

# Gynecologic Cancer InterGroup Cervix Cancer Research Network



## NEO-ADJUVANT CHEMOTHERAPY FOLLOWED BY SURGERY IN CERVICAL CANCER:

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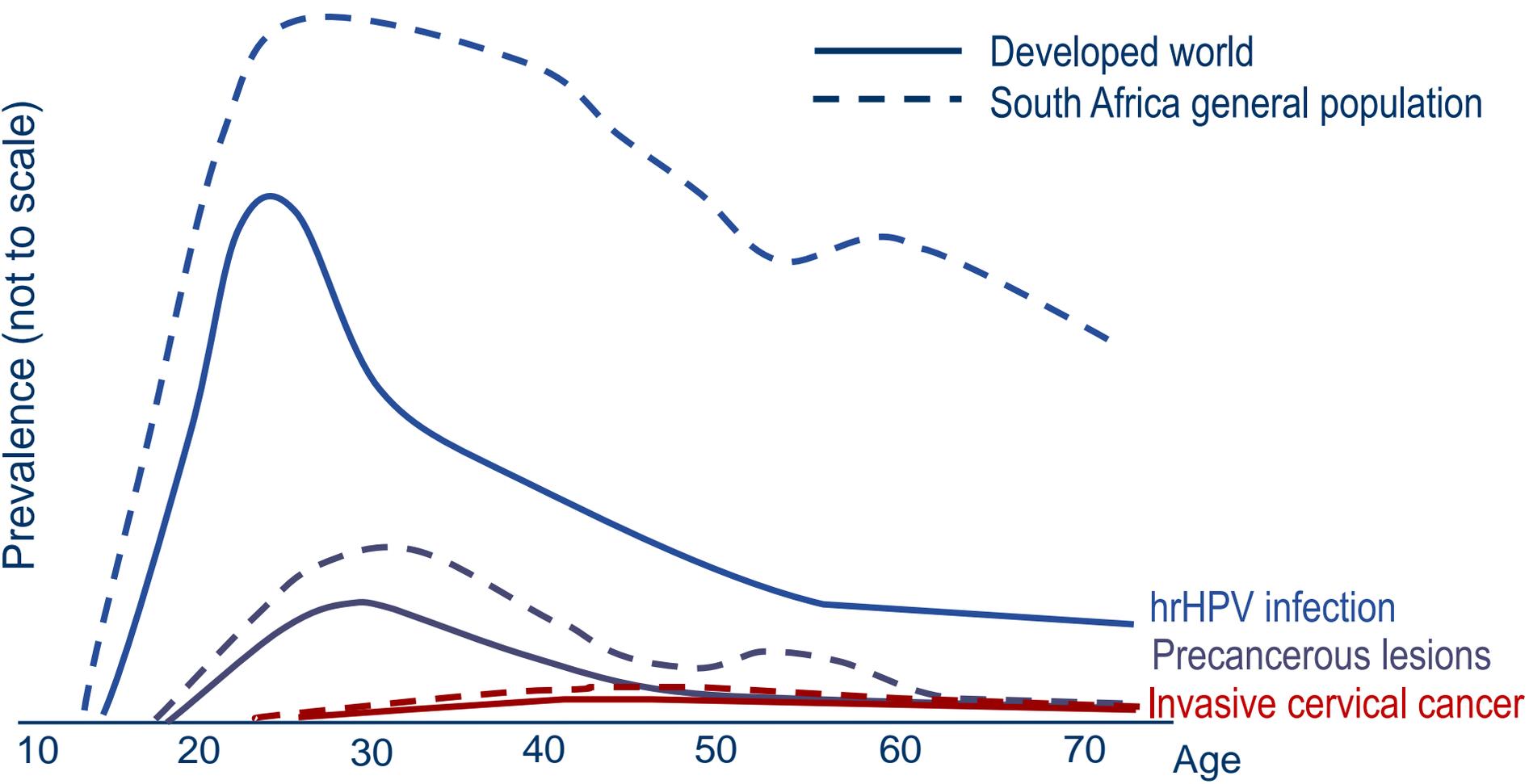
health

Department:  
Health  
REPUBLIC OF SOUTH AFRICA



Cervix Cancer Education Symposium, January 2019, South Africa

# Prevalence of HPV infection & cervical lesions in the developed world and South African population



Richter KL, Dreyer G. South Afr Med J 2013;103(5);291-2.

# INDICATION OR POSSIBLE ADVANTAGE

Induce fertility saving

Improve fertility outcomes

Induce operability

Reduce radicality of surgery

Easier surgery

Buy time to radiation

Alternative to radiation



# INDICATION OR POSSIBLE ADVANTAGE

Reduce Rx modalities

Increase Rx modalities

Reduce Rx costs

Predictor of response

Improve central control

Improve PFS

Improve OS



# APPLES vs. PEARS....

## available literature

Inclusion criteria

Aims

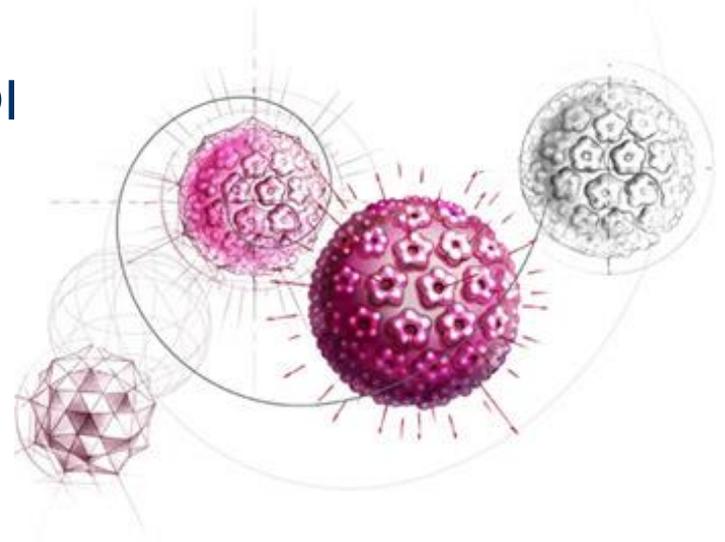
Chemo-mix

Secondary treatment options

Adjuvant options

Comparator

Outcome measures



# **Entry criteria and treatment options**

**Indication:**

**EARLY STAGE , mixed**

**LOCALLY ADVANCED**

**Secondary treatment options:**

**Surgery (radical / not)**

**CRT / RT**

**according to response**

**Adjuvant or tertiary treatment options:**

**Surgery or RT / CRT or CT**

# **OUTCOME MEASURES - LATE STAGE**

## **RESPONSE RATES**

**Histopathological**

**Clinical**

**Complete**

**Partial**

## **LOCAL CONTROL**

**PFS**

## **SYSTEMIC DISEASE**

**OS**



# **NACT FOR EARLY STAGE**

**Fertility saving possible or not**

**Operable or not**

**Large volume or small**

**Node positive or negative**

**Single vs multimodality Rx**

# Single institute RCT

Gupta 2018

**Entry criteria (635)**

Stage IB2 to IIB

**Secondary treatment**

simple or radical surgery

**Adjuvant treatment**

None or RT or CRT

**Comparator**

RT / CRT

**No improvement in OS / DFS**



# Meta-analysis

Yijie Fu; 2017

## **Secondary treatment**

simple or radical surgery

## **Adjuvant treatment**

None or RT or CRT

## **Comparator**

Radical surgery +/- adj CRT

## **Outcome**

No benefit for DFS or OS

# Meta-analysis de Azevedo et al. 2016

## **Entry criteria**

Mixed

## **Secondary treatment**

CRT, mixed

## **Comparator**

None, historical

**Outcomes much better than historical controls**

# **NACT FOR LOCALLY ADVANCED DISEASE**

**Stage II or III (+IB)**

**Large volume or small**

**Node positive or negative**

**Followed by surgery or (C)RT**

**MRI findings or histopathology**

# Single institute Ferrandina 2018

## **Entry criteria**

LACC, IB2- IIIB

## **Secondary treatment**

radiation or CRT

## **Adjuvant treatment**

Surgery

## **Outcomes**

High surgical complication rates

## **Feasibility and toxicity**

# Cochrane

## Marta Briarava 2017

### **Secondary treatment**

simple or radical surgery

### **Adjuvant treatment**

None or RT or CRT

### **Comparator**

RT

### **Outcomes similar**

RCT ongoing  
EORTC GCG 55994

**Entry criteria**

IB2 to IIB

**Secondary treatment**

surgery

**Comparator**

CRT

**Outcomes**

20-30% discontinue

PFS, OS 2019

# Single institute Marita 2017

## **Entry criteria**

LACC IIB-IIIB

## **Secondary treatment**

radiation or CRT  
or surgery

## **Comparator**

Historical

## **Outcomes**

OS same; PFS better

# POSSIBLE ADVANTAGE

useful vs not useful

Fertility saving

2015

? Robova

Induce operability

cost

✓ Gaducci 2017,

Buy time to radiation

2013

✓ Singh

Alternative to radiation

X

Reduce Rx modalities / \$

X

Increase Rx modalities

✓

ES: Better than surgery +adj

X

# POSSIBLE ADVANTAGE

useful vs possibly useful vs not

useful

Response rate

70%+

✓ Gaducci 2017:

He 2018: 80%,  
McCormack 2013 70-

80%

Predictor of RT response

2017

✓ Zu 2018, Chen

Reduce need for adj RT ✓ Kim 2013, Mallman 2016

LACC: Better than CRT X

Improve central control

vs 15%

? Dastidar 2016 10

Improve PFS

? ✓ Marita 2018

# **APPLES vs. PEARS....**

## **available literature in early stage**

**Induces short term chemo-response in 70%+**

**Small becomes smaller; early becomes earlier**

**Opens window or buys time**

**pregnant, fertility sparing, radiation alternative**

**Operable becomes more operable**

**Nodes and parametrium may become negative**

# **APPLES vs. PEARS....**

## **available literature in late stage**

**Induces short term chemo-response in 70%+**

**Late becomes less late**

**Inoperable becomes less inoperable**

**Huge need for three treatments**

**Treatment complications considerable**

**Outcomes better than RT; similar than CRT**

**Radio-resistance induced OR predicted?**

## **CONCLUSIVE REMARKS**

### **Local control debate**

**Large central disease not sterilised by RT**

**Need for multimodality treatment + surgery**

**Rescue hysterectomy option**

### **Sequence debate**

**surgery upfront less complications**

**RT first selects candidates in need**

**CT first then surgery then adjuvant ??**

**Opens the IB2 debate widely**

## **CONCLUSIVE REMARKS**

**Treatment of control arm**

**Must be optimal**

**Meaning of histologically “sterilised”**

**Remove or radiate?**

**Individualised treatment options**

**Some value for individual patient**

**Theoretical role of NACT poorly outlined**

**To reduce or**

**to increase radicality of treatment??**