

FERRARA, 21/03/2014

HOTEL OROLOGIO

OSTETRICIA e GINECOLOGIA 2014

Centro Salute Donna

Azienda USL Ferrara

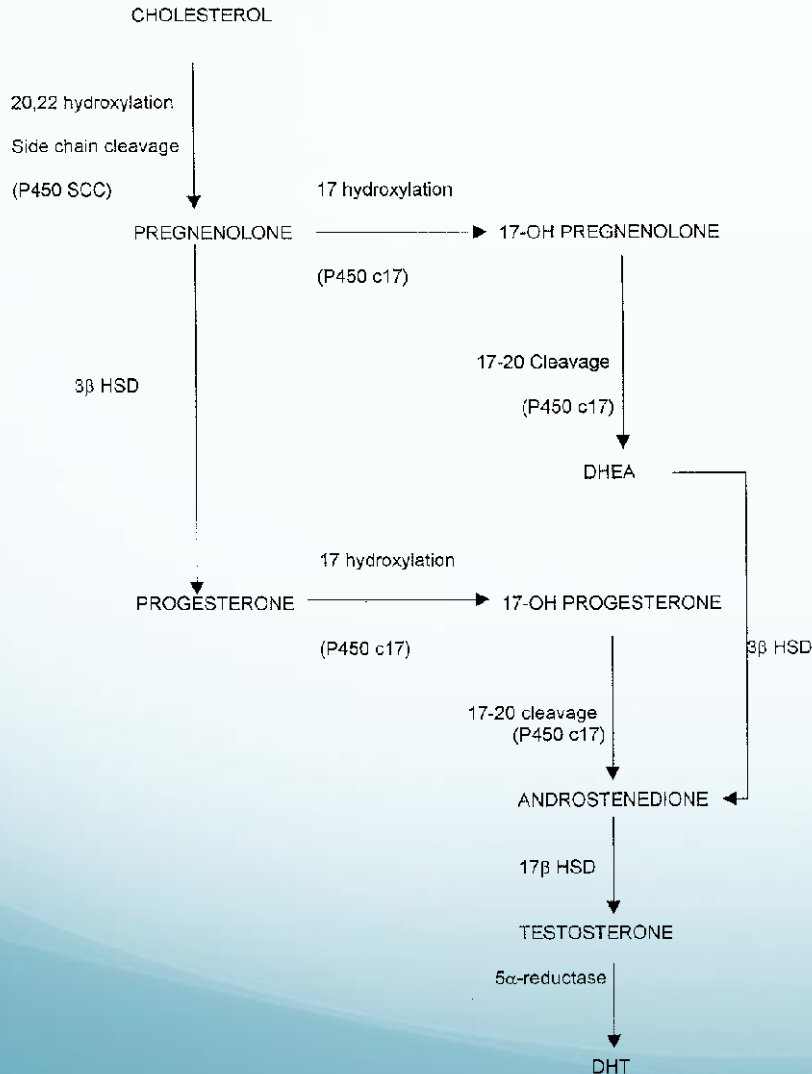
Approccio

contraccettivo

nell'iperandrogenismo



Iperandrogenismo



Influenzano il comportamento e l'umore

[Weiner CL. Psychosom Med 2004;66:356–62.](#)

Modificano la composizione corporea

[Rebuffe-Scrive. Horm Metab Res 1989;21: 391–7.](#)

[Lindstedt G. Diabetes 1991;40:123–8.](#)

Alterano il metabolismo glicidico

[DeFronzo RA. Diabetes Care 1991;14:173–94.](#)

Iperandrogenismo

Irregolarità mestruali

Acne

Irsutismo

Seborrea

Adiposità androgenica

Irsutismo

A livello dell'unità pilo-sebacea è presente l'enzima 5- α -reduttasi di tipo 1 e 2 che converte DHEA e testosterone in forme attive come DHT

L'eccesso di DHT agisce attivando fattori come IGF-1 che hanno un effetto mitogeno sui follicoli piliferi e prolunga la fase anagen

Randall VA. Lippincott-Raven Publishers, 1997

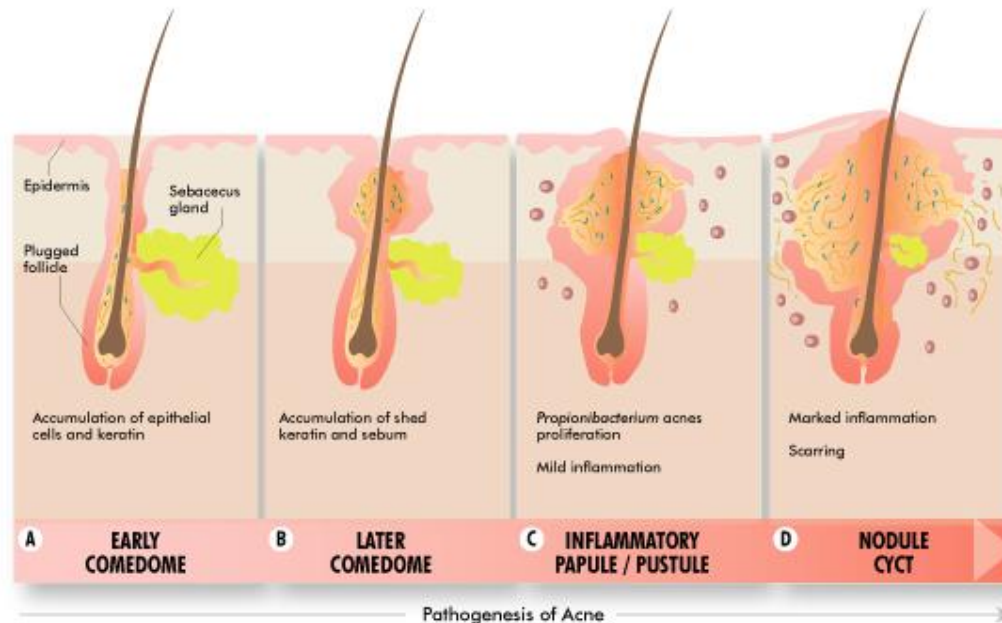
Table 2. Distribution of terminal hair under endocrine conditions.

| Endocrine condition | Type of terminal hair | | | | | |
|-------------------------------------|-----------------------|-------|-------|-------|---------------------|--------|
| | Eyelash | Scalp | Axial | Pubic | Abdominal/ chest | Facial |
| Normal child | + | + | - | - | - | - |
| Adult female androgens | + | + | + | + | - | - |
| Excess female androgens | + | + | + | + | ± | ± |
| Adult male androgens | + | + | + | + | + | + |
| 5 α -Reductase II deficiency | + | + | + | + | - | - |
| Androgen receptor deficiency | + | + | - | - | - | - |

Acne - Seborrea

L'eccesso di DHT stimola la produzione di sebo a livello dell'unità pilosebacea

Si forma il comedone chiuso che colonizzato dai batteri permette la formazione di lesioni infiammatorie



Alopecia

Scala di Ludwig

Sistema di Classificazione della Calvizie Femminile

I-1



I-2



I-3



I-4



II-1



II-2



III



Advanced



Frontal



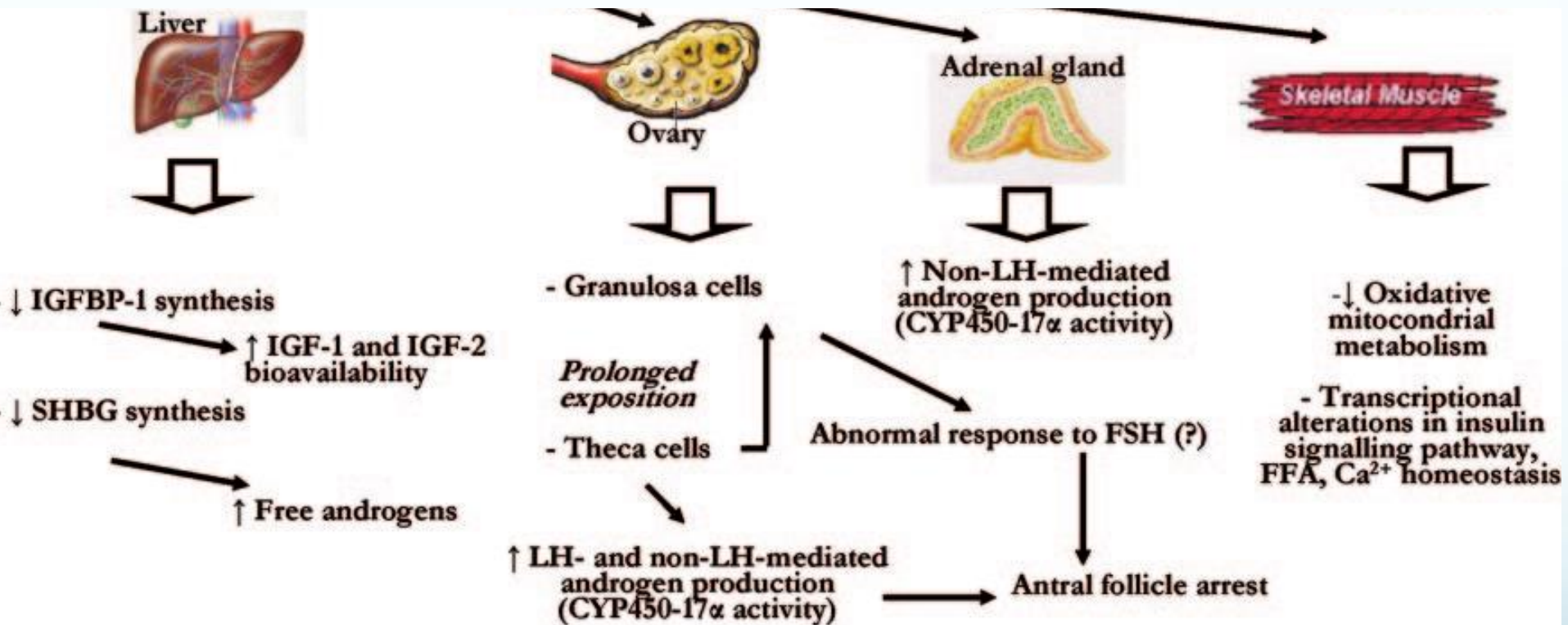
La fase anagen è più breve e la fase telogen più lunga

Continuo e diffuso assottigliamento dei capelli a partire dalla loro punta

Elevati livelli di 3-alfa-androstenedione solfato e androsterone solfato

Alterato meccanismo di solfatazione degli androgeni nelle iperandrogeniche con alopecia

Irregolarità mestruali



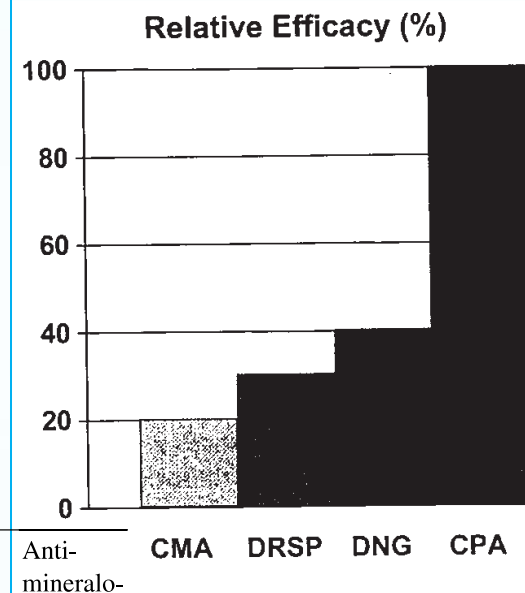
Quale terapia?

Desiderio di gravidanza?

Quale contraccettivo?



Quale progestinico?



Biological activities of natural progesterone and synthetic progestins

| Progestin | Progesterogenic | Anti-gonadotropic | Anti-estrogenic | Estrogenic | Androgenic | Anti-androgenic | Glucocorticoid | Anti-mineralocorticoid |
|----------------------------------|-----------------|-------------------|-----------------|------------|------------|-----------------|----------------|------------------------|
| Progesterone | + | + | + | - | - | ± | + | + |
| Dydrogesterone | + | - | + | - | - | ± | - | ± |
| Medrogestone | + | + | + | - | - | ± | - | - |
| 17 α -Hydroxy-derivatives | | | | | | | | |
| Chlormadinone acetate | + | + | + | - | - | + | + | - |
| Cyproterone acetate | + | + | + | - | - | +++ | + | - |
| Megestrol acetate | + | + | + | - | ± | + | + | - |
| Medroxy-progesterone-acetate | + | + | + | - | ± | - | + | - |
| 19-Nor-progesterone-derivatives | | | | | | | | |
| Nomegestrol acetate | + | + | + | - | - | ± | - | - |
| Promegetone | + | + | + | - | - | - | - | - |
| Trimegestone | + | + | + | - | - | ± | - | ± |
| Spirolactone-derivatives | | | | | | | | |
| Drospirenone | + | + | + | - | - | + | - | + |
| 19-Nortestosterone derivatives | | | | | | | | |
| Norethisterone | + | + | + | + | + | - | - | - |
| Lynestrenol | + | + | + | + | + | - | - | - |
| Norethinodrel | ± | + | ± | + | ± | - | - | - |
| Levonorgestrel | + | + | + | - | + | - | - | - |
| Norgestimate | + | + | + | - | + | - | - | - |
| 3-Keto-desogestrel | + | + | + | - | + | - | - | - |
| Gestoden | + | + | + | - | + | - | + | + |
| Dienogest | + | + | ± | ± | - | + | - | - |

Combined oral contraceptive pills for treatment of acne (Review)

Arowojolu AO, Gallo MF, Lopez LM, Grimes DA



**THE COCHRANE
COLLABORATION®**

COC vs placebo

Di 10 trial analizzati, ben 9 erano concordi nell'affermare un miglioramento delle lesioni cutanee nelle pz in tp ep.

**Combined oral contraceptive pills for treatment of acne
(Review)**

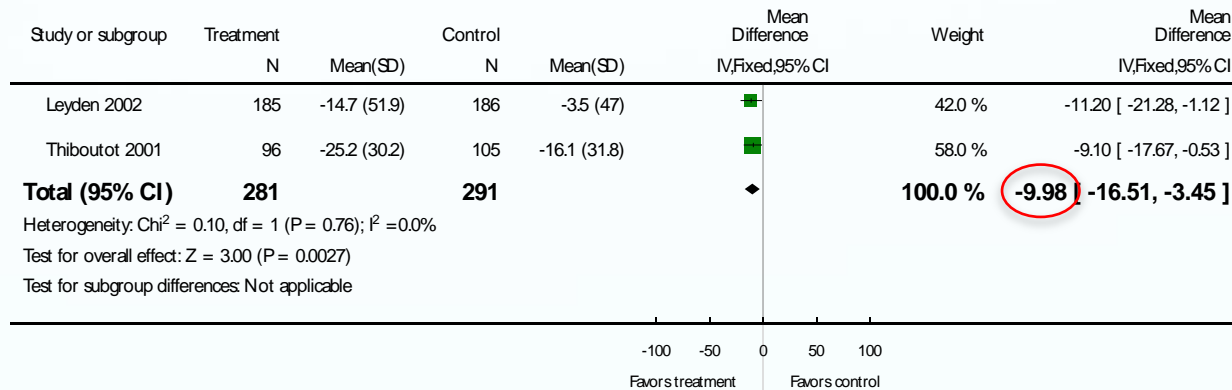
Arowojolu AO, Gallo MF, Lopez LM, Grimes DA



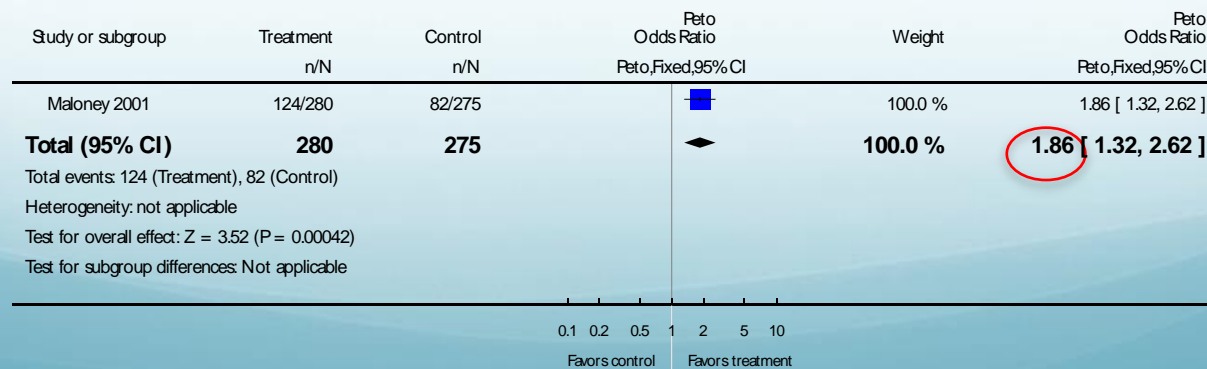
**THE COCHRANE
COLLABORATION®**

COC vs placebo

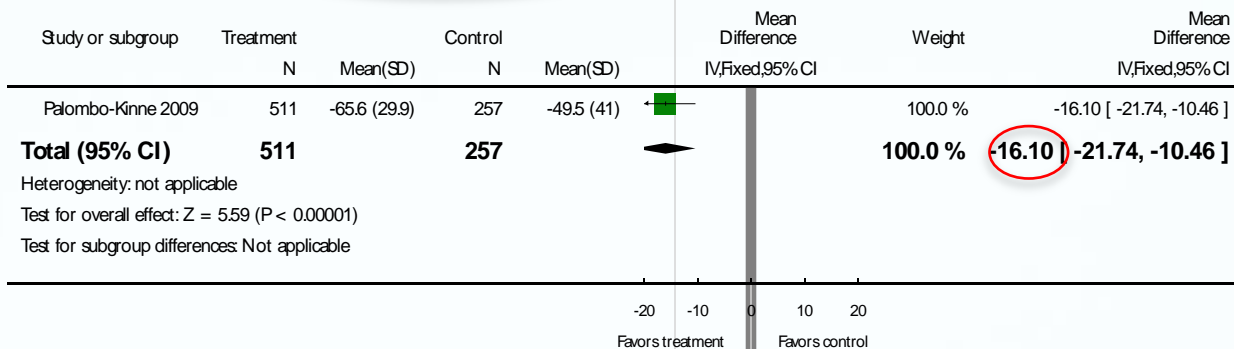
Comparison 1 LNG 100 µg / EE 20 µg versus placebo, Outcome 1 Mean change in total lesion count.



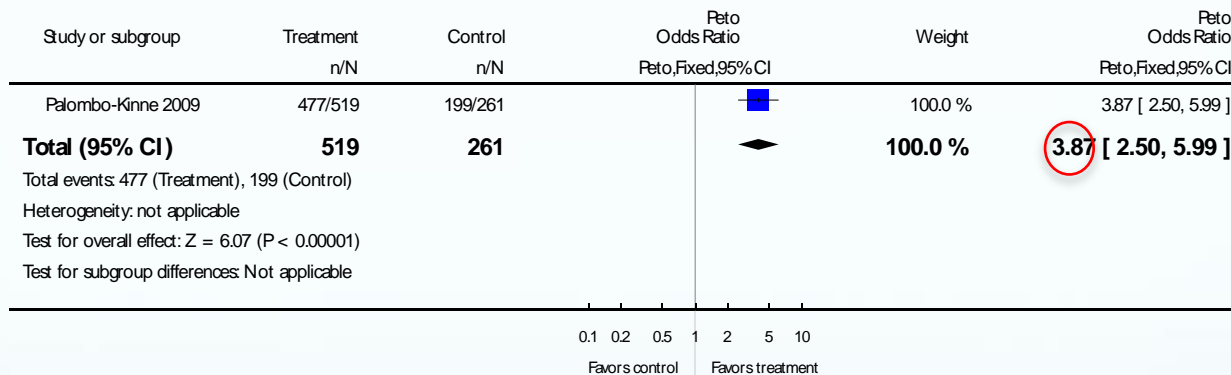
Comparison 2 NA 1 mg / EE 20-30-35 µg versus placebo, Outcome 1 Clinician assessment of no, minimal or mild acne at cycle 6.



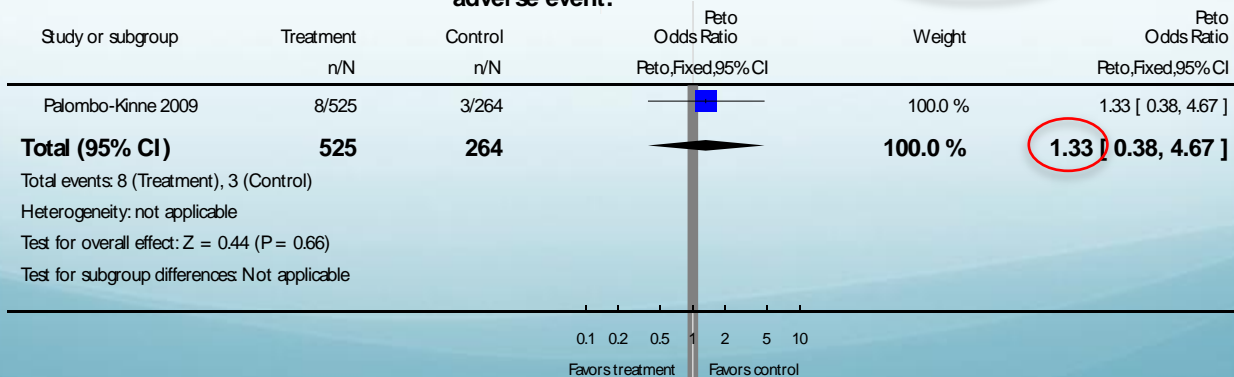
Comparison 4 Dienogest 2 mg / EE 30 µg versus placebo, Outcome 1 Mean percentage change in inflammatory lesion count after cycle 6.



Comparison 4 Dienogest 2 mg / EE 30 µg versus placebo, Outcome 3 Improvement of facial acne (clinical assessment).



Comparison 4 Dienogest 2 mg / EE 30 µg versus placebo, Outcome 4 Discontinuation due to adverse event.

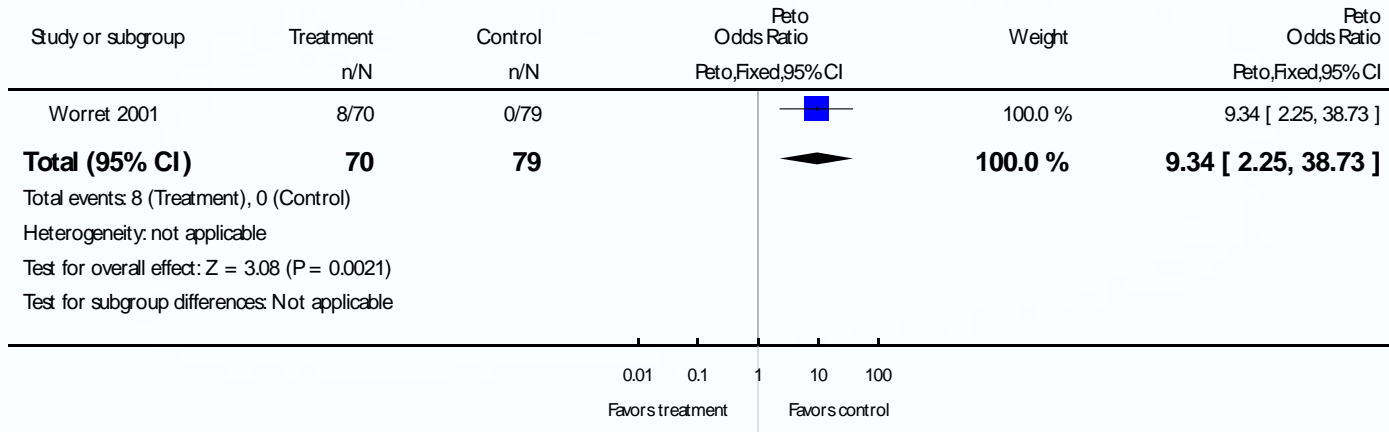


Comparison 5 DRSP 3 mg / EE 20 µg versus placebo, Outcome 1 Mean percent change in lesion counts at cycle 6.

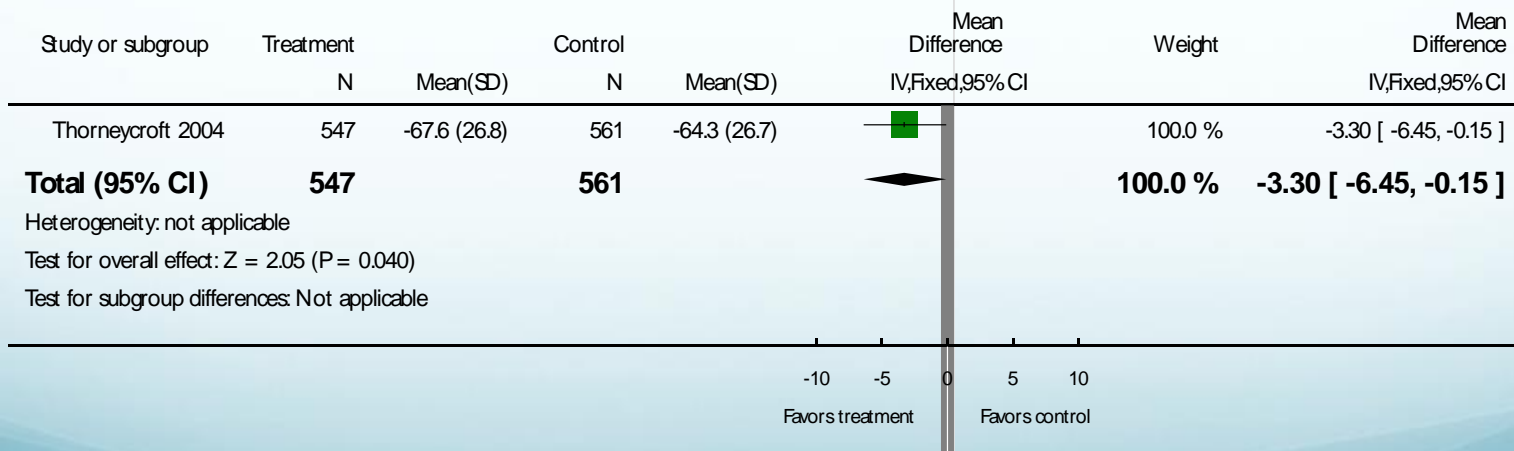
| Study or subgroup | Treatment | | Control | | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|--|-----------|---------------|-----------|----------------|------------------------------------|----------------|------------------------------------|
| | N | Mean(SD) | N | Mean(SD) | | | |
| 1 Mean percent change in total lesion count | | | | | | | |
| Bayer 2011 | 87 | 66.79 (31.45) | 86 | 37.71 (118.73) | | 100.0 % | 29.08 [3.13, 55.03] |
| Subtotal (95% CI) | 87 | | 86 | | | 100.0 % | 29.08 [3.13, 55.03] |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 2.20 (P = 0.028) | | | | | | | |
| 2 Mean percent change in inflammatory lesion count | | | | | | | |
| Bayer 2011 | 75 | 75.49 (28.11) | 71 | 60.88 (29.92) | | 100.0 % | 14.61 [5.18, 24.04] |
| Subtotal (95% CI) | 75 | | 71 | | | 100.0 % | 14.61 [5.18, 24.04] |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 3.04 (P = 0.0024) | | | | | | | |
| 3 Mean percent change in non-inflammatory lesion count | | | | | | | |
| Bayer 2011 | 75 | 69.27 (33.75) | 71 | 50.24 (49.93) | | 100.0 % | 19.03 [5.13, 32.93] |
| Subtotal (95% CI) | 75 | | 71 | | | 100.0 % | 19.03 [5.13, 32.93] |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 2.68 (P = 0.0073) | | | | | | | |
| 4 Mean percent change in papule count | | | | | | | |
| Bayer 2011 | 75 | 72.36 (31.32) | 71 | 55.03 (40.19) | | 100.0 % | 17.33 [5.60, 29.06] |
| Subtotal (95% CI) | 75 | | 71 | | | 100.0 % | 17.33 [5.60, 29.06] |

COC vs COC

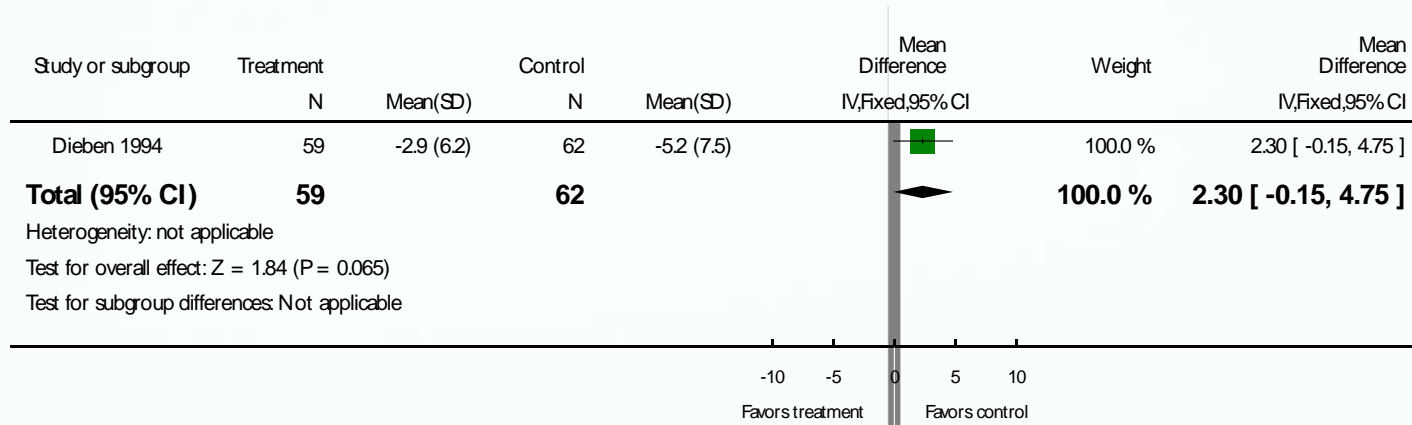
Comparison 16 LNG 150 µg / EE 30 µg versus CMA 2 mg / EE 30 µg, Outcome 3 Women with increased pustules or papules lesion count at cycle 12.



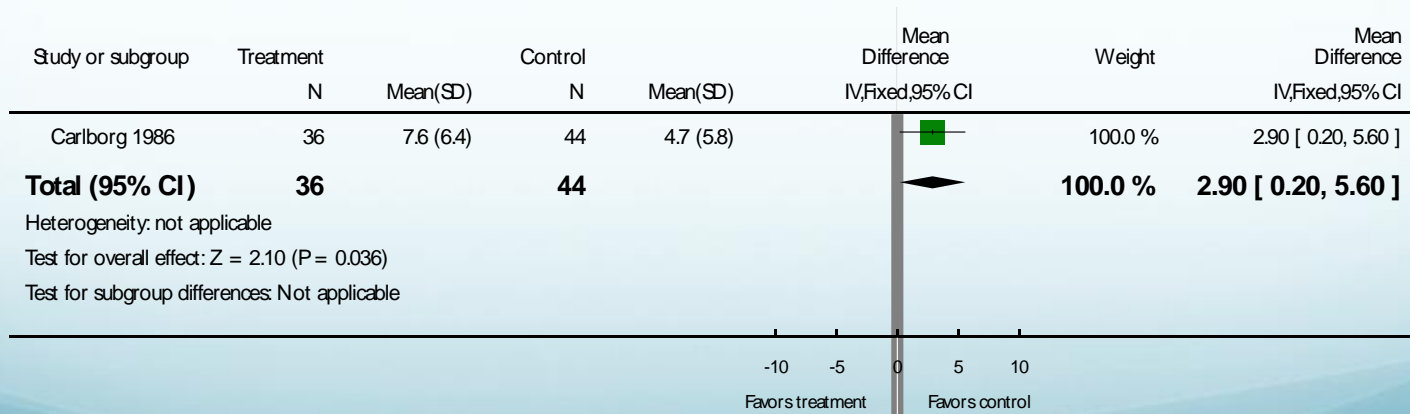
Comparison 9 DRSP 3 mg / EE 30 µg versus NGM 180-215-250 µg / EE 35 µg, Outcome 2 Mean percentage change in total lesion count after cycle 6.



Comparison 11 DSG 25-125 µg / EE 40-30 µg versus CPA 2 mg / EE 35 µg, Outcome 5 Mean change in pustule count at cycle 4.

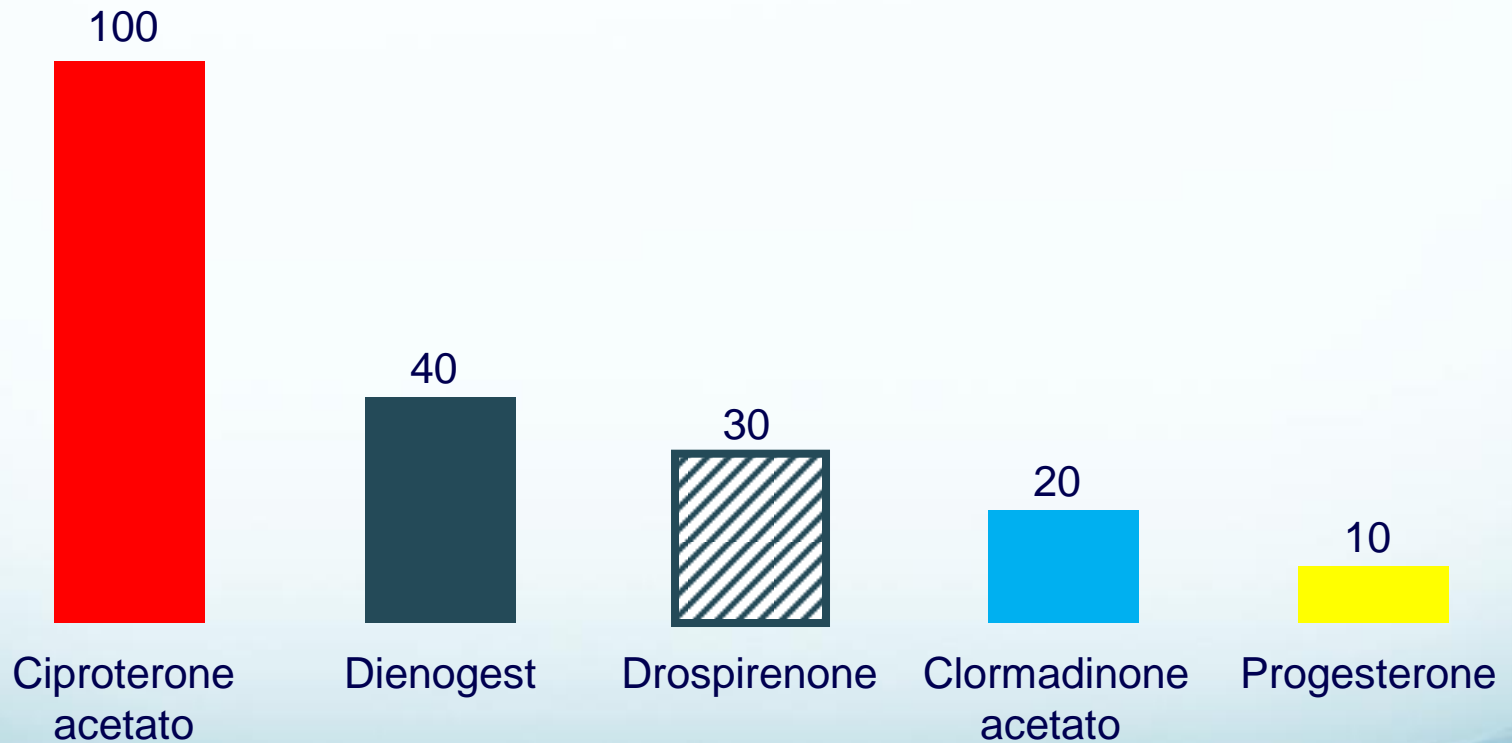


Comparison 17 LNG 150 µg / EE 30 µg versus CPA 2 mg / EE 35 µg, Outcome 3 Mean papule count at cycle 6.



Cosa scegliere?

Attività antiandrogenica relativa di diversi progestinici



Valutata col test di Hershberger (rodent seminal vesicle hypertrophy test)

CPA vs DRSP

Multicentrico doppio cieco

Pz con acne lieve-moderata

82 pz DRPS

43 pz CPA

9 cicli di tp

Outcomes: *numero di lesioni cutanee, dosaggio testosterone, androstenedione, DHEAS, SHBG*

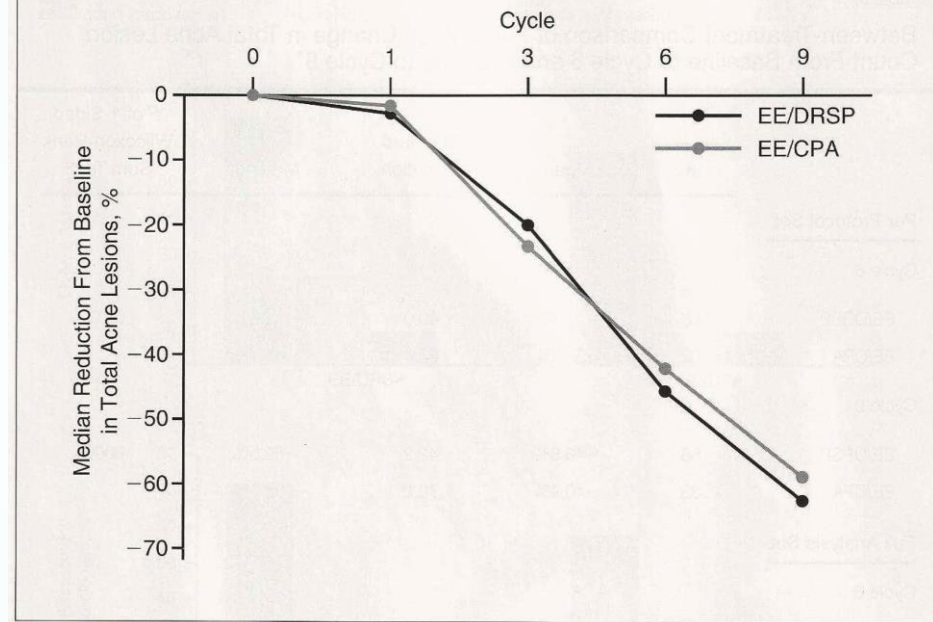
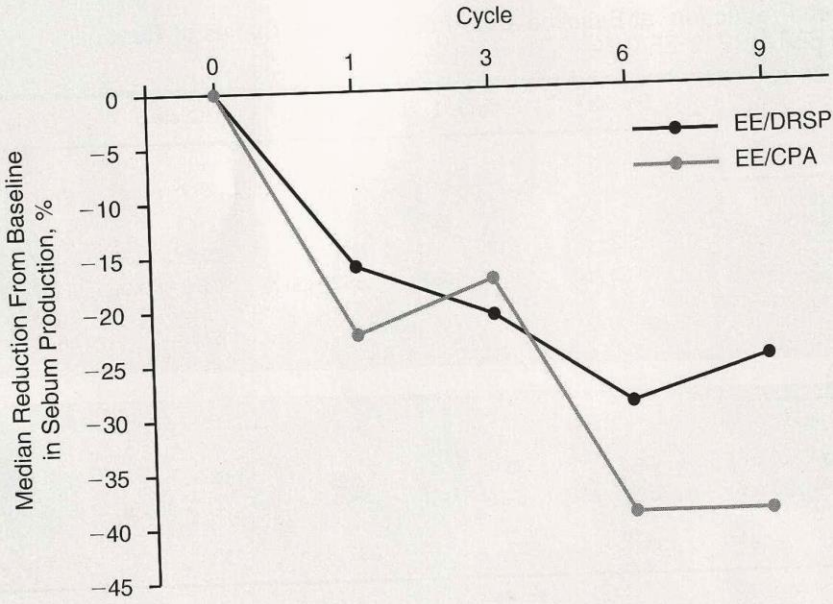


Figure 1. Median percentage reduction from baseline in total acne lesions (per protocol set). EE/DRSP indicates 30 µg ethinyl estradiol/3 mg drospirenone; EE/CPA, 35 µg ethinyl estradiol/2 mg cyproterone acetate.

Median (25th–75th Quartile) Acne Lesion Count for the Per Protocol Set at Baseline and at the End of Treatment With EE/DRSP (n=58) or EE/CPA (n=33)*

| | Cycle 0 | | Cycle 1 | | Cycle 3 | | Cycle 6 | | Cycle 9 | |
|-------------------------|-------------|------------|------------|------------|------------|------------|-------------|------------|--------------|-----------|
| | EE/DRSP | EE/CPA | EE/DRSP | EE/CPA | EE/DRSP | EE/CPA | EE/DRSP | EE/CPA | EE/DRSP | EE/CPA |
| All lesions | 50 (23–68) | 43 (30–76) | 48 (27–74) | 49 (27–74) | 35 (23–46) | 46 (19–61) | 24 (15–38) | 22 (13–44) | 17.5 (10–29) | 18 (8–31) |
| Noninflammatory lesions | 23 (8–52) | 21 (6–53) | 25 (10–50) | 20 (10–47) | 20 (8–28) | 20 (8–37) | 12.5 (5–25) | 12 (5–30) | 9 (5–20) | 6 (4–20) |
| Inflammatory lesions | 16 (11–29) | 20 (13–25) | 19 (11–28) | 19 (12–28) | 13 (8–21) | 13 (9–29) | 8 (5–12) | 7 (4–14) | 4 (3–8) | 5 (2–10) |
| Open comedos | 6.5 (0–20) | 11 (0–25) | 6 (0–20) | 11 (3–20) | 7 (0–12) | 10 (0–20) | 6 (0–10) | 5 (0–12) | 3.5 (0–10) | 3 (0–8) |
| Closed comedos | 10.5 (4–22) | 11 (0–30) | 12 (6–26) | 9 (5–25) | 9 (5–18) | 10 (3–20) | 5 (3–12) | 7 (0–18) | 4 (2–13) | 4 (0–10) |
| Papules | 10.5 (8–18) | 15 (10–23) | 12 (7–21) | 13 (9–22) | 9 (5–14) | 10 (6–18) | 6 (4–10) | 7 (3–11) | 3.5 (2–6) | 5 (2–7) |
| Pustules | 5 (2–10) | 3 (2–8) | 5 (1–10) | 4 (2–7) | 2 (0–7) | 2 (0–7) | 1 (0–3) | 0 (0–1) | 0 (0–2) | 0 (0–1) |
| Nodules | 0 (0–0) | 0 (0–0) | 0 (0–0) | 0 (0–1) | 0 (0–0) | 0 (0–0) | 0 (0–0) | 0 (0–0) | 0 (0–0) | 0 (0–0) |

*EE/DRSP indicates 30 µg ethinyl estradiol/3 mg drospirenone; EE/CPA, 35 µg ethinyl estradiol/2 mg cyproterone acetate.



Sebum Production* at Baseline and After 3, 6, and 9 Cycles of Treatment With EE/DRSP or EE/CPA[†]

| | Baseline | Cycle 1 | Cycle 3 | Cycle 6 | Cycle 9 |
|---|-----------------------|-----------------------|----------------------|----------------------|----------------------|
| EE/DRSP | | | | | |
| Median Sebum | | | | | |
| Production, $\mu\text{g}/\text{cm}^2$ (25th–75th Quartile) | 126.2 (94.7–165) | 112.7 (62.7–146.3) | 91.2 (65.3–130.7) | 79.0 (55.3–121.0) | 84.0 (54.0–132.3) |
| n | 58 | 57 | 58 | 57 | 58 |
| EE/CPA | | | | | |
| Median Sebum | | | | | |
| Production, $\mu\text{g}/\text{cm}^2$ (25th–75th Quartile) | 120.7 (87.3–165.7) | 78.0 (66.3–115.3) | 79.3 (57.3–140.0) | 62.3 (41.7–108.0) | 72.7 (51.0–105.0) |
| n | 33 | 33 | 33 | 33 | 33 |

*Per protocol set.

[†]EE/DRSP indicates 30 μg ethinyl estradiol/3 mg drospirenone; EE/CPA, 35 μg ethinyl estradiol/2 mg cyproterone acetate.

Hormone Levels* Before and After 9 Cycles of Treatment With EE/DRSP or EE/CPA[†]

| | EE/DRSP | | EE/CPA | |
|---|---------------|---------------|---------------|---------------|
| | Baseline | Cycle 9 | Baseline | Cycle 9 |
| LH, U/L (mean±SD) | 6.23±8.10 | 1.38±2.19 | 4.99±3.85 | 1.09±1.62 |
| Total testosterone, nmol/L (mean±SD) | 1.31±0.66 | 0.94±0.50 | 1.24±0.66 | 1.05±0.61 |
| Free testosterone, nmol/L (mean±SD) | 0.0065±0.0055 | 0.0023±0.0027 | 0.0074±0.0062 | 0.0028±0.0036 |
| DHEAS, nmol/L (mean±SD) | 6390±2840 | 4320±2110 | 6943±4011 | 4166±2028 |
| Androstenedione, nmol/L (mean±SD) | 8.85±3.18 | 6.68±3.15 | 8.88±3.26 | 6.59±2.65 |
| SHBG, nmol/L (mean±SD) | 55.5±35.0 | 184.2±48.5 | 58.9±35.1 | 190.3±53.9 |

CPA vs DRSP

Studio prospettico randomizzato

91 pz con diagnosi di irsutismo

DRSP CPA per 12 mesi

**Outcomes: free T2, androstenedione,
DHEAS, SHBG, miglioramento dei
sintomi (Ferriman-Gallwey)**

Percentuale di riduzione irsutismo :

0.70 (0-0.58) vs. 0.57 (0.10-1.00) (*p = 0.028*) a 6 mesi

0.80 (0-0.42) vs. 0.81 (0-0.75) (*p = 0.6*) a 12 mesi

DNG

DIAG

VS

CPA??

The European Journal of Contraception and Reproductive Health Care 1999; 4: 155–164

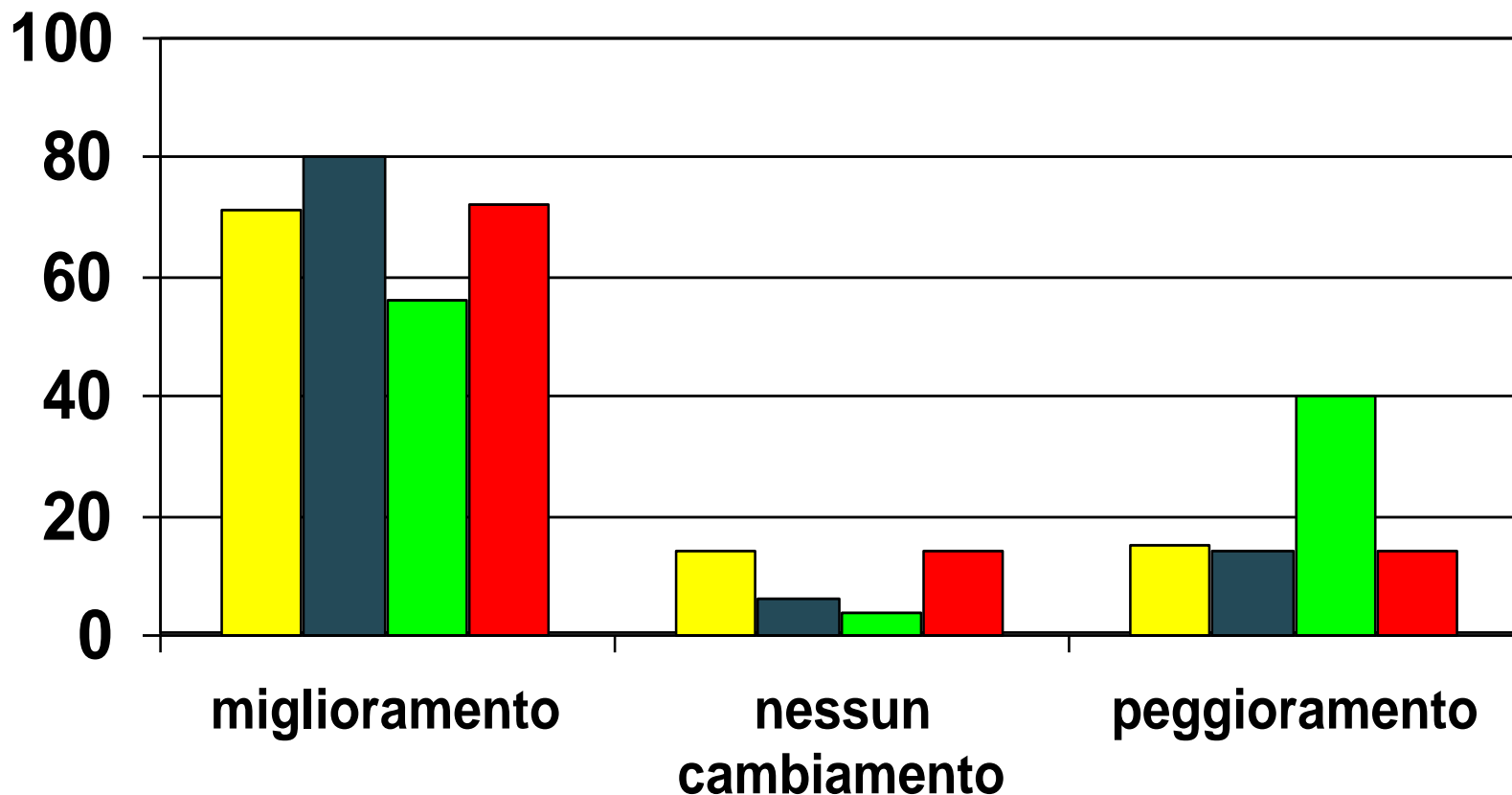
The efficacy and tolerability of Valette[®]: a postmarketing surveillance study

T. Zimmermann, H. Dietrich, K.-H. Wisser and H. Hoffmann*

Department of Medical Affairs and *Drug Safety Unit, Jenapharm GmbH & Co. KG, Jena, Germany

per cento su 1110 donne

acne pelle grassa capelli irsutismo



effetto al sesto ciclo di trattamento con EE30+DNG2 vs basale

Zimmermann T et al, 1999

Clinical Findings with the Oral Contraceptive Combination Ethinylestradiol/Dienogest in Poland

S. Golbs, R. Domhardt, S. Radowicky¹, Z. Kałuzny², K.H. Wisser and T. Zimmermann

Department of Medical Affairs, Jenapharm GmbH & Co. KG, Jena, Germany; ¹Medical Academy Warsaw; ²Schering Office, Warsaw, Poland

Inestetismi cutanei

Multicentrico
N = 431 pz per 12 mesi di tp

TABLE 4. Shifts in the severity of skin blemishes during the use of EE/DNG.

| Status | Cycle 3 | | Cycle 6 | | Cycle 12 | |
|-----------|----------|------|----------|------|----------|------|
| | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % |
| Improved | 75 | 18.8 | 101 | 27.1 | 75 | 26.7 |
| Unchanged | 321 | 80.7 | 271 | 72.7 | 206 | 73.3 |
| Worsened | 2 | 0.5 | 1 | 0.3 | 0 | 0 |
| All | 398 | 100 | 373 | 100 | 281 | 100 |

Acne vulgaris

TABLE 6. Shifts in severity of acne in the patients with acne vulgaris during the use of EE/DNG.

| | Cycle 6 | | Cycle 12 | |
|-----------|----------|------|----------|------|
| | <i>n</i> | % | <i>n</i> | % |
| Healed | 1 | 2.0 | 13 | 37.1 |
| Improved | 40 | 80.0 | 19 | 54.3 |
| Unchanged | 8 | 16.0 | 3 | 8.6 |
| Worsened | 1 | 2.0 | 0 | 0 |
| Total | 50 | 100 | 35 | 100 |

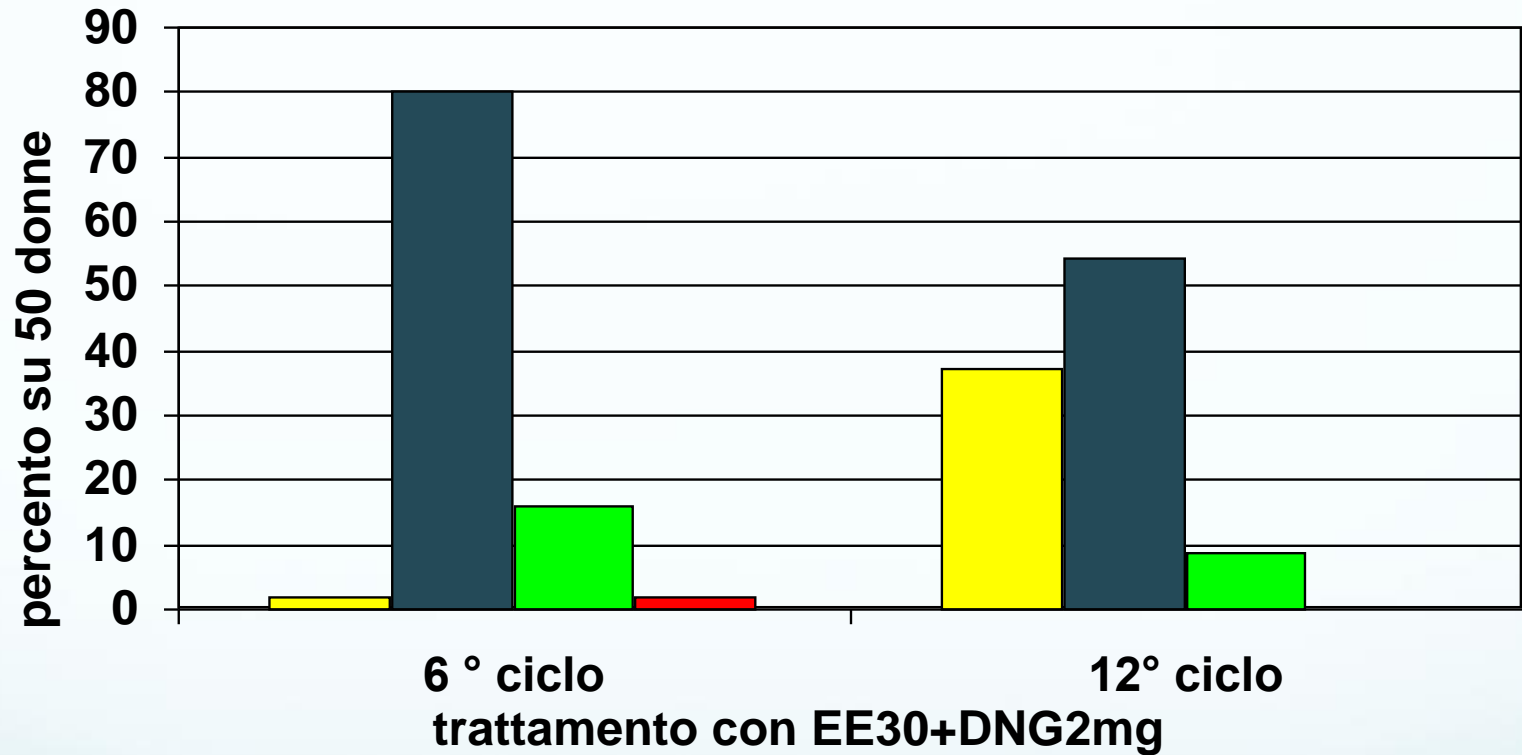
Seborrea

Multicentrico
N = 431 pz per 12 mesi di tp

TABLE 5. Shifts in the severity of the hair greasiness during the use of EE/DNG.

| Status | Cycle 3 | | Cycle 6 | | Cycle 12 | |
|-----------|----------|------|----------|------|----------|------|
| | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % |
| Improved | 131 | 32.6 | 187 | 49.3 | 159 | 53.9 |
| Unchanged | 270 | 67.2 | 191 | 50.4 | 136 | 46.1 |
| Worsened | 1 | 0.2 | 1 | 0.3 | 0 | 0 |
| All | 402 | 100 | 379 | 100 | 295 | 100 |

■ guarita ■ migliorata ■ immodificata ■ peggiorata



Golbs S et al, 2002;24:585-92



ELSEVIER

Contraception 79 (2009) 282–289

Contraception

Original research article

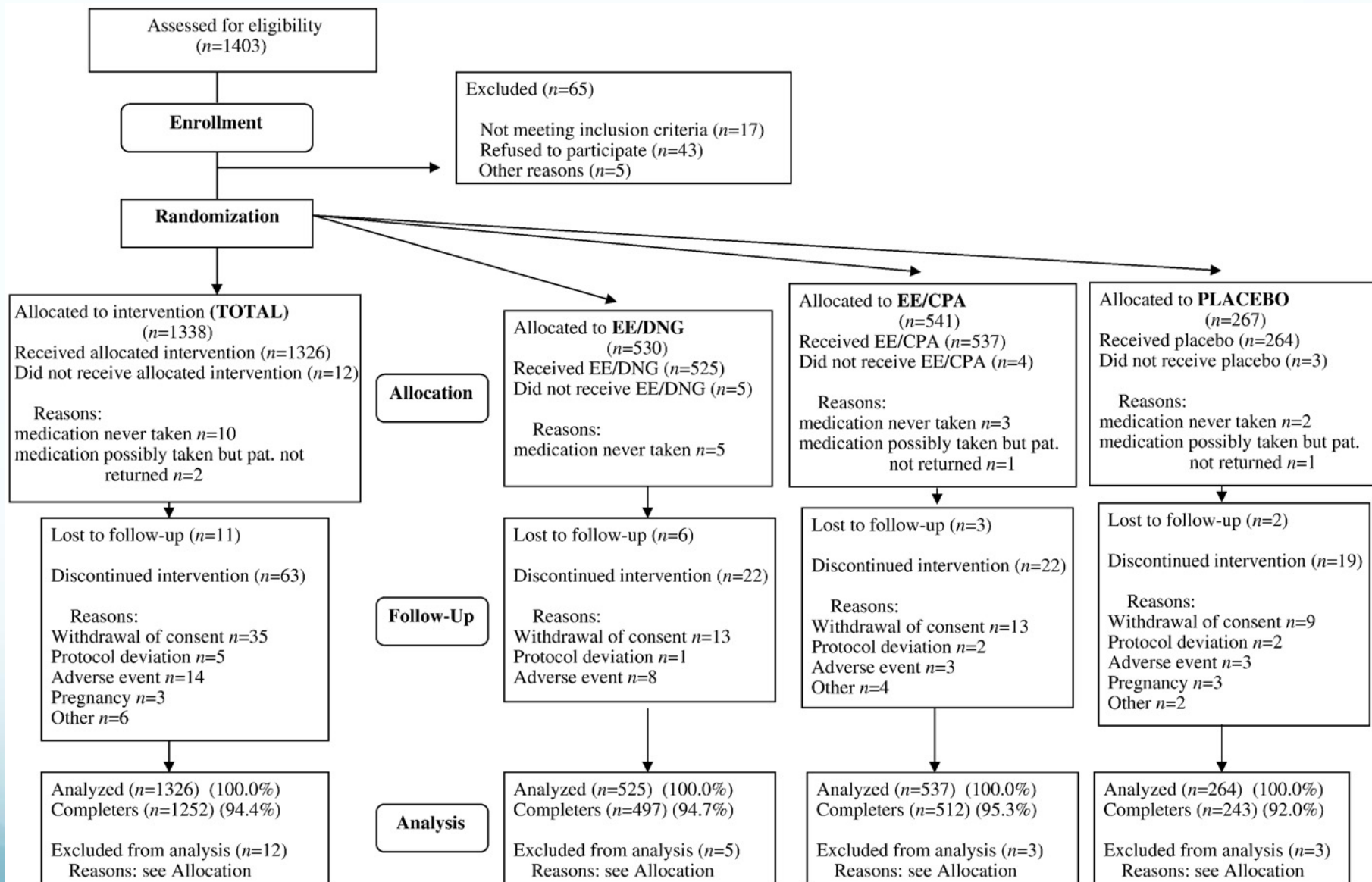
Efficacy of a combined oral contraceptive containing 0.030 mg ethinylestradiol/2 mg dienogest for the treatment of papulopustular acne in comparison with placebo and 0.035 mg ethinylestradiol/2 mg cyproterone acetate[☆]

Ernesta Palombo-Kinne^{a,*}, Ilka Schellschmidt^b, Ulrike Schumacher^a, Thomas Gräser^a

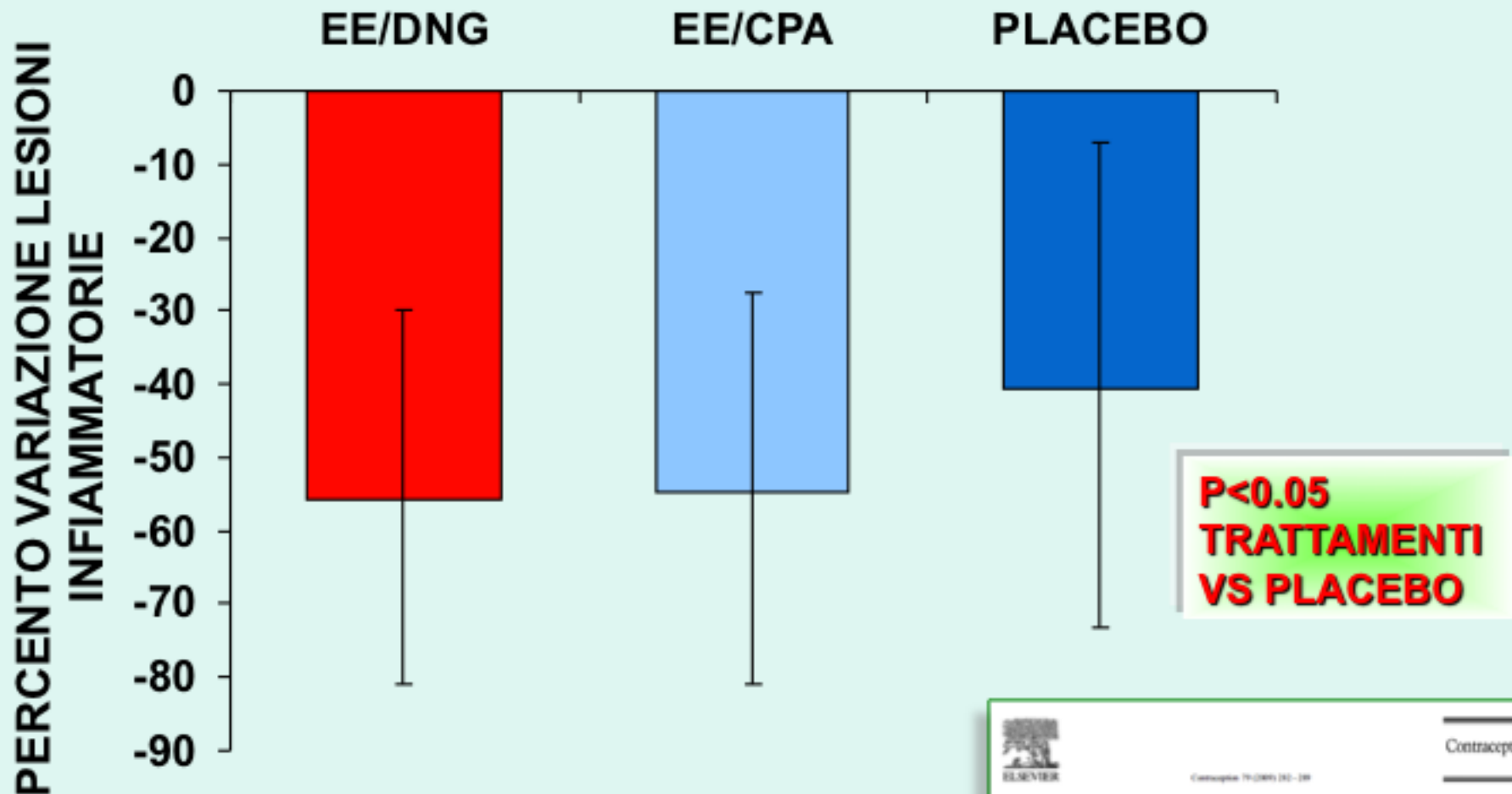
^a*Jenapharm GmbH & Co. KG, 07745 Jena, Germany*

^b*Bayer Schering Pharma AG, 13353 Berlin, Germany*

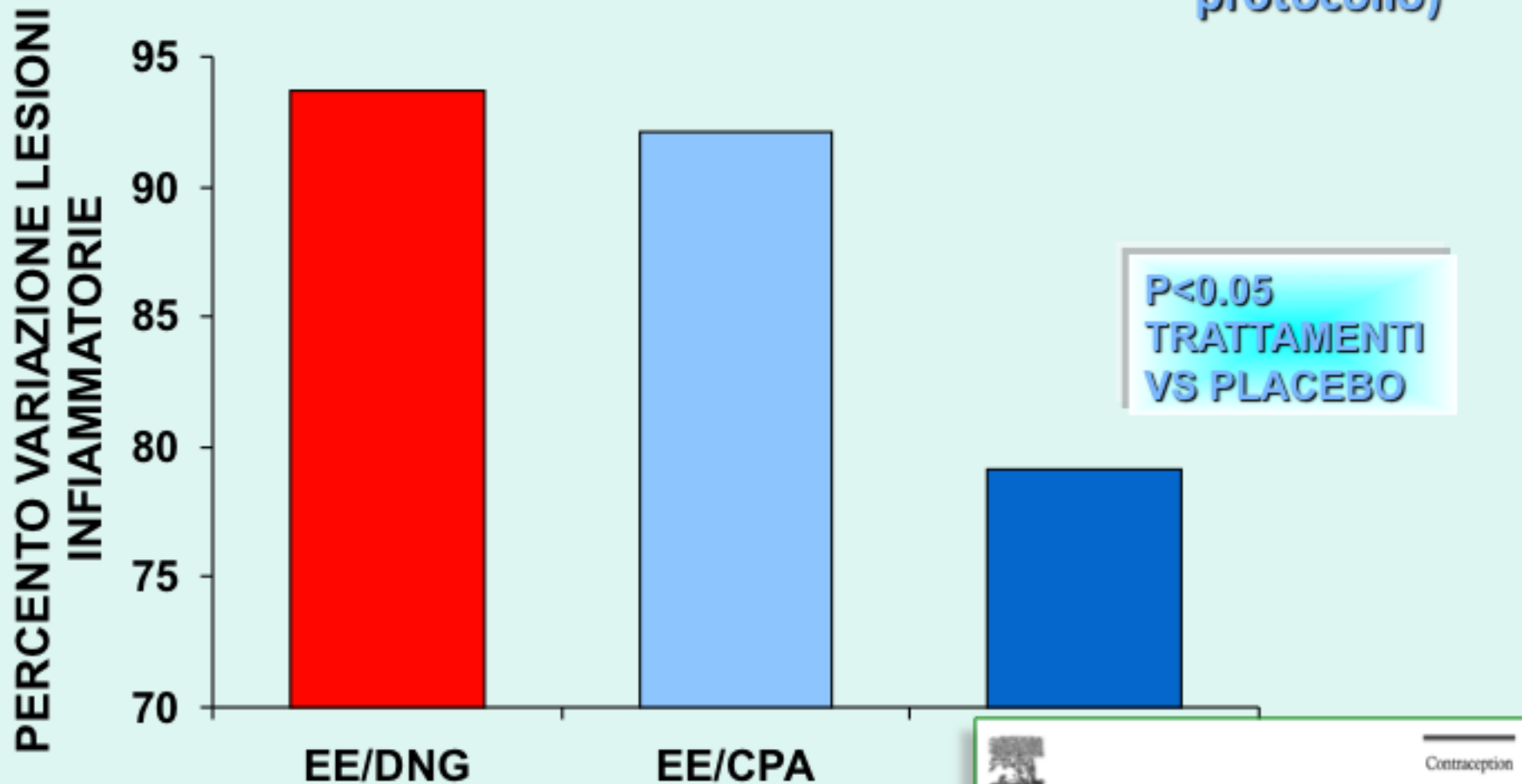
Received 30 April 2008; revised 20 October 2008; accepted 20 October 2008



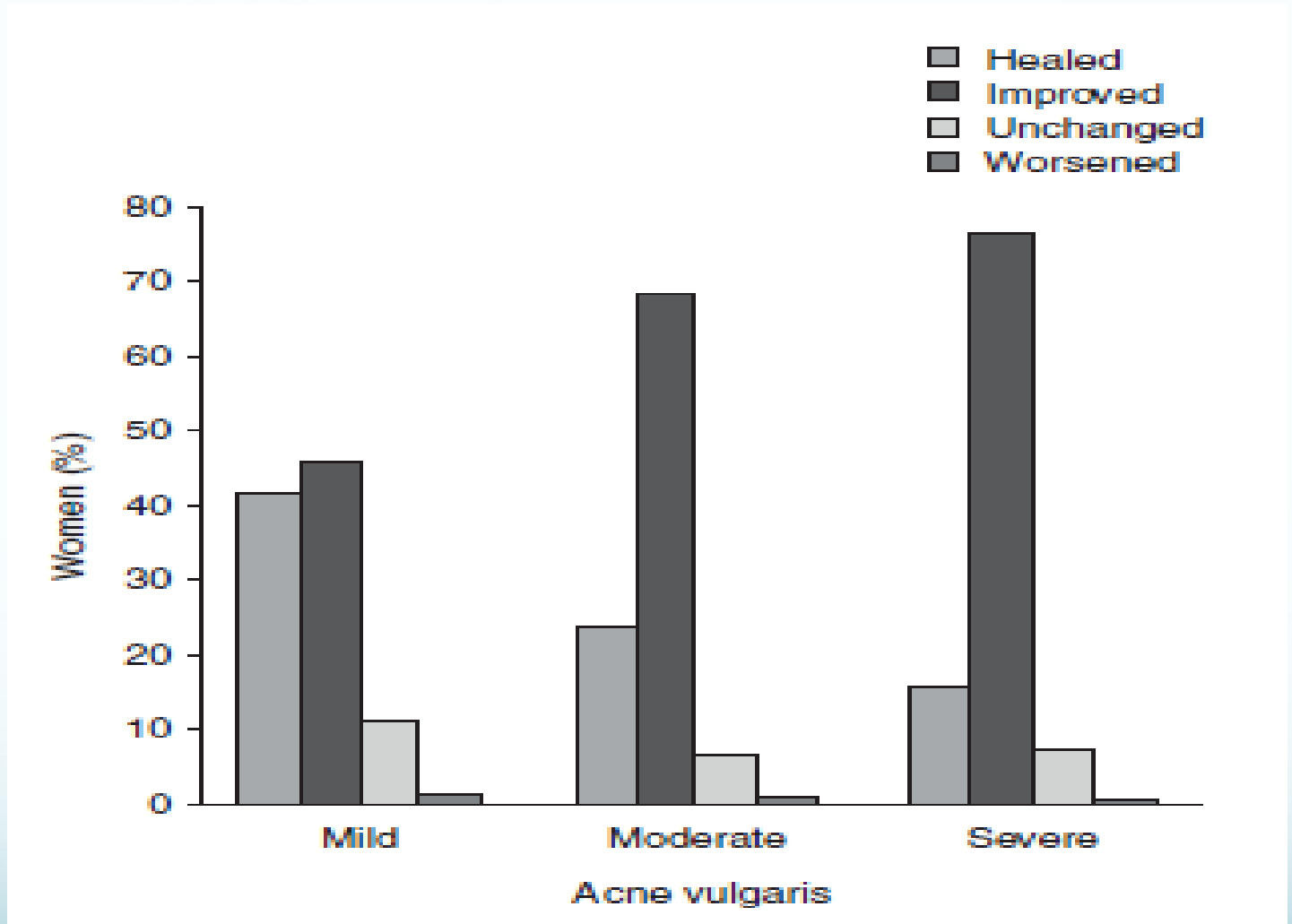
Primary efficacy . Percento di variazione delle lesioni TOTALI al 6° ciclo vs basale (FAS intent-to-treat Per protocol set (escluso pazienti con grosse variazioni da protocollo))



Primary efficacy . Percento di PAZIENTI CON MIGLIORAMENTO al 6° ciclo vs basale (FAS intent-to-treat Per protocol set (escluso pazienti con grosse variazioni da protocollo))



Contraception
Original research article
Efficacy of a combined oral contraceptive containing 0.030 mg ethinylestradiol/2 mg dienogest for the treatment of papulopustular acne in comparison with placebo and 0.035 mg ethinylestradiol/2 mg cyproterone acetate[©]
Ernesta Palombo-Kinne^{a,*}, Ilka Schellischmidt^b, Ulrike Schumacher^c, Thomas Geiser^d

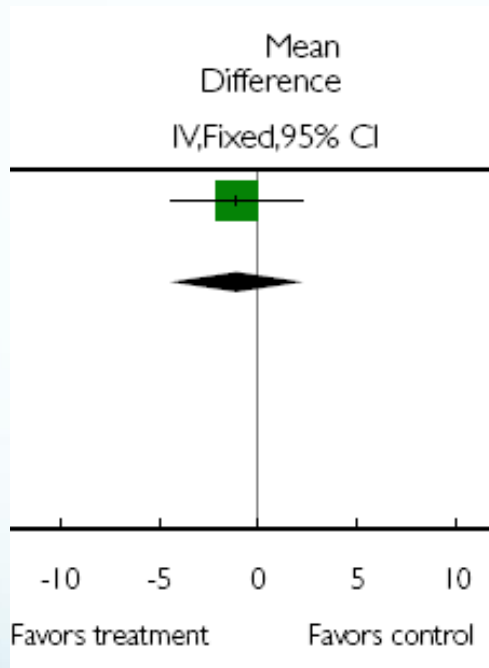


Most frequent adverse events (related and unrelated; number and percentage of affected patients)

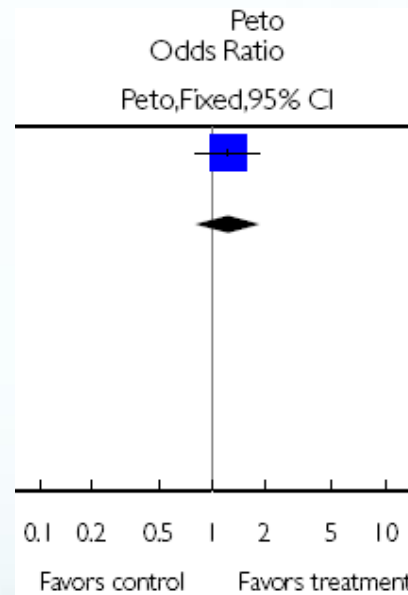
| | EE/DNG (n=525) | EE/CPA (n=537) | Placebo (n=264) |
|-----------------------------|-------------------|-------------------|--------------------|
| Total adverse events | 170 (32.4%) | 188 (35.0%) | 86 (32.6%) |
| Most common adverse events | | | |
| Headache | 28 (5.3%) | 28 (5.2%) | 14 (5.3%) |
| Nausea | 22 (4.2%) | 34 (6.3%) | 7 (2.7%) |
| Vomiting | 16 (3.0%) | 21 (3.9%) | 5 (1.9%) |
| Breast pain | 11 (2.1%) | 9 (1.7%) | – |
| Influenza | 11 (2.1%) | 14 (2.6%) | 3 (1.1%) |
| Metrorrhagia | 11 (2.1%) | <1.0% | – |
| Nasopharyngitis | 9 (1.7%) | 14 (2.6%) | 8 (3.0%) |
| Breast tenderness | 8 (1.5%) | 15 (2.8%) | <1.0% |
| Respiratory tract infection | 8 (1.5%) | <1.0% | – |
| Diarrhea | 7 (1.3%) | 11 (2.0%) | 6 (2.3%) |
| Breast edema | <1.0% | 11 (2.0%) | <1.0% |
| Weight increase | <1.0% | 7 (1.3%) | <1.0% |

DNG vs CPA

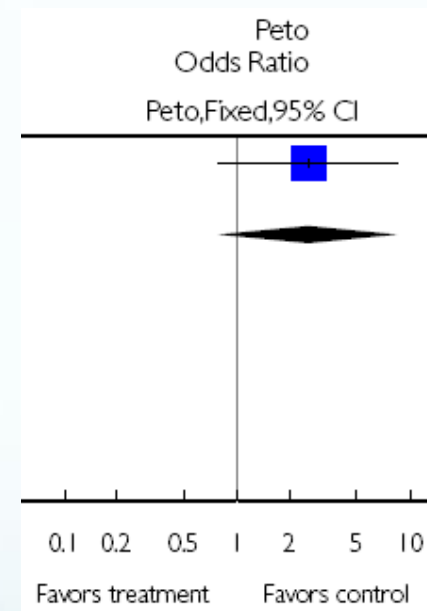
% riduzione del numero di lesioni dopo 6 mesi
P = 0.51



Miglioramento clinico dell'acne vulgaris
P = 0.34



Sospensione tp per effetti collaterali
P = 0.12



➤ DNG/EE non è inferiore al „gold standard” CPA/EE

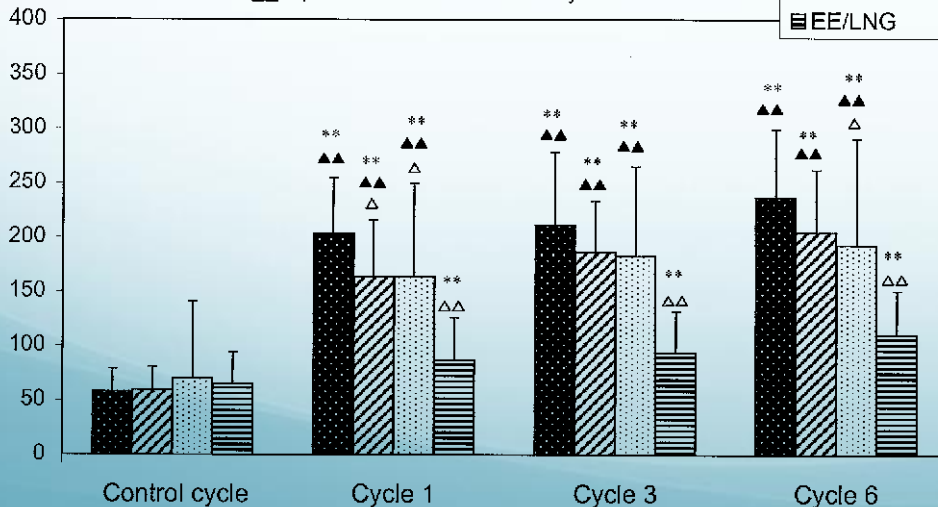
Quale estrogeno?

Serum concentration of free testosterone (pg/mL), DHEAS ($\mu\text{g/mL}$), and prolactin ($\mu\text{IU/mL}$) in the control cycle and in the first, third and sixth cycle of treatment with 30EE/DNG, 20EE/DNG, EE/EV/DNG or EE/LNG

| Formulation | Control cycle | Cycle 1 | Cycle 3 | Cycle 6 |
|-------------------|-----------------|-------------------|-------------------|-------------------|
| Free testosterone | | | | |
| 30EE/DNG | 1.40 \pm 0.87 | 0.45 \pm 0.35** | 0.38 \pm 0.29** | 0.56 \pm 0.52** |
| 20EE/DNG | 1.83 \pm 1.20 | 0.68 \pm 0.45** | 0.52 \pm 0.32** | 0.59 \pm 0.45** |
| EE/EV/DNG | 1.90 \pm 1.80 | 0.89 \pm 0.64** | 0.74 \pm 0.50** | 0.86 \pm 0.66** |
| EE/LNG | 1.56 \pm 0.79 | 0.82 \pm 0.60** | 0.59 \pm 0.42** | 0.63 \pm 0.47** |
| DHEAS | | | | |
| 30EE/DNG | 1.69 \pm 1.06 | 1.25 \pm 0.59** | 1.19 \pm 0.69** | 1.06 \pm 0.51** |
| 20EE/DNG | 2.22 \pm 1.10 | 1.75 \pm 0.99** | 1.63 \pm 0.83** | 1.57 \pm 0.76** |
| EE/EV/DNG | 2.03 \pm 0.99 | 1.78 \pm 1.00** | 1.70 \pm 1.04** | 1.52 \pm 0.96** |
| EE/LNG | 2.01 \pm 0.92 | 1.81 \pm 0.85** | 1.76 \pm 0.85** | 1.53 \pm 0.86** |
| Prolactin | | | | |
| 30EE/DNG | 275 \pm 149 | 316 \pm 189 | 328 \pm 207 | 339 \pm 169 |
| 20EE/DNG | 331 \pm 257 | 274 \pm 135 | 315 \pm 159 | 311 \pm 137 |
| EE/EV/DNG | 310 \pm 177 | 369 \pm 264 | 361 \pm 192* | 438 \pm 276** |
| EE/LNG | 363 \pm 261 | 392 \pm 245 | 356 \pm 209 | 380 \pm 252 |

SHBG

nmol/L



Take at home....

Valutare la gravità delle lesioni dermatologiche

Acne moderata-grave ed irsutismo rappresentano un'indicazione assoluta per un CO con progestinico ad azione anti-androgenica

Eventuali sintomi associati (ad es. menorragia, endometriosi)

Take at home...

Valutare fattori di rischio associati e l'impatto metabolico considerando anche i diversi regimi di terapia (per l'acne miglioramenti evidenti già dopo 3 mesi di trattamento)

Table 1: Estimates of risk of nonfatal venous thromboembolism

| Group* | Estimated 1-year risk of nonfatal venous thromboembolism |
|---|--|
| Baseline (women not using OC) ^{6,13} | 1 in 20 000 to 1 in 9090 |
| Women using OC containing levonorgestrel ^{13,14} | 1 in 6666 to 1 in 6211 |
| Women using OC containing desogestrel ^{†13} | 1 in 3333 |
| Women using any low-dose OC ^{6,13} | 1 in 3333 |
| Women not using OC but who have factor V Leiden mutation ⁶ | 1 in 1754 |
| Women using OC containing cyproterone [‡] | 1 in 1666 |
| Pregnant women and those post partum ^{13,15} | 1 in 1666 to 1 in 1500 |
| Women using OC and who have factor V Leiden mutation ⁶ | 1 in 350 |

Take at home....

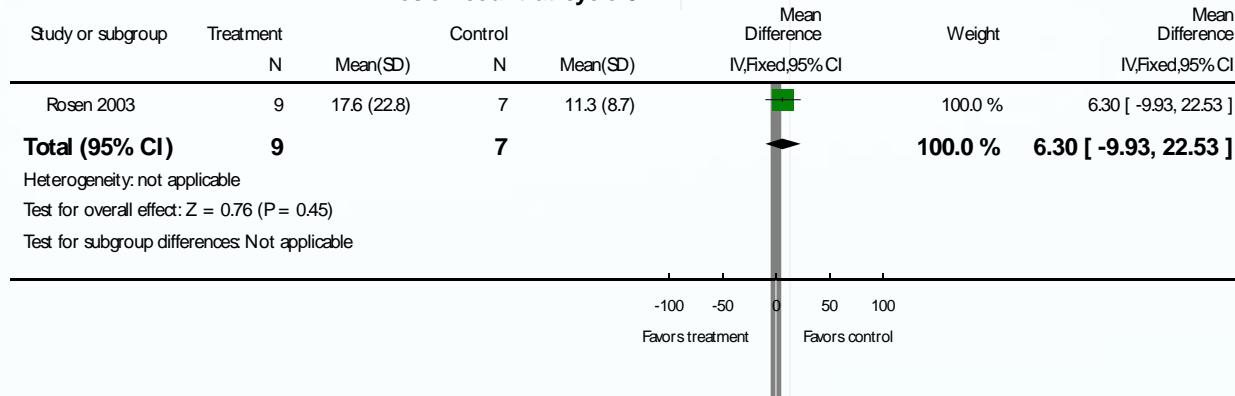
La superiorità *in vitro* del CPA non è tale *in vivo*

DRSP è un'ottima alternativa.....tuttavia i numeri che supportano l'uso del DNG sono talmente "importanti" da farlo considerare come prima scelta

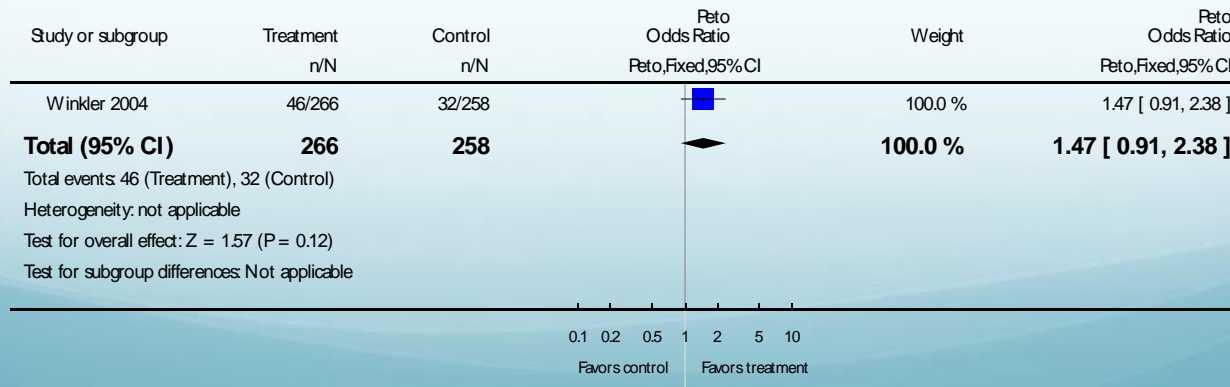
***Grazie per
l'attenzione!!!!***

LNG vs. DSG

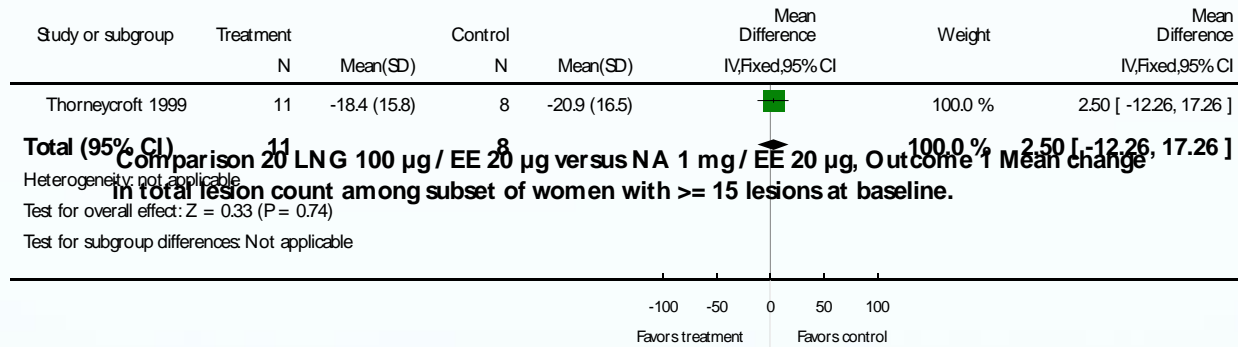
Comparison 15 LNG 150 µg / EE 30 µg versus DSG 150 µg / EE 30 µg, Outcome 2 Mean total lesion count at cycle 9.



Comparison 14 DSG 150 µg / EE 20 µg versus LNG 100 µg / EE 20 µg, Outcome 5 Improvement in pustules at week 25.



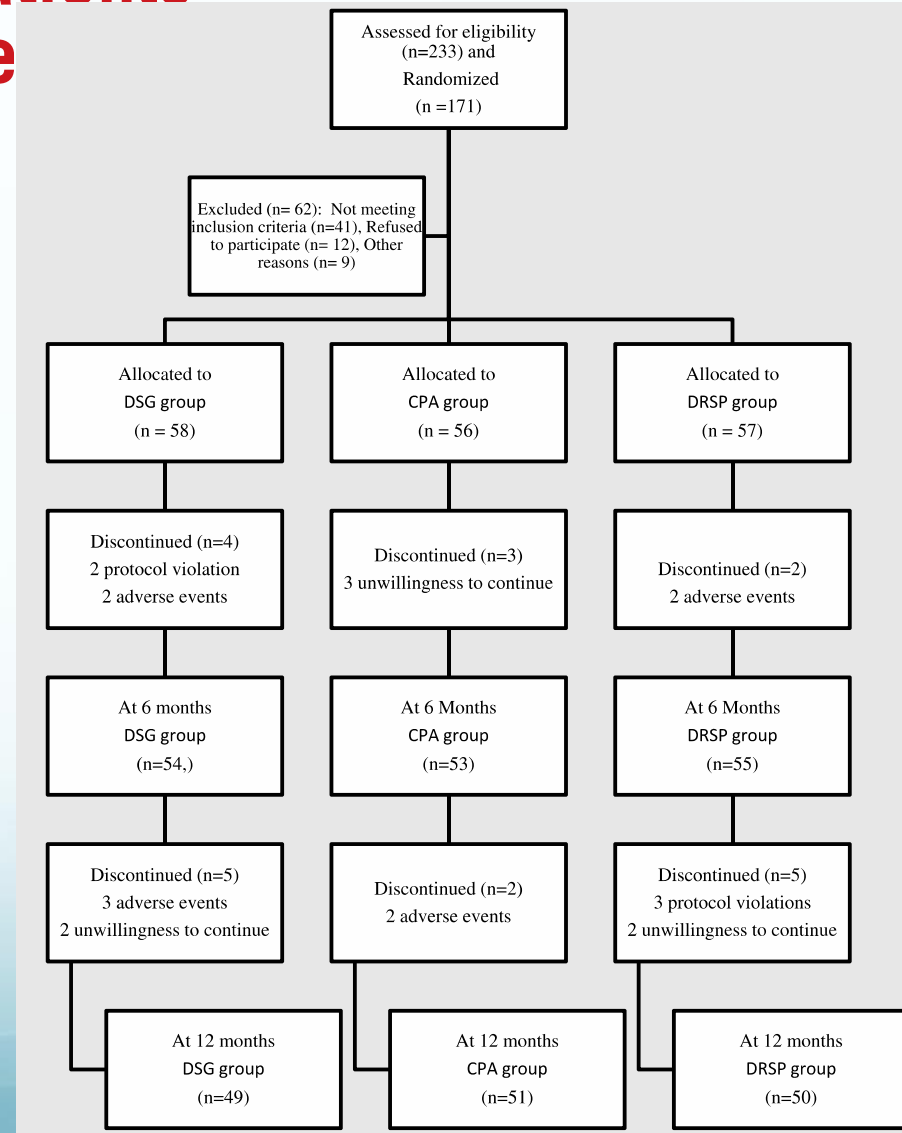
LNG vs NA



Solo 3 cicli di tp

Comparative study of the therapeutic effects of oral contraceptive pills containing desogestrel, cyproterone acetate, and drospirenone in patients with polycystic ovary syndrome

Sudhindra Mohan Bhattacharya, M.D.,^a and Ayan Jha, D.P.H.^b



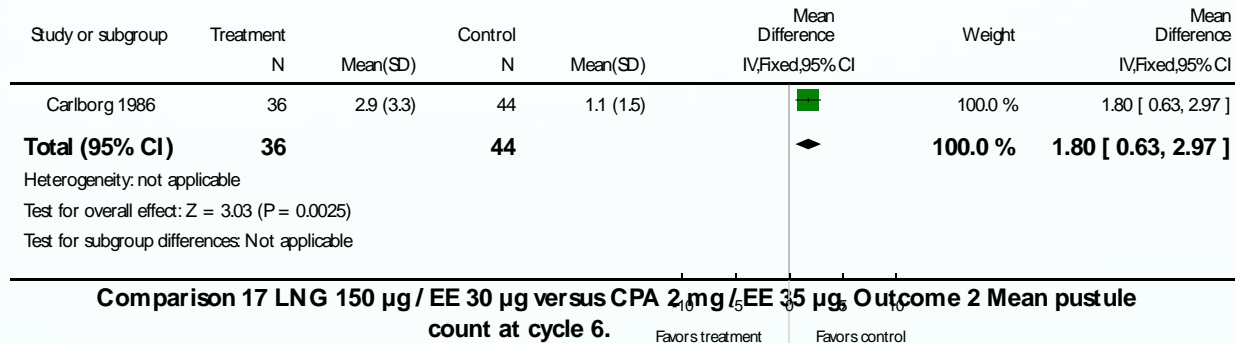
Change from baseline at 6 months of therapy.

| Parameters | Change from baseline | | | | | | P value of changes from baseline (ANOVA) |
|--------------------------|----------------------|-------|------------------------------|-------|-----------------------|-------|--|
| | Desogestrel (n = 58) | | Cyproterone acetate (n = 56) | | Drospirenone (n = 57) | | |
| | Mean | SD | Mean | SD | Mean | SD | |
| BMI | -0.19 | 0.89 | -0.29 | 1.28 | -0.19 | 3.71 | .97 |
| Abdominal circumference | -0.17 | 1.57 | 0.25 | 1.49 | 0.32 | 3.41 | .48 |
| Waist-hip ratio | 0.00 | 0.05 | 0.00 | 0.03 | 0.01 | 0.06 | .65 |
| m-FG score | -1.57 | 1.97 | -2.09 | 3.29 | -1.53 | 3.98 | .58 |
| Acne | -0.95 | 1.21 | -0.48 | 1.18 | -0.63 | 1.17 | .10 |
| Acanthosis nigricans | 0.00 | 0.26 | -0.09 | 0.72 | -0.11 | 0.94 | .69 |
| Systolic blood pressure | 1.59 | 10.96 | 0.79 | 10.97 | 2.60 | 13.75 | .72 |
| Diastolic blood pressure | 0.21 | 7.76 | -0.54 | 9.48 | 1.93 | 11.09 | .37 |
| T | -0.09 | 0.22 | -0.04 | 0.24 | -0.04 | 0.28 | .50 |
| SHBG | 76.05 | 79.41 | 93.75 | 85.71 | 97.52 | 94.55 | .37 |
| Free androgen index | -5.13 | 8.72 | -6.09 | 7.51 | -5.27 | 9.22 | .81 |
| Fasting glucose | -2.26 | 6.92 | -0.91 | 10.84 | -0.53 | 7.63 | .53 |
| Fasting insulin | -1.08 | 12.71 | 1.65 | 8.21 | 0.43 | 12.93 | .45 |
| Glucose-insulin ratio | -0.82 | 9.75 | -1.16 | 5.36 | -0.38 | 4.53 | .84 |
| HOMA | -0.36 | 2.92 | 0.26 | 2.39 | 0.03 | 2.99 | .48 |

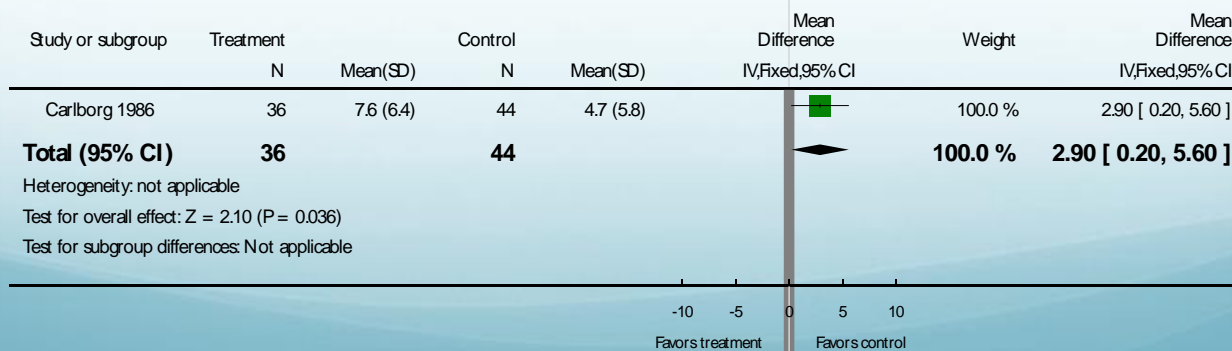
Change from baseline at 12 months of therapy.

| Parameters | Change from baseline | | | | | | P value of changes from baseline (ANOVA) |
|--------------------------|----------------------|-------|------------------------------|-------|-----------------------|-------|--|
| | Desogestrel (n = 58) | | Cyproterone acetate (n = 56) | | Drospirenone (n = 57) | | |
| | Mean | SD | Mean | SD | Mean | SD | |
| BMI | -0.45 | 6.75 | -0.59 | 4.76 | 0.11 | 5.54 | .79 |
| Abdominal circumference | -0.28 | 5.27 | -0.21 | 5.21 | 1.07 | 5.70 | .33 |
| Waist-hip ratio | 0.00 | 0.08 | -0.02 | 0.08 | 0.02 | 0.09 | .07 |
| m-FG score | -1.69 | 5.69 | -5.29 | 5.88 | -2.12 | 6.58 | .003 ^{a,b} |
| Acne | -1.41 | 1.32 | -1.52 | 1.25 | -1.42 | 1.27 | .89 |
| Acanthosis nigricans | 0.03 | 1.66 | -0.30 | 1.45 | 0.04 | 1.83 | .46 |
| Systolic blood pressure | 1.62 | 17.04 | 0.32 | 19.71 | 0.84 | 17.74 | .93 |
| Diastolic blood pressure | -0.07 | 12.16 | 2.04 | 16.12 | 2.70 | 14.10 | .55 |
| T | -0.10 | 0.39 | -0.03 | 0.42 | -0.06 | 0.32 | .62 |
| SHBG | 99.53 | 67.52 | 142.91 | 60.71 | 131.52 | 72.89 | .002 ^{c,d} |
| Free androgen index | -5.58 | 9.15 | -10.57 | 7.93 | -7.89 | 9.13 | .01 ^e |
| Fasting glucose | -4.28 | 11.66 | -2.46 | 16.86 | -2.11 | 14.02 | .68 |
| Fasting insulin | -0.02 | 17.35 | 6.38 | 15.22 | 2.78 | 17.27 | .12 |
| Glucose-insulin ratio | -1.70 | 8.30 | -4.64 | 13.44 | -0.57 | 9.59 | .12 |
| HOMA | -0.28 | 3.98 | 1.21 | 4.03 | 0.42 | 3.82 | .14 |

CPA vs LNG



Comparison 17 LNG 150 µg / EE 30 µg versus CPA 2 mg / EE 35 µg, Outcome 3 Mean papule count at cycle 6.



Pharmacodynamics – anti-androgen character

- Hersberger test of in vivo potency shows 40% anti-androgenic activity compared to CPA. (weight of seminal vesicle and m. levator ani referring to anabolic effect).
- DNG is the 2nd strongest anti-androgen used in COCs.
- DNG binds to the progesterone receptor of the human uterus with only 10% of the relative affinity of progesterone.
- Despite its low affinity to the progesterone receptor, DNG has a strong progestogenic effect in vivo.
- DNG has no significant androgenic, mineralocorticoid or glucocorticoid activity in vivo.

