Adjuvant Radiation in Early Stage Vulvar Cancer: A Review of Indications and Optimal Dose

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Abstract

Vulvar cancer is a relatively rare gynecologic malignancy for which surgery remains the cornerstone of treatment. A wide local excision with curative intent in patients with early stage vulvar cancer is the gold standard. Adverse pathologic features have been shown to increase risk of local recurrence. Specifically, the presence of positive or close margins of < 8 mm or 2 or more positive nodes have been shown to significantly increase the risk of recurrence and have informed guidelines for risk-adapted adjuvant radiation, although the optimal dose for adjuvant radiation is yet to be established. Given the rarity of vulvar cancer, guidelines regarding the indications and dose for adjuvant radiation are based largely on retrospective studies. The purpose of this review is to summarize the evidence underlying the current indications for adjuvant radiation in early stage vulvar cancer as well as to determine the optimal dose for adjuvant radiation.

Keywords: vulvar cancer, early stage, management, radiation dose, adjuvant radiation

Vulvar cancer is a relatively rare malignancy accounting for 5% of gynecologic tumors, with an incidence of 6,120 cases and 1,550 deaths in the United States in 2021.[1] While the incidence of vulvar cancer increases with age, there has been an increase in younger patients in recent years, likely due to the association with human papillomavirus (HPV) infections.[2] One of the most common presenting symptoms of vulvar cancer is pruritis, but other less commonly reported symptoms include bleeding, dysuria, discharge, and pain.[3] Many patients experience a delay in diagnosis due to misdiagnosis as an inflammatory condition due to the lack of specificity in presenting symptoms.[4] Squamous cell carcinoma is the predominant histology of vulvar cancer, accounting for 95% of all histological types. Approximately 30% of patients who present with early stage vulvar cancer have existing lymph node metastases — most commonly to the inguinal and femoral nodes followed by metastases to the pelvic nodes.[3] Lymph node status has been shown to be the most important independent prognostic factor for disease-free survival in vulvar cancer.[5,6]

Early stage vulvar cancer is generally considered to be T1 or T2 disease with clinically nonsuspicious lymph nodes.[7] The cornerstone of treatment for early stage vulvar cancer remains surgery with the goal of achieving a wide-margin resection. Historically, the standard surgical approach was an en bloc radical vulvectomy with a bilateral lymph node dissection.[8] However, this surgery was associated with significant morbidity and mortality, with up to 70% to 85% of patients reporting chronic lymphedema and wound breakdown[9] and an operative mortality rate of up to 16%.[10] In recent years, this radical surgical approach has been largely replaced by a wide local excision and modified radical vulvectomy with a 1 cm margin.[11] Furthermore, a separate skin vulvar-groin incision can be performed for nodal assessment rather than an en bloc groin dissection,[12]

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Table 1. Studies of Vulvar Cancer Patients With Close or Positive Margin

AUTHOR	YEAR	NUMBER OF VULVAR CANCER PATIENTS S/P SURGERY	MARGIN STATUS	INTERVENTION	RESULTS
Heaps et al[19]	1990	135 patients	91 patients with ≥ 8 mm margins and 44 patients with < 8 mm margins	LR examined by margin status	LR 0% in patients with ≥ 8 mm margins and 50% in patients with < 8 mm margins
Faul et al[20]	1997	62 patients	All patients had positive or < 8 mm margins	31 patients were observed and 31 patients received adjuvant radiation	LR 58% in observed vs 16% in the radiation group, *P* = 0.036
Chan et al[21]	2007	90 patients	30 patients with > 8 mm and 53 patients with ≤ 8 mm margins	Differences in recurrence examined	LR 0% with a margin > 8 mm and 23% with ≤ 8 mm margins
Viswanathan et al[22]	2013	205 patients	69 patients (negative margins), 116 (< 1 cm margins), 20 patients (positive margins)	Freedom from vulvar relapse was examined	4-year freedom from vulvar relapse rates: 82% (negative margins), 63% (close margins), 37% (positive margins), *P* = .005
Ignatov et al[24]	2016	257 patients	65 patients had close or positive margins ≤ 10 mm	34 patients received postoperative brachytherapy and 31 were observed	5-year overall survival improved with adjuvant radiation (67.6% vs 29%, *P* < .0001)
Groenen et al[26]	2010	93 patients	54% of the patients had < 8 mm margin	LR was examined by margin status	No significant difference in LR (23% vs 22%) between those with close margins or clear margins
Nooij et al[25]	2016	148 patients	122 patients with margins < 8 mm	40% patients with close margins received either local excision or radiation	No difference in LR between those who received treatment and those who did not (14% vs 7%, *P* = 0.323)
Barlow et al[23]	2020	122 patients	All had close or positive margins	146 patients were treated with re-excision or adjuvant radiation and 76 patients were observed	LR significantly decreased in those who were treated (8.7% vs 30.2%, *P* = 0.005)
Nomura et al[27]	2021	34 patients	10 patients positive, 3 with < 3 mm, 4 with < 5 mm, 5 with < 8 mm, 12 with ≥ 8 mm margins	Differences in recurrence patterns in patients based on margin status were examined	LR-free survival increased with narrower surgical margins: 32%, 30.3%, 42.5%, 55.5%, and 73% for positive, < 3 mm, < 5 mm, < 8 mm, and ≥ 8 mm margins, respectively

Key: s/p = status post, LR = local recurrence

and an ipsilateral node dissection can be considered in well-lateralized tumors.[13] However, given that an inguinofemoral nodal dissection can be associated with significant morbidity, sentinel lymph node biopsy is becoming integrated into standard treatment for early stage vulvar cancers on the basis of two major trials. Specifically, GOG 173 found that sentinel lymph node biopsy was a viable alternative to an inguinofemoral lymphadenectomy with a sensitivity of 91.7%,[14] and GROINSS-V showed that the recurrence rate with a negative sentinel node assessment was 2.3% with significantly lower complications than those with a positive sentinel node who ultimately underwent an inguinofemoral lymphadenectomy.[15]

Radiation therapy is often used in the adjuvant setting in vulvar cancer to reduce local recurrence and improve survival in patients who have adverse pathologic features. However, given the relative rarity of vulvar cancer, there are limited randomized controlled trials to inform the use and optimal dose of adjuvant radiation. Current treatment guidelines are largely based on retrospective studies and extrapolated from cervical and anal canal cancers. The purpose of this review is to determine the indications for adjuvant radiation in early stage vulvar cancer as well as to report the evidence regarding the optimal dose for adjuvant radiation.

Indications for Adjuvant Radiation in Early Stage Vulvar Cancer

The role of adjuvant radiation in vulvar cancer is to reduce local recurrence. The two strongest predictors of local recurrence, which have informed current guidelines, include margin status and nodal involvement:

Adjuvant Radiation for Close or Positive Margins

One of the indications for adjuvant radiation in early stage vulvar cancer is a close or positive margin. While re-excision can be considered for close or positive margins, it can often have significant morbidity and psychosocial impact on the patient in terms of lymphedema and sexual function.[16] Thus, adjuvant radiation is often recommended in situations where re-excision would result in excessive morbidity.[17] While there is some variation in the definition of margin status, much of the literature traditionally defines margins of < 8 mm as close margins – corresponding to a 1 cm surgical margin given the 20% shrinkage in formalin – and classifies any tumor at the surgical edge of the specimen as positive margins.[18] Studies addressing the impact of margin status and/or adjuvant radiation on local recurrence in vulvar cancer patients are summarized in **Table 1**. A study by Heaps et al reviewed 135 patients with squamous cell carcinoma of the vulva; among the 91 patients with a margin ≥ 8 mm, none had a local recurrence. By contrast, among 44 patients with margins < 8 mm, 50% of patients had a local recurrence.[19] In a subsequent study, 62 patients with vulvar cancer with positive or close margins defined as < 8 mm were retrospectively reviewed. Thirty-one patients were observed after surgery and 31 patients received adjuvant radiation to a mean dose of 5,654 cGy for those with positive margins and 4,867 cGy for those with close margins. The local recurrence rate in the observation group was 58% vs 16% in the radiation group, and adjuvant radiation significantly decreased local recurrence rates in both the close margin (≤ 8 mm, $P = 0.036$) and positive margin groups ($P = 0.0048$). On multivariate analysis, adjuvant radiation and margin status were significant predictors for local control ($P = 0.009$ and $P = 0.0001$ respectively).[20] Finally, a study by Chan et al examined 90 vulvar cancer patients who underwent surgery and found margin status to be an important predictor of recurrence. Specifically, among the 30 patients with a margin > 8 mm, none had a local recurrence, whereas 23% of the women with ≤ 8 mm had a recurrence.[21]

In a large retrospective study by Viswanathan et al, 205 vulvar cancer patients who underwent surgery were categorized by margin status as follows: negative margins, close margins of < 1 cm, and positive margins. The 4-year freedom from vulvar relapse rates for the groups were 82%, 63% and 37% respectively ($P = 0.005$). Additionally, while recurrences were seen with margins up to 9 mm, the risk of recurrence was significantly increased with margins < 5 mm ($P = 0.002$).[22] Barlow et al examined 122 vulvar cancer patients who underwent surgery with close or positive margins — defined as between 0.1 mm and 8 mm or tumor on any surgical skin edge, respectively — of which 46 patients underwent re-excision or adjuvant radiation and 76 patients were observed. Local recurrence was significantly decreased in patients who underwent re-excision or adjuvant radiation compared with those who were observed (8.7% vs 30.2%, $P = 0.005$).[23] In addition, in a retrospective review of 257 patients with vulvar squamous cell carcinoma by Ignatov et al, 65 patients had close or positive margins — defined as ≤ 10 mm — of which 34 patients received postoperative brachytherapy (median dose of 50 Gy) and 31 patients did not receive adjuvant therapy. The 5-year overall survival was significantly improved in patients with close or positive margins who received adjuvant brachytherapy compared with those who did not receive adjuvant treatment (67.6% vs 29%, $P < 0.0001$).[24] In a meta-analysis of 10 studies consisting of 1,276 vulvar cancer patients and 255 local recurrences, the risk of recurrence nearly doubled for patients with margins < 8 mm compared with those with margins > 8 mm (RR 1.99, CI: 1.1 to 3.5).[25]

While the aforementioned studies have demonstrated that margin status is an important predictor of local recurrence and have largely focused on 8 mm as an appropriate margin, other studies have challenged the association between margin status and local recurrence and have shown that narrower margins may be appropriate. In a study by Groenen et al, 93 patients who underwent surgery for squamous cell carcinoma of the vulva were retrospectively reviewed and 54% of these patients had a margin of < 8 mm. After a median follow-up of 31 months, the recurrence rate did not significantly differ between patients with margins > 8 mm or < 8 mm (23% vs 22%), respectively. However, it is important to note that among patients with < 8 mm margins, 48% received additional treatment with either radiation or re-excision. Thus, the results should be interpreted with caution, since the additional treatment may have impacted the findings of this study.[26] Furthermore, Nooij et al conducted a cohort study of 148 patients with vulvar squamous cell carcinoma and found no significant difference in local recurrence between those who had < 8 mm margins vs those who had > 8 mm margins (HR 1.18, CI: 0.32 to 4.35). Additionally, among the 122 patients who had margins

< 8 mm, 40% received either local excision or radiation, and there was no significant reduction in recurrence between those who received additional treatment compared with those who received no additional treatment (14% vs 7%, $P = 0.323$).[25]

Furthermore, a Japanese study examined 34 patients with vulvar cancer who underwent surgery with curative intent. On univariate analysis, local recurrence-free survival generally increased with wider surgical margins, with rates of 32%, 30.3%, 42.5%, 55.5%, and 73% for positive, < 3 mm, < 5 mm, < 8 mm, and ≥ 8 mm margins, respectively. However, on multivariate analysis, only a tumor size of > 2 cm and a positive surgical margin — defined as tumor at the edge of the specimen — were risk factors for local recurrence (HR 17.7, 95% CI: 1.39 to 226 and HR 0.0092, 95% CI: 0.011 to 0.53, respectively), thereby suggesting that narrower surgical margins may be acceptable.[27] Lastly, a review by Milliken et al examined articles from 2005 to 2020 and concluded that a 2- to 3-mm margin was not associated with higher local recurrence rates compared with an 8-mm margin.[28]

While earlier literature has traditionally classified < 8 mm margin as close margins requiring adjuvant radiation to reduce local recurrence, some series have questioned the adequate width of surgical margin and its impact on local recurrence. In a systematic review by te Grootenhuis et al, 11 studies examined the role of margin status and local recurrence and only 6 studies showed a decreased local recurrence with margins > 8 mm vs ≤ 8 mm.[29] Nevertheless, the most conservative recommendation put forth in the ACR Appropriateness Criteria for adjuvant therapy in vulvar cancer is to continue to offer adjuvant radiation in vulvar cancer patients with margins < 8 mm,[17] although if there is concern for a patient's ability to tolerate the radiation or for significant morbidity then omission is reasonable in light of recent studies.

Nodal Involvement

Adjuvant Radiation With 2 or More Positive Nodes or Extracapsular Extension

The role of adjuvant radiation for patients with ≥ 2 positive lymph nodes or fixed ulcerated groin nodes has been supported by a randomized trial. Specifically, GOG 37 randomized 114 patients with invasive vulvar cancer and positive nodal status post radical vulvectomy and bilateral groin lymphadenectomy between pelvic node resection or adjuvant radiation therapy to a dose of 45 to 50 Gy bilaterally to the groins. The 2-year overall survival rates were significantly improved in the adjuvant radiation arm compared with pelvic resection (68% vs 54%, $P = 0.03$),[30] but at 6 years, the overall survival did not remain significant for the entire cohort (51% vs 41%, $P = 0.18$). The incidence of cancer-related death, however, significantly favored the radiation arm (29% vs 51%, $P = 0.015$), and the overall survival benefit persisted for patients with fixed ulcerated groin nodes and 2 or more positive groin nodes ($P = 0.004$ and $P = < 0.001$ respectively), or those with ≥ 20% lymph node positivity.[31]

The AGO-CaRE-1, a large retrospective study, evaluated the role of adjuvant radiation in patients with node-positive vulvar cancer. A total of 1,249 patients were included of which 447 patients had node-positive disease, with 38.5% of patients having 1 positive node, 22.8% having 2 positive nodes, 33.3% having ≥ 3 positive nodes, and 5.4% having an unknown number of positive nodes. Among the node-positive patients, 54.6% received adjuvant therapy: 183 patients had inguinal nodal irradiation and 117 patients had inguinal and pelvic nodal irradiation. For all node-positive patients, regardless of the field irradiated, the median dose was 50.4 Gy. After a median follow-up of 39.4 months, adjuvant radiation in node-positive patients significantly improved the progression-free survival (PFS) compared with observation (39.6% vs 25.9%, $P = 0.004$, respectively). On multivariate analysis, adjuvant radiation was significantly associated with superior PFS in patients with 2 or 3 positive nodes. Although the overall survival was also improved, it was not statistically significant (57.7% vs 51.4%, $P = 0.17$).[32]

A subset analysis of this study examined 360 patients with positive nodes, known radiation status, and known radiation volumes. In this cohort, 15.8% received adjuvant radiation to the inguinal and pelvic nodes, 40.5% received adjuvant radiation to the vulva in addition to the inguinal and pelvic nodes, and 43.6% of patients did not receive any adjuvant treatment. After a median follow-up of 17.2 months, local recurrence was significantly higher in node-positive patients without adjuvant radiation compared with those who received adjuvant radiation to the vulva in addition to the groins and pelvis (HR 1.79, CI: 1.09 to 2.91, $P = 0.019$). Additionally, median disease-free survival was significantly improved (18.3 months vs 12.7 months) in node-positive patients who received radiation to the vulva, groins, and pelvis compared with those who did not receive adjuvant radiation ($HR_{withoutradiation}$ 1.53, CI: 1.10 to 2.13, $P = 0.010$). Thus, this study concluded that node-positive patients benefit from adjuvant radiation, particularly in the case of comprehensive radiation to the vulva, groins and pelvis.[33]

Finally, a study by van der Velden et al also substantiated the role of adjuvant radiation not only for those with 2 or more positive nodes, but also for patients who have nodes with extracapsular extension. Specifically, 71 patients with squamous

cell carcinoma of the vulva were reviewed, and extracapsular extension, 2 or more positive nodes, and > 50% replacement of lymph nodes by tumor were found to be independent predictors of poor survival ($P = 0.00$, $P = 0.02$, and $P = 0.03$, respectively). Moreover, extracapsular extension was found to be the most significant independent predictor of survival, thereby underscoring the potential benefit of adjuvant radiation in these patients.[34]

Adjuvant Radiation with 1 Positive Node

While the role of radiation in patients with 2 or more positive nodes is well-supported by the literature, the role of radiation in patients with a single positive node remains controversial. In a small retrospective review, 75 vulvar cancer patients with lymph node metastasis underwent radical vulvectomy and an inguino-femoral lymphadenectomy, of which 31 patients were treated with adjuvant radiation therapy to a dose of 46 Gy. There was no significant difference in the 5-year disease-free survival and disease-specific survival between those who received radiation therapy and those who did not receive radiation therapy (63% and 69%, $P = 0.97$ vs 62% and 68%, $P = 0.96$ respectively).[35] Van der Velden et al further supported the omission of radiation therapy for vulvar cancer patients with a single intracapsular positive node. A total of 96 patients with vulvar cancer with a single positive intracapsular node who did not receive radiation therapy were reviewed. After a median follow-up of 64 months, only 1 patient (1%) had an isolated groin recurrence in a contralateral groin that had been assessed as node-negative at the time of surgery, and 2 patients (2.1%) had a local and groin recurrence. Of the patients with a combined local and groin recurrence, 1 patient had a large vulvar recurrence with lymphangitis carcinomatosa of the skin in the groin and the other had a vulvar recurrence and a groin nodal recurrence in the undissected left groin. The risk of recurrence or survival did not depend on the size of the node or lymph node ratio. Furthermore, the 5-year disease-specific survival, overall survival, and recurrence-free survival were 79%, 62.5%, and 97%, respectively. Given the low risk of groin recurrence, the authors concluded that radiation therapy could be omitted in this patient cohort.[36]

By contrast, Parthasarathy et al suggested a potential benefit from adjuvant radiation in vulvar cancer patients with a single positive node. This study examined 490 patients with node-positive vulvar cancer of which 208 patients had a single positive node. Radiation therapy significantly improved survival in the subset of patients with ≤ 12 lymph nodes removed (76.6% vs 55.1%, $P = 0.035$), but the improvement in survival did not reach significance in those with >12 lymph nodes removed (77.3% vs 66.7%, $P = 0.23$). However, an important limitation of this study was that the size and characteristics of the nodal metastases were not reported.[37] Finally, a multicenter study examined 176 patients with vulvar cancer and 1 positive node. While there were significant differences in 5-year overall survival between women with no lymph node metastases and women with 1 intracapsular metastasis ($P < 0.0001$), 1 extracapsular metastasis ($P = 0.0006$) and with 3 node metastases ($P < 0.0001$), there were no significant differences in survival between women with 1 intracapsular, 1 extracapsular, or 2 nodal metastases. Additionally, lymphovascular space invasion (LVSI) was a negative predictor of recurrence-free survival while adjuvant radiation was a positive predictor of recurrence-free survival (HR 0.10, CI: 0.01 to 0.90, $P = 0.04$ and HR 5.87, CI: 1.21 to 28.5, $P = 0.02$, respectively). These results suggest that adjuvant radiation would be beneficial regardless of the number of positive nodes, particularly if negative risk factors such as LVSI are present.[38]

Thus, adjuvant radiation should be recommended in patients with > 2 positive nodes and in those with extracapsular extension, and could be considered in patients with 1 positive

Adjuvant Radiation in Early Stage Vulvar Cancer: Highlights

- Early stage vulvar cancer is managed with wide local excision and nodal assessment followed by risk-adapted adjuvant radiation.
- Indications for adjuvant radiation are based on factors shown to increase risk of local recurrence.
- Close (< 8 mm) or positive margins (tumor on the edge of the surgical specimen) are an indication for adjuvant radiation.
- Two or more positive lymph nodes, extracapsular extension, or gross residual nodal disease are also indications for adjuvant radiation.
- The role of adjuvant radiation for a single positive node remains controversial.
- Dose escalation to > 56 Gy has been shown to reduce local recurrence compared with 45 to 50 Gy in patients with close or positive margins.
- Prospective trials are needed to validate the use of adjuvant radiation and to clarify the role of systemic therapy in patients with early stage vulvar cancer.

node in the presence of additional negative risk factors such as LVSI.

Optimal Dose for Adjuvant Radiation

With regard to radiation technique and volumes for postoperative vulvar cancer, intensity-modulated radiation therapy has become a standard option for vulvar cancer and consensus recommendations have been developed. Specifically, for a vulvar primary with negative margins, the CTV should encompass the entire operative bed, while if a case has positive margins, the CTV should have a margin of approximately 2 cm. Furthermore, the lymph node volumes for lesions involving the vulva or distal vagina include bilateral inguinofemoral, bilateral obturator, bilateral internal, and external iliac groups, with perirectal and presacral nodes added for anal involvement.[39] While adjuvant radiation has been shown to decrease the risk of local recurrence in vulvar cancer, relatively few studies have been conducted to ascertain the optimal dose of adjuvant radiation. The randomized study by Homesley et al established the dose of 45 to 50 Gy as standard dose for adjuvant pelvic and inguinal nodal irradiation.[30] More recent studies explored the benefit of dose escalation particularly in the presence of close or positive margins. The aforementioned study by Viswanathan et al not only found that margins ≤ 5 mm were significantly associated with an increased risk of local recurrence but also examined the relationship between radiation dose and recurrence. A total of 61 patients received adjuvant radiation of which 25% had negative margins, 66% had close margins, and 10% had positive margins.[22] The median vulvar radiation dose was 50.4 Gy, 47.4 Gy, and 47.6 Gy for those with negative, close, and positive margins, respectively. The vaginal recurrence rates were 21% and 34% for patients who received ≥ 56 Gy and ≤ 50.4 Gy, respectively. There were significantly more recurrences in patients who received < 56 Gy compared with those who received ≥ 56 Gy ($P = 0.046$).[22]

A study published in 2017 examined 3,075 patients with vulvar squamous cell carcinoma with positive margins of which 35.3% received adjuvant radiation to a median cumulative dose of 54.0 Gy. Patients were stratified by the following radiation dose categories: 30.0 to 45.0 Gy, 45.1 to 53.9 Gy, 54.0 to 59.9 Gy, and ≥ 60 Gy. The unadjusted 3-year overall survival in these groups was 54.3%, 55.7%, 70.1%, and 65.3%, respectively, ($P < 0.001$). On multivariate analysis, patients receiving 54 Gy to 59.9 Gy and ≥ 60 Gy had the greatest mortality reduction compared with patients receiving < 54 Gy (HR 0.75, $P = 0.024$ and HR 0.71, $P = 0.015$, respectively). This mortality reduction for patients receiving ≥ 54 Gy persisted for both node-positive and node-negative patients (HR 0.73, $P < 0.001$ and HR 0.79, $P = 0.001$, respectively). However, there was no significant overall survival benefit between patients who received ≥ 60 Gy compared with those who received 54.0 to 59.9 Gy (HR 0.95, $P = .779$).[40]

In summary, while early literature suggested that doses of 45 to 50 Gy were appropriate for adjuvant radiation, recent studies support dose escalation to > 56 Gy in patients with close or positive margins as mentioned in the ACR Appropriateness Criteria.[17]

Conclusion

Early stage vulvar cancer is managed by wide local excision with nodal assessment followed by risk-adapted adjuvant radiation. Despite the lack of large, randomized trials in vulvar cancer, a multitude of retrospective studies has shown benefits of adjuvant radiation therapy, including lower recurrence rates, improved PFS, and improved overall survival. The strongest indications for adjuvant radiation are close or positive margins – often defined in the literature as margins < 8 mm and tumor on the edge of the surgical specimen, respectively – and positive nodes due to the increased risk of local recurrence with the presence of these factors. Thus, patients with vulvar cancer with positive or close margins should undergo adjuvant radiation therapy unless concerns for excessive morbidity would outweigh potential benefit of decreasing local recurrence and improving PFS. Additionally, patients with 2 or more positive nodes or ≥ 1 node with extracapsular extension should undergo adjuvant radiation therapy, with radiation for patients with 1 intracapsular positive node reserved for those with additional risk factors such as LVSI. Future trials are needed to investigate the role of adjuvant radiation therapy in patients with a single positive node. Moreover, while optimal dose of adjuvant radiation is still being defined, dose escalation to > 56 Gy has shown a benefit in the presence of close or positive margins and should be utilized in cases where adjuvant radiation is indicated. Although adjuvant radiation has shown benefit in patients with close or positive margins and in node-positive disease, prognosis still remains relatively poor. Intensification of adjuvant therapy with the addition of chemotherapy to radiation may be a potential strategy to improve outcomes analogous to anal or cervical cancers. Prospective trials are needed to further inform the use of appropriate adjuvant therapy in patients with early stage vulvar cancer.

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