

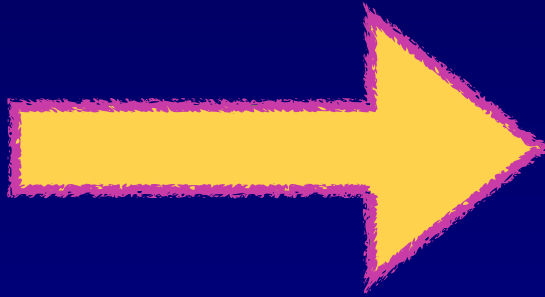
Anogenital warts management algorithm

Sergio Delmonte

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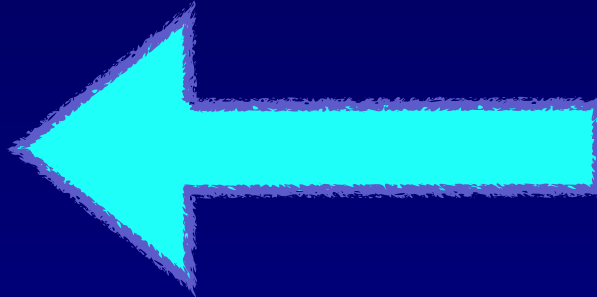
Biologic struggle

Viral replication



- Appearance of many warts
- Rapid dissemination
- Many recurrences
- Long lasting infection

Immune response



- Appearance of few warts
- Slow dissemination
- No or few recurrences
- Short lasting infection

The recurrences

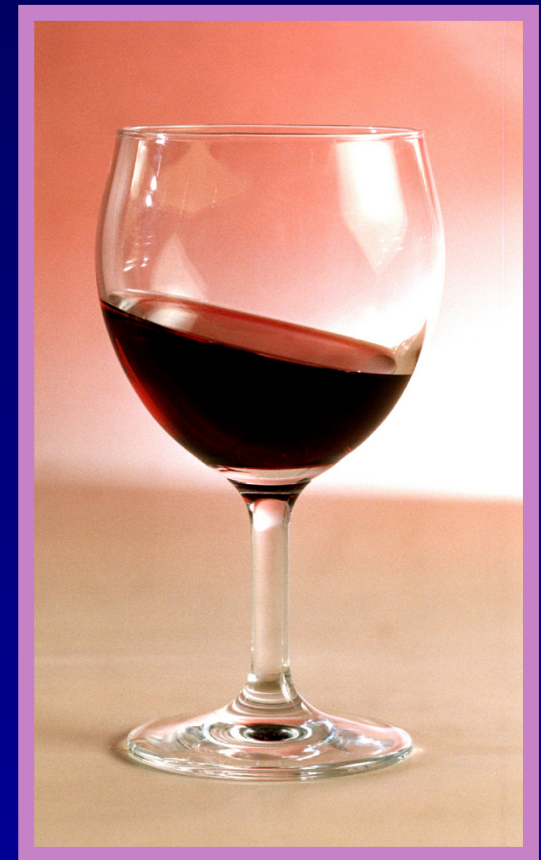
DEFINITION:

“ Appearance of new lesions at previously treated or new sites “

Recurrences appear in 30-50% of patients
Usually in the first 3 months ... and later !

RISK FACTORS

- high number of lesions
- male > female sex
- anal > genital site
- immunosuppressed (think diabetes and HIV !)
- oversize (inguinal moist folds)
- hair removal (any kind)
- after use of topical corticosteroids
- smoking



The impact of the infection

- | | | |
|----|---|-------|
| 1. | Physical discomfort (itching, pain, bleeding) | + |
| 2. | Aesthetic problem | +++ |
| 3. | Fear of transmission. | ++++ |
| 4. | Psychological impact | +++++ |



TREATMENT EFFICACY: clearance and recurrence rates

Table 1: Summary of the results of randomized controlled trials of therapies for anogenital warts among HIV negative patients (modified from Lacey et al ²¹ with permission)

Treatment	Range of clearance rates based on an 'intention to treat analysis'	Range of clearance rates based on a 'per protocol analysis' (determined at time in weeks; range)	Range of recurrence rates (determined at time in weeks; range)
Podophyllotoxin solution 0.5%	45-83%	55-83% (3-6)	13-100% (8-21)
Podophyllotoxin cream 0.15%	43-70%	43-70% (4)	6-55% (8-12)
Imiquimod cream 5%	35-68%	55-81% (16)	6-26% (10-24)
Cryotherapy	44-75%	67-92% (6-10)	21-42% (4-12)
TCA	56-81%	81-84% (8-10)	36% (8)
Electrosurgery	94-100%	94-100% (1-6)	22% (12)
Scissors excision	89-100%	89-100% (6)	19-29% (40-48)

Sinecatechine 15% ung | 47-59%

| 50-58%

| 7-11%

Nitrizinc complex

| 49-92%

| -

| 29% (3rd month)

PROs and CONs

ABLATIVE TREATMENTS

(provider administered)

- Electrosurgery
- CO2 Laser
- Surgical excision

- High clearance rate (100%) in a single procedure
- Longlasting healing of wounds
- Painful wounds
- High recurrence rate (20-50%)

IMMUNOMODULATORS

(patient applied)

- Imiquimod
- Sinecatechins

- Good clearance rate (60%)
- Long treatment > 2 months
- Common appearance of local side effects (burning, itching, erythema)
- Lowest recurrence rate (6-15%)

The goals of Treatment

1. Removal or reduction of visible warts

any treatment

2. Reduction of infectiousness

3. Prevention of recurrences

Immunomodulators

4. Relief of the patient's stress

medical
counselling

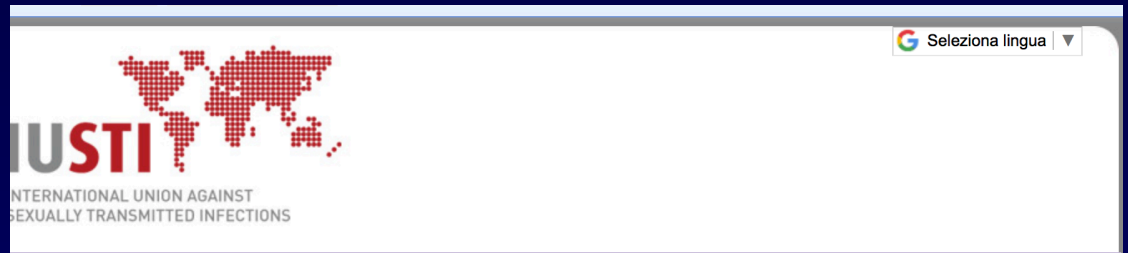
Guidelines

UK National Guidelines on the Management of Anogenital Warts 2015

Centers for Disease Control and Prevention
MMWR
Recommendations and Reports / Vol. 64 / No. 3

Morbidity and Mortality

Sexually Transmitted Diseases Treatment Guidelines



Società Italiana di Dermatologia
(SIDEmaST)

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VERRUCHE

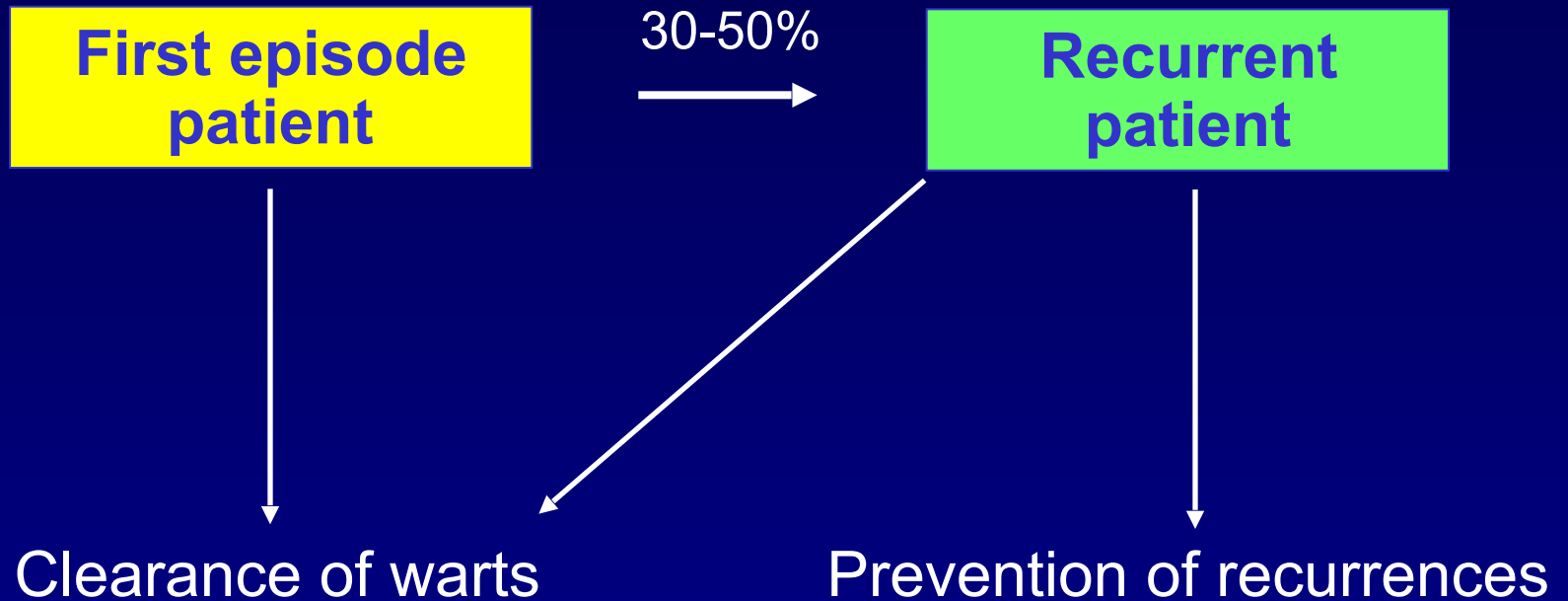
Ano-Genitali e Cutanee

Linee Guida e Raccomandazioni SIDEmaST
2016 - 2017

[Pediculosis Pubis \(2017\)](#) under review, contact [Jonathan Ross](#) with comments

[Scabies \(2016\)](#)

Treatment Strategy



Treatment Strategy

**First episode
patient**



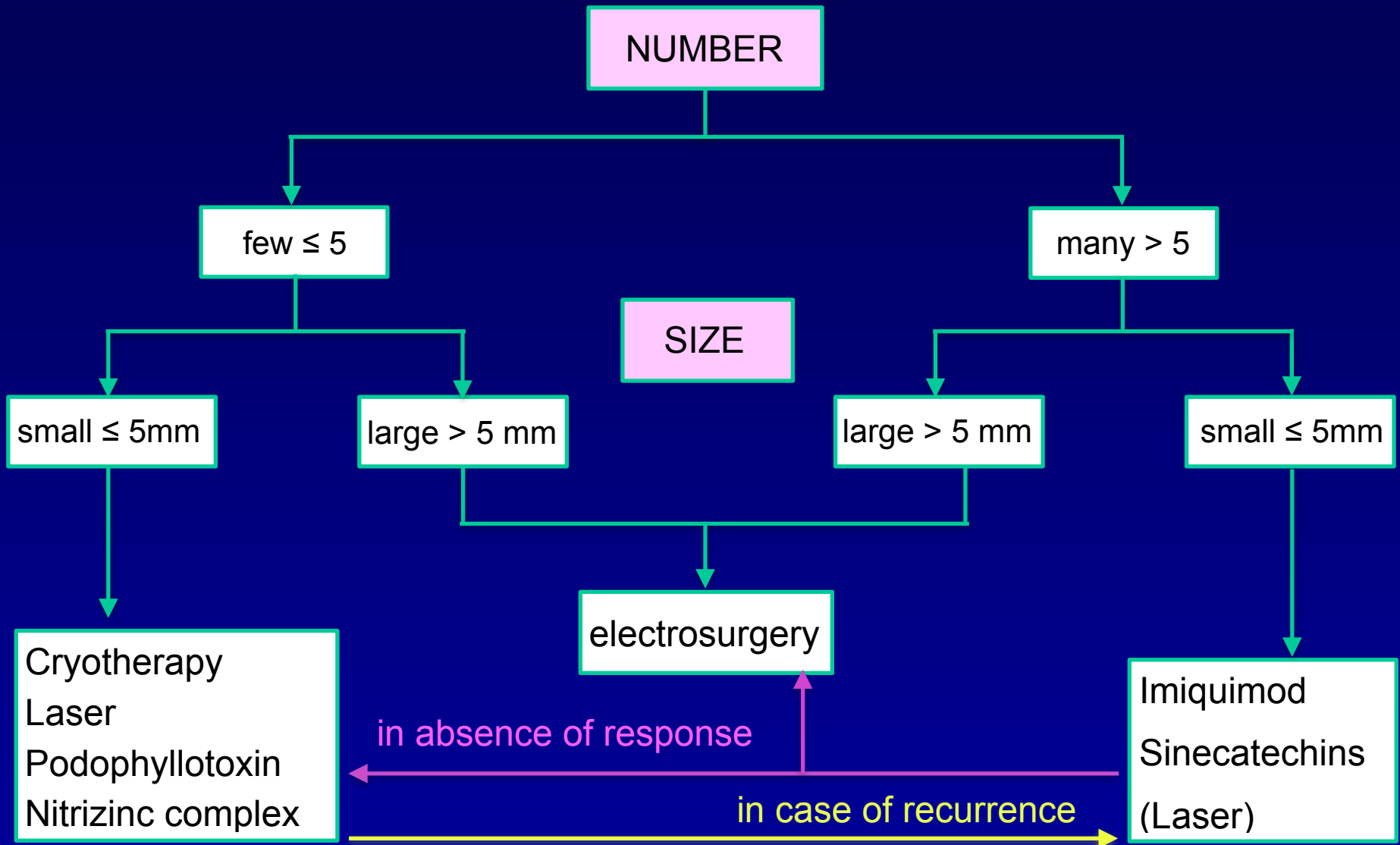
Clearance of warts

- cryotherapy
- Electrosurgery / laser
- TCA
- Podophyllotoxin
- Nitrizinc compl,ex



**Astonished and frightened patient
urging for prompt warts removal**

First episode of warts



Comparison of ablative TTT

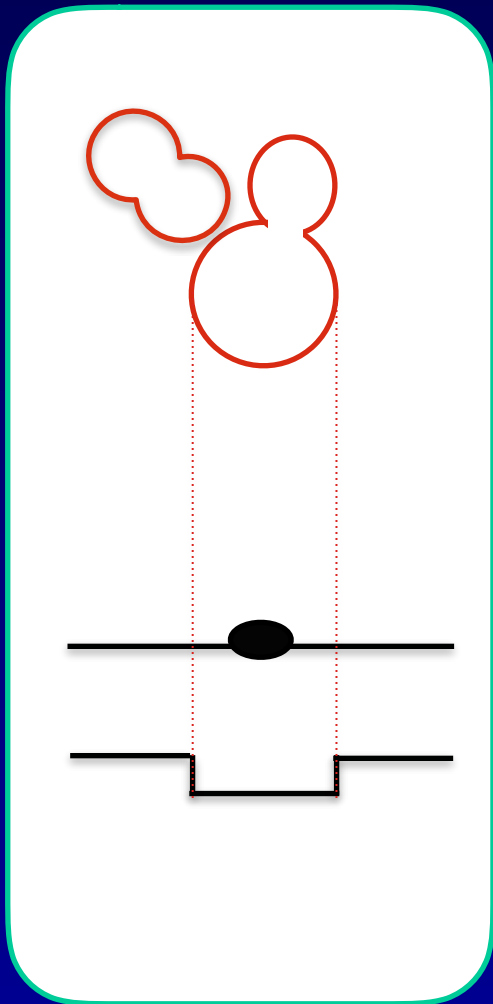
Electrosurgery (ELS)

- The best for large and thick lesions
- Infiltrative local anesthesia is required
- Long and painful healing time
- Possible hyperpigmentation or scars

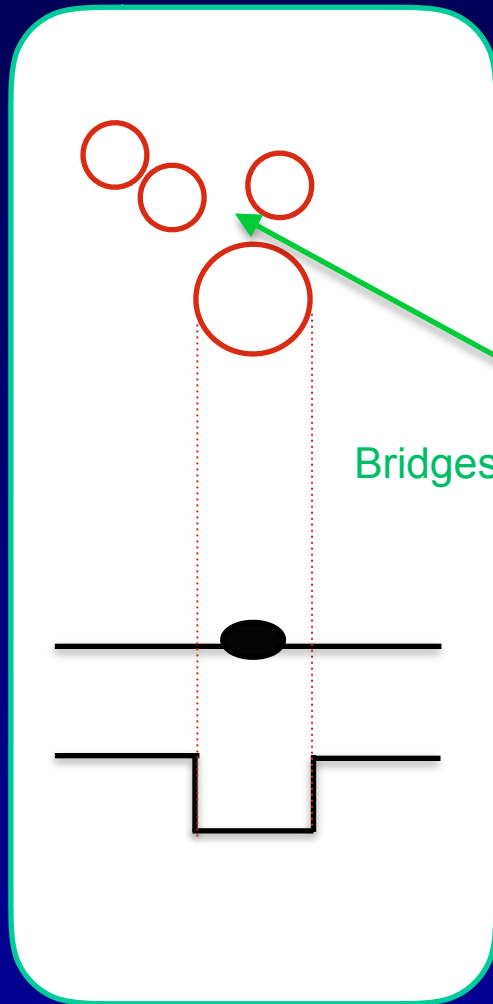
CO2 Laser

- The best for numerous small lesions (healthy skin bridges)
- Topical or infiltrative local anesthesia
- Short and painless healing time
- Time consuming
- Smoke evacuators are required

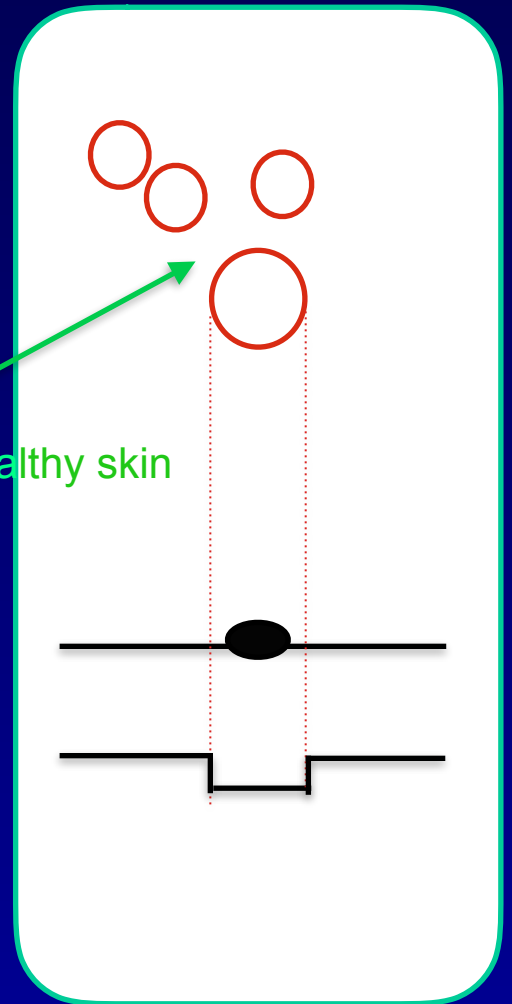
Criotherapy



Electrosurgery



LASER



Bridges of healthy skin

Treatment Strategy



Discouraged
and depressed
patient tired of
ablative treatments

**Recurrent
patient**

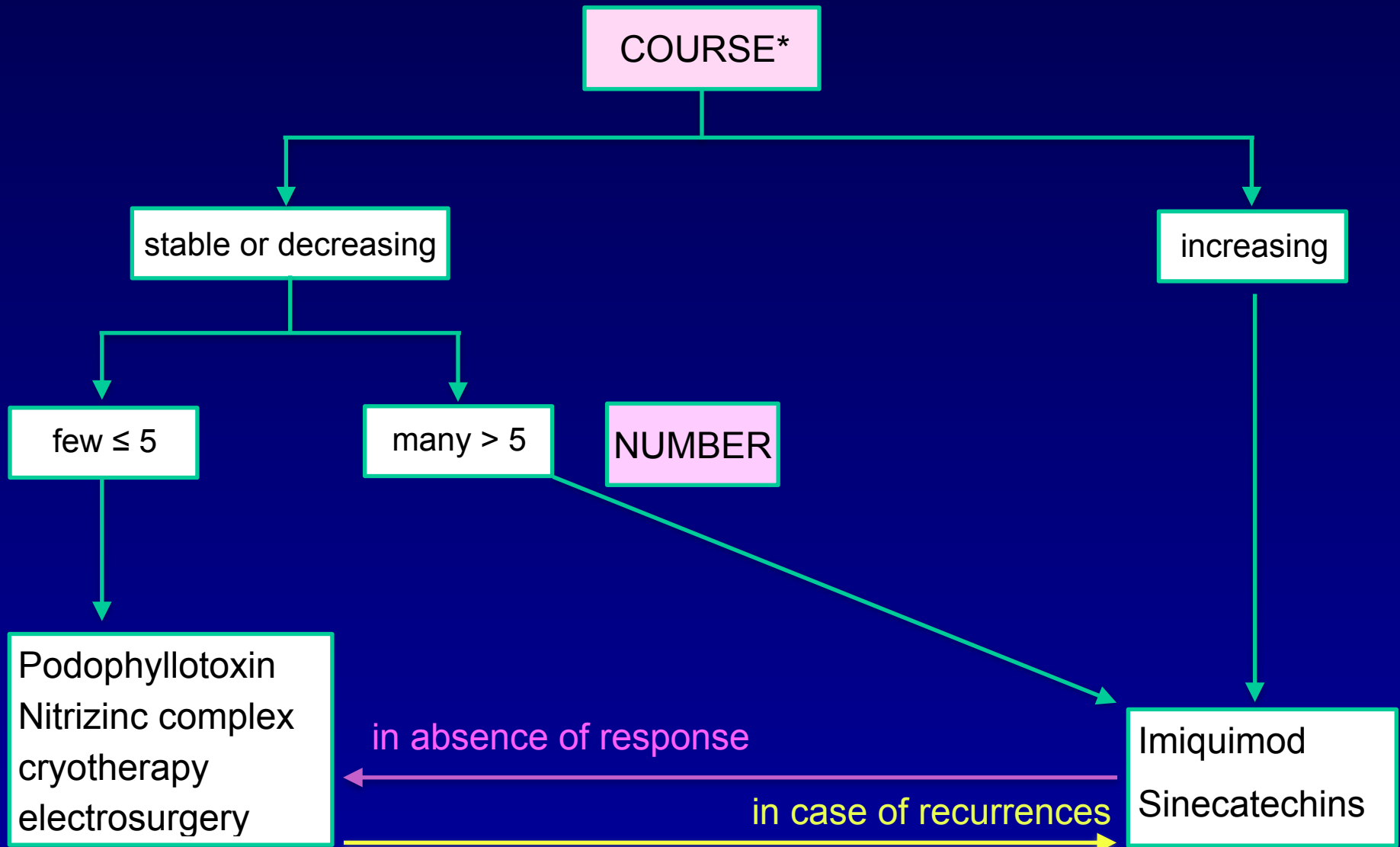
Clearance of warts

- cryotherapy
- Electrosurgery / laser
- TCA
- Podophyllotoxin
- Nitrizinc compl,ex

Prevention of recurrences

- Imiquimod
- Sinecatechins

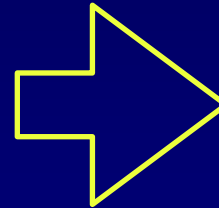
The recurrent patient



Therapeutic switch

When treated lesions are not removed (treatment failure) or recur a change of treatment is advisable:

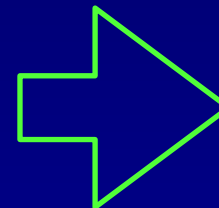
No or partial regression* of the lesions after a complete course of treatment



Change ablative TTT
(i.e. ELS for Cryo)

or switch to ablative TTT
(i.e. ELS for IMQ)

Appearance of recurrences after a complete regression of treated lesions



Switch to
immunomodulators
(i.e. IMQ for cryo)

NB. A change in treatment is indicated even when therapy is not tolerated for severe side effects or poor compliance

Combination therapies

Ablation provides rapid and complete clearance but has high Recurrence rates while immunotherapy shows low clearance rates but lower RR
Different treatments may be used in combination to improve the overall efficacy

1. Imiquimod 5% cr + Surgery (Neo adjuvant IMQ)

1. Ablative LASER + imiquimod 5% cr (adjuvant IMQ)

3. Cryotherapy + Sinecatechins 10% ont (adjuvant SCT)

2. Ablative LASER + Sinecatechins 10% ont (adjuvant SCT)

The rationale is promising but there is still a lack of evidence confirmed by larger clinical trials

Adjuvant IMQ after LASER treatment

1. Effect of adjuvant IMQ 5% cream on sustained clearance of AGW following laser treatment Hoyne UB et al. Infect Dis Obstet Gynecol 2002;10:79-88.

Open-labelled, prospective, multi center study on 211 German patients treated with CO2 laser + IMQ 3 x week for 12 weeks with a 6 months follow-up

Recurrence Rate: 11.8% at the end of follow-up

The RR in LASER + IMQ were lower then in LASER alone, as reported in literature

2. Randomized, comparative trial on the sustained efficacy of IMQ 5% cream versus conventional ablative methods in EGW. Schöfer H et al. Eur J Dermatol 2006;16:642-648.

Three arm, open-label, randomized study on 358 German patients comparing

	RR
A) LASER alone	26%
B) IMQ 3 x week for 12 weeks 6 month F-UP.....	6%
C) LASER + IMQ 3 x week for 12 wk	8%

The RR in LASER + IMQ were similar to IMQ alone

Adjuvant sinecatechins after LASER treatment

Efficacy of sinecatechins 10% as proactive sequential therapy after laser CO2 therapy...
Puviani M et al. Int J STD & AIDS 2019; 30(2):131-136.

Randomized, masked outcome assessment, prospective multi center trial
on 87 Italian patients treated with CO2 laser followed by application of
sinecatechins 10% ointment in 60 pts (TS) vs placebo in 27 pts (CTR)

All patients had already been treated in the last year (recurrent patients)
in external genital area with a mean number of 6.5 lesions

The ointment was applied 2 weeks later on LASER treated areas (healthy skin)
Patients applied the ointment twice a day for 3 months

RESULTS (at the 3^o month)

Recurrence rate : 5% in the TS group vs 29% in the CTR group

Mild to moderate burning sensation was reported in 56% of TS group

In conclusion...

“ Any surgeon can remove ano-genital warts but our role, as STI specialists, is to provide the best available TTT, to explain the disease to the patients and to support them during the cure “

