Presentaciones más destacadas en tumores germinales y otros tumores genitourinarios

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EPIC-A: phase II trial of cemiplimab plus SoC chemotherapy followed by maintenance cemiplimab in locally advanced or metastatic penile carcinoma

Prospective COTRIMS trial: final results.
(*Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma*)

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¿Cambio en el paradigma del manejo de estas patologías?

EPIC-A: Phase II trial of cemiplimab plus standard of care chemotherapy followed by maintenance cemiplimab in locally advanced or metastatic penile carcinoma.

Amit Bahl[1], Amarnath Challapalli[1], Balaji Venugopal[2], Mehran Afshar[3], Constantine Alifrangis[4], Alastair Thomson[5], Anna Tran[6], Andrew Hudson[6], Christopher Kent[7], Jim Barber[8], Helen Dearden[9], Rachel Pearson[10], Vivekanandan Kumar[11], Robert Wade[11], Alicia Bravo[1], Emily Foulstone[1], Paul White[12]

EPIC-A: phase II trial of cemiplimab plus SoC chemotherapy followed by maintenance cemiplimab in locally advanced or metastatic penile carcinoma

NHS Health Research Authority

ELIGIBILITY

- Patient with locally advanced or metastatic carcinoma of the penis: TxN3M0 or TxN2M0 or T3N1M0 or T4anyN or M1
- No previous chemotherapy for treatment of penile cancer
- Histologically–proven squamous cell carcinoma of penis or penile urethra
- ECOG performance status 0, 1 or 2
- Adequate renal, liver and bone marrow function
- Measurable disease as per RECIST 1.1

INTERVENTION

4 cycles cisplatin based chemotherapy* IV Q3W + cemiplimab 350mg IV D1
Followed by maintenance with:
30 cycles cemiplimab 350mg IV D1 Q3W

2 years of treatment in total

Tumour assessments per RECIST 1.1

*SoC chemotherapy: 1) Cisplatin (80mg/m2) D1 / 5FU (4000mg/m2) D1-4
2) TIP (cisplatin 75mg/m2, paclitaxel 175mg/m2 and ifosfamide 3600mg/m2)

Primary end point:
- Investigator assessed (RECIST 1.1) Clinical Benefit Rate (CBR) at 12 weeks

Secondary Endpoints:
- Safety
- CBR at 1, 2, 3 years
- Overall response rate (ORR)
- Progression Free survival (PFS)
- Overall survival (OS)
- Quality of Life (QoL)

Research sites: 11 across UK

Period of enrolment: Jan 2022- Dec 2023

Statistical Considerations: A'Hern (2001) study design with $\alpha = 0.05$ + power $(1-\beta) = 0.8$, assuming 25% meeting the clinical end point is poor treatment ($p0 = 0.25$) and 50% is a good treatment ($p1 = 0.5$). Assuming a 10% drop out rate, 29 patients were recruited.

Presented by Amit Bahl.

EPIC-A: phase II trial of cemiplimab plus SoC chemotherapy followed by maintenance cemiplimab in locally advanced or metastatic penile carcinoma

NHS Health Research Authority

Demographics	All patients (N=29)
Age in years - Median (range)	61 (range 38-76)
ECOG Performance score	
0	13 (45%)
1	14 (48%)
2	2 (7%)
Disease stage	
Locally advanced	7 (24%)
Metastatic	22 (76%)
Lung	16 (55.2%)
Bone	6 (23%)
Liver	2 (6.9%)
Number of cycles – Median (range)	5 (1-34)
Follow-up (months) – Median (range)	15.0 (IQR 6.2-21.6)

TIP 2 / cisplatin-5FU 27

Presented by Amit Bahl.

EPIC-A: phase II trial of cemiplimab plus SoC chemotherapy followed by maintenance cemiplimab in locally advanced or metastatic penile carcinoma

NHS Health Research Authority

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Number of cycles – Median (range)	5 (1-34)
Follow-up (months) – Median (range)	15.0 (IQR 6.2-21.6)

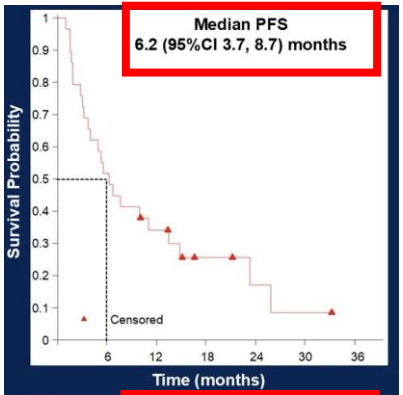
Efficacy outcome	N=29
12 weeks	
Clinical benefit rate (CBR)	62.1% (95%CI 44.4%, 79.7%)
CR	0
PR	15 (51.7%)
SD	3 (10.3%)
Objective response rate (ORR)	51.7% (95%CI 34.4%, 68.6%)
21 (12+9) weeks	
Clinical benefit rate (CBR)	48.3% (95%CI 31.4%, 65.6%)
CR	1 (3.4%)
PR	12 (41.4%)
SD	1 (3.4%)
Objective response rate (ORR)	44.8% (95%CI 28.4%, 62.4%)

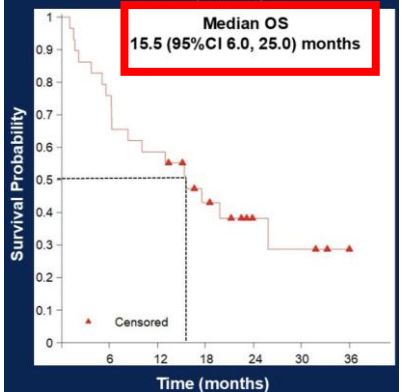
TIP 2 / cisplatin-5FU 27

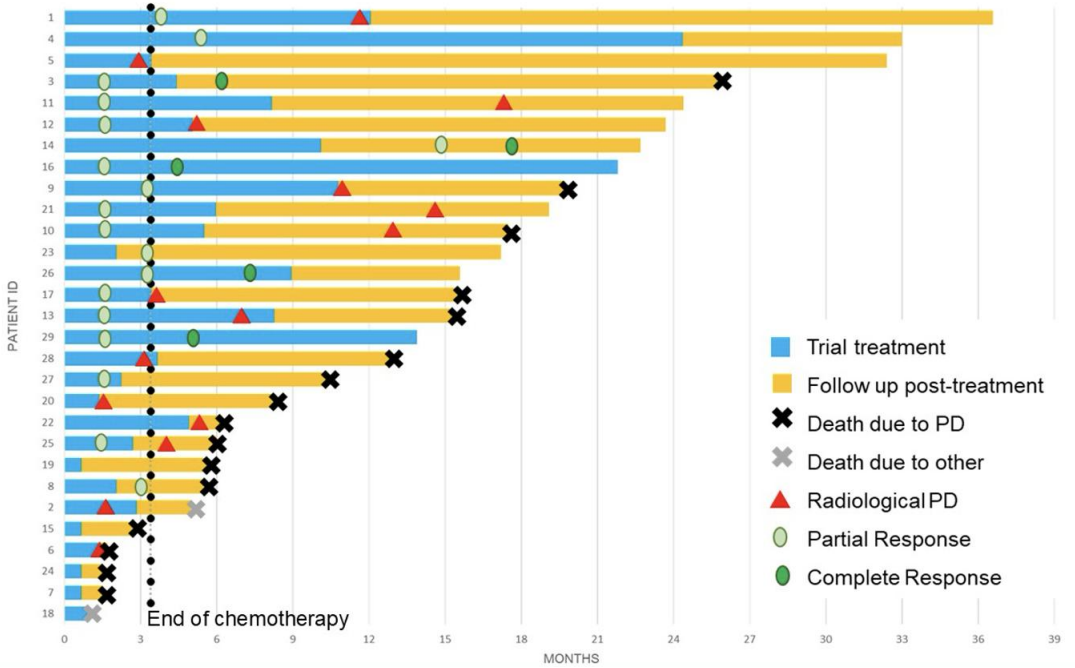
Presented by Amit Bahl.

EPIC-A: phase II trial of cemiplimab plus SoC chemotherapy followed by maintenance cemiplimab in locally advanced or metastatic penile carcinoma

NHS Health Research Authority







Presented by Amit Bahl.

EPIC-A: phase II trial of cemiplimab plus SoC chemotherapy followed by maintenance cemiplimab in locally advanced or metastatic penile carcinoma

NHS Health Research Authority

Table: List of AEs ≥ Grade 3 related to chemotherapy or cemiplimab.

AE CTC Cat 0	Chemotherapy Related		Cemiplimab Related	
	N	%	N	%
Gastrointestinal disorders	3	13.6	1	11.1
Blood and lymphatic system	2	9.1	---	
Infections and infestations	2	9.1	2	22.2
Cardiac disorders	1	4.5	---	
Ear and labyrinth disorders	1	4.5	---	
Immune system disorders	1	4.5	1	11.1
Musculoskeletal & connective tis	1	4.5	1	11.1
Respiratory, thoracic and medias	1	4.5	---	
Vascular disorders	---		1	11.1
Total	22	100	9	100

- Safety profile is in keeping with reported data on cisplatin-based chemotherapy and cemiplimab.

- 23% related to cemiplimab, 31% related to chemotherapy.

- 2 grade 5 AEs, neither related to cemiplimab but 1 related to chemotherapy.

- 7 patients discontinued treatment, 4 were related to cemiplimab (14%).

Presented by Amit Bahl.

EPIC-B: phase II trial of cemiplimab as first line treatment in advanced penile carcinoma.

NHS Health Research Authority

ELIGIBILITY

- Patient with locally advanced or metastatic carcinoma of the penis: TxN3M0 or TxN2M0 or T3N1M0 or T4anyN or M1
- No previous chemotherapy for treatment of penile cancer
- Histologically–proven squamous cell carcinoma of penis or penile urethra
- ECOG performance status 0, 1 or 2
- Adequate renal, liver and bone marrow function
- Measurable disease as per RECIST 1.1

INTERVENTION

34 cycles of cemiplimab 350mg IV D1 Q3W

2 years of treatment in total

Tumour assessments per RECIST 1.1

Primary end point:

- Investigator assessed (RECIST 1.1) Clinical Benefit Rate (CBR) at 12 weeks

Secondary Endpoints:

- Safety
- CBR at 1, 2, 3 years
- Overall response rate (ORR)
- Progression Free survival (PFS)
- Overall survival (OS)
- Quality of Life (QoL)

Research sites: 11 across UK

Period of enrolment: Nov 2021- Apr 2024

Statistical Considerations: A'Hern (2001) study design with $\alpha = 0.05$ + power $(1-\beta) = 0.8$, assuming 5% meeting the clinical end point is poor treatment ($p0 = 0.05$) and 25% is a good treatment ($p1 = 0.25$). Assuming a 10% drop out rate, 18 patients were recruited.

Presented by Amarnath Challapalli.

EPIC-B: phase II trial of cemiplimab as first line treatment in advanced penile carcinoma.

NHS Health Research Authority

Demographics	All patients (N=18)
Age in years - Median (range)	72 (range 44-88)
ECOG Performance score	
0	1 (5%)
1	10 (56%)
2	7 (39%)
Disease stage	
Locally advanced	3 (17%)
Metastatic	15 (83%)
Lung	6 (33.3%)
Bone	1 (5%)
Liver	1 (5%)
Number of cycles – Median (range)	4 (1-32)
Follow-up (months) – Median (IQR)	5.5 (IQR 2.3-8.1)

Presented by Amarnath Challapalli.

EPIC-B: phase II trial of cemiplimab as first line treatment in advanced penile carcinoma.

NHS Health Research Authority

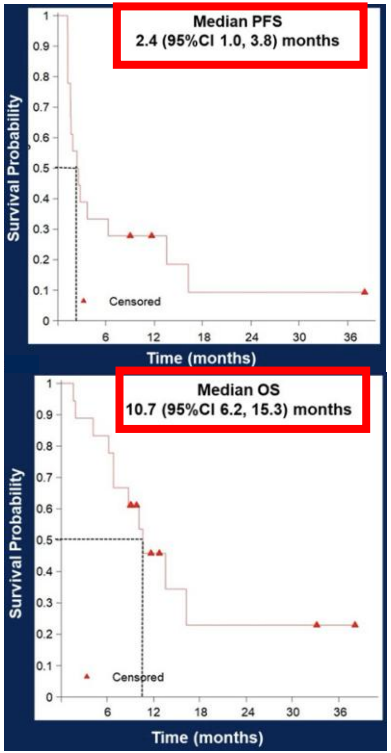
Demographics	All patients (N=18)
Age in years - Median (range)	72 (range 44-88)
ECOG Performance score	
0	1 (5%)
1	10 (56%)
2	7 (39%)
Disease stage	
Locally advanced	3 (17%)
Metastatic	15 (83%)
Lung	6 (33.3%)
Bone	1 (5%)
Liver	1 (5%)
Number of cycles – Median (range)	4 (1-32)
Follow-up (months) – Median (IQR)	5.5 (IQR 2.3-8.1)

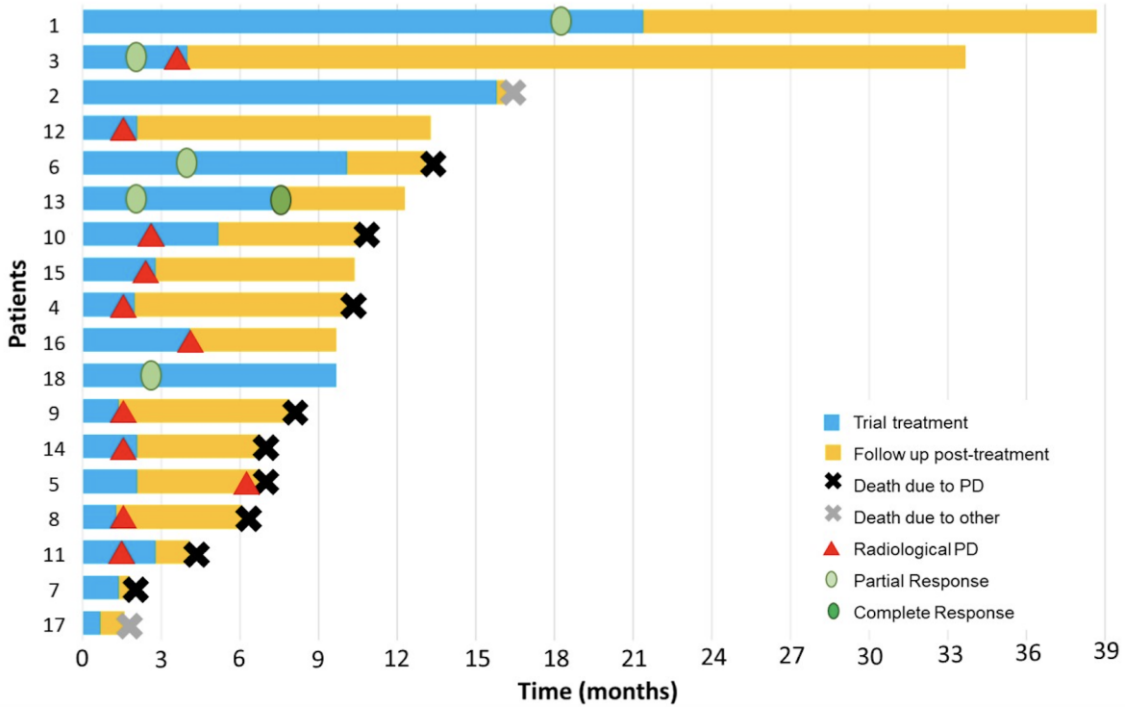
Efficacy outcome	N=18
12 weeks	
Clinical benefit rate (CBR)	38.9% (95%CI 20.3%, 61.4%)
CR	0
PR	3 (16.6%)
SD	4 (22.2%)
Objective response rate (ORR)	16.6% (95%CI 5.8%, 39.2%)
Best response	
Clinical benefit rate (CBR)	49.9% (95%CI 29.0%, 71.0%)
CR	1 (5.5%)
PR	4 (22.2%)
SD	4 (22.2%)
Objective response rate (ORR)	27.7% (95%CI 12.5%, 50.9%)

Presented by Amarnath Challapalli.

EPIC-B: phase II trial of cemiplimab as first line treatment in advanced penile carcinoma.

NHS Health Research Authority





Presented by Amarnath Challapalli.

EPIC-B: phase II trial of cemiplimab as first line treatment in advanced penile carcinoma.

NHS Health Research Authority

CTCAE SOC (number)	AE term	Grade
Skin and subcutaneous tissue disorders (1)	Toxic epidermal necrolysis (SUSAR)	5
Gastrointestinal disorders (2)	Proctitis (SAR)	3
	Colitis (SAR)	3
Investigations (2)	Increased neutrophils	3
	Increased white blood cells	3
Immune system disorders (1)	Allergic reaction (SAR)	3
Infections and infestations (1)	Abscess infection (SAR)	3

Related to cemiplimab (31%):

- AEs of any grade: 75, (median per patient was 3)
- Gr3 AEs: 6, most common being infection.
- No G4 AES reported
- Gr 5 AEs: 1 Toxic epidermal necrolysis

There was 1 Gr 5 no related to cemiplimab: Cardiorespiratory event

4 patients discontinued treatment due to toxicity,

2 related to cemiplimab (11%)

Presented by Amarnath Challapalli.

Studies of systemic therapy in metastatic or relapsed PSCC

Regimen	Authors	Study design	No. Patients Evaluable	ORR/CR	G3-4 Toxicities	Median PFS/OS
Paclitaxel	Di Lorenzo et al. 2011	Phase II in pretreated pts	25	20%/0	28% neutropenia	2.75 months/ 5.75 months
5-FU + Cisplatin	Di Lorenzo et al. 2012	Retrospective first line stage 3/4	25	32%/0%	20% neutropenia	5 months/ 8 months
Vinflunine[1]	Nicholson S, et al. 2022	Single-arm, Phase II trial Chemonaive pts	26	27%/0%	68% at least 1 G3 TRAE	2.9 months/ 8.4 months
Dacomintinib[2]	Necchi et al. 2018	Single-arm, Phase II trial Chemonaive pts	28	32.1%/3.5%	-10 % skin rash	4.1 months/ 13.7 months
Nimotuzumab	Huang et al. 2019	Pilot study in pretreated advanced disease	6	33%/16%	NA	4.8 months/ 9.2 months

1. Nicholson S , et al. Br J Cancer . 2022 Jan;126(1):34 41 / 2. Necchi A, et al. BJU Int . 2018 Mar;121(3):348 356

Single agent immunotherapy or combination therapies

EPIC-B
ORR: 16.6%
PFS: 2.4 mo
OS: 10.7 mo

CaboNivo (N=59)
CaboNivolpi (N=49)
- PSCC: N=9
- 4 PR; 5 SD (all with CaboNivolpi)

Apolo AB, et al. *J Clin Oncol*. 2024 Sep 1;42(25):3033-3046

PERICLES study:
- **Atezo w/wo locoregional RT**
- 32 stage IV PSCC
- ORR: 33% (44% A+RT; 17% A)
- Median PFS: 2.5m
- Median OS: 11.5m
- hrHPV+ > Improved PFS/OS

De Vries HM, et al. *J Clin Oncol*. 2023 Nov 1;41(31):4872-4880

GSRGT retrospective study:
- N=92
- Stage IV PSCC
- Chemonaive (20%) + chemorefractory (80%) PSCC
- Various IO regimens
- **ORR: 13%**
- **Median PFS: 3.2 months**

El Zarif T, et al. *J Natl Cancer Inst*. 2023 Dec 6;115(12):1605-1615

HERCULES Trial (LACOG 0218)

ELIGIBILITY CRITERIA (N=33)

- ✓ ECOG PS 0-1
- ✓ Patients with penile squamous cell carcinoma:
  - Metastatic disease (de novo or recurrent),
  - Locally advanced disease (TanyN3M0 or T4NanyM0) not amenable to curative-intent therapy,
  - Loco-regional recurrence not amenable to curative-intent therapy
- ✓ No prior exposure to chemotherapy for advanced disease
- ✓ Prior (neo)adjuvant chemotherapy is allowed if progression after 12 months

INTERVENTION

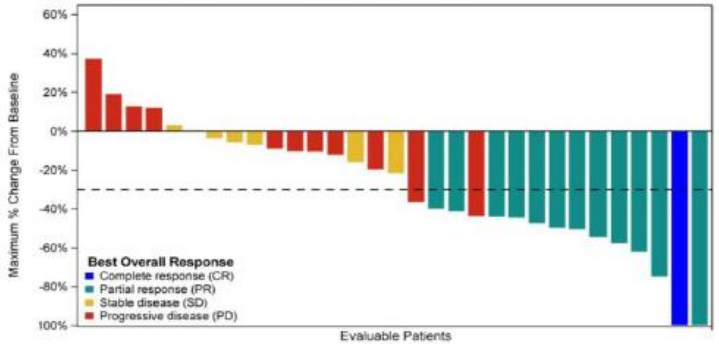
Cisplatin 70mg/m² or **Carboplatin** AUC 5 D1 +
5-FU 1000mg/m²/day D1-D4 +
Pembrolizumab 200mg IV Q3W for 6 cycles

Followed by maintenance with:
Pembrolizumab 200mg IV Q3W up to 34 cycles

Tumor assessment per RECIST v1.1 by investigator every 6 weeks.

- 11 Brazilian centers

Tumor shrinkage of any magnitude was observed in 75.8% of patients.



- **ORR: 39.4% (13/33)**
- Median FUP: 24 months
- Median PFS: 5.4 months
- Median OS: 9.6 months

Responses enriched in:

- **TMB-high tumors: ORR: 75%**
- **HPV+ tumors: ORR: 55.6%**

EPIC-A
ORR: 51.7%
PFS: 6.2 mo
OS: 15.5 mo

J Clin Oncol. 2024;42(suppl 16):abstr 5009.

ASCO GU 2025 Conclusions on Penile Carcinoma

These data support combination cisplatin-based chemotherapy + cemiplimab as a first line treatment option to potentially improve outcomes in this rare cancer

These data support cemiplimab alone as new standard of care first line treatment in Ia/mPC patient's ineligible for chemotherapy.

GONORTE
Grupo Oncológico

ACTUALIZACIONES TRAS EL CONGRESO AMERICANO DE ONCOLOGÍA CLÍNICA GU

NCCN Guidelines Version 2.2025
Penile Cancer

First-Line Systemic Therapy for Metastatic/Recurrent Disease
Preferred Regimen • TIP
Other Recommended Regimens • 5-FU + cisplatin • 5-FU + cisplatin + pembrolizumab followed by pembrolizumab maintenance therapy • 5-FU + carboplatin + pembrolizumab followed by pembrolizumab maintenance therapy

- Not recommended: Bleomycin-containing regimens are associated with unacceptable toxicity.[5]
- TIP is a reasonable first-line treatment for patients with metastatic penile cancer, including palliative treatment of patients with distant metastases.[2]
- 5-FU + cisplatin has been used historically for metastatic penile cancer and can be considered as an alternative to TIP.[4] It appears to be effective for some patients, although the toxicities may be limiting and may require dose reductions.[3,4]
- There are no randomized clinical trials due to the rarity of penile cancer in industrialized countries.

Subsequent-Line Systemic Therapy for Metastatic/Recurrent Disease
Preferred Regimen • Clinical trial • Pembrolizumab, if unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) tumor that has progressed following prior treatment and no satisfactory alternative treatment options,[6,7,8] or if tumor mutational burden-high (TMB-H), TMB ≥10 mut/Mb in patients who have progressed on previously approved lines of therapy[9]
Useful in Certain Circumstances • Paclitaxel • Cetuximab

- No standard subsequent-line systemic therapy exists.
- A clinical trial is preferred. The evidence to support the palliative use of second-line therapy is limited.[10]
- Paclitaxel[11] or cetuximab[12] may be considered in select patients, especially if not previously treated with a similar class of agent.
- Any tumor-agnostic labels that cover penile cancer can be used based on results of broad next-generation sequencing (NGS).

EAU-ASCO Collaborative Guidelines on
Penile Cancer

Summary of evidence	LE
Low-level data support the use of platinum-based chemotherapy as first-line systemic therapy in advanced disease.	3
Effective second-line palliative chemotherapy regimens are lacking. Second-line chemotherapy in multiple studies was associated with median OS of six months or less.	3
Initial phase II or basket studies assessed anti-EGFR therapy or checkpoint inhibition, as monotherapy or combination therapy, in advanced disease. Early evidence of promising clinical activity has been reported in patients with penile cancer.	2b

Recommendations	Strength rating
Systemic therapies	
Offer patients with distant metastatic disease, platinum-based chemotherapy as the preferred approach to first-line palliative systemic therapy.	Weak
Do not offer bleomycin because of the pulmonary toxicity risk.	Strong
Offer patients with progressive disease under platinum chemotherapy the opportunity to enroll in clinical trials, including experimental therapies within phase I or basket trials.	Strong
Radiotherapy	
Offer radiotherapy for symptom control (palliation) in advanced disease.	Strong

Prospective COTRIMS (Cologne Trial of Retroperitoneal Lymphadenectomy in Metastatic Seminoma): final results

Axel Heidenreich, MD, PhD

Professor of Urology

University Hospital Cologne, Germany

Presented by Axel Heidenreich.

Prospective COTRIMS trial: final results.
(*Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma*)

- single modality approach without delivery of DNA damaging agents
- retroperitoneal nerve sparing lymphadenectomy unilateral, modified template dissection
- no adjuvant systemic chemotherapy following RPLND
- guideline recommended follow-up according to EAU guidelines
- 3-4 cycles of PEB in case of relapsing disease depending on IGCCCG classification

Presented by Axel Heidenreich.

Prospective COTRIMS trial: final results. (*Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma*)

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Inclusion criteria

- pure testicular seminoma
- tumor markers AFP and ß-hCG negative, LDH < 1.5 times USN
- clinical stages IIA and IIB (CT chest, CT/MRI abdomen, pelvis) at time of diagnosis or during active surveillance
- repeat CT scan in equivocal findings at primary staging after 6-8 weeks
- evaluation of circulating miR371 to predict histology

Presented by Axel Heidenreich.

Prospective COTRIMS trial: final results.
(*Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma*)

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Objectives: to evaluate the following issues in in low volume metastatic seminomas

1) Feasibility

2) Oncological outcome

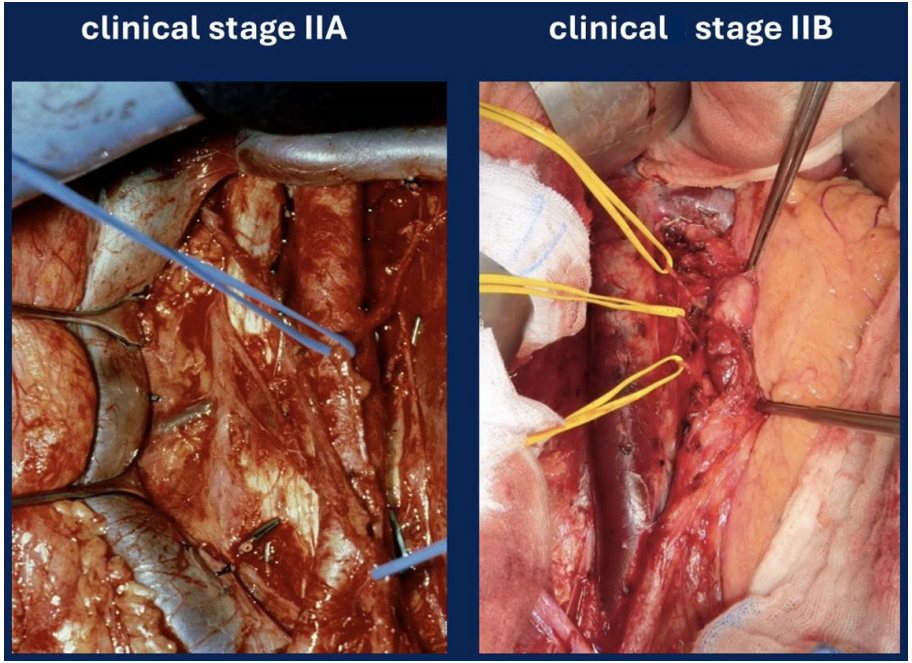
PFS & OS, biomarker to predict pathohistology

3) Functional outcome

antegrade ejaculation

4) Complications

Clavien-Dindo classification



Presented by Axel Heidenreich.

Prospective COTRIMS trial: final results.
(*Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma*)

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Patient characteristics	number (n = 34)
age (years), median (IQR)	34.2 (21-54)
Primary orchiectomy, n (%) right left pT1 pT2 Rete testis Invasion	 11 (32) 23 (68) 22 (65) 12 (35) 6/22 (28)
Tumo diameter (cm), median (IQR)	4.3 (2.1 – 5.1)
Clinical stage at diagnosis, n (%) CS I CS IIA CS IIB	 16 (47) 14 (41) 4 (12)
Clinical stage at RPLND, n (%) CS IIA CS IIB	 22 (65) 12 (35)
number lymph nodes on preop. CT, median (IQR)	1.6 (1-3)
Size of lymph nodes (cm), median (IQR)	2.2 (1.3-4.5)

- 31 (91.2%) open nsRPLND
- 3 (8.8%) robotic RPLND

- antegrade ejaculation 30 (88.2%)

- Clavien-Dindo IIIa-IV 4 (11.7%)

(lymphocele, chylous ascites, paralytic ileus)

	Definition
Grade I	any deviation from the ordinary post-operative course without giving pharmacological and surgical interventions.
Grade II	complication requires pharmacological treatment
Grade IIIa	complication requires surgical intervention under local anesthesia
Grade IIIb	complications requires surgical intervention under general anesthesia
Grade IV	complications are related to life-threatening complications that require intensive care unit management
Grade V	complications are related to patient's death.

Ann Surg. 2004;240:205-213.
Presented by Axel Heidenreich.

Prospective COTRIMS trial: final results.
(*Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma*)

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Retroperitoneal lymph nodes (preoperative distribution)

Paracaval	*6/11 - 54.5%*	*Paraaortal*	*15/23 - 65.2%*
Precaval	*5/11 - 45.4%*	*Preaortal*	*4/23 - 17.4%*
Interaortocaval	*3/21 - 27.3%*	*Bifurcation*	*4/23 - 17.4%*

Retroperitoneal lymph nodes (postoperative)

Number of resected lymph nodes	19 (7 - 57)
Number of positive lymph nodes.	1.4 (1 – 2)
Median diameter of positive lymph nodes	2.3 (1.0 – 4.5) cm

Histology

Seminoma	*29 (85%)*
Extracapsular extension	*8 (27.6%)*
Non malignancy	*3 (8.9%)*
Embryonal carcinoma	*2 (5.9%)*

Presented by Axel Heidenreich.

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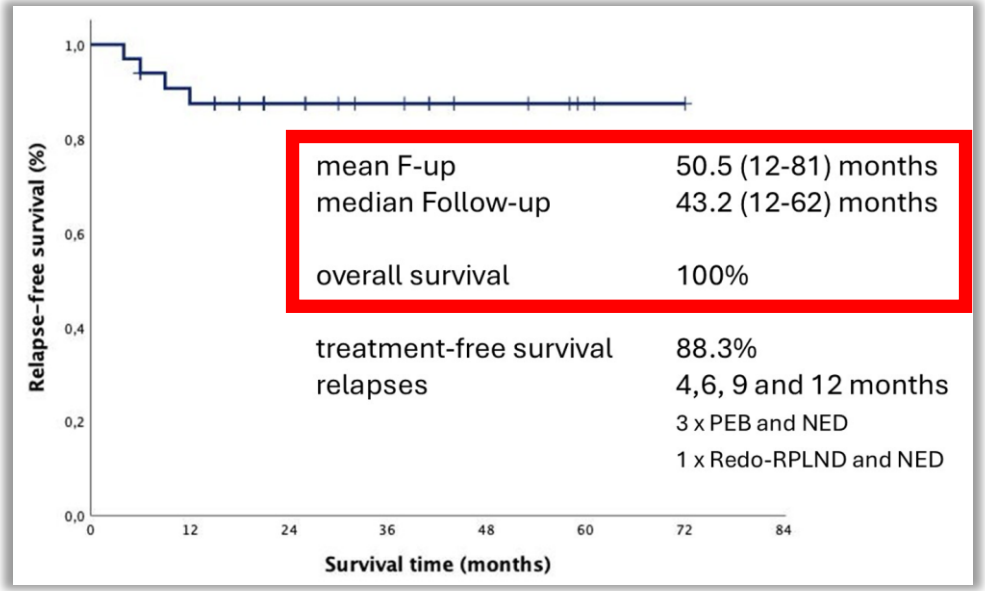
Oncological outcome



Relapse

Pulmonary nodule, mediastinal, pelvic contralateral, paraaortic contralateral

Low relapse rate might be due to:

- patient cohort (*80% CS IIA / small vol CS IIB*)
- the template (*always retrocaval or -aortal, always common iliac artery down to iliac bifurcation, always lateral to ureters, always resection of ipsilateral testicular vein and vas deferens*)

Presented by Axel Heidenreich.

Summary of world´s experience

	SEMS	PRIMETEST	COTRIMS	Indiana	MSK	SWENOTECA
Country	US/Canada	Germany	Germany	US	US	Norway/Sweden
Study period	2016-2021	2015-2020	2018-202?	2014-2021	2013-2023	2019-2022
N	55	33	34	67	45	62
Treatment	RPLND	RPLND	RPLND	RPLND	RPLND	RPLND
Stage	IIA-B (1-3cm)	IIA-C (1-5cm)	IIA-B (1-5cm)	IIA-B (1-3cm)	IIA-B (1-3cm)	IIA-B (1-3cm)
Pathologic stage	pN0: 9 (16%)	pN0: 3 (9%)	pN0: 3 (9%)	pN0: 1 (1%)	pN0: 2 (4%)	pN0: 4 (6%)
Follow up	33 months	32 months	22 months	22 months	18 months	23 months
Adjuvant tx	1 (2%)	0	0	2 (3%)	16 (36%)	18 (29%)
RFS	81% @ 24m	70% @ 36m	88%	80.2% at 24m	84% at 24m	90% at 24m

Risks / Adverse Events

	SEMS	PRIMETEST	COTRIMS	Indiana	MSK	SWENOTECA
Country	US/Canada	Germany	Germany	US	US	Norway/Sweden
Study period	2016-2021	2015-2020	2018-202?	2014-2021	2013-2023	2019-2022
N	55	33	34	67	45	62
Complication • Grade □3	4 (7%) 2 (4%)	6 (18%) 4 (12%)	4 ? 4 (12%)	5 (7%) 3 (4%)	5 (11%) 2 (4%)	5 (8%) 3 (5%)
Deaths	0	0	0	0	0	0
Nerve-sparing • Antegrade ejac	87% NR	100% 94%	100% 88%	70% 98%	71% NR	NR

Retroperitoneal relapses

	SEMS	PRIMETEST	COTRIMS	Indiana	MSK	SWENOTECA
Country	US/Canada	Germany	Germany	US	US	Norway/Sweden
Study period	2016-2021	2015-2020	2018-202?	2014-2021	2013-2023	2019-2022
N	55	33	34	67	45	62
Bilateral template	19 (35%)	0	0	31 (46%)	45 (100%)	2 (3%)
Total relapse	12	10	4	11	5	6
Contralateral RP relapse following unilateral template	4	4	1	2	0	NR

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NCCN Guidelines Version 1.2025
Testicular Cancer - Pure Seminoma

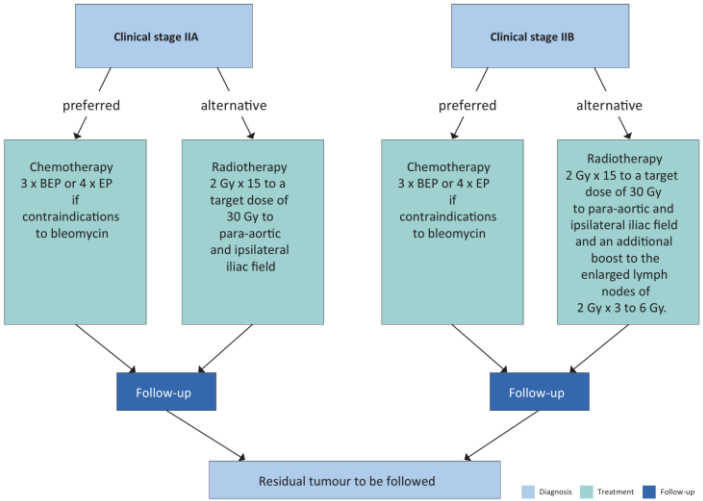
CLINICAL STAGE		PRIMARY TREATMENT[i]
Stage IIA/IIB[h,q]	<3 cm[r] →	RT[l] to include para-aortic and ipsilateral iliac lymph nodes to a dose of 30 Gy (1–2 cm) or 36 Gy (2–3 cm) or First-line chemotherapy[s]: BEP[u] for 3 cycles or EP for 4 cycles or Nerve-sparing RPLND[t,v,w] (category 2B for 2–3 cm) or Carboplatin + RT[x,y] (category 2B)
	3–5 cm →	First-line chemotherapy[s]: BEP[u] for 3 cycles or EP for 4 cycles

Note: All recommendations are category 2A unless otherwise indicated.

EAU Guidelines on Testicular Cancer

Summary of evidence	LE
At this stage all de-escalation strategies, including RPLND remain under evaluation and should only be considered in high volume specialised centres within a prospective cohort or clinical trial.	3

Figure 2: Treatment options in patients with seminoma clinical stage IIA and B*



ASCO GU 2025 Conclusions on COTRIMS trial

- Primary RPLND without adjuvant chemothreapy → standard treatment option across several major guidelines for IIA/selected IIB seminoma
- Needs to be done at experienced centers

Future research: biomarkers to refine patient selection; mild elevated HCG levels; predicting who benefits from adjuvant chemotherapy; miR371 to avoid unnecessary surgery

Presented by Clint Cary.

Prospective COTRIMS trial: final results.
(*Cologne trial of retroperitoneal lymphadenectomy in metastatic seminoma*)

UNIKLINIK KÖLN

Micro-RNA 371 and histology

Evaluation of a miRNA-371a-3p Assay for Predicting Final Histopathology in Patients Undergoing Primary Nerve-sparing Retroperitoneal Lymphadenectomy for Stage IIA/B Seminoma or Nonseminoma European Urology Oncology 2024

Felix Seelemeyer[a], David Pfister[a], Robert Pappesch[b], Sabine Merkelbach-Bruse[b], Pia Paffenholz[a], Axel Heidenreich[a,b,]*

miR371 (n=18)

true positive 23/24 (95.8%)

true negative 3/3 (100%)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Overall	95.7	100	100	75
Clinical stage IIA	91.7	100	100	67
Clinical stage IIB	100	100	100	100

PPV = positive predictive value; NPV = negative predictive value.

Presented by Axel Heidenreich.

Landscape of New Trials and Targets in Refractory Germ Cell Tumors

Darren R. Feldman, MD
Section Head, Germ Cell Cancer
Genitourinary Oncology Service
Department of Medicine
Memorial Sloan Kettering Cancer Center

Relapsed / refractory GCT (RR-GCT)

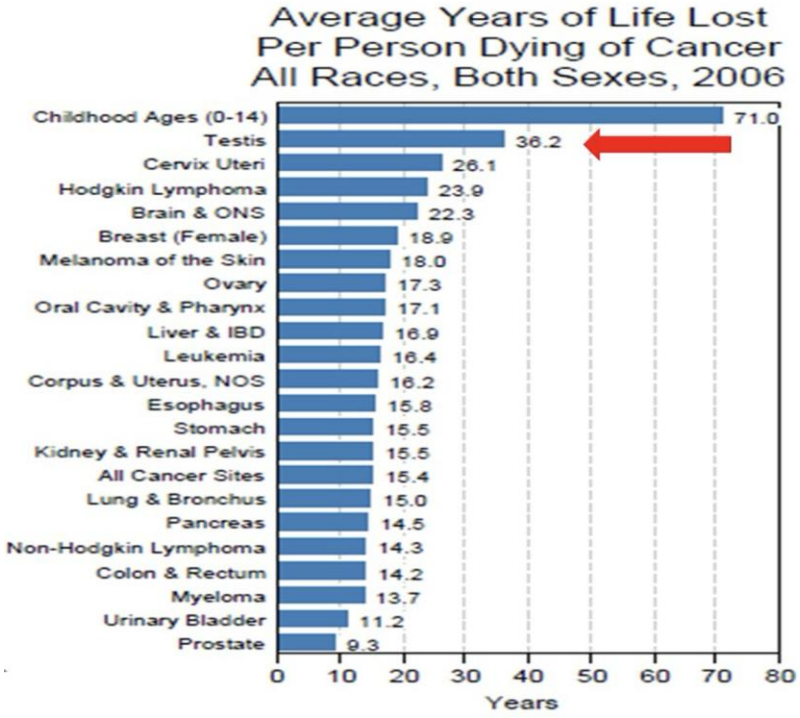
GCT that is probably not curable

Includes most patients with:

- PD after HDCT
- absolute refractory GCT (not response to 1L ChT)
- PD after 2 CDCT regimens who are not candidate to HDCT
- unresectable late relapse CDCT

No curative systemic therapy for progressors after HDCT

When death occurs, still accounts on average for largest number of life years lost of any non-childhood malignancy



Cancer Epidemiol Biomarkers Prev. 2020;29(12):2591-2598.
Presented by Darren Feldman.

Post HDCT options: single agent and combinations

Drug(s)	No. Trials	N	ORR, %	CR, %
Oxaliplatin[1]	1	32	6-19*	0
Gemcitabine[2-3]	2	51	15-19	0-5
Paclitaxel[4-8]	5	98	11-30	0-10
Oral Etoposide[9-10]	2	42	29-33	0-10
Gem / Oxali[11-14]	4	92	17 – 46	5 – 18**
Gem / Paclitaxel[15]	1	32	31	19**
Gem / Oxali / Paclitaxel[16-17]	2	71	31 – 51	7-15

* 2 dose levels studied; ** not all CRs durable

- Other agents with activity include: Vinblastine, Actinomycin-D, Epirubicin

GCT essentially not curable after HDCT failure – the one exception is desperation surgery (solitary RP or lung met)

Presented by Darren Feldman.

Phase 2 trials of PD1/PD-L1 inhibition in pts with platinum refractory GCTs

	GU14-206[1]	APACHE-A[2]	Slovakia[3]	Japan[4]	MDACC[5]
Total Evaluable Patients	12	11	8	16	12 (2 women)
Treatment	Pembrolizumab	Durvalumab	Avelumab	Nivolumab	Pembrolizumab
Best response					
Partial response	0 (0%)	0 (0%)	0 (0%)	1 (6)%	0 (0%)
Stable disease	2 (17%)	0 (0%)	0 (0%)	3 (19%)	3 (25%)
Progressive disease	10 (83%)	11 (100%)	8 (100%)	12 (75%)	0 (0%)
Median # doses (range)	2 (1-8)	NR	NR	3 (2-46)	3 (1-14)
Landmark PFS	12 wk – 17%	9 wk – 0%	12 wk - 0%	NR	3 mo – 33%
Median PFS, mo (CI)	NR	1.5 (NR)	0.9 (0.5-1.9)	1.5 (0-23.6)	2.4 (1.5-4.5)
Median OS, mo (CI)	NR	3.1 (NR)	2.7 (1.0-3.3)	4.1 (1.6-29.8)	10.6 (4.6-27.1)

Presented by Darren Feldman.

Phase 2 trials of combination ICB in pts with platinum refractory GCTs

	APACHE-B[1]	Alliance[2]	Alliance[2]	DFCI[3]	MSKCC[4]
Total Evaluable Patients	11	4	2	5	29 (1 woman)
Treatment	Durva + Treme	Nivo + Cabo	Ipi + Nivo + Cabo	Ipi + Nivo	Durva + Treme
Best response					
Partial response	1 (9%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Stable disease	1 (9%)	1 (17%)	0 (0%)	1 (20%)	4 (14%)
Progressive disease	9 (82%)	3 (83%)	2 (100%)	4 (80%)	24 (83%)
Landmark PFS	9 wk – 18%	NR	NR	NR	16 wk – 14%
Median PFS (CI)	1.7 mo (NR)	NR	NR	NR	6.0 wks (4.1 – 7.1)
Median OS (CI)	3.1 (NR)	NR	NR	NR	7.3 mo (3.2 – 10.9)

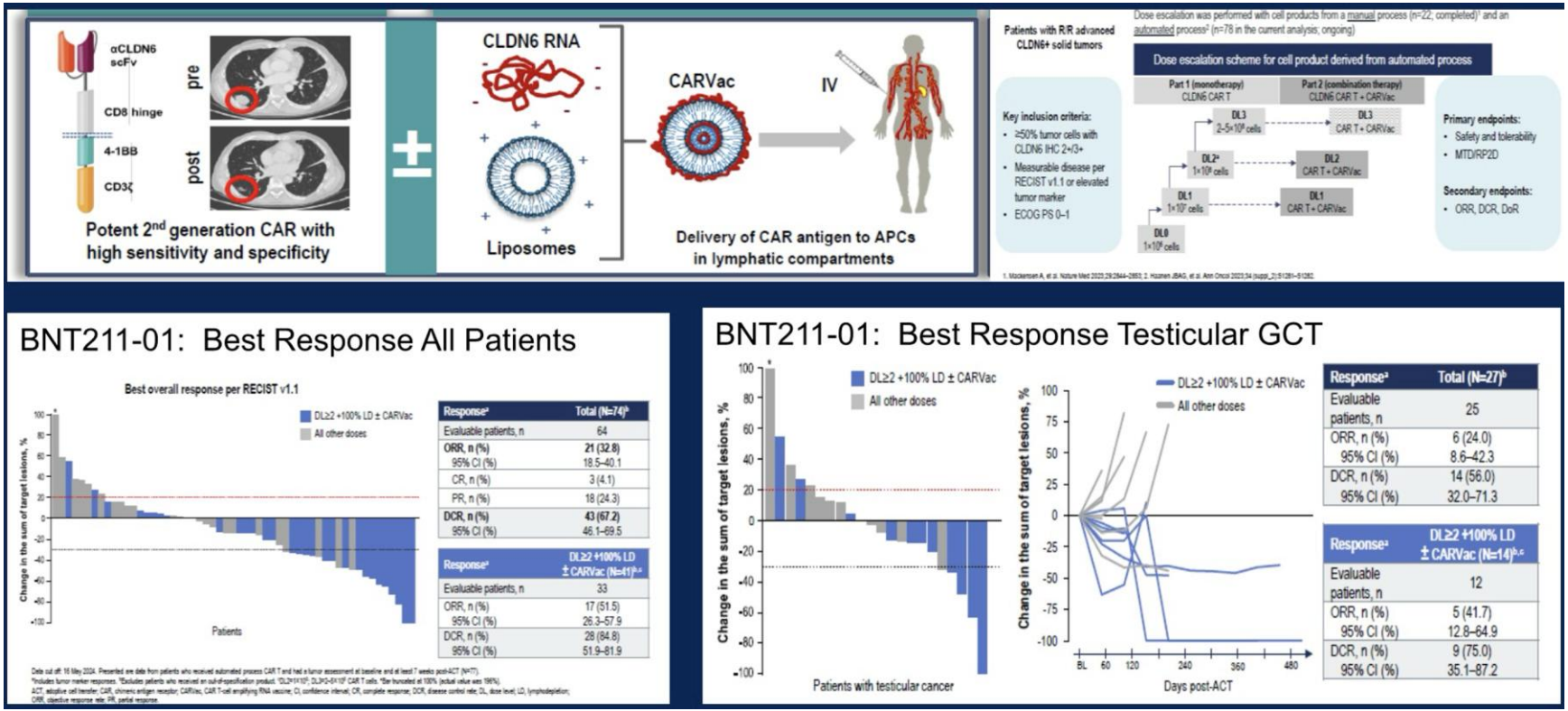
Presented by Darren Feldman.

Claudin-6 ADCs

Characteristic	TORL-1-23[1]	DS9606a[2]
Payload	MMAE (microtubule inhibitor)	Pyrolobenzodiazepine (cross-links DNA)
Study Design	Phase I/II	Phase I with dose exp.
N, total (n, GCT)	68 (5)	53 (11)
ORR (%), all pts	33%	NR
N, GCT evaluable for ORR	5	7
ORR (%), GCT (by RECIST)	"activity seen"	2 (29%)
ORR (%), STMs >90%	"activity seen"	5 (71%)
Future Development	Registrational trial in Ovarian CA, further investigation in NSCLC	Phase II trial in RR-GCT opening in 2025

Presented by Darren Feldman.

Claudin-6 CAR-T +/- CAR-VAC for RR-GCT



BNT211-01: Best Response All Patients

Response[a]	Total (N=74)[b]
Evaluable patients, n	64
ORR, n (%)	**21 (32.8)**
95% CI (%)	18.5–40.1
CR, n (%)	3 (4.1)
PR, n (%)	18 (24.3)
DCR, n (%)	**43 (67.2)**
95% CI (%)	46.1–69.5

Response[a]	DL≥2 +100% LD ± CARVac (N=41)[b,c]
Evaluable patients, n	33
ORR, n (%)	17 (51.5)
95% CI (%)	26.3–57.9
DCR, n (%)	28 (84.8)
95% CI (%)	51.9–81.9

Data cut off: 16 May 2024. Presented are data from patients who received automated process CAR T and had a tumor assessment at baseline and at least 7 weeks post-ACT (N=77).
[a]Includes tumor marker responses. [b]Excludes patients who received an out-of-specification product. [c]DL2=1×10⁸, DL3=5×10⁸ CAR T cells. [d]Bar truncated at 100% (actual value was 196%).
ACT, adoptive cell transfer; CAR, chimeric antigen receptor; CARVac, CAR T-cell amplifying RNA vaccine; CI, confidence interval; CR, complete response; DCR, disease control rate; DL, dose level; LD, lymphodepletion; ORR, objective response rate; PR, partial response.

BNT211-01: Best Response Testicular GCT

Response[a]	Total (N=27)[b]
Evaluable patients, n	25
ORR, n (%)	6 (24.0)
95% CI (%)	8.6–42.3
DCR, n (%)	14 (56.0)
95% CI (%)	32.0–71.3

Response[a]	DL≥2 +100% LD ± CARVac (N=14)[b,c]
Evaluable patients, n	12
ORR, n (%)	5 (41.7)
95% CI (%)	12.8–64.9
DCR, n (%)	9 (75.0)
95% CI (%)	35.1–87.2

Presented by Darren Feldman.

Glipican-3 (GPC3)

Cell surface glycoprotein in which heparin sulfate glycosaminoclycane chains are covalently linked to a protein core.

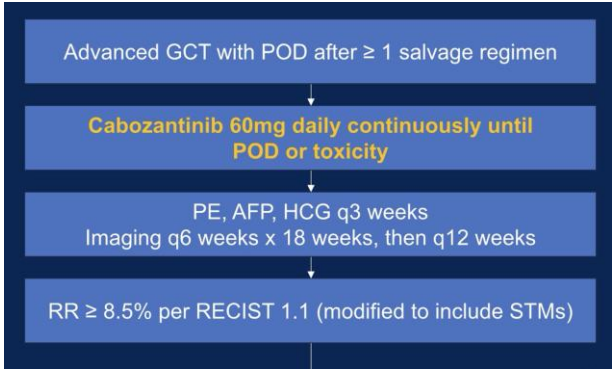
Plays a role in regulating cell proliferation.

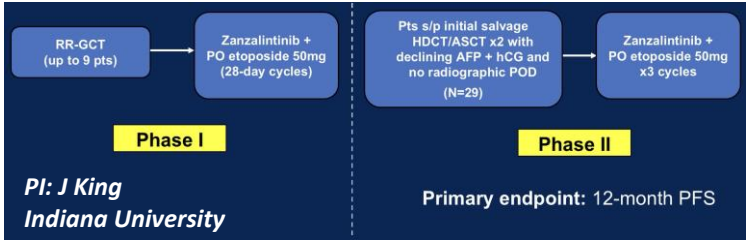
Expressed on nearly all yolk sac tumours (>95%) as well as HCCs but not normal liver .

Ongoing Studies:

Approach	Agent	Trial Number
Monoclonal Antibody	Codrituzumab	NCT04928677
Bispecific Antibody	BGB-B2033 (Anti-GPC3 + Anti-4-1BB)	NCT06427941
CAR-T	IL-15-armored GPC-3 CAR-T	NCT04377932; NCT06198296

VEGFR and cMET





Presented by Darren Feldman.

Conclusiones / Reflexiones

La inmunoterapia en cáncer de pene ofrece resultados prometedores. ¿Debemos incluirla -cemiplimab- en los esquemas de quimioterapia basado en platino? ¿En monoterapia cuando el paciente no sea *fit* para cisplatino?

La *RPLND* es otra alternativa a la quimio y a la radioterapia en lo seminomas II-A / II-B. ¿Debemos considerarlas alternativas similares? ¿Están “nuestros” cirujanos preparados para ello? ¿Están dispuestos?

Es necesario continuar con la investigación en tumores germinales refractarios / recidivantes tras *HDCT* ya que su pronóstico continúa siendo sombrío.

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