starpharma

ASX Announcement

DEP® cabazitaxel presentation at ASCO 2024 Annual Meeting

Melbourne, Australia; 3 June 2024: Starpharma (ASX: SPL, OTCQX: SPHRY) today provides a copy of the DEP® cabazitaxel presentation that was delivered at the American Society of Clinical Oncology (ASCO) 2024 Annual Meeting in Chicago, US. The presentation was part of an oral abstract session showcasing the final results of the DEP® cabazitaxel Phase 1/2 clinical trial.

The ASCO Meeting is the most comprehensive gathering of oncology clinicians, researchers, and pharmaceutical companies in the world. It provides a platform to hear the latest breakthroughs and advancements in cancer treatment. Only a small proportion of submitted abstracts are accepted for presentation at the ASCO Annual Meeting. This year, fewer than 4% of these accepted abstracts were designated for full or rapid oral presentation.

It is a significant achievement that both DEP® cabazitaxel and DEP® irinotecan abstracts were selected for oral presentation at the ASCO Meeting, a demonstration of the quality and potential clinical impact of the findings.

The DEP® cabazitaxel ASCO Meeting abstract (#3004) has been published in the Journal of Clinical Oncology (JCO) (Volume 42, Number 16)[1]. Professor James Spicer, MBBS FRCP PhD, professor of experimental cancer medicine at King's College London, consultant in medical oncology, and Principal Investigator of the DEP® cabazitaxel trial at Guy's and St Thomas' NHS Foundation Trust in London, delivered the presentation over the weekend.

The presentation is appended.

[1] https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.3004

About Starpharma

Starpharma (ASX: SPL, OTCQX: SPHRY) is dedicated to helping patients with significant illnesses, such as cancer, achieve improved health outcomes and quality of life through the application of our unique dendrimer technology.

Dendrimers are precise, synthetically manufactured, nanoscale molecules. Their unique properties—including their size, structure, high degree of branching, polyvalency, and water solubility—are advantageous in medical and pharmaceutical applications.

Starpharma uses its dendrimer technology to develop novel therapeutics and to enhance the performance of existing pharmaceuticals. The Company's portfolio includes multiple clinical-stage oncology products, which utilise its Dendrimer Enhanced Product ('DEP®') drug delivery technology, as well as marketed products, including VIRALEZE™ and VivaGel® BV, which utilise SPL7013, a proprietary dendrimer with antimicrobial properties. Starpharma's DEP® drug delivery platform is being used to enhance the effectiveness of existing and novel therapies and to reduce drug-related toxicities through controlled and specified drug delivery.

For more information about Starpharma, visit www.starpharma.com or connect with Starpharma on LinkedIn.

WE Communications
Hannah Howlett
+61 450 648 064
WE-AUStarPharma@we-worldwide.com

Starpharma Holdings Limited
Cheryl Maley, Chief Executive Officer
Justin Cahill, CFO and Company Secretary
+61 3 8532 2704
investor.relations@starpharma.com
4-6 Southampton Crescent
Abbotsford Vic 3067

Disclosure
This ASX Announcement was authorised for release by Chair, Mr Rob Thomas.

Forward-Looking Statements
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2024 ASCO® ANNUAL MEETING

Efficacy and safety of dendrimer-enhanced cabazitaxel (DEP CTX) in patients with advanced solid cancers; a Phase 1/2 trial

James Spicer[1], David J. Pinato[2], Martin D. Forster[3], Anthony M. Joshua[4], James Korolewicz[5], Karam Aboud[6], Cienne Morton[1], Jia Liu[4], Rasha Cosman[4], Nicola J. Main[7], Julia Le Meur[7], Jeremy R.A. Paull[7], Stephanie R. Edmondson[7], Robert H. Jones[6]

[1]King's College London, Guy's Hospital, London, UK, [2]Imperial College London, London, UK, [3]University College London (UCL) Cancer Institute, UCL Hospital NHS Trust, London, UK, [4]The Kinghorn Cancer Centre, St Vincent's Hospital, Sydney, Australia, [5]University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK, [6]Velindre Cancer Centre and Cardiff University, Cardiff, UK, [7]Starpharma Pty Ltd, Abbotsford, Australia

James Spicer FRCP PhD

Study funded and sponsored by Starpharma Pty Ltd

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Dendrimer nanoparticle delivery of cabazitaxel (DEP CTX)

- 3D lysine polymer provides a scaffold for targeting payloads including cytotoxics to tumor microenvironment
- Cabazitaxel is a taxane approved for treatment of prostate cancer
- We conducted a Phase 1/2 trial of DEP CTX in advanced solid tumors
- Safety compares favourably with standard cabazitaxel
- Efficacy in patients with tumors including prostate, ovary and upper GI

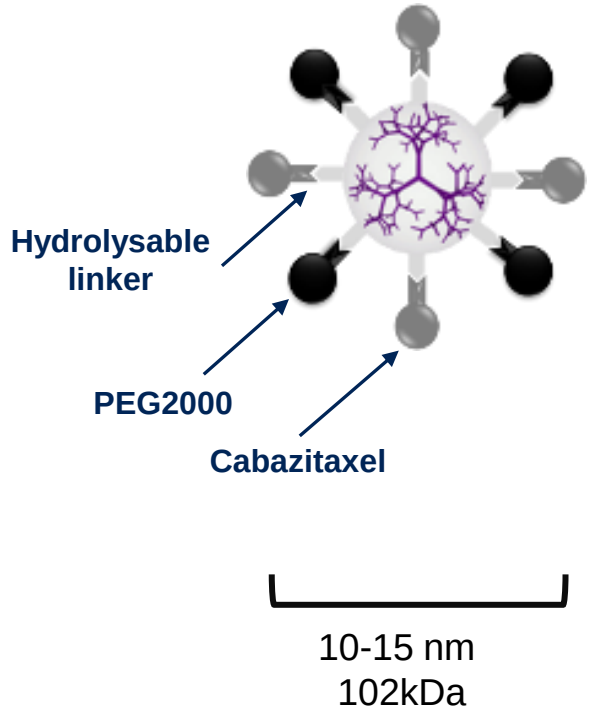
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Dendrimer platform[1]

DEP CTX designed to improve safety and efficacy of cytotoxic payload

- Branched poly-lysine polymer
- Scalable, precise manufacturing in concentric layers
  - 5 generations, 64 attachment points per dendrimer
- Covalent linkage (1:1) to:
  - **cabazitaxel** (CTX) - linker renders payload inert until released
  - **PEG** - solubility without polysorbate; molecular weight/PK
- Hydrolysis of linker in tumor interstitium releases free drug

DEP dendrimer (1:1 ratio CTX:PEG)

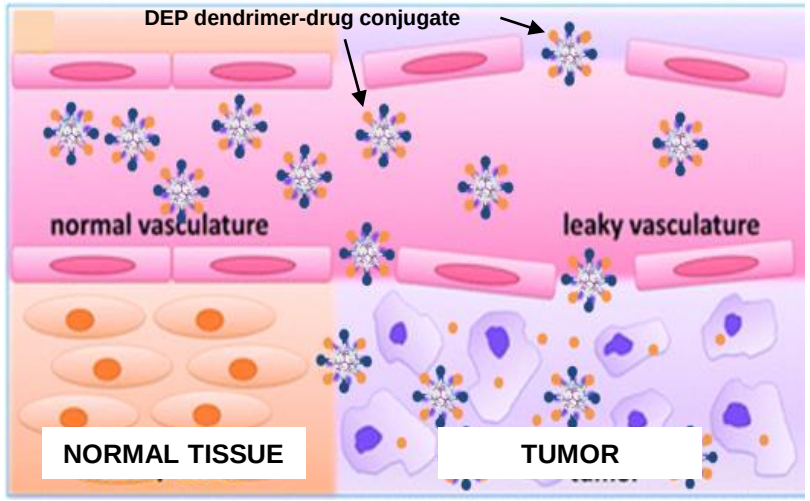


1. Kaminskas et al, Nanomedicine 2011, 6(6):1063-1084

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Preclinical selective delivery and anti-tumor activity

Size-dependent tumor accumulation[1,2]



- DEP CTX preferentially escapes from permeable tumor vasculature
- Prolonged retention in tumor interstitium

Tumor accumulation PET-CT image

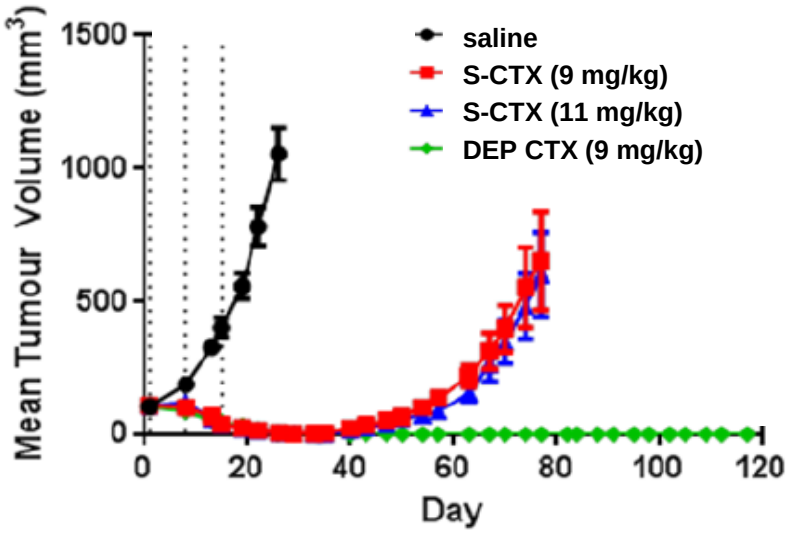


^{89}Zr-labelled DEP CTX

DU145 (human prostate cancer) xenograft

48 hours post IV injection

DEP CTX enhanced efficacy: xenograft model



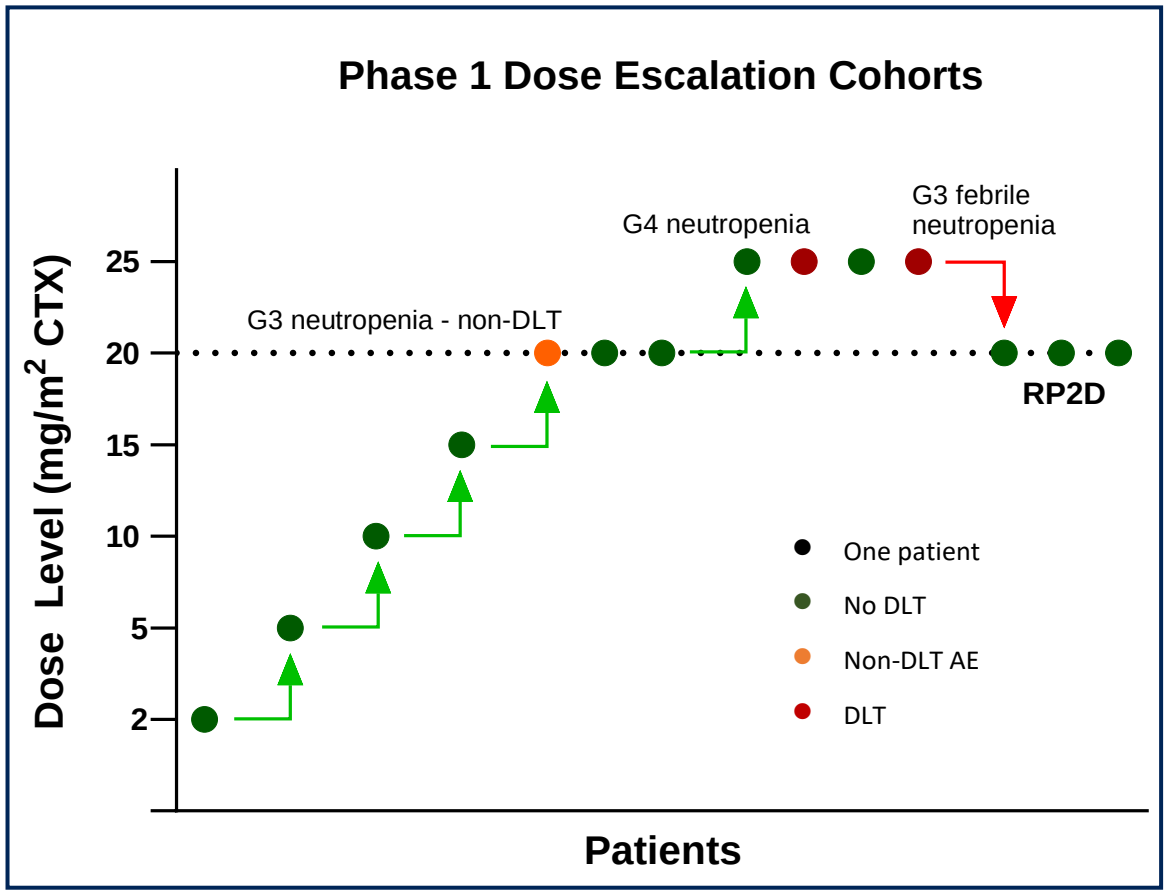
- DEP CTX or s-CTX IV on days 1, 8 & 15; n=10/group
- SCID mice; DU-145 human prostate xenograft

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

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Dendrimer cabazitaxel Phase 1/2 trial

- **Phase 1 - primary objective**: safety profile; MTD & DLTs; **secondary objectives**: preliminary efficacy, PK
- Single patient cohorts, followed by 3+3 escalation[1]. Expansion cohorts in selected tumor types



- **DEP CTX 3-weekly IV infusion**
- **no corticosteroid pre-medication**
- **no routine use of G-CSF**

Phase 1 outcomes (n=14)

- **DLTs**: G4 neutropenia, G3 febrile neutropenia
- **RP2D**: 20 mg/m^2 cabazitaxel, Q3W

Phase 2 dose expansion (n=75)

Prostate (n=25)	**Ovary** (n=22)	**Esophago-gastric** (n=15)	**Other** (n=13*)

* hepatobiliary, head & neck, lung, thymic carcinoma

1. Jones RH, Pinato DJ, Joshua A, et al. *Ann Oncol*, 2022:33(suppl_7):S616-S652

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ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Phase 2 patient characteristics

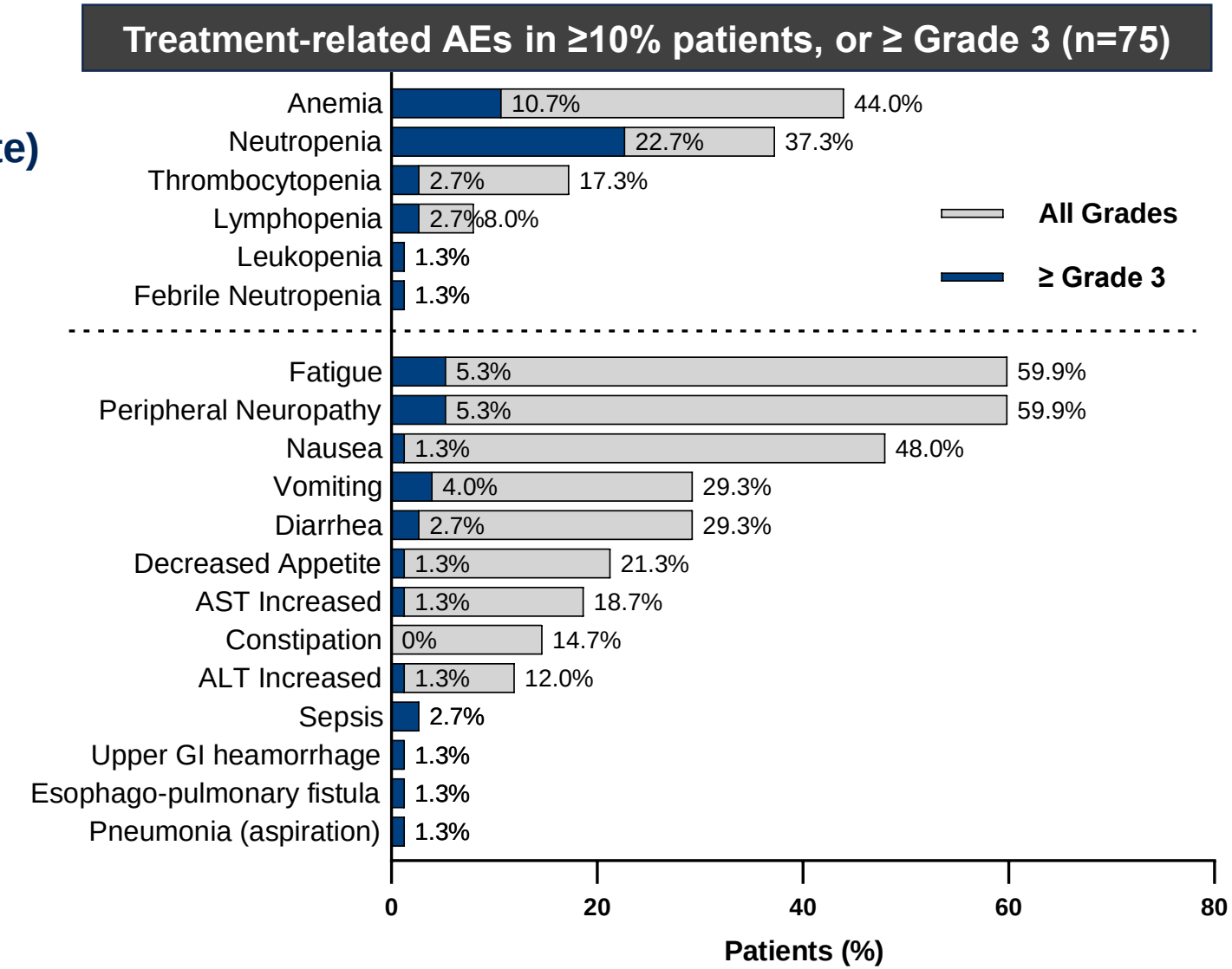
PATIENT BASELINE CHARACTERISTICS		PROSTATE	OVARIAN	EGC	HNSCC	HEPATO-BILIARY	OTHER*	TOTAL
Patients enrolled (n, %)		25 (33%)	22 (29%)	15 (20%)	7 (9%)	4 (5%)	2 (3%)	75 (100%)
Age (years)	**Median (range)**	73 (57-83)	62 (43-76)	61 (25 – 73)	60 (49-69)	65 (57-75)	73 (66-80)	65 (25-83)
Sex (n, %)	**Male**	25 (100%)	0 (100%)	10 (67%)	6 (86%)	2 (50%)	1 (50%)	44 (59%)
	Female	0 (0%)	22 (100%)	5 (33%)	1 (14%)	2 (50%)	1 (50%)	31 (41%)
ECOG PS	**0**	15 (60%)	12 (55%)	8 (53.3%)	4 (57%)	2 (50%)	0	41 (55%)
	1	10 (40%)	10 (45%)	7 (46.7%)	3 (43%)	2 (50%)	2 (100%)	34 (45%)
Prior lines of therapy	**Median (range)**	**4 (2-9)**	**4 (1-11)**	**1 (1-3)**	3 (2-4)	2 (1-4)	3 (2-4)	3 (1-11)
Prior systemic exposure (n, %)	**Platinum**	**2 (8%)**	**22 (100%)**	**13 (87%)**	7 (100%)	4 (100%)	2 (100%)	49 (65%)
	Taxane	**24 (96%)**	**22 (100%)**	**3 (20%)**	4 (57%)	0 (0%)	1 (50%)	54 (72%)
Prior surgery (n, %)	**Any**	7 (28%)	21 (95%)	6 (40%)	3 (43%)	4 (100%)	2 (100%)	43 (57%)
Radiotherapy (n, %)	**Any**	21 (84%)	7 (32%)	6 (60%)	6 (86%)	2 (50%)	1 (50%)	46 (61%)

**lung and thymic carcinoma*

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DEP CTX Phase 2 safety

- **G3/4 neutropenia 23% (16% in prostate)**
- **Febrile neutropenia 1% (none in prostate)**
- **G-CSF:**
  - primary prophylaxis: 0%
  - any: 9%
- **Most common symptomatic AEs:** fatigue, PSN, nausea; mostly mild/moderate
- **>90% of PSN was G1/2**
- **G3/4 non-heme TRAEs 21%**
- **No prominent hypersensitivity signal or anaphylaxis:** no routine steroid premedication
- **G1 alopecia 4% (3/75)**



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Pharmacokinetics

Phase 1 PK:

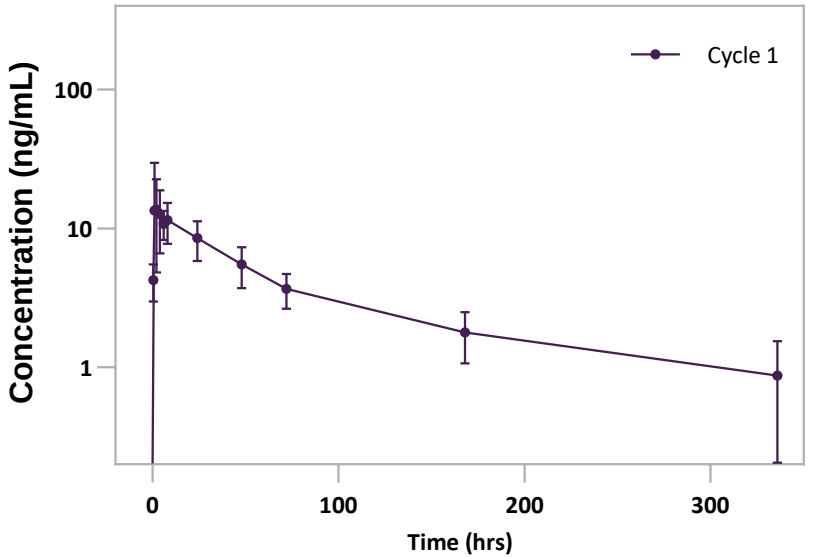
Linear PK parameters across dose range (2-25 mg/m^2 CTX)

No evidence of cycle-to-cycle accumulation

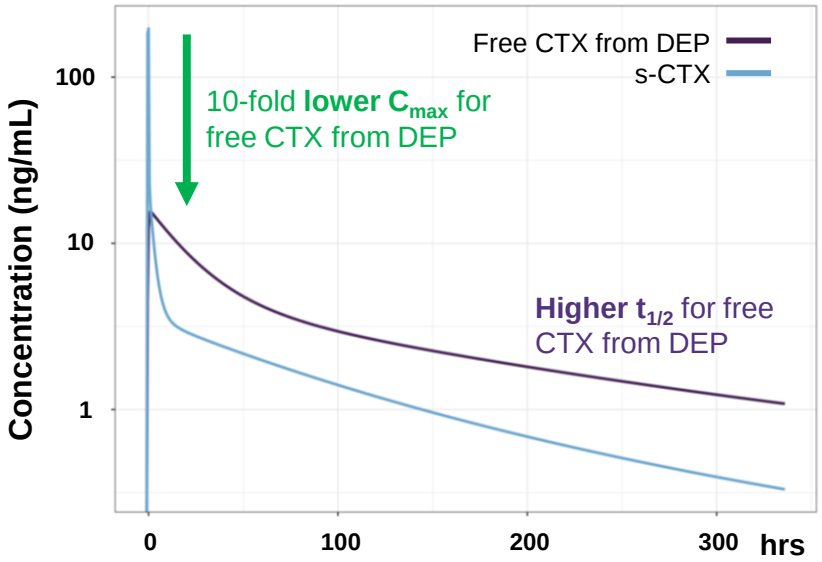
Slow-release depot

PK at RP2D	DEP CTX 20mg/m^2	
	Free CTX (mean)	Total CTX (mean)
C_{max} (ng/mL)	19.2	9,870
AUC_{inf} (ng.h/mL)	1,190	173,000
$t_{1/2}$ (h)	~100	>100

DEP CTX Pharmacokinetics – Free CTX (mean ± SD)



Free CTX vs standard CTX† – simulated population PK profiles



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† Ferron et al., *Cancer Chemother Pharmacol*, 2013; 71:681-692

Phase 2 anti-tumor activity

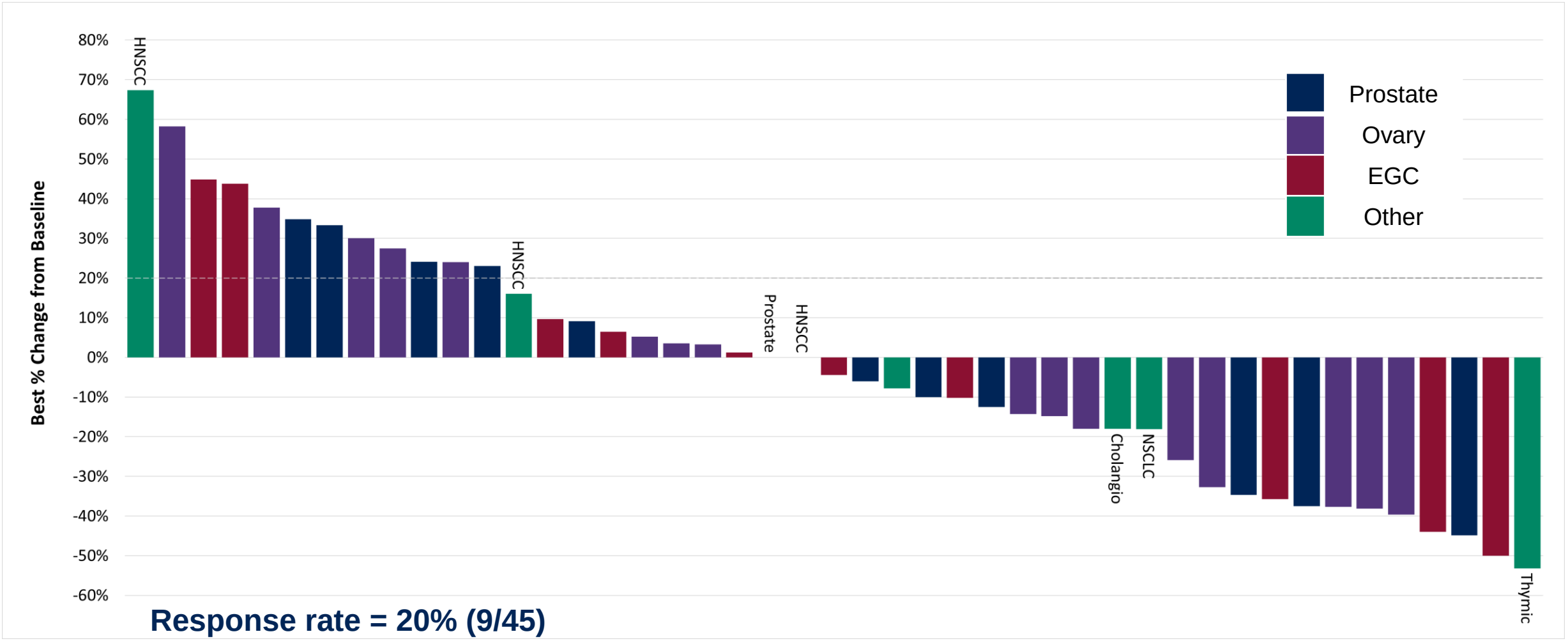
	mCRPC (n = 25)	Ovary (n = 22)	EGC (n = 15)	HNSCC (n = 7)	Hepato-biliary (n = 4)	Other† (n = 2)	Total (n = 75)
Evaluable, n	17	18	10	3	1	2	51
RECIST measurable, n	12	17	10	3	1	2	45
ORR % [95% CI]	**16.7%** [2.1 - 48.4]	**17.6%** [3.8 - 43.4]	**30.0%** [6.7 - 65.2]	**0.0%** [0.0 - 70.8]	**0.0%** [0.0 - 97.5]	**50.0%** [1.3 - 98.7]	**20.0%** [9.6 - 34.6]
DCR % [95% CI]	**70.6%** [44.0 - 89.7]	**66.7%** [41.0 - 86.7]	**80.0%** [44.4 - 97.5]	**33.3%** [0.8 - 90.6]	**100%** [2.5 - 100.0]	**100%** [15.8 - 100.0]	**70.6%** [56.2 - 82.5]
Median PFS (mths) [95% CI]	**4.4*** [3.8 - 5.9]	**3.1** [1.9 - 4.0]	**4.0** [1.9 - 5.6]	**1.7** [1.2 - 1.9]	**0.8** [0.5 - 9.3]	**6.3** [- ; -]	**3.8** [2.1 - 4.1]
Median OS (mths) [95% CI]	**14.7** [6.2 - 19.6]	**Not reached** [4.9 - -]	**8.6** [4.5 - 12.0]	**2.1** [1.5 - 15.1]	**1.9** [0.6 -]	**9.0** [- ; -]	**9.0** [7.0 - 15.1]

*Composite disease progression outcome: RECIST soft tumor / bone / PSA (RECIST v1.1, PCWG3)
Evaluable: received ≥ 1 dose of DEP CTX and had a post-baseline scan at ≥8 weeks,
or efficacy measurement for prostate patients.
RECIST-measurable at baseline (ORR data)

HNSCC: Head & Neck Squamous Cell Cancers
† Other cancers: thymic carcinoma, NSCLC

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Phase 2 anti-tumor activity – RECIST

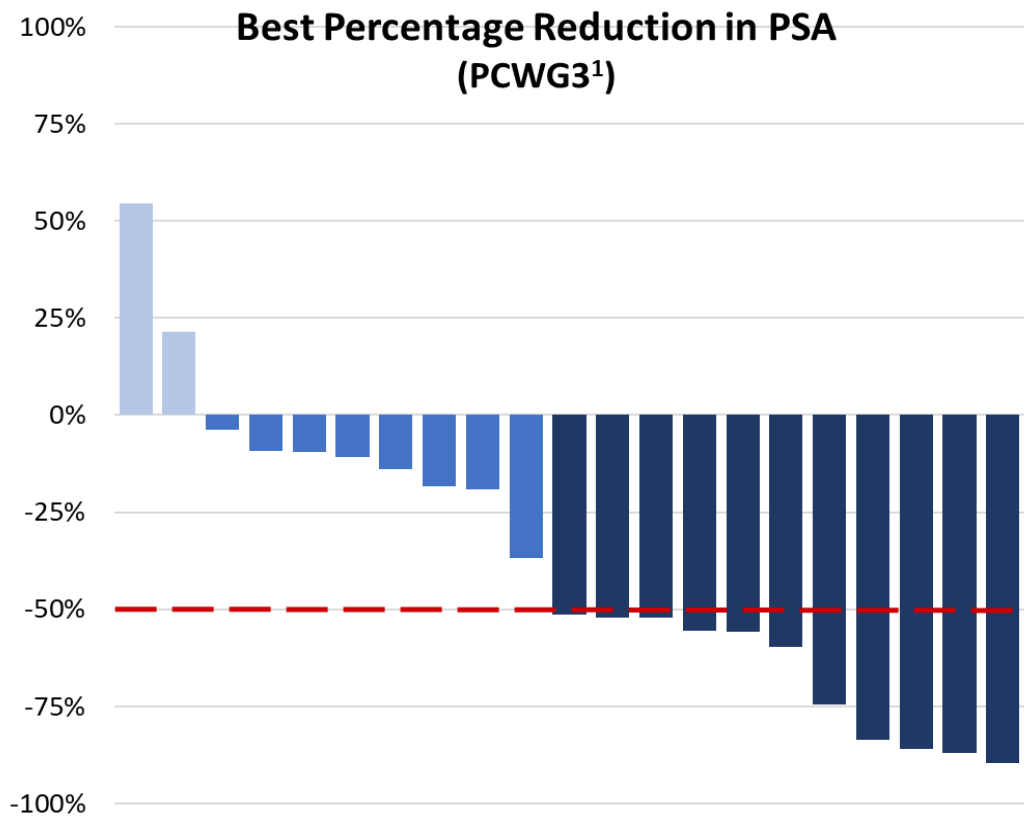


Response rate = 20% (9/45)

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Phase 2 prostate cancer

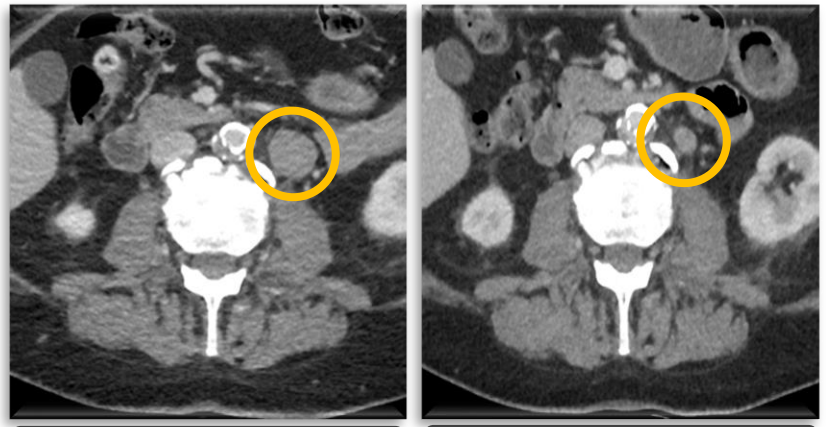
Prostate



1. Scher H et al. *J Clin Oncol* 2016

- **PSA reduction in 91%**
  >50% reduction ('PSA50') in 52%

- **62% reduction abdominal LNs**
- **87% PSA reduction**



Baseline | On treatment

- **87% stable or improved bone disease**
- **Durable PRs and SDs up to 55 weeks**

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Conclusions

- **Dendrimer cabazitaxel is safe and well tolerated:**
  - **no pre-medication** (due to lack of toxic excipients)
  - **potential for less severe myelosuppression** compared with standard CTX
    - **despite little use of G-CSF**
  - **no AEs related to dendrimer scaffold**
- **Clinical benefit even in patients previously exposed to taxanes**
- **DEP platform has potential to deliver other cytotoxics, targeted therapies & radioisotopes**
- **Further clinical development of DEP CTX is justified**

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Acknowledgements

- **All patients participating in the study, and their families**
- All investigators and research personnel who conducted this trial
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