Presentaciones más destacadas en tumores germinales y otros tumores genitourinarios

Dra. Geòrgia Anguera
Hospital de la Santa Creu i Sant Pau - Barcelona

Agenda

- Tumores germinales
- Tumores no germinales

Agenda

- Tumores germinales
- Tumores no germinales

2026 ASCO ANNUAL MEETING

First Interim Analysis of SWOG S1823/GCC.1: Operating Characteristics of Circulating microRNA 371a-3p (miR371) in Predicting Active Germ Cell Malignancy (aGCM) in Patients (pts) With Early-Stage Testicular Cancer

Lucia Nappi*, Sarah Colby, Robert W. Hamilton, Andrea Harzstark, Nabil Adra, Siamak Daneshmand, Christopher W. Ryan, Scott E. Eggener, Chunkit Fung, Rebecca Johnson, Seth P. Lerner, Kathryn B. Arnold, Banu Arun, James M. Rae, Charles D. Blanke, Michael LeBlanc, Wendy R. Parulekar, Lawrence H. Einhorn, Christian K. Kollmannsberger, Craig R. Nichols, on behalf of the SWOG S1823 / CCTG GCC.1 investigators

*Department of Urologic Sciences, University of British Columbia, Vancouver, BC Canada

LuciaNappi4

SWOG Canadian Cancer Trials Group

Background and Rationale

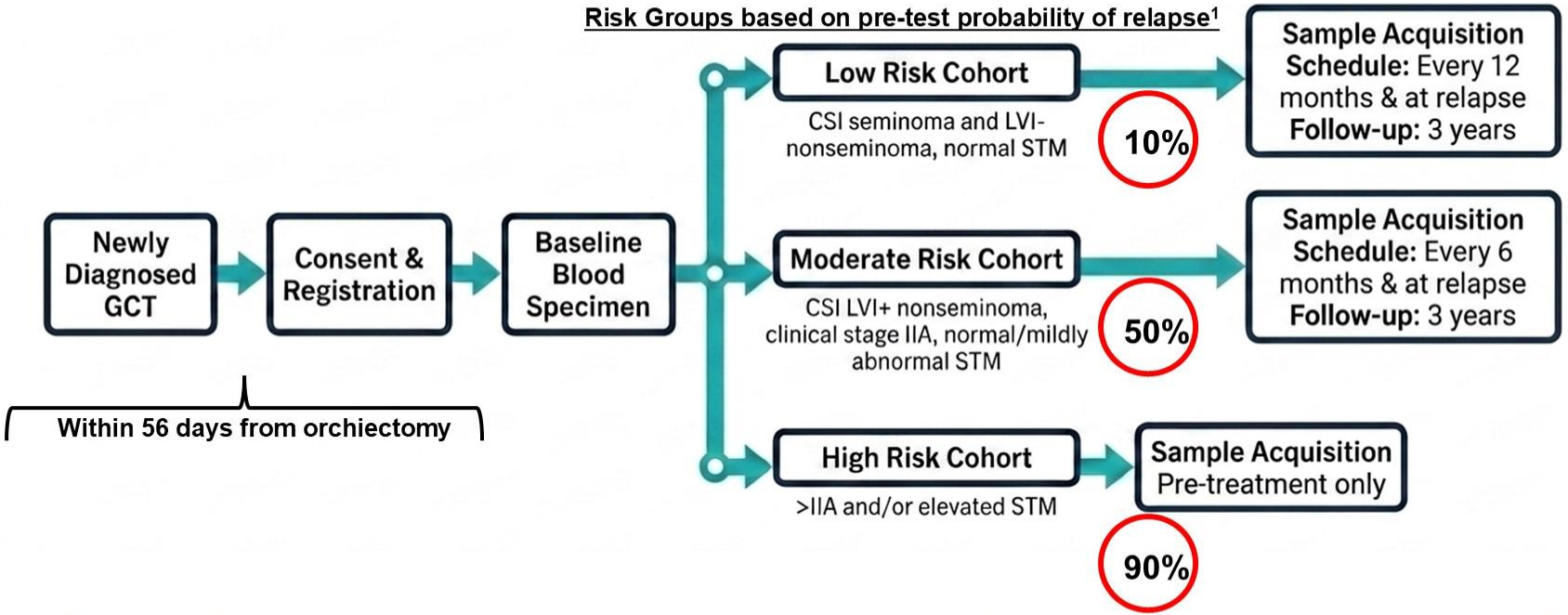
The Clinical Gap: Active Surveillance (AS) is the most commonly used management for patients with Clinical Stage I (CSI) germ cell tumors (GCT) but lacks reliable and highly accurate diagnostic tools

	CT scans & Serum Tumor Markers – standard of care for AS	miR371 Biomarker
Diagnostic Accuracy	Limited accuracy in < 2 cm retroperitoneal nodes and in seminoma	Specific for non-teratoma germ cell tumors
Operating Metrics	Serum tumor markers: Specificity: 50-60% Sensitivity: 15-60%	miR371 AUC confirmed to be >0.90 by independent retrospective studies
Material Required	Radiation exposure via CT scans	miR371 detectable in 50-400 uL of plasma or serum

Prospective validating studies for miR371 in early stage GCT are needed to reduce imaging reliance and improve detection

Voorhoeve et al, 2007; Palmer et al, 2010; Gillis et al, 2010; Dieckman et al,2019; Nappi et al, 2019; Milose et al., 2011; Dalal et al., 2006; Fankhauser et al, 2022; Dieckman et al, 2022; Tran, oral presentation ASCO GU 2026.

Methods – S1823/GCC.1 Study Design



Primary Endpoint: To evaluate miR371 operating characteristics at the time of clinical relapse diagnosis in patients with CSI/CSIIA disease on Active Surveillance (Low and Moderate Risk Groups)

1. Nappi et al, JCO 2019

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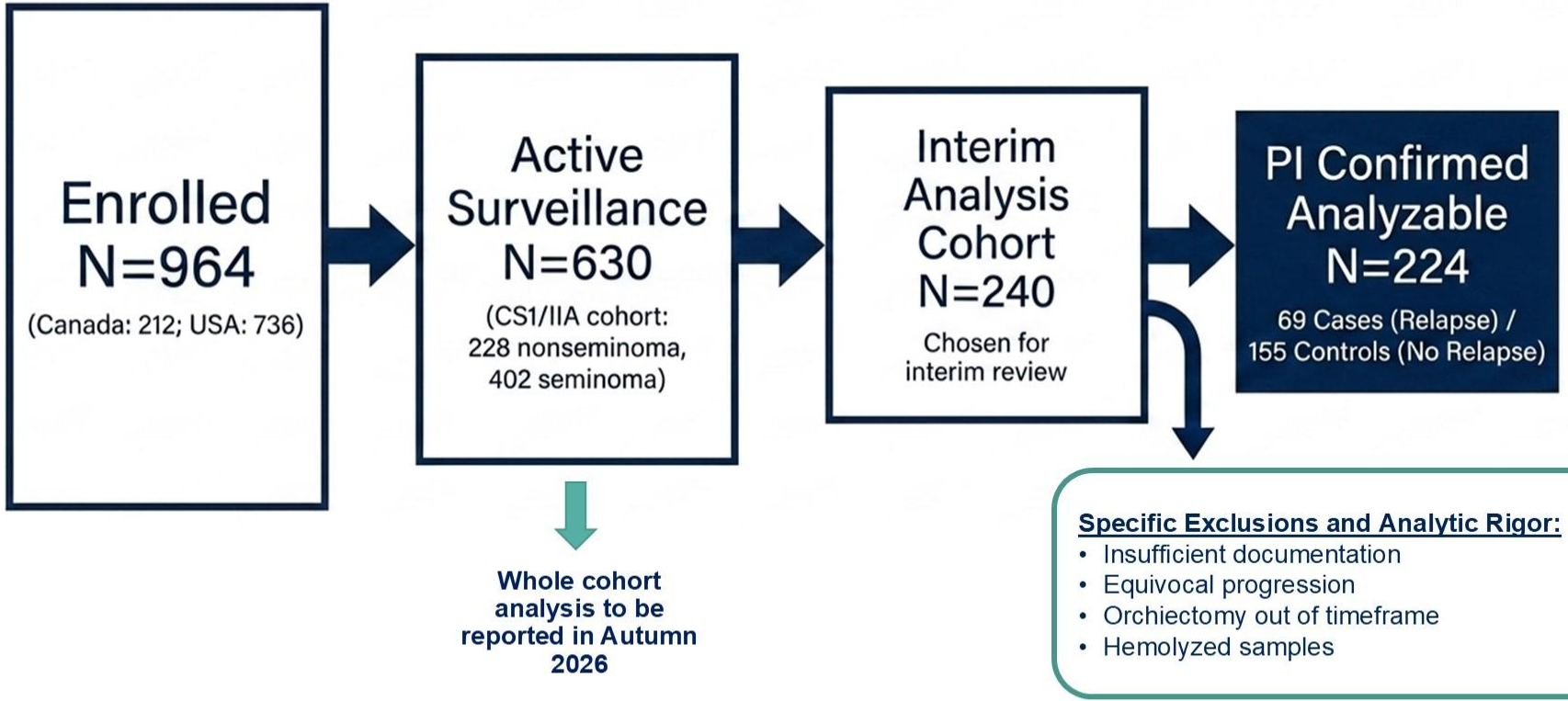
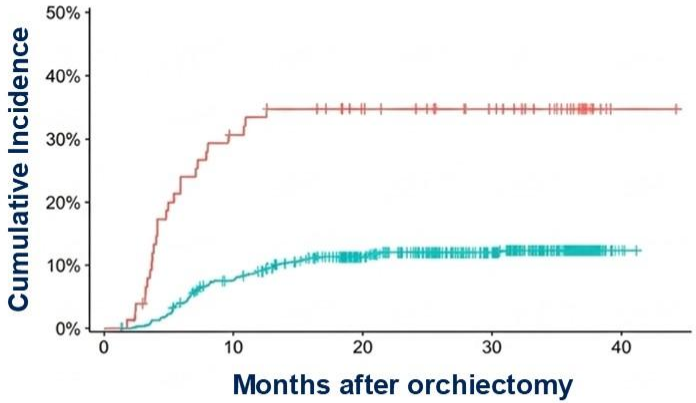
Results – Patients enrolled



Results – Cumulative incidence of relapse in the whole study



Milestone	Low Risk	Moderate Risk
At 6 Months	4%	24%
At 12 Months	9.1%	33.3%
At 24 Months	12%	34.7%

Overall relapse rate: **14.63%**

Median Time to Relapse: **5.8 months (1.8-21.5)**

- Sem: **7.4 mo (3.2-21.5)**; Nonsem: **5.3 mo (1.8-15.5)**
- Low risk: **6.6 mo (2.2-21.5)**; Moderate risk: **4.1mo (01.8-12.6)**

Note: Relapses were strictly confirmed by consistent STM elevation, growing lesions on subsequent CT scans or pathologically. Insufficient evidence of relapse resulted in exclusion of patients from the analysis

Results – Patient characteristics

		Cases	Controls
N		69	155
Risk of relapse	Low	48 (70%)	136 (88%)
	Moderate	21 (30%)	19 (12%)
Histology	Seminoma	33 (48%)	75 (48%)
	Nonseminoma	36 (52%)	80 (52%)
Stage at Registration	I	67 (97%)	154 (99%)
	IIA	2 (3%)	1 (1%)
Follow-up (months)		--	**35.1 [14.7, 40.2]**

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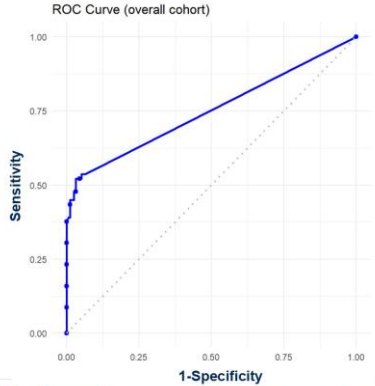
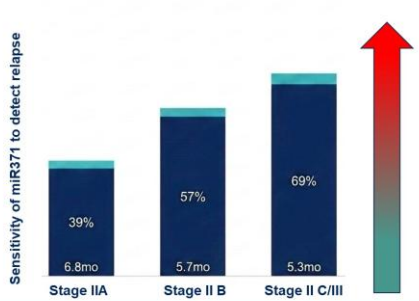
Results – Primary Endpoint: operating characteristics of miR371 at the time of relapse



Specificity	Negative Predictive Value (NPV)
0.94 (95% CI: 0.90, 0.97)	0.90 (95% CI: 0.88, 0.92)
Sensitivity	**Positive Predictive Value (PPV)**
0.54 (95% CI: 0.42, 0.65)	0.65 (95% CI: 0.51, 0.80)
AUC	
0.75 ($p < 0.001$)	

Blood Collection relative to clinical relapse:
14% collected 1-2 months prior to relapse
80% collected 0-1 months post relapse

Results – Sensitivity of miR371 increased with higher stage at relapse



2/3 of relapses were detected at stage IIB or higher using gold standard CT scan and STM

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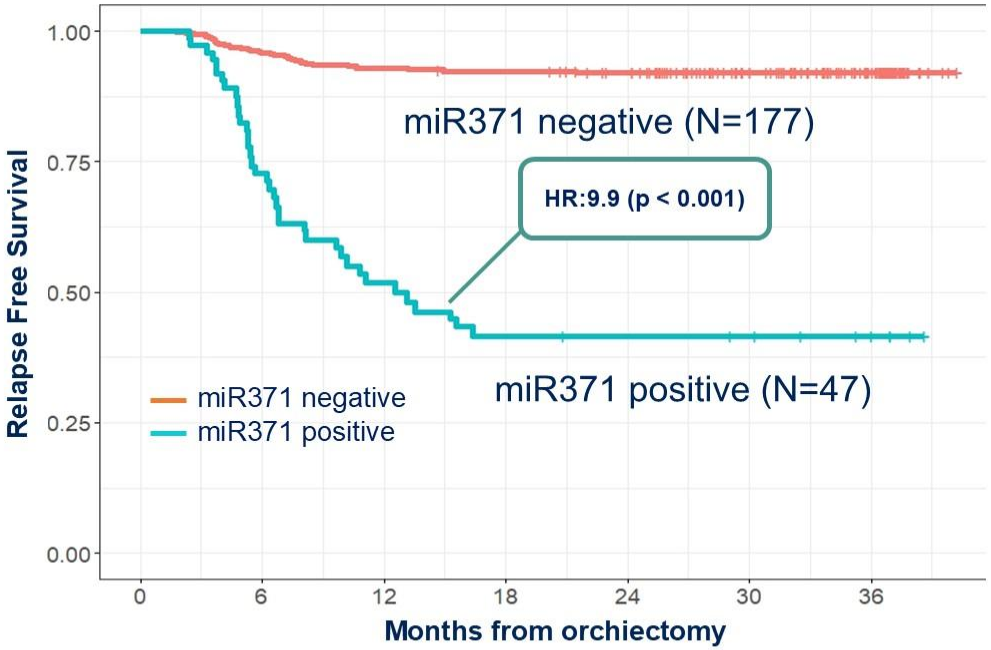
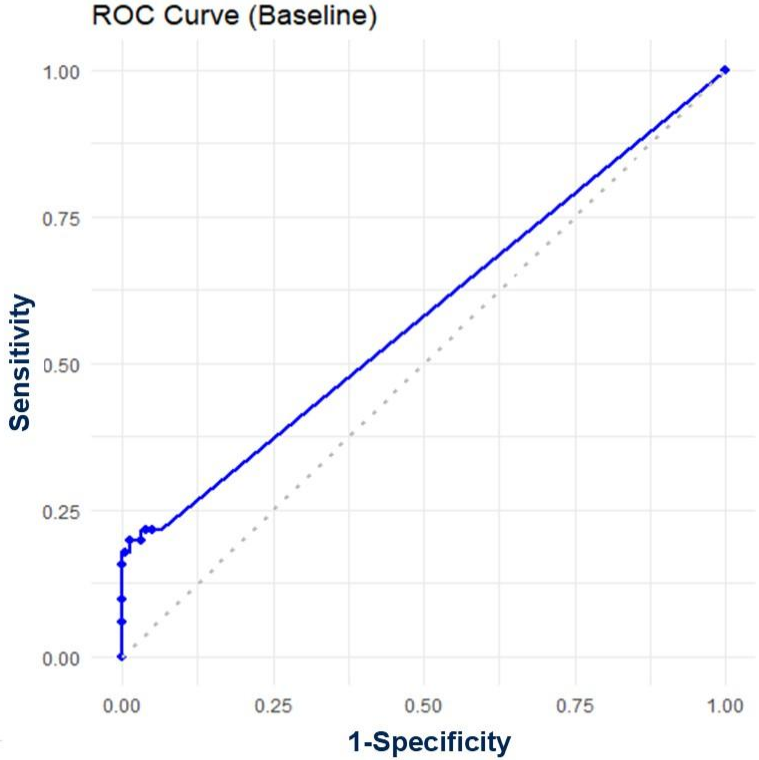
Results – Post-orchiectomy miR371 predicts Relapse Free Survival



Results – Operating characteristics of miR371 at baseline in patients who subsequently relapsed



Specificity	Negative Predictive Value (NPV)
0.94 (95% CI: 0.90, 0.97)	0.84 (95% CI: 0.82, 0.86)
Sensitivity	**Positive Predictive Value (PPV)**
0.22 (95% CI: 0.10, 0.33)	0.43 (95% CI: 0.24, 0.63)

AUC
0.58 (p=0.005)

N=206 patients; 51 relapsed patients with baseline data, median time to relapse: 6.3 months

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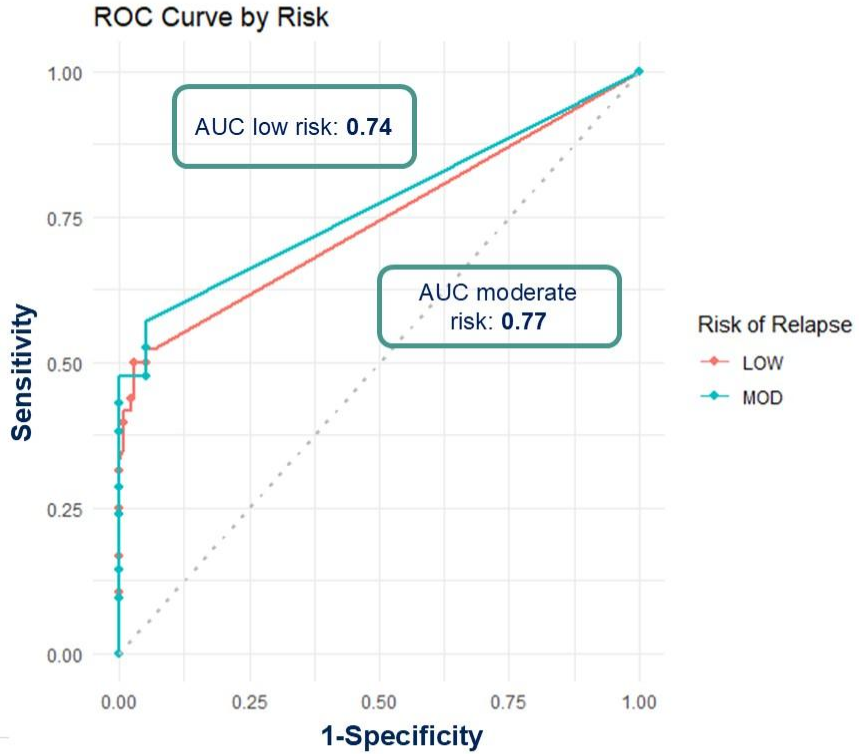
Results – Accuracy of miR371 in detecting relapse according to risk of relapse



- Low risk and moderate risk cohorts ROC curves are overlapping
- In aggregate, these data strongly suggest that miR371 outperforms historical accuracy of tumor markers (AFP, HCG), especially in seminoma
- miR371 specificity for GCT is superior to cross sectional imaging and sensitivity of miR371 is competitive with imaging

Results – False positive results in control patients

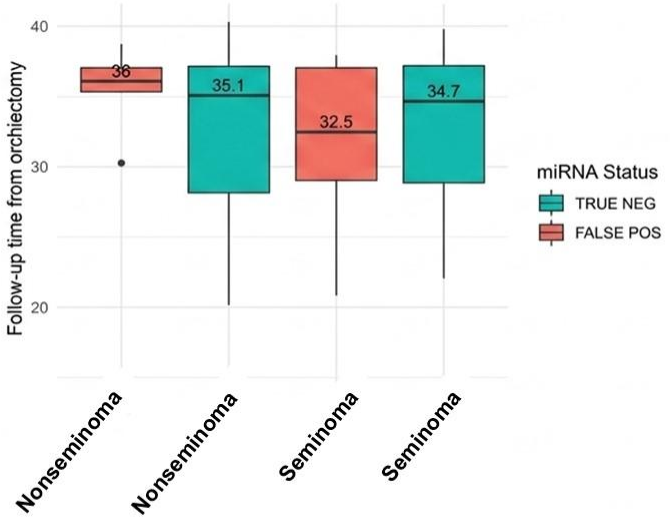
False Positive Breakdown

Overall False Positive Rate: 6% (10 out of 155 controls)

Distribution by Histology:
- Nonseminoma (5 pts)
- Seminoma (5 pts)

Distribution by Risk:
- Low Risk (9 pts)
- Moderate Risk (1 pt)

Follow-up Context



With a follow-up of 37.5 months, only 10 controls (6%) exhibited a false positive miR371 result, confirming an overall specificity of 94%

Limitations

- Selected patients (pre-planned interim analysis on the first 69 relapses, case-control design)
- Limited number of baseline samples analyzed
- Only qualitative miR371 analysis; miR371 quantification at baseline and over time during surveillance to be presented with the whole cohort analysis

Key Takeaway Points/Conclusions

1

S1823/GCC.1 results showed high specificity (94%) and NPV (90%) in detecting relapse of patients with early-stage germ cell tumor on surveillance

2

miR371 sensitivity and PPV were higher in more advanced disease, confirming the association between miR371 expression and tumor burden

3

Clinical utility of miR371 remains to be defined, with additional miR371-informed trials underway

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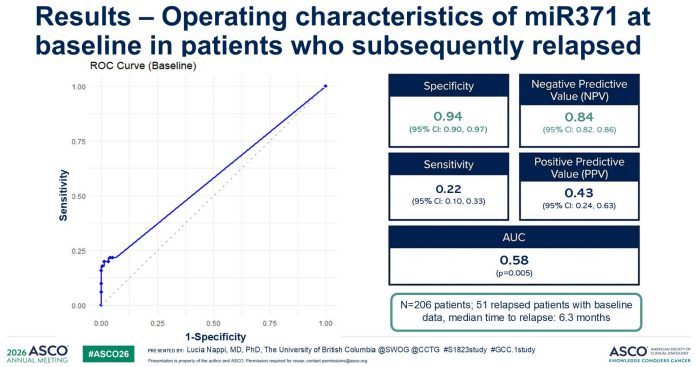
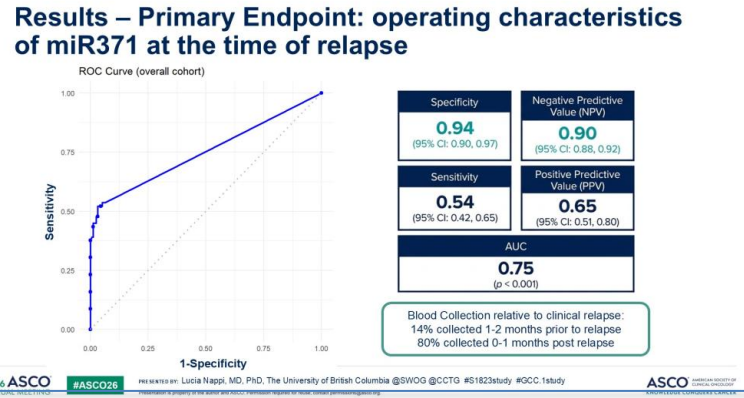
Discusion



- Sensibilidad baja post orquiectomía: 22 %
- VPP 43%: más de la mitad de los pacientes con miRNA + no recaen
  - ¿¿Útil para definir paciente candidato a adyuvancia? (57% de sobretratamiento..)
- Especificidad alta
- VPN de 0,84 = 16 % de paciente recaerán



- Sensibilidad de miRNA en la recaída 54% (46% de las recaídas no se detectan a pesar de tener TC+)
  - ¿Suficiente para reducir /reemplazar el seguimiento radiológico?
- La sensibilidad aumenta con el estadio→ biomarcador de carga tumoral
- ¿Cúal es el objetivo de AS?–detectar a quien recaerá para evitar sobretratamiento
  - Prevalencia de recaída es del 16,3% (83,7% no recaen)
  - Tener miRNA negativo 83,7% → 90 %

Agenda

- Tumores germinales
  - posters
- Tumores no germinales

Abstract #5025: Implementation of serum microRNA-371a-3p testing for testicular germ cell tumors in a pathology department: real-world data from a comprehensive cancer center

João Lobo, Nuno Tiago Tavares, Bruno Oliveira-Lopes, Rui Silva-Santos, Isaac Braga, Alina Rosinha, Joaquina Maurício, Carmen Jerónimo, Rui Henrique

Background

- *Classical serum tumor markers (**AFP, HCG, LDH**) have **limited** sensitivity and specificity for testicular germ cell tumor (TGCT) detection*
- ***MicroRNA-371a-3p** emerged as a promising non-invasive liquid biopsy biomarker for TGCT patients*
- *The **M371 test** is a **CE-IVDR** approved test which is commercially available, offering a standardized protocol for reporting serum miR-371a-3p in patients with testicular masses*

The *M371 serum test alone* showed a *superior diagnostic performance* for detecting active TGCT in an unselected, consecutive cohort of testicular cancer patients spanning different settings of the disease, when compared to AFP, HCG or LDH, isolated or in combination

The *high NPV* of the M371 test (0.99) may *aid in the decision of de-escalating intervention* (treatment or intensity of follow-up) of young TGCT patients

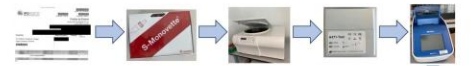
These real-world data, using a *standardized pipeline and a CE-IVDR approved protocol*, underscore the potential advantages of introducing microRNA-371a-3p as an additional test to combine with classical serum tumor markers and imaging

Methods

*M371 test was **adopted** at IPO Porto in Aug 2024*
- *Testicular masses, at presentation*
- *Follow-up of TGCTs*

*Serial collections, **coincident** with AFP, HCG, LDH measurements*

*Pipeline (RTqPCR-based) performed at the **Department of Pathology** once per week, strictly following **SOP**, issuing a **report***



Possible test results	Interpretation
POSITIVE	Probable TGCT presence
NEGATIVE	Probable TGCT absence
INCONCLUSIVE	New sample collection and test repeat

Results/Graphs/Data

***Total** of **128** M371 tests performed at the Molecular Pathology Lab of the Department of Pathology in 16 months*

Turnaround time** (from receiving blood sample to issuing report) of **5.6 days

Biomarker	Sensitivity	Specificity	PPV	NPV
AFP	0.43	0.96	0.76	0.85
HCG	0.57	0.98	0.89	0.88
LDH	0.37	0.91	0.55	0.82
AFP+HCG+LDH	0.80	0.92	0.77	0.93
M371	0.96	0.96	0.87	0.99

Case study #1
34yo, 2cm testicular mass
AFP, HCG, LDH within normal range
M371 test POSITIVE

Mixed TGCT (90% EC, 10% SE) pT2

Case study #2
28yo, previous mixed TGCT → BEP → 7cm RP mass
AFP, HCG, LDH within normal range
M371 test POSITIVE

Necrosis/fibrosis (70%) + Teratoma (10%) + EC/YST (20%)

Future Directions for Research

***Cross-validation** spanning different clinical settings*

*Assessment of **serum versus plasma** as the optimal sample source for the test*

*Continuing assessing the **threshold** of positivity and better defining the **"grey zone"** of the test*

*Evaluating the impact of **pre-analytics** on the test performance*

Acknowledgements

João Lobo, MD, PhD
jpedro.lobo@ipoporto.min-saude.pt
joaomachadolobo@gmail.com
@JoaoPedroLobo89

Abstract #538778: Genomic Determinants of Cisplatin Resistance in Germ Cell Tumors

Vincent D. D'Andrea, Timothy N. Clinton, Carissa Chu, Fady Baky, Andrea Knezevic, Vignesh Ravichandran, Anna Lee, Jahwa Hossain, Jordan E. Eichholz, Mary Chapman, Aliza Katz, Adam Price, Allison L. Richards, Mark T.A. Donoghue, Richard S. Matulewicz, Joel Sheinfeld, Manjit S. Bains, David R. Jones, Anis Hamid, Deaglan McHugh, Samuel A. Funt, David B. Solit, Darren R. Feldman

Memorial Sloan Kettering Cancer Center, New York, NY, USA

Memorial Sloan Kettering Cancer Center

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BACKGROUND

- **Cisplatin-based chemotherapy cures most patients** with advanced germ cell tumors (GCTs), but a subset develop **chemotherapy-resistant disease**
- Prior studies have shown that ***TP53/MDM2* gene alterations** and **chromosome 3p25.3 gain** are linked to cisplatin resistance[1,2]
- We sought to identify **additional genomic determinants** of cisplatin resistance in GCT

METHODS

- Eligibility criteria: Patients with advanced GCT treated with first-line cisplatin-based chemotherapy with **MSK-IMPACT** (NGS)
- Standard first-line chemotherapy: **≥3 cycles** of a cisplatin-based combination regimen: EP, BEP, VIP, or TIP (on trial)[3,4]
- **Cisplatin resistance:**

(1) IR to first-line cisplatin-based chemotherapy
(2) nonteratomatous tumor progression after first-line cisplatin-based chemotherapy
(3) viable nonteratomatous GCT identified at post-chemotherapy surgery

- Associations determined between **cisplatin response** and genetic alterations, clinicopathologic features, progression-free survival (PFS), and overall survival (OS)*

*Survival analyses include left truncation with entry delayed until sample sequenced

RESULTS

Table 1. Patient Characteristics (N=557)

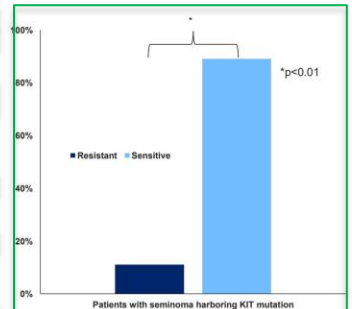
	All patients (N=557)	Sensitive (N=217)	Resistant (N=340)
Age at diagnosis, years – median (Q1, Q3)	30.8 (24.6, 38.8)	29.8 (24.6, 38.2)	31.1 (24.5, 38.8)
Sex			
Male	533 (95.7%)	201 (92.6%)	332 (97.6%)
Female	24 (4.3%)	16 (7.4%)	8 (2.4%)
Overall histology			
Seminoma	115 (20.6%)	62 (28.6%)	53 (15.6%)
Non-seminoma	442 (79.4%)	155 (71.4%)	287 (84.4%)
Primary Site			
Testis	440 (79.0%)	178 (82.0%)	262 (77.1%)
Mediastinum	84 (15.1%)	20 (9.2%)	64 (18.8%)
Ovary	25 (4.5%)	16 (7.4%)	9 (2.6%)
Retroperitoneum	6 (1.1%)	3 (1.4%)	3 (0.9%)
Other	2 (0.4%)	0 (0%)	2 (0.6%)
IGCCCG			
Good	233 (41.8%)	123 (56.7%)	110 (32.4%)
Intermediate	84 (15.1%)	33 (15.2%)	51 (15.0%)
Poor	212 (38.1%)	46 (21.2%)	166 (48.8%)
Missing/Unknown	28 (5.0%)	15 (6.9%)	13 (3.8%)
Initial chemotherapy			
BEP	234 (42.0%)	69 (31.8%)	165 (48.5%)
EP	199 (35.7%)	111 (51.2%)	88 (25.9%)
VIP/TIP	122 (21.9%)	36 (16.6%)	86 (25.3%)
Other	2 (0.4%)	1 (0.5%)	1 (0.3%)
Sample type			
Primary tumor	330 (59.2%)	162 (74.7%)	168 (49.4%)
Metastatic sample	227 (40.8%)	55 (25.3%)	172 (50.6%)

Table 2. Gene Mutations and Copy Number Alterations in the Overall Cohort

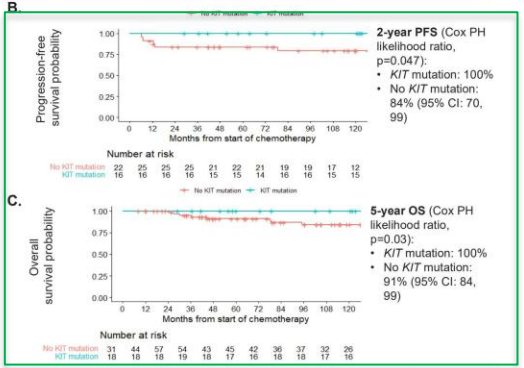
Overall	All patients (N=557)	Sensitive (N=217)	Resistant (N= 340)	Fisher's p-value
Mutations				
TP53	58 (10%)	4 (1.8%)	54 (16%)	<0.001
KIT	48 (8.6%)	31 (14%)	17 (5.0%)	<0.001
CDK12	13 (2.3%)	9 (4.1%)	4 (1.2%)	0.04
Copy number amplifications				
MDM2.Amp	25 (4.5%)	2 (0.9%)	23 (6.8%)	<0.001
CRKL.Amp	15 (2.7%)	1 (0.5%)	14 (4.1%)	0.007
MAPK1.Amp	12 (2.2%)	1 (0.5%)	11 (3.2%)	0.034
NSGCT	**All patients (N=442)**	**Sensitive (N=155)**	**Resistant (N= 287)**	**Fisher's p-value**
Mutations				
TP53	57 (13%)	4 (2.6%)	53 (18%)	<0.001
MGA	8 (2.2%)	0 (0%)	8 (3.5%)	0.03
Copy number amplifications				
MDM2.Amp	21 (4.8%)	1 (0.6%)	20 (7.0%)	0.002
Seminoma	**All patients (N=115)**	**Sensitive (N=62)**	**Resistant (N=53)**	**Fisher's p-value**
Mutations				
KIT	27 (23%)	24 (39%)	3 (5.7%)	<0.001
Copy number amplifications				
RECQL.Amp (12p)*	12 (24%)	1 (5.6%)	11 (34%)	0.036
KRAS.Amp (12p)	25 (22%)	7 (11%)	18 (34%)	0.006
PIK3C2G.Amp (12p)	15 (13%)	4 (6.5%)	11 (21%)	0.028

*50 patients included in analysis

Figure 2. (A) Frequency of cisplatin-resistance and cisplatin-sensitivity among patients with seminoma harboring *KIT* mutations; (B) PFS and (C) OS for patients with seminoma stratified by whether a *KIT* mutation is present.



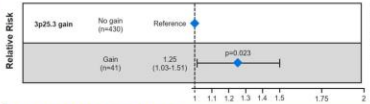
Among patients with **seminoma**, 24/27 (**89%**) patients with *KIT*-mutated tumors were **cisplatin-sensitive**, compared to 3/27 (**11%**) patients who were **cisplatin-resistant** (p<0.01)



2-year PFS (Cox PH likelihood ratio, p=0.047):
- *KIT* mutation: 100%
- No *KIT* mutation: 84% (95% CI: 70, 99)

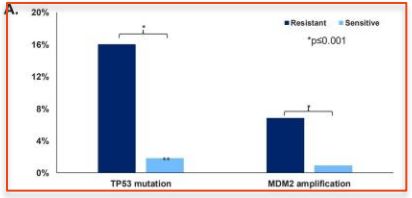
5-year OS (Cox PH likelihood ratio, p=0.03):
- *KIT* mutation: 100%
- No *KIT* mutation: 91% (95% CI: 84, 99)

Figure 3. Relative risk of cisplatin resistance in patients with chromosome 3p25.3 gain compared to those without.



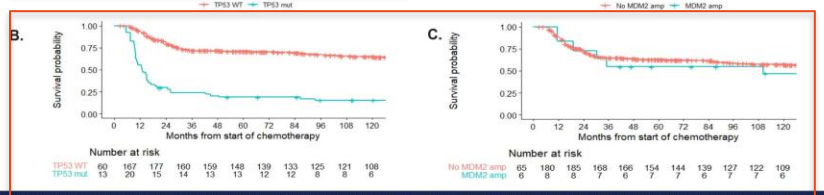
Chromosome 3p25.3 gain was **associated with cisplatin resistance**

Figure 1. (A) Comparison of *TP53* mutation and *MDM2* amplification frequencies; (B) Kaplan-Meier OS curve stratified by *TP53* mutation status and (C) Kaplan-Meier OS curve stratified by *MDM2* amplification status.



A.) *TP53* mutations (left) and *MDM2* amplifications (right) were significantly **more frequent in cisplatin-resistant tumors** compared to cisplatin-sensitive tumors (approximately 16% vs. 2% and 7% vs. 1%, respectively; p≤0.001 for both comparisons).
B.) Significant decrease in OS in patients with *TP53* mutation compared to those without.
C.) No significant difference in OS in patients with *MDM2* amplifications compared to those without.

**3/4 (75%) cisplatin-sensitive patients had teratoma with atypical cells on pathology in their index tumor or subsequent resection which did not meet the criteria for a diagnosis of secondary somatic transformation



CONCLUSIONS

- Our study confirms previous findings that link ***TP53/MDM2* gene alterations** and **chromosome 3p25.3 gain** to cisplatin resistance
- ***TP53* mutation is associated with inferior OS**, but not *MDM2* amplification
- In seminoma, ***KIT* mutations are associated with cisplatin sensitivity and improved PFS and OS**
- ~75% of cisplatin resistance in GCT remains unexplained by genomic alterations and **future studies** are required to elucidate further mechanisms

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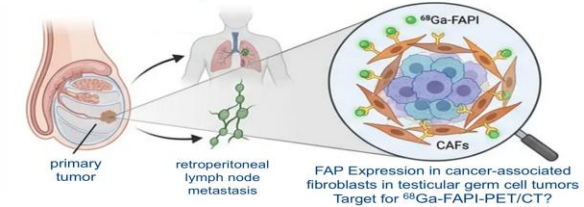
Clinical implications and diagnostic utility of ^{68}Gallium FAPI PET CT in patients with testicular germ cell tumors: The prospective phase Ib FAPI-TEST study

Rölz N[1], Spektor AM[2], Frey L[1], Porubsky[3], Frey LJ[1], Duwe G[1], Haack M[1], Lache N[1], Haferkamp A[1], Röhrich M[2], **Brandt MP[1]**

[1]University Medical Center Mainz, Department of Urology and Pediatric Urology, [2] Department of Nuclear Medicine, University Medical Center Mainz, Mainz [3] Institute of Pathology, University Medical Center Mainz, Mainz

UNIVERSITÄTSmedizin. MAINZ
Klinik und Poliklinik für Urologie und Kinderurologie

Introduction & Objective



Material and Methods

12 TGCT Patients
Mean Age: 34.5

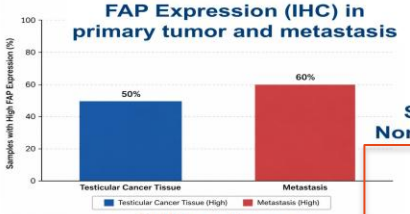
CS II (9) | CS I (1) | CS III (1) | Extragonadal (1)

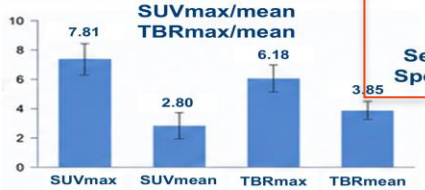
Pre-Chemo (8) | Post-Chemo (4)

^{68}Ga-FAPI-PET/CT Scan
SUV max/mean
TBR max/mean

Histology
FAP staining (neg., med., high)
Lymph node tissue (RPLND n=3)
Retroperitoneal Biopsy (n=1)
Mediastinal tumor tissue (n=1)

Results





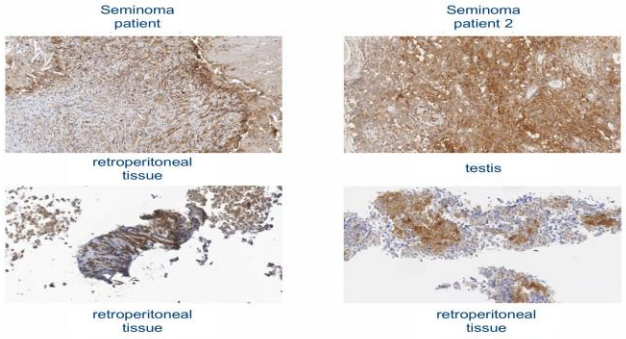
Seminoma: n=5
Non-Seminoma: n= 7

Cut off: mean SUVmax 7.81

Sensitivity: 57%
Specificity: 100 %

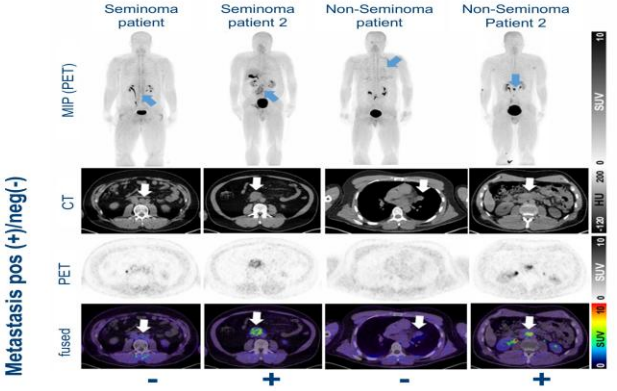
Conclusion

- IHC FAP expression was 50% and 60% in primary testicular cancer and metastatic tissue
- Stratification of SUVmax lesions above 7.81 showed excellent specificity of 100% and acceptable sensitivity with 57%.
- ^{68}Ga-FAPI-PET/CT might serve as a promising tool to distinguish metastatis from benign lesions especially after curative chemotherapy with residual mass.



Patient 1: Biopsy and RPLND with prominent FAPI expression in peritumoral fibroblasts without viable tumor tissue availabe.

Patient 2: primary testicular tumor and RPLND showed prominent FAPI expression.



Abstract #TPS5131

Randomized phase 1 trial of cisplatin-based chemotherapy with or without sodium thiosulfate (STS) for men with metastatic germ cell tumor (GCT)

Koral Shah[1], Xiaochen Li[1], Tanya Dorff[1], Sumanta Pal[1], Abhishek Tripathi[1], Charles Nguyen[1], Pierre Sayad[2], Alex Chehrazi-Raffle[1]
[1]City of Hope Comprehensive Cancer Center, Duarte, CA USA; [2]Fennec Pharmaceuticals, Inc, Research Triangle Park, NC USA

To evaluate the **safety and efficacy** of sodium thiosulfate in reducing cisplatin-induced **ototoxicity** in **adults with metastatic testicular GCT**

BACKGROUND

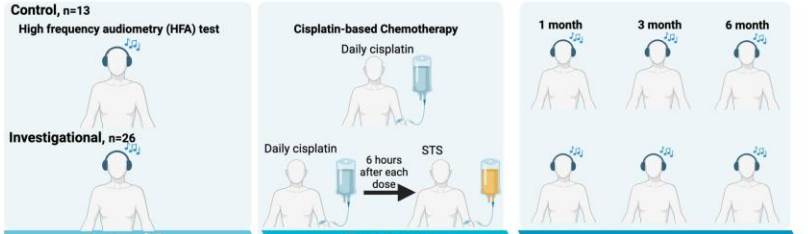
- Ototoxicity from cisplatin affects 75% of adult GCT survivors, with severity correlated to cumulative exposure[1]
- STS (PEDMARK®) was FDA-approved in 2022 for reducing cisplatin-induced ototoxicity in the pediatric setting
- Prospective adult data for otoprotective strategies, particularly in metastatic disease are lacking

ACCRUAL

- Two patients have been enrolled as of May 2026

STUDY DESIGN

Sodium Thiosulfate (STS) in Adults Receiving Cisplatin for Metastatic Germ Cell Tumor



- **Eligibility Criteria:**
  - Histologically confirmed seminoma or non-seminoma
  - Stage II and III
  - Receiving first or second line cisplatin-based chemotherapy
  - Planned cumulative cisplatin dose of ≥ 300mg/m² (including previous treatment)
  - No known hypersensitivity to thiol compounds or sulfites
- **Exclusion Criteria:**
  - Symptomatic CNS disease
  - Chronic steroid use
  - Baseline ≥ moderate hearing loss per ASHA
  - Cisplatin within 4 weeks of enrollment
- **Primary Treatment:**
  - Physician choice cisplatin-based chemotherapy regimen (BEP, EP, TIP, VeIP, VIP, etc) per standard of care
  - 20g/m² of STS will be infused 6 hours after completion of daily cisplatin infusion
  - Patients in control arm will not receive STS
- **Sample Size:** 39 patients, 2:1 randomization
- **Primary Endpoints**
  - Incidence of *clinically meaningful ototoxicity** per ASHA criteria
    *Ototoxicity affecting frequencies 250–8000 Hz
- **Secondary Endpoints**
  - Incidence of high-frequency ototoxicity (8-12.5 kHz)
  - Severity & progression of ototoxicity
  - Rate of adverse events
  - Two-year Progression Free Survival
- **Exploratory Endpoints**
  - Incidence of tinnitus
  - Disease assessment 6 months post-treatment

Figure made by BioRender

METHODS

- Phase I, open-label, single-center
- Randomized 2:1 (STS vs control), N=39
- Assuming ototoxicity incidence of 70% in the control arm and 35% in the investigational arm, the study design yields 81% power to detect the hypothesized difference using a one-sided significance level of α = 0.20

STUDY SITE

City of Hope Comprehensive Cancer Center, Duarte, CA

CONTACT INFORMATION

Principle Investigator: Alex Chehrazi-Raffle, MD
achehraziraffle@coh.org @arafflemd

Co-investigator: Koral Shah, MD
koshah@coh.org

Agenda

- Tumores germinales
- Tumores no germinales
  - **Cáncer de pene**
  - Carcinoma de uraco

Abstract 5034: Efficacy and Safety of Disitamab Vedotin Combined with Toripalimab for Cisplatin-Refractory Advanced Penile Cancer：A Prospective Single-Center Study (SAVE)

重庆大学附属肿瘤医院 CHONGQING UNIVERSITY CANCER HOSPITAL 重庆市肿瘤医院 CHONGQING CANCER HOSPITAL

Background

- *Patients with advanced penile cancer progressing on cisplatin-based chemotherapy have limited subsequent options.*
- *This study evaluated DV combined with a PD-1 inhibitor (Toripalimab, T) in patients with advanced penile cancer refractory to cisplatin-based chemotherapy.*

The combination of DV and T shows promising antitumor activity and a manageable safety profile in cisplatin-refractory advanced penile cancer patients, independent of HER-2 or PD-L1 status. These findings support further evaluation in this patients with high unmet clinical need.

Methods

Key Eligibility Criteria:

- No age limit and expected survival ≥8 weeks.
- III stage(cT1-3,N1-2,M0) or IV stage(cT4/N3/M1)
- Progression or intolerance by cisplatin-based chemotherapy

n=8

TMB
PD-L1
HER-2

RC48(q2w 2mg/kg) + Toripalimab (q2w 3mg/kg or q3w 240mg)

until disease progression or intolerance

CT/MRI every 8 weeks

Primary objectives: ORR

Secondary objectives: OS, PFS, Safety

Results/Graphs/Data

- *8 patients were enrolled (demographics are shown in Table 1).*
- *The overall response rate (ORR) after treatment was 37.5% ,the disease control rate (DCR) after treatment was 50%(shown in Table 2).*
- *Median progression-free survival and overall survival were 3 and 5 months, respectively (Kaplan-Meier estimate).*
- *One grade ≥3 adverse event occurred (immune-mediated colitis with hematochezia). The most common Grade 1-2 adverse events were fatigue (75%) and peripheral neuropathy (62.5%) (shown in Table 3)*
- *HER-2 expression was negative in all patients. The patient with clearance of MRD had high TMB but low PD-L1 expression; others evaluable tumors had PD-L1 CPS >40 (TMB not assessed).*

Table 1. Baseline characteristics of patients

Characteristics	Number (n) or Specific Description	Characteristics	Number (n) or Specific Description
Median Age (Range)	52 (38-66 years)	Baseline Staging	
SD	1 (12.5)	T4	25% (2/8)
PD	4 (50%)	N3	87.5% (7/8)
Size of all target lesions	87.5%(>5 cm)	M1	62.5% (5/8)
HER-2 expression	100% negative (8/8)	PD-L1 expression	62.5% tested (5/8: 4/5 CPS>40; 1/5 low PD-L1 but high TMB)

Results/Graphs/Data

Table 2. Response to treatment

Response to therapy	N (%)	Response to therapy	N (%)
PR	3 (37.5)	ORR	3 (37.5%)
SD	1 (12.5)	DCR	4 (50%)
PD	4 (50%)		

Table 3. Treatment-Emergent Adverse Events

Adverse Events	Grade 1-2 N (%)	Grade≥3 N (%)	Adverse Events	Grade 1-2 N (%)	Grade≥3 N (%)
Overall	8(100%)	1(12.5%)	Leukopenia	2(25%)	0
Immune-Mediated Colitis	0	1 (12.5%)	Infusion-Related Pyrexia	1(12.5%)	0
Fatigue	6(75%)	0	Sinus Tachycardia	1(12.5%)	0
Peripheral Neuropat	5(62.5%)	0	Rash	1(12.5%)	0

Acknowledgements

- Corresponding author: Fang Yuan (cqchyuanfang@126.com); Chongqing University Cancer Hospital, Chongqing, China, 400030

TPS5133 : DEPECA-1 (DEfeating PEnile CAncer 1) – A Phase II study to evaluate a first-line systemic therapy with enfortumab vedotin plus avelumab for advanced and metastatic penile carcinoma

2026 ASCO ANNUAL MEETING

DEPECA1

Universitätsklinikum Tübingen

IKF Frankfurter Institut für Klinische Krebsforschung

Tsaur I[1], Barcena ML[1], Feng YS[2], Pyrgidis N[3], Thomas C[4], Gäbel C[5], Müller DW[5], Al-Batran SE[5], Thomas A[6], Borkowetz A[7], Meister B[8], Schnabel MJ[9], Retz M[10], Reimann M[11], Niegisch G[12, 13], Uhlig A[1], Erne E[1], Rausch S[1]

[1] University Hospital Tübingen, Department of Urology, Tübingen, Germany; [2] University Hospital Tübingen, Institute for Clinical Epidemiology and Applied Biostatistics (IKEAB), Tübingen, Germany; [3] Department of Urology, University Hospital Munich, LMU, Munich, Germany; [4] Universitätsklinikum Carl Gustav Carus, Department of Urology, Dresden, Germany; [5] The Frankfurt Institute of Clinical Cancer Research IKF GmbH, University Cancer Center Frankfurt, Frankfurt am Main, Germany; [6] University Medical Center of Johannes Gutenberg-University, Department of Urology and Pediatric Urology, Mainz, Germany; [7] Rostock University Medical Center, Department of Urology, Rostock, Germany; [8] Medical Faculty Mannheim of Heidelberg University, Department of Urology and Uro-Surgery, Mannheim, Germany; [9] Caritas Hospital St. Josef, Department of Urology, Regensburg, Germany; [10] Technical University of Munich, School of Medicine and Health, Department of Urology, TUM University Hospital Munich, Germany; [11] Charité – Universitätsmedizin Berlin, Department of Urology, Berlin, Germany; [12] Department of Urology, University Hospital and Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany; [13] Centre for Integrated Oncology (CIO) Düsseldorf, CIO Aachen-Bonn-Cologne-Düsseldorf (ABCD), Düsseldorf, Germany

Introduction and objectives

Squamous cell carcinoma of the penis (PeCa) is a rare malignancy with unfavorable outcomes in advanced stage. Since the 1990s, platinum-based chemotherapy has been the standard of care for the first-line treatment of metastatic disease. Unfortunately, it is characterized by a response rate of 30-40%, overall survival (OS) of 17 months and progression free survival (PFS) of 6 months at most. Thus, there is a critical medical need to assess novel systemic strategies for PeCa in the first-line setting, given that current regimens are of a limited clinical benefit and associated with considerable chemotherapy-associated toxicities.

In this context, the PD-1 inhibitor pembrolizumab yielded a promising activity in squamous cell carcinomas of various origins.[1,2] Meanwhile, enfortumab vedotin (EV), a Nectin-4 directed antibody-drug-conjugate, in combination with pembrolizumab has been recently approved for the treatment of metastatic urothelial cancer. The incidence of ≥3 grade adverse events with this regimen was > 55%.[3] Notably, a PD-L1 inhibitor avelumab provided a comparable activity as pembrolizumab but a lower overall rate of endocrine adverse events in patients with urothelial carcinoma.[4,5] Interestingly, avelumab monotherapy yielded a response rate of 17% and a median duration of response of 16 months in males with a platinum-refractory PeCa or those unfit for platinum chemotherapy in ALPACA trial.[6] Given that approximately 60% of PeCa tissues express both PD-L1 and Nectin-4, the combination of EV with avelumab represents a potentially synergistic therapeutic strategy, leveraging both direct cytotoxicity and immune-mediated anti-tumor activity through complementary mechanisms of action.[7]

Study Design

The DEPECA-1 trial is an investigator-initiated, open label, single-arm, multicenter phase II trial, enrolling 25 males with locally advanced or metastatic PeCa at 10 sites in Germany. Patients must be ineligible for curative surgery and not have received any prior systemic palliative therapy. Participants (ECOG ≤ 2) will receive 1200 mg avelumab on day 1 and EV (1,25 mg/kg) on day 1 and day 8 in a 3-week cycle for a maximum of 24 months and 32 cycles. Primary endpoint is the objective response rate (ORR) assessed per RECIST 1.1. Secondary endpoints include PFS, OS, duration of response (DOR), disease control rate (DCR) and patient-related outcomes. Exploratory analysis comprises tumor biomarker profiling. DEPECA-1 has received regulatory approval on 29th October 2025. First patient was enrolled on 16th December 2025. Up to May 12 2026, 5 patients were enrolled.

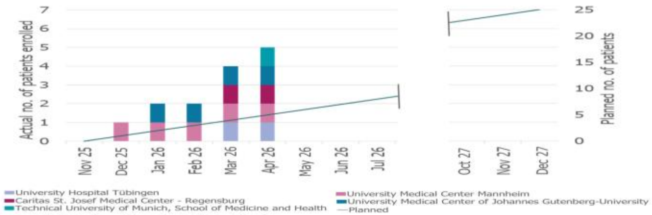


Figure 1: Overview of recruitment per trial site

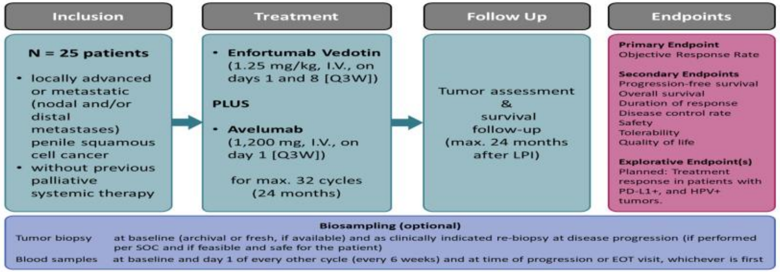


Figure 2: Overview of study design

Table 1: Overview of key inclusion and exclusion criteria

Key Inclusion criteria

- Histologically confirmed diagnosis of PeCa
- Non-eligible for curative surgical management. Presence of either distant metastatic disease (M1) OR at least one of the following scenarios (UICC/AJCC 8th edition, TNM classification):
  a. Stage 3 (cT3) disease with a single lymph node involved (N1)
  b. Stage 4 disease (cT4)
  c. Any T stage with either N2 (involvement of multiple or bilateral inguinal nodes) or N3 (fixed inguinal nodal mass or pelvic lymphadenopathy) disease
  d. Patients without distant metastases are eligible if multidisciplinary team review concludes that they are unsuitable for curative surgery.
- ECOG performance status of ≤ 2.
- Measurable disease per RECIST 1.1 criteria.

Key Exclusion criteria

- Previous systemic therapy for metastatic or locally advanced PeCa in the palliative setting.
- Known active central nervous system (CNS) metastases and/or carcinomatous meningitis.
- Active, known, or suspected autoimmune disease requiring systemic treatment within the past 2 years.
- Ongoing sensory or motor neuropathy Grade 2 or higher.
- History of uncontrolled diabetes (HbA1c > 8%).

First author contact information:
Prof. Dr. med. Igor Tsaur
igor.tsaur@med.uni-tuebingen.de / depeca-1@ikf-khnw.de

Sponsor: Frankfurter Institut für Klinische Krebsforschung IKF GmbH
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EU-CT-No: 2025-521644-37-00
Clinicaltrials.gov: NCT07110038

First author conflicts of interest:

Prof. Dr. med. Igor Tsaur is employed at University Hospital Tübingen

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Lecturing/Proctoring: Bayer, Sanofi, Astellas, Janssen, Recordati, Intuitive, neoConnect GmbH
Funding of Congress trips: Bayer, Astellas, Janssen, Pfizer, Merck KGaA, Apogepha

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1 Grob, J.-J., Gonzalez, R., Basset-Seguin, N., et al. (2020). Pembrolizumab Monotherapy for Recurrent or Metastatic Cutaneous Squamous Cell Carcinoma: A Single-Arm Phase II Trial (KEYNOTE-629). *JCO 38*, 25, 2916–2925.
2 Chahoud, J., Skelton, W.P., Spiess, P.E., et al. (2020). Case Report: Two Cases of Chemotherapy Refractory Metastatic Penile Squamous Cell Carcinoma With Extreme Durable Response to Pembrolizumab. *Front. Oncol. 10.*
3 POWLES, T., VALDERRAMA, B.P., GUPTA, S., ET AL. 2024. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. New England Journal of Medicine 390, 10, 875–888.
4 Zacchi, F., Sordo, A., Torresan, I., et al. (2025). Clinical outcomes of avelumab and pembrolizumab in advanced [illegible] retro-prospective study on patients undergoing treatment in clinical practice (AVePEm study). [illegible]
5 Shindo, T., Hashimoto, K., Takahashi, A., et al. (2024). Comparison of Oncological [illegible] Therapy in Advanced Urothelial Carcinoma After Platinum-based Chemo[illegible]
6 Muneer, A., Bandini, M., Compérat, E., et al. 2024. Penile cance[illegible]
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Agenda

- Tumores germinales
- Tumores no germinales
  - Cáncer de pene
  - **Carcinoma de uraco**

2026 ASCO ANNUAL MEETING

Phase II Study of Frontline Gemcitabine, 5-Fluorouracil/Leucovorin, and Cisplatin (GemFLP) in Advanced Urachal and Non-Urachal Urinary Tract Adenocarcinoma

Emanuele Crupi[1], Jianjun Gao[1], Paul Corn[1], Lance C. Pagliaro[2], Charles C. Guo[3], Bogdan Czerniak[3], Mohammad Jad Moussa[1], Zachariah Thomas[1], Cindy Y. Jiang[1], Omar Alhalabi[1], Matthew T. Campbell[1], Arlene O. Siefker-Radtke[1]

[1] Department of Genitourinary Medical Oncology, UT MD Anderson Cancer Center, Houston, TX. [2] Department of Oncology, Mayo Clinic, Rochester, MN. [3] Department of Pathology, UT MD Anderson Cancer Center, Houston, TX.

CONQUER CANCER® THE ASCO FOUNDATION MERIT AWARD

Walter & Lisa Stadler Endowed Merit Award

*Supported by **Dr. Walter and Mrs. Lisa Stadler***

@emanuele_crupi

Background

- Urinary tract adenocarcinoma is a very rare disease with no standard-of-care frontline therapy in the advanced setting[1]
- Evidence has largely been retrospective, although fluoropyrimidine-based regimens have shown activity[1,2]
- More recently, the ULTIMA trial reported promising prospective activity of modified FOLFIRINOX in advanced urachal cancer [3]

[1] Siefker AO et al. 2012 Semin Oncol DOI: 10.1053/j.seminoncol.2012.08.011 [2] Moussa MJ et al. 2024 J Clin Oncol DOI: 10.1200/JCO.2024.42.4_suppl.630 [3] Park I et al. 2026 Cancer Res Treat DOI: 10.4143/crt.2024.1231

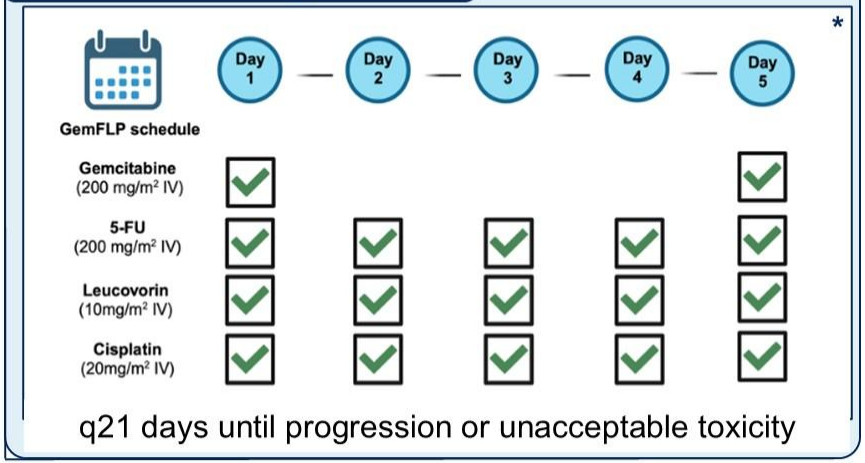
Methods

Patient Selection

- Adult patients (≥ 18 years old)
- Predominant (≥50%) urinary tract adenocarcinoma histology
- Patients with metastatic or unresectable disease
- Measurable or evaluable disease*
- Zubrod PS ≤2 and adequate hematologic, hepatic, and renal function

* Patients without measurable disease were eligible if a serum marker (CEA, CA 125, CA 19-9, β-hCG) was elevated (≥4 xULN)

GemFLP Regimen



Study Strategy

- **Phase II single-arm single-center study**
- **Primary end points:** Objective response rate (ORR) and overall survival (OS)
- **Secondary endpoints:** Safety
- Progression-free survival (PFS) and duration of response (DoR) were additional outcomes endpoints

*Figure courtesy of M.J. Moussa et al.

Baseline Characteristics (N=46)

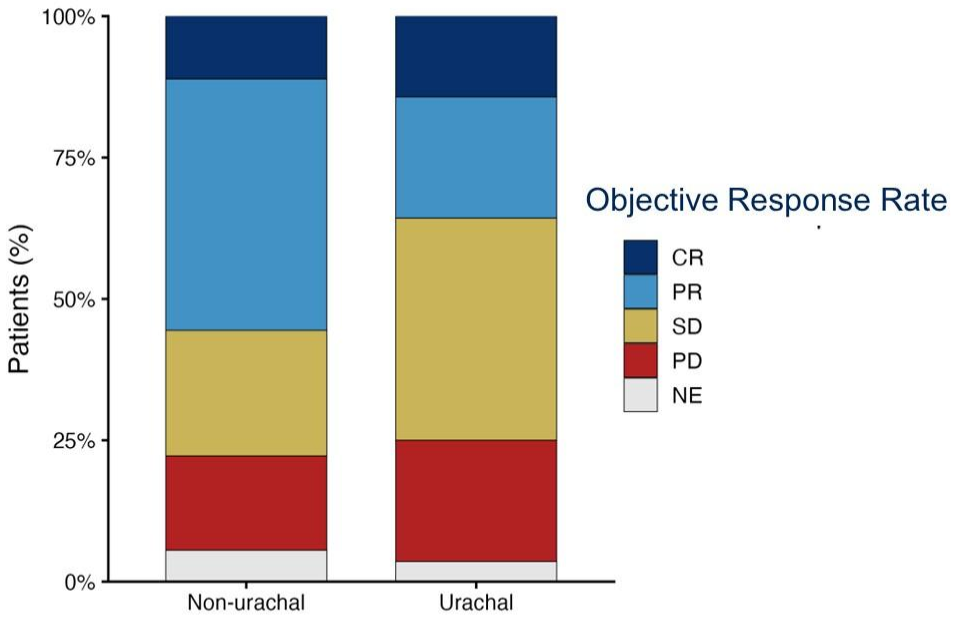
Variable	Site of Disease	
	UA (n=28)	NUA* (n=18)
Female sex, n (%)	11 (39)	15 (83)
Age, median [ICR]	58 [54– 62]	67 [62-72]
Race, n (%)		
White	22 (79)	11 (61)
Black	6 (21)	6 (33)
Other	0	1 (6)
Prior surgery for localized disease, n (%)	18 (64)	5 (28)
ECOG performance status, n (%)		
0	15 (54)	8 (44)
1	11 (39)	8 (44)
2	2 (7)	2 (11)
Stage		
cT4bN0M0	1 (4)	5 (28)**
Any T N1 M0	0	5 (28)***
Any T N≥2 M0	4 (14)	2 (11)
any T any N, M+		
Lung	6 (21)	4 (22)
Liver	3 (11)	0
Peritoneum	17 (61) #	0
Bone	3 (11)	4 (22)

* 9/18 (50%) pts with NUA originated from the urethra (100% occurred in female pts)

** Bladder primary tumor site in 4/5 patients.
*** Urethral primary tumor site in 4/5 patients

likely reflecting proximity to the peritoneal cavity

Results: Objective Response Rate

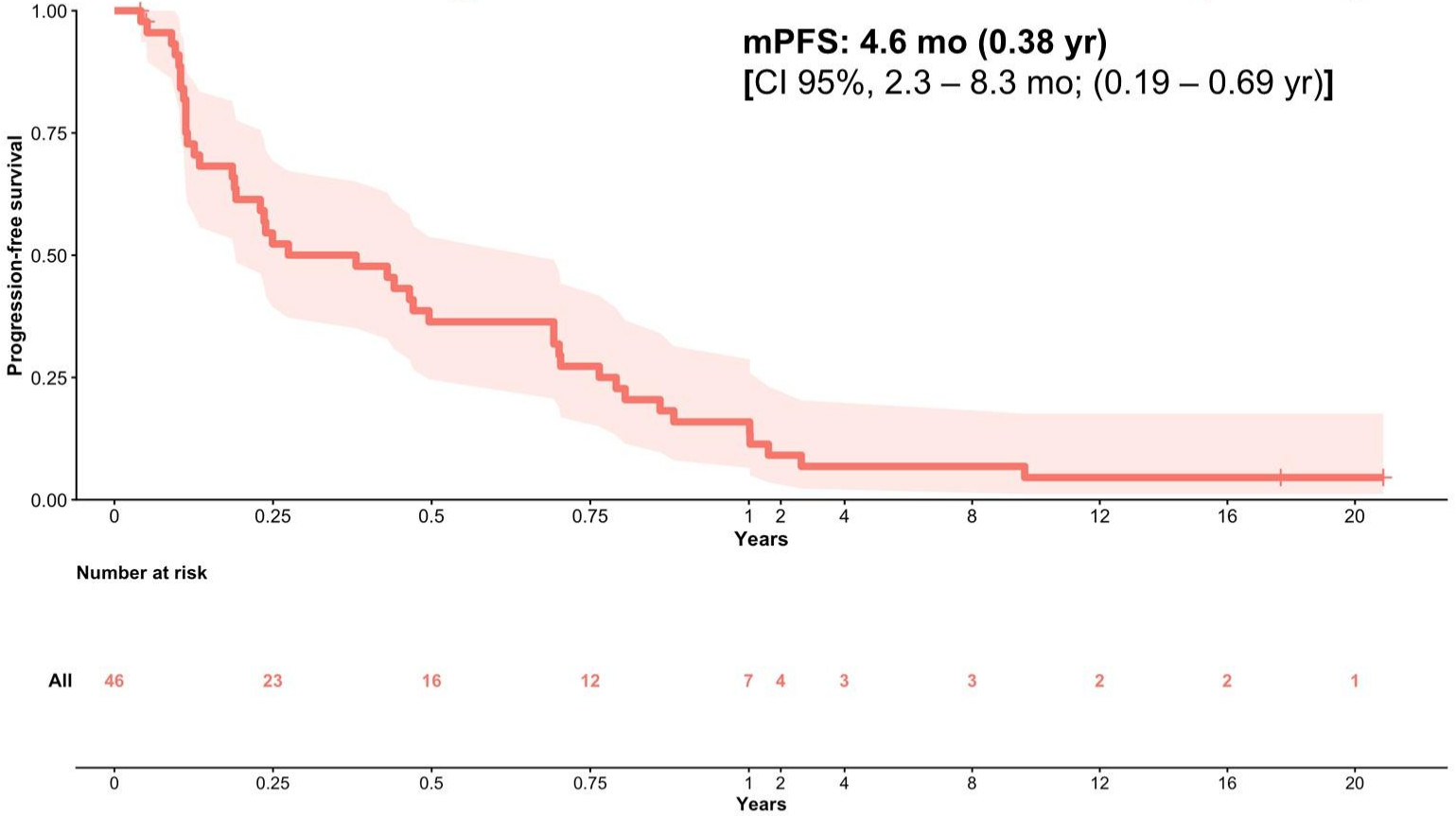


Radiographic Response	UA (n=28)	NUA (n=18)	All (n=46)
ORR	**10 (35.7%)**	**10 (55.6%)**	**20 (43.5%)**
CR	4 (14.3%)	2 (11.1%)	6 (13%)
PR	6 (21.4%)	8 (44.4%)	14 (30.4%)
SD	11 (39.3%)	4 (22.2%)	15 (32.6%)
PD	6 (21.4%)	3 (16.7%)	9 (19.6%)
NE *	1 (3.6%)	1 (5.6%)	2 (4.3%)

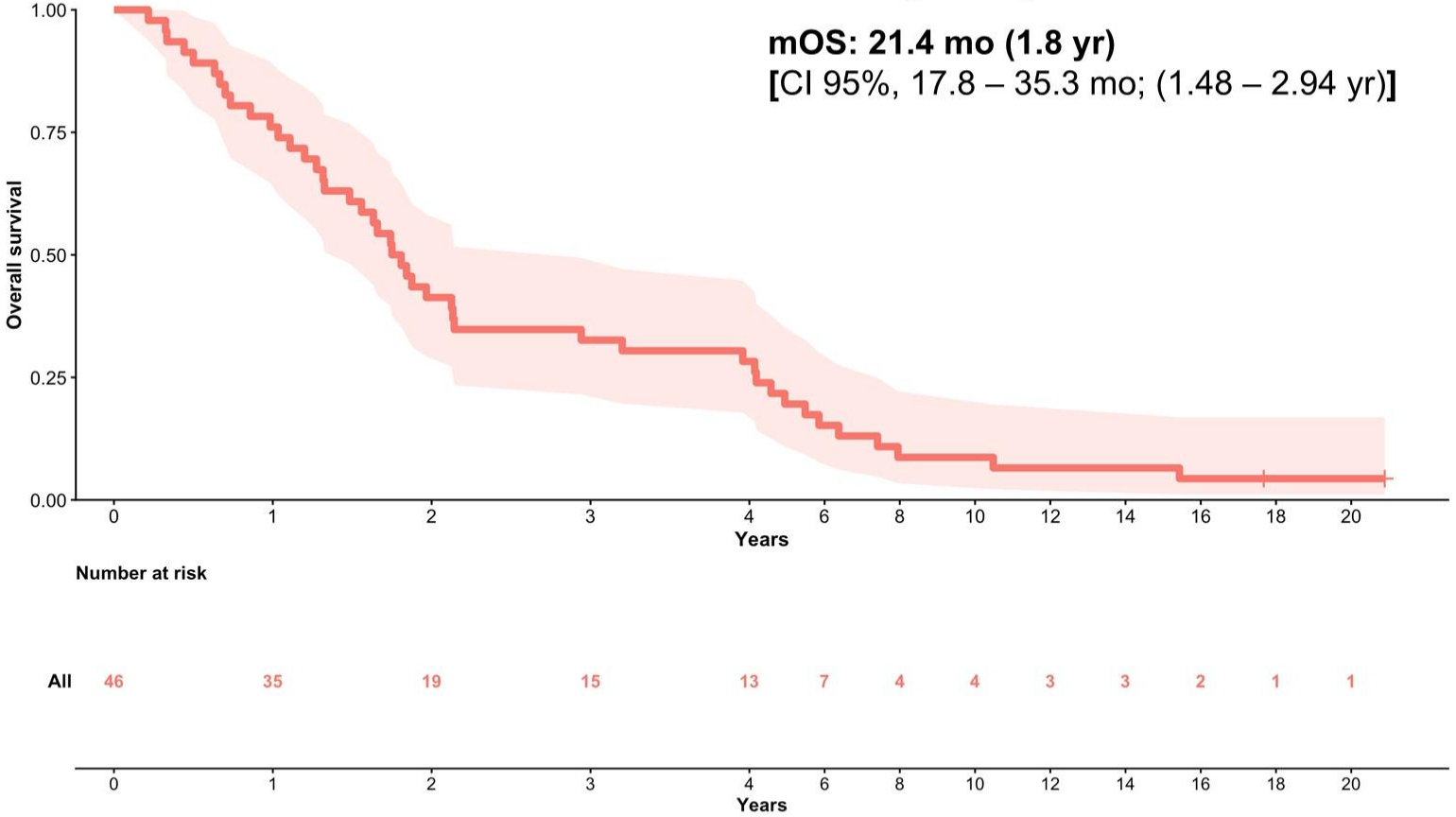
* 1 pts NE due to unacceptable toxicity at C1D3 (anasarca), 1 pts off trial due to insurance coverage issue after C1

Legend: CR – Complete Response; NE – Not Evaluable; NUA – Non-Urachal Adenocarcinoma; ORR – Overall Response Rate; PD – Progressive Disease; PR – Partial Response; SD – Stable Disease; UA – Urachal Adenocarcinoma

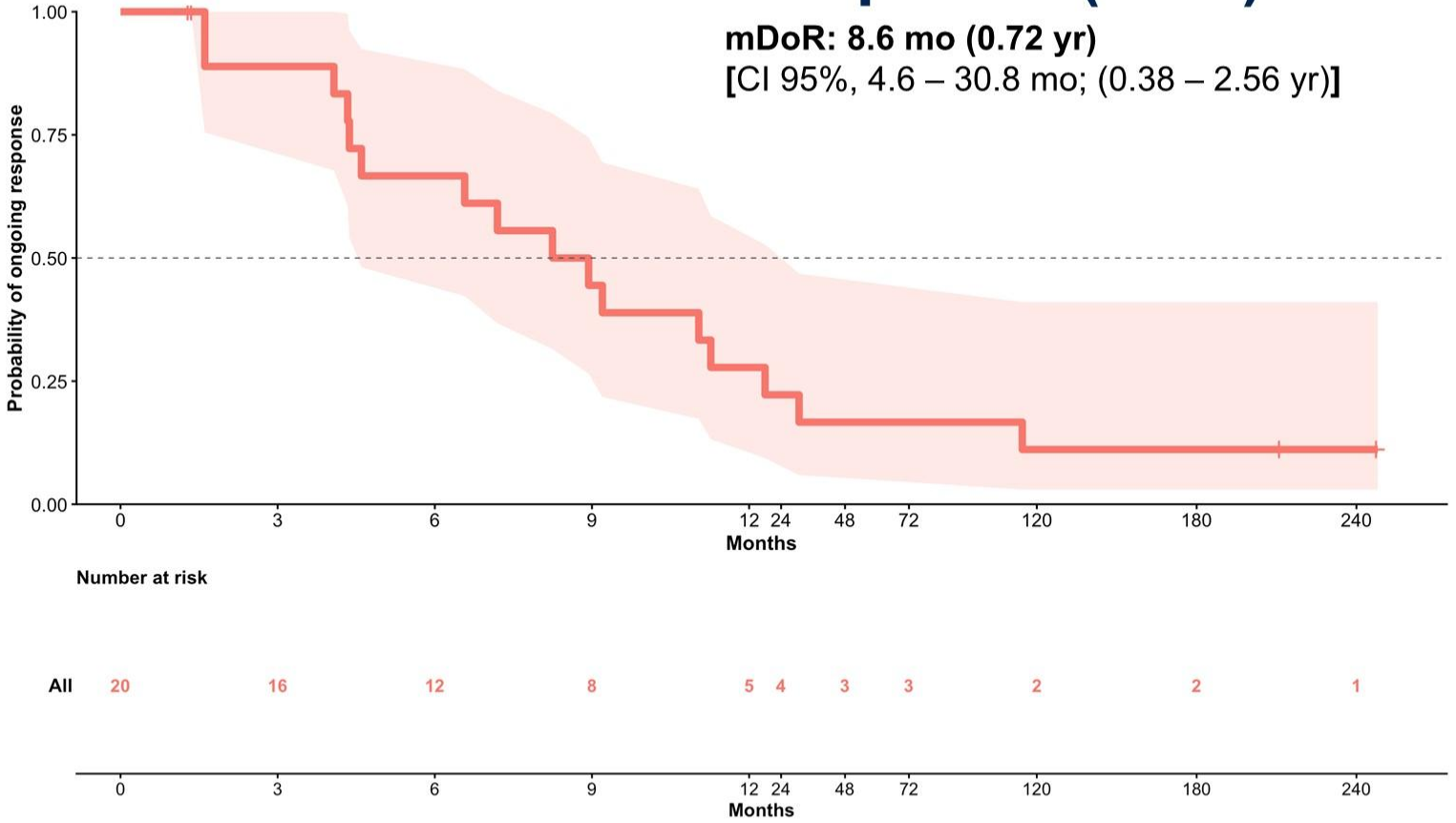
Results – Progression Free Survival (PFS)



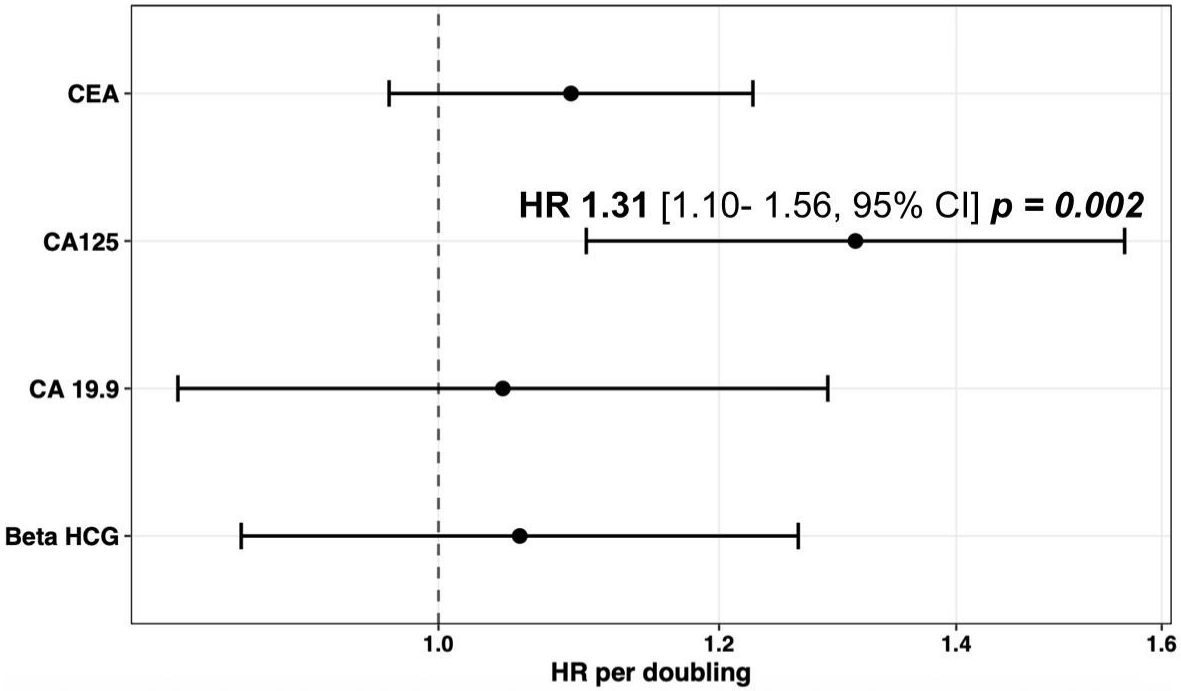
Results – Overall Survival (OS)



Results – Duration of Response (DoR)



Results – Biomarkers at baseline correlation with OS



Biomarker	HR (95% CI)	*p*-value
β-hCG	1.05 (0.88–1.26)	0.7
CA 125	**1.31 (1.10–1.56)**	**0.002**
CA19-9	1.04 (0.84–1.29)	0.7
CEA	1.09 (0.97–1.23)	0.1

Legend: β-hCG = beta-human chorionic gonadotropin; CA125 = cancer antigen 125; CA19-9 = carbohydrate antigen 19-9; CEA = carcinoembryonic antigen. HR= hazard ratio

Safety

TRAEs n (%)	Any	Grade 1	Grade 2	Grade 3	Grade 4
Any TRAE	32 (69)	14 (30)	21 (46)	20 (44)	8 (17)
Hematological TRAEs					
Anemia	9 (28)	2 (6)	3 (9)	4 (12)	0
Neutropenia	4 (12)	0	1 (3)	1 (3)	2 (6)
Thrombocytopenia	7 (22)	1 (3)	2 (6)	2 (6)	2 (6)
Non-hematological TRAEs					
Fatigue	10 (31)	2 (6)	4 (12)	4 (12)	0
Infection	8 (25)	0	3 (9)	5 (15)	0
Dehydration	7 (22)	0	5 (15)	2 (6)	0
Mucositis/stomatitis	7 (22)	0	3 (9)	3 (9)	1 (3)
Hypomagnesemia	7 (22)	6 (19)	1 (3)	0	0
Thrombosis/embolism	5 (15)	0	0	2 (6)	3 (9)
Neuropathy-sensory	4 (12)	3 (9)	0	1 (3)	0
Diarrhea	3 (9)	1 (3)	0	2 (6)	0
Vomiting	3 (9)	0	0	3 (9)	0
Transaminase increased	3 (9)	1 (3)	1 (3)	0	1 (3)
Creatinine increase	2 (6)	1 (3)	1 (3)	0	0
Hemorrhage	2 (6)	1 (3)	0	1 (3)	0
Hyperglycemia	2 (6)	1 (3)	0	1 (3)	0
Hypophosphatemia	2 (6)	0	0	2 (6)	0

No Grade 5 treatment-related adverse events identified

Key Takeaway Points

1

GemFLP achieved a **44% ORR** and **21.4-month median OS** in advanced UA and NUA

2

GemFLP was **safe** and **manageable**, with no grade 5 events

3

CA125 at baseline was associated with **worse OS**, but warrants independent validation

Limitations

- Single-arm design
- Small sample size (N=46) inherent to rare disease, single-arm, single-center study, limiting precision and subgroup analyses
- Biomarker analyses were exploratory and require independent validation

Key Takeaway Points/Conclusions

- GemFLP achieved a **44% ORR** and **21.4-month median OS** in advanced urachal (UA) and non-urachal (NUA) urinary tract adenocarcinoma
- **GemFLP** was safe and manageable, with no grade 5 events; the main toxicities were anemia, dehydration, thrombocytopenia, and neutropenia
- Baseline **CA 125** was associated with **worse OS**, but this finding requires validation in larger independent prospective cohorts

- **Clinical Implication**: In the absence of a standard-of-care, GemFLP provides a prospective reference regimen for future studies and a reasonable current option in appropriately selected patients

Conclusiones

- Tumores germinales
  - miRNA371 papel prometedor en la detección de recaídas, con alta especificidad
- Tumores no germinales
  - Cáncer de pene
    - Posible llegada de ADC+IO en futuro próximo (DV + Toripalimab ORR 37% , EV +Avelumab en ensayo)
  - Carcinoma de uraco
    - GemFLP nueva opción de tratamiento en primera línea

Gracias

Geòrgia Anguera
ganguera@santpau.cat