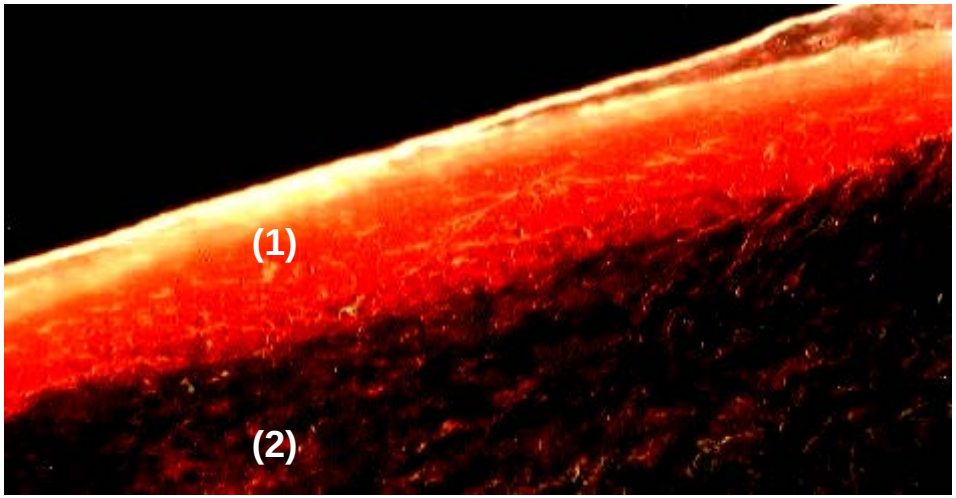
CEVIRA®
FINAL RESULTS OF PHASE 2B CLINICAL TRIAL

April 11, 2013

Introduction

- Cevira® (hexaminolevulinate) is a key late stage asset for treatment of pre-cancerous lesions and HPV
- Human Papilloma Virus (HPV) is a highly prevalent sexually transmitted disease impacting women of child-bearing age
- High unmet medical need for non-invasive, safe treatment options
- Cevira removes HPV and CIN selectively, preserving underlying normal tissue and the cervix remains competent



1) Selectively Fluorescing HPV-infected precancerous tissue

- Successful Phase 2b results of Cevira at 5% optimal dose demonstrated
  - significant and sustained efficacy in CIN 2 patients after 6 months
  - sustained clearance of HPV 16/18, the high risk subtypes, after 6 months
- Results are significant and lay the foundation for the Phase 3 registration program, to be undertaken with a global development and commercialization partner

Photo courtesy: of Dr. Hillemanns, Hannover

Breakthrough Platform Technology Designed for Ease of Use

- First fully integrated drug-delivery device in photodynamic technology
- Novel single use, disposable intra-vaginal device developed for ease of use
  - Obviates clinical and commercial barriers
- Simple application in office setting
  - Does not require additional equipment
  - Auto-activation
  - Patient free to resume normal daily activities
- Designed to treat the entire epithelial sheet
- Outstanding Physician and Patient Acceptance

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Program

- HPV Related Diseases of the Cervix
  The Need for Novel Therapies
  - *Ole Erik Iversen, MD, PhD*
    Department of Obstetrics and Gynecology
    Haukeland University Hospital, Bergen, Norway
- Results of Phase 2b Clinical Trial
  - *Peter Hillemanns, MD, PhD*

    Principal Investigator
    Department of Gynecology and Obstetrics
    University Hospital, Hannover, Germany
- Conclusion and Q&A
  - *Kjetil Hestdal, MD, PhD*

    President & CEO

HPV Related Diseases of the Cervix
The Need for Novel Therapies

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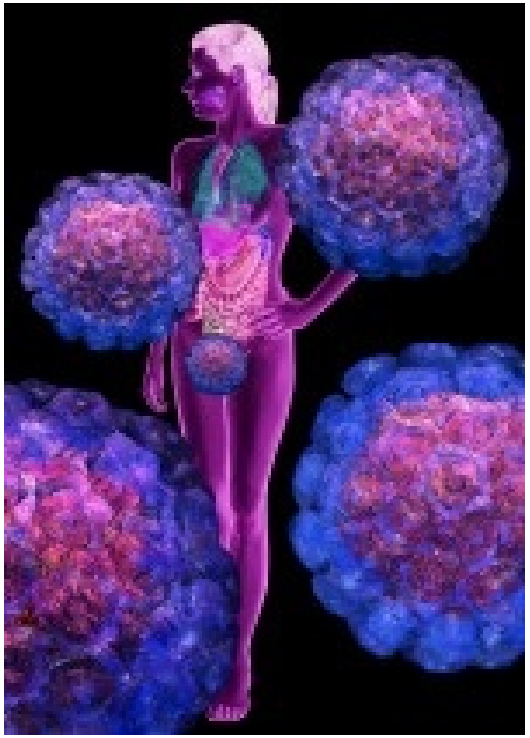
Bergen, Norway

Human Papilloma Virus

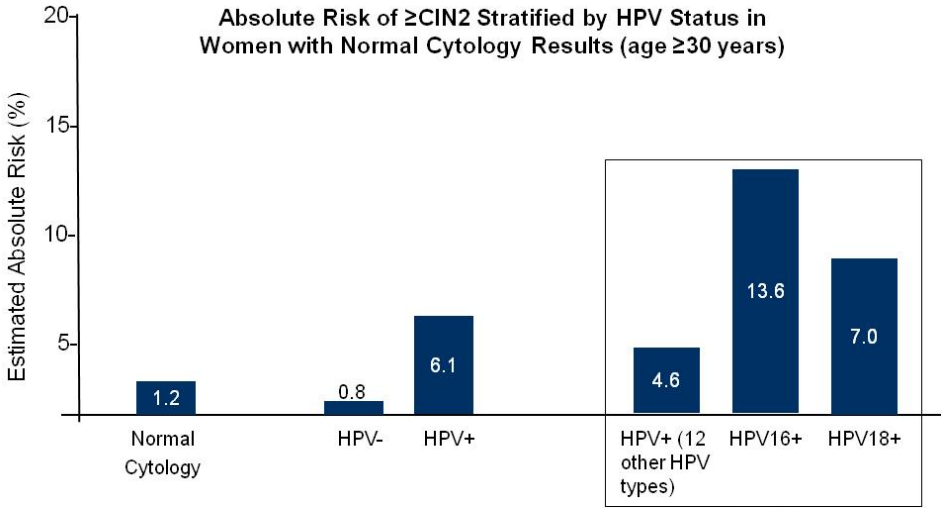
- Human Papilloma Virus (HPV) is a highly prevalent sexually transmitted disease
- Affects 80% women of all women during their lifetime
  - 300 million woman infected worldwide
  - 11.4% prevalence in the general population
  - Highest incidence in ages 18-35 years
- Well established cause of Cervical Intraepithelial Neoplasia (CIN) and cervical cancer
- Highly oncogenic subtypes 16 and 18 causal factor in
  - ~70% all cervical cancers
  - ~50% all high grade lesions
  - ~25% all low grade lesions



References: WHO, 2010

Progression of HPV to CIN and Cervical Cancer

- Although majority of HPV infections will spontaneously regress, ~10- 20% progress to precancerous lesions (CIN) within 2 years
- CIN
  - Close association between HPV induced cell changes and invasive cancer
  - Disease within its own right, CIN 2+ requires treatment
  - 30 million women globally with low grade lesions/CIN 1
  - 10 million women globally with high grade lesions/CIN 2
- Cervical cancer
  - 2nd most frequent cancer in females worldwide
  - ~530,000 new cases diagnosed annually
  - ~280,000 deaths



References: WHO, 2010; NEJM 2003;Clin Can Res 2002, Wright 2011

Current Screening Programs are Insufficient

- PAP testing (cytology), although considered gold standard for screening, misses 30-50% of cancers
  - Sensitivity of a single PAP test ~50%
- Current consensus guidelines in US recommend primary HPV Co-testing only in patients ≥ 30 years of age
  - Recent data supportive of HPV testing without cytology as sufficient screening tool
- Adherence to recommended screening and surveillance variable across geographies, even in developed countries
  - 30-75% of patients adhere to protocol
- Colposcopy, used to diagnose lesion severity, has limited sensitivity ~70%

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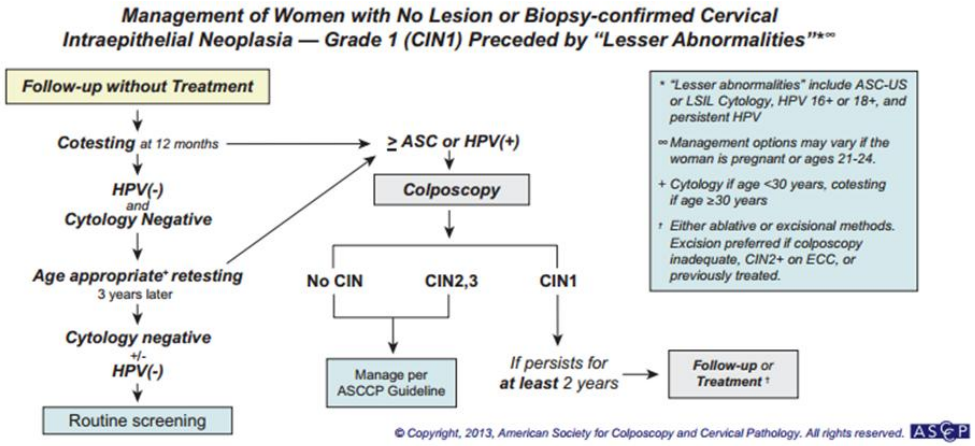
References: Saslow 2012, Dillner 2008

Shortcomings of Current Management
HPV and Low Grade Lesions

- No standard treatment exists
- Complicated, tedious surveillance recommendations
- Low adherence to surveillance protocol
  - Geographic relocations
  - Insurance migrations
  - High numbers lost to follow up



- Vaccines aimed at preventing HPV are significantly underutilized
  - 44% of parents in US rejecting vaccine recommendations
  - Only 1/3 of eligible girls in US are receiving vaccination
  - Offers no protection once virus is contracted

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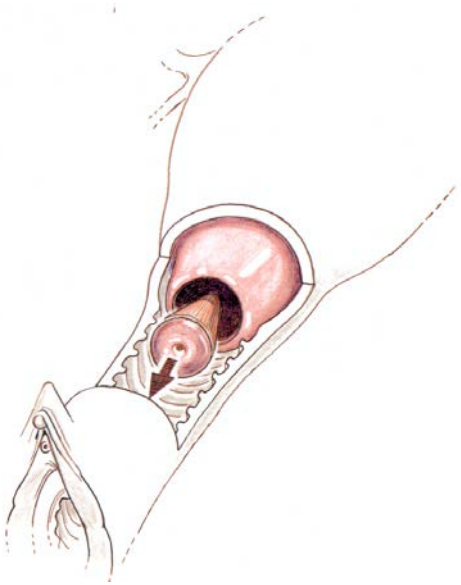
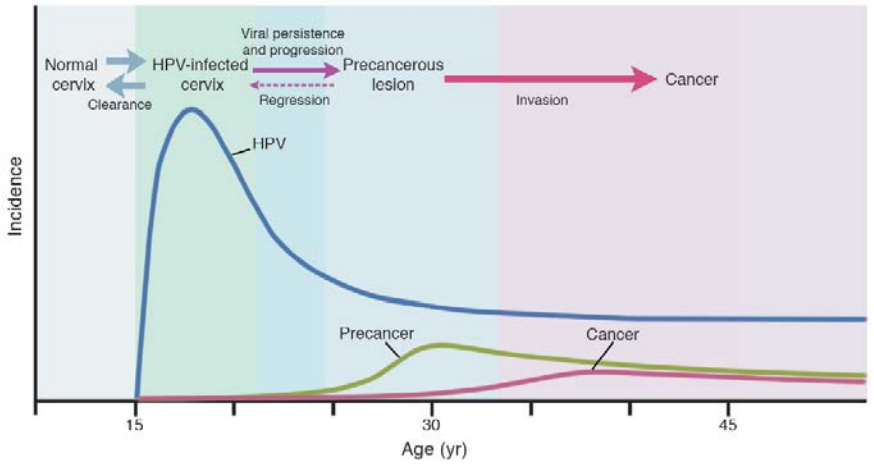
Shortcomings of Current Management High Grade Lesions

- CIN 2/3 treated with invasive surgery
  - Most commonly LEEP
- Morbidities associated with the surgery are significant and particularly devastating in women of child bearing potential
  - Bleeding, infections, cervical stenosis, infertility, preterm labor, low birth weight infants
- Mean age of conization approaches mean age of first pregnancy
- 5-30% recurrence
  - Requires long term follow up
  - Unsatisfactory colposcopy





Cervical Conization Influences the Outcome in Pregnancy

BMJ

RESEARCH

Pregnancy outcome in women before and after cervical conisation: population based cohort study

Susanne Albrechtsen, obstetrician,[1,2] Svein Rasmussen, professor,[2,3] Steinar Thoresen, professor,[4] Lorentz M Irgens, professor,[2] Ole Erik Iversen, professor[3]

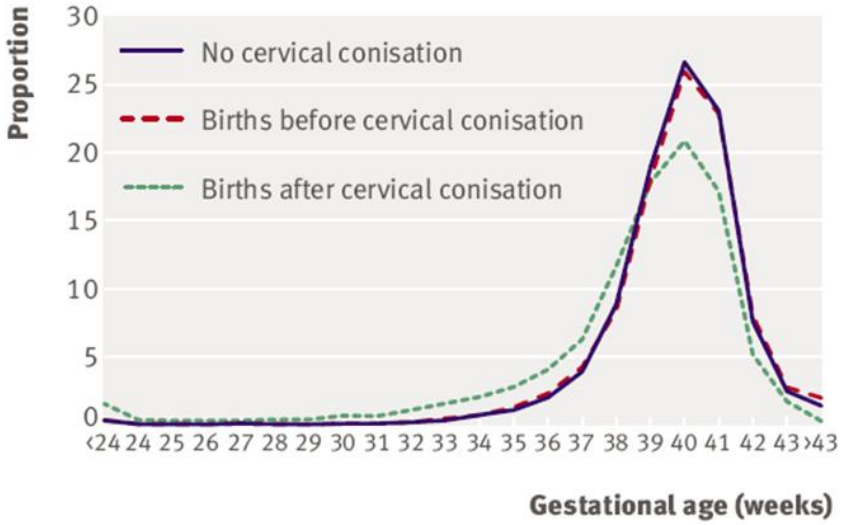


Fig 1 | Births before and after cervical conisation or with no cervical conisation by gestational age, Norway 1967-2003

- Increased risk of preterm delivery
- High impact on health care costs
- Relative risk of late miscarriages 4.0

Summary

- HPV related disease of cervix affects majority of women and risk of development of cervical cancer if not managed appropriately
  - 10 million women globally with high grade lesions
  - 30 million women globally with low grade lesions
- Current screening and surveillance of low grade lesions (CIN1) complicated with high risk of women lost to follow up and possible disease progression
  - Need for new treatments in women with associated high risk HPV related infections
- Need for new treatment options of high grade lesions (CIN 2)

Need for non-invasive, safe alternatives to ensure rapid clearance of HPV and lesions

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A Randomized Phase 2b Study of HAL Photodynamic Therapy in Patients with Low/Moderate Grade Cervical Intraepithelial Neoplasia (CIN 1/2)

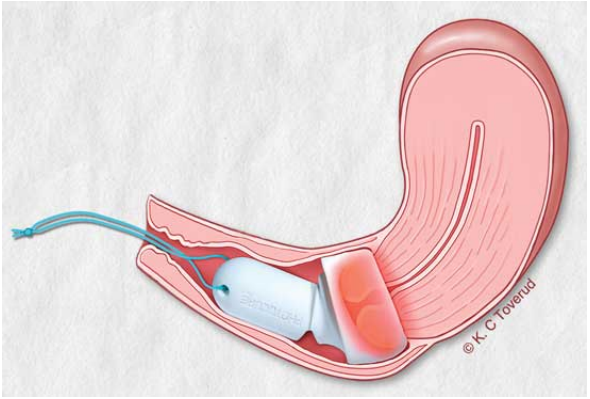
Peter Hillemanns, MD, PhD
Principal Investigator
Department of Gynecology and Obstetrics
University Hospital
Hannover, Germany

Objectives of Cevira Phase 2b Study

- To verify feasibility, efficacy and safety of the new Cevira photodynamic treatment in a placebo controlled multicenter Phase 2b study in patients diagnosed with CIN 1/2

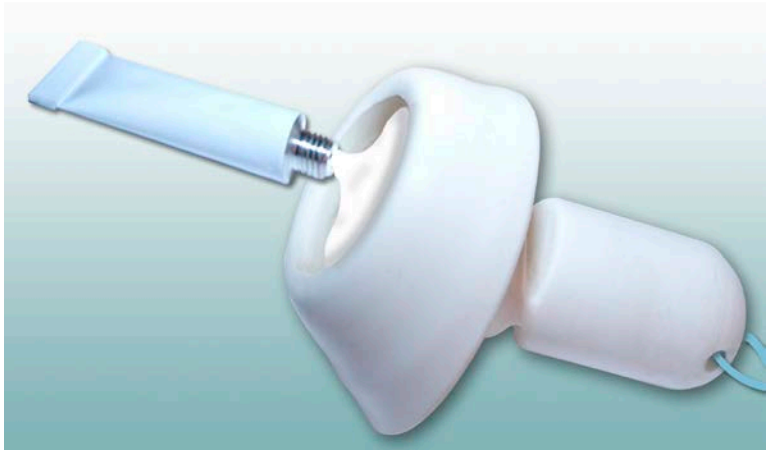
- To define the optimal efficacy endpoint(s) and patient population(s) to enable design of further clinical program

- To determine the preferred dose of hexylaminolevulinate (HAL)



Cevira Fully Integrated Drug-Device

- Cevira ointment containing HAL applied into the device and placed on the cervix by the gynecologist
- Automatic photoactivation 5 hours after drug application
- Integrated light source delivers 100J/cm^2 of red (629nm) light photoactivation lasting 4.6 hours
- Patient removes device after completion of treatment



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Phase 2b Clinical Trial End Points

3 months after last treatment
Histology, Cytology, HPV

6 months after last treatment
Cytology, HPV

- **Primary efficacy/Patient response**
  - Histology (central review)
  - Cytology
  - HPV DNA genotyping
- **Safety assessments**
  - Local tolerance
  - Adverse events

- **Secondary efficacy**
  - Cytology
  - HPV DNA genotyping of 12 high-risk oncogenic subtypes

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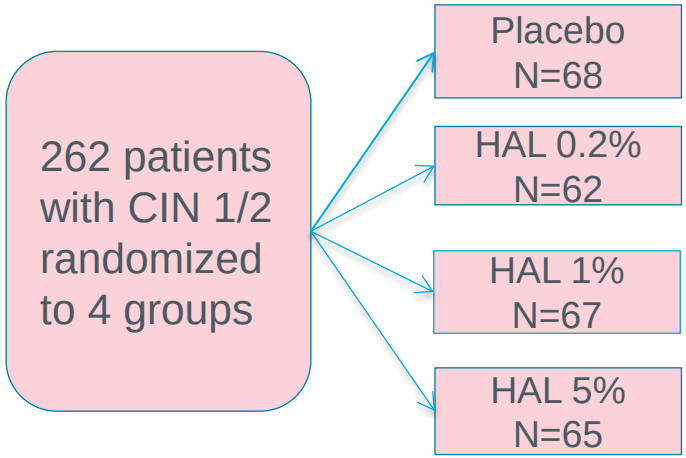
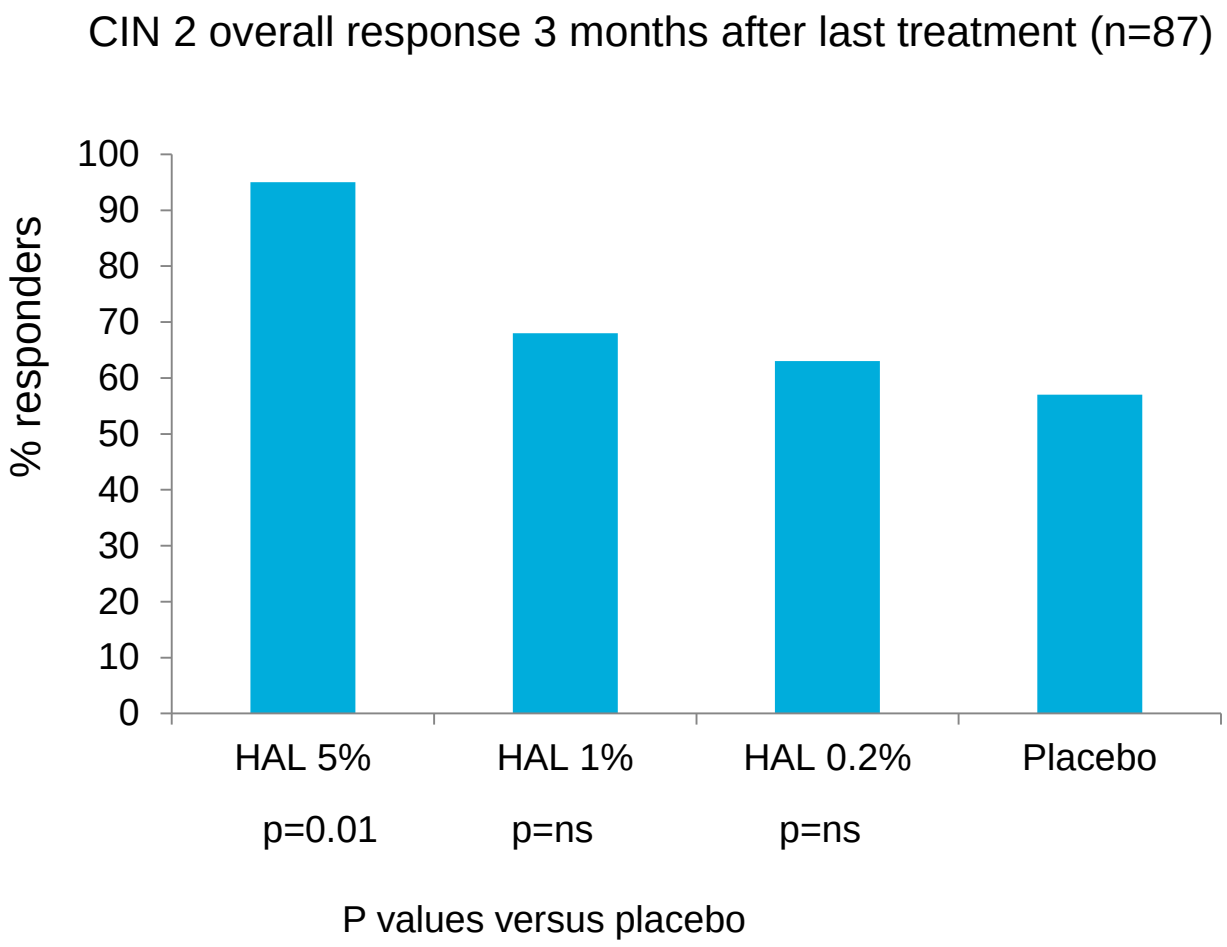
Main Study Metrics

- Enrolled 262 patients (average age 27 years) with local histology confirmed CIN 1 or CIN 2 (safety population)
- 190 patients with CIN 1 (103) and CIN 2 (87) verified by central blinded review (efficacy population)
- 51% CIN 1 and 83% CIN 2 patients with positive HPV DNA status
- 50 CIN 1/2 patients with positive HPV 16/18 DNA status
- 1 or 2 treatments depending on results at 3 months
  - 52% of the patients received 2 treatments
- Patients enrolled at 23 centers in EU and US

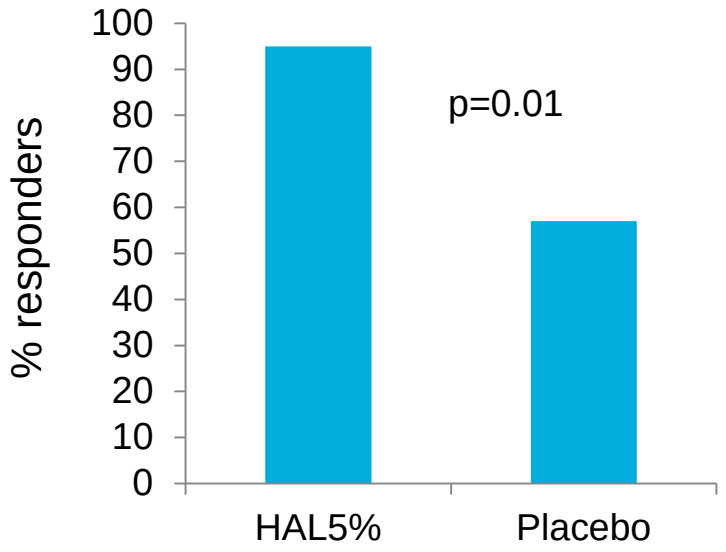


Study Demonstrated a Clear Dose Response 5% is Optimal Dose

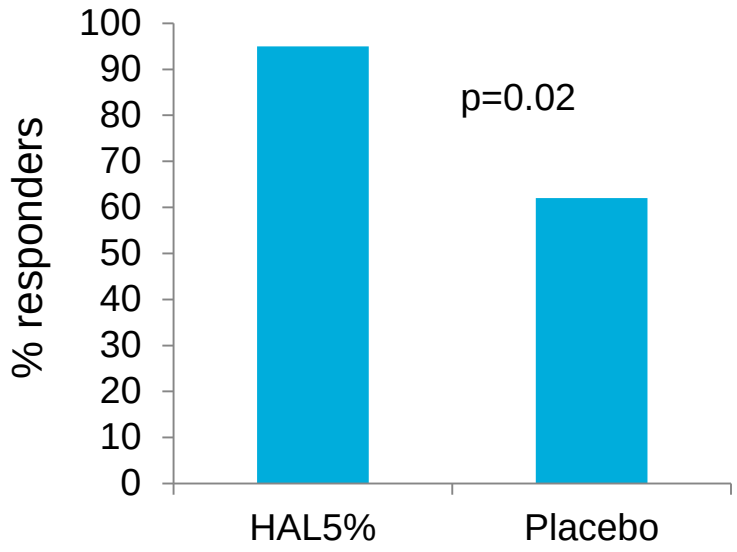


Cevira Demonstrated Significant and Sustained Efficacy in **CIN2** Patients after 6 months

CIN2 overall response 3 months after last treatment (n=40)

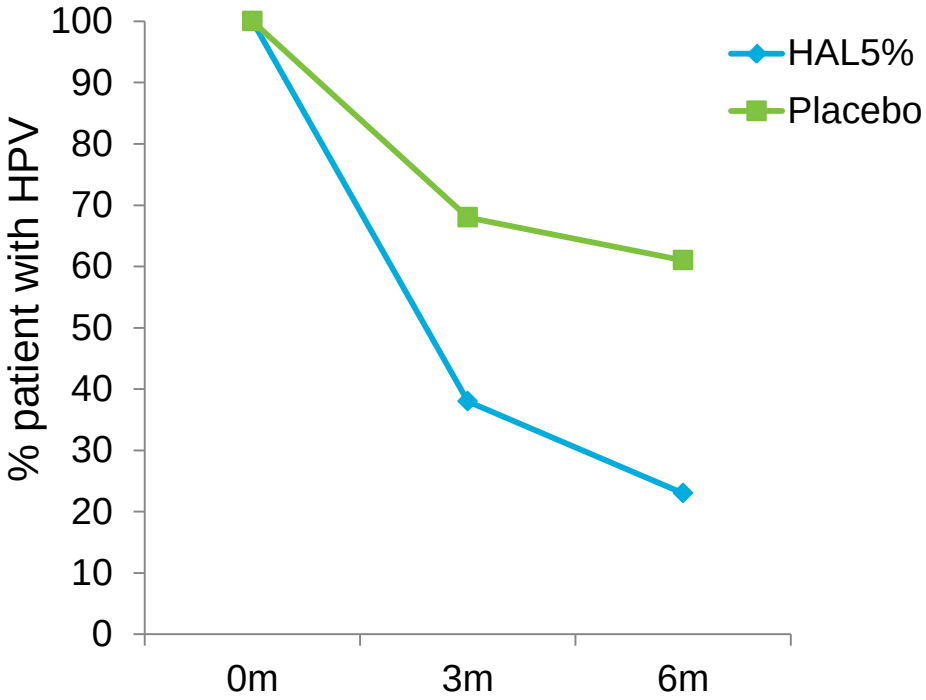


CIN2 overall response 6 months after last treatment (n=40)

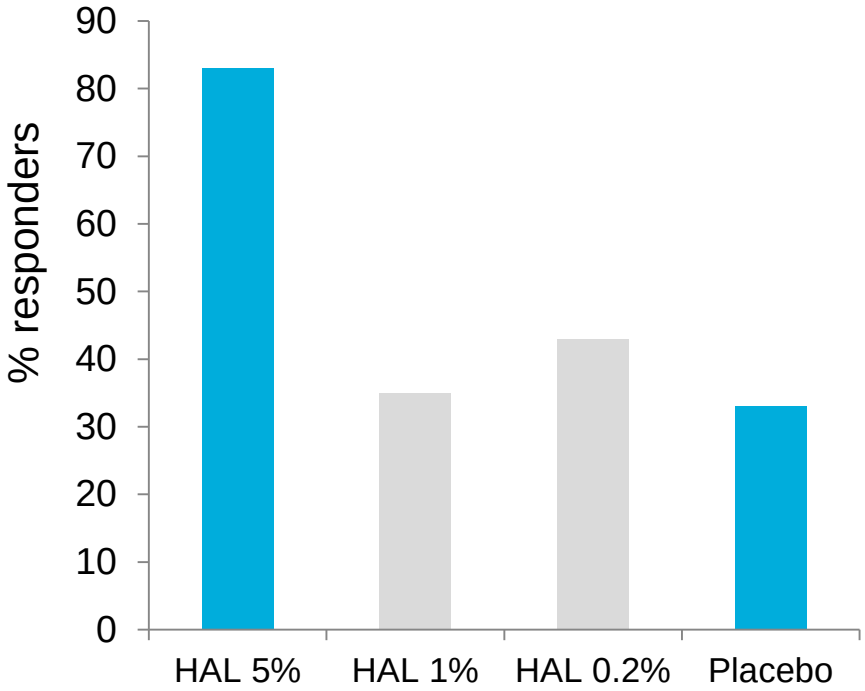


Cevira Demonstrated Sustained Clearance of HPV including HPV 16/18 at 6 months

HPV* clearance in CIN 2 patients 3-6 months after last treatment (n=31)



HPV16/18 clearance in CIN 2 patients 6 months after last treatment (n=33)

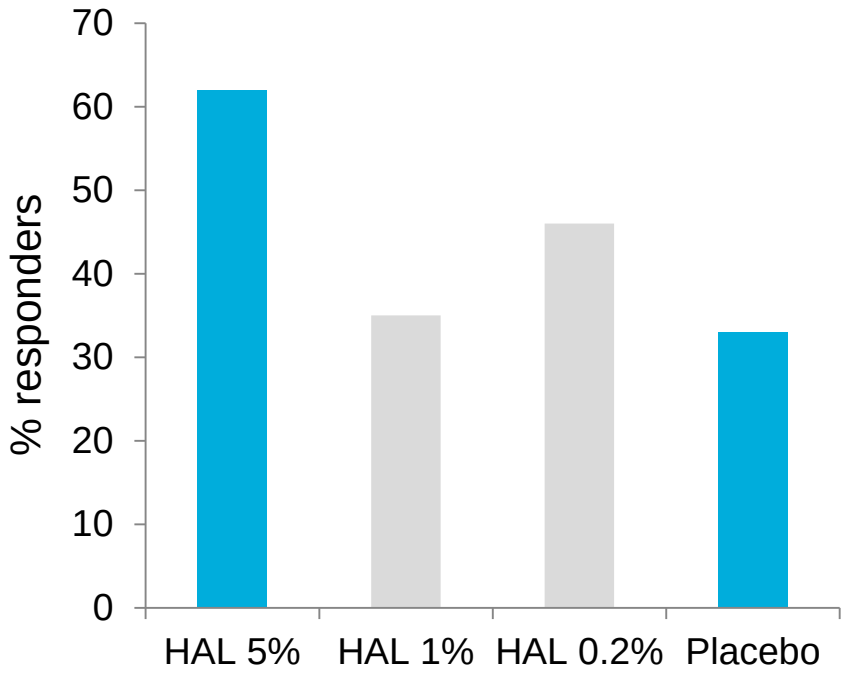


*12 oncogenic HPV subtypes

Cevira Showed a Superior Clearance of HPV 16/18 in the Overall Population

- Several HPV subtypes can cause precancerous lesions which lead to cervical cancer
- HPV 16 and 18 have the highest risks, accounting for
  - 70% of all cervical cancers
  - 50% of all high grade lesions
  - 25% of all low grade lesions
- Cevira showed superior clearance of high risk HPV 16/18 in the overall study population
- By clearing the virus rapidly, Cevira has the potential to significantly reduce the potential of progression to cervical cancer

HPV 16/18 clearance in CIN 1/2 patients 6 months after last treatment (n=50)



Cevira Tolerability and Acceptance

- No serious or systemic treatment related events were reported
- Treatment was well tolerated by the patients at all doses
  - Only self-limiting local events (e.g. discharge, discomfort, bleeding) were reported in 38% of the patients
- Several pregnancies reported during study
  - all normal full term deliveries
- High acceptance by patients and gynecologists

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Summary of Results

- Cevira at the optimal dose demonstrated sustainable efficacy in CIN 2 patients
  - Significant sustained overall response
  - High and sustained clearance of high risk HPV 16/18
- Cevira at the optimal dose showed a clear effect in overall response and HPV 16/18 clearance in the CIN 1/2 study population, though not statistically significant
- The study confirmed the strong patient and gynecologist acceptability and safe use of Cevira
- The study forms an excellent basis for selecting patient populations and endpoints for further clinical development

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Conclusion

Kjetil Hestdal, MD, PhD
President & CEO

Conclusion

- High unmet medical need for novel therapies to treat epidemic proportions of HPV/CIN populations
- Breakthrough technology allows for convenience and simplicity which can be integrated in even under-developed healthcare systems
- Results of the Phase 2b trial are significant and lay the foundation for the Phase 3 registration program
  - Significant overall response in CIN 2
  - High clearance of HPV, including highly oncogenic HPV 16/18
  - Excellent tolerability and high physician & patient acceptance
- Discussions underway to secure ideal global development and commercialization partner
- Photocure continues to deliver on the milestones as the evolution into a profitable specialty pharma company continues

Q & A

Moderated by K Hestdal