Penile Cancer: Diagnostics, Treatments, Outcomes, and Recent Advances

Literature Review (2020–2025)

Prepared for Presentation

Introduction

- Penile cancer is a rare malignancy, mostly squamous cell carcinoma.
  HPV-related and HPV-unrelated subtypes exist with distinct biology.
  Incidence is higher in developing regions.
  Diagnosis, staging, and treatment require multidisciplinary care.

Muneer A et al., ESMO Open, 2024

Clinical and Pathological Evaluation

- Primary diagnosis requires biopsy of suspicious lesions.
  Histologic subtype, grade, depth of invasion, and margins are crucial.
  p16 and HPV testing stratify prognosis.
  Pathology follows WHO 2016/2022 classification.

Compérat E et al., ESMO Open, 2024

Imaging

- Clinical exam is first-line; imaging supports staging.
  CT chest/abdomen/pelvis recommended for metastasis assessment.
  MRI or penile ultrasound helps detect cavernosum invasion.
  FDG-PET/CT useful in high-risk cases but not routine.

Switlyk MD et al., Cancers (Basel), 2023

Lymph Node Staging

- Ultrasound with FNAC for suspicious nodes.
  Sentinel lymph node biopsy (DSLNB) is standard in cNo high-risk tumors.
  Modified lymphadenectomy with frozen section if DSLNB unavailable.
  Node-positive disease requires full inguinal dissection.

Hakenberg OW et al., ESMO Guidelines, 2022

Biomarkers

- No validated serum biomarker yet.
  SCC antigen has low sensitivity and specificity.
  Elevated CRP is linked to poor survival and nodal metastasis.
  HPV/p16 and PD-L1 status carry prognostic implications.

Qin T et al., World J Surg Oncol, 2025

Surgery

- Surgical excision remains the cornerstone of treatment.
  Organ-sparing techniques preferred for small distal tumors.
  Radical penectomy reserved for advanced disease.
  Robotic/ laparoscopic ILND reduces morbidity vs open.

Høyer S et al., Eur Urol Open Sci, 2022

Radiotherapy

- Brachytherapy or EBRT is an option for early tumors.
  Used when surgery contraindicated or refused.
  Local control is lower than surgery.
  Adjuvant radiotherapy for node-positive cases is debated.

Naushad N et al., Urol Res Pract, 2023

Chemotherapy

- Cisplatin-based chemo is standard in advanced disease.
  TIP (paclitaxel-ifosfamide-cisplatin) shows ~50% response.
  Adjuvant chemo may be considered in node-positive cases.
  Outcomes remain poor in metastatic setting.

Pagliaro LC et al., Cancers (Basel), 2024

Targeted Therapies

- EGFR inhibitors (cetuximab, dacomitinib) show limited efficacy.
  Genomic profiling reveals TP53, NOTCH1, PIK3CA alterations.
  Nectin-4 and TROP-2 targeted ADCs under investigation.
  Still experimental in clinical practice.

Pagliaro LC et al., Cancers (Basel), 2024

Immunotherapy

- Checkpoint inhibitors (PD-1/PD-L1) show modest responses.
  ORR ~16% in atezolizumab trial, better in MSI-high cases.
  Combination regimens under evaluation.
  Pembrolizumab approved for MSI-H/TMB-high tumors.

Taghizadeh H et al., Cancers (Basel), 2025

Outcomes

- 5-yr survival ~79% in localized, 51% in regional disease.
  Drops to 9% with distant metastases.
  Local recurrence manageable after organ-sparing surgery.
  Advanced disease median OS ~12 months.

Taghizadeh H et al., Cancers (Basel), 2025

Recurrence & Follow-up

- Most recurrences occur within 2 years.
  Local relapses can often be salvaged.
  Nodal relapse predicts worse prognosis.
  Close surveillance is essential.

Muneer A et al., ESMO Open, 2024

Quality of Life

- Radical surgery impairs sexual function and body image.
  Organ-sparing approaches preserve QoL better.
  Psychological distress is common among survivors.
  Multidisciplinary support crucial for rehabilitation.

Irizarry VMT et al., Cancers (Basel), 2024

Recent Advances

- Molecular profiling distinguishes HPV+ vs HPV- tumors.
  Robotic ILND shows reduced complications.
  Fluorescence-guided sentinel biopsy improves staging.
  ADCs and ICI combinations are promising.

Pagliaro LC et al., Cancers (Basel), 2024

Conclusion

- Penile cancer requires multimodal, individualized management.
  Diagnostics rely on pathology, imaging, and nodal staging.
  Organ preservation prioritized whenever possible.
  Emerging therapies (ICI, ADCs) may improve outcomes.

Muneer A et al., ESMO Open, 2024

References

- Muneer A, Bandini M, Compérat E, De Meerleer G, Fizazi K, Gietema JA, et al. Penile cancer: ESMO–EURACAN clinical practice guideline for diagnosis, treatment and follow-up. *ESMO Open*. 2024;9(7):103481pmc.ncbi.nlm.nih.govpmc.ncbi.nlm.nih.gov .
- Switlyk MD, Hopland A, Reitan E, Sivanesan S, Brennhovd B, Axcrona U, Hole KH. Multiparametric magnetic resonance imaging of penile cancer: a pictorial review. *Cancers (Basel)*. 2023;15(22):5324mdpi.compubmed.ncbi.nlm.nih.gov.
- Naushad N, Deb AA, Agag AA, Serag HA, Sangar VK. Prognostic markers and trials in penile cancer. *Urol Res Pract*. 2023;49(3):138–46pmc.ncbi.nlm.nih.govpmc.ncbi.nlm.nih.gov.
- Qin T, Du S, Zhang K, Wang L, Zong L, Wang L, Yu W. Evaluation of C-reactive protein levels in penile cancer: a systematic review and meta-analysis. *World J Surg Oncol*. 2025;23:78wjso.biomedcentral.com.
- Irizarry VMT, Paster IC, Ogbuji V, Gomez DM, McCormick K, Chipollini J. Improving quality of life and psychosocial health for penile cancer survivors: a narrative review. *Cancers (Basel)*. 2024;16(7):1309pmc.ncbi.nlm.nih.govpmc.ncbi.nlm.nih.gov.

References

- Pagliaro LC, Tekin B, Gupta S, Herrera Hernandez L. Therapeutic targets in advanced penile cancer: from bench to bedside. *Cancers (Basel)*. 2024;16(11):2086mdpi.commdpi.com.
- Taghizadeh H, Fajkovic H, Stief CG, et al. Immunotherapy in the management of penile cancer: a systematic review. *Cancers (Basel)*. 2025;17(5):883pmc.ncbi.nlm.nih.govpmc.ncbi.nlm.nih.gov.
- Høyer S, Nauschad N, Hakenberg OW, et al. What is the most effective management of the primary tumor in men with invasive penile cancer? A systematic review of the available treatment options and their outcomes. *Eur Urol Open Sci*. 2022;40:58–94. (cited inpmc.ncbi.nlm.nih.govpmc.ncbi.nlm.nih.gov for surgical outcomes).
- Horiguchi A, Ko A, Mullane S, et al. Systematic review of quality of life in penile cancer survivors. *J Clin Med*. 2021;10(19):4506 (summarized inpmc.ncbi.nlm.nih.gov).