



Southern African HIV Clinicians Society 3rd Biennial Conference

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**Our Issues, Our Drugs,
Our Patients**

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VICAR 2
LEEP vs Cryotherapy for treatment
for CIN 2+ in HIV infected women

SA HIV Clinician Society
April 2016
Cindy Firnhaber

Introduction

- Invasive cervical cancer incidence rates are higher among HIV seropositive women.
- Little is currently known about the comparative effectiveness of different treatment modalities in HIV-seropositive women to optimize successful treatment.
- Data based on a randomized controlled study design would be optimal to determine comparative treatment effectiveness.

Study Aims

Primary Aim:

➤PA1: To compare the efficacy of cryotherapy and LEEP (Loop Electrosurgical Excision Procedure) methodologies for the treatment of high-grade cervical intra-epithelial neoplasia (CIN 2/3) among HIV-seropositive women.



Infection with HPV →



Persistent / Recurrent HPV infection ↓



HIV negative
around late 40s-50s

HIV positive late 20s
-mid 30s



Study Eligibility & Population Enrollment



- HIV-seropositive woman with confirmed histology-proven CIN 2 or 3 disease
- Between ages of 18 & 65 and not pregnant
- Absence of previous treatment for HSIL (e.g. cryotherapy, LEEP or cone biopsy); no prior hysterectomy (i.e. removal of uterus)
- No currently active STD determined by clinical history and/or physical exam
- Eligible for cryotherapy treatment (e.g. no lesions or lesions not too large, nor endocervical)
- Absence of significant medical or mental illness that may hinder protocol compliance or place patient at medical risk



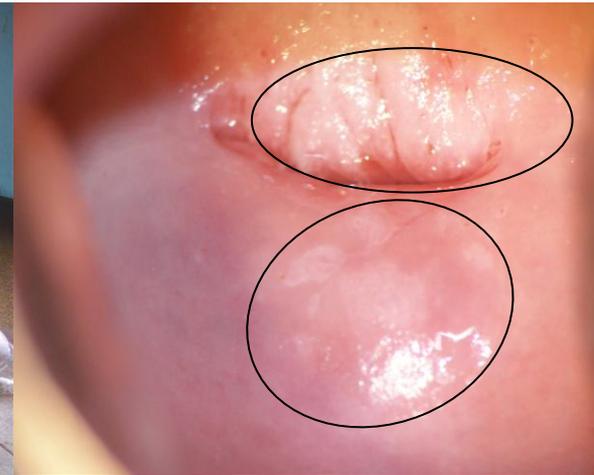
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Methods

- VIA (Visual Inspection with Acetic Acid) photograph was read by two clinicians to determine whether cervical lesions were amenable to cryotherapy treatment.
- Eligible women with CIN2/3 were then randomized to 1 of 2 treatment arms:
 - Cryotherapy
 - LEEP



LEEP vs CRYO



Statistical Analyses

- Treatment comparisons using:
 - Fisher's exact test
 - Wilcoxon rank-sum test
 - Cochran-Armitage test for trend.
- Log-rank test - Differences in the survival distributions.
- Kaplan Meier estimates - Time until an event of CIN.
- Cox proportional hazards model – Effect of baseline CD4 count on treatment outcome.
- Subgroup analyses - Compare the incidence of high grade biopsy result via stratification of baseline CD4 count (≤ 350 vs > 350).

Baseline Attributes

Covariates	CRYOTHERAPY (N=80)	LEEP (N=86)	p-value
Age (years) [¶]	37.5 (26-52)	35.0 (22-57)	0.17
CD4 count (per mm ²) [¶]	412.0 (54-1158)	413.0 (99-1561)	0.46
Age of first sex (years) [¶]	17.5 (10-25)	17 (12-28)	0.39
Lifetime sexual partners [¶]	4 (2-98)	7 (1-180)	0.04
HPV DNA positivity	89.7%	92.5%	0.59
Pap Smear result [†]			
Negative	2.5%	2.4%	0.92
ACUS & LSIL	22.5%	23.5%	
ASC-H & HSIL	75.0%	74.1%	
Detectable HIV viral load [‡]	30.4%	16.3%	0.04

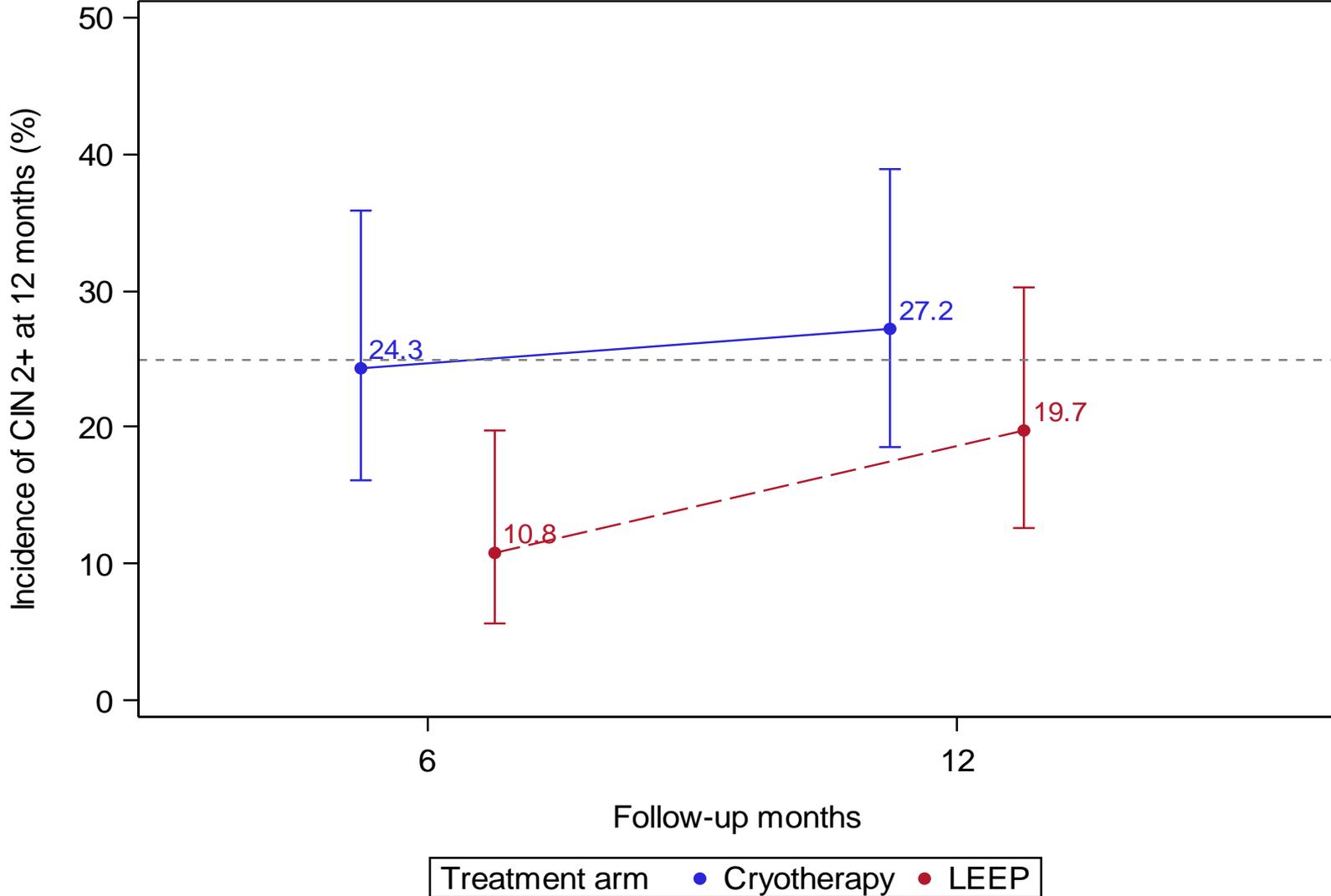
[¶] Median (Min-Max)

[†] ASCUS = Atypical Squamous Cells of Undetermined Significance, LSIL = Low grade Squamous Intraepithelial Lesion, HSIL = High grade Squamous Intraepithelial Lesion, ASC-H = Atypical Squamous Cells – cannot exclude HSIL

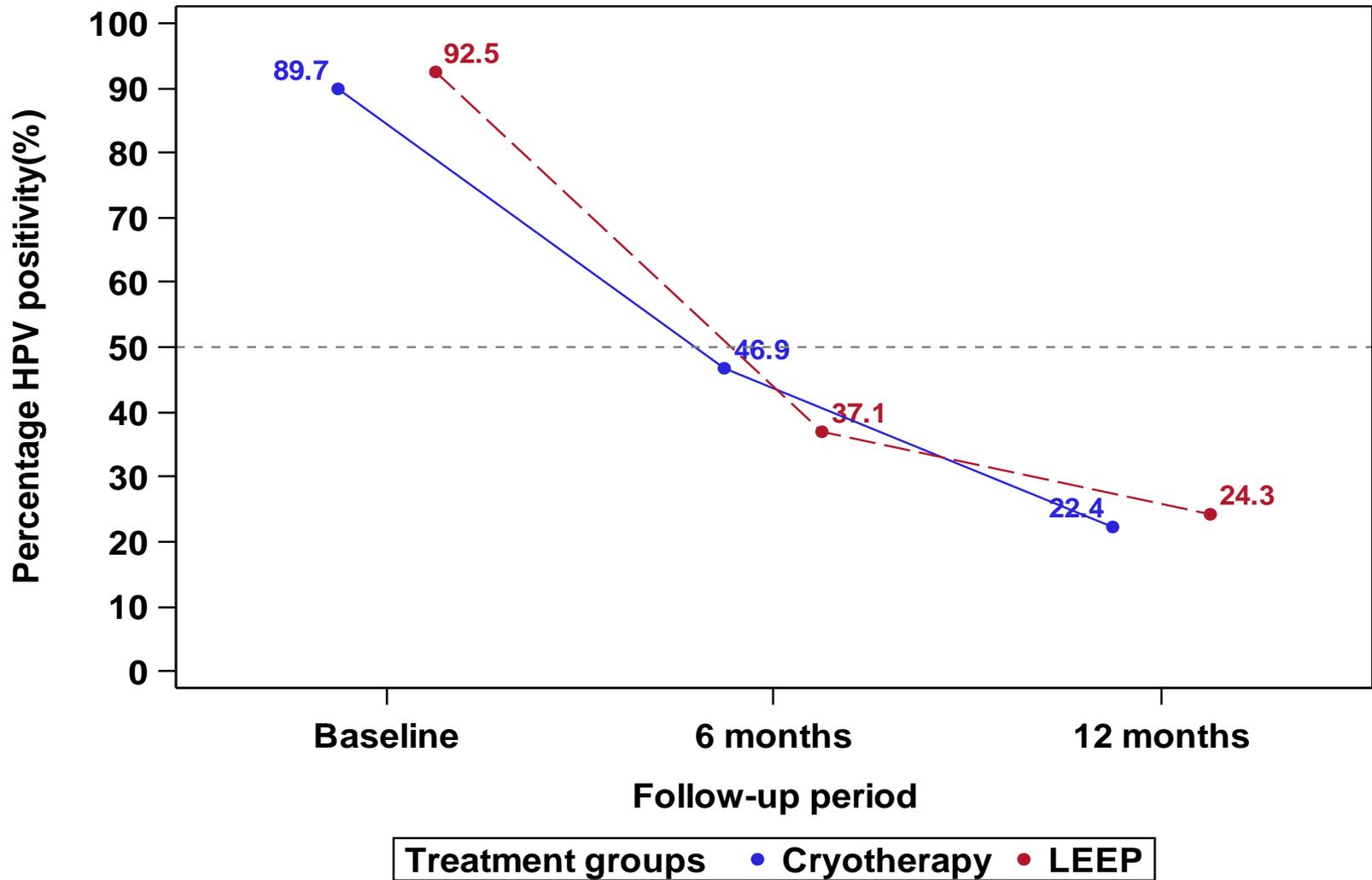
[‡] Least detectable viral load was 400 copies



Cumulative risk of CIN 2+ with 95% CI



Prevalence of HPV positivity in HIV seropositive women comparing Cryotherapy to LEEP



Conclusion

Survival probability in treating CIN 2+ at 12 months:

- LEEP – 80.3%
- Cryotherapy – 72.8%

This difference was not statistically significant ($p=0.21$).

Treatment outcomes of primary endpoints:

CIN2+

LEEP out-performed cryotherapy at 6 months ($p=0.02$). However at 12 months, there was no difference in the efficacy of both treatments ($p=0.21$).

THANK YOU

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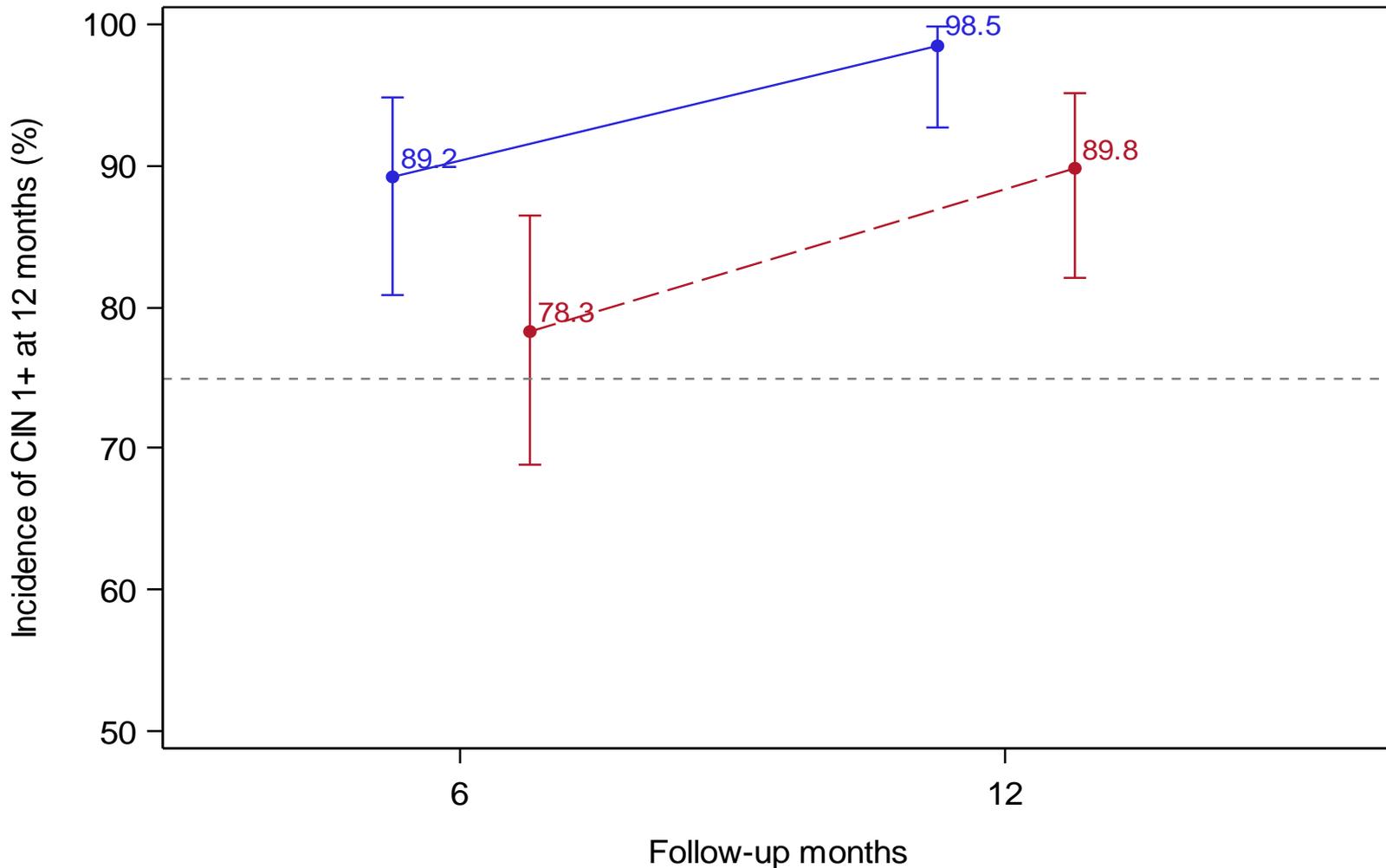


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Cumulative risk of CIN 1+ with 95% CI



Treatment arm • Cryotherapy • LEEP



Results: Cumulative incidence of CIN over 12 months follow-up stratified by baseline CD4 count

Cumulative Biopsy Result	CRYOTHERAPY (N=74)		LEEP (N=83)		p-value
	No.	Probability % (95% CI)	No.	Probability % (95% CI)	
CIN 1+					
<i>Baseline CD4 350</i>					
6 months	29	87.9 (74.5 – 96.2)	23	74.2 (58.2 – 87.8)	0.16
12 months	32	100.0 (N/A)	28	90.3 (77.1– 97.5)	0.08
<i>Baseline CD4 350</i>					
6 months	37	90.2 (78.9 – 96.9)	42	80.7 (69.1 – 90.1)	0.21
12 months	40	97.6 (88.9 – 99.8)	46	89.3 (78.9 – 95.9)	0.11
CIN 2+					
<i>Baseline CD4 350</i>					
6 months	6	18.2 (8.6 – 36.1)	4	12.9 (5.1 – 30.8)	0.56
12 months	7	21.6 (10.9 – 40.1)	5	16.1 (7.1– 34.5)	0.58
<i>Baseline CD4 350</i>					
6 months	12	29.3 (17.9 – 45.8)	5	9.6 (4.1 – 21.6)	0.02
12 months	13	31.8 (19.9 – 48.4)	10	20.1 (11.4 – 34.2)	0.15