CLINICAL TRIAL
PALOMA

ClinicalTrials.gov
NCT04002154

PAPILOCARE®

PALOMA CLINICAL TRIAL
FINAL RESULTS

1ST TREATMENT TO PREVENT AND TREAT HPV-DEPENDENT CERVICAL LESIONS◊

30% OF CIN I WILL PROGRESS TO CIN II/CIN III WITHIN 10 YEARS[1]

HIGH-RISK HPV VIRAL DNA IS FOUND IN 87% OF CERVICAL CANCERS[2]

(HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68)

Procare Health
Naturally woman

◊Low grade lesions: ASCUS / LSIL

www.papilocare.com
www.procarehealth.com

FINAL RESULTS

EFFICACY AND SAFETY ENDORSED BY CLINICAL STUDIES[3]

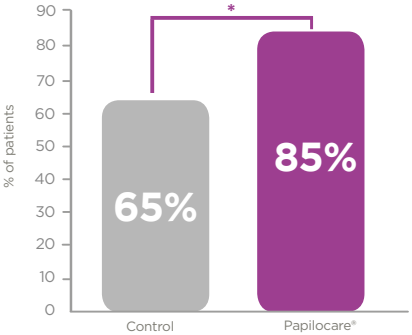
CLINICAL TRIAL
PALOMA[3]
ClinicalTrials.gov NCT04002154

PAPILOCARE®

TOTAL POPULATION

NORMALIZATION OF ASCUS/LSIL LESIONS
(Primary Endpoint)

Cytological normalization with concordant colposcopy at **6 months** vs control



NNT=4.90

n=84
p=0.0311
NNT= 4.90
Chi-Square Test

NORMALIZATION OF HPV-DEPENDENT CERVICAL LESIONS IN

85%*

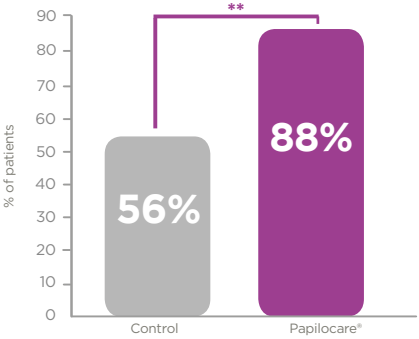
of the total population **at 6 months vs 65%** in the control group

* Statistically significant: p<0,05

HIGH-RISK HPV SUBPOPULATION

NORMALIZATION OF ASCUS/LSIL LESIONS
(Primary Endpoint)

Cytological normalization with concordant colposcopy at **6 months** vs control



NNT=3.84

n=66
p=0.0034
NNT= 3.84
Chi-Square Test

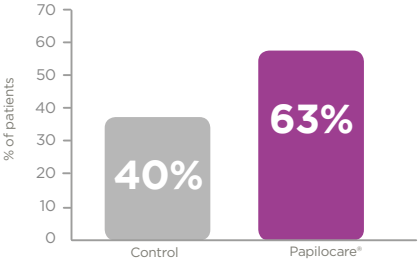
NORMALIZATION OF HPV-DEPENDENT CERVICAL LESIONS IN

88%**

of High-Risk HPV+ patients **at 6 months vs 56%** in the control group

** Statistically significant: p<0,01

HPV CLEARANCE AT 6 MONTHS
(Secondary Endpoint)



NNT=4.44

n=65
p=0.0767
NNT= 4.44
Test Chi-cuadrado

HPV CLEARANCE IN

63%

of High-Risk HPV+ patients **at 6 months vs 40%** in the control group

High Risk virus of genotype: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

PAPILOCARE®

ABSTRACTS PRESENTED AT ASCCP 2019

Clinical Studies[4]

ASCCP

Annual Scientific Meeting on Anogenital & HPV-Related Diseases
April 4-7 | Atlanta, GA

APRIL 4-7TH, 2019
ATLANTA, USA

EFFECT OF A *CORIOLUS VERSICOLOR*-BASED VAGINAL GEL IN HIGH-RISK HPV INFECTED PATIENTS. RESULTS OF DIFFERENT STUDIES[4].

Authors: Javier Cortés[1], Gilles T. Seydoux[2], Damián Dexeus[3], Santiago Palacios[4], Luis Serrano[5], Clara Gajino[6], Elena Marín[7], Margarita Riera[8]
[1]Senior Consultant in Gynecological Oncology, Private practice, Palma de Mallorca, (Spain), [2]Procare Health SL, Barcelona (Spain), [3]Women's Health Institute, Barcelona, (Spain), [4]Instituto Palacios de Salud y Medicina de la Mujer, Madrid (Spain),
[5]Centro Médico Gabinete Velázquez, Madrid (Spain), [6]Hospital Materno Infantil Teresa Herrera, A Coruña, (Spain), [7]Hospital Álvaro Cunqueiro, Vigo (Spain), [8]Institut Català de la Salut. Hospitalet de LLobregat, (Spain)

BACKGROUND AND OBJECTIVE

A new multi-ingredient *Coriolus versicolor*-based vaginal gel has been recently marketed in Europe to prevent and treat HPV-dependent low-grade cervical lesions. Objective: to evaluate the consistency of the results observed with the gel on the HPV clearance criteria in high-risk HPV-infected women in different studies.

METHODS

Results from 3 independent, observational, non-comparative studies carried out in 3 different public university centers in Spain with similar design characteristics **(figure 1)** were evaluated together with the pre-analysis of the final results of one clinical trial (Paloma clinical trial)[1] whose design is observed in **Table 1 and figure 2**.

Vigo prospective study[2]: HPV clearance at 6 months of 25 patients infected by HPV 16 and/or 18 was evaluated as secondary endpoint.

Coruña retrospective study[3]: 57 medical records of patients with high-risk HPV were analyzed. HPV clearance at 6 months was evaluated as primary endpoint.

Hospitalet retrospective study[4]: Data from 91 high-risk HPV patients were evaluated. Primary endpoint: composite efficacy consisting in percentage of patients with normal cytology and/or HPV clearance at 6 months.

RESULTS

The pre-analysis of the final results of the Paloma clinical trial **showed 63% of high-risk HPV clearance vs 42% in the control group (wait and see approach) at 6 months (data from 64 patients), as observed in figure 3.** Concerning independent studies, after 6 months of treatment, 48% of HPV 16-18 infected patients have cleared (Vigo study), a reduction of 58% was observed in the number of high-risk HPV-positive patients (Coruña study) and 72.5% of patients negativized cytology and/or cleared HPV (Hospitalet study) vs baseline ($p \leq 0.0001$ for all results, Chi-square). These results show strong consistency among the Paloma clinical trial and the 3 independent Phase IV studies **(figure 4)**.

CONCLUSION

The use of a *Coriolus versicolor*-based vaginal gel in clinical practice shows a significant and consistent benefit for high-risk HPV clearance.

Data from further ongoing studies and clinical trials should confirm these exciting results.

1.Paloma Clinical Trial data on file . **2.** Gil Andrés M et al. ASCCP 2018, Las Vegas, US. Late-Breaking abstracts. Poster#71. **3.** Gajino C. 32nd IPCV 2018. Sydney, Australia. Abstract #IPVC8-0489.
4. Riera M et al. J Low Genit Tract Dis. 2018;22(April 2, suppl 1): oral communication

PAPILOCARE®

ABSTRACTS PRESENTED AT EFC 2019

Clinical Studies[5,6]
& Scientific Innovation[7] Data

EFC 2019
EUROPEAN CONGRESS

SEPTEMBER 25-28TH, 2019
ROME, ITALY

CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN THE CLEARANCE AND/OR CYTOLOGY NORMALIZATION IN HIGH-RISK HPV POSITIVE PATIENTS[5]

Authors:
M. Riera, B. Rupérez, I. Lázaro, A. Felgueroso, E. Fontanet, Y. Tena.
Institut Català de la Salut. L'Hospitalet de Llobregat - Barcelona (Spain)

Objective

- To evaluate the efficacy of a *Coriolus versicolor*-based vaginal gel to clear and/or normalize cytology in high-risk HPV (HR-HPV+) patients.

Methods

- Observational, case-control study:
  - Cases: HR-HPV+ patients aged between 20 and 65 with ASCUS/LSIL or normal cytology at baseline, treated with a daily application of a *Coriolus versicolor*-based vaginal gel for 3 weeks and then alternate days up to 6 months.
  - Controls: Population with the same characteristics managed according to usual clinical practice by another gynecologist of the same unit.
- Patient data were obtained from the hospital database. Cases and controls had been derived from the general Gynecology Consultation to the Cervical Pathology Unit and managed following the protocols of the Catalan Institute of Oncology (ICO): control visit at 6 months for cases and at 12 months for controls.
- HR-HPV+ evaluation was performed by hybrid capture. Vaccinated, immunosuppressed and pregnant patients were excluded. Follow-up duration: 6 months. Recruitment period: December 2016 to October 2017.
- Endpoint: % of responders (composite efficacy variable consists of percentage of patients with normal cytology and/or HPV clearance) at control visit according to ICO protocols vs baseline.

Results

- A total of 91 HR-HPV+ patients were included as cases (46 with ASCUS/LSIL and 45 with normal cytology) and 65 as controls.
- At control visit, 72.5% of cases (66/91) vs 24.6% (16/65) of controls negativized the cytology and/or cleared HPV, so were classified as responders (Chi-square, p<0.0001 between groups) (figure 1).

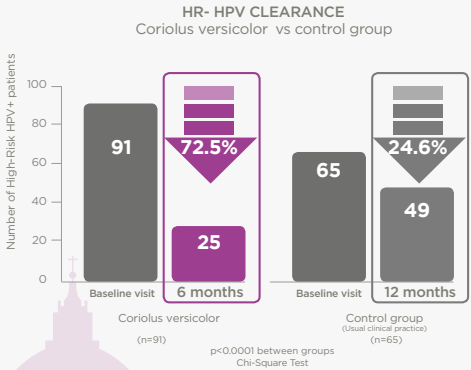


Figure 1: HR-HPV clearance.

Conclusions

- After 6 months of treatment, the *Coriolus versicolor*-based vaginal gel appears to be effective both in normalizing ASCUS and LSIL cytology alterations caused by high-risk HPV and in the clearance of high-risk HPV.
- Further prospective studies are needed to confirm these exciting results.

EFC2019 EUROPEAN CONGRESS

EFFECT OF A *CORIOLUS VERSICOLOR*-BASED VAGINAL GEL IN HPV INFECTED WOMEN: NORMALIZING HPV-DEPENDENT CERVICAL LESIONS (ASCUS/LSIL) AND HIGH-RISK HPV CLEARANCE[6]

Authors:
L. Serrano[1], A.C. López[2], S. González[1], S. Palacios[3], D. Dexeus[4], C. Centeno[5], P. Coronado[6], J. de la Fuente[7], J A. López Fernández[8], C. Vanrell[9] and J. Cortés[10]
[1]Centro Médico Gabinete Velázquez, Madrid, [2]Hospital Quironsalud, Málaga, [3]Instituto Palacios, Salud y Medicina de la Mujer, Madrid, [4]Women´s Health Institute, Barcelona, [5]Clínica Diatros, Barcelona, [6]Hospital Clínico San Carlos, Madrid, [7]Hospital Universitario Infanta Leonor, Madrid, [8]Hospital General Universitario, Alicante, [9]Hospital de la Santa Creu i Sant Pau, Barcelona, [10]Private Practice, Palma de Mallorca.

Objective

• To evaluate the efficacy of a *Coriolus versicolor*- based vaginal gel (CVVG) repairing HPV-dependent cervical lesions (ASCUS/LSIL cytology with concordant colposcopy image) and in the clearance of high-risk HPV (HR-HPV).

Methods

• Randomized, open-label, parallel-group, controlled clinical trial (Paloma Clinical Trial).

• HPV+ women aged between 30 and 65 withcytology of ASCUS or LSIL and concordant colposcopy image were randomized into 3 groups:

- A) CVVG 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months.
- B) CVVG 1 cannula/day for 3 months + 1 cannula/alternate days for 3 months.
- C) Control group: no treatment (usual clinical practice).

• Main results of the Paloma trial are presented:
- Percentage of HPV+ and HR-HPV+ subpopulation of patients with normal cytology and concordant colposcopy image at 3 and 6 months (primary endpoint).
- Percentage of patients with HR-HPVclearance at 6 months (clearance: total and partial clearance with concordant cytological normalization).

• Pap smear and PCR (Clart®) evaluations were centrally-conducted at the IECM laboratory (Lugo, Spain). *Coriolus versicolor* arms (A+B) were combined and chi-square test was used.

Results

• In the total population, at 3 and 6 months respectively, 78% (46/59) and 85% (45/53) of patients treated with CVVG had negative cytology with concordant colposcopy vs. 55%(17/31) and 65% (20/31) in control group (p=0.02 and p=0.03; Chi-square).

• In the HR-HPV+ subpopulation, normal cytology and concordant colposcopy image was observed in 80% (35/44) and 88% (36/41) of patients treated by CVVG vs 52% (13/25) and 56% (14/25) of patients in control group (p=0.01 and p=0.003 respectively; Chi-square) (figure 1).

• HR-HPV clearance at 6 months was observed in 63% (25/40) vs 40% (10/25) patients treated with CVVG vs. control group (p=0.07; Chi-square), respectively (figure 2).

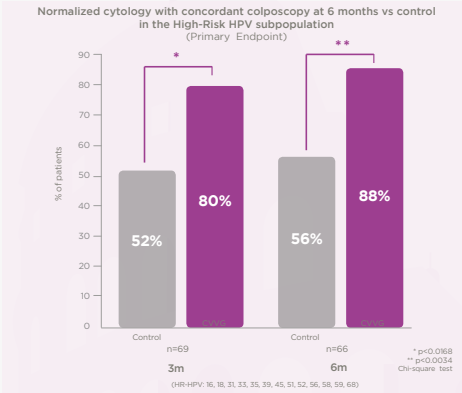


Figure 1: Papilocare® on repairing cervical lesions (ASCUS/LSIL) in the High-Risk hpv subpopulation.

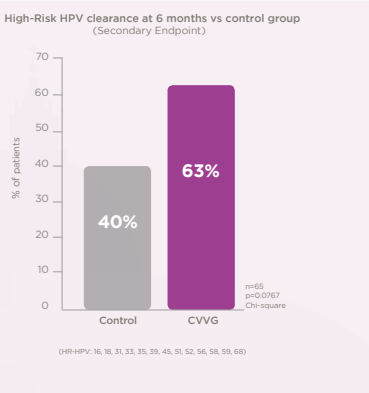


Figure 2: Papilocare® on High-Risk HPV clearance.

Conclusions

• *Coriolus versicolor*-based vaginal gel shows a statistically significant efficacy in normalizing HPV-dependent cervical lesions.

• *Coriolus versicolor*-based vaginal shows a trend to facilitate HPV clearance, especially in HR-HPV subpopulation.

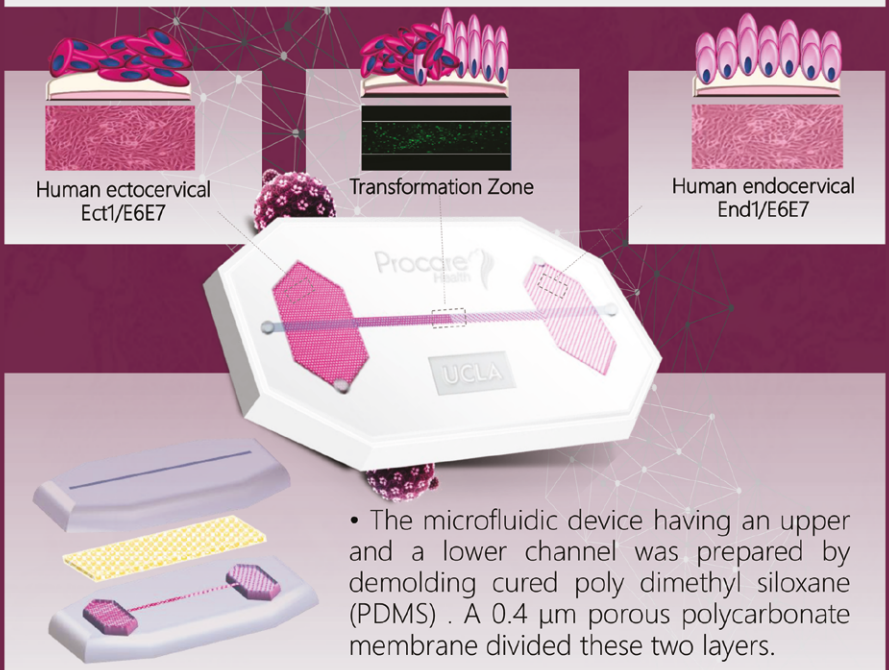
EFC2019 EUROPEAN CONGRESS

HUMAN UTERINE CERVIX-ON-A-CHIP: ESTABLISHING THE FIRST IN VITRO MODEL TO STUDY THE DEVELOPMENT OF CERVICAL CARCINOMA AND HUMAN PAPILOMA VIRUS MECHANISM OF ACTION [7]

D. Khorsandi [1, 2], R. Haghniaz [2], Y. Gaslain [3], J. Combalia [3], C. Emsellem [3], S. Palacios [4], A. Khademhosseini [2]

[1]Faculty of Pharmacy, University of Barcelona - Barcelona (Spain), [2]California NanoSystems Institute (CNSI), University of California - Los Angeles - Los Angeles (United States of America), [3]Medical Department, Procare Health Iberia SL - Barcelona (Spain), [4]Instituto Palacios de Salud y Medicina de la Mujer - Madrid (Spain)

The cost of drug discovery is steadily increasing owing to the limited predictability of two-dimensional (2D) cell culture and animal models. The objective of this study was to develop a microfluidic 'uterine cervix-on-a-chip', a dynamic 3D platform that let the cultured cells mimic the native human uterine cervix histomorphology *in vitro* aiming to study the transformation zone of cervix during Human Papilloma virus (HPV) infection and cervical cancer development.



• The microfluidic device having an upper and a lower channel was prepared by demolding cured poly dimethyl siloxane (PDMS) . A 0.4 µm porous polycarbonate membrane divided these two layers.

Conclusion

Uterine cervix-on-a-chip may provide the first *in vitro* model for studies on cervix physiology, real-time and high-resolution imaging, and analysis of biological responses in the cervix, as well as drug development. This technology can allow both types of epithelial cells to grow on from both sides of the chip to reach each other and make the Squamo-columnar junction, which is the target zone of HPV.

EFC2019
EUROPEAN CONGRESS

PAPILOCARE®

ABSTRACTS PRESENTED AT ESGO 2019

Clinical Studies[3,8,9]

ESGO
European Society of Gynaecological Oncology

NOVEMBER 2-5TH, 2019
ATHENS, GREECE

Effect of a multi-ingredient vaginal gel in HPV infected women: normalizing HPV-dependent cervical lesions (ASCUS/LSIL) and high-risk HPV clearance[3]

Authors:
L. Serrano[1], A.C. López[2], S. González[1], S. Palacios[3], D. Dexeus[4], C. Centeno[5], P. Coronado[6], J. de la Fuente[7], J A. López Fernández[8], C. Vanrell[9] and J. Cortés[10]
[1]Centro Médico Gabinete Velázquez, Madrid, [2]Hospital Quironsalud, Málaga, [3]Instituto Palacios, Salud y Medicina de la Mujer, Madrid, [4]Women´s Health Institute, Barcelona, [5]Clínica Diatros, Barcelona, [6]Hospital Clínico San Carlos, Madrid, [7]Hospital Universitario Infanta Leonor, Madrid, [8]Hospital General Universitario, Alicante, [9]Hospital de la Santa Creu i Sant Pau, Barcelona, [10]Private Practice, Palma de Mallorca.

Background/Objective:

In previous clinical studies Papilocare®, a non-hormonal multi-ingredient vaginal gel, has shown to significantly influence the re-epithelialization of the cervix and the rebalancing of the vaginal microbiota that favors the natural process of vaginal immunity.

The objective of this study was to evaluate the effect of Papilocare® on the normalization of cervical HPV-dependent atypia (ASCUS and LSIL) and associated colposcopic alterations, and on the clearance of high-risk HPV (HR-HPV).

Methods

Multicenter, randomized, open-label, parallel-group, usual practice-controlled clinical trial (Paloma Clinical Trial).

Unvaccinated HPV+ women aged between 30 and 65 with cytology of ASCUS or LSIL and concordant colposcopy image were randomized into 3 groups:

- **A)** Papilocare® 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months
- **B)** Papilocare® 1 cannula/day for 3 months + 1 cannula/alternate days for 3 months
- **C)** Control group: no treatment (usual clinical practice)

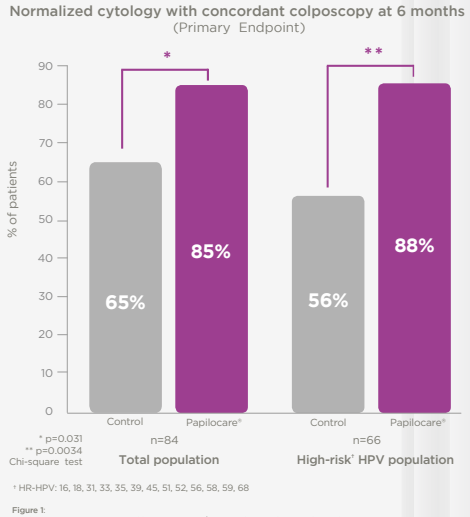
Percentage of patients with normalization of the lesions (normal cytology and concordant colposcopy image) as the primary endpoint and percentage of patients with HR-HPV clearance (total clearance or baseline-HPV partial clearance together with cytological and colposcopy normalization) were evaluated at 6 months.

Pap smear evaluation and HPV identification (Clart® HPV4) were blind and centrally-conducted by an independent researcher at the IECM laboratory (Lugo, Spain). Papilocare® arms (A+B) were combined as treatment group and Chi-square test was used.

Results

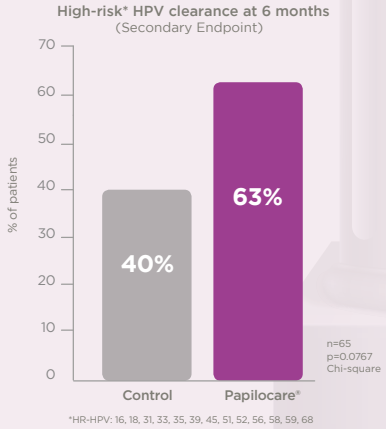
A total of 84 patients (mean age of 41 yo, evenly distributed among groups; total population) were evaluated (53 vs 31 in treatment and control groups, respectively) of which 66 were HR-HPV (HR-HPV subpopulation; 41 vs 25 in treatment and control groups, respectively). Results of patients with cytology normalization and concordant colposcopy at 6 months in both total and HR-HPV populations are shown in **Figure 1.**

Figure 2 shows clearance results in HR-HPV subpopulation at 6 months.



† HR-HPV: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

Figure 1:
Papilocare® on repairing cervical lesions (ASCUS/LSIL cytology and concordant colposcopy image)



*HR-HPV: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

Figure 2:
Papilocare® on high-risk HPV clearance.

Conclusions

After the six-month treatment period, Papilocare® has shown statistically significant efficacy in normalizing HPV-dependent cervical lesions (cytology of ASCUS/LSIL and concordant colposcopy images), especially in HR-HPV subpopulation. A trend to increase HPV clearance has also been observed in HR-HPV subpopulation.

ESGO European Society of Gynaecological Oncology

21st European Congress on Gynaecological Oncology
Nov 2-5, 2019 | Athens, Greece

Efficacy of a multi-ingredient vaginal gel in repairing HPV-dependent cervical lesions (ASCUS/LSIL) according to the risk of HPV strains[8]

Authors:
L. Serrano[1], A.C. López[2], S. González[1], S. Palacios[3], D. Dexeus[4], C. Centeno[5], P. Coronado[6], J. de la Fuente[7], J A. López Fernández[8], C. Vanrell[9] and J. Cortés[10]
[1]Centro Médico Gabinete Velázquez, Madrid, [2]Hospital Quironsalud, Málaga, [3]Instituto Palacios, Salud y Medicina de la Mujer, Madrid, [4]Women´s Health Institute, Barcelona, [5]Clínica Diatros, Barcelona, [6]Hospital Clínico San Carlos, Madrid, [7]Hospital Universitario Infanta Leonor, Madrid, [8]Hospital General Universitario, Alicante, [9]Hospital de la Santa Creu i Sant Pau, Barcelona, [10]Private Practice, Palma de Mallorca.

Background/Objective:

High-risk strains of HPV are well established as the causative agents for cervical dysplasia and cervical cancer. It is also well known that pre-cancerous cervical lesions persist longer and progress quickly in women infected by high-risk HPV than in women with non-oncogenic HPV strains.

The aim of this study was to evaluate the efficacy of Papilocare® -a multi-ingredient vaginal gel- in repairing HPV-dependent cervical lesions (ASCUS/LSIL) in three groups of patients according to the oncogenic potential of HPV strains.

Methods

Multicenter, randomized, open-label, parallel-group, usual practice-controlled clinical trial (Paloma Clinical Trial).

Unvaccinated HPV+ women aged between 30 and 65 with cytology of ASCUS or LSIL and concordant colposcopy image were randomized into 3 groups:

- **A)** Papilocare® 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months
- **B)** Papilocare® 1 cannula/day for 3 months + 1 cannula/alternate days for 3 months
- **C)** Control group: no treatment (usual clinical practice)

Primary endpoint of the Paloma Clinical trial, percentage of patients with normalization of lesions (normal cytology and concordant colposcopy image) at 6 months, evaluated in total population, high-risk subpopulation (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) and the subpopulation infected by any combination of 16, 18 and 31 , is presented.

Pap smear evaluation and HPV identification (Clart® HPV4) were blind and centrally-conducted by an independent researcher at the IECM laboratory (Lugo, Spain). Papilocare® arms (A+B) were combined as treatment group and chi-square test was used.

Results

A total of 84, 66 and 29 patients corresponding to total population, and high-risk and 16-18-31 subpopulations were evaluated, respectively.

At 6 months, normal cytology and concordant colposcopy image was observed in 85% (45/53), 88% (36/41) and 73% (11/15) of patients treated with Papilocare® vs 65% (20/31), 56% (14/25) and 43% (6 /14) of patients in control group, in the total population, and high-risk and 16-18-31 subpopulations (p=0.0311; p=0.0034; p=0.0959), respectively **(figure 1)**.

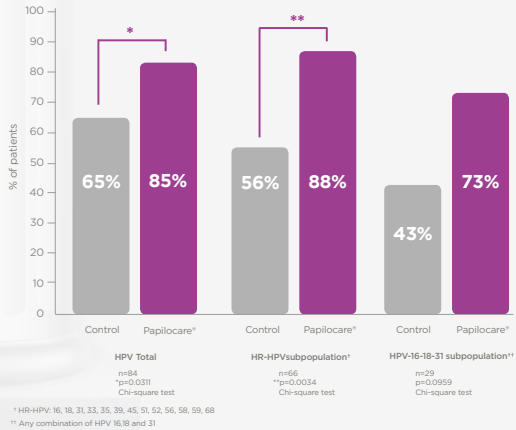


Figure.1
Papilocare® on repairing HPV-dependent cervical lesions (ASCUS/LSIL cytology and concordant colposcopy image) at 6 months in three groups of patients according to the oncogenic potential of HPV strains.

Conclusion

While the spontaneous normalizations of HPV-dependent cervical lesions clearly decreased according to the risk of HPV strains, the robust efficacy of Papilocare® in normalizing cervical lesions was maintained in the 3 subgroups, with statistically significant difference versus control group in the total population and HR-HPV subpopulation.

ESGO European Society of Gynaecological Oncology
21st European Congress on Gynaecological Oncology
Nov 2-5, 2019 | Athens, Greece

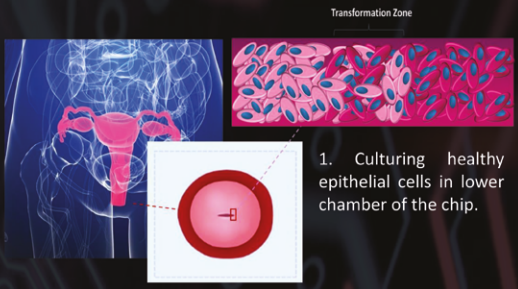
HUMAN UTERINE CERVIX-ON-A-CHIP: ESTABLISHING THE FIRST IN VITRO MODEL TO STUDY THE DEVELOPMENT OF CERVICAL CARCINOMA AND HUMAN PAPILOMA VIRUS MECHANISM OF ACTION [9]

D. Khorsandi [1,2], R. Haghniaz [2], Y. Gaslain [3], J. Combalia [3], C. Emsellem [3], S. Palacios [4], A. Khademhosseini [2]

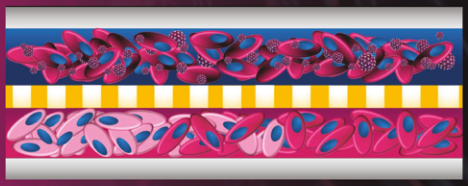
[1]Faculty of Pharmacy, University of Barcelona - Barcelona (Spain), [2]California NanoSystems Institute (CNSI), University of California - Los Angeles - Los Angeles (United States of America), [3]Medical Department, Procare Health Iberia SL - Barcelona (Spain), [4]Instituto Palacios de Salud y Medicina de la Mujer - Madrid (Spain)

INTRODUCTION

The cost of drug discovery is steadily increasing owing to the limited predictability of two-dimensional (2D) cell culture and animal models. The objective of this study was to develop a microfluidic 'uterine cervix-on-a-chip', a dynamic 3D platform that let the cultured cells mimic the native human uterine cervix histomorphology *in vitro* aiming to study the transformation zone of cervix during Human Papilloma virus (HPV) infection and cervical cancer development.

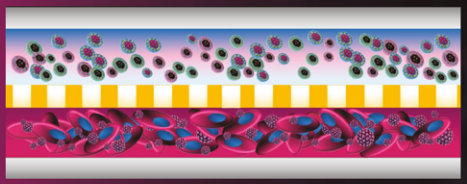


1. Culturing healthy epithelial cells in lower chamber of the chip.



2. Adding infected cell via upper chamber of the chip to mimic the infection and let the viruses go over the porous membrane.

3. By changing the upper layer, the infected model is ready to test new drugs and treatments.



4. By adding the new treatment/ drug compound to the system through upper chamber, we can detect the treatment's mechanism of action on the infected viruses real time.

CONCLUSION

Uterine cervix-on-a-chip may provide the first *in vitro* model for studies on cervix physiology, real-time and high-resolution imaging, and analysis of biological responses in the cervix, as well as drug development. This technology can allow both types of epithelial cells to grow on from both sides of the chip to reach each other and make the Squamo-columnar junction, which is the target zone of HPV.

ESGO European Society of Gynaecological Oncology

21st European Congress on Gynaecological Oncology
Nov 2-5, 2019 | Athens, Greece

PAPILOCARE®

ORAL COMMUNICATIONS[10-12] & ABSTRACTS[13] PRESENTED AT EUROGIN 2019

Clinical Studies

EUROGIN 2019
INTERNATIONAL MULTIDISCIPLINARY HPV CONGRESS

DECEMBER 4-7TH, 2019
MONACO

EFFECT OF A CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN HPV INFECTED WOMEN: NORMALIZING HPV-DEPENDENT CERVICAL LESIONS (ASCUS/LSIL) AND HIGH-RISK HPV CLEARANCE[10]

Authors:
L. Serrano[1], A.C. López[2], S. González[1], S. Palacios[3], D. Dexeus[4], C. Centeno[5], P. Coronado[6], J. de la Fuente[7], J. A. López and J. Cortés[10] Fernández[8], C. Vanrell[9]
[1]Centro Médico Gabinete Velázquez, Madrid, [2]Hospital Quironsalud, Málaga, [3]Instituto Palacios, Salud y Medicina de la Mujer, Madrid, [4]Women´s Health Institute, Barcelona, [5]Clínica Diatros, Barcelona, [6]Hospital Clínico San Carlos, Madrid, [7]Hospital Universitario Infanta Leonor, Madrid, [8]Hospital General Universitario, Alicante, [9]Hospital de la Santa Creu i Sant Pau, Barcelona, [10]Private Practice, Palma de Mallorca.

Objective

In previous clinical studies a non-hormonal Coriolus versicolor-based vaginal gel (CVVG) has shown to significantly influence the re-epithelialization of the cervix and the rebalancing of the vaginal microbiota that favors the natural process of vaginal immunity. The objective was to evaluate the effect of the CVVG on the normalization of cervical HPV-dependent atypia (ASCUS and LSIL) and associated colposcopic alterations, and on the clearance of high-risk HPV (HR-HPV).

Methods

Multicenter, randomized, open-label, parallel-group, usual practice controlled clinical trial (Paloma Clinical Trial). Unvaccinated HPV+ women aged between 30 and 65 (mean age of 41 yo, evenly distributed among groups) with cytology of ASCUS or LSIL and concordant colposcopy image were included. Patients were randomized into 3 groups:

A) CVVG 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months;

B) CVVG 1 cannula/day for 3 months + 1 cannula/alternate days for 3 months;

C) Control group: no treatment (usual clinical practice).

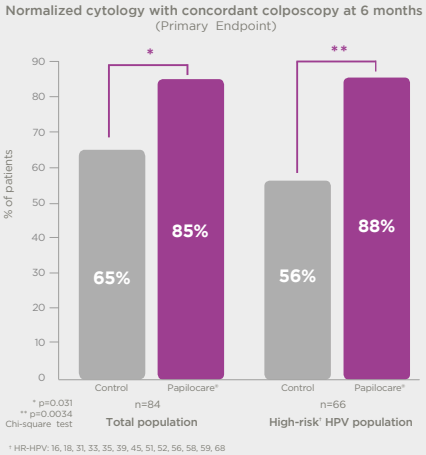
Percentage of patients with normalization of the lesions (normal cytology and concordant colposcopy image) as the primary endpoint and percentage of patients with HR-HPV clearance (secondary endpoint) were evaluated at 6 months. Pap smear evaluation and HPV identification (Clart® HPV4) were blind and centrally- conducted by an independent researcher at the IECM laboratory (Lugo, Spain). CVVG arms (A+B) were combined as treatment group and chi-square test was used.

Conclusions

After the six-month treatment period, CVVG has shown statistically significant efficacy in normalizing HPV-dependent cervical lesions (cytology of ASCUS/LSIL and concordant colposcopy images), especially in HR-HPV subpopulation. A trend to increase HPV clearance has also been observed in HR-HPV subpopulation.

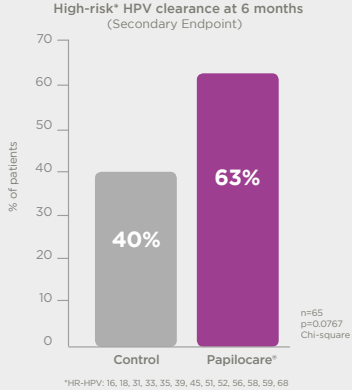
Results

A total of 84 patients (total population) were evaluated (53 vs 31 in treatment and control groups, respectively) of which 66 were HR-HPV (HR-HPV subpopulation) (41 vs 25 in treatment and control groups, respectively). In the total population, 85% (43/53) of patients treated with CVVG had normal cytology with concordant colposcopy vs 65% (20/31) in control group (p=0.031). In the HR-HPV subpopulation, normal cytology and concordant colposcopy image was observed in 88% (36/41) of patients treated by CVVG vs 56% (14/25) of patients in control group (p=0.003). HR- HPV clearance was observed in 63% (25/40) vs 40% (10/25) of patients treated with CVVG and control group, respectively (p=0.076).



† HR-HPV: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

Figure 1:
Papilocare® on repairing cervical lesions (ASCUS/LSIL cytology and concordant colposcopy image)



*HR-HPV: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

Figure 2:
Papilocare® on high-risk HPV clearance.

EFFECT OF A CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN HPV INFECTED WOMEN: CERVICAL REEPITHELIZATION, PERCEIVED STRESS AND TOLERABILITY EVALUATION[11]

Authors:

L. Serrano[1], A.C. López[2], S. González[1], S. Palacios[3], D. Dexeus[4], C. Centeno[5], P. Coronado[6], J. de la Fuente[7], J A. López and J. Cortés[10] Fernández[8], C. Vanrell[9]
[1]Centro Médico Gabinete Velázquez, Madrid, [2]Hospital Quironsalud, Málaga, [3]Instituto Palacios, Salud y Medicina de la Mujer, Madrid, [4]Women´s Health Institute, Barcelona, [5]Clínica Diatros, Barcelona, [6]Hospital Clínico San Carlos, Madrid, [7]Hospital Universitario Infanta Leonor, Madrid, [8]Hospital General Universitario, Alicante, [9]Hospital de la Santa Creu i Sant Pau, Barcelona, [10]Private Practice, Palma de Mallorca.

Objective

In previous clinical studies a non-hormonal Coriolus versicolor-based vaginal gel (CVVG) has shown to significantly influence the re- epithelization of the cervix and the rebalancing of the vaginal microbiota that favors the natural process of vaginal immunity. The objective was to evaluate the tolerability and the effect of the CVVG on the cervical re-epithelialization and the perceived stress in patients with HPV-dependent atypia (ASCUS and LSIL) and associated colposcopic alterations.

Methods

Multicenter, randomized, open-label, parallel-group, usual practice controlled clinical trial (Paloma Clinical Trial). Unvaccinated HPV+ women aged between 30 and 65 (mean age of 41 yo, evenly distributed among groups) with cytology of ASCUS or LSIL and concordant colposcopy image were included. Patients were randomized into 3 groups:

A) CVVG 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months;

B) CVVG 1 cannula/day for 3 months + 1 cannula/alternate days for 3 months;

C) Control group: no treatment (usual clinical practice).

Changes in epithelialization of the cervix evaluated by standard colposcopy (and rated by investigators with a likert scale from 0= severe ectopy + bleeding to 5= normal) and in perceived stress evaluated by PSS14 were assessed at 6 months as secondary endpoints. Satisfaction and tolerability of gel were also evaluated. CVVG arms (A+B) were combined as treatment group and chi-square or Fisher test were used as appropriate.

Conclusions

After the six-month treatment period, CVVG has shown a statistically significant difference in cervix re-epithelization and a positive trend in perceived stress reduction. CVVG has shown a high satisfaction level and a good tolerability. Data of further studies should confirm these exciting results.

Results

A total of 84 patients were evaluated (53 vs 31 in treatment and control groups, respectively). At 6 months, a statistically significant difference in cervix re-epithelization likert scale was observed: 4,51 vs 4.10 in CVVG and control group, respectively, p=0.017. A trend vs baseline was also observed in both groups: a stress reduction in CVVG group (21.13 vs 18.98) vs a stress increase in control group (17.72 vs 20.68). 58% of CVVG patients improved the PSS14 score vs 39% in control group. 87% of patients reported some degree of satisfaction with CVVG and none was unsatisfied. 11 out of 64 CVVG patients included in the safety sample reported 22 adverse events (AA): 7AA were possible/probable related to treatment (burning/stinging/itching), of which all were classified as mild/moderate and only in 2 cases caused permanent treatment withdrawal.

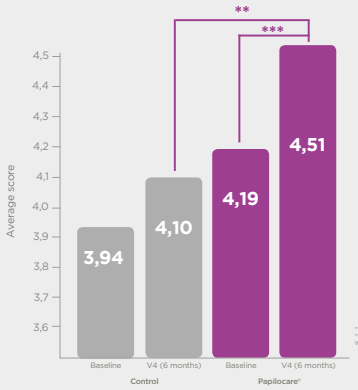


Figure 1:
Cervical Mucosa Reepithelialization Degree (Likert scale) (Secondary Endpoint)

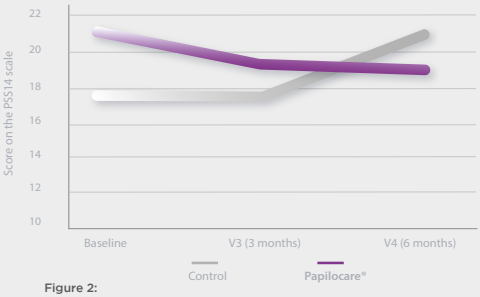


Figure 2:
Stress evolution (Secondary Endpoint)

EFFECTIVENESS OF A MULTI-INGREDIENT CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN REPAIRING CERVICAL MUCOSA WITH HPV LESIONS. INTERIM ANALYSIS RESULTS OF AN OBSERVATIONAL STUDY.[12]

Authors:

J. Cortés[1], J. de Santiago[2], A. Cos[3], I. Lago[4], G. Espinosa[5], M.A. Olalla[6], G. Fiol[7], C. Lozada[3], C. Garcia[8], M. Agenjo[2]

[1]Senior Consultant in Gynecological Oncology. Private Practice, Palma de Mallorca, [2] Head of the Gynecology Service.MD Anderson Cancer Center, Madrid, [3]Barcelona/Spain, [4]Pontevedra/Spain, [5]Sevilla/Spain, [6]Málaga/Spain, [7]Almería/Spain, [8]Burgos/Spain

Introduction

Real-life studies are mandatory for complementation of RCT. They inform on the "effectiveness" of a treatment what is intended to do in routine circumstances.

Objective: to evaluate the effectiveness of Papilocare® -a Coriolus versicolor-based vaginal gel- on repairing HPV-dependent low-degree cervical lesions and HPV clearance.

Methods

Observational, multicenter, prospective, one-cohort study (PAPILOBS study). Currently recruiting 300 vaccinated or not vaccinated HPV-positive women aged > 25y with pap result of ASC-US or LSIL and concordant colposcopy image during routine clinical visits in Spain. Patients are treated with Papilocare® 1 cannula/day for 21 days the first month + 1 cannula/alternate days for 5 months. After this 6-month period, patients with altered cytology and HPV persistency are treated for a 6-month extension period with the same dosage.

Interim analysis of patients with normal pap smear and concordant colposcopy image (primary endpoint) and patients with HPV clearance at 6/12 months is presented. The study was approved by the ethical committee of Public University Hospital of Puerta de Hierro (Madrid). Informed consent was signed by all patients.

Conclusions

In this preliminary analysis, Papilocare® has shown a notable effect in both repairing HPV-dependent low-degree cervical lesions and clearing HPV, in real life conditions. Objectives can be obtained after a 6-month treatment period in most of the patients, achieving 94% extending the treatment to 12 months. These findings need to be confirmed upon study completion.

Results

At 6 months, data of 72 and 71 patients for pap smear/colposcopy and HPV presence, respectively, are available. 65% of patients (47/72) had negative pap smear and concordant colposcopy. HPV clearance was observed in 54% of patients (38/71).

Data of 18 patients included in the 6-month extension treatment period, are available. At 12 months, 94% of patients (17/18) had negative pap and colposcopy and HPV clearance was observed in 83% of patients (15/18).

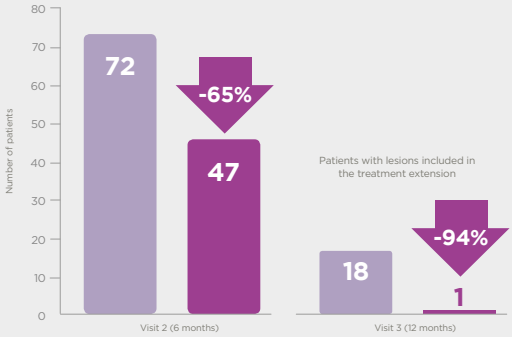


Figure 1:
Normalization of cervical lesions (ASCUS/LSIL) in the TOTAL POPULATION (Primary Endpoint)

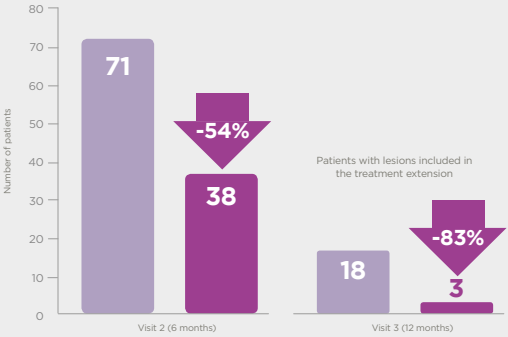


Figure 2:
HPV Clearance in the TOTAL POPULATION (Secondary Endpoint)

EFFECT OF A CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN A HIGH-RISK HPV INFECTED PATIENTS. RESULTS OF DIFFERENT STUDIES[13]

Authors:
Cortés Javier[1], Dexeus Damián[2], Palacios Santiago[3], Serrano Luis[4], Seydoux Gilles[5], Gajino Clara[6], Marín Elena[7], Riera Margarita[8].
[1]Senior Consultant in Gynecological Oncology, Private practice, Palma de Mallorca, (Spain), [2]Women's Health Institute, Barcelona, (Spain), [3]Instituto Palacios de Salud y Medicina de la Mujer, Madrid (Spain), [4]Centro Médico Gabinete Velázquez, Madrid (Spain), [5]Procare Health, Barcelona (Spain), [6]Hospital Materno Infantil Teresa Herrera, A Coruña, (Spain), [7]Hospital Álvaro Cunqueiro, Vigo (Spain), [8]Institut Català de la Salut. Hospitalet de LLobregat, (Spain)

Objective

New and independent real-life data about the high-risk HPV (HR-HPV) clearance effect of a non-hormonal Coriolus versicolor-based vaginal gel (Papilocare® vaginal gel) have been presented in the last years. The objective of this work was to evaluate the consistency of the HPV clearance effect of this gel in patients infected by HR-HPV across these studies and a clinical trial.

Methods

Results from 3 independent observational non-comparative studies carried out in 3 different public centers of Spain were evaluated and compared to results from a randomized, open, parallel and controlled clinical trial comparing the Papilocare® vaginal gel vs wait and see approach (The Paloma RCT). One of the independent studies was prospective (Vigo study)[1] and the two others were retrospective (Coruña and Hospitalet studies).[2,3]

The patients included in the three observational studies were treated with Papilocare® vaginal gel 1 cannula/day for 1 month + 1 cannula/ alternate days for 5 months (except menstrual days).

Vigo study[1]: HPV clearance at 6 months of 25 patients older than 24 years infected by HPV 16 and/or 18 was evaluated as a secondary endpoint.

Coruña study[2]: 57 medical records of patients with HR-HPV (mean age 38.4 years) were analyzed. HPV clearance at 6 months was evaluated as primary endpoint.

Hospitalet study[3]: Data of 91 HR-HPV patients aged between 20 and 65 were evaluated. Primary endpoint: composite efficacy variable (percentage of patients with normal cytology and/or HPV clearance at 6 months).

Paloma RCT: 66 HR-HPV patients (mean age 39,73 years) were evaluated (41 vs 25 in Papilocare® vaginal gel and control groups, respectively). Percentage of patients with HR-HPV clearance (total clearance + partial clearance with concordant cytological and colposcopy normalization) at 6 months was assessed as secondary endpoint.

Results

After the 6-month treatment period, 48% of patients cleared HPV 16-18 (Vigo study), a reduction of 58% was observed in number of HR-HPV patients (Coruña study) and 72.5% of patients negativized cytology and/or cleared HR-HPV (Hospitalet study) vs baseline ($p \leq 0.0001$ for all results, Chi-square). In the Paloma RCT, HR-HPV clearance was observed in 63% of patients treated with Papilocare® vaginal gel vs 40% in the control group (p=0.076).

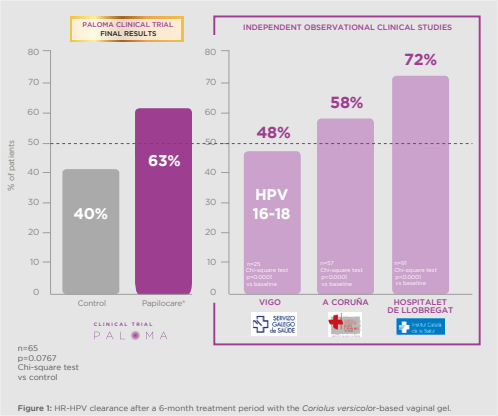


Figure 1: HR-HPV clearance after a 6-month treatment period with the *Coriolus versicolor*-based vaginal gel.

Conclusions

After the 6-month treatment period, Papilocare® vaginal gel has shown significant and consistent rates of HR-HPV clearance ranging from 50% to 70% in the 4 different studies carried out. Data of further studies should confirm these exciting results.

1- Gil Andrés M et al. ASCCP 2018, Las Vegas, US. Late-Breaking abstracts #71.
2- Gajino C. 32nd IPCV 2018. Sydney, Australia. Abstract #IPVC8-0489.
3- Riera M et al. J Low Genit Tract Dis. 2018;22(April 2, suppl 1): oral communication

PAPILOCARE®

PREVIOUS COMMUNICATIONS IN INTERNATIONAL CONGRESSES

5 POSTERS PRESENTED

EUROGIN 2016

1 POSTER PRESENTED
1 ORAL COMMUNICATION

IFCPC2017 World Congress
for Cervical Pathology and Colposcopy
April 4-7, 2017 | Orlando, Florida

4 POSTERS PRESENTED

5 POSTERS PRESENTED

7 POSTERS PRESENTED

AWARD BEST POSTER IN CLINICAL RESEARCH

EUROGIN
INTERNATIONAL MULTIDISCIPLINARY HPV CONGRESS
WWW.EUROGIN.COM/2017
Amsterdam

5 POSTERS PRESENTED
1 ORAL COMMUNICATION

EUROGIN 2018
International multidisciplinary HPV congress
DECEMBER 2-5, 2018
LISBON, PORTUGAL

6 POSTERS PRESENTED

PAPILOCARE®

ABSTRACTS PRESENTED AT ASCCP 2018

Clinical Studies Data[14]

& Public University Hospitals Independent Studies[15,16]

ABSTRACTS PUBLISHED IN:

JOURNAL OF
Lower Genital
Tract Disease

VOLUME 22, SUPPLEMENT 2S
APRIL 2018

PAPILOCARE® CLINICAL STUDY RESULTS

EFFECT OF A NON-HORMONAL CORIOLUS VERSICOLOR VAGINAL GEL AMONG POSITIVE-HPV WOMEN WITH NO COLPOSCOPY CERVICAL LESIONS. A PILOT STUDY[14]

ID: 370

Authors:
S. González. L. Serrano Gabinete Médico Velázquez, Madrid. (Spain)

Authors: J. Gálvez, A. Rodríguez Nogales, Teresa Vezza, José Garrido Mesa, Francesca, Algieri and M. Elena Rodríguez Cabezas.
Center for Biomedical Research (CIBM), Department of Pharmacology, University of Granada, Granada, (Spain).

Objective

To evaluate the effect of a Coriolus versicolor-based vaginal gel (Papilocare®) on both cervical epithelization and vaginal microbiota in positive - HPV women with no colposcopy lesions.

Methods

An exploratory, prospective, observational study. Sexually active HPV-positive women aged > 25y with negative pap and no colposcopy cervical lesions were included during routine clinical visits and treated with Papilocare® once daily for 21 consecutive days.

Primary endpoint: change vs baseline in epithelialization degree of the cervix mucosa evaluated by standard colposcopy and rated by investigator from 5 = No ectopy o 1= severe ectopy and bleeding.

Secondary endpoints:
1) changes in vaginal signs and symptoms evaluated by likert-type scale from 7= severity to 28= absence,
2) changes in vaginal microbiota evaluated by 16S rRNA gene pyrosequencing and proportion of both bacterial phyla and species were evaluated
3) patient satisfaction.

Results

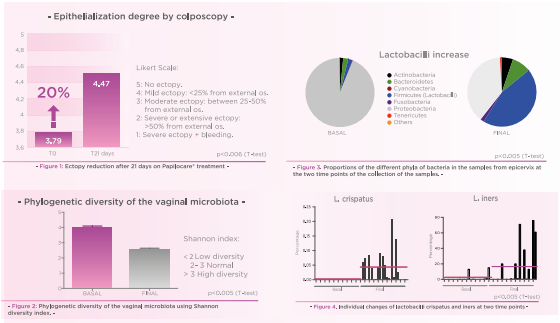
21 patients were included. Papilocare® showed:

• A positive trend to improve the re-epithelialization of the cervix:
- Results of mean score are shown in figure 1.
- 52.6% of patients improved cervix epithelialization and a score of 5 was observed in 63% of women.

• A reduction in vaginal diversity (figure 2) and an increase proportion of Firmicutes (phylum to which the lactobacilli belong) (figure3). Specifically, the significant increases of Lactobacillus crispatus and iners are are shown in (figure 4).

• A trend to improve symptoms was observed despite of few symptoms at baseline: 71% of patients reached maximum symptoms score at the end of treatment period. Eight patients improved the symptoms score and 3 worsened.

• A "moderate/complete satisfaction" and some degree of «positive impact on wellness» were reported by 84% and 90% of evaluated patients.



Conclusions

Papilocare has demonstrated to improve significantly the cervix epithelisation among HPV-positive women without cervical lesions. The treatment was able to modify the composition of the microbiome, associated with a reduction of the microbiome diversity, clear marker of vaginal dysbiosis. The increase concentration of specific species of the genus Lactobacillus (iners and crispatus) suggests a restoration of the altered microbiota composition in these women at the end of the study. These results might explain the mechanism of action of Papilocare in providing positive results on normalizing cervical lesions.

Funding: This study was carry out with no external funding.
Disclosures: Dr Serrano and Dr González have received honorarium as a speaker from Procare Health SL. Rest of co-authors: there are no relationships to disclose

ASCCP2018
Annual Meeting
April 18-21,2018
Las Vegas,NV

PUBLIC UNIVERSITY HOSPITALS INDEPENDENT STUDIES WITH PAPILOCARE

Efficacy of a Coriolus versicolor-based vaginal gel in high risk HPV+ women[15]

Authors:
E. Marín Ortiz, MP. Vázquez Caamaño, M. Porto Quintans, O. Valenzuela Besada, M. Gil Andrés and A. Iñarrea Fernández.
Servicio de Ginecología y Obstetricia, Unidad de Patología Cervical. Hospital Álvaro Cunqueiro (Vigo-Spain)

HOSPITAL ÁLVARO CUNQUEIRO

Objective

To evaluate the efficacy of Papilocare® - a Coriolus versicolor - based vaginal gel - to clear HPV and to normalize pap smear in high risk HPV + women

Methods

An exploratory, prospective, observational non-controlled study. High risk HPV+ vaccinated and unvaccinated women older than 24 years were included during routine follow-up visits and treated with Papilocare® 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months (except menstrual days).

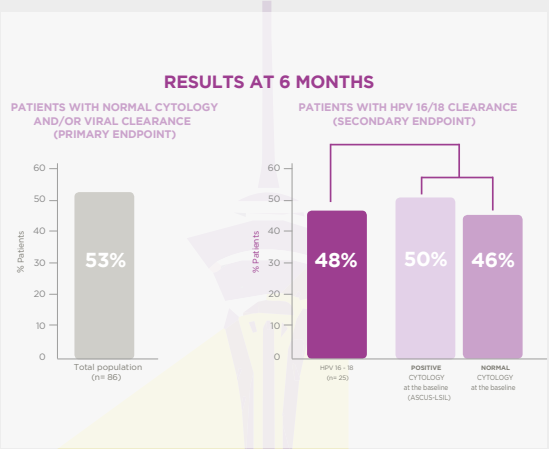
Primary endpoint: composite efficacy variable consists of percentage of patients with normal pap smear and/or HPV clearance at month 6 vs baseline.

Secondary variable: percentage of patients clearing HPV 16-18 vs baseline.

Results

A total of 86 patients, mean age 42.1 years (24 to 81) were included. At 6 months, 53% of women negativized pap smear and/or cleared HPV and were classified as responders to treatment (Primary endpoint - figure 1). A total of 25 patients were positive to HPV 16-18 at baseline (12 and 13 with positive and negative pap smear, respectively).

Results of secondary endpoint at 6 months are shown in figure 2.



Conclusions

In this preliminary analysis, Papilocare® shows a positive trend to improve pap smear alterations and HPV clearance in women infected by high risk HPV, after 6 months; these findings are consistent with other clinical studies results.

Funding: Procare Health SL (PH)
Disclosures: J Cortés, S Palacios and D Dexeus work as consultants for PH. L Serrano, S González and AC López have been speakers for PH.
Rest of authors: There are no relationships to disclose
Approvals: Study protocol was approved by Ethical Committees of all participant hospitals.

ASCCP2018 Annual Meeting
April 18-21,2018
Las Vegas,NV

PUBLIC UNIVERSITY HOSPITALS INDEPENDENT STUDIES WITH PAPILOCARE®[16]

2018 ASCCP Oral Communication

Journal of Lower Genital Tract Disease • Volume 22, Number 2, Supplement 1, April 2018 Abstracts

Papilocare® in the clearance of High-Risk HPV[11]

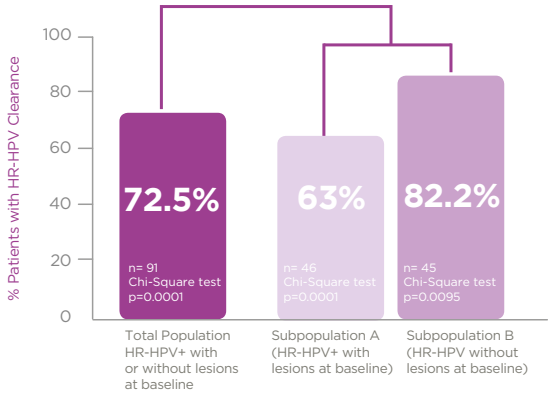
Principal Investigator:
Dr. Margarita Riera Blasco
Gynecologist and Obstetrician of the Catalan Health Institute
Assir Delta Del Llobregat, Barcelona.
Member of the AEPCC

Objective:
• Evaluate the efficacy of a Corioulus versicolor-based vaginal gel, Papilocare®, in High-Risk HPV+ patients

Design:
Observational study carried out between December 2016 and October 2017.
• The determination of High Risk Papilloma Virus was carried out by hybrid capture
• When the result was positive, colposcopy and biopsy were performed (if applicable), following the protocols of the ICO **(Catalan Institute of Oncology)**

Patients:
• A total of 91 patients:
46 patients High-Risk HPV+ with cervical lesions at baseline (subpopulation A=50.5%)
45 patients High-Risk HPV+ without cervical lesions at baseline (subpopulation B=49.5%)

High-Risk HPV Clearance after 6 months of Papilocare® treatment



Conclusions

- The *Coriolus versicolor*-based vaginal gel appears to be **effective against ASCUS and LSIL lesions**
- There is a viral **clearance at 6 months of Papilocare® treatment** in HR-HPV+ patients, presenting or not cervical lesions at baseline

PAPILOCARE®

ABSTRACTS PRESENTED AT IPVC 2018

Public University Hospitals Independent Study[17]

IPVC 2018
32ND INTERNATIONAL PAPILLOMAVIRUS CONFERENCE
In conjunction with AOGIN 2018

OCTOBER 2-6TH, 2018
SYDNEY, AUSTRALIA

PUBLIC UNIVERSITY HOSPITALS INDEPENDENT STUDIES WITH PAPILOCARE®

USE AND RESULTS OF A CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN WOMEN HPV+ AND/OR ABNORMAL PAP SMEAR ATTENDED IN A REGIONAL SPANISH HOSPITAL. PRELIMINARY ANALYSIS[17]

SERVIZO GALEGO de SAÚDE | Complexo Hospitalario Universitario A Coruña | A Coruña

Author:
Clara Gajino Suárez. Hospital Materno Infantil Teresa Herrera, Ginecology and Obstetrics, A Coruña, Spain.

OBJECTIVE

A Coriolus versicolor-based vaginal gel (Papilocare®) is recently available in Spain to prevent and treat the HPV-dependent low-grade cervical lesions. Recommended dose: 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months (except menstrual days).

To analyze how Papilocare® is being used in our hospital and to evaluate the treatment results in our patients.

METHODS

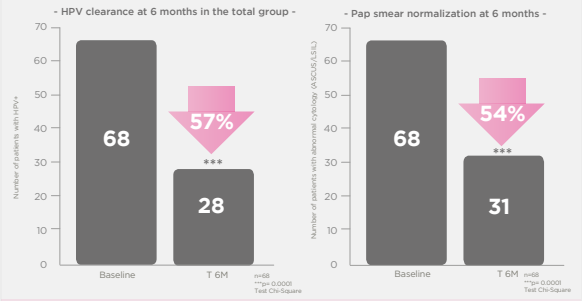
A retrospective, observational study. Medical records of patients who completed 3 or 6 months treatment period during 2017 were analyzed. Baseline characteristics of Papilocare® users were described.

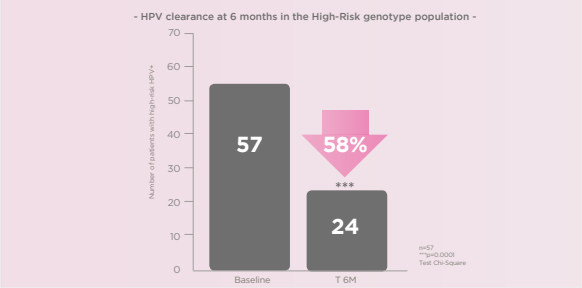
Pre and post treatment number of patients with ASCUS/LSIL, positive-HPV and high risk positive HPV were assessed.

RESULTS

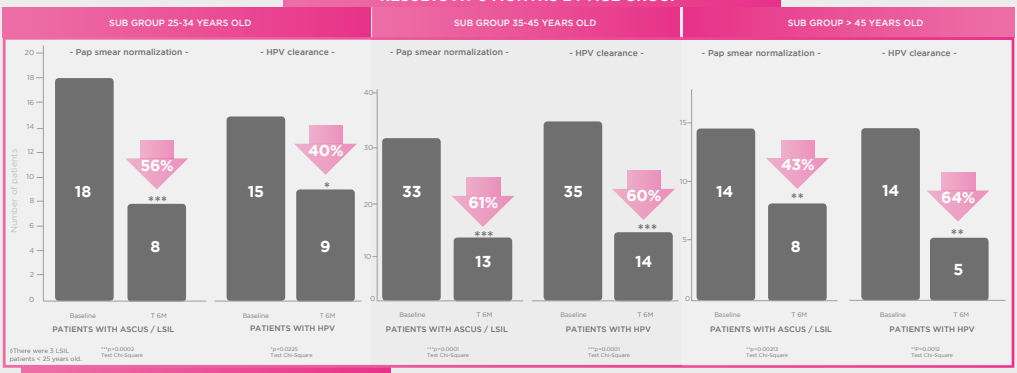
A total of 86 medical records were analyzed. Most of them (84%) were treated for 6 months. Mean age was 38.4 years (from 18 to 72 years), 43.5% were vaccinated before treatment with Papilocare®, 32,5% were smokers and 42% used condoms regularly in all their sexual relationships. Baseline pap smear: Normal 11(13%), ASCUS 3 (3.5%), LSIL 65 (75.5%) and HSIL 7 (8%). HPV test was performed in 68 patients of which 57 (89%) were high-risk HPV.

Results after treatment are shown in figures





RESULTS AT 6 MONTHS BY AGE GROUP◊



◊There were 3 LSIL patients < 25 years old.

*p=0.0225 Test Chi-Square
**p=0.0002 Test Chi-Square
***p=0.0001 Test Chi-Square
*p=0.00213 Test Chi-Square
**p=0.0012 Test Chi-Square

CONCLUSIONS

In our hospital, most of patients using Papilocare® had LSIL. In this preliminary analysis, significant reductions of patients with pap smear alterations and significant High-Risk HPV clearance were observed after 3-6 months of Papilocare® application. The treatment with Papilocare® manages to solve the medical situation in almost 1 out of 2 women treated, avoiding more aggressive treatments such as destructive and/or excisional therapies and with no side effects reported.

The authors declares no conflict of interest related to the conduct of study

PAPILOCARE®

RESEARCH & CLINICAL DEVELOPMENT PLAN

PILOT STUDY | epicervix | CLINICAL TRIAL PALOMA | CLINICAL TRIAL PALOMA2 | CLINICAL TRIAL PAPILOCAN | PAPILOBS

Ongoing studies

Phase I
Asymptomatic women
12 days
21 patients

Phase IIa
HPV+ Women
21 days
21 patients

Phase IIb
HPV+ with LSIL/ASCUS
6 months vs control
96 patients

Phase IIb
HR-HPV+ with LSIL/ASCUS
6 months vs control
288 patients

Phase III
HPV+ with LSIL/ASCUS
6 months vs placebo
200 patients

Phase IV
HPV+ with LSIL/ASCUS
12 months
300 patients

SCIENTIFIC INNOVATION

FIRST HUMAN CERVIX-ON-A-CHIP

CERVIX-ON-A-CHIP

Procare Health
Naturally woman

PHASE IV INDEPENDENT PUBLIC UNIVERSITARY HOSPITAL STUDIES

Patients High Risk HPV+
6 months

86 patients	91 patients	86 patients	98 patients
SERVIZO GALEGO de SAÚDE	Institut Català de la Salut	Complejo Hospitalario Universitario Juan Canalejo A Coruña	Prof. Giovanni Miniello

FINAL RESULTS

CLINICAL TRIAL
PALOMA
ClinicalTrials.gov NCT04002154

PAPILOCARE®

1ST TREATMENT TO PREVENT AND TREAT HPV-DEPENDENT CERVICAL LESIONS◊

THE EFFICACY OF PAPILOCARE® IN THE CLEARANCE OF HIGH RISK-HPV AT 6 MONTHS IS BETWEEN 50% TO 70% IN

the Paloma clinical trial[3], the Papilobs observational study[12], and 3 independent clinical studies[13] carried out by university public hospitals, with a total of 700 patients

NORMALIZATION OF HPV-DEPENDENT CERVICAL LESIONS IN

88%**

of High-Risk HPV+ patients at 6 months vs 56% in the control group

FINAL RESULTS on High-Risk HPV

HPV CLEARANCE IN

63%

of High-Risk HPV+ patients at 6 months vs 40% in the control group

**p<0.01 Chi-square Test

ClinicalTrials.gov NCT04002154

RECOMMENDED TREATMENT DURATION: 6 MONTHS

◊ Low grade lesions: ASCUS / LSIL

Recommended for:

- Controlling and re-epithelizing the cervical transformation zone to prevent the risk of HPV-induced lesions (LSIL).
- Coadjuvant treatment of HPV-induced intra-epithelial lesions.
- Repairing and re-epithelizing lesions of the cervical-vaginal mucosa.
- Rebalancing vaginal microbiota.
- Improving vaginal health.
- Creating the conditions for rapid healing of lesions caused by scratching due to burning and pruritus.

Instructions for use:

Insert a single-dose cannula into the vagina, preferably before bedtime. Start treatment after period. The recommended posology is one single-dose cannula for 21 consecutive days, then one single-dose cannula every other day for the 5 following months (off during the period).

1. Holowaty P. et al. Natural History of Dysplasia of the Uterine Cervix. J Natl Cancer Inst. 1999, 91(3):253-258. **2.** Saraiya M. et al. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. J Natl Cancer Inst. 2015, 107(6): djv086. **3.**Serrano L, López A, González S, Palacios P. Dexeus D, Centeno C, Coronado P, de la Fuente J, López Fernández JA, Vanrell C, Combalia J and Cortés J. EP274 Effect of a Coriolus versicolor-based vaginal gel in HPV infected women: normalizing HPV-dependent cervical lesions (ASCUS/LSIL) and high-risk HPV clearance. International Journal of Gynecologic Cancer 2019;29:A206. **4.** Cortés J, Seydoux G, Dexeus D, Palacios S, Serrano L, Gajino C, Marin E, Riera M. EFFECT OF A CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN A HIGH-RISK HPV INFECTED PATIENTS. RESULTS OF DIFFERENT STUDIES. Poster presented at ASCCP 2019, 4-7th April. Atlanta, USA **5.** Riera MB, Rupérez, I, Felgueroso, E, Fontanet E, Tena Y. CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN THE CLEARANCE AND/OR CYTOLOGY NORMALIZATION IN HIGH-RISK HPV POSITIVE PATIENTS. Poster P11 presented at EFC Congress 2019, 25-28th September. Rome, Italy. **6.** Serrano L, López ACs, GonzálezS, Palacios S, Dexeus D, Centeno C, Coronado P, de la Fuente J, López Fernández JA, Vanrell C, Cortés J. Effect of a coriolus versicolor-based vaginal gel in HPV infected women: normalizing HPV-dependent cervical lesions (ascus/lsil) and high-risk HPV clearance.Poster P12 presented at EFC Congress 2019, 25-28th September. Rome, Italy. **7.** Khorsandi D, Haghniaz R, Gaslain Y, Combalia J, Emsellem C, Palacios S, Khadmhosseini A. Human uterine cervix-on-a-chip: Establishing the first in vitro model to study the development of cervical carcinoma and human Papiloma Virus mechanism of action. Poster P28 presented at EFC Congress 2019, 25-28th September. Rome, Italy. **8.** Serrano L, López A, González S, et al P158. Efficacy of a coriolus versicolor-based vaginal gel in repairing HPV-dependent cervical lesions (ASCUS/LSIL) in three patients' groups according to the risk of HPV strains International Journal of Gynecologic Cancer 2019;29:A154. **9.** Khorsandi D, Palacios S, Gaslain Y, et al. P159 Human uterine cervix-on-a-chip: establishing the first in vitro model to study the development of cervical carcinoma and human papiloma virus mechanism of action International Journal of Gynecologic Cancer 2019;29:A155. **10.** Serrano L, López AC, González S, Palacios S, Dexeus D, Centeno C, Coronado P, de la Fuente J, López JA, Vanrell C, Cortés J. EFFECT OF A CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN HPV INFECTED WOMEN: NORMALIZING HPV-DEPENDENT CERVICAL LESIONS (ASCUS/LSIL) AND HIGH-RISK HPV CLEARANCE. Oral Communication presented at EUROGIN Congress 2019, 4-7th December, Monaco. **11.** Serrano L, López AC, González S, Palacios S, Dexeus D, Centeno C, Coronado P, de la Fuente J, López Fernández JA, Vanrell C, Cortés J. EFFECT OF A CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN HPV INFECTED WOMEN: CERVICAL REEPITHELIZATION, PERCEIVED STRESS AND TOLERABILITY EVALUATIONA. Oral Communication presented at EUROGIN Congress 2019, 4-7th December, Monaco. **12.** Cortés J, de Santiago J, Cos A, Lago I, Espinosa G, Olalla MA, Fiol G, Lozada C, Garcia C, Agenjo M. EFFECTIVENESS OF A MULTI-INGREDIENT CORIOLUS VERSICOLOR-BASED VAGINAL GEL IN REPAIRING CERVICAL MUCOSA WITH HPV LESIONS. INTERIM ANALYSIS RESULTS OF AN OBSERVATIONAL STUDY. Oral Communication presented at EUROGIN Congress 2019, 4-7th December, Monaco **13.** Cortés J, Dexeus D, Santiago P, Serrano L, Seydous G, Gajino C, Marin E, Riera M. Effect of a Coriolus versicolor-based vaginal gel in high-risk HPV infected patients. Results of different studies. P24-11 Poster presented at EUROGIN Congress 2019, 4-7th December, Monaco. **14.** Serrano L, González S, Gálvez J, Rodríguez Nogales AB, Vezza T, Garrido Mesa JR, Algieri F, Rodríguez Cabezas ME. Effect of a Coriolus versicolor-Based Vaginal Gel in HPV+ Women with no colposcopy cervical lesions. A pilot study. Low Genit Tract Dis 2018, 22(2S):S22 **15.** Gil Andrés M, et al. Efficacy of a Coriolus versicolor-based vaginal gel in high risk HPV+ women. Preliminary results. In: Proceedings of the Annual Meeting of ASCCP; April 18-21 2018; Las Vegas, USA. [Conference Proceedings on the internet. ASCCP Publication; 2018. [cited May 2018]. p:8-9. Available from URL: http://www.asccp.org/asccp2018-late-breaking-abstracts. **16.** Riera Blasco MR, Rupérez Pérez B, Lázaro Vicario I, Felgueroso A, Fontanet Pérez E, Águayo Alba A. Coriolus versicolor and treatment of high Risk HPV . J Low Genit Tract Dis 2018, 22:2(S1):59. **17.** Gajino Suárez C. et al. Use and results of a Coriolus versicolor-based vaginal gel in women HPV+ and/or abnormal pap smear attended in a regional Spanish hospital. Preliminary analysis. Poster 0489 presented at the IPVC 2018, October 2-6 2018. Sidney, Australia.

Procare Health
Naturally woman

www.papilocare.com

PAPINT-0050 04/2020.