Overview of the ongoing clinical trials in rare tumors

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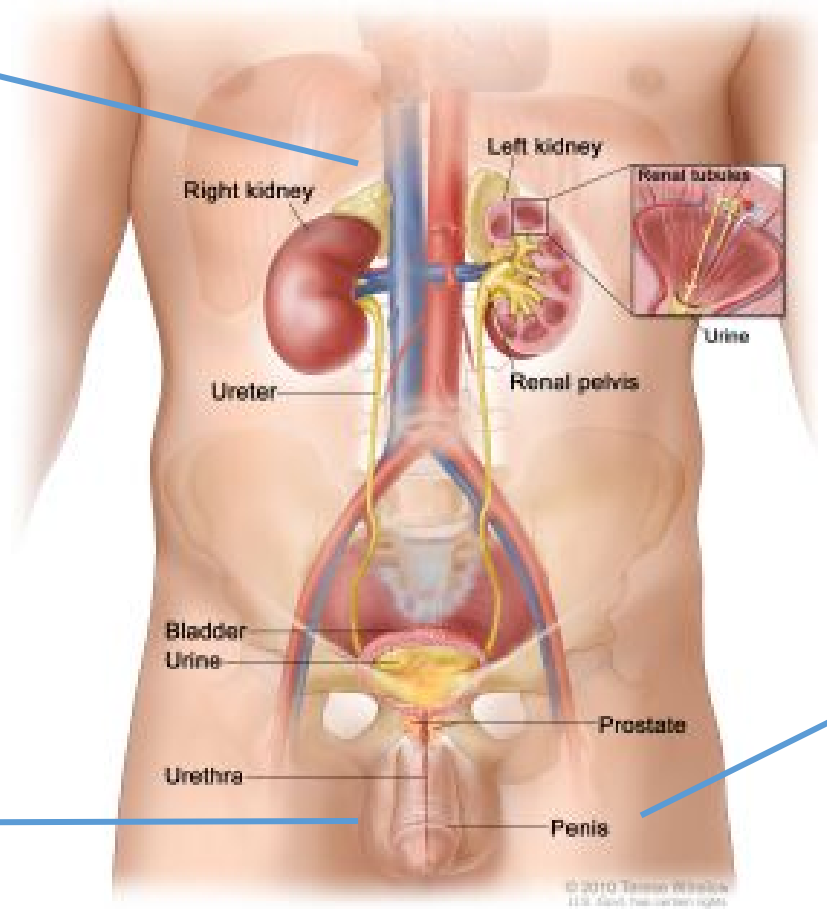
Rare GU tumors

Adrenal tumours



Penile cancer

Testicular cancer

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Challenges in Rare GU Tumors

https://dailynews.ascopubs.org/do/improving-management-rare-genitourinary-tumors-through-international-collaborations

Global Society of Rare Genitourinary Tumors (GSRGT)

- Multidisciplinary collaboration
- Medical Education
- Development of guidelines
- Clinical Research

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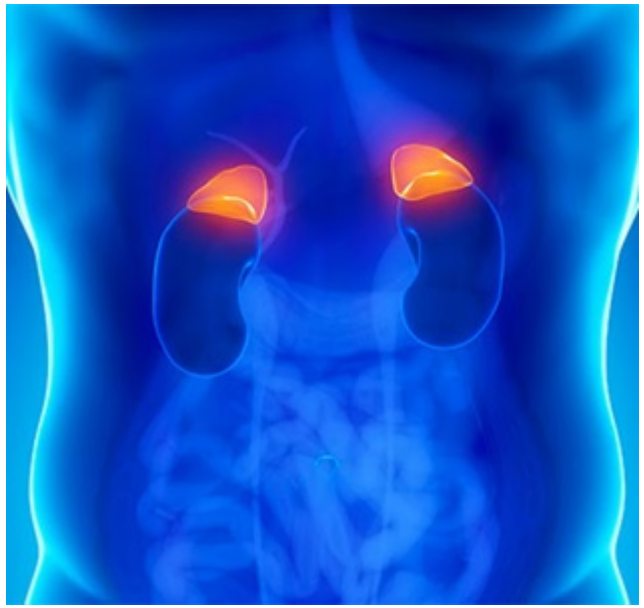
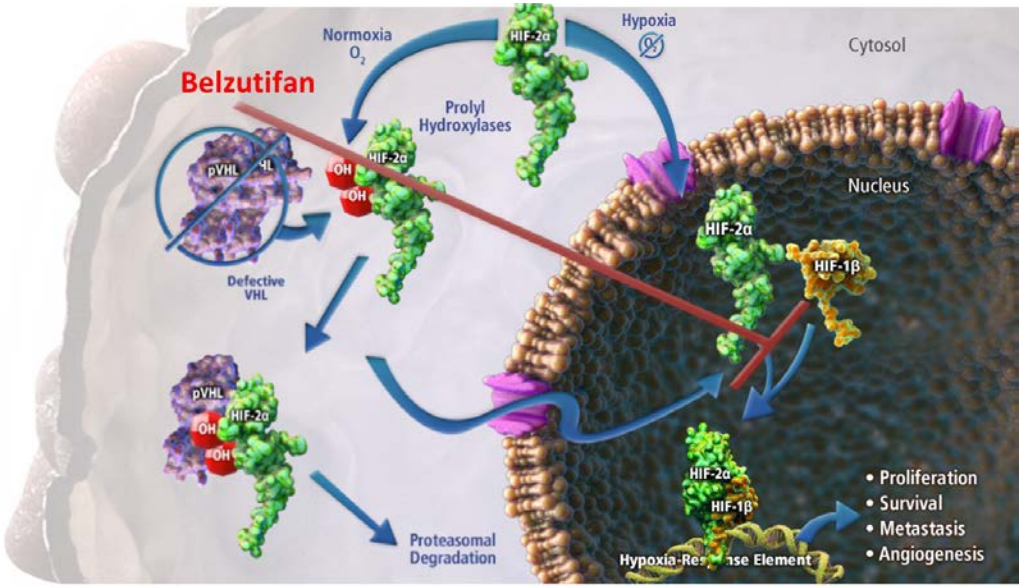
Adrenal tumors



A Phase 2 Study to Evaluate the Efficacy and Safety of Belzutifan Monotherapy in Participants with Advanced Pheochromocytoma/Paraganglioma (PPGL) or Pancreatic Neuroendocrine Tumor (pNET)

Belzutifan



1. Linehan WM, Rickets CJ. *Nat Rev Urol*. 2019;16:539-552. 2. Couvé S et al. *Cancer Res*. 2014;74:6554-6564.

- FDA approved for VHL mutated RCC
- PPGL: Hypoxic signaling with HIF-2α as one of the major drivers of tumorigenesis

- Sporadic malignant pheochromocytomas: 17% VHL gene abnormalities
- Germline VHL mutations: 9.6% to 17.6% of PPGL in larger cohorts

Dannenberg, H., et al 2003; Mannelli, M., et al 2009] [Buffet, A., et al 2012;

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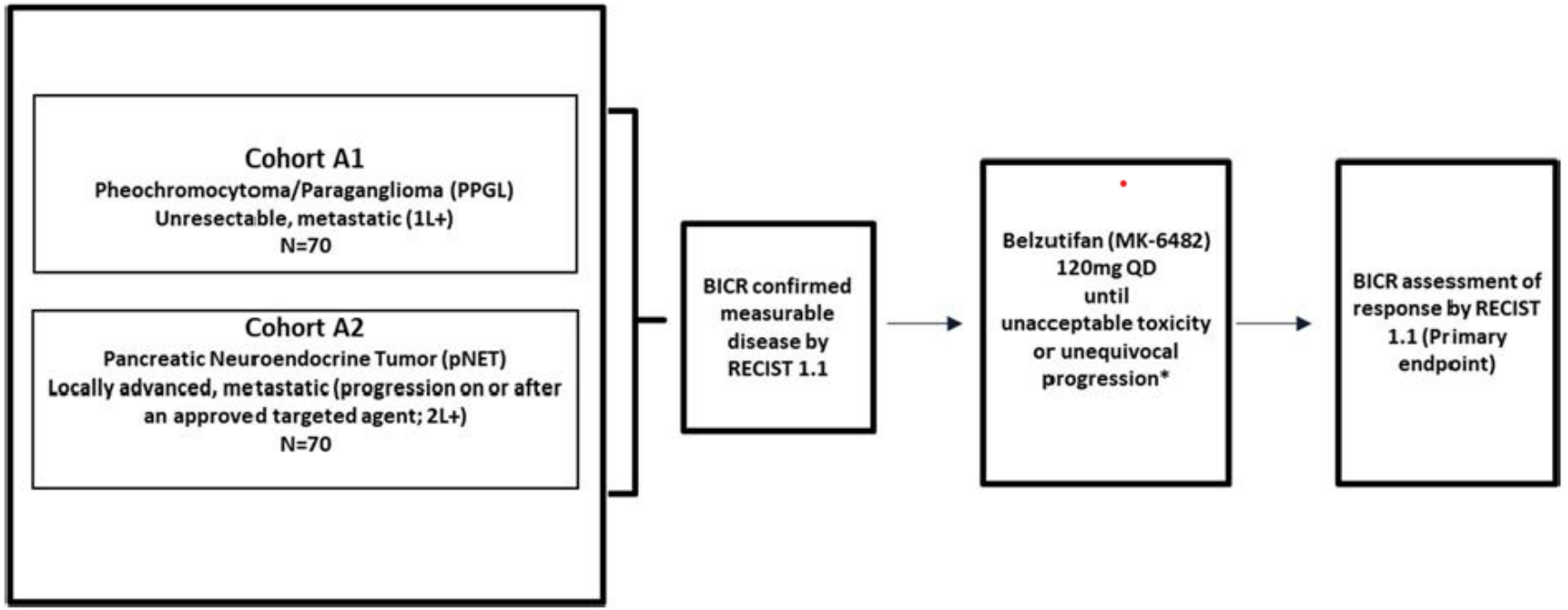
Study design



- Primary endpoint: Objective Response (OR): CR or PR
- Secondary Endpoints: DOR, TTR, Disease control, PFS, OS, safety

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Inclusion criteria

- Has locally advanced or metastatic disease that is not amenable to surgery or curative intent treatment
- Has measurable disease per RECIST v1.1 by CT or MRI
- Participants are allowed to receive therapy in first line where a satisfactory treatment option does not exist and if participants are not candidates for systemic chemotherapy or have refused such therapy. There is no limit on number of prior systemic therapies.
- Adequately controlled blood pressure defined as blood pressure ≤150/90 mm Hg

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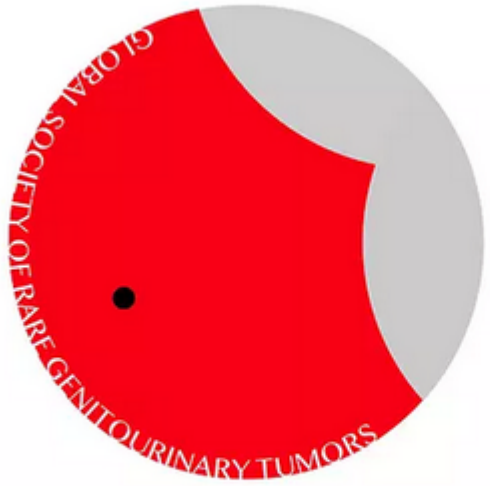
www.adrenalmass.org



AdrenalMass.org

A resource from the Global Society of Rare Genitourinary Tumors dedicated making high-quality, up-to-date guidance on management of tumors of the adrenal gland freely available at the point of care.

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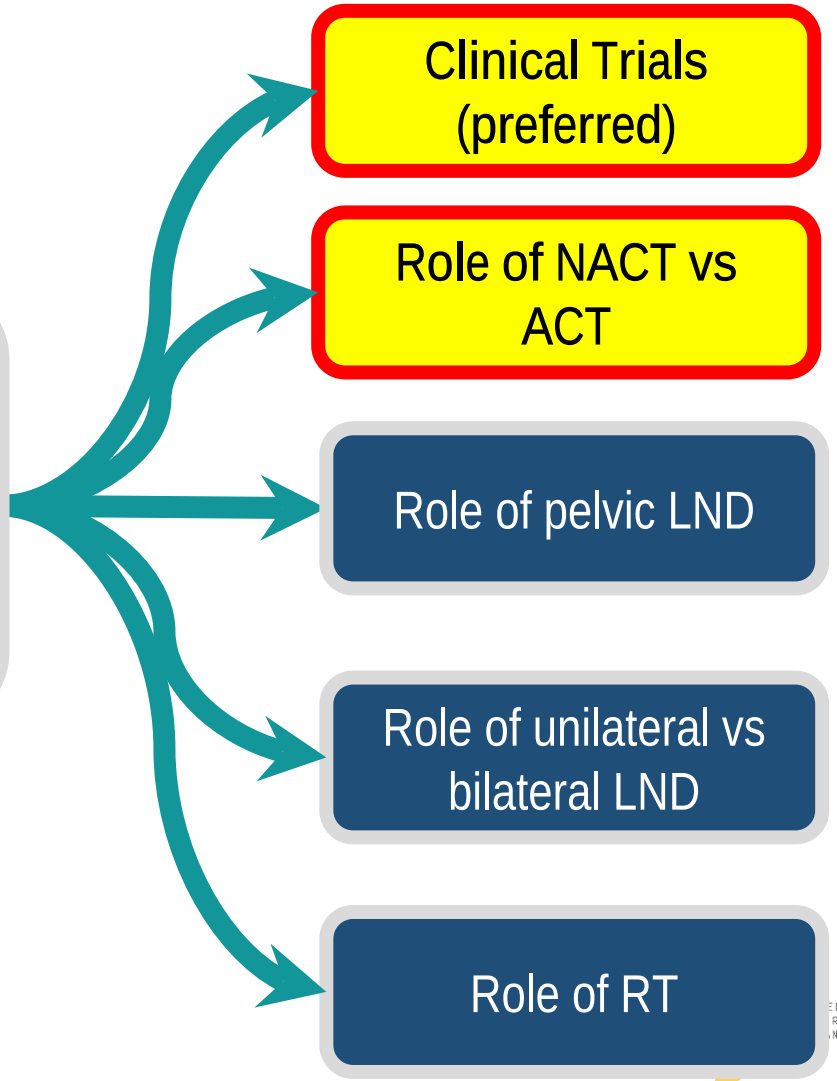
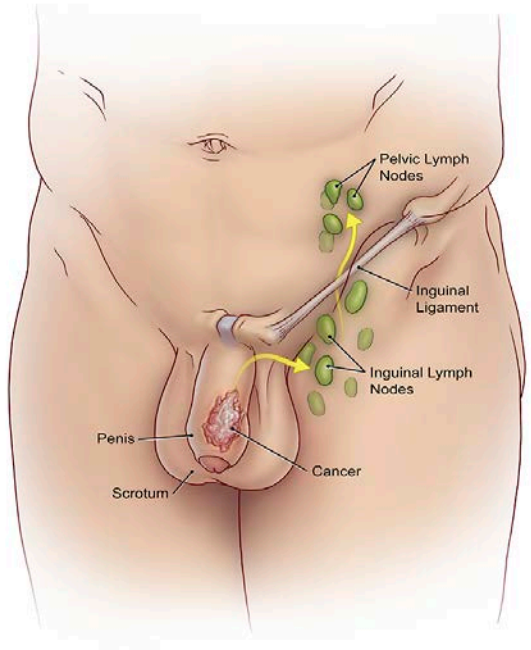
Penile cancer

Locally-advanced

- Clinical lymph node involvement
- Surgery, chemotherapy, and radiotherapy (RT)



Penile cancer



INPACT trial
International Penile Advanced Cancer Trial

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INPACT- NCT02305654

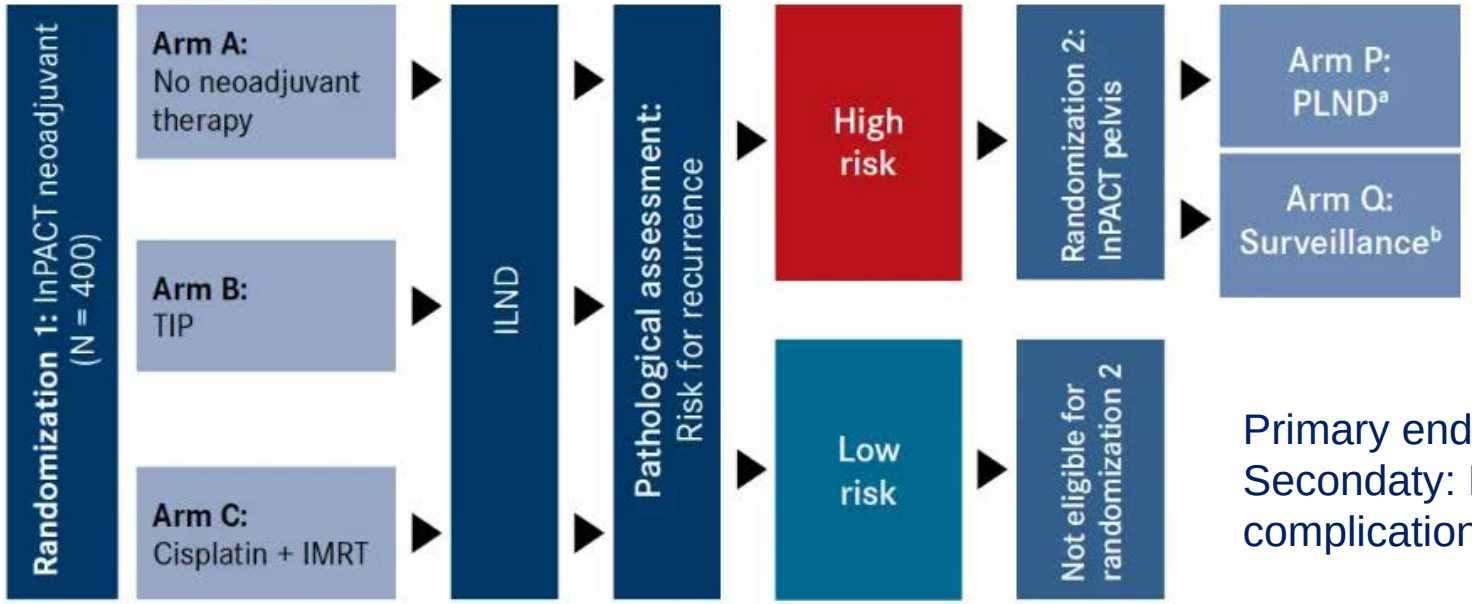
Bayesian design

InPACT Neoadjuvant

InPACT Pelvic

Eligibility criteria

- Written informed consent
- Histologically confirmed squamous cell carcinoma of the penis N1-3, M0
- Measurable disease by RECIST 1.1 criteria
- ECOG PS of 0-2



No neoadjuvant chemotherapy -> adjuvant CRT + PLND
Neoadjuvant chemotherapy -> PLND alone

No neoadjuvant chemotherapy -> IMRT

Primary endpoint: OS
Secondaty: DFS, safety, surgical complications

Stratification by disease burden (nodal involvement), radiological features and renal function

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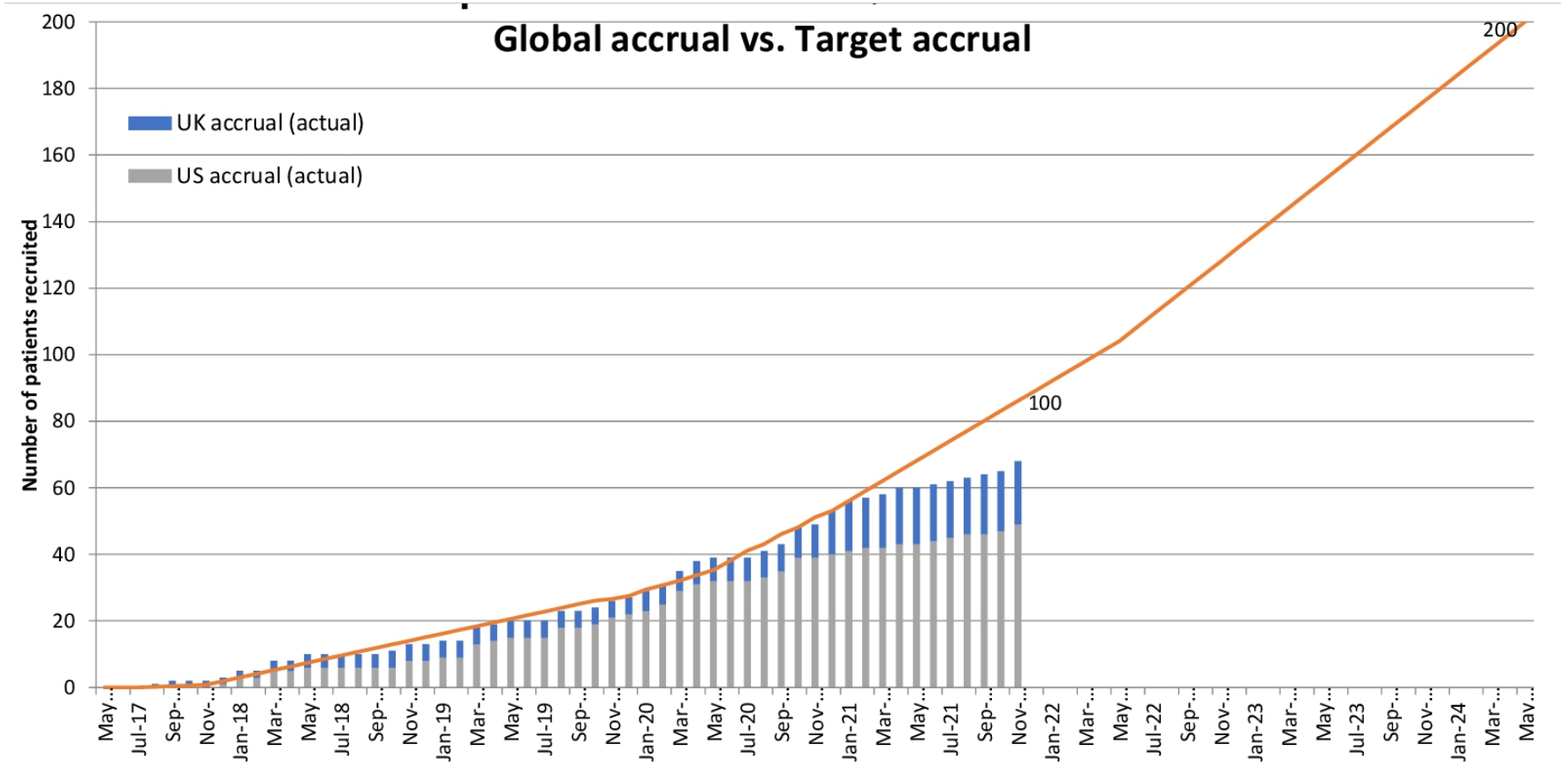
Accrual fev/22

- 69/200 patients to InPACT neoadjuvant
- 10 participants recruited to InPACT pelvis



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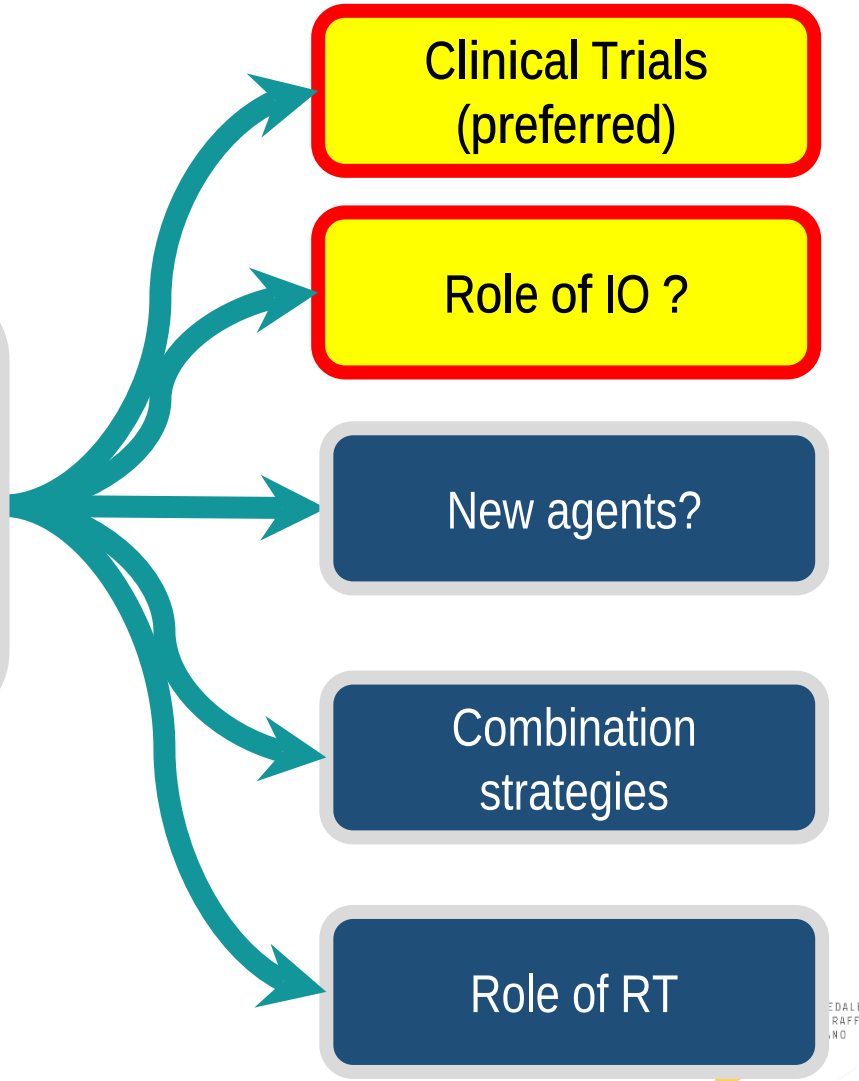
Advanced penile cancer: very poor prognosis

Metastatic disease

- SOC: Platinum-based chemotherapy
- Second-line: low response rates

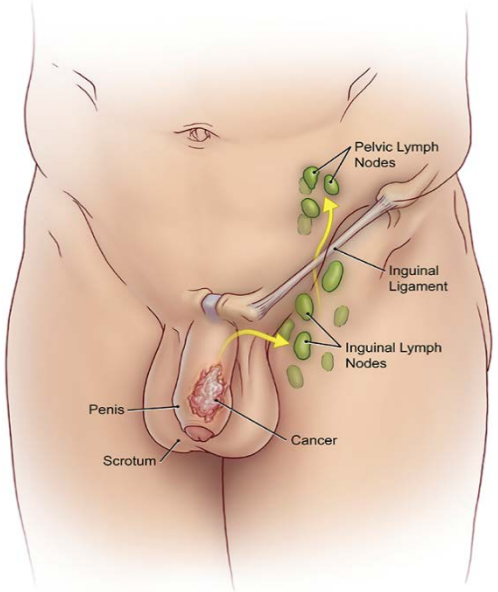


Ongoing clinical trials in PSCC

Identifier	Phase	Diagnosis (planned *n*)	Intervention	Study dates	Sites	Country
Studies enrolling only patients with penile cancer (n = 8)						
NCT03686332 (PERICLES)	II	Unresectable penile carcinoma (32)	Atezolizumab + radiotherapy	2018–2022	1	Netherlands
NCT04475016	II	Neoadjuvant locally advanced penile carcinoma (29)	Albumin-bound paclitaxel + ifosfamide + cisplatin + nimotuzumab + triprilimab	2020–2025	1	China
NCT04224740 (HERCULES)	II	Advanced penile carcinoma (33)	Pembrolizumab + standard-of-care chemotherapy	2020–2025	4	Brazil
NCT02817958 (AFU-GETUG 25 MEGACEP)	II	Node-positive penile carcinoma eligible to lymph-node dissection (37)	Paclitaxel + ifosfamide + cisplatin	2016–2022	17	France
NCT03391479	II	Unresectable/metastatic penile carcinoma (24)	Avelumab + best supportive care	2018–2022	1	Canada
NCT03774901 (PULSE)	II	Advanced penile carcinoma after PBT (32)	Avelumab	2019–2022	1	France
NCT04231981 (ORPHEUS)	II	Unresectable/metastatic penile carcinoma (18)	INCMGA0012	2020–2022	12	Italy, Spain
NCT02305654 (InPACT)	III	Node-positive penile carcinoma (400)	Multi-arm, two randomizations (chemotherapy, lymph-node dissection, radiotherapy)	2017–2022	17	UK, USA

Bandini M et al, Nat Rev Urol. 2022; 19(4): 231–239.

Penile cancer- advanced disease



ORPHEUS
A phase 2 study of the efficacy and safety of INCMGA00012 (Retifanlimab) in advanced penile squamous cell carcinoma (PSqCC)

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ORPHEUS

- International, multicenter, open-label, single-arm, phase 2 trial
- Sample size: 18 patients

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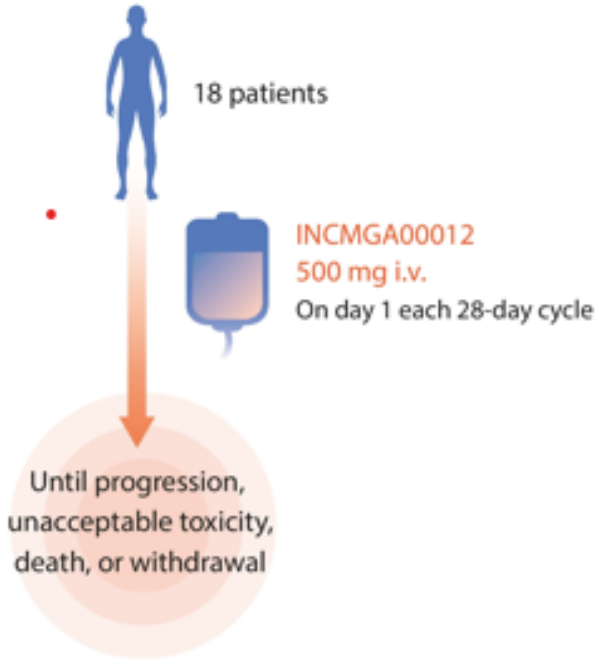
ORPHEUS

Key inclusion criteria:

- Radiologic evidence of locally advanced unresectable or metastatic stage 4 PSqCC (T4 or N3 or M1).
- Treatment naïve or ≥1 prior chemotherapy regimens or radiotherapy for locally recurrent and/or metastatic disease.
- Measurable or evaluable disease per RECIST 1.1.
- ECOG Performance status 0 or 1.

Key exclusion criteria:

- Prior anti-PD-1–, anti-PD-L1–, or anti-PD-L2–based regimens.
- Diagnosis of immunodeficiency or ongoing treatment with systemic steroids or immunosuppressors.
- Known active CNS metastases and/or carcinomatous meningitis.



OBJECTIVES

Primary objective

- To determine the investigator-assessed ORR as per RECIST 1.1.

Secondary objectives

- To determine the CBR, PFS, 6-month PFS, DoR, TTP, and maximum tumor shrinkage as per RECIST 1.1.
- To determine the OS.
- To evaluate the safety and tolerability of INCMGA00012 as per NCI-CTCAE 5.0.

Exploratory objectives

- To evaluate the ORR, CBR, and 6-month PFS as per irRECIST.
- To evaluate tumor- and immune-related factors associated with disease activity status or response to treatment.
- To assess impact of INCMGA00012 on HIV control in HIV-positive patients.

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Results will be presented soon!

Recruitment Status :	Active, not recruiting
Actual Primary Completion Date :	June 1, 2022
Estimated Study Completion Date :	December 2022

Clinicaltrials.org

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Testicular cancer

TIGER Trial: A Randomized Trial of TIP vs TI-CE as Initial Salvage Chemotherapy for Patients with Germ Cell Tumors

Advanced germ cell tumors: salvage chemotherapy

- Approximately 20 to 30% require salvage chemotherapy
- Options: conventional-dose chemotherapy (VIP or TIP) or high-dose chemotherapy (HDCT)
- Important geographical variation

Country or Institution	Initial Salvage Approach
United Kingdom	CDCT
Germany	HDCT
MSKCC	Risk-stratified approach Favorable pts[1] → CDCT (TIP) Unfavorable pts[2] → HDCT (TI-CE)
Indiana	HDCT for all pts except those with late relapse

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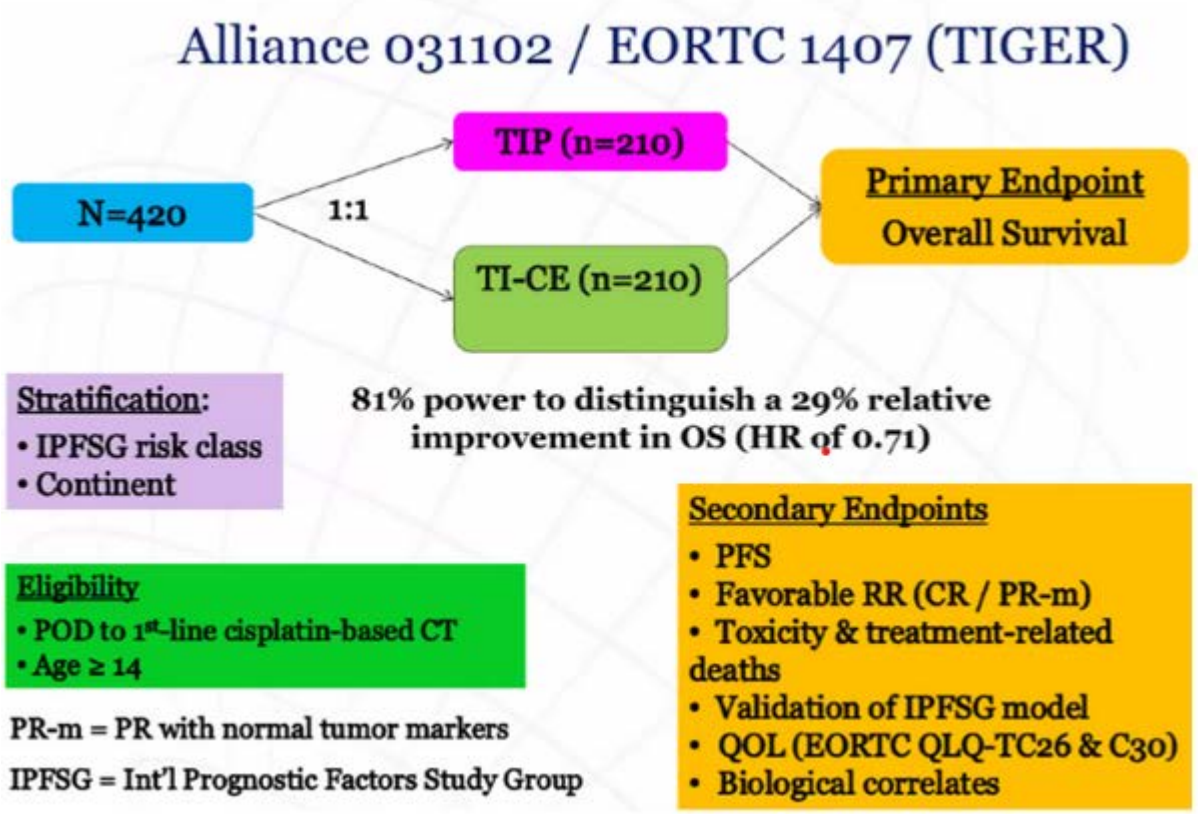
DOI: 10.1200/EDBK_201189 American Society of Clinical Oncology Educational Book 38 (May 23, 2018) 324-329.

TIGER trial

- International collaboration among many centers in North America, Europe, and Australia

- Objective: determine the optimal initial salvage chemotherapy approach in patients with advanced GCT



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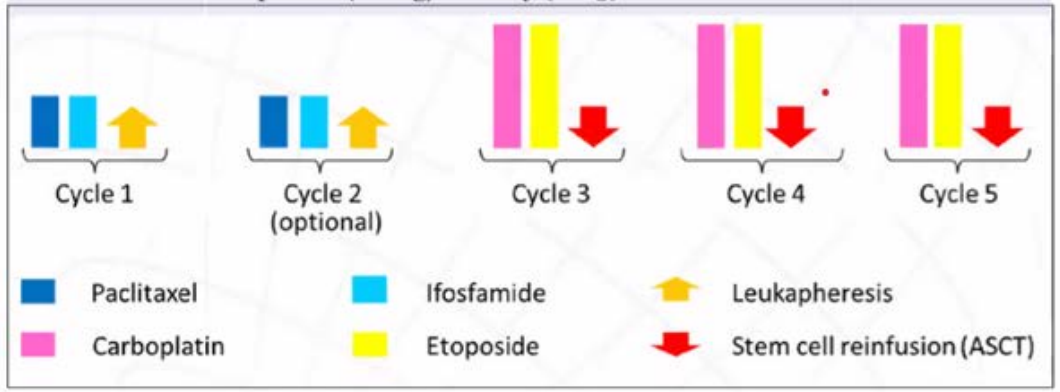
Inclusion Criteria

- Confirmation of GCT histology (both seminoma and nonseminoma)
- Evidence of progressive or recurrent GCT following one line of cisplatin-based chemotherapy:
- Tumor biopsy of new or growing or unresectable lesions
- Consecutive elevated serum tumor markers (HCG or AFP) that are increasing.
- Development of new or enlarging lesions in the setting of persistently elevated HCG or AFP, even if the HCG and AFP are not continuing to increase.
- Must have received 3-6 cycles of cisplatin-based chemotherapy as part of first-line (initial) chemotherapy
- No more than one prior line of chemotherapy for GCT

MSKCC: TI-CE Regimen

Cycle	Drug Daily Dose	Cycle Length
1, 2	Paclitaxel 200mg/m² (D1) Ifosfamide 2000mg/m² mixed 1:1 with mesna (D1-3)	14 days
3, 4, 5	Carboplatin AUC=8 daily (D1-3) Etoposide 400mg/m² daily (D1-3)	21 days



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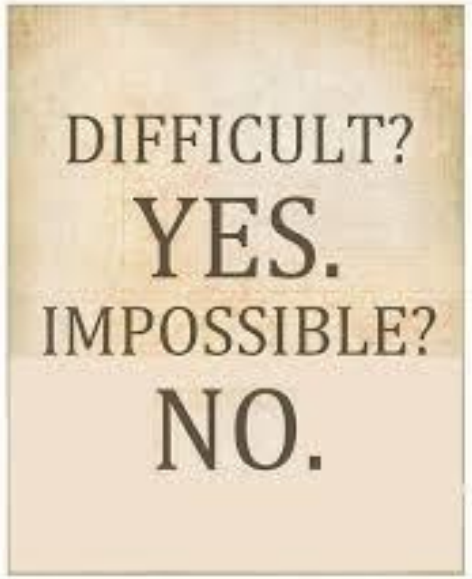
Clinical Research in Rare Tumors



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Thank you!

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