

VULVAR SQUAMOUS INTRAEPITHELIAL LESIONS (SIL)

Dr Somayeh Nikfar, Gynecolgy Oncology fellowship student, TUMS

VULVAR SIL

- Previously referred as vulvar intraepithelial neoplasia (VIN)
- A group of premalignant conditions of vulva
- There are no routine screening methods for vulvar SIL or vulvar carcinoma

CLASSIFICATION

• Low-grade squamous intraepithelial lesion (LSIL) of vulva

- Vulvar LSIL, flat condyloma, or HPV effect
- Previously \rightarrow VIN 1
- High-grade squamous intraepithelial lesion (HSIL) of vulva
 - vulvar HSIL, VIN usual type [uVIN]
 - Previously \rightarrow VIN 2 and VIN 3.

• Differentiated VIN (dVIN)

- Includes lesions that are not associated with HPV but are associated with vulvar dermatoses, mainly lichen sclerosus
- Previously \rightarrow VIN simplex

1986 ISSVD	2004 ISSVD	2012 LAST	2015 ISSVD
VIN 1 (mild dysplasia)*	Condyloma (HPV effect)*	LSIL*	LSIL of the vulva (vulvar LSIL, flat condyloma, or HPV effect)*
VIN 2 (moderate dysplasia)* VIN 3 (severe dysplasia)* VIN 3 (carcinoma in situ)*	 VIN, usual type:* VIN, warty type VIN, basaloid type VIN, mixed (warty or basaloid type) 	HSIL*	HSIL (vulvar HSIL, VIN usual type)*
Differentiated VIN [¶]	VIN differentiated [¶]	N/A (no alternative terminology for dVIN) ¶	Differentiated VIN [¶]

EPIDEMIOLOGY

- Prevalence of vulvar SIL is higher in premenopausal than in postmenopausal women
- Average age at diagnosis is 46 yr
- Women younger than 50 yr account for 75 percent of cases
- Vulvar LSIL is a benign lesion and is not considered a premalignant lesion
- dVIN and HSIL are neoplastic (premalignant) changes
- HSIL occurs much more frequently than dVIN
- dVIN is more likely to progress to invasive carcinoma

RISK FACTORS AND PREVENTION

- Human papillomavirus (HPV)
 - The majority of cases of vulvar SIL are associated with HPV infection.
 - Risk factors \rightarrow genital, anal, or oral contact to vulva
 - Low-grade SIL is most often associated with low-risk HPV subtypes
 - HSIL is most often associated with high-risk HPV subtypes
 - HPV-associated squamous neoplasia at other lower genital tract sites
 - ~60% of patients with vaginal intraepithelial neoplasia 3 or VIN have preexisting or synchronous CIN
 - HPV vaccines decrease risk of vulvar SIL

RISK FACTORS AND PREVENTION

Cigarette smoking

- Associated with development of vulvar SIL and recurrence
- Patients should be encouraged to stop using tobacco to reduce the risk of vulvar SIL.

Immunodeficiency

• Vulvar SILs are more common in patients infected with HIV than in uninfected controls

RISK FACTORS AND PREVENTION

- Premenopausal patients are more likely to have HPV-associated vulvar HSIL
- Postmenopausal patients are more likely to have non-HPV associated vulvar SIL.
- Major risk factor for dVIN →associated vulvar dermatosis (eg. lichen sclerosus)
 - Earlier detection and proactive management of lichen sclerosus may lead to a reduction in risk of development of squamous cell carcinoma

PATHOGENESIS

- Anogenital epithelium is derived from embryonic cloaca and includes cervix, vagina, vulva, anus, and lower 3 cm rectal mucosa up to the dentate line
- →susceptible to similar exogenous agents (eg, HPV infection),
- $\cdot \rightarrow$ SILs in this area are often both **multifocal** and **multicentric**
- → patients with vulvar SIL may have synchronous or metachronous squamous neoplasia of other lower genital tract sites

PATHOGENESIS

- dVIN
 - usually unifocal and unicentric
 - often associated with lichen sclerosus but not with HPV infection
 - found adjacent to 80% of vulvar squamous cell carcinomas
 - Diagnosis of solitary dVIN is very challenging and appears to be associated with more rapid progression to SCC
- Patients with lichen sclerosus with dyskeratosis and parakeratosis, hyperplasia, and/or basal cellular atypia tend to have the highest risk of progression to SCC
- There are no known biomarkers

NATURAL HISTORY

- If left untreated, vulvar SIL may persist, progress, or resolve
- Vulvar low-grade SILs
 - Benign manifestations to a HPV
 - Often self-limited and usually resolve within one to two years
 - Should not be considered as potentially neoplastic, except in rare cases
- Vulvar high-grade SILs
 - Estimated to be associated with ~20% of SCC of vulva
- Differentiated VIN
 - Has the highest risk of progression to SCC (estimated at 33%)
 - Putative precursor lesion of ~80% of keratinizing vulvar SCC

CLINICAL PRESENTATION

- Vulvar SIL can be asymptomatic
- Vulvar pruritus
 - Most common complaint among symptomatic patients
 - vulvar pain, burning
 - **Dysuria** may occur if there is a periurethral lesion or if urine comes into contact with a lesion at another site

Vulvar lesion

- Detected during a routine gynecologic examination, or at colposcopy for abnormal cervical cytology
- A visible lesion or a palpable abnormality may be noted.
- Persistent abnormal cervical cytology with no abnormality identified on cervical biopsy
 - Vulvar SIL can initially present with an abnormal cervical cytology result, which is actually representative of disease in other nearby genital tract sites

• History

- Should include questions about symptoms and risk factors associated with vulvar SIL
- Should be asked about a prior history of vulvar SIL, genital warts, or vulvar cancer, and about other HPV associated lower genital tract neoplasia
- Should include questions about smoking, conditions associated with immunosuppression, and HPV vaccination status.

Physical examination

- A gynecologic examination should be performed, with thorough inspection and palpation of vulva and groin for lesions, color changes, masses, or ulceration.
- Most vulvar SILs are multifocal and are located in nonhairy part of vulva
- raised orThe lesions are often verrucous and white ,
- the color may be red
- pink, gray, or brown
- Macular lesions mostly occur on adjacent mucosal surfaces.
- There is no pathognomonic clinical appearance

WHITE PLAQUES OF VULVAR HSIL

• Raised whitish plaques as a manifestation of HSIL of the vulva.

RED MACULAR HSIL OF THE VULVA

• Red macular lesion as a manifestation of HSIL of the vulva

BROWN MACULAR HSIL OF THE VULVA

• HSIL manifesting as a brown macular lesion of the vulva.

- Condylomata acuminata (genital warts)
 - May be difficult to differentiate on examination from vulvar lowgrade SIL, high-grade SIL, dVIN, and invasive vulvar squamous carcinoma
 - Can present as a plaque, ulcer, or mass (fleshy, nodular, or warty), and both may coexist in a patient
- Vulvar lesions may mimic VIN
 - Lichen sclerosus or lichen planus
 - Condyloma latum

- **Colposcopy** Perform colposcopy in patients with any of following characteristics:
 - Visible vulvar lesion
 - Visible lesion should be biopsied, but because of high prevalence of multicentric synchronous intraepithelial lesions, colposcopic evaluation of entire lower genital tract and perianal area may detect additional lesions
 - Persistent symptoms consistent with vulvar SIL but no visible lesions
 - Persistent abnormal cervical cytology with no CIN on biopsy
- Colposcopy of the vulva can identify subclinical lesions not appreciated on gross visual examination and helps to define extent of disease and guide biopsy
- If colposcopy is not available, a hand lens provides similar magnification and is easy to use

- Biopsy
 - Any vulvar lesion found on exam and/or colposcopy that is not known to be benign/non-neoplastic warrants a biopsy
 - A vulva with multiple areas of abnormalities warrants multiple biopsies
 - If a lesion is treated w/o biopsy and does not completely resolve or is refractory to a defined course of empiric therapy, it should be biopsied to obtain a definitive diagnosis.
 - Infrequently, a biopsy is appropriate in absence of a visible lesion
 - If no lesion is found at colposcopy and symptoms cannot be explained by another diagnosis, a biopsy from symptomatic area of vulva should be performed

- Diagnosis of vulvar SIL is based on histologic findings observed in a biopsy specimen
- Appropriate sites for biopsy are identified by physical examination and colposcopy
- Characteristics of the three histopathologic entities are described below (table 2)

listologic characteristics and terminology of vulvar squamous intrapeithelial lesions

Low grade squamous intraepithelial lesion (LSIL) of the vulva (vulvar LSIL, flat condyloma or human papillomavirus [HPV] effect)

Cytologic atypia is most often represented by koilocytosis or basal cell hyperplasia and increased mitotic activity, with squamous maturation occurring in the upper two-thirds of the epithelium.

High grade squamous intraepithelial lesion (HSIL) of the vulva (vulvar HSIL, VIN usual type [uVIN])

Loss of maturation includes the middle (formerly VIN 2) and upper third to full thickness (formerly VIN 3) of the squamous epithelium. Cytologic changes may be significant with bizarre mitotic figures and significant pleomorphism. Stromal invasion is not present.

Vulvar intraepithelial neoplasia differentiated type (dVIN)

Differentiated VIN lesions affect the parabasal layer and exhibit keratin formation. The epithelium is generally thickened and parakeratotic with elongated and anastomosing rete ridges. The abnormal cells have prominent eosinophilic cytoplasm and are confined to the parabasal and basal portion of the rete pegs with little or no atypia above.

Vulvar low-grade SIL (LSIL)

 Characterized by cytologic atypia, most prominent in upper keratinocytes, increased mitotic activity in basal or parabasal epithelium, and squamous maturation in upper two-thirds of epithelium.

• Vulvar high-grade SIL (HSIL)

- characterized by loss of maturation of middle (formerly VIN 2) and upper third to full thickness (formerly VIN 3) of squamous epithelium.
- HSILs can be subdivided based on their morphologic and histologic features .
- Mixtures of warty and basaloid HSIL are common and are classified together as vulvar HSIL

HSIL

VULVAR SQUAMOUS INTRAEPITHELIAL LESION HISTOLOGY

- Vulvar HSIL
 - **Basaloid subtype:** thickened epithelium with a relatively flat, smooth surface.
 - Consists of atypical, immature parabasal-type cells with numerous mitotic figures and enlarged hyperchromatic nuclei.
 - Warty (condylomatous) subtype: a surface that is undulating or spiking, giving it a condylomatous appearance
 - Histologically, it consists of marked cellular proliferation with numerous mitotic figures and abnormal maturation, but it may have some maturation (not all basaloid cells).

Vulvar HSIL

- Often multifocal.
- Interlabial grooves, posterior fourchette, and perineum are most frequently affected by multifocal lesions
- More extensive disease is often confluent, involving the labia majora, minora, and perianal skin
- Confluent or multifocal lesions exist in up to two-thirds of patients with HSIL

Differentiated VIN

- dVIN is commonly found adjacent to keratinizing SCC or in patients with a history of vulvar cancer
- The differentiated (simplex) type refers to lesions in which epithelium is thickened and parakeratotic with elongated and anastomosing rete ridges
- The abnormal cells are confined to parabasal and basal portion of rete pegs with little or no atypia above basal or parabasal layers
- The basal cells may stain positively for p53, and p53-positive cells extend above basal layers into upper layers of epidermis.
- dVIN is putative precursor of human papillomavirus-negative vulvar cancer
- Distinguishing dVIN from reactive squamous proliferations can be quite difficult.

DIFFERENTIAL DIAGNOSIS

- Vulvar SILs are typically multifocal, and vary in appearance
- Vulvar cancer, condyloma acuminatum, lichen sclerosus, lichen planus, or condyloma latum
- Can be differentiated with vulvar biopsy
- Vulvar lesions associated with vulvar pruritus and pain
 - Candidiasis, dermatitis, molluscum contagiosum, lichen sclerosus, lichen planus, lichen simplex chronicus, psoriasis, and herpes simplex virus

• Low-grade squamous intraepithelial lesions

- LSIL are equivalent to condylomata acuminata (anogenital warts)
- Are not precancerous lesions,
- Should not be considered as potentially neoplastic lesions, and
- Do not need to be treated unless symptomatic.

High-grade squamous intraepithelial lesions

- Goals for treatment HSIL→ Prevent development of vulvar squamous carcinoma and to relieve symptoms while preserving normal vulvar anatomy and function
- Management options: excision, ablative therapy, and topical treatment.
- Approach depends on level of concern for invasive disease based on examination and biopsy results, prior treatment history, and the location and focality of the lesion(s)

- High-grade squamous intraepithelial lesions
- Excision is generally indicated for those patients with vulvar HSIL who have the following:
 - Possible invasive lesion (eg, raised, ulcerative, or with irregular borders), irrespective of results from colposcopy/biopsy.
 - Setting of clinically significant risk factors for invasive disease (eg, previous vulvar HSIL, differentiated VIN [dVIN], or vulvar carcinoma; immunosuppression; or lichen sclerosus)

- High-grade squamous intraepithelial lesions
- For patients lacking any of features listed above, approach at initial presentation is the following:
 - Single lesions \rightarrow excision
 - Any of the following characteristics → ablative therapy with CO₂ laser or argon beam coagulator rather than excision:
 - Multifocal disease.
 - Lesions that involve clitoris, urethra, anus, or vaginal introitus (as excision may impair function or cause dyspareunia).
- Topical therapy with imiquimod can be used for carefully selected patients (eg, patients with clitoral lesions) who prefer to avoid excision and ablation, provided that they are able to comply with a long treatment course (typically 16 weeks)

- High-grade squamous intraepithelial lesions
- For patients with recurrent lesions w/o evidence of invasion: ablative or topical therapy to avoid multiple excisional procedures
 - Especially relevant in patients with risk factors for recurrent disease (eg, heavy smokers, immunocompromised patients).
 - The choice between ablative and topical therapy (or combined modality treatment) is based on many patient-specific factors, including prior treatment history, location and focality of lesion(s), and coexisting vulvar dermatoses.
 - Careful colposcopic examination with biopsies to exclude invasive disease is mandatory prior to beginning treatment

PREFERRED INITIAL OPTIONS
EXCISION

- Provides both treatment and a diagnostic specimen
- Wide local excision is the preferred excisional procedure
- Simple or skinning vulvectomy
 - Rarely indicated
 - Reserved for lesions that are extensive or multifocal and highly symptomatic, particularly when prior treatments (eg, topical treatments, laser ablation, smaller excisions) have failed

WIDE LOCAL EXCISION

- Excision of an individual lesion with a 1 cm margin, generally provides satisfactory cosmetic results
- A 1 cm margin is often hard to accomplish as the surgeon has to balance the desire for complete excision with preservation of vulvar anatomy and function.
- In terms of depth of excision, removal of epidermis provides sufficient depth for treatment of HSIL
 - Removing a small amount of underlying dermis helps to ensure the absence of early invasive disease.
- Positive epithelial margins are common and a risk factor for recurrent disease
- If there is a grossly visible residual lesion, it should be treated.

WIDE LOCAL EXCISION

- If there is a grossly visible residual lesion, it should be treated.
- If a margin is positive microscopically, but there is no visible residual disease, the patient may be followed by close clinical observation and colposcopy
- Retreatment is provided if another visible lesion occurs.
- Because HSILs are often multifocal in nature, a negative margin will only reduce the recurrence risk at that site, not the lifelong risk of recurrence of HSIL elsewhere on the vulva

EXCISION

- Simple, or total, vulvectomy
 - Simple, or total,
 - Removal of entire vulva together with perineal tissues, as indicated, and usually includes some subcutaneous tissue

Skinning vulvectomy

- Removing vulvar skin along a relatively avascular plane beneath epidermis while preserving subcutaneous tissue
- Primary closure can be achieved by either reapproximation or by using a split thickness skin graft

ABLATIVE THERAPY

- For vulvar HSIL in whom there is no concern for invasive disease and who have multifocal disease or have lesions involving the clitoris, urethra, anus, and/or vaginal introitus,
 - Best option to preserve anatomy
- Major limitations of laser ablation
 - Special training is required and this equipment may not be readily available at all institutions
 - Coexistence of invasive cancer must be carefully excluded by liberal use of colposcopically directed biopsies prior to the procedure.

ABLATIVE THERAPY

- CO₂ laser vaporization is the most commonly used ablative therapy
- Argon beam ablation and ultrasonic surgical aspiration can also be used
- It is most advantageous when there are multiple small lesions
- Goal of ablative therapy is to treat entire area of intraepithelial abnormality.
- Colposcopy is used to control depth of tissue destruction to less than 1 mm (for hair-free epithelium), which will ablate the intraepithelial lesion and allow for rapid healing

ABLATIVE THERAPY

- Ablation to 3 mm of depth is required in hairy areas of vulva because the hair root sheet tends to extend as deep as 2.5 mm and is at significant risk for harboring HSIL
- Superficial ablative therapy may offer cosmetic advantages over excisional procedures
 - deep laser vaporization results in destruction of the skin appendage, which leads to hypertrophic scar formation
 - Another method may be preferred for lesions in hair-bearing areas because laser treatment destroys the hair follicle

ALTERNATIVES AND LATER-LINE TREATMENTS

TOPICAL THERAPIES

- Imiquimod
 - Preferred initial treatment for recurrent vulvar HSIL
 - Can also be used as initial therapy for carefully selected patients who prefer to avoid excision and ablation, provided that they are able to comply with a long treatment course (typically 16 wks)
 - Applied topically to individual lesions, not to entire vulva.
 - A typical course involves applying a thin layer of cream 3 to 5 times per wk (alternating days) for a total duration of 16 wks.

TOPICAL THERAPIES

- Imiquimod
 - Side effects are common and consist mostly of inflammation at application site, including mild to moderate erythema or erosions.
 - Up to two-thirds of patients reduce the number of applications due to local side effects→ some experts suggest an escalating dose regimen starting with an application once a wk for two wks, then twice a wk for two wks, then, if tolerated well, three times a wk

TOPICAL THERAPIES

Fluorouracil

- Rarely and as a last resort when other therapies have failed.
- Causes a chemical desquamation of HSIL
- Response rates as high as 75 %
- Disadvantage → poorly tolerated because of significant burning, pain, inflammation, edema, or painful ulcerations (topical fluorouracil has a limited role in primary therapy of HSIL).

COMBINED MODALITY THERAPY

- Data are limited
- Reserve this option for a very select group of patients whose disease distribution requires multimodality therapy to allow for organ preservation and to avoid significant disruption of normal vulvar anatomy

INVESTIGATIONAL THERAPIES

• Topical cidofovir,

- Potent antiviral agent
- Similar efficacy to imiquimod in clearing vulvar HSIL
- Use of vaccines designed to elicit a cellular immune response (commercially available vaccines elicit only a humoral response), indole-3carbinol, sinecatechins, photodynamic therapy, and use of chemopreventive agents, such as retinyl acetate gel

DIFFERENTIATED VIN

- We recommend **surgical excision** rather than ablation or pharmacologic therapy since dVIN is associated with a high risk of developing invasive carcinoma.
- Decision making regarding the type of excision follows the same decision-making process as for HSIL

POSTTREATMENT SURVEILLANCE

- After treatment has been completed, long-term surveillance of the entire genital tract is mandatory, given the possibility of late recurrences
- Follow-up with a gynecologic examination (including visual inspection of the vulva) **every six months** for five years and then annually.
- Further evaluation with colposcopy and biopsies is warranted if patient exhibits symptoms and/or examination findings concerning for additional disease

DISEASE RECURRENCE

- With prolonged follow-up, approximately one-third of patients develop recurrent vulvar SIL regardless of treatment modality employed
- Risk factors for recurrent disease include:
 - Immunosuppression
 - Presence of multifocal or multicentric disease
 - Large lesion size (eg, 3 cm [range 1 to 7 cm])
 - Age >50 years
 - Positive margins on excisional specimen (risk of recurrent vulvar SIL is ~threefold higher among patients with positive margins on excisional specimen
 - Cigarette smoking
 - Some studies report higher rates of recurrence associated with laser ablation than with excision

DISEASE RECURRENCE

• The risk of synchronous or subsequent vulvar carcinoma also differs by histologic type:

• Vulvar high-grade SIL (HSIL)

 Risk of subsequent locally invasive squamous carcinoma following initial treatment of VIN 3 has been reported to be 2 to 15

Differentiated VIN (dVIN)

- Risk of invasive carcinoma is not well established however, appears to be quite high
- Low-grade SILs are benign lesions and, therefore, do not contribute to the development of vulvar carcinoma, except in rare cases

SPECIAL CONSIDERATIONS

RISK OF OCCULT CARCINOMA

At initial diagnosis

 Retrospective case series have reported the presence of occult squamous carcinoma in 10 to 22 percent of patients with a preoperative diagnosis of VIN who were treated with surgical excision

At the time of recurrence

• In the systematic review of data from 3322 patients treated for VIN, occult carcinoma was found in 3.3 percent of patients who were diagnosed with disease recurrence during follow-up

MANAGEMENT OF VULVAR SIL IN PREGNANCY

- Data are extremely limited.
- ~15 % of vulvar carcinomas have been reported to occur under age of 40
- → any vulvar lesion noted during pregnancy should be biopsied as outlined above for the nonpregnant patient
- Management options for the pregnant patient with vulvar SIL fall principally into two main categories:

Surgical therapy

- local excision or ablative therapy should follow the same general principles as for nonpregnant patient
- These are the preferred treatment options for HSIL in pregnancy, especially for the patient remote from delivery.

MANAGEMENT OF VULVAR SIL IN PREGNANCY

• Expectant management until after delivery

- If invasive carcinoma has been ruled out histologically, clinicians may consider deferring treatment of HSIL to postpartum period, especially in patients who are diagnosed in third trimester.
- Small series suggest a possibility for spontaneous regression, particularly in asymptomatic patients who are younger than 30 years of age and who present with multifocal pigmented HSIL

• Medical therapy is generally not recommended

- Imiquimod is classified as a category C drug
 - Its safety during pregnancy has not been clearly established nor are there efficacy data on the use of imiquimod for the treatment of HSIL in pregnancy.

MANAGEMENT OF VULVAR SIL IN HIV-INFECTED PATIENTS

- Individuals infected with HIV are at greater risk of HPV related cancers.
- Vulvar SIL occurs commonly among patients infected with HIV

- Vulvar low-grade squamous intraepithelial lesion (LSIL)
- Vulvar high-grade squamous intraepithelial lesion (HSIL)
- Differentiated vulvar intraepithelial neoplasia (dVIN)
- Vulvar LSIL is a benign lesion and is not considered a premalignant lesion
- HSIL and dVIN are premalignant conditions

- Risk factors for vulvar HSIL include HPV, cigarette smoking, and immunosuppression.
- The major risk factor for dVIN is having an associated vulvar dermatosis, such as lichen sclerosus.
- Vulvar SILs are usually multifocal and multicentric
 - →having diseases in more than one location (vulva, vagina, cervix, or perianal area) is relatively common.
 - By contrast, dVIN is usually unifocal and unicentric

- Vulvar SIL can be asymptomatic and diagnosed when a visible lesion or palpable abnormality is incidentally found on pelvic examination.
- Among symptomatic patients, pruritus is the most common complaint.
- Other presentations include pain or dysuria
- Vulvar SIL can be difficult to distinguish clinically from lichen sclerosus or lichen planus, especially when they occur concurrently.
- Any lesion on vulva that is not known to be benign warrants biopsy, as does any lesion that does not resolve with a defined course of medical therapy.
- Appropriate sites for biopsy are identified by physical examination and colposcopy. Tissue biopsy is necessary for a definitive diagnosis.

- The goals of treatment are
 - to prevent development of invasive vulvar carcinoma and
 - relieve symptoms while preserving normal vulvar anatomy and function
- Treatment is individualized based on examination and biopsy results, prior treatment history, and the location and focality of the lesion(s).
- Vulvar **LSILs** are not precancerous lesions and do not need to be treated unless symptomatic.

- For vulvar **HSIL**, our approach is as follows (algorithm 1):
 - Lesions that have high-risk features (raised, ulcerative, or with irregular borders), or for patients with HSIL and significant risk factors for invasive disease (eg, previous vulvar HSIL, dVIN, or vulvar carcinoma; immunosuppression; or lichen sclerosus), we suggest initial treatment with surgical excision rather than ablation or medical therapy (Grade 2C)

- For vulvar **HSIL**, our approach is as follows (algorithm 1):
 - Patients with multifocal disease and/or lesions that involve urethra, anus, clitoris, and/or vaginal introitus, we suggest initial treatment with ablation rather than excision (Grade 2C).
 - Topical treatments may be an appropriate alternative in select patients. However, excision in these areas carries risk for impairment of anatomy or function and is not an appropriate option.

- For vulvar **HSIL**, our approach is as follows (algorithm 1):
 - Management of patients with recurrent vulvar HSIL needs to be individualized to ensure disease control while maintaining vulvar anatomy and function.
 - For many of these patients, we suggest topical therapy with imiquimod rather than repeat excision if invasive disease is not suspected (Grade 2C).
 - Careful colposcopic examination with biopsies to exclude invasive disease is mandatory prior to beginning treatment.

• For patients with **dVIN**, we suggest surgical excision rather than ablation or pharmacologic therapy given the high risk of developing invasive carcinoma (Grade 2C).

- Despite treatment, ~ one-third of patients develop recurrent vulvar SIL.
- The risk of recurrence with progression to invasive carcinoma is ~8%
- →long-term surveillance of entire lower genital tract is mandatory.
- We suggest follow-up every six months for five years after the last treatment and then annually.









SEBACEOUS CYSTS



INFANTILE HAEMANGIOMA


ANGIOKERATOMA

LYMPHANGIOMA



SYRINGOMA`



MELANOSIS









PIGMENTED VIN

SQUAMOUS CELL CARCINOMA



THANK YOU FOR YOUR ATTENTION