Last update: Feb ‘26

COLPOFIX®

Global Launch Pack

Global Medical Brands Team

Laborest

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Product Description and Key Ingredients

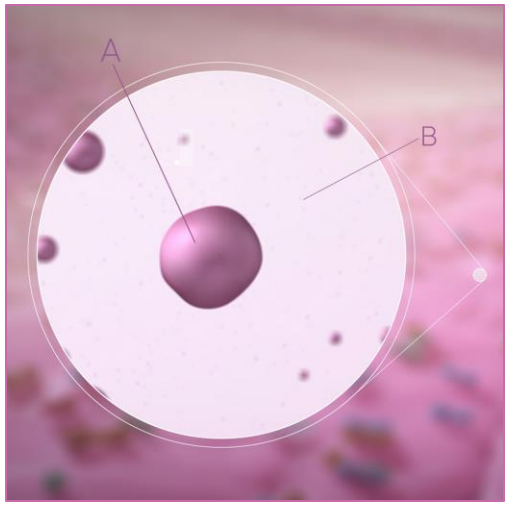
COLPOFIX® is an **innovative vaginal spray gel** indicated for the **prevention and treatment of cervical lesions caused by Human Papillomavirus (HPV). COLPOFIX®** is a **medical device** that acts by **helping restore** and **control the physiological conditions** of the **cervico-vaginal transformation zone**. Its spray formulation allows a uniform and effective distribution of the gel on the cervico-vaginal mucosa.

INGREDIENTS INFORMATION

A) Carboxymethyl β-glucan

It is a **yeast-derived β-glucan** (*Saccharomyces cerevisiae*) that **supports cervico-vaginal healing and vaginal health**.

- **Immune stimulation activity**: interacts with innate immune cells (e.g., macrophages and dendritic cells), **supporting immune activation and HPV clearance**.
- **Tissue repairing activity**: promotes r**e-epithelialization** and **supports regression of cervical lesions**, helping tissue repair (also after excisional treatment).
- **Prebiotic activity**: supports a *Lactobacillus*-dominant **vaginal microbiota** and helps maintain a **low vaginal pH**, improving vaginal health.



B) Polycarbophil

It is a **mucoadhesive**, **high-molecular-weight acrylic polymer** that forms a **protective film** through strong hydrogen bonding with mucins.

- **Protection activity**: the mucoadhesive film supports **epithelium integrity** and acts as a **mechanical protective barrier**, making HPV access to the basal layer more difficult.
- **Acidifying activity**: once attached to the mucosa, polycarbophil releases H+ ions, contributing to **a lower vaginal pH** and **supporting an optimal vaginal microbiota**, which may help reduce infection and persistence risk.

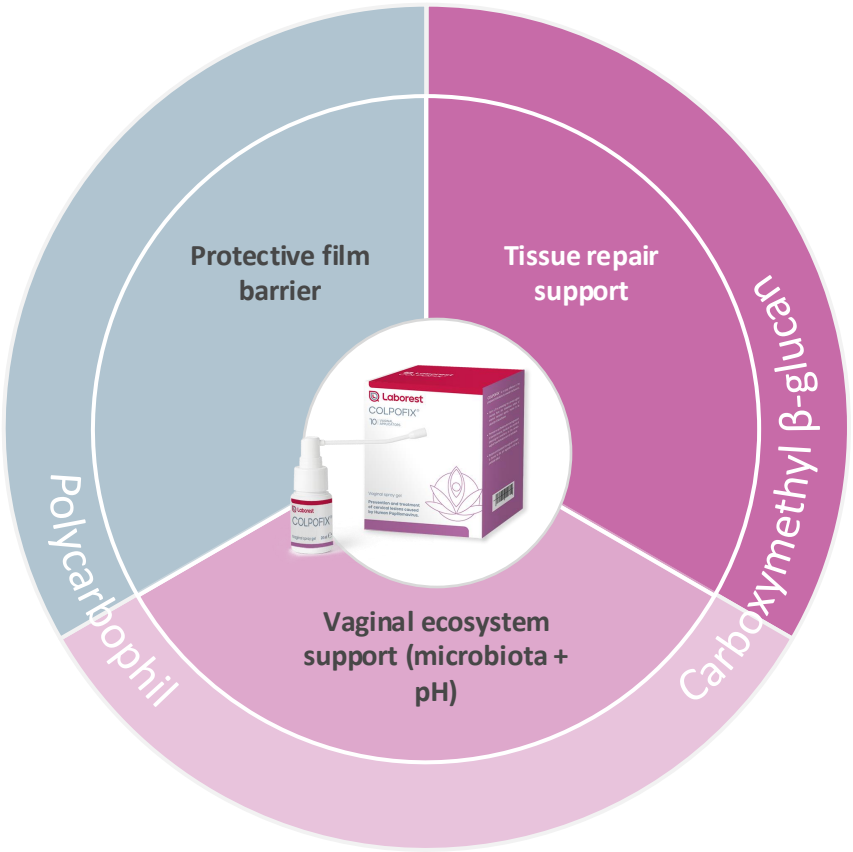
Claims and Benefits

COLPOFIX® is an **innovative vaginal spray gel medical device** for the **prevention and treatment of cervical lesions caused by Human Papillomavirus (HPV).** It acts through the control of physiological conditions on the cervico-vaginal transformation zone.

MAIN CLAIMS

- Prevention and treatment of cervical lesions caused by Human Papillomavirus (HPV).
- It acts through the control of physiological conditions on the cervico-vaginal transformation zone.

Mechanism of action: Restoring physiological conditions in the cervico-vaginal transformation zone



Protective barrier (film-forming action)

Polycarbophil forms a **mucoadhesive protective film over the vaginal mucosa**. This mechanical barrier helps protect the affected area from the deleterious action of external microbial agents and supports epithelium integrity.

Tissue repair support (re-epithelialization)

Carboxymethyl β-glucan supports tissue repair by promoting r**e-epithelialization**, contributing to the **regression of cervical lesions**, and **supporting healing** (including after excisional treatment).

Microbiota & pH support (prebiotic/acidifying action)

Carboxymethyl β-glucan supports a *Lactobacillus*-dominant vaginal microbiota, while **polycarbophil** contributes to a lower vaginal pH. Together**, they help maintain an optimal vaginal environment and support vaginal health**.

Mechanism of action: control of physiological conditions in the cervico-vaginal transformation zone

The combination of polycarbophil and carboxymethyl β-glucan supports a protective local environment on the cervico-vaginal mucosa

Cervico-vaginal environment and HPV-related lesions

The **cervico-vaginal transformation zone** is a key site for **HPV-related cervical lesions**. Local physiological conditions and mucosal protection are relevant to support tissue integrity and cervico-vaginal homeostasis. Beyond physical implications, an HPV diagnosis may also be associated with **psychological burden**, including stress, anxiety, and concerns about sexual health and relationships.

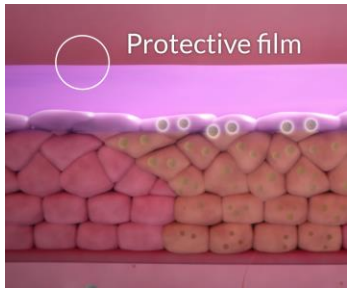
ROLE OF THE KEY INGREDIENTS

Carboxymethyl β-glucan

- Yeast-derived β-glucan that supports cervico-vaginal healing and vaginal health.
- Supports **innate immune activation** relevant to HPV clearance and promotes re-epithelialization, contributing to cervical lesion regression.
- **Prebiotic effect**: supports a *Lactobacillus*-dominant vaginal microbiota.

Polycarbophil:

- Mucoadhesive, high-molecular-weight acrylic polymer that forms a protective film on the vaginal mucosa.
- Supports **epithelium integrity** (mechanical barrier) and contributes to a **lower vaginal pH**, helping maintain an optimal vaginal microbiota.

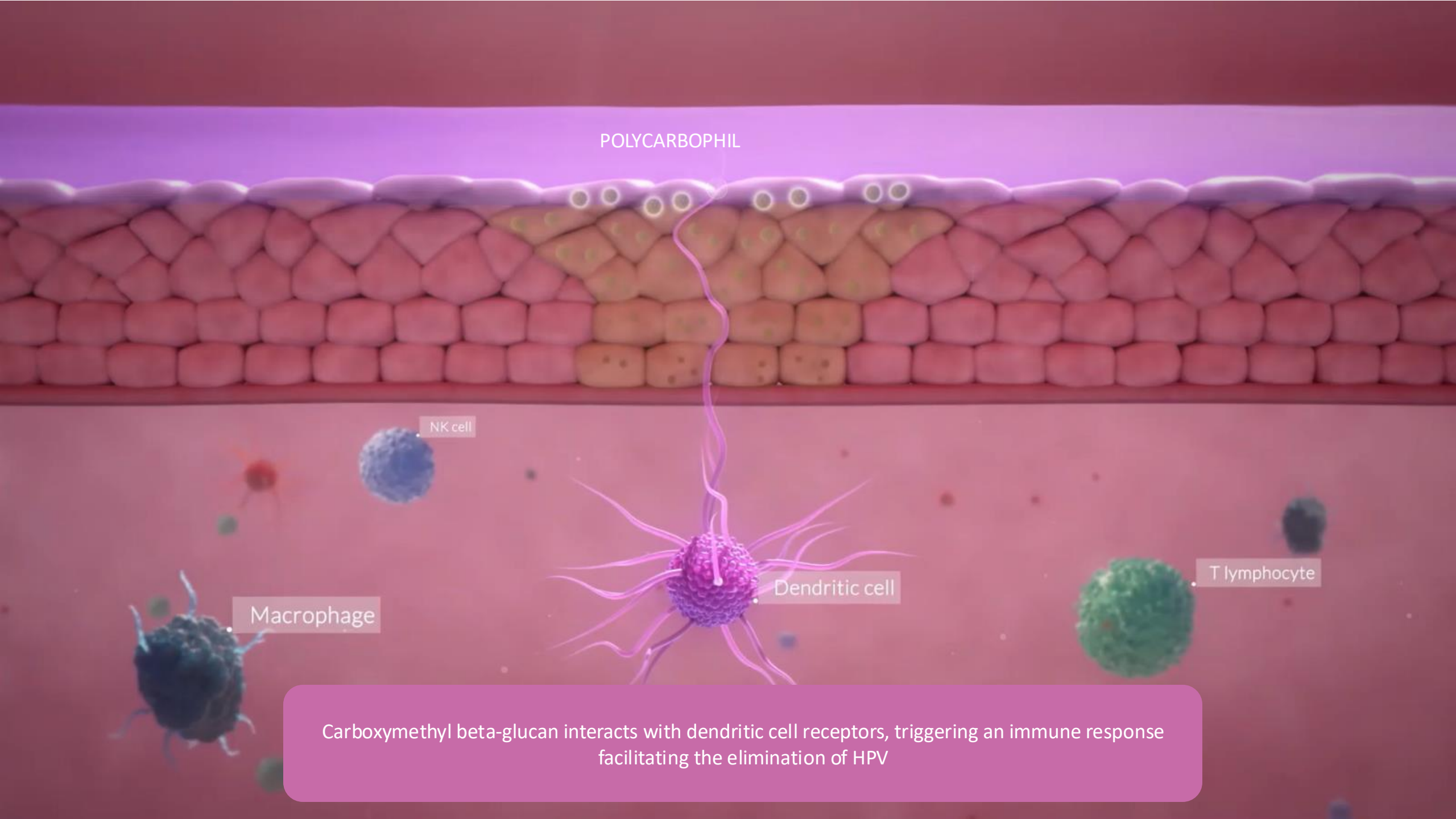


Local supportive action

- Supports the formation of a mucoadhesive protective film on the cervico-vaginal mucosa, helping maintain **epithelium integrity.**
- Contributes to maintaining **physiological conditions** in the transformation zone (pH and microbiota balance) and supports **re-epithelialization** processes associated with cervical lesion regression.

In COLPOFIX®...

The combination of **polycarbophil** and **carboxymethyl β-glucan** supports local physiological conditions on cervico-vaginal transformation zone through **protective film formation**, **tissue repair** support, and **vaginal ecosystem support**.


POLYCARBOPHIL
NK cell
Dendritic cell
T lymphocyte
Macrophage
Carboxymethyl beta-glucan interacts with dendritic cell receptors, triggering an immune response facilitating the elimination of HPV


Macrophage infiltrations stimulate tissue granulation, collagen deposition, and epithelialization

Product Formula and Specifications

SUPPLEMENT FACTS

Polycarbophil; Carboxymethyl β-glucan

PRODUCT FORM

Vaginal spray gel

SUGGESTED USE

1 application (5 sprays) a day, 20 days per month for 3-6 months

AVAILABLE IN

- 1 x 20 ml bottle + 10 disposable single-use vaginal applicators
- 2 x 20 ml bottles + 20 disposable single-use vaginal applicators

Medical device, Class IIa. CE marked.

PRODUCT POSITIONING

- Target Audience
- Value Proposition
- Product Messaging

Target Audience

Focus on women diagnosed with **HPV infection and HPV-related cervical abnormalities** who are managed by gynecologists during screening, follow-up, and post-treatment care. In addition to the physical implications (cervical lesions and procedures), HPV findings can be associated with **psychological burden,** such as **anxiety**, **stress,** and **concerns about sexual health and relationships**.

Colpofix® is used in two main clinical settings:

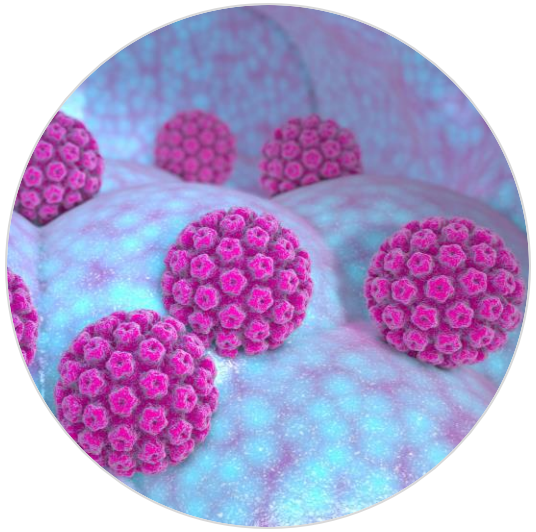
- **Indication 1: HPV+ / low-grade cervical lesions (CIN1; ASCUS/LSIL).** Women with a positive HPV test and/or abnormal Pap smear who enter a "wait and see" pathway with planned follow-up.
- **Indication 2: After cervical surgery (CIN2/3; HSIL).** Women in the post-excisional treatment phase who require support for local tissue recovery and maintenance of a healthy cervico-vaginal environment.

SEGMENTATION

- **Age**
  - Women of any age diagnosed with HPV-related cervical lesions and managed by a gynecologist.
- **Gender**
  - Women under gynecological follow-up for HPV-related cervical lesions.

Value Proposition: targeted protection and support for HPV-related cervical lesions

PROBLEM STATEMENT/ PAIN POINT



HPV is the **most common sexually transmitted infection worldwide**, and some genotypes can lead to cervical lesions that are implicated in cervical cancer. Many women enter a **"wait and see"** follow-up pathway, often needing a non-invasive local option that helps protect the cervico-vaginal area and supports a healthy environment over time.

HOW COLPOFIX® HELPS?

COLPOFIX® is an innovative vaginal spray gel indicated for the **prevention and treatment of cervical lesions** caused by **HPV**. It acts through the control of physiological conditions on the cervico-vaginal transformation zone. Its exclusive spray formulation enables uniform distribution of the gel on the cervico-vaginal mucosa without spills, and the ergonomic applicator helps the cervix to be reached.

BENEFITS

Protective barrier on the cervico-vaginal mucosa
- Polycarbophil forms a film that protects the affected area from the deleterious action of external microbial agents

Supports tissue recovery
- Carboxymethyl ß-glucan promotes re-epithelialization and regression of cervical lesions

Supports vaginal health and microbiota balance
- The protective film-forming action of polycarbophil helps preserve mucosal conditions, while carboxymethyl β-glucan supports restoration and maintenance of the vaginal microbiota through its prebiotic effect

Easy, targeted application
- Uniform and effective distribution over the cervico-vaginal mucosa, with an ergonomic applicator designed to reach the cervix

Product Messaging

COLPOFIX®
SURE TO HIT THE TARGET

COLPOFIX® is an innovative vaginal spray gel designed to support women with HPV-related cervical abnormalities during follow-up. Thanks to its ergonomic applicator and spray technology, it enables targeted application to the cervico-vaginal transformation zone, supporting local physiological conditions where HPV-related changes occur.

SURE TO HIT THE TARGET: With its exclusive ergonomic cannula and spray formulation, COLPOFIX® helps the cervix to be reached and ensures uniform distribution over the cervico-vaginal mucosa without spills, maximizing local coverage where it matters most.

SUPPORT LOCAL RECOVERY: By forming a protective, mucoadhesive film and supporting mucosal integrity, COLPOFIX® helps maintain a healthy cervico-vaginal environment during the “wait & see” period, promoting comfort and supporting epithelial recovery.

Stay confident during follow-up, with targeted local support.

MARKET ANALYSIS

- Market Trends
- Papilocare® Vaginal Gel: competitor deep dive (Procare Health)
- Competitive Landscape
- Positioning vs. Papilocare® (Laborest wins)

Market Trends: Addressing the needs of women in HPV “wait and see” pathways

HPV is very common, and most infections clear naturally, but HPV-based screening identifies many women who enter follow-up (“wait and see”) pathways over months, creating a need for supportive, non-invasive local options and clear education.

The “wait and see” burden: anxiety and uncertainty

Testing HPV-positive can trigger elevated short-term **anxiety, fear, and distress**, especially when women are told to wait for repeat testing. This increases the need for reassurance, a clear explanation of risk, and structured follow-up communication[1,2,3].

Women actively ask about alternatives during surveillance

Because **“wait and see”** is often the standard approach, many women actively seek supportive options they can use during the waiting period and ask clinicians about alternatives to surveillance[4].

Preference for non-invasive options to limit procedure-related harms

There is growing awareness that excisional cervical treatments are associated with increased risks in subsequent pregnancies (e.g., preterm birth). This supports a market trend toward **non-invasive approaches whenever clinically appropriate[5].**

[1]McBride E, et al. **Emotional response to testing positive for human papillomavirus at cervical cancer screening: a mixed-method systematic review with meta-analysis**. Health Psychol Rev. 2021;15(3):395-429. doi:10.1080/17437199.2020.1762106.; [2]McBride E, Marlow LAV, Bennett KF, Stearns S, Waller J. **Exploring reasons for variations in anxiety after testing positive for human papillomavirus with normal cytology: a comparative qualitative study**. Psychoncology. 2021;30(1):84-92. doi:10.1002/pon.5540.; [3]Symmons SM, Waller J, McBride E. **Testing positive for Human Papillomavirus (HPV) at primary HPV cervical screening: A qualitative exploration of women’s information needs and preferences for communication of results**. Prev Med Rep. 2021;24:101529. doi:10.1016/j.pmedr.2021.101529.; [4]McGee AE, Hawco S, Bhattacharya S, Hanley SJB, Cruickshank ME. **Alternatives to surveillance for persistent human papillomavirus after a positive cervical screen: A systematic review and meta-analysis**. Eur J Obstet Gynecol Reprod Biol. 2024;302:332-338. doi:10.1016/j.ejogrb.2024.09.019.; [5]Kyrgiou M, Athanasiou A, Paraskevaidi M, et al. **Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis.** BMJ. 2016;354:i3633. doi:10.1136/bmj.i3633.

Market Trends – Key ingredients in HR-HPV supportive management

There is no direct antiviral therapy recommended to eradicate HPV; standard care relies on risk-based surveillance (“wait & see”) and treating lesions when indicated. This has driven interest in non-invasive topical and oral options, which are positioned as supportive approaches during follow-up.

***Lactobacillus* probiotics** Microbiome-focused adjuvant trend	**Probiotics** are widely used as an adjunct approach **in HR-HPV/LSIL follow-up**, reflecting evidence that a *Lactobacillus*-dominant cervico-vaginal microbiome may be associated with better HPV-related outcomes; recent meta-analyses evaluate clearance and cytology endpoints.
Hyaluronic acid (vaginal) Mucosal repair + supportive local care	**Hyaluronic acid** is frequently used in local vaginal products to support hydration and mucosal integrity. Clinical studies have combined vaginal HA with oral supplements to improve CIN1/LSIL regression and follow-up parameters.
Coriolus versicolor extract (vaginal) Immune-support positioning	**Coriolus** versicolor is a well-known **differentiating ingredient** in multi-ingredient vaginal gels evaluated against “wait and see”, with trials reporting HR-HPV clearance and low-grade lesion repair outcomes.
AHCC® (oral) Nutraceutical immune modulation under clinical study	**AHCC® (Lentinula edodes mycelia extract)** is one of the most studied **oral nutraceuticals** for persistent HR-HPV; a phase II randomized, double-blind, placebo-controlled study[1] investigated durable HR-HPV clearance/negativity outcomes.

COLPOFIX® aligns with the trend toward **non-invasive local support** during “wait and see”: a cervico-vaginal spray gel combining a mucoadhesive protective polymer (polycarbophil) and a bioactive component positioned for re-epithelialization and microbiota support (carboxymethyl β-glucan).

[1]Smith JA, Gaikwad AA, Mathew L, Rech B, Faro JP, Lucci JA 3rd, Bai Y, Olsen RJ, Byrd TT. AHCC® Supplementation to Support Immune Function to Clear Persistent Human Papillomavirus Infections. Front Oncol. 2022 Jun 22;12:881902. doi: 10.3389/fonc.2022.881902. PMID: 35814366; PMCID: PMC9256908.

Papilocare® Vaginal Gel: competitor deep dive (Procare Health)

Main Actives & Mechanism of action

- **Coriolus versicolor extract:** Beta-glucan-rich mushroom extract; supports **local immune response and epithelial repair**
- **BioEcolia® (α-oligoglucan, prebiotic)**: promotes **growth of beneficial *Lactobacillus*** (including *L. crispatus*) to help rebalance cervico-vaginal microbiota
- **Hyaluronic acid (encapsulated in niosomes)**: hydrates and improves **tissue elasticity/comfort**; supports mucosal recovery
- **β-glucan (encapsulated in niosomes):** helps **reinforce barrier function** and supports **repair/soothing of irritated mucosa**
- **Centella asiatica (phytosomes):** supports **re-epithelialization and tissue regeneration** (wound-healing support)
- **Neem extract (Azadirachta indica):** soothing + antimicrobial/anti-inflammatory support for **mucosal comfort**
- **Aloe vera extract** soothes and supports **mucosal repair**; contributes to hydration/comfort
- **Delivery technology (niosomes + phytosomes):** improves ingredient availability and helps action in deeper epithelial layers; preserves actives

Main Claims

- **Re-epithelializing vaginal gel** for the **prevention and management of HPV-related low-grade cervical lesions (ASC-US/LSIL)**
- Forms a **protective film** on the cervical mucosa (transformation zone), creating a **defensive barrier** to help reduce HPV integration risk and support mucosal repair/lesion normalization
- Helps **restore the cervico-vaginal environment** (hydration, comfort) and supports microbiota balance (prebiotic support for beneficial *Lactobacillus*).
- **Scientific background:** https://pro.papilocare.com/personal-sanitario/evidencia-clinica-y-estudios-en-curso/

Format Posology Pricing

- **Format**: Intravaginal gel (Medical device). Available presentations: 7 single-dose cannulas +5 ml (monodose); 21 single-dose cannulas x 5ml (monodose); 2 tubes x 40 ml + applicators (up to 21 applications; 3 ml/application with reusable applicator)
- **Posology** (standard 6-month regimen): Month 1: 1 application/day 21 days; months 2-6: 1 application every other day for 21 days. Pause during menstruation.
- **PVP**:
  - **Italy**: 7×5 ml ~€20–25 | 21×5 ml — | 2×40 ml — → Monthly cost: Month 1 ~€60–75 | Maintenance ~€31–39/month
  - **Romania**: 7×5 ml ~99.9 Lei | 21×5 ml — | 2×40 ml — → Monthly cost: Month 1 ~300 Lei | Maintenance ~157 Lei/month
  - **Spain**: 7×5 ml ~€25–30 | 21×5 ml ~€52 | 2×40 ml ~€47 → Monthly cost: Month 1 ~€52 | Maintenance ~€40–47/month
  - **Greece**: 7×5 ml ~€22.8–26.0 | 21×5 ml ~€60 | 2×40 ml — → Monthly cost: Month 1 ~€60 | Maintenance ~€36–41/month

Competitive Landscape

	Finderm Forte Beta Vaginal Cream	**Papilocare** Vaginal gel	**AP 16** Vaginal spray
			
Main Actives	- Xalifin 15NP - Glicmonos A2000 - Polycarbophil - hyaluronic acid - beta-glucan - stearic acid	- Coriolus versicolor - BioEcolia (α-oligoglucan, prebiotic) - Hyaluronic acid (niosomes) - Beta-glucan (niosomes) - Centella asiatica (Phytosomes) - Neem extract; Aloe vera extract	- **Carboxymethyl beta-glucan** - **Curcumin** - **Resveratrol** - **Green tea**
Main Claims	Indicated as an adjuvant in the **repair processes of genital tract damage induced by Human Papillomavirus (HPV)**. The presence of **hyaluronic acid** promotes **tissue re-epithelialization**, **hydration**, and **healing** of the **cervico-vaginal skin and mucosa**, helping to **reduce pain and itching**.	**Re-epithelializing vaginal gel for HPV-related cervical lesions**. Forms a protective barrier in the cervical transformation zone and supports tissue repair during follow-up, helping maintain a healthy cervico-vaginal environment and microbiota balance. Medical device. **Scientific background:** https://pro.papilocare.com/personal-sanitario/evidencia-clinica-y-estudios-en-curso/	- AP16 spray is ideal to protect the cervical and vaginal mucosa and assists the reparative process during infectious or traumatic phlogistic processes. - AP16 spray contains principles with proven anticancer properties and therefore it is an effective therapeutic agent in patients with cytological alterations of low degree due to HPV infection.
Format Posology Pricing	FARMITALIA - 7 applicators - 1 applicator/day for 21 days, then 1 each 2 days - PVP: 27€ (**7 applicators** – 81€/1stmonth, then 57€/month)	PROCARE - Intravaginal gel (medical device) - Posology: 6 months. Month 1: 1 application/day 21 days; months 2-6: 1 application every other day for 21 days. Pause during menstruation.	EUTYLIA - 10 canules - 1 canule/day - PVP: 30€ (30€/month)

Competitive Landscape

	Papilocare Vaginal gel	**SiloffGyn** Vaginal cream	**Eva intima cervasil** Vaginal cream-gel	**Deflagyn** Vaginal gel
				
Main Actives	- Coriolus versicolor - BioEcolia (α-oligoglucan, prebiotic) - Hyaluronic acid (niosomes) - Beta-glucan (niosomes) - Centella asiatica (Phytosomes) - Neem extract; Aloe vera extract	- Curcumin (Curcuma longa) - Docosanol - Emblica officinalis (Indian gooseberry) - Aloe vera (Aloe barbadensis gel) - Polidocanol - CM β-glucan - Lactic acid	- Curcumin - Docosanol - Aloe vera & amla extracts - CM β-glucans	- Colloidal anhydrous silica (silicon dioxide) - Deflamin®: citric acid & sodium selenite pentahydrate
Main Claims	**Re-epithelializing vaginal gel for HPV-related cervical lesions**. Forms a protective barrier in the cervical transformation zone and supports tissue repair during follow-up, helping maintain a healthy cervico-vaginal environment and microbiota balance. Medical device. **Scientific background:** https://pro.papilocare.com/personal-sanitario/evidencia-clinica-y-estudios-en-curso/	**Vaginal cream for HPV-related epithelial lesions (incl. SIL) and dryness:** supports the transformation zone, promotes re-epithelialization and micro-lesion healing, helps recovery after procedures, and relieves burning/itching. Class IIa medical device.	Vaginal cream gel for the management of cervical lesions due to HPV. Helps strengthen local defenses, supports re-epithelialization of epithelial micro-lesions, and helps restore normal vaginal conditions (post-procedures and symptom relief such as burning/itching) Medical device.	Promotes spontaneous remission and regression of unclear cervical smears or HPV-induced or p16/Ki-67 positive cervical lesions or cervical erosions. **Scientific background:** **https://www.deflagyn.com/scientific/**
Format Posology Pricing	PROCARE - Intravaginal gel - Posology: 6 months. Month 1: 1 application/day 21 days; months 2-6: 1 application every other day for 21 days. Pause during menstruation.	HEREMCO - 30g tube + 6 single-use applicators. - Posology: **LSIL** week 1 → 1 vaginal app for 6 days; then 3-6 months → 1 vag app 2 days/week. **Post-surgery/ post-laser,** same regimen as LSIL. **Vaginal dryness**: 1 vag app for 6 days; repeat after 1 week. **Acute condylomata**: 1 app for 6 days; topical vulvar use. **PVP**: 15€ (month 1: ~30 €/month; maintenance: ~20 €/month)	INTERMED - Vaginal cream-gel 30 ml tube + 6 disposable vaginal applicators - Posology: **intraepithelial lesions/post-surgical or laser** week 1 → 1 vag app for 6 days; then 3-6 months → 1 vag app 2 days/week. - **PVP**: 19€ (30 ml x 6 vaginal applicators). Induction month: ~€40/month (≈2 packs); Maintenance: ~€27/month (≈1–2 packs)	VIRTUS PHARMA - Intravaginal gel (150 ml) with 2 applicators - Posology: 5ml intravaginal application using an applicator; typically 3x28-day courses with 3 day breaks between cycles; pause during menstruation. - PVP: 72,23€ (150 ml & 2 applicators); monthly cost ~72.23€/month (150 ml ≈ 30 applications if 5 ml/application).

Positioning vs. Papilocare® (Laborest wins)

	Colpofix® vaginal gel spray	Papilocare vaginal gel
Pharmaceutical form	Vaginal spray gel	Vaginal gel
Product presentation	1 x 20 ml bottle + 10 disposable single-use vaginal applicators 2 x 20 ml bottles + 20 disposable single-use vaginal applicators	7 single-dose cannulas +5 ml (monodose); 21 single-dose cannulas x 5ml (monodose); 2 tubes x 40 ml + applicators (up to 21 applications; 3 ml/application with reusable applicator)
Posology	3-6 months. 5 puffs (~1 ml) daily for 20 days/month	**Month 1:** 1 application/day 21 days; **months 2-6:** 1 application every other day for 21 days. Pause during menstruation.
Units needed per month	10 disposable applicators: 2 units per month 20 disposable applicators: 1 unit per month	Month 1: 21 applications → 3×7 monodose OR 1×21 monodose OR 1 pack (2×40 ml). Months 2–6: 11 applications/month → 2×7 monodose OR 1×21 monodose every ~2 months OR 1 pack every ~2 months.
Clinical evidence	Yes, 4 clinical studies + 1 under publication (Fix study)	Yes
Total patients enrolled	**n = 2732** (4 clinical studies + 1 under publication)	> 600
Clinical trials with control group	Yes	Yes
Proven efficacy in HPV + patients	Yes	Yes
Proven efficacy in ASCUS diagnosed patients	Yes	Yes
Proven efficacy in LSIL and CIN1+ diagnosed patients	**Yes**	Yes
Proven efficacy in HSIL and CIN2+ and CIN3+ diagnosed patients	No	No
MoA description and active ingredient association with:		
Cervix epithelization	Yes	Yes
Immune system enhancement	Yes	Yes
Eubiotic microbiota promotion	Yes	Yes

SALES AND MARKETING MATERIALS

- Key Sales Tools
- Visuals and Assets
- FAQs

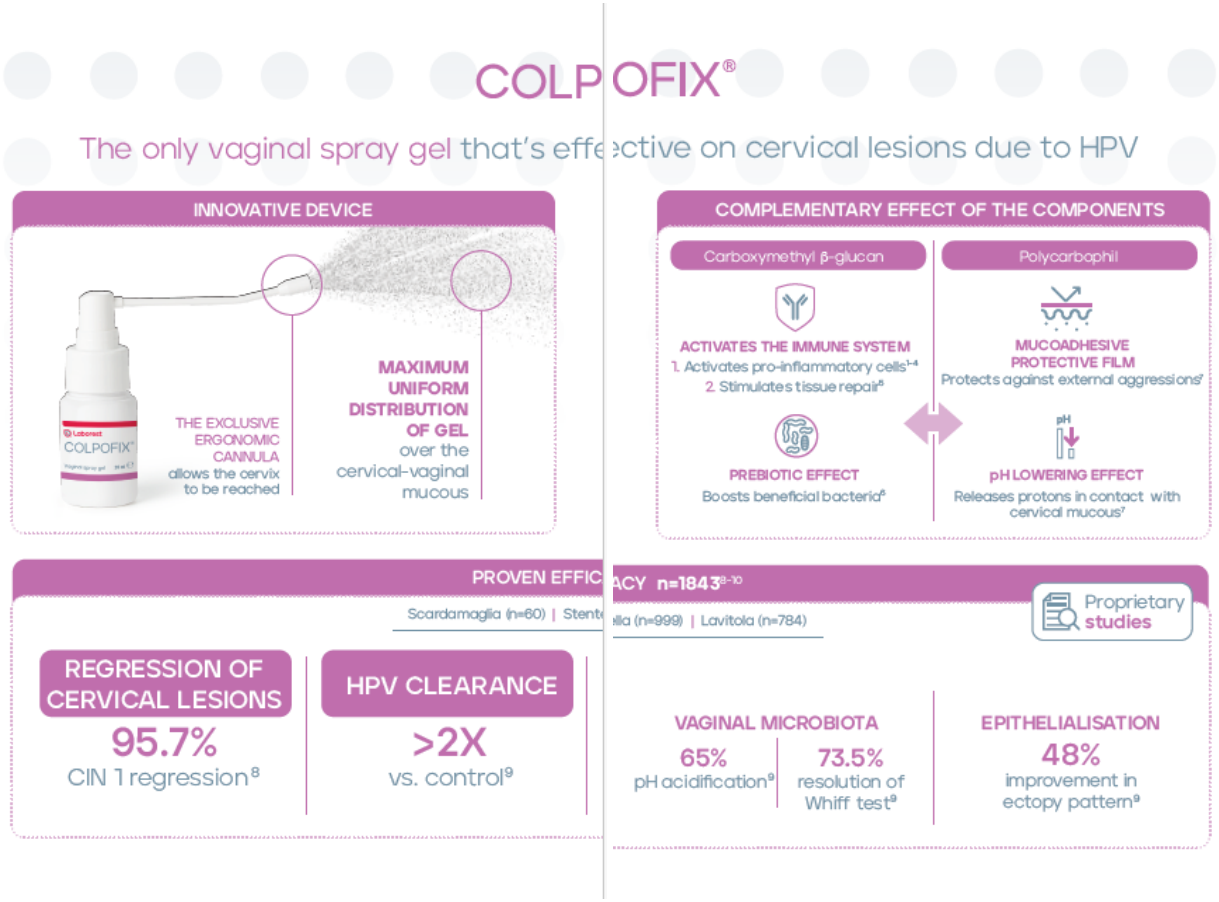
Key Sales Tools

New materials on going

Colpofix tablet material, available in:
https://brandcenter.uriach.com/downloads#@4054

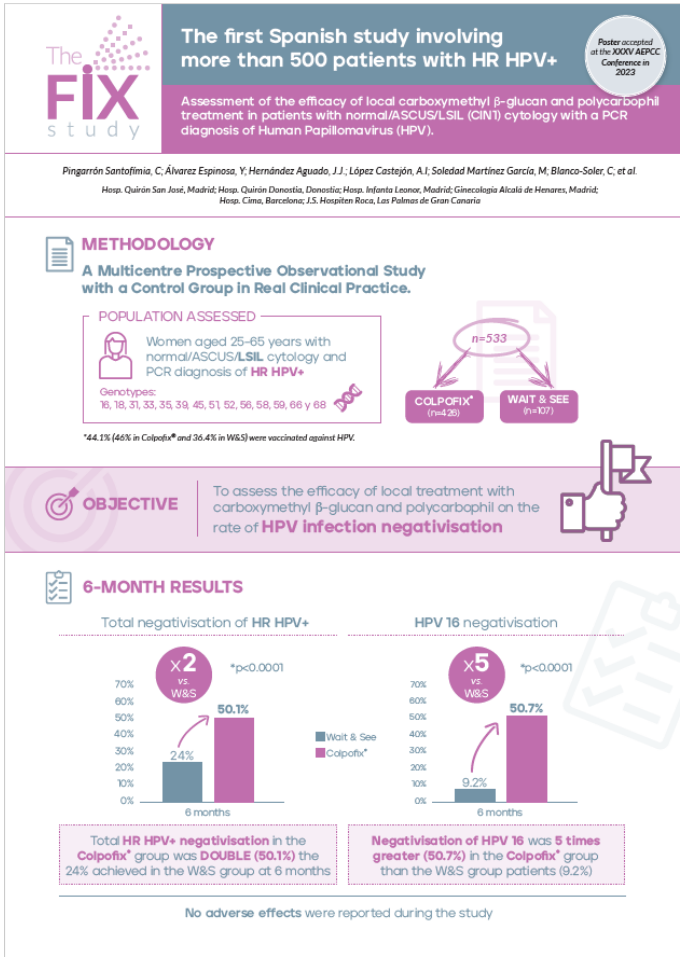
Key Sales Tools

New materials on going



Colpofix leaflet, available in:
https://brandcenter.uriach.com/downloads#@4053

Key Sales Tools



New materials on going

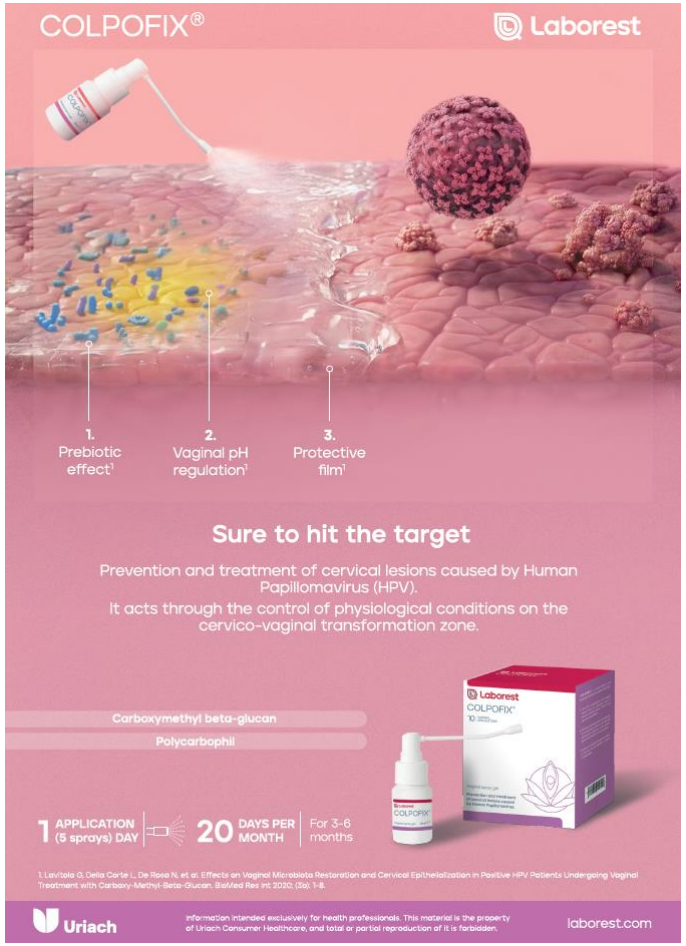
Fix study infographic:
https://brandcenter.uriach.com/downloads#@4052

Key Sales Tools

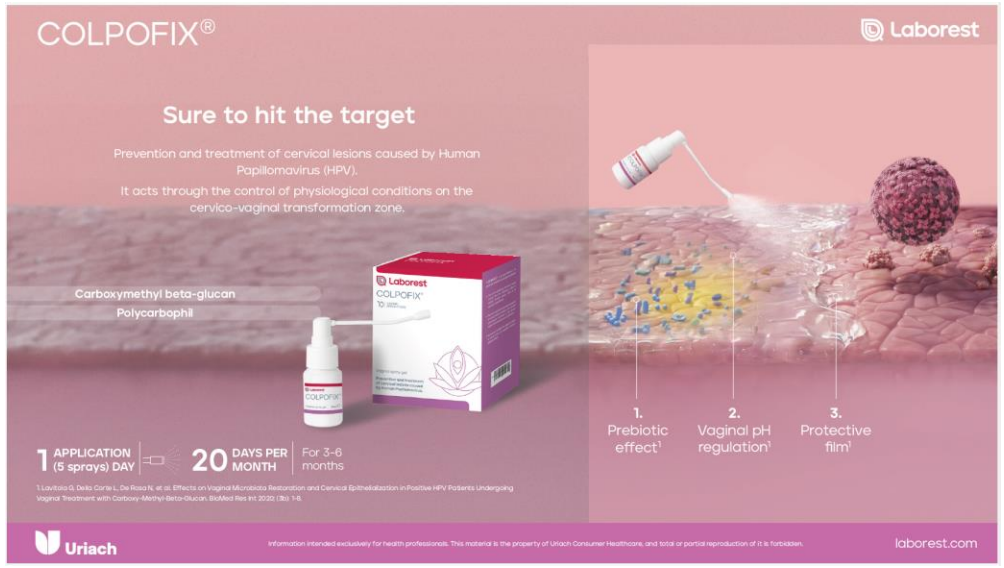
Available in:
https://brandcenter.uriach.com/downloads#@4771

Available in:
https://brandcenter.uriach.com/downloads#@4769

Key Visuals



Vertical format – Key Visual
https://brandcenter.uriach.com/downloads#@5798



Horizontal format – Key Visual
https://brandcenter.uriach.com/downloads#@5799

Visuals and Assets

Colpofix RO-GR
Available in BC:
https://brandcenter.uriach.com/downloads#@5035

Colpofix ES-IT
Available in BC:
https://brandcenter.uriach.com/downloads#@3311

Colpofix ENG
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Colpofix ENG
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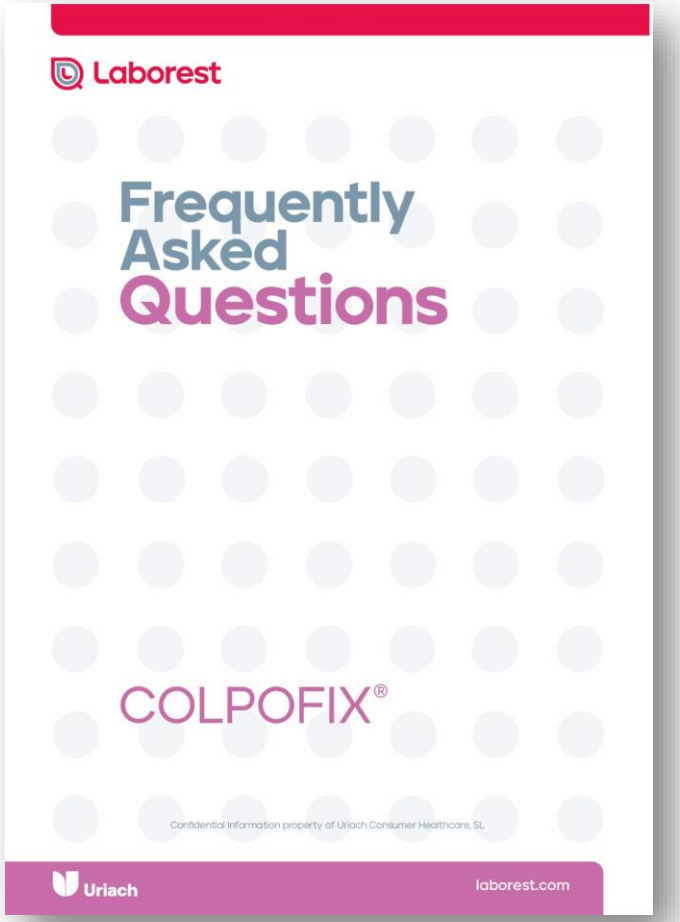
FAQs



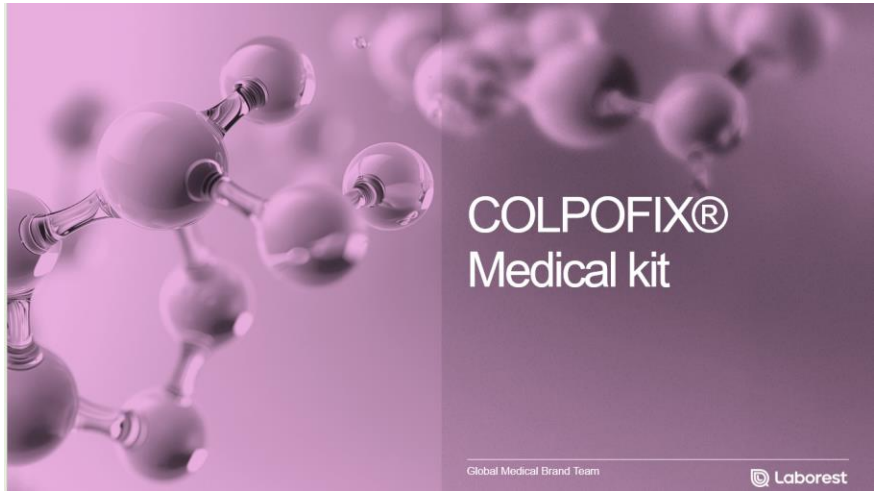
Available in Brandcenter:

https://brandcenter.uriach.com/downloads#@4412

MEDICAL TRAINING

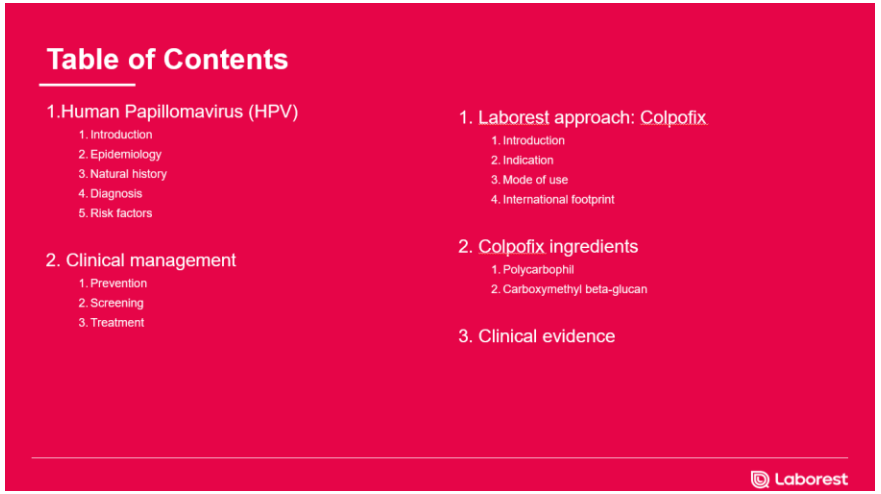
- **Medical Tool Kit – on going**

MEDICAL TOOLKIT



COLPOFIX® MEDICAL KIT

Content



CLINICAL STUDIES & EVIDENCE

- Overview Of Clinical Studies
- Clinical Evidence For Key Ingredients
- List Of Relevant Studies/ Bibliography

Overview Of Clinical Studies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MINERVA GINECOL 2010;62:389-94

Efficacy of carboximethyl beta-glucan in the regression of HVP correlated, low-grade cervical cytological alterations

P. SCARDAMAGLIA [1, 2], C. CARRARO [1, 2], P. MANCINO [1, 2], P. STENTELLA [1, 2]

EFFECTIVENESS OF THE TREATMENT WITH BETA-GLUCAN IN THE HPV-CIN1 LESIONS

Aim. The aim of the study was to evaluate the effectiveness of the beta-glucan in women with abnormal cytology, including the women with a positive screening for ASCUS-LSIL further divided in women with positive cytology (ASCUS or LSIL) and negative colposcopy and women with abnormal cytology, positive colposcopy and human papilloma virus (HPV)-CIN1 hystology who opted for follow-up.

Methods. From September 2007 to December 2008, 60 women whit ASCUS-LSIL diagnosis were recruited at the ambulatory of Laser surgery and Cervico-Vaginal Patology, Department of Gynecology and Obstetrics of Policlinico Umberto I of Rome. The women was subdivided in two groups: 1) women with cytological diagnosis of ASCUS or LSIL and negative colposcopy; 2) women with abnormal cytology, positive colposcopy and HPV-CIN1 histology, who opted for follow-up. All the women were treated with two cycles of a daily topical application of beta-glucan for 20 consecutive days with a suspension of 10 days. The effects of beta-glucan were analyzed with colposcopy and cytology at 3,6 and 12 months from the beginning of the therapy.

Result. After 3 months of treatment, of the 30 women with positive cytology and negative colposcopy, 80% with ASCUS diagnosis resulted negative, 35% with LSIL diagnosis resulted negative; after 6 months 100% with ASCUS diagnosis resulted negative, 70% with LSIL diagnosis resulted negative; after 12 months 85% with LSIL diagnosis resulted negative. Of the 30 women with positive cytology, positive colposcopy and HPV-CIN1 histology after 3 months 20% resulted negative, after 6 months 60% resulted negative and after 12 months 80% resulted negative. The persistence of the HPV-CIN1 histology was verified in the 15% of the women. For these women the definitive treatment was the TFD.

Conclusion. Our study demonstrate the effectiveness of the treatment with beta-glucan in the women with ASCUS-LSIL lesions and HPV-CIN1 lesions, increasing of the regressions rate after 12 months of the treatment of the 15-20%.

Key words: **Beta-glucans - Colposcopy - Cell biology.**

[1] Ambulatory of Lasersurgery and Cervico-Vaginal Patology, Sapienza University, Rome, Italy; [2] Department of Gynecological Studies, Perinatology and Neonatal Nursing, Umberto I Policlinic, Rome, Italy.

Received on 1st June, 2010.
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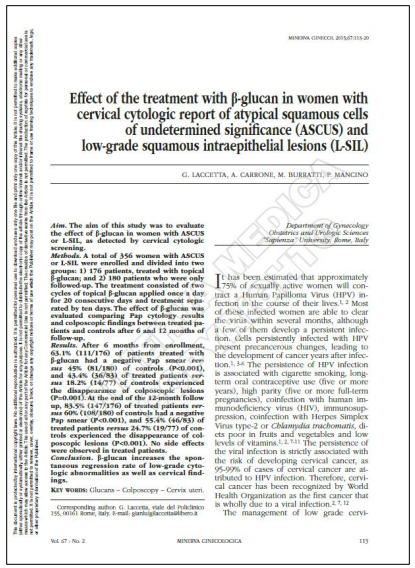
The correlation between genital infection with human papillomavirus (HPV) and cervical cancer was first theorized in the early 1980s by German virologist Harald zur Hausen and later confirmed by numerous authors throughout the following years.


MINERVA GINECOL 2015;67:115-20

Effect of the treatment with β-glucan in women with cervical cytologic report of atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesions (L-SIL)

G. LACCETTA, A. CARRONE, M. BURRATTI, P. MANCINO

Department of Gynecology Obstetrics and Urologic Sciences "Sapienza" University, Rome, Italy

Aim. The aim of this study was to evaluate the effect of β-glucan in women with ASCUS or L-SIL, as detected by cervical cytologic screening.

Methods. A total of 356 women with ASCUS or L-SIL were enrolled and divided into two groups: 1) 176 patients, treated with topical β-glucan; and 2) 180 patients who were only followed-up. The treatment consisted of two cycles of topical β-glucan applied once a day for 20 consecutive days and treatment separated by ten days. The effect of β-glucan was evaluated comparing Pap cytology results and colposcopic findings between treated patients and controls after 6 and 12 months of follow-up.

Results. After 6 months from enrollment, 63.1% (111/176) of patients treated with β-glucan had a negative Pap smear (versus 45% (81/180) of controls (P<0.001), and 43.4% (36/83) of treated patients versus 18.2% (14/77) of controls experienced the disappearance of colposcopic lesions (P<0.001). At the end of the 12-month follow up, 83.5% (147/176) of treated patients versus 60% (108/180) of controls had a negative Pap smear (P<0.001), and 55.4% (46/83) of treated patients versus 24.7% (19/77) of controls experienced the disappearance of colposcopic lesions (P<0.001). No side effects were observed in treated patients.

Conclusion. β-glucan increases the spontaneous regression rate of low-grade cytologic abnormalities as well as cervical findings.

KEY WORDS: Glucans – Colposcopy – Cervix uteri.

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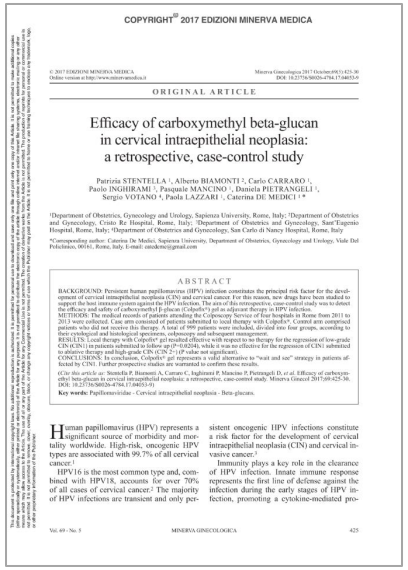
It has been estimated that approximately 1.75% of sexually active women will contract a Human Papilloma Virus (HPV) infection in the course of their lives.[1, 2] Most of these infected women are able to clear the virus within several months, although a few of them develop a persistent infection. Cells persistently infected with HPV present precancerous changes, leading to the development of cancer years after infection.[3, 3,4] The persistence of HPV infection is associated with cigarette smoking, long-term oral contraceptive use (five or more years), high parity (five or more full-term pregnancies), coinfection with human immunodeficiency virus (HIV), immunosuppression, coinfection with Herpes Simplex Virus type-2 or *Chlamydia trachomatis*, diets poor in fruits and vegetables and low levels of vitamins.[3, 5, 7,11] The persistence of the viral infection is strictly associated with the risk of developing cervical cancer, as 95-99% of cases of cervical cancer are attributed to HPV infection. Therefore, cervical cancer has been recognized by World Health Organization as the first cancer that is wholly due to a viral infection.[2, 7, 12]

The management of low grade cervi-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Minerva Ginecologica 2017 October;69(5):425-36
DOI: 10.23736/S0026-4784.17.04053-9

ORIGINAL ARTICLE

Efficacy of carboxymethyl beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study

Patrizia STENTELLA [1], Alberto BIAMONTI [2], Carlo CARRARO [1], Paolo INGHIRAMI [1], Pasquale MANCINO [1], Daniela PIETRANGELI [1], Sergio VOTANO [4], Paola LAZZARI [1], Caterina DE MEDICI [1]*

[1]Department of Obstetrics, Gynecology and Urology, Sapienza University, Rome, Italy; [2]Department of Obstetrics and Gynecology, Cristo Re Hospital, Rome, Italy; [3]Department of Obstetrics and Gynecology, Sant'Eugenio Hospital, Rome, Italy; [4]Department of Obstetrics and Gynecology, San Carlo di Nancy Hospital, Rome, Italy

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ABSTRACT

BACKGROUND: Persistent human papillomavirus (HPV) infection constitutes the principal risk factor for the development of cervical intraepithelial neoplasia (CIN) and cervical cancer. For this reason, new drugs have been studied to support the host immune system against the HPV infection. The aim of this retrospective, case-control study was to detect the effects of carboxy-methyl-beta-glucan (Colpofix®) on cervical cytology and HPV-CIN1 lesions.

METHODS: The medical records of patients attending the Colposcopy Service of four hospitals in Rome from 2011 to 2013 were collected. Case sets consisted of patients submitted to local therapy with Colpofix®. Control sets comprised patients who did not receive this therapy. A total of 999 patients were included, divided into four groups, according to their cytological and histological specimens, colposcopy and subsequent management.

RESULTS: Local therapy with Colpofix® gel resulted effective with respect to no therapy for the regression of low-grade CIN (CIN1) in patients submitted to follow up ($P<0.0234$), while it was no effective for the regression of CIN1 submitted to conization for high-grade CIN (CIN2 and CIN3) ($P>0.1$ value).

CONCLUSIONS: In clinical practice, Colpofix® gel represents a valid alternative to "wait and see" strategy in patients affected by CIN1. Further prospective studies are warranted to confirm these results.

© De Medici et al. Scardaglia P, Biamonti A, Carraro C, Inghirami P, Mancino P, Pietrangeli D, *et al.*, Efficacy of carboxymethyl-beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study. Minerva Ginecol 2017;69:425-36.
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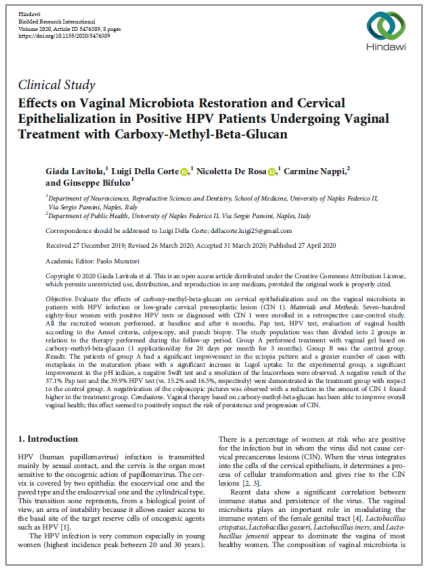
Key words: Papillomaviridae - Cervical intraepithelial neoplasia - Beta-glucans.

Human papillomavirus (HPV) represents a significant source of morbidity and mortality worldwide. High-risk, oncogenic HPV types are associated with 99.7% of all cervical cancer.[1]

HPV16 is the most common type and, combined with HPV18, accounts for over 70% of all cases of cervical cancer.[2] The majority of HPV infections are transient and only persistent oncogenic HPV infections constitute a risk factor for the development of cervical intraepithelial neoplasia (CIN) and cervical invasive cancer.[3]

Immunity plays a key role in the clearance of HPV infection. Innate immune response represents the first line of defense against the infection during the early stages of HPV infection, promoting a cytokine-mediated pro-


Hindawi
Biomed Research International
Volume 2020, Article ID 5476309, 9 pages
https://doi.org/10.1155/2020/5476309

Clinical Study

Effects on Vaginal Microbiota Restoration and Cervical Epithelialization in Positive HPV Patients Undergoing Vaginal Treatment with Carboxy-Methyl-Beta-Glucan

Giada Lavitola,[1] Luigi Della Corte,[1] Nicoletta De Rosa,[1] Carmine Nappi,[2] and Giuseppe Bifulco[1]

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Objective. Evaluate the effects of carboxy-methyl-beta-glucan on cervical epithelialization and on the vaginal microbiota in patients with HPV infection or low-grade cervical preneoplastic lesion (CIN 1). *Materials and Methods.* Seven-hundred eighty-four women with positive HPV tests or diagnosed with CIN 1 were enrolled in a retrospective case-control study. All the recruited women performed, at baseline and after 6 months, Pap test, HPV test, evaluation of vaginal health according to the Amsel criteria, colposcopy, and punch biopsy. The study population was then divided into 2 groups in relation to the therapy performed during the follow-up period. Group A performed treatment with vaginal gel based on carboxy-methyl-beta-glucan (1 application/day for 20 days per month for 3 months). Group B was the control group. *Results.* The patients of group A had a significant improvement in the ectopia pattern and a greater number of cases with metaplasia in the maturation phase with a significant increase in Lugol uptake. In the experimental group, a significant improvement in the pH indices, a negative Swift test and a resolution of the leucorrhoea were observed. A negative result of the 37.1% Pap test and the 39.9% HPV test (vs. 15.2% and 16.5%, respectively) were demonstrated in the treatment group with respect to the control group. A negativization of the colposcopic pictures was observed with a reduction in the amount of CIN 1 found higher in the treatment group. *Conclusions.* Vaginal therapy based on carboxy-methyl-beta-glucan has been able to improve overall vaginal health; this effect seemed to positively impact the risk of persistence and progression of CIN.

1. Introduction

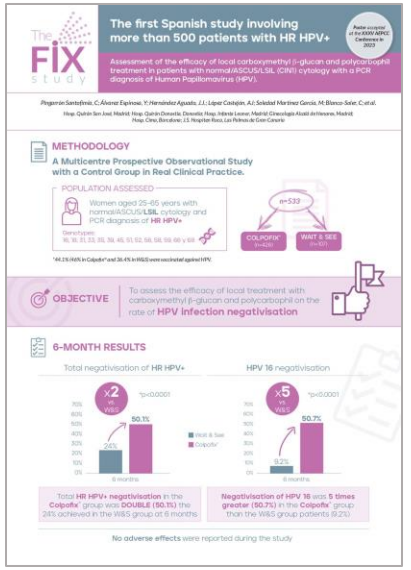
HPV (human papillomavirus) infection is transmitted mainly by sexual contact, and the cervix is the organ most sensitive to the oncogenic action of papillomavirus. The cervix is covered by two epithelia: the exocervical one and the paved type and the endocervical one and the cylindrical type. This transition zone represents, from a biological point of view, an area of instability because it allows easier access to the basal site of the target reserve cells of oncogenic agents such as HPV [1].

The HPV infection is very common especially in young women (highest incidence peak between 20 and 30 years).

There is a percentage of women at risk who are positive for the infection but in whom the virus did not cause cervical precancerous lesions (CIN). When the virus integrates into the cells of the cervical epithelium, it determines a process of cellular transformation and gives rise to the CIN lesions [2, 3].

Recent data show a significant correlation between immune status and persistence of the virus. The vaginal microbiota plays an important role in modulating the immune system of the female genital tract [4]. *Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus iners*, and *Lactobacillus jensenii* appear to dominate the vagina of most healthy women. The composition of vaginal microbiota is

UNDER PUBLICATION



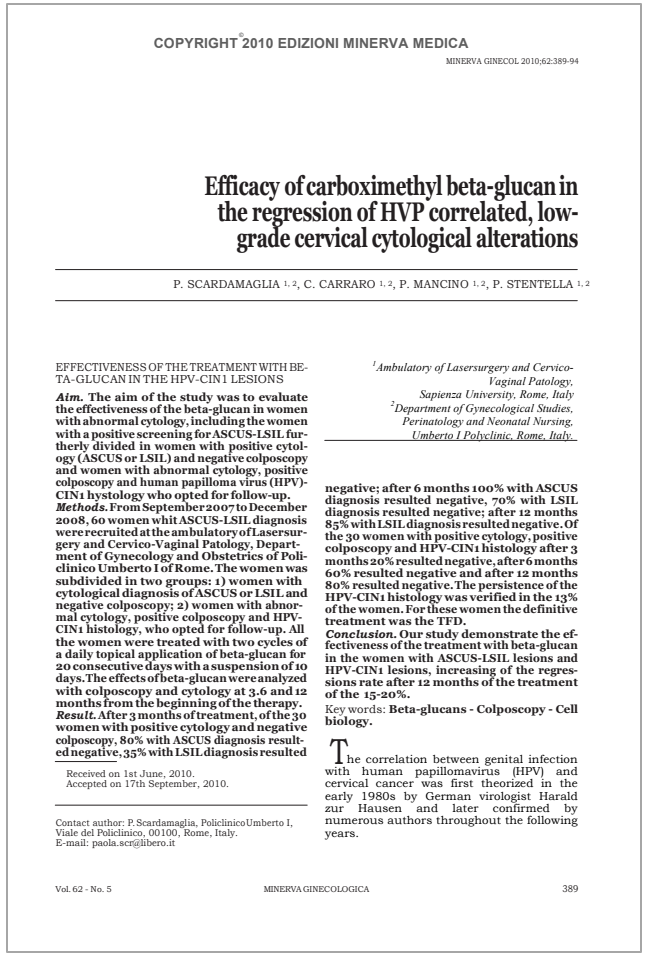
PROVEN EFFICACY n= 2199

Scardamaglia (n=60) – Laccetta (n=356) - Stentella (n=999) – Lavitola (n=784)

Fix Study (Spain): n=533

Infographic available in BC:
https://brandcenter.uriach.com/downloads#@4052

Overview Of Clinical Studies



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MINERVA GINECOL 2010;62:389-94

Efficacy of carboximethyl beta-glucan in the regression of HVP correlated, low-grade cervical cytological alterations

P. SCARDAMAGLIA [1, 2], C. CARRARO [1, 2], P. MANCINO [1, 2], P. STENTELLA [1, 2]

[1] Ambulatory of Lasersurgery and Cervico-Vaginal Patology, Sapienza University, Rome, Italy
[2] Department of Gynecological Studies, Perinatology and Neonatal Nursing, Umberto I Polyclinic, Rome, Italy.

EFFECTIVENESS OF THE TREATMENT WITH BETA-GLUCAN IN THE HPV-CIN1 LESIONS

Aim. **The aim of the study was to evaluate the effectiveness of the beta-glucan in women with abnormal cytology, including the women with a positive screening for ASCUS-LSIL further divided in women with positive cytology (ASCUS or LSIL) and negative colposcopy and women with abnormal cytology, positive colposcopy and human papilloma virus (HPV)-CIN1 hystology who opted for follow-up.**

Methods. **From September 2007 to December 2008, 60 women whit ASCUS-LSIL diagnosis were recruited at the ambulatory of Lasersurgery and Cervico-Vaginal Patology, Department of Gynecology and Obstetrics of Policlinico Umberto I of Rome. The women was subdivided in two groups: 1) women with cytological diagnosis of ASCUS or LSIL and negative colposcopy; 2) women with abnormal cytology, positive colposcopy and HPV-CIN1 histology, who opted for follow-up. All the women were treated with two cycles of a daily topical application of beta-glucan for 20 consecutive days with a suspension of 10 days. The effects of beta-glucan were analyzed with colposcopy and cytology at 3.6 and 12 months from the beginning of the therapy.**

Result. **After 3 months of treatment, of the 30 women with positive cytology and negative colposcopy, 80% with ASCUS diagnosis resulted negative, 35% with LSIL diagnosis resulted negative; after 6 months 100% with ASCUS diagnosis resulted negative, 70% with LSIL diagnosis resulted negative; after 12 months 85% with LSIL diagnosis resulted negative. Of the 30 women with positive cytology, positive colposcopy and HPV-CIN1 histology after 3 months 20% resulted negative, after 6 months 60% resulted negative and after 12 months 80% resulted negative. The persistence of the HPV-CIN1 histology was verified in the 13% of the women. For these women the definitive treatment was the TFD.**

Conclusion. **Our study demonstrate the effectiveness of the treatment with beta-glucan in the women with ASCUS-LSIL lesions and HPV-CIN1 lesions, increasing of the regressions rate after 12 months of the treatment of the 15-20%.**

Key words: **Beta-glucans - Colposcopy - Cell biology.**

Received on 1st June, 2010.
Accepted on 17th September, 2010.

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The correlation between genital infection with human papillomavirus (HPV) and cervical cancer was first theorized in the early 1980s by German virologist Harald zur Hausen and later confirmed by numerous authors throughout the following years.

Efficacy of carboxymethyl β-glucan in regression of HPV-correlated, low-grade cervical cytological alterations

Scardamaglia, et.al., 2010

- **Objective:** To evaluate the effectiveness of topical β-glucan in women with abnormal cytology (ASCUS/LSIL), including women with negative colposcopy and women with positive colposcopy and HPV-CIN1 histology.
- **Study model/design:** Retrospective study (single-centre; recruitment Sep 2007-Dec 2008). Population: N=**60 women** with ASCUS/LSIL cytology; mean age 24 years (18-35). Groups:
  - **Group 1:** ASCUS/LSIL cytology + **negative colposcopy** (n=30)
  - **Group 2:** abnormal cytology + **positive colposcopy** + HPV-CIN1 histology; follow-up (n=30)

  Both groups were treated with Colpofix: one application per day (5 doses) for 20 days, followed by a 10-day suspension, for 2 months.

  Assessments: colposcopy and cytology at 3, 6, and 12 months
- **Results:**

Group 1 (cytology+ / colposcopy-):

- **3 months**: ASCUS 80% -; LSIL 35% -
- **6 months**: ASCUS 100% -; LSIL 70% -
- **12 months**: LSIL 85% -

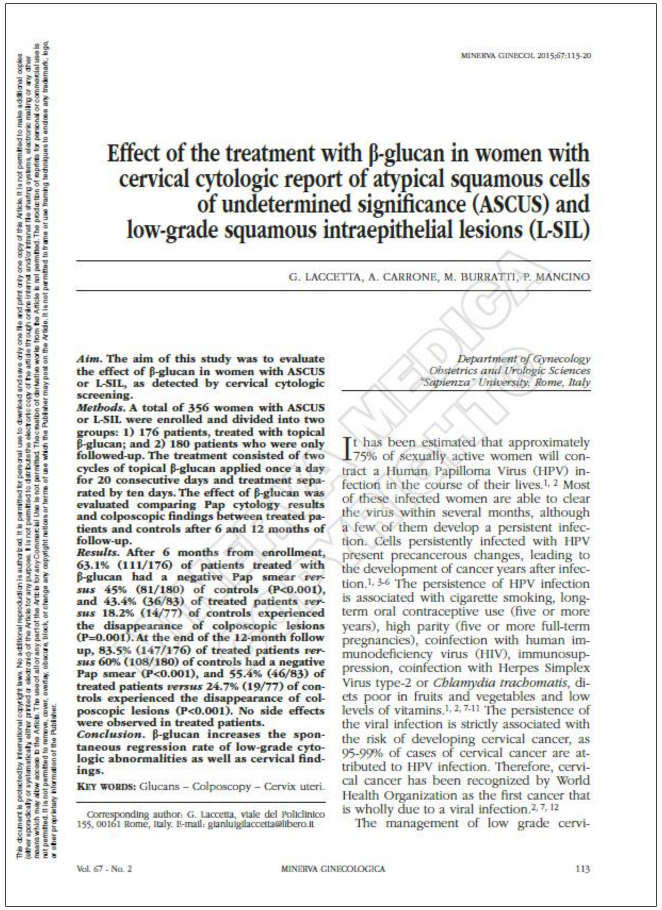
Group 2 (HPV-CIN1 histology):

- **3 months**: 20% -
- **6 months**: 60% -
- **12 months**: 80% -

Topical β-glucan treatment was associated with high regression/negativisation rates over 12 months in ASCUS/LSIL and HPV-CIN1 follow-up patients.

Scardamaglia P, Carraro C, Mancino P, Stentella P. Efficacia del carbossimetilbetaglucano nella regressione delle alterazioni citologiche cervicali di basso grado HPV correlate [Effectiveness of the treatment with beta-glucan in the HPV-CIN 1 lesions]. Minerva Ginecol. 2010 Oct;62(5):389-93. Italian. PMID: 20938424.

Overview Of Clinical Studies



MINERVA GINECOL 2015;67:113-20

Effect of the treatment with β-glucan in women with cervical cytologic report of atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesions (L-SIL)

G. LACCETTA, A. CARRONE, M. BURRATTI, P. MANCINO

Department of Gynecology Obstetrics and Urologic Sciences "Sapienza" University, Rome, Italy

Aim. **The aim of this study was to evaluate the effect of β-glucan in women with ASCUS or L-SIL, as detected by cervical cytologic screening.**

Methods. **A total of 356 women with ASCUS or L-SIL were enrolled and divided into two groups: 1) 176 patients, treated with topical β-glucan; and 2) 180 patients who were only followed-up. The treatment consisted of two cycles of topical β-glucan applied once a day for 20 consecutive days and treatment separated by ten days. The effect of β-glucan was evaluated comparing Pap cytology results and colposcopic findings between treated patients and controls after 6 and 12 months of follow-up.**

Results. **After 6 months from enrollment, 63.1% (111/176) of patients treated with β-glucan had a negative Pap smear *versus* 45% (81/180) of controls (P<0.001), and 43.4% (36/83) of treated patients *versus* 18.2% (14/77) of controls experienced the disappearance of colposcopic lesions (P=0.001). At the end of the 12-month follow up, 83.5% (147/176) of treated patients *versus* 60% (108/180) of controls had a negative Pap smear (P<0.001), and 55.4% (46/83) of treated patients *versus* 24.7% (19/77) of controls experienced the disappearance of colposcopic lesions (P<0.001). No side effects were observed in treated patients.**

Conclusion. **β-glucan increases the spontaneous regression rate of low-grade cytologic abnormalities as well as cervical findings.**

KEY WORDS: Glucans – Colposcopy – Cervix uteri.

Corresponding author: G. Laccetta, viale del Policlinico 155, 00161 Rome, Italy. E-mail: gianluigilaccetta@libero.it

It has been estimated that approximately 75% of sexually active women will contract a Human Papilloma Virus (HPV) infection in the course of their lives.[1, 2] Most of these infected women are able to clear the virus within several months, although a few of them develop a persistent infection. Cells persistently infected with HPV present precancerous changes, leading to the development of cancer years after infection.[1, 3-6] The persistence of HPV infection is associated with cigarette smoking, long-term oral contraceptive use (five or more years), high parity (five or more full-term pregnancies), coinfection with human immunodeficiency virus (HIV), immunosuppression, coinfection with Herpes Simplex Virus type-2 or *Chlamydia trachomatis*, diets poor in fruits and vegetables and low levels of vitamins.[1, 2, 7-11] The persistence of the viral infection is strictly associated with the risk of developing cervical cancer, as 95-99% of cases of cervical cancer are attributed to HPV infection. Therefore, cervical cancer has been recognized by World Health Organization as the first cancer that is wholly due to a viral infection.[2, 7, 12]

The management of low grade cervi-

Effect of the treatment with β-glucan in women with cervical cytologic report of ASCUS and L-SIL

Lacetta, et.al., 2015

- **Objective:** To assess the efficacy of a topical β-glucan-based local treatment (Colpofix®) in women with abnormal cervical cytology (ASCUS / L-SIL), compared with follow-up only ("wait & see").
- **Study model/design:** Prospective randomized 1:1, controlled study. Population: N=**356 women**, 16-75 years (mean age 33.3). Inclusion criteria: HPV+ women with ASCUS and/or LSIL cytology. Groups:
  - **Case:** Colpofix® (n=176). One application per day for 20 days, followed by a 10-day suspension, repeated for 2 months.
  - **Control:** Wait & see (n=180)

  Assessments: cytology and colposcopy at 6 and 12 months
- **Results:**

Negative cytology:

- **6 months**: 63.1% vs 45.0% (Colpofix vs control) (+18%)
- **12 months**: 83.5% vs 60.0% (+24%)

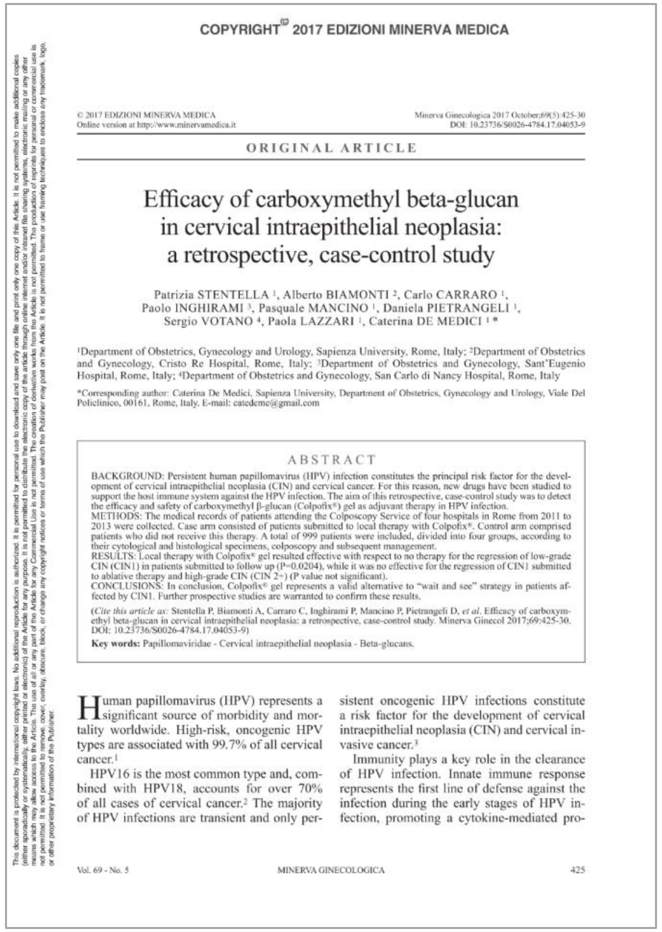
Negative colposcopy (baseline positive colposcopy subgroup: n=83 treated; n=77 control):

- **6 months**: 43.4% vs 18.2% (+25%)
- **12 months**: 55.4% vs 24.7% (+31%)

Topical β-glucan treatment was associated with higher rates of negative cytology and negative colposcopy at 6 and 12 months versus "wait & see".

Laccetta G, Carrone A, Burratti M, Mancino P. Effect of the treatment with β-glucan in women with cervical cytologic report of atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesions (L-SIL). Minerva Ginecol. 2015 Apr;67(2):113-20. Epub 2015 Feb 5. PMID: 25668505

Overview Of Clinical Studies



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ORIGINAL ARTICLE

Efficacy of carboxymethyl beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study

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[1]Department of Obstetrics, Gynecology and Urology, Sapienza University, Rome, Italy; [2]Department of Obstetrics and Gynecology, Cristo Re Hospital, Rome, Italy; [3]Department of Obstetrics and Gynecology, Sant'Eugenio Hospital, Rome, Italy; [4]Department of Obstetrics and Gynecology, San Carlo di Nancy Hospital, Rome, Italy

*Corresponding author: Caterina De Medici, Sapienza University, Department of Obstetrics, Gynecology and Urology, Viale Del Policlinico, 00161, Rome, Italy. E-mail: catedeme@gmail.com

ABSTRACT

BACKGROUND: Persistent human papillomavirus (HPV) infection constitutes the principal risk factor for the development of cervical intraepithelial neoplasia (CIN) and cervical cancer. For this reason, new drugs have been studied to support the host immune system against the HPV infection. The aim of this retrospective, case-control study was to detect the efficacy and safety of carboxymethyl β-glucan (Colpofix®) gel as adjuvant therapy in HPV infection.
METHODS: The medical records of patients attending the Colposcopy Service of four hospitals in Rome from 2011 to 2013 were collected. Case arm consisted of patients submitted to local therapy with Colpofix®. Control arm comprised patients who did not receive this therapy. A total of 999 patients were included, divided into four groups, according to their cytological and histological specimens, colposcopy and subsequent management.
RESULTS: Local therapy with Colpofix® gel resulted effective with respect to no therapy for the regression of low-grade CIN (CIN1) in patients submitted to follow up (P=0.0204), while it was no effective for the regression of CIN1 submitted to ablative therapy and high-grade CIN (CIN 2+) (P value not significant).
CONCLUSIONS: In conclusion, Colpofix® gel represents a valid alternative to "wait and see" strategy in patients affected by CIN1. Further prospective studies are warranted to confirm these results.

(*Cite this article as:* Stentella P, Biamonti A, Carraro C, Inghirami P, Mancino P, Pietrangeli D, *et al*. Efficacy of carboxymethyl beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study. Minerva Ginecol 2017;69:425-30. DOI: 10.23736/S0026-4784.17.04053-9)

Key words: Papillomaviridae - Cervical intraepithelial neoplasia - Beta-glucans.

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HPV16 is the most common type and, combined with HPV18, accounts for over 70% of all cases of cervical cancer.[2] The majority of HPV infections are transient and only persistent oncogenic HPV infections constitute a risk factor for the development of cervical intraepithelial neoplasia (CIN) and cervical invasive cancer.[3]

Immunity plays a key role in the clearance of HPV infection. Innate immune response represents the first line of defense against the infection during the early stages of HPV infection, promoting a cytokine-mediated pro-

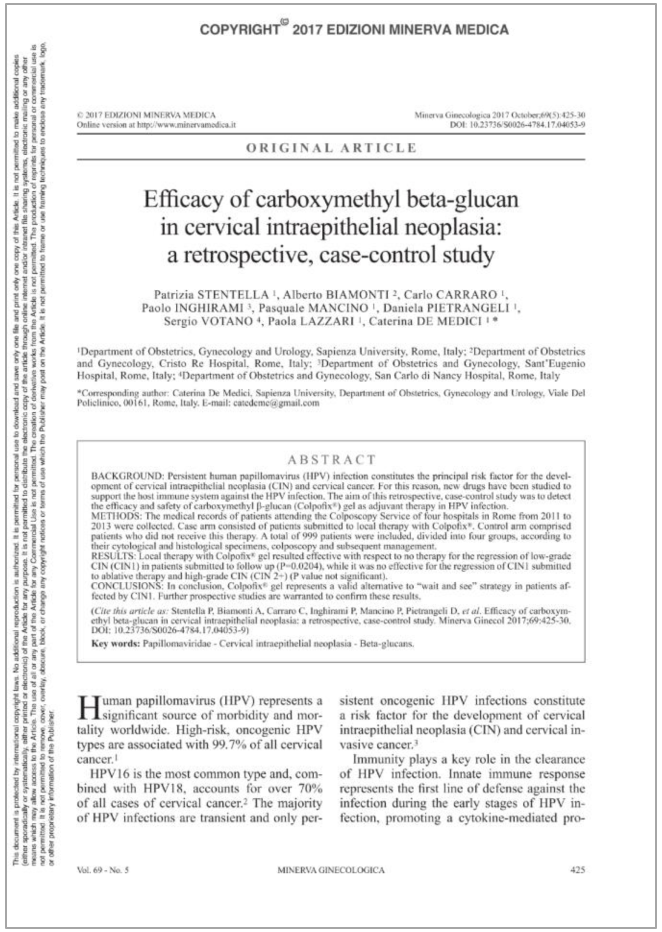
Efficacy of carboximethyl β-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study

Stentella, et.al., 2017

- **Objective:** To evaluate Colpofix® effectiveness versus no treatment on regression of ASCUS/LSIL and CIN1 during 12-month follow-up in a multicentre real-world cohort.
- **Study model/design:** Retrospective case-control study. Multicentric (4 hospitals). Follow-up: 12 months. Population: N=**999 women**; mean age 36.1 (+/- 10); 18-65 years. Inclusion: patients attending colposcopy for an abnormal Pap test. Arms and groups:
    - **Case-arm:** received Colpofix® treatment
    - **Control-arm:** did not receive Colpofix® treatment
    - **Distribution:**
        - **Group 1:** ASCUS/LSIL + negative colposcopy (187 / 124) → follow-up
        - **Group 2:** ASCUS/LSIL + positive colposcopy + CIN1 histology (168 / 144) → follow-up
        - **Group 3:** ASCUS/LSIL + positive colposcopy + CIN1 histology (99 / 98) → ablative therapy
        - **Group 4:** HSIL + positive colposcopy + CIN2/3 histology (81 / 98) → LEEP
    - **Treatment regimen and timeline:**
        - Colpofix®: 1 application/day for 20 days/month for 2 months
        - Follow-up assessments: cytology + colposcopy at 6 and 12 months
        - Post-procedure (groups 3-4): Colpofix® started one month after excisional treatment

Stentella P, Biamonti A, Carraro C, Inghirami P, Mancino P, Pietrangeli D, Votano S, Lazzari P, DE Medici C. Efficacy of carboxymethyl beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study. Minerva Ginecol. 2017 Oct;69(5):425-430. doi: 10.23736/S0026-4784.17.04053-9. PMID: 28675291.

Overview Of Clinical Studies



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ORIGINAL ARTICLE

Efficacy of carboxymethyl beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study

Patrizia STENTELLA [1], Alberto BIAMONTI [2], Carlo CARRARO [1], Paolo INGHIRAMI [3], Pasquale MANCINO [1], Daniela PIETRANGELI [1], Sergio VOTANO [4], Paola LAZZARI [1], Caterina DE MEDICI [1] *

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ABSTRACT

BACKGROUND: Persistent human papillomavirus (HPV) infection constitutes the principal risk factor for the development of cervical intraepithelial neoplasia (CIN) and cervical cancer. For this reason, new drugs have been studied to support the host immune system against the HPV infection. The aim of this retrospective, case-control study was to detect the efficacy and safety of carboxymethyl β-glucan (Colpofix®) gel as adjuvant therapy in HPV infection.
METHODS: The medical records of patients attending the Colposcopy Service of four hospitals in Rome from 2011 to 2013 were collected. Case arm consisted of patients submitted to local therapy with Colpofix®. Control arm comprised patients who did not receive this therapy. A total of 999 patients were included, divided into four groups, according to their cytological and histological specimens, colposcopy and subsequent management.
RESULTS: Local therapy with Colpofix® gel resulted effective with respect to no therapy for the regression of low-grade CIN (CIN1) in patients submitted to follow up (P=0.0204), while it was no effective for the regression of CIN1 submitted to ablative therapy and high-grade CIN (CIN 2+) (P value not significant).
CONCLUSIONS: In conclusion, Colpofix® gel represents a valid alternative to "wait and see" strategy in patients affected by CIN1. Further prospective studies are warranted to confirm these results.

(*Cite this article as:* Stentella P, Biamonti A, Carraro C, Inghirami P, Mancino P, Pietrangeli D, *et al*. Efficacy of carboxymethyl beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study. Minerva Ginecol 2017;69:425-30. DOI: 10.23736/S0026-4784.17.04053-9)

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Human papillomavirus (HPV) represents a significant source of morbidity and mortality worldwide. High-risk, oncogenic HPV types are associated with 99.7% of all cervical cancer.[1]

HPV16 is the most common type and, combined with HPV18, accounts for over 70% of all cases of cervical cancer.[2] The majority of HPV infections are transient and only persistent oncogenic HPV infections constitute a risk factor for the development of cervical intraepithelial neoplasia (CIN) and cervical invasive cancer.[3]

Immunity plays a key role in the clearance of HPV infection. Innate immune response represents the first line of defense against the infection during the early stages of HPV infection, promoting a cytokine-mediated pro-

Efficacy of carboximethyl β-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study

Stentella, et.al., 2017

RESULTS:

- **Key outcomes (6 and 12 months):**
  - **ASCUS/LSIL regression**: 96.8% vs 78% at 6 months; 98% vs 87% at 12 months (Colpofix vs control)
  - **CIN1 regression**: 95.7% vs 71% at 6 months; 95.7% vs 79% at 12 months (Colpofix vs control)
- **Post-conization / re-epithelialization (Groups 3-4):**
  - Negative histology (<CIN2+) at 6 and 12 months: no meaningful difference between Colpofix® and control (NS), consistent with the effect of surgical removal of abnormal tissue

ASCUS/LSIL regression:

- **6 months**: 96.8% vs 78% (p=0.02)
- **12 months**: 98% vs 87%

CIN1 regression:

- **6 months**: 95.7% vs 71% (p=0.02)
- **12 months**: 95.7% vs 79%

In a large multicentre real-world cohort, Colpofix® was associated with higher regression rates of ASCUS/LSIL and CIN1 at 6 and 12 months versus control.

Stentella P, Biamonti A, Carraro C, Inghirami P, Mancino P, Pietrangeli D, Votano S, Lazzari P, DE Medici C. Efficacy of carboxymethyl beta-glucan in cervical intraepithelial neoplasia: a retrospective, case-control study. Minerva Ginecol. 2017 Oct;69(5):425-430. doi: 10.23736/S0026-4784.17.04053-9. PMID: 28675291.

Overview Of Clinical Studies

Effects on Vaginal Microbiota Restoration and Cervical Epithelialization in Positive HPV Patients Undergoing Vaginal Treatment with Carboxy-Methyl-β-glucan

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Hindawi

Clinical Study

Effects on Vaginal Microbiota Restoration and Cervical Epithelialization in Positive HPV Patients Undergoing Vaginal Treatment with Carboxy-Methyl-Beta-Glucan

Giada Lavitola,[1] Luigi Della Corte,[1] Nicoletta De Rosa,[1] Carmine Nappi,[2] and Giuseppe Bifulco[1]

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Objective. Evaluate the effects of carboxy-methyl-beta-glucan on cervical epithelialization and on the vaginal microbiota in patients with HPV infection or low-grade cervical preneoplastic lesion (CIN 1). *Materials and Methods.* Seven-hundred eighty-four women with positive HPV tests or diagnosed with CIN 1 were enrolled in a retrospective case-control study. All the recruited women performed, at baseline and after 6 months, Pap test, HPV test, evaluation of vaginal health according to the Amsel criteria, colposcopy, and punch biopsy. The study population was then divided into 2 groups in relation to the therapy performed during the follow-up period. Group A performed treatment with vaginal gel based on carboxy-methyl-beta-glucan (1 application/day for 20 days per month for 3 months). Group B was the control group. *Results.* The patients of group A had a significant improvement in the ectopia pattern and a greater number of cases with metaplasia in the maturation phase with a significant increase in Lugol uptake. In the experimental group, a significant improvement in the pH indices, a negative Swift test and a resolution of the leucorrhoea were observed. A negative result of the 37.1% Pap test and the 39.9% HPV test (vs. 15.2% and 16.5%, respectively) were demonstrated in the treatment group with respect to the control group. A negativization of the colposcopic pictures was observed with a reduction in the amount of CIN 1 found higher in the treatment group. *Conclusions.* Vaginal therapy based on carboxy-methyl-beta-glucan has been able to improve overall vaginal health; this effect seemed to positively impact the risk of persistence and progression of CIN.

1. Introduction

HPV (human papillomavirus) infection is transmitted mainly by sexual contact, and the cervix is the organ most sensitive to the oncogenic action of papillomavirus. The cervix is covered by two epithelia: the esocervical one and the paved type and the endocervical one and the cylindrical type. This transition zone represents, from a biological point of view, an area of instability because it allows easier access to the basal site of the target reserve cells of oncogenic agents such as HPV [1].

The HPV infection is very common especially in young women (highest incidence peak between 20 and 30 years). There is a percentage of women at risk who are positive for the infection but in whom the virus did not cause cervical precancerous lesions (CIN). When the virus integrates into the cells of the cervical epithelium, it determines a process of cellular transformation and gives rise to the CIN lesions [2, 3].

Recent data show a significant correlation between immune status and persistence of the virus. The vaginal microbiota plays an important role in modulating the immune system of the female genital tract [4]. *Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus inners*, and *Lactobacillus jensenii* appear to dominate the vagina of most healthy women. The composition of vaginal microbiota is

Lavitola, et.al., 2020

- **Objective:** To evaluate the effect of vaginal treatment with carboxy-methyl-beta-glucan on vaginal microbiota restoration and cervical epithelialization in HPV-positive women, compared with an untreated control group.
- **Study model/design:** Retrospective case-control study. Multicentric. N=**784 women** (392 treated/392 control). Mean age: 34.11 (+/- 6.35) years. T=6 months.
- **Inclusion criteria:** women 18-60 years old; HPV-positive and/or CIN1 positive by punch biopsy.
- **Groups**:
  - **Group A:** 392 treated women with Colpofix® (1 application/day for 20 days per month for 3 months)
  - **Group B:** 392 untreated women (control group)
- **Timeline:** baseline examination → Months 1-3: treatment cycles; T1: 6-month follow-up
- **Endpoints:**
  - HPV-related outcomes
  - HPV test, Pap smear (cytology), colposcopy, biopsy (when performed)
  - Vaginal health and epithelialization markets → vaginal pH>4.5, Whiff test, leucorrhea, Lugol test (non-captive), ectopy >2/3, metaplasia >20%

Lavitola G, Della Corte L, De Rosa N, Nappi C, Bifulco G. Effects on Vaginal Microbiota Restoration and Cervical Epithelialization in Positive HPV Patients Undergoing Vaginal Treatment with Carboxy-Methyl-Beta-Glucan. Biomed Res Int. 2020 Apr 27;2020:5476389. doi: 10.1155/2020/5476389. PMID: 32420349; PMCID: PMC7201736.

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Clinical Study

Effects on Vaginal Microbiota Restoration and Cervical Epithelialization in Positive HPV Patients Undergoing Vaginal Treatment with Carboxy-Methyl-Beta-Glucan

Giada Lavitola,[1] Luigi Della Corte,[1] Nicoletta De Rosa,[1] Carmine Nappi,[2] and Giuseppe Bifulco[1]

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- **RESULTS:** Colpofix® improves HPV-related outcomes and vaginal/cervical health at 6 months

HPV/cervix outcomes

A) HPV test positivity:

- Colpofix®: 98.7% → 59.3% (-39.1%)
- Control: 97.8% → 81.7% (-16.5%)

= ~2.3× greater improvement vs control (p<0.001)

B) Positive cytology (Pap smear):

- Colpofix®: 81.3% → 51.1% (−37.1%)
- Control: 80.4% → 68.1% (−15.2%)

= ~2.4× greater improvement vs control

C) Positive colposcopy:

- Colpofix®: 82.1% → 40.8% (−50.3%)
- Control: 82.0% → 60.5% (−26.2%)

= ~1.9× greater improvement vs control

D) Positive biopsy:

- Colpofix®: 63.4% → 39.7% (−37.4%)
- Control: 62.9% → 56.1% (−10.8%)

= ~3.4× greater improvement vs control (p<0.001)

Vaginal microenvironment + epithelialization

A) Whiff test (dysbiosis marker)

- Colpofix®: 47.5% → 12.6% (-73.5%)
- Control: 44.4% → 42.2% (-4.9%)

B) Leucorrhoea

- Colpofix®: 84.1% → 27.4% (−67.4%)
- Control: 79.3% → 68.1% (−14.1%)

= ~5× lower vs control at 6 months

C) Ectopy >2/3

- Colpofix®: 39.7% → 20.4% (−48.6%)
- Control: 33.5% → 29.2% (−13%) (p=0.006)

D) Metaplasia >20%

- Colpofix®: 23.2% → 49.7% (+115%)
- Control: 28.3% → 32.4% (+4%) (p<0.001)

Lavitola G, Della Corte L, De Rosa N, Nappi C, Bifulco G. Effects on Vaginal Microbiota Restoration and Cervical Epithelialization in Positive HPV Patients Undergoing Vaginal Treatment with Carboxy-Methyl-Beta-Glucan. Biomed Res Int. 2020 Apr 27;2020:5476389. doi: 10.1155/2020/5476389. PMID: 32420349; PMCID: PMC7201736.

APPENDIX

- **Additional Information**

Additional Information: EFSA-Approved Claims

EFSA-APPROVED CLAIMS

- Prevention and treatment of cervical lesions caused by Human Papillomavirus

Thank you!