# The 2015 International Society for the Study of Vulvovaginal Disease Terminology of Vulvar Squamous Intraepithelial Lesions

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### Table 1: 2015 ISSVD Terminology of Vulvar Squamous Intraepithelial Lesions

Low grade squamous intraepithelial lesion (Flat condyloma or HPV effect)
High grade squamous intraepithelial lesion (VIN usual type)
Vulvar Intraepithelial neoplasia, differentiated-type

#### **Comments:**

#### A. The rationale for introducing a change in terminology:

Lower Anogenital Squamous Terminology (LAST) was introduced in 2012 by The American Society of Colposcopy and Cervical Pathology and the College of American Pathologists, with the support and participation of many professional organizations, including the International Society for the Study of Vulvovaginal Disease (ISSVD) [1], to unify the nomenclature of HPV-associated squamous lesions of the lower genital tract. It recommends the terms low-grade squamous intraepithelial lesion (LSIL) and high-grade intraepithelial lesion (HSIL) for histopathologic diagnoses of productive HPV infections (which includes external genital warts) and precancers, respectively.

However, in relation to vulvar lesions, the ISSVD raised the following concerns [2]:

- 1. In LAST, that considers only HPV associated lesions, differentiated vulvar intraepithelial neoplasia (VIN) generally a non-HPV associated intraepithelial neoplasia, is not recognized, although differentiated VIN has a higher risk of progression to invasive cancer. Studies have demonstrated there are two types of intraepithelial and invasive neoplasia in the vulva [3]. These observations have led, in the 2004 ISSVD terminology, to the definition of two different types of squamous VIN [4]: "usual VIN" (HPV associated, with approximately 20% of the burden of invasive cancer) and "differentiated VIN" (not HPV associated, with approximately 80% of the burden of invasive cancer) [5,6]
- 2. By including vulvar LSIL, LAST has recreated the potential for over diagnosis and over treatment for benign and at times, self-limiting lesions. The ISSVD 2004 terminology [4] of VIN has explicitly stated that "Low grade SIL" (formerly VIN 1) is not a precancerous lesion in the vulva, but rather the reaction of the skin to HPV infection. Accordingly, vulvar LSIL, as with other HPV infections in any sites of the lower genital tract, should not be considered or treated as potentially neoplastic lesions. However, LAST pathologists argued that LSIL does have a significant role in the vulva [7].

## **B.** the ISSVD terminology discussions:

The ISSVD terminology committee was asked to discuss these issues and propose a solution. Members of the ISSVD 2013-2015 terminology committee included: **Chairman**: Jacob

Bornstein. **Members** (alphabetically): Fabrizio Bogliatto, Tanja Bohl, Deborah Coady, Hope Haefner, Mario Preti, Jason Reutter, Priya Selva-Nayagam, Colleen Stockdale, Marc Van-Beurden

Several proposals were raised and discussed in depth. However, during discussions, we learned that the World Health Organization has adopted the LAST Project's recommendations for cervix, vagina, and vulva but revised them to include the term "Differentiated-type vulvar intraepithelial neoplasia" for these non HPV-associated precancerous lesions [8]. Dr. Teresa M. Darragh, the leader of LAST project recommended, when consulted, that the ISSVD adopt the WHO modification of LAST, for classification of vulvar squamous cell precursors.

WHO classification of tumors of the vulva still uses LSIL. During discussions with Dr. Christopher Crum and Dr. Ed Wilkinson, two of authors of the WHO classification, they recommended that the ISSVD adopt the WHO classification and explain that LSIL is preferable to "condyloma" because it encompasses a range of HPV-associated vulvar lesions.

The terminology committee discussed all options by e-mail correspondence and finally, in a conference call. The decision was to propose a modified WHO classification. The ISSVD Executive Council accepted that proposal. This was presented twice to the members at the 2015 World Congress. All suggestions and corrections were reviewed and discussed, and a final version was accepted by a majority vote at the Business Meeting of the ISSVD in July 28, 2015 (Table 1).

The final version (Table 1) does contain "low grade squamous intraepithelial lesion", which, as discussed above, is controversial. However, the word 'neoplasia' is not used, and in parentheses it is stated that the meaning is that of flat condyloma or HPV effect. This expresses the approach of the ISSVD that LSIL in not pre-cancerous and does not need to be treated, unless symptomatic.

Then HSIL is used, and in parentheses, the previous term is mentioned (usual VIN). 'VIN differentiated' is the third, just as in the previous ISSVD terminologies.

The 2015 terminology is close to the WHO classification that is used by pathologists, and to the LAST that is used by the ASCCP and CAP. It gives a reasonable solution to the two concerns that were raised by ISSVD in regard to LAST.

#### References

- 1. Darragh TM, Colgan TJ, Thomas Cox J, Heller DS, Henry MR, Luff RD, McCalmont T, Nayar R, Palefsky JM, Stoler MH, Wilkinson EJ, Zaino RJ, Wilbur DC; Members of the LAST Project Work Groups. The Lower Anogenital Squamous Terminology Standardization project for HPV associated lesions: background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. Int J Gynecol Pathol. 2013 Jan;32(1):76-115.
- 2. Bogliatto F, Bohl T, Reutter J, Sideri M, Bornstein J. LAST terminology applied to the vulva: the challenge of VIN continues. J Low Genit Tract Dis. 2015;19:e47-8.

- 3. van de Nieuwenhof HP, van der Avoort IAM, de Hullu JA: Review of squamous premalignant vulvar lesions H.P. Critical Reviews in Oncology/Hematology 68 (2008) 131–156.
- 4. Sideri M, Jones RW, Wilkinson EJ, Preti M, Heller DS, Scurry J, Haefner H, Neill S. Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD Vulvar Oncology Subcommittee. J Reprod Med. 2005 Nov;50(11):807-10.
- 5. Del Pino M, Rodriguez-Carunchio L, Ordi J. Pathways of vulvar intraepithelial neoplasia and squamous cell carcinoma. Histopathology. 2013;62:161-75.
- 6. Eva LJ, Ganesan R, Chan KK, Honest H, Luesley DM. Differentiated type vulval intraepithelial neoplasia has a high risk association with vulval squamous cell carcinoma. Int J Gynecol Cancer. 2009;19(4):7414.
- 7. Srodon M, Stoler MH, Baber GB, Kurman RJ. The distribution of low risk and high risk types in vulvar and vaginal intraepithelial neoplasia (VIN and VAIN). Am J Surg Pathol 2006;30:1513-1518.
- 8. Crum CP, Herrington CS, McCluggage WG, Regauer S, Wilkinson EJ. Tumours of the vulva; epithelial tumors. In: Kurman RJ et al. ed. WHO Classification of Tumours of Female Reproductive Organs. 4th Edition. IARC Press, Lyon 2014.