

SINGLE AND MULTIPLE EXPOSURE TOLERANCE STUDY OF THREE CONCENTRATIONS OF C31G: ONCE- AND TWICE-DAILY EXPOSURE

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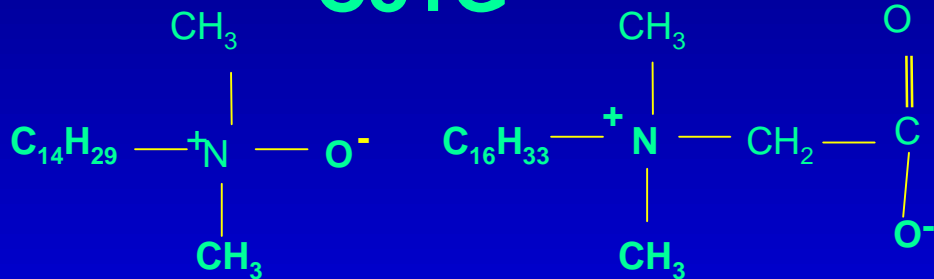
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Inc

C31G: Background:

- ◆ Product of Biosyn, Inc. ("Savvy")
- ◆ Surfactant, like N-9, but different structure and behavior

C31G vs. N-9: Chemistry

C31G



Alkyl dimethyl
amine oxide

Alkyl dimethyl
glycine (betaine)

1:1 Mixed Micelle

Amphoteric Surfactant

Nonoxynol 9



Nonylphenol (polyethoxy)
ethanol

Nonionic Ethoxylated
Alcohol Surfactant

C31G – comparisons with N-9

- ◆ Faster diffusion into cervical mucus
- ◆ *In vitro* spermicidal activity equal to N-9
- ◆ *In vitro* activity against HIV, chlamydia, gonorrhea, syphilis, HSV, chancroid, candida, e coli
- ◆ More selective effects on cell membranes
- ◆ Less toxic to vaginal keratinocytes than N-9:
 - ▶ At 100 ug/ml C31G, 100% viable
 - ▶ At 100 ug/ml N-9, 0% viable
 - ▶ At 800 ug/ml C31G, 50% still viable

Clinical studies on C31G completed prior to this one

- ◆ PCT using 1.2% C31G in hydroxyethylcellulose (HEC)
 - ▶ No difference from N-9 in sperm counts
 - ▶ Genitourinary AEs: 30% in C31G vs. 8% in N-9 group
- ◆ 8-day irritation study using 1.2% C31G in HEC
 - ▶ Irritation seen in 80% of C31G group
- ◆ 3-day irritation study using 7 formulations of C31G
 - ▶ 1.2% C31G in HEC least tolerated
 - ▶ New formulation well-tolerated
 - ▶ New formulation carried forward into this study

C31G Safety study - Objectives

Assess:

- ◆ Genital irritation:
 - ▶ Symptoms
 - ▶ Findings on naked eye exam
 - ▶ Colposcopic findings
- ◆ Vaginal leakage
- ◆ Systemic safety
- ◆ Absorption
- ◆ Changes in microflora
- ◆ Changes in vaginal cytology
- ◆ Acceptability

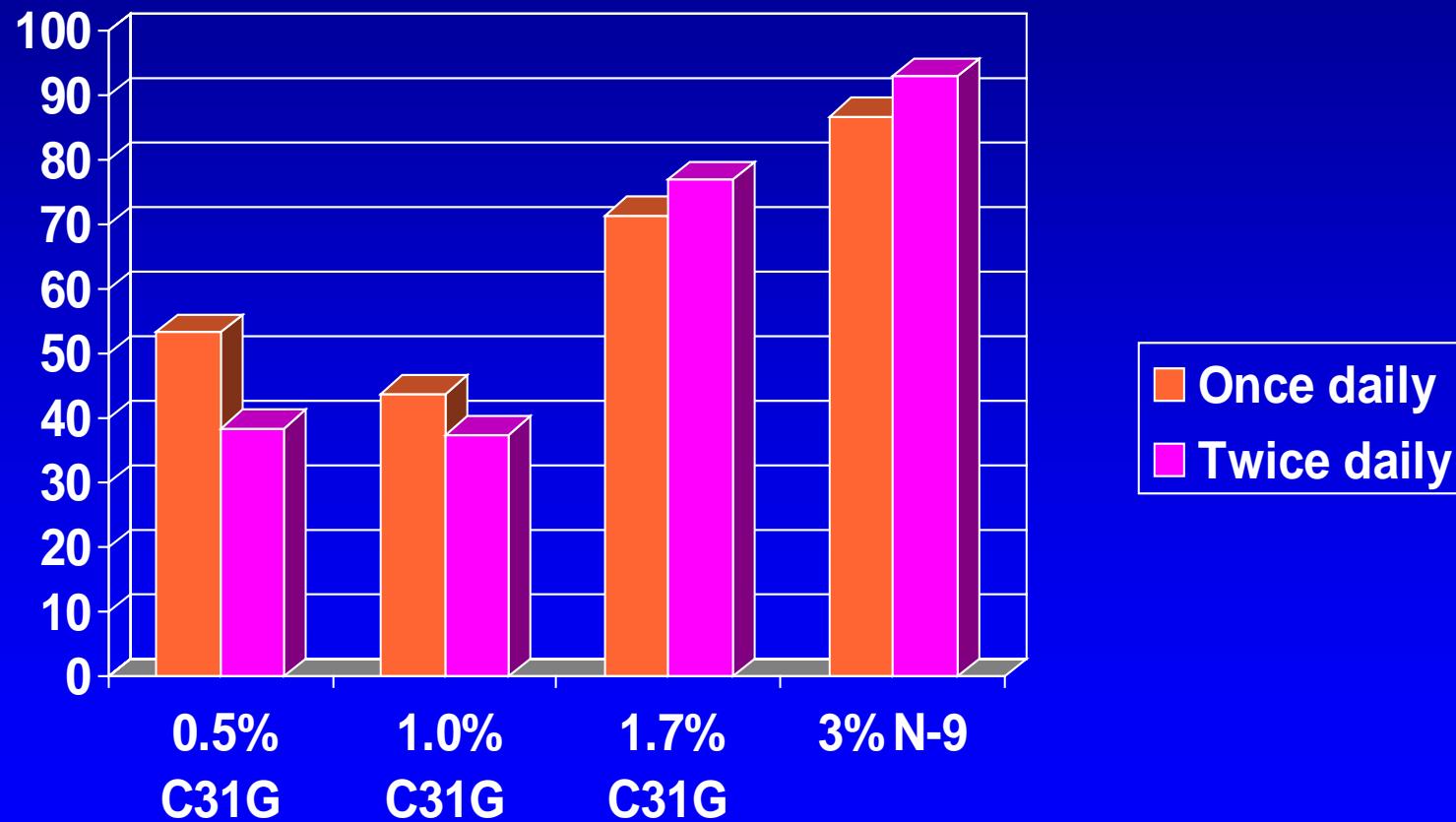
C31G safety study - design

- ◆ Blinded, randomized
- ◆ Treatment groups (all 3.5 ml):
 - ▶ 0.5% C31G
 - ▶ 1.0% C31G
 - ▶ 1.7% C31G
 - ▶ 3% N-9
- ◆ 16 women per group, 64 total
- ◆ Two sites:
 - ▶ Magee-Womens Hospital in Pittsburgh
 - ▶ University of Pennsylvania in Philadelphia

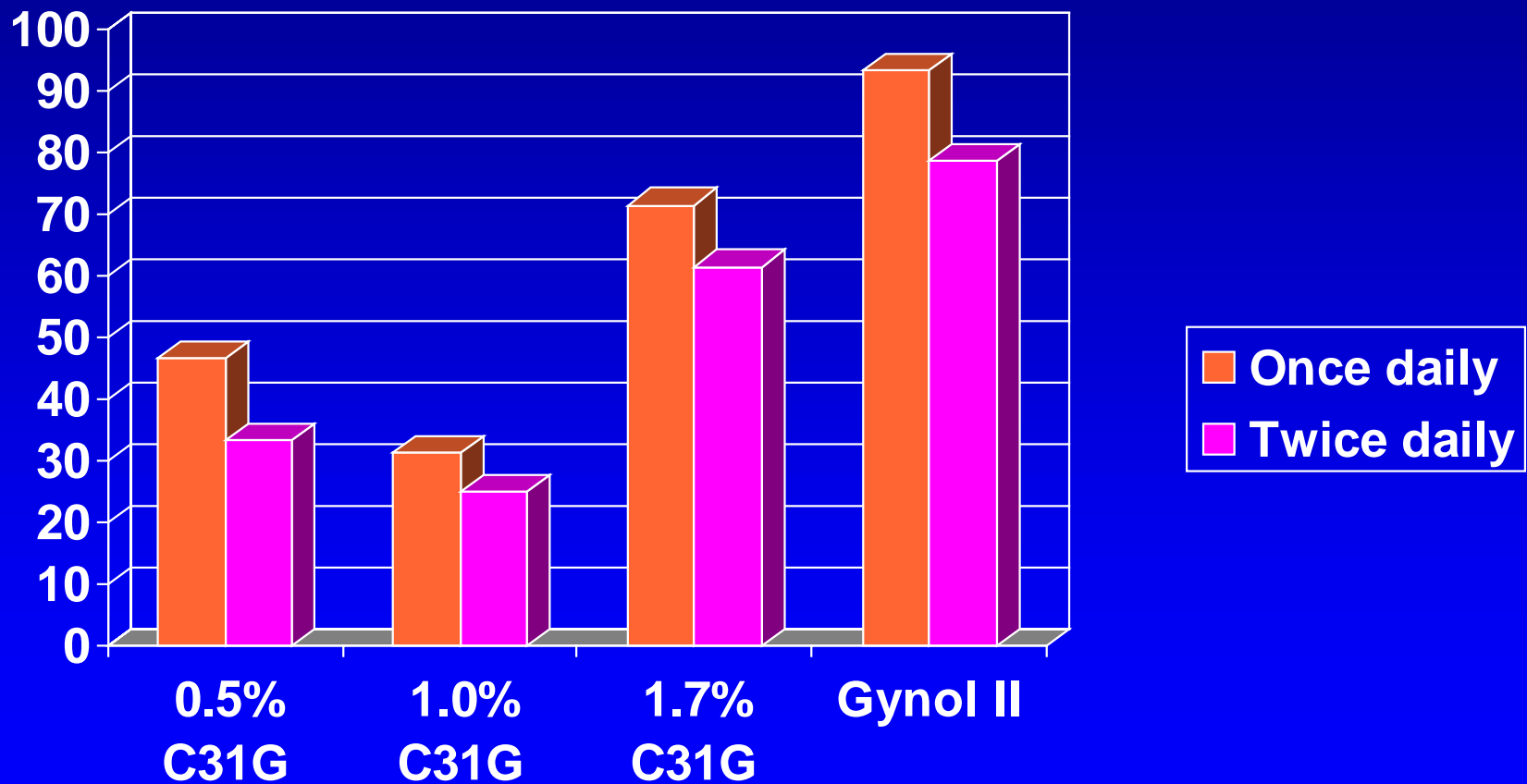
Design - continued

- ◆ Participants at low risk for pregnancy and STDs
- ◆ Product used once daily for 7 days, then twice daily for 7 days
- ◆ No intercourse
- ◆ Participants seen at :
 - ▶ Screening
 - ▶ Enrollment
 - ▶ After 7 days once-daily use
 - ▶ After 14 days twice-daily use

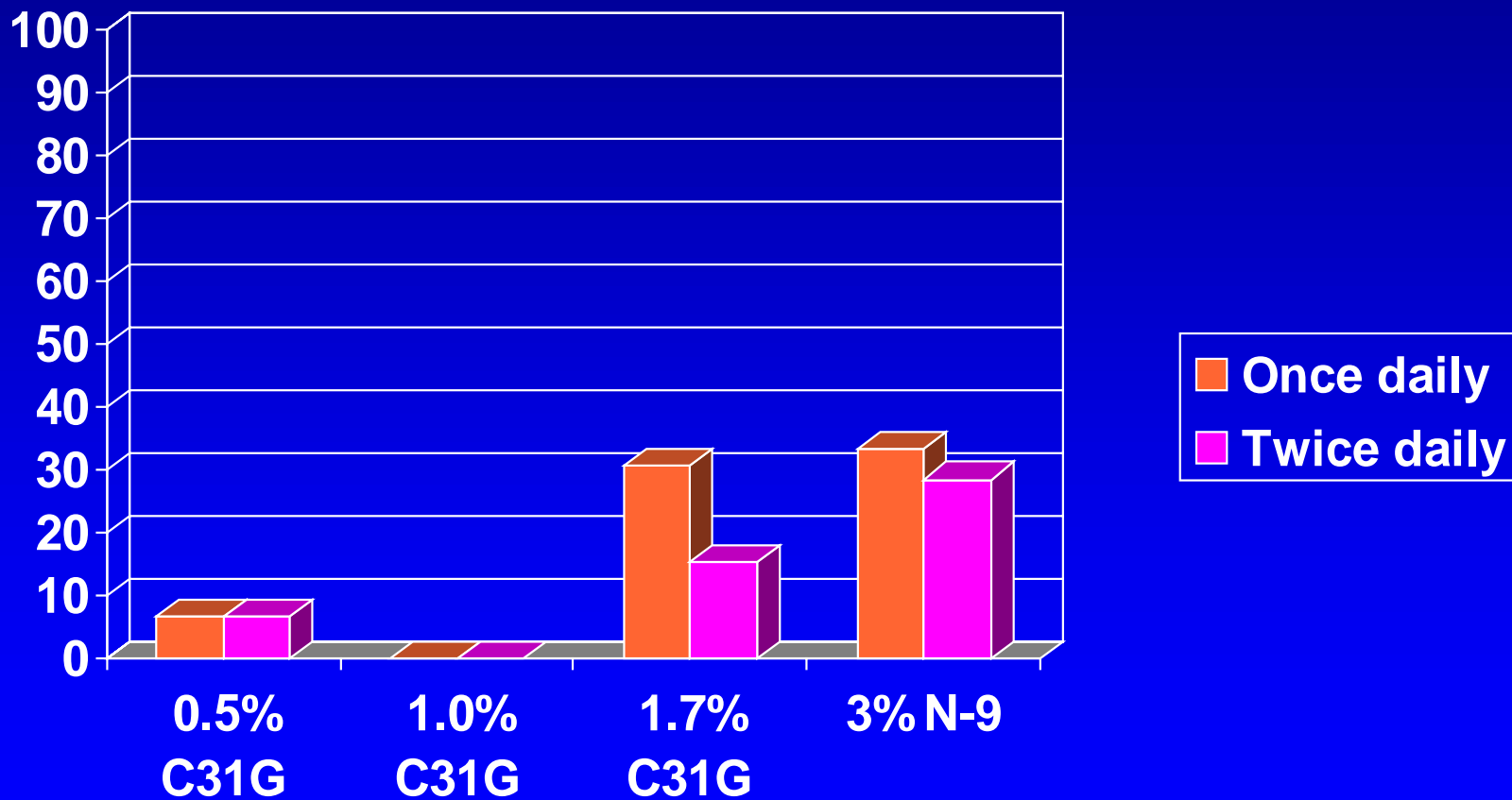
C31G Safety study – % of women with any evidence of irritation



C31G Safety study – % of women with product-related irritation



C31G Safety study – % women with “non-mild” product-related AEs



C31G Safety study – other results

- ◆ % of women reporting moderate-severe leakage
 - ▶ Once-daily use: 19-27%
 - ▶ Twice-daily use: 14-46%
 - ▶ More leakage in 1.7% C31G group than N-9 group during twice-daily use; otherwise no significant differences between groups
- ◆ Systemic safety:
 - ▶ Few changes, no differences between groups
- ◆ No evidence of absorption

Other results - continued

- ◆ Microflora
 - ▶ Very few changes
 - ▶ No significant differences between groups
- ◆ Cytology
 - ▶ More inflammation in N-9 & 1.7% C31G groups
- ◆ Acceptability
 - ▶ 50-67% would buy to prevent pregnancy
 - ▶ 47-58% would buy to prevent STDs

Conclusions

- ◆ 0.5% and 1.0% C31G significantly less irritating than N-9.
- ◆ Both 0.5% and 1.0% C31G performed well in postcoital testing
- ◆ 1.0% chosen for further study in male tolerance study.