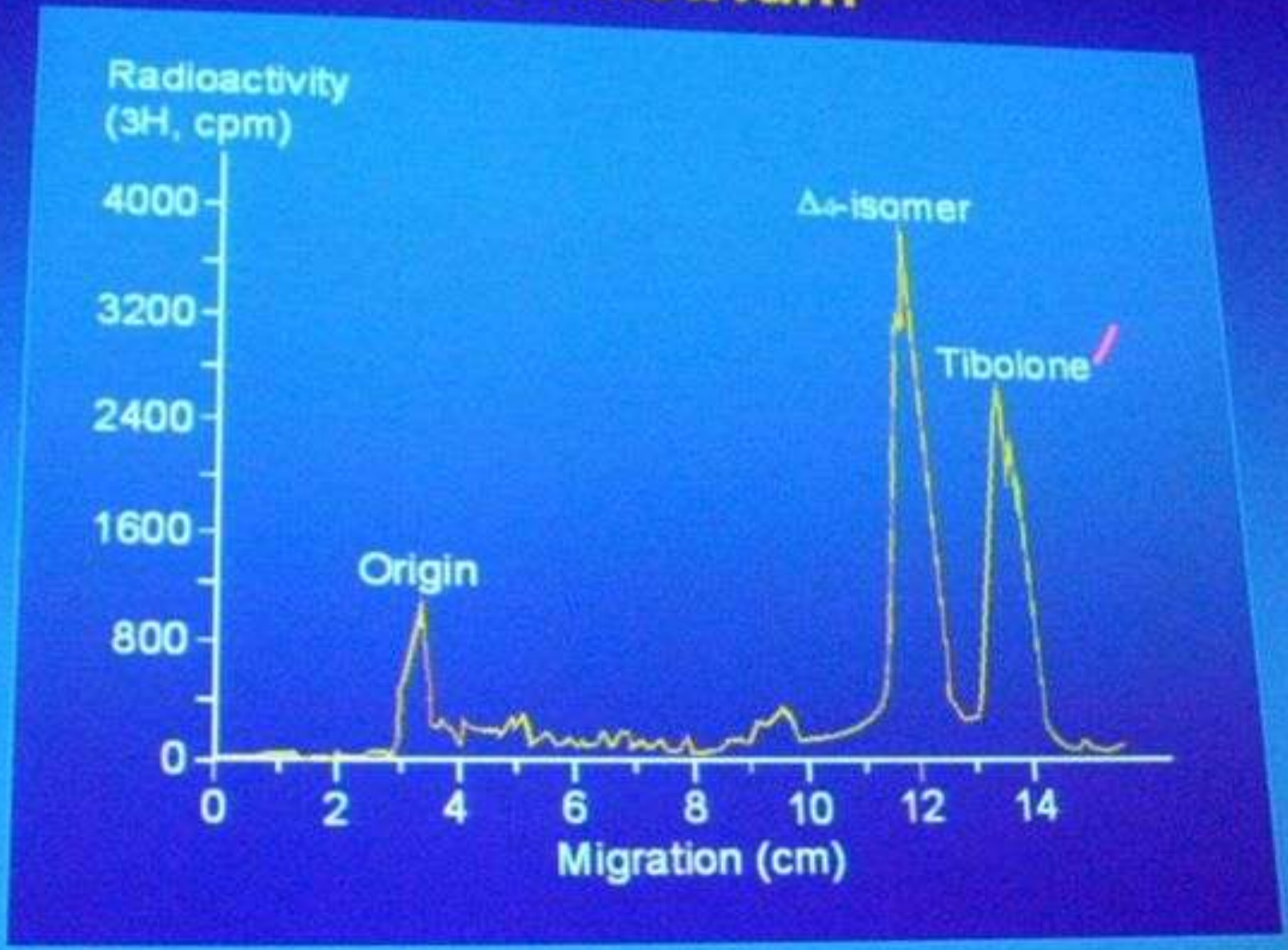
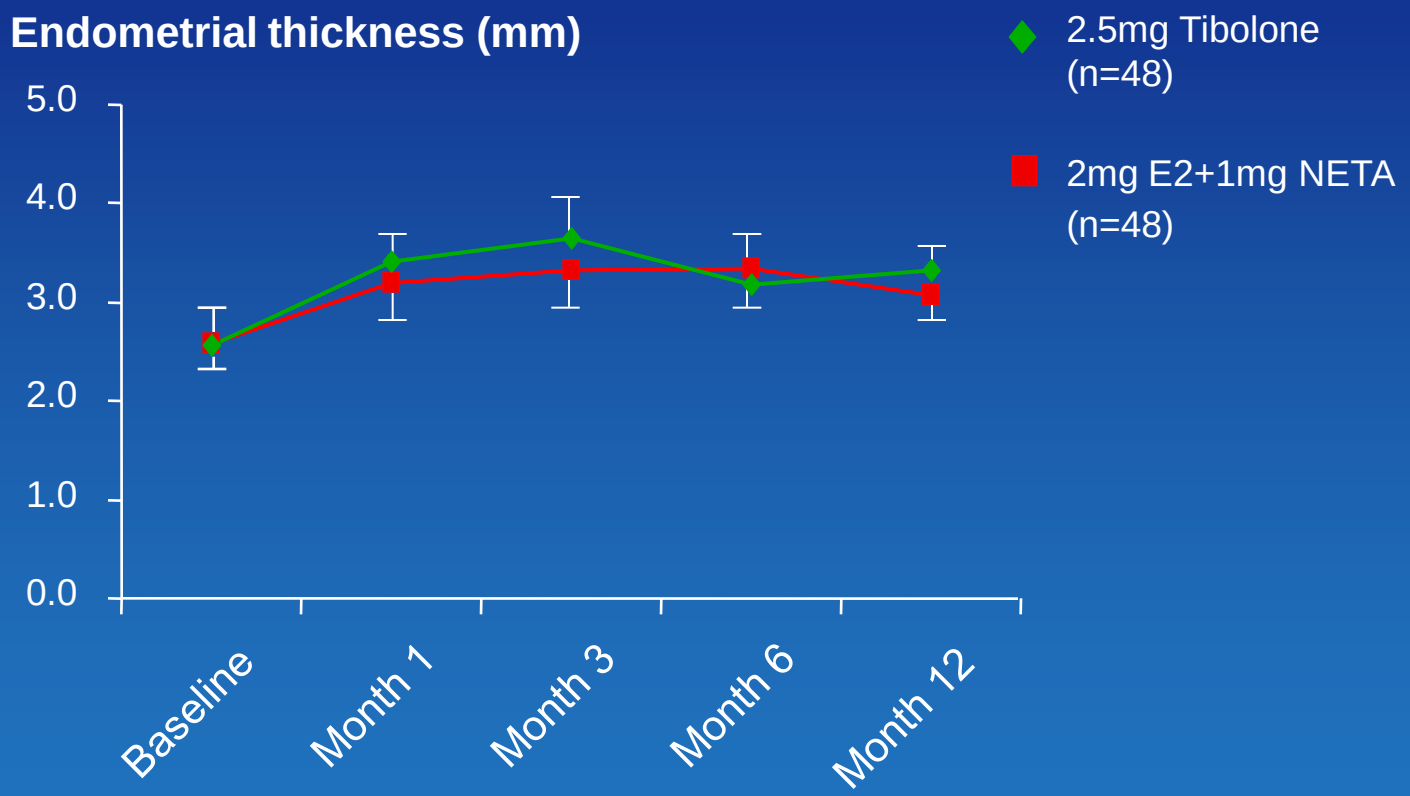
# TIBOLONA

# Metabolism of 3H-tibolone in human endometrium



# Effect on the endometrium

## Endometrial thickness during 12 months treatment



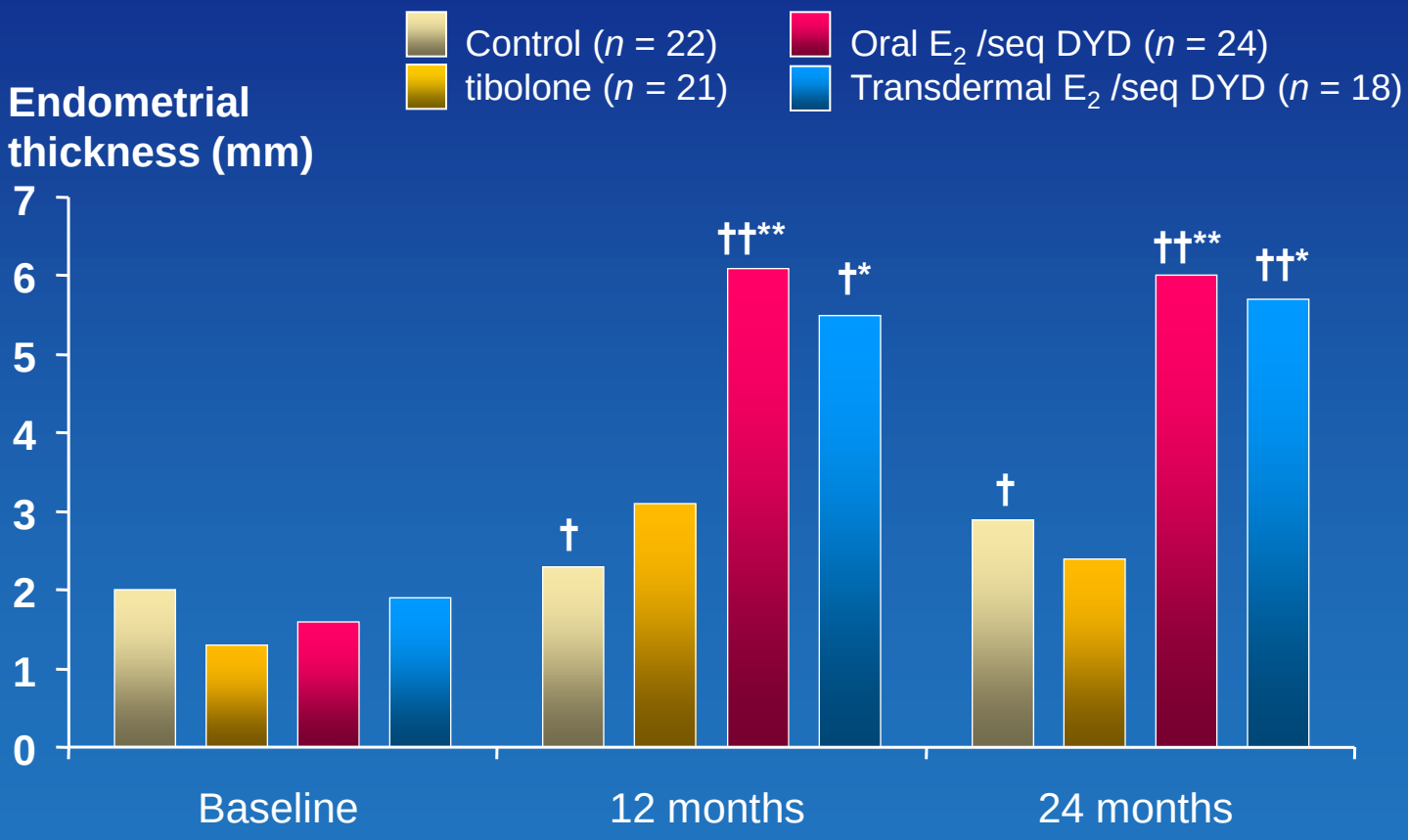

Datapoints represent mean and SE

Groups were not statistically different at any timepoint

Dören *et al., Menopause 1999*

# Effect on the endometrium

## Effect on endometrial thickness




*$p$ < 0.01; **$p$ < 0.001 vs change in controls;
†$p$ < 0.01; ††$p$ < 0.001 vs baseline

Haenggi *et al., Maturitas 1997*

# Effect on urogenital system

## Hysteroscopy and endometrial thickness after one-year treatment with tibolone

| Hysteroscopy findings | Tibolone | Placebo |
|---|---|---|
| | n= 15 | n= 9 |
| Atrophic | 14 (93.3%) | 7 (77.7%) |
| Polypoid lesions | 1 (6.6%) | 2 (22.2%) |

| Endometrial thickness | Tibolone | Placebo |
|---|---|---|
| | n= 17 | n= 17 |
| Baseline | 4.8 ± 1.0 mm | 4.0 ± 1.0 mm |
| After 12 months | 4.7 ± 2.0 mm | 4.2 ± 2.0 mm |

Wender *et al., Menopause* 2004

**TABLE 3.** *Histological diagnoses and semiquantitative histological scores of endometrial samples in 11 women at the end of 1 and 2 years of treatment with tibolone*

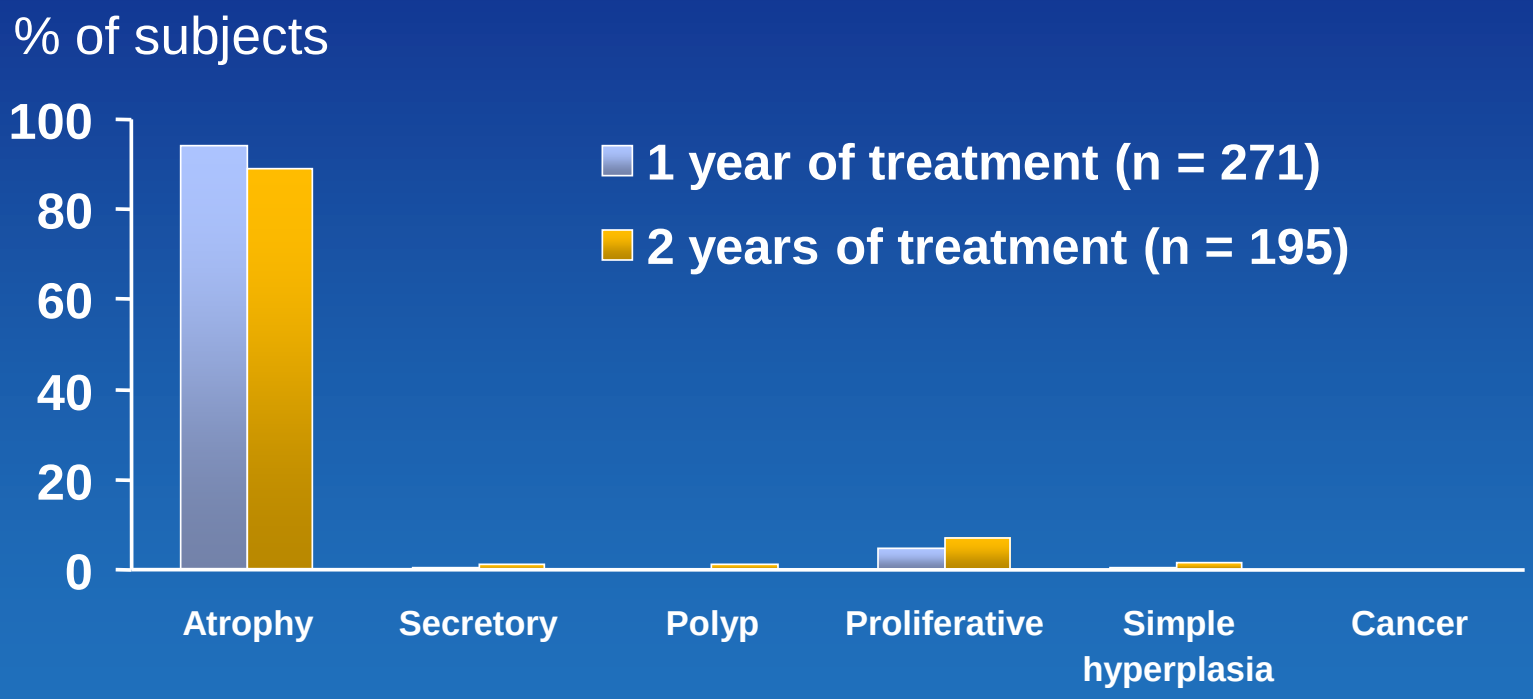
| Patient # | Endometrial histology after 12 mo of treatment | Semiquantitative histological score | Endometrial histology after 24 mo of treatment | Semiquantitative histological score |
|---|---|---|---|---|
| 12 | Weakly proliferative | 2a | Hypotrophic with incipient secretory alterations | 1 |
| 16 | Hypotrophic with incipient secretory alterations | 1 | Insufficient material for diagnosis | 0 |
| 21 | Atrophic | 0 | Insufficient material for diagnosis | 0 |
| 26 | Atrophic | 0 | Atrophic | 0 |
| 30 | Atrophic + endometrial polyp | 0 | Insufficient material for diagnosis | 0 |
| 31 | Hypotrophic with incipient secretory alterations | 1 | Insufficient material for diagnosis | 0 |
| 32 | Insufficient material for diagnosis | 0 | Insufficient material for diagnosis | 0 |
| 36 | Insufficient material for diagnosis | 0 | Atrophic | 0 |
| 38 | Atrophic | 0 | Hypotrophic with incipient secretory alterations | 1 |
| 42 | Insufficient material for diagnosis | 0 | Insufficient material for diagnosis | 0 |
| 43 | Insufficient material for diagnosis | 0 | Atrophic | 0 |

Semiquantitative histological score: 0, atrophic endometrium; 1, secretory endometrium; 2a, weakly proliferative endometrium; 2b, proliferative endometrium.

Wender M et al. Menopause 2004;11:423-9

# Effect on the endometrium

## Endometrial histology after tibolone treatment




Subjects with pathology at baseline were excluded from the analysis

*M Mol-Arts, Climacteric suppl* 1999

# Effect on the endometrium

## Endometrial histology of women treated with tibolone

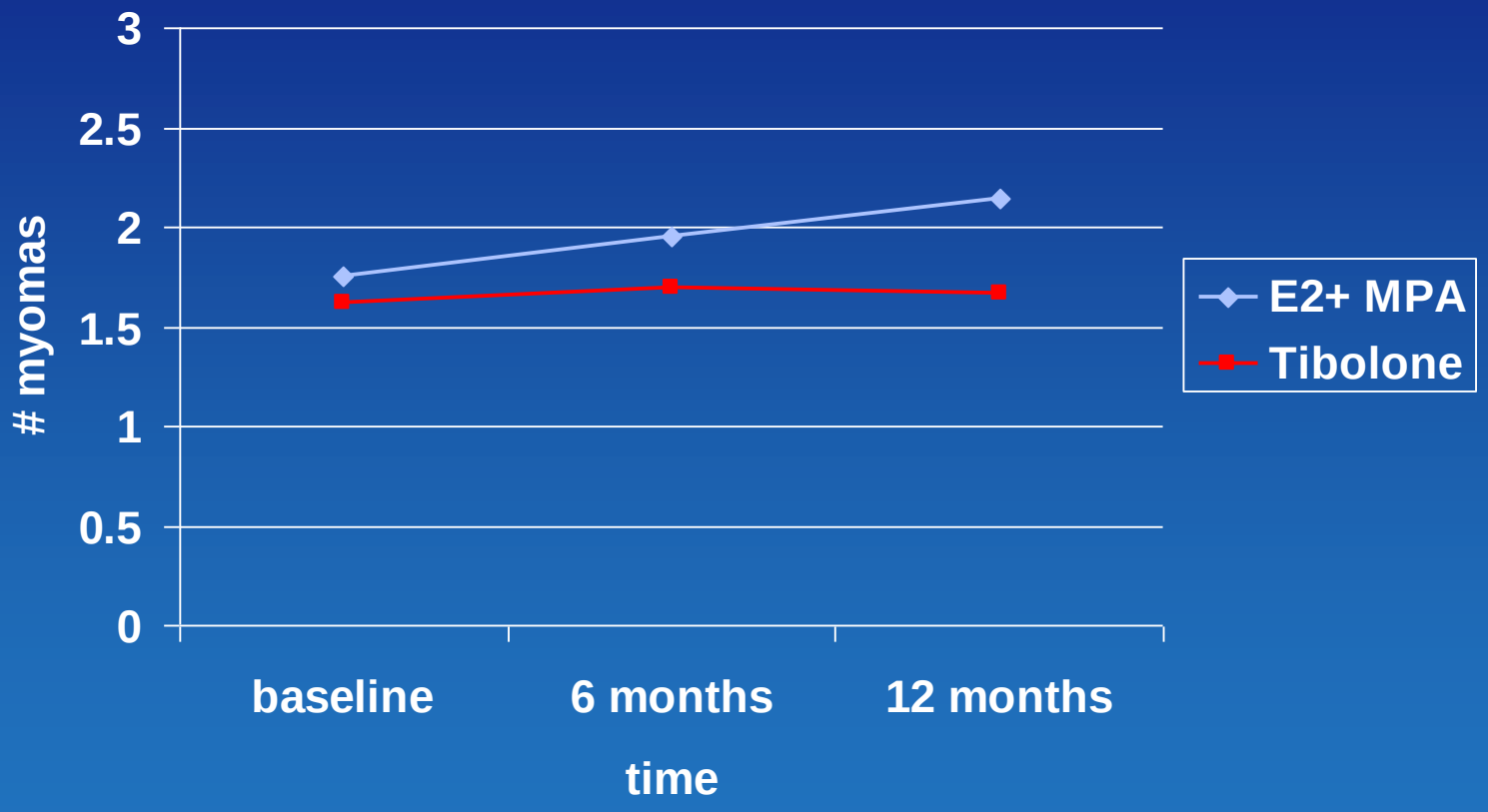
| Endometrial histology | Baseline (n= 146) | 12 months (n=112) | 24 months (n=62) |
|---|---|---|---|
| Atrophy | 146 (100.0%) | 110 (98.2%) | 57 (91.9%) |
| Proliferation | | 2 (1.8%; 0.22-6.45) | 4 (6.5%;1.20-7.51) |
| Hyperplasia | | 0 (0%; 0.0-3.29) | 1*(1.6%;0.01-3.20) |

* simple hyperplasia “worst-case approach” was used: tissue sample was insufficient for full diagnosis

Völker *et al., Climacteric 2001*

# Effect on urogenital system

## Tibolone and Myomas



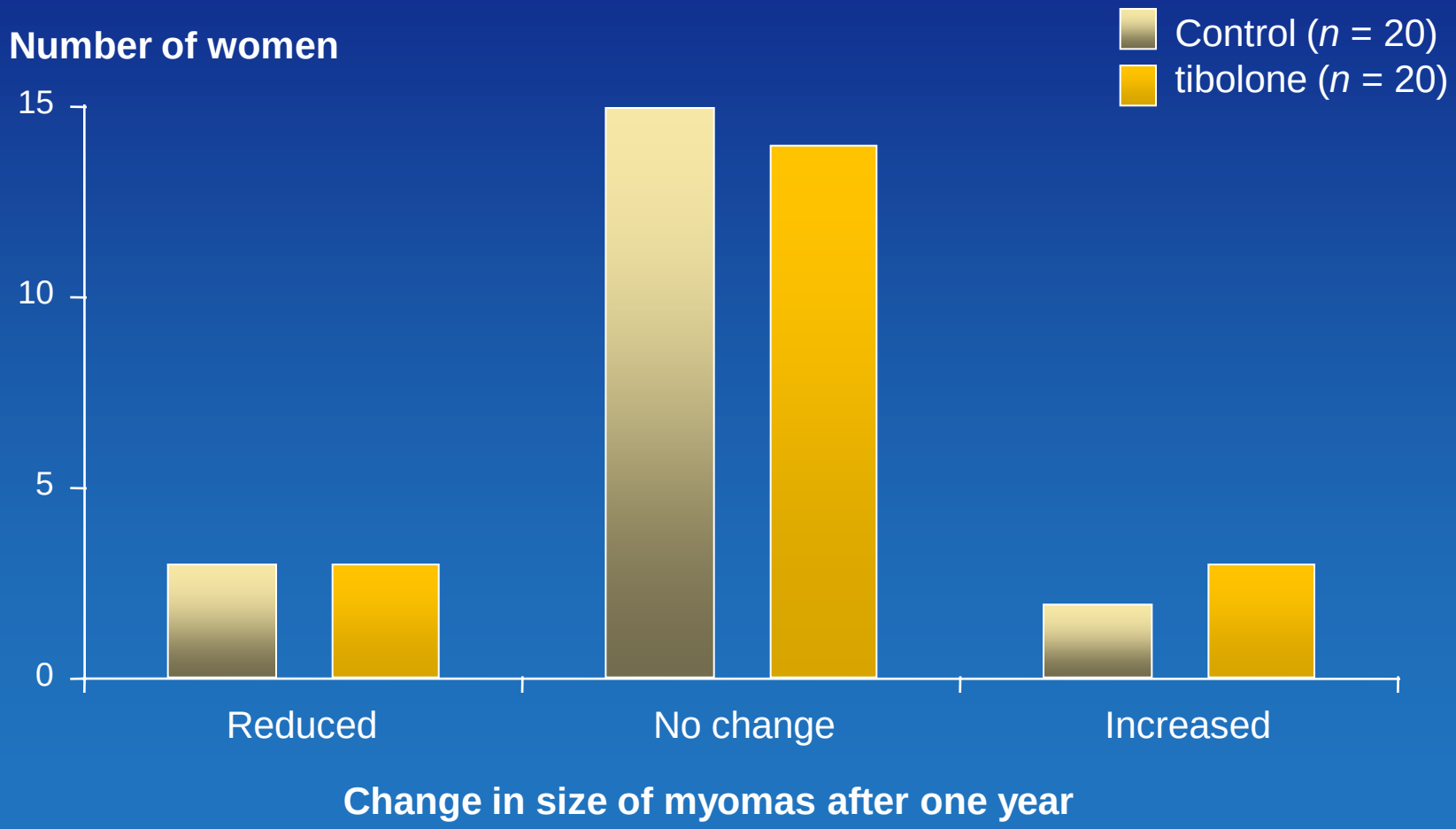

**Change in number of myomas after one year**

P< 0.01 vs baseline

Fedele *et al.,Eur J Obstet 2000*

# Effect on urogenital system

## Tibolone and fibroids




Gregoriou *et al., Maturitas 1997*

# Livial: effect on the endometrium

Incidence of endometrial cancer in the clinical database

| | Placebo/ untreated controls | Tibolone (all doses) |
|---|---|---|
| N | 1074 | 3288 |
| Woman-years | 1665 | 3637 |
| Endometrial cancers (n) | 2 | 3 |
| Incidence/1000 Woman-years | 1.20 | 0.82 |
| Relative risk (95% confidence interval) | 0.69 (0.08- 8.22) | |

# Tibolone and the endometrium
## Conclusions

Tissue-selective conversion into the $\Delta^4$-metabolite

- progestogenic dominant effect on the endometrium
- low incidence of hyperplasia
- low incidence of vaginal bleeding

Tissue-selective on sulfatase/sulfotransferase

- lowers estrogenic activity in endometrium

Therefore, no endometrial stimulation

- high amenorrhea rate (> 90% within 3 months)
- no progestogen needed