

Evidence Discussion Anal Cancer and Cancers of the External Genitalia (ONC-24)

Anal Cancer

The anal canal is predominantly formed by squamous epithelium; hence, the most common histology of anal cancers is squamous cell carcinoma, with cloacogenic variants that include large cell keratinizing, large cell non-keratinizing (transitional), or basaloid.^{1,2} Squamous cell carcinoma of the perianal region (up to 5 cm from the anal verge) is imaged the same as anal carcinoma due to many perianal cancers having involvement of the anal canal or precancerous lesions in the anal canal.³

Suspected/Diagnosis (ONC 24.1): Advanced imaging prior to biopsy is not indicated as most tumors are staged clinically by direct examination and microscopic confirmation (biopsy).³

Initial work-up/Staging (ONC 24.2): All individuals undergo CT chest with contrast and either CT abdomen and pelvis with contrast or CT abdomen with contrast and MRI pelvis with/without contrast. CT allows information on whether there is other organ involvement or possible disease spread.³ PET/CT is supported in stage II-III disease with no evidence of distant metastatic disease by conventional imaging or if conventional imaging is inconclusive. PET/CT is useful in assessing pelvic nodes and has been shown to change the nodal status/TNM stage in up to 41% of patients.⁴ PET/CT does not replace a diagnostic CT in initial staging.³

Restaging/Recurrence (ONC 24.3): Due to low risk of recurrence, stage I treated with complete surgical resection would follow surveillance guidelines that do not recommend any routine imaging. For stages I, II, and III treated with chemoradiation, CT abdomen and pelvis, or MRI abdomen and pelvis should be obtained upon completion of therapy. Stage IV disease on treatment should undergo CT abdomen and pelvis every 2 cycles with imaging of the chest if chest x-ray is abnormal or symptoms develop. If recurrence is suspected, CT chest with either CT abdomen and pelvis or MRI abdomen and pelvis should be performed. PET/CT is indicated for inconclusive findings on conventional imaging.

Surveillance/Follow-up (ONC 24.4): For individuals with Stage II-III disease or had definitive treatment of a local recurrence, CT chest with or without contrast plus either CT abdomen and pelvis with contrast or MRI abdomen and pelvis with/without contrast is indicated annually for 3 years.³

References:

1. Cummings BJ, Ajani JA, Swallow CJ. Cancer of the anal region. In: DeVita Jr. VT, Lawrence TS, Rosenberg SA, et al., eds. *Cancer: Principles & Practice of Oncology*, Eighth Edition. Philadelphia, PA: Lippincott, Williams & Wilkins; 2008.
2. Jass JR, Sobin LH. *Histological Typing of Intestinal Tumours*: Springer-Verlag Berlin Heidelberg; 1989.
3. Benson III AB, Venook AP, Adam M, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – December 20, 2023. Anal Carcinoma, available at: https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for anal carcinoma V2.2023– April 28, 2023. ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
4. Jones M, Hruby G, Solomon M, et al. The role of FDG-PET in the initial staging and response assessment of anal cancer: a systematic review and meta-analysis. *Ann Surg Oncol* 2015;22:3574-3581. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25652048>.

Cancers of the External Genitalia

This information applies to squamous cell carcinomas arising from the vulva, vagina, penis, urethra, and scrotum.

Initial work-up/Staging (ONC 24.6): Unilateral or bilateral inguino-femoral lymphadenectomy (IFL) may be complicated by up to 40% rate of wound complications and up to 70% of individuals experiencing lymphedema.^{1,2,3} A systemic review and meta-analysis comparing IFL to sentinel lymph node biopsy (SLN) showed similar recurrence rates of 1.4% versus 2.8%, respectively, with less morbidity for SLN.^{4,5} For clinically node-negative vulvar cancer with either the lesion > 2 cm or any size with stromal invasion > 1 mm, sentinel lymph node biopsy with SPECT/CT is indicated. For stage II or higher, either CT abdomen and pelvis or CT abdomen and MRI pelvis can be completed. CT chest is indicated for further evaluation of chest x-ray abnormality or signs/symptoms of chest involvement due to the uncommon involvement of the chest at presentation.⁶ PET/CT is only indicated for inconclusive findings on conventional imaging.

Restaging/Recurrence (ONC 24.7): Upon signs/symptoms of recurrence to include a difficult or abnormal exam, elevated LFTs or biopsy proven recurrence, CT chest with either CT abdomen and pelvis or MRI abdomen and pelvis is indicated. Individuals on systemic therapy can obtain CT abdomen and pelvis every 2 cycles and may also include chest if clinically indicated.

Surveillance (ONC 24.8): Routine imaging is not indicated for any stage of vulvar or vaginal cancer but is recommended as indicated by suspicious examination findings or symptoms of recurrence.⁶ Stage I-III A penile cancer does not require routine advanced imaging, while Stage IIIB and higher should have CT abdomen and pelvis every 3 months for year 1 and every 6 months for year 2.⁷

References:

1. Carlson JW, Kauderer J, Hutson A, et al. GOG 244-The lymphedema and gynecologic cancer (LEG) study: Incidence and risk factors in newly diagnosed patients. *Gynecol Oncol* 2020;156:467-474. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31837831>.
2. DiSaia PJ, Creasman WT, Rich WM. An alternate approach to early cancer of the vulva. *Am J Obstet Gynecol* 1979;133:825-832. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/434024>.
3. Cacciamani GE, Medina LG, Sayegh AS, et al. Assessment and Reporting of Perioperative Adverse Events and Complications in Patients Undergoing Inguinal Lymphadenectomy for Melanoma, Vulvar Cancer, and Penile Cancer: A Systematic Review and Meta-analysis. *World J Surg* 2023;47:962-974. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/36709215>.
4. Covens A, Vella ET, Kennedy EB, et al. Sentinel lymph node biopsy in vulvar cancer: Systematic review, meta-analysis and guideline recommendations. *Gynecol Oncol* 2015;137:351-361. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25703673>.
5. Oonk MH, van Os MA, de Bock GH, et al. A comparison of quality of life between vulvar cancer patients after sentinel lymph node procedure only and inguino-femoral lymphadenectomy. *Gynecol Oncol* 2009;113:301–305.
6. Abu-Rustum NR, Yashar CM, Arend R. et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2024 – May 1, 2024. Vulvar Cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/vulvar.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Vulvar Cancer V4.2024 – May 1, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.
7. Flaig TW, Spiess PE, Agarwal N. National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2024 – October 25, 2023. Penile Cancer, available at: https://www.nccn.org/professionals/physician_gls/pdf/penile.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Penile Cancer V1.2024 – October 25, 2023. ©2023 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines™, go online to NCCN.org.