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Estrogen and Tamoxifen vs. Breast Cancer Benefits: Prevention vs. Adjuvant Setting

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Background

Breaking News!

- **US FDA November 10, 2025 News Release**: Removal of the "black box" warnings from HRT side effects…those which were blocking the widespread use of HRT…
- "*Tragically, tens of millions of women have been denied the life-changing long-term HRT health benefits because of a medical dogma rooted in a distortion of risk,*" said FDA Commissioner Makary.
- As a result, HHS now Advances Women's Health, Removes Misleading FDA Warnings on Hormone Replacement Therapy…

Introduction

- Despite prior HRT consensus of BrCa harms, the 2020 WHI-2 shows E-HRT reduction of both Incidence AND mortality rates.

Table 1: E-alone HRT **BrCa**

Analysis 1: WHI HRT Trials 2 vs. 1	Trial 2, **RRs** [*E-alone HRT vs. Placebo*] RR [95% C.I.]	Trial 1, **RRs** [*E+P HRT vs. Placebo*] RR [95% C.I.]	**Ratio of "hazards" –** *[or Ratio of "Risk Ratios"]* [**R-RRs**]	P
BrCa Incidence	0.78 [0.65-0.93]	1.28 [1.13-1.45]	**R-RR** *incidence* 0.61 [0.49-0.76]	*<0.001*
BrCa Mortality	0.60 [0.37-0.97]	1.35 [0.94-1.95]	**R-RR** *mortality* 0.44 [0.25-0.81]	*0.008*

Results

WHI-2: All-cause Mortality: E-HRT Benefits

- **Bone loss & fractures:** RR: **0.55 - 0.70**
- **Metabolic &diabetes:** RR: **0.70 - 0.80**
- **Breast Cancer**: RR: **0.60** [0.37-0.97]
- **Alzheimer dementia:** RR: **0.74** [0.59-0.94]
  - for women age <60 at E-HRT start
- **Coronary Heart Dis:** RR: **0.65** [0.44-0.96]
- **All-cause mortality:** RR: **0.79** [0.64-0.96]

And Tamoxifen vs. Estrogen-HRT? *Ref 1, 3, 9*

Estrogen HRT vs. Tamoxifen: Prevention setting

Ref 9

- **BrCa incidence:**
  - E-HRT: RR: 0.78 [0.65-0.93] *Ref 1*
  - Tamoxifen: RR: 0.71 [0.60-0.83] *Ref 3*

BUT – have a look:

- **BrCa mortality**:
  - E-HRT: RR: **0.60** [0.37-0.97] *Ref 1*
  - Tamoxifen: RR: 1.19 [0.68-2.10] *Ref 3*

Results

Estrogen HRT vs. Tamoxifen: Stage IV BrCa

Estrogen [Stilboestrol]: 35%

Tamoxifen: 16%

Adjusted "p": *p = 0.039*

CONCLUSIONS: Benefits of E-HRT over Tamoxifen are now fully evident in BrCa Prevention & and Stage IV settings…

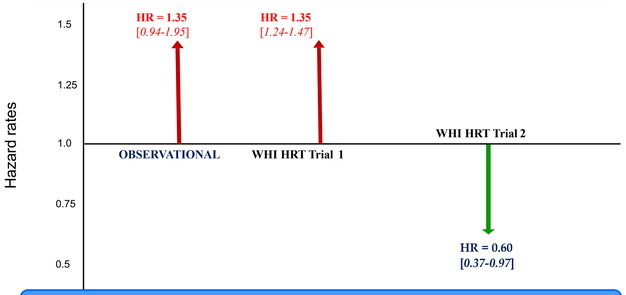
QUESTIONS:

- Should we expect "*E-HRT-over-Tamoxifen*" benefits also in Adjuvant setting?
- More importantly, should both E-HRT and Tamoxifen be combined in Adjuvant Therapy?

Conclusions

- The observed BrCa and non-BrCa benefits of E-HRT over Tamoxifen in both prevention and stage IV settings are **sufficiently compelling** to seek Tamoxifen guideline approval in breast cancer adjuvant therapy.
- **COMMENT:** Approval of E-HRT in both prevention and adjuvant settings will likely avoid tens of thousands of deaths each year just in USA alone, with concomitant dramatic improvements in QOL.

Figure 1: WHI vs. Observational Trials: Rates of Mortality



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