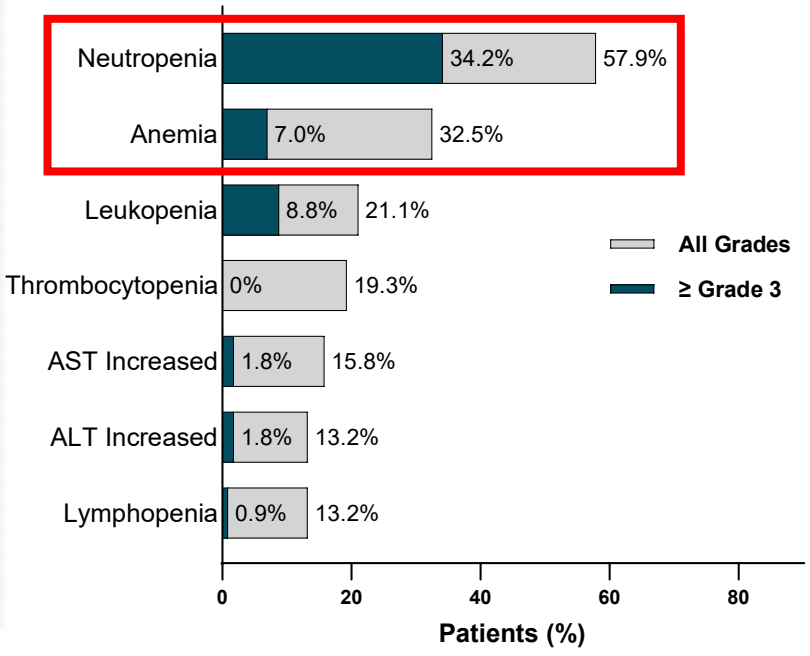
Treatment-related AEs in ≥10% patients (N=114)

Non-hematological AEs



Mostly mild/moderate GI AEs, and lack of cholinergic effects

Hematological / Lab AEs



DEP SN38 cycles administered: median 4 (1 – 38 to date)

RP2D 12.5 mg/m² for Q2W and Q3W

Dose Level / Regimen	DLT
12.5 mg/m² Q3W	G4 neutropenia >7 days
15 mg/m² Q2W	G3 febrile neutropenia
15 mg/m² Q2W	G3 neutropenic colitis

Treatment-related dose modifications (N=114)

Delay, n (%)	27 (23.7%)
Reduction, n (%)	12 (10.5%)
Discontinuation, n (%)	4 (3.6%)

DEP SN38 GI toxicity profile improved vs known toxicity of irinotecan

TRAE	DEP SN38 (Q2W, Q3W)	Irinotecan† (Q3W)
Diarrhea ≥ Grade 3	0.9%	~20%
Vomiting ≥ Grade 3	0.9%	~10%
Nausea ≥ Grade 3	1.8%	~10%
Cholinergic Syndrome	0%	47%
	N=114	N=765

† https://www.medicines.org.uk/emc/product/6506- UK SmPC April 2022

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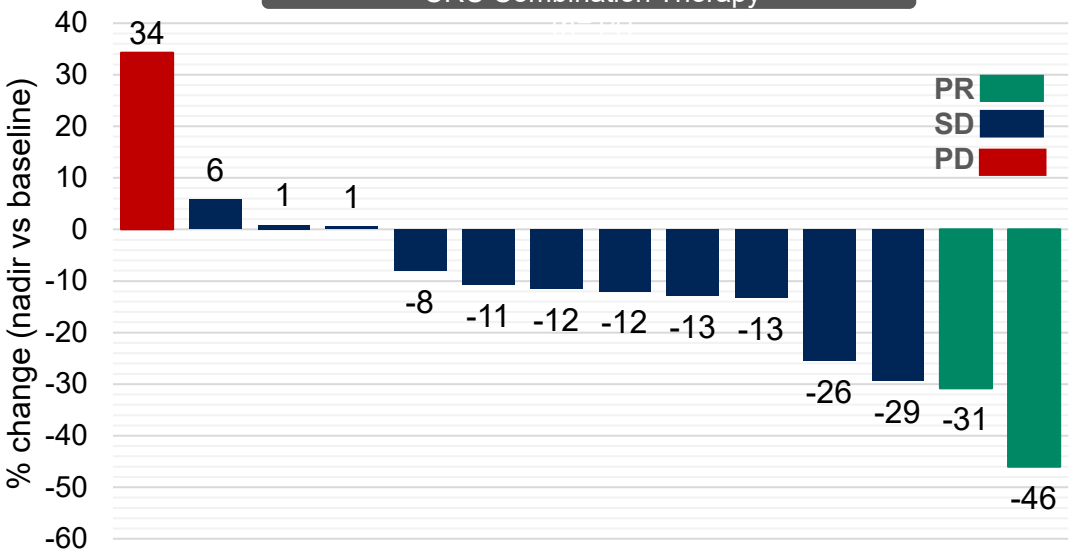
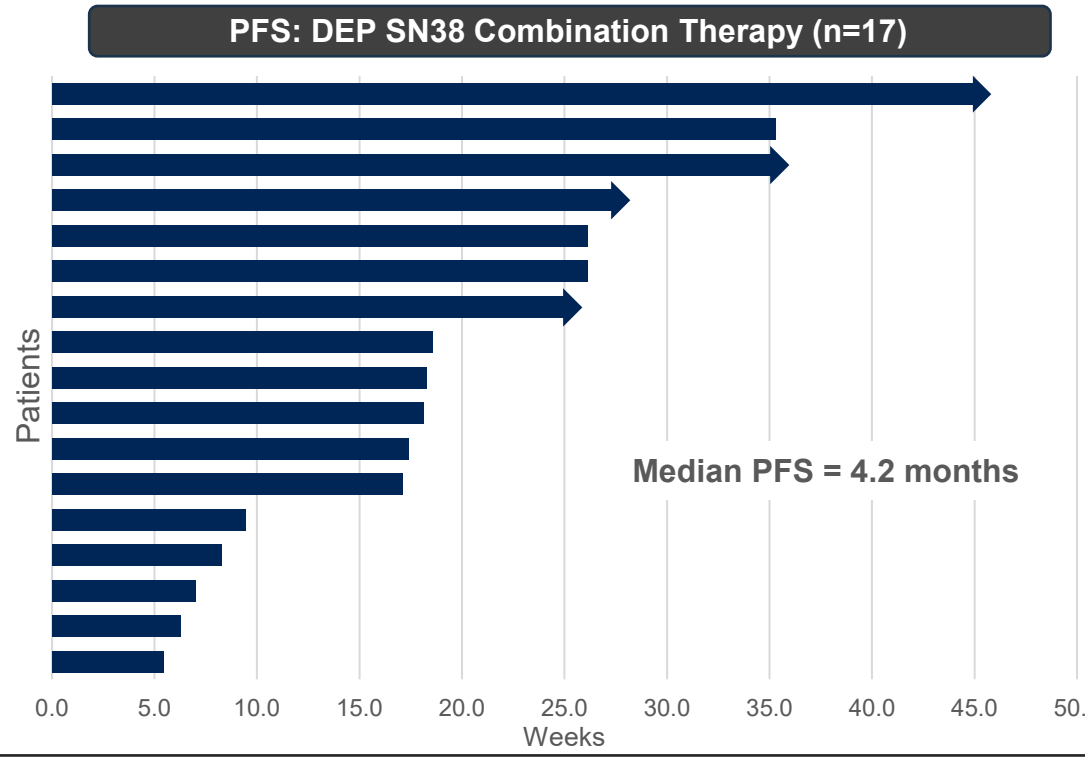
CRC Efficacy Overview

Efficacy Response		
DEP SN38 Monotherapy Q3W/Q2W (N=38)	**Median number of prior lines (range)**	**4 (2-9)**
	RECIST 1.1 Evaluable (n)	**31**
	DCR (n)	48% (15)
	ORR (n)	0% (0)
	Duration of response	up to 72 weeks
	Median PFS [95% CI]	2.1 months [9.9-18.4]
DEP SN38 + 5-FU/LV Combination Q2W (N=17)	**Median number of prior lines (range)**	**3 (2-6)**
	RECIST 1.1 Evaluable (n)	**14**
	DCR (n)	86% (12)
	ORR (n)	14% (2)
	Duration of response	up to 45 weeks*
	Median PFS [95% CI]	4.2 months [14.5-26.2]

**** 4 patients ongoing treatment***

Evaluable: patients who received ≥ 1 dose DEP SN38 and a CT scan at ≥ ~week 8 after first dose.
DCR: : Disease Control Rate (CR+PR+SD/RECIST Evaluable).





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Ovarian Efficacy Overview

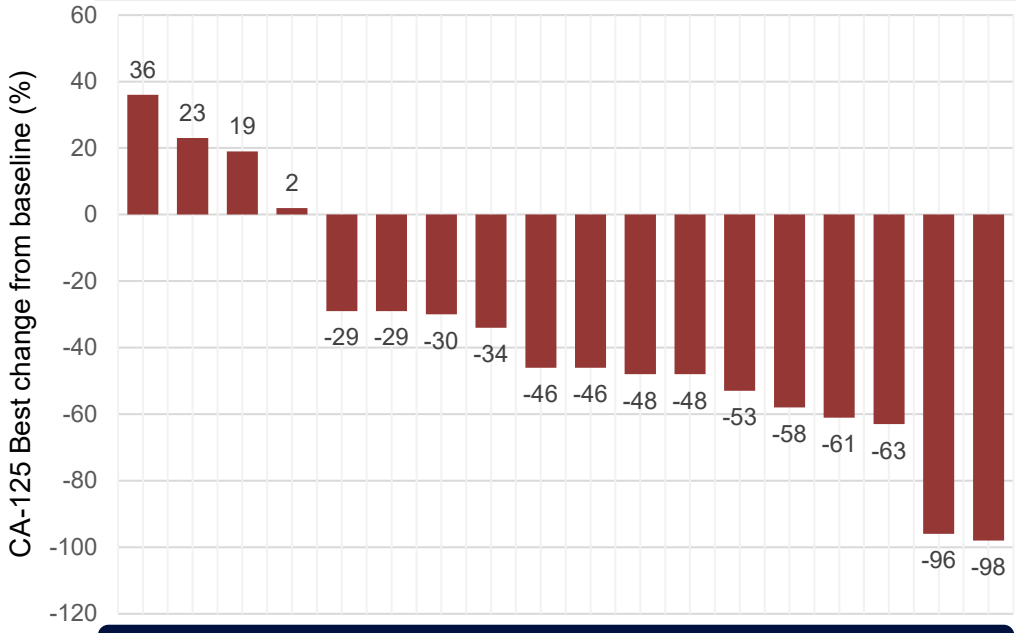
Efficacy Response		Total (n=23)	Q2W (n=8)	Q3W (n=15)
DEP SN38 Monotherapy	Median prior lines (range)	6 (3-9)	6 (4-8)	6 (3-9)
	RECIST 1.1 Evaluable (n)	18	7	11
	ORR % (n)	22% (4†)	43% (3†)	9% (1)
	DCR % (n)	72% (13)	100% (7)	55% (6)
	Duration of response	up to 62 weeks*	up to 62 weeks*	up to 33 weeks
	Median PFS [95% CI]	3.2 months [12.6 – 29.5]	9.3 months [14.4 – 56.3]	1.9 months [7.3 – 17.7]

**** 2 patients – ongoing treatment***

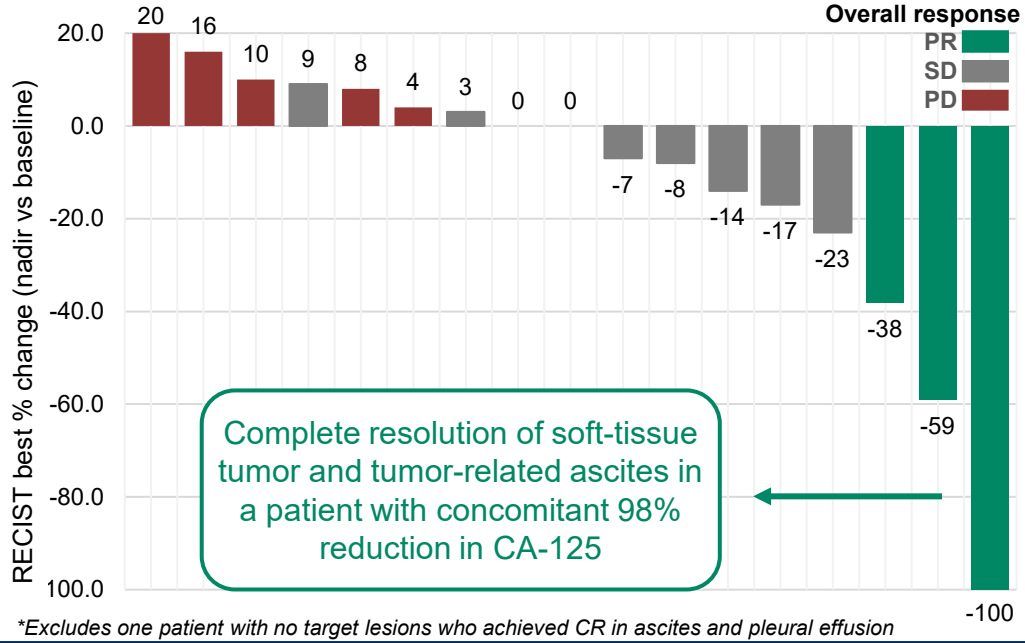
Evaluable Patients: received ≥ 1 dose DEP SN38 and a CT scan at ≥ ~week 8 after first dose.
DCR: Disease Control Rate (CR+PR+SD/RECIST Evaluable).

† Includes a patient with no target lesions had complete resolution in tumor ascites and pleural effusion.

CA-125 biomarker reduced in >75% patients - up to 98% ↓



Best % Change in Sum of Target Lesion Size (n=17*)



**Excludes one patient with no target lesions who achieved CR in ascites and pleural effusion*

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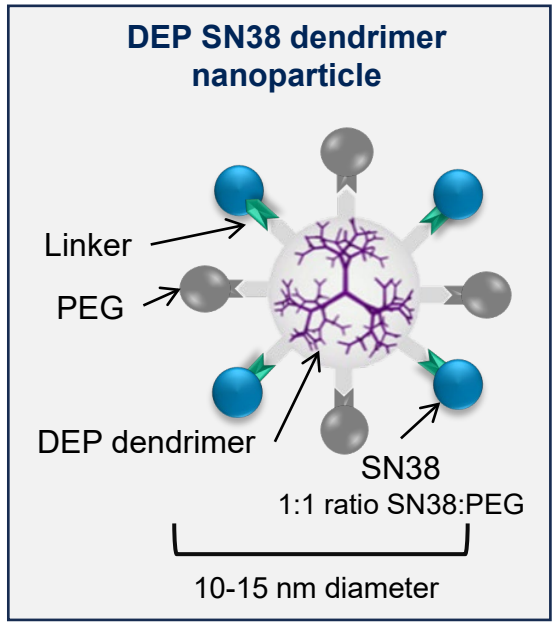
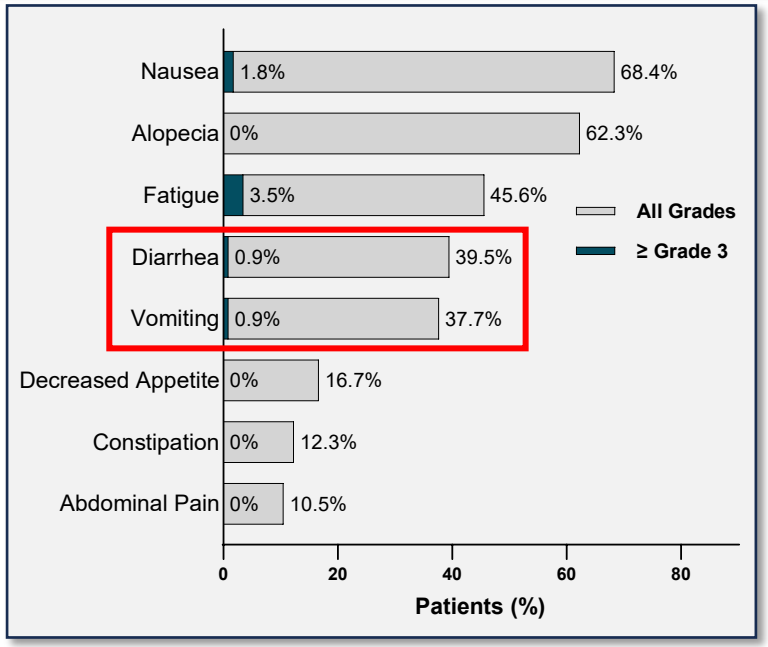
Key Points

Dendrimer nanoparticles offer a better way to deliver chemotherapy, focusing the treatment on cancer cells and sparing healthy tissue, helping to improve effectiveness and reduce side effects

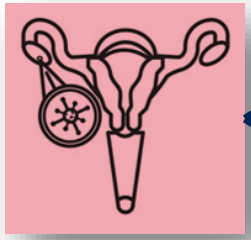




(n=55)

Monotherapy
DCR 48%

Combo + 5FU/LV
DCR 86%



(n=23)

Q2W ORR 43%
Q2W+Q3W DCR 72%

CA125 ↓ 75%

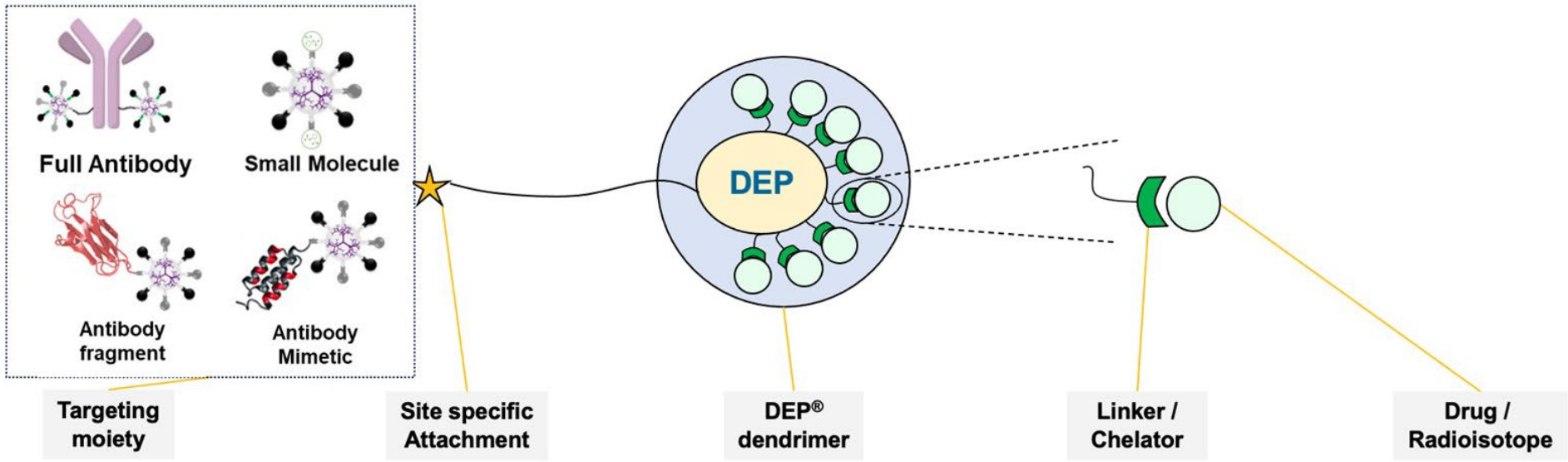
Dendrimer technology has potential to deliver a range of payloads with improved safety / efficacy

DEP SN38 (12.5 mg/m^2) IV Q2W / Q3W well-tolerated, with mostly mild/moderate GI AEs, no cholinergic toxicity

Promising efficacy in irinotecan-treated CRC and platinum-resistant/refractory ovarian cancer

Future Directions

- Confirm efficacy of DEP SN 38 vs irinotecan in randomized trials
- Explore synergy of DEP SN38 in combination with checkpoint / PARP inhibition
- Dendrimer platform to improve efficacy and safety profile of different payloads



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