

Adjuvante endocriene behandeling: hoe langer hoe beter?

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Adjuvante therapie

- ✓ Overlijden aan borstkanker:
 - 21.3%↓ tussen 1975-2000
- ✓ Mediane afname: 30%
(range: 25-38%)
 - Screening: 15% (range: 7-23%)
 - Adjuvante therapie: **19%** (range: 12-21%)

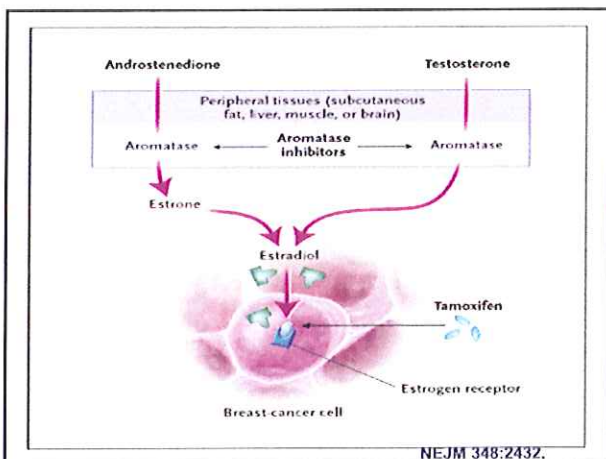
Berry DA et al. NEJM 2005

Adjuvante endocriene therapie

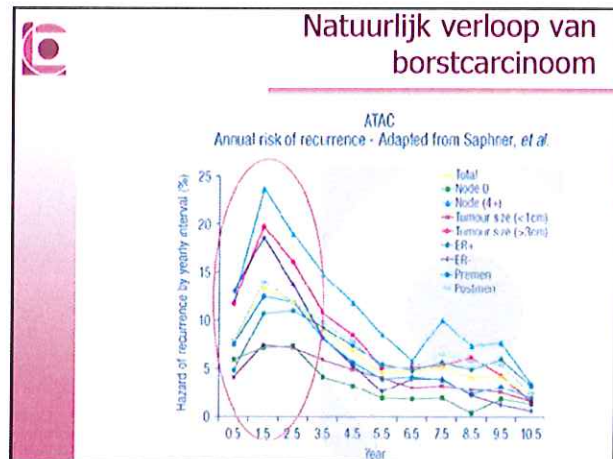
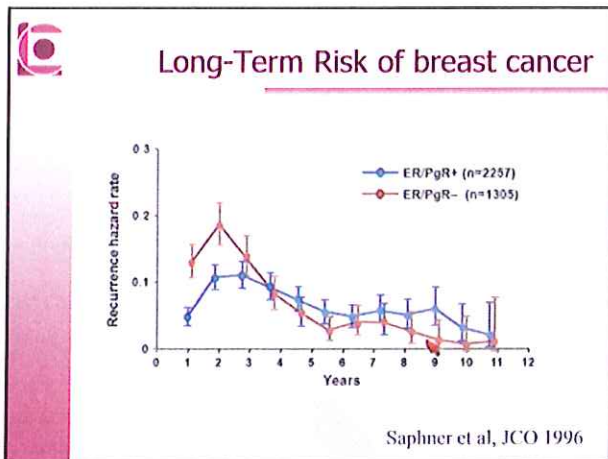
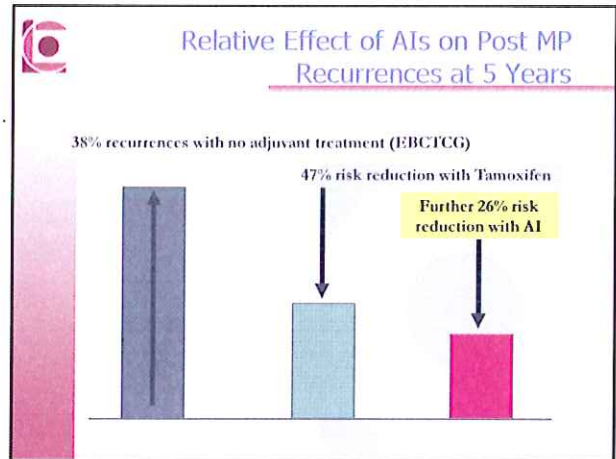
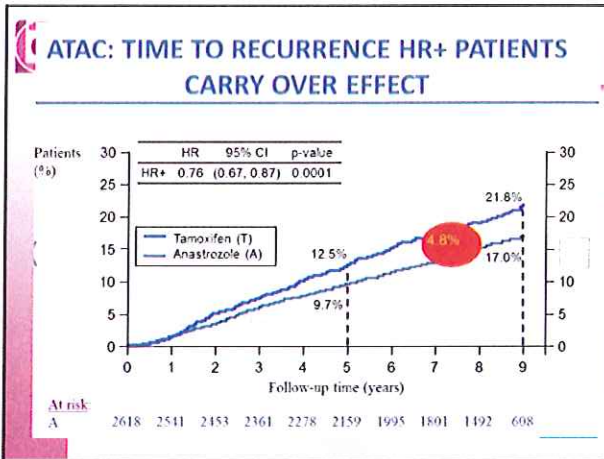
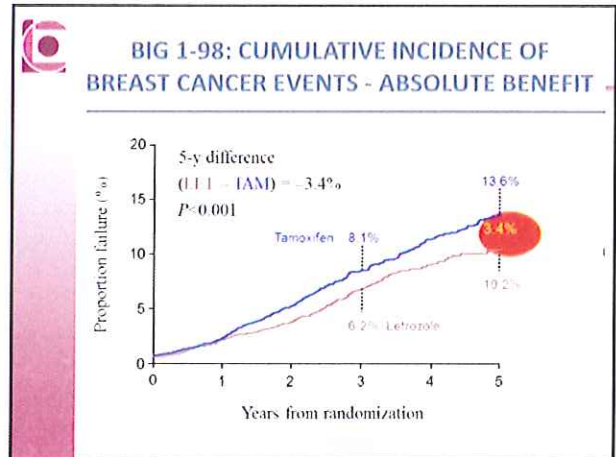
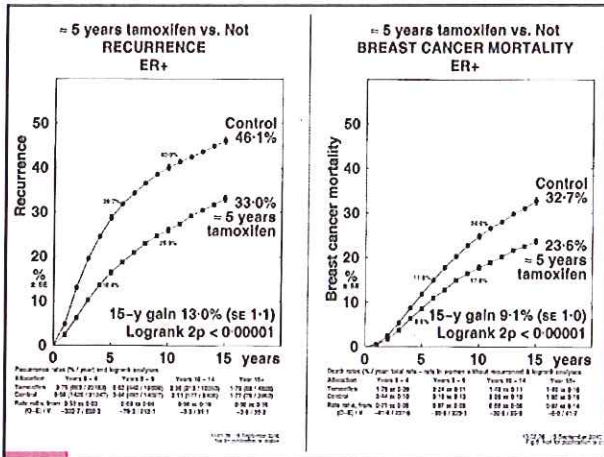
- ✓ Wie?
 - HR +
 - Pre- of postmenopausaal
 - +/- chemotherapie
- ✓ Belang van kwaliteitslabo
 - Europa: 20% vals-negatief

Hormonaal arsenaal

- Ovariële ablatie**
 - Chirurgisch
 - LHRH-agonisten
- SERMS**
 - Tamoxifen
 - Raloxifen, Toremifeen
- Aromatase Inhibitoren**
 - Anastrozole
 - Letrozole
 - Exemestane
- SERD**
 - Fulvestrant
- Progestagenen**
 - Medroxyprogesteron
 - Megestrol acetat



Waarom endocriene therapie?





ATLAS (Adjuvant Tamoxifen: Longer Against Shorter)

- International (36 countries) 1996 - 2005
- 12 894 women early bc 5 years tamoxifen
- Randomised 5 more years (10 in all) or stop
- 6845 women with known ER+ve disease (53%) 60% of remainder assumed ER+ve on basis of subset analysis

Davies et al Lancet 2013 381 801

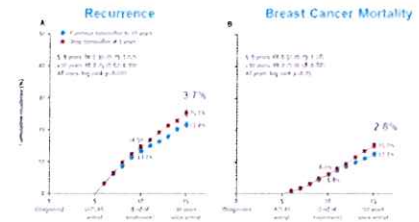
aTOM (Adjuvant Tamoxifen to Offer More)

- UK trial 1991 - 2005
- 6934 pts >4 years tamoxifen
- Known ER+ve 39% (assumed 60% of remainder +ve)
- Randomised 5 more years or not
- N=ve 53%

Gray et al ASCO Abstract 5-2013



Atlas Trial



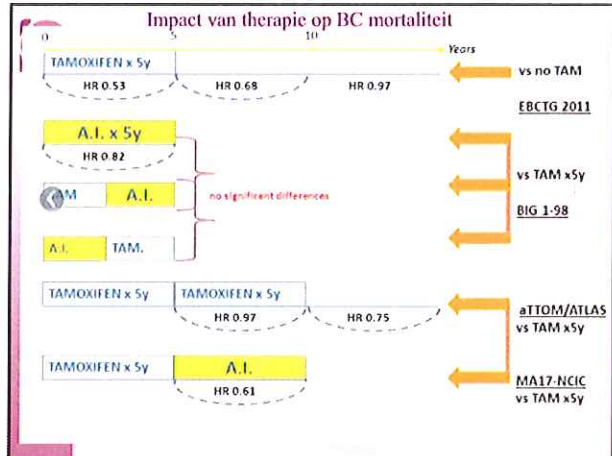
N= 6846 patients

Davies C et al Lancet 2013 381 805-16

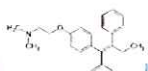


Gepoolde analyse: ATTOM en ATLAS: Gray et al, ASCO 2013

RR in ER + pt	Atlas	Attom	Combined BC mortaliteit	Combined OS mortaliteit
Jaar 5-9	0,92	1,08	0,97	HR 0,99
Jaar 10+	0,75	0,75	0,75	HR 0,84
Alle jaren	0,83	0,88	0,85	HR 0,91



Verschillen in nevenwerkingen



Tamoxifen

- Vasomotor symptomen
- Gynaecologische compl
- vag bleeding, flux
- verminderd libido
- endometriële ca
- Veneuze thrombo-embolie

Aromatase inhibitoren

- Muskuloskeletale symptomen
- artralgie, myalgie
- CTS
- Vasomotor symptomen
- Vaginale droogte, afn libido
- Botverlies
- osteopenie/-porose
- fractuur



Toxicities

ATLAS (Adjuvant Tamoxifen: Longer Against Shorter)

- Pulmonary embolus RR 1.87 (p=0.01) 0.2% mortality both groups
- Stroke RR 1.06 (0.83-1.36)
- Ischaemic heart disease RR 0.76 (p=0.02)
- Endometrial cancer RR 1.74 (p=0.0002) Cumulative risk years 5-14 3.1% (mortality 0.4%) for continued versus 1.6% (mortality 0.2%) for controls

Davies C et al Lancet 2013 381 805-16

aTOM (Adjuvant Tamoxifen to Offer More)

- Endometrial cancers RR 2.20 (1.31-3.34) p<0.0001
 - 10 yrs (2.9%) 5 yrs (1.3%)
- Death from endometrial cancers RR 1.83 (1.09-3.09) p=0.02
 - 10 yrs (1.1%) 5 yrs (0.6%)

Gray RG et al ASCO 2013 (Abstract 5)



Patiënt factoren

- TNM,
- Biologie,
- Leeftijd,
- comorbiditeiten

Therapie factoren



Studies met verlengde AI therapie

Study	n	Treatment Pre-randomization	Arms at Randomization	Study number
MA 17R	1800	T (3-5 yr) + Any extended AI (5 yr) + 0-2 yr prior randomization	L (5 yr) vs placebo (5 yr)	NCT00754845
BALSA	3488	Any endocrine therapy (5 yr)	A (5 yr) vs A (2 yr)	NCT00295620
LEAD	4050	T (2-3 yr)	L (5 yr) vs L (2-3 yr)	NCT01064635
DATA	1900	T (2-3 yr)	A (6 yr) vs A (3 yr)	NCT00301457
NSABP-B42	3968	AI or T-AI (5 yr)	L (5 yr) vs placebo (5 yr)	NCT00382070
SOLE	4800	Any endocrine therapy (5 yr)	L (5 yr) vs intermittent (5 yr)	NCT00553410

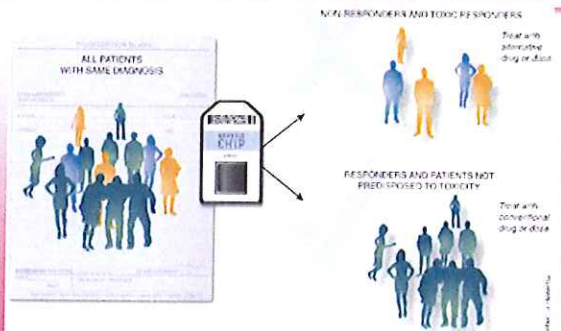


Behandelings algoritme

Menopauze status bij diagnose	Initiële therapie	Extended therapie
Pre/peri	Tam5	Tam5
	Tam5	AI5 (indien post-menopauze)
Post	AI5	
	Tam5	Tam5
	Tam5	AI5
	Tam2-3	AI5



Toekomst: personalised medicine



Take Home Messages

- ✓ Tamoxifen nog steeds zeer waardevol!
- ✓ Combinaties van AI en Tam bij menopauze patiënten
- ✓ Langere hormoontherapieën vnl. ifv patiënt kenmerken en nevenwerkingen en invloed van QOL



Dank voor Uw aandacht