

Breast Cancer Tumor Board

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Douglas K Hawley MD
Medical Oncology



ASSOCIATION OF VA HEMATOLOGY/ONCOLOGY



U.S. Department
of Veterans Affairs

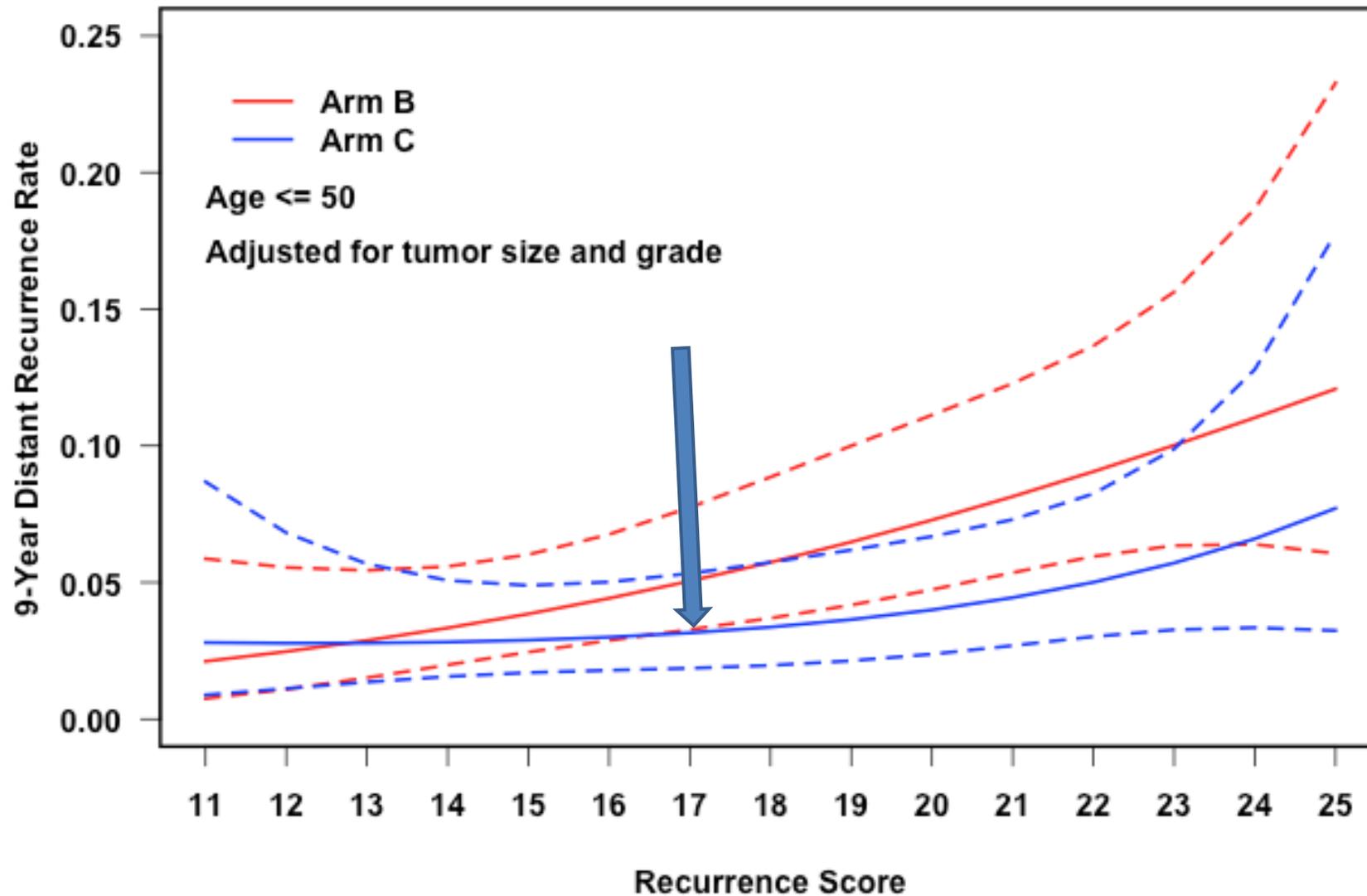
Initial presentation: Premenopausal, ER/PR+, HER2-, Gr III; SNBx neg. Chemo? Hormonal therapy (ET)?

- ▶ “21 gene assay” on all Stage I ER+ for *Recurrence Score*
- ▶ Score <11: ET; Score >25: ET + Chemo;
Score 11-25: usually chemo but less clear
- ▶ TAILORx Score 11-25 : randomized to ET vs ET + chemo
- ▶ 10,273 randomized; overall no different w or w/o chemo
- ▶ But if Age <50:
 - 11-15 no chemo benefit.
 - 16-20 mild benefit
 - 21-25 6% bigger benefit

TAILORx recurrence rate age <50

B= ET alone

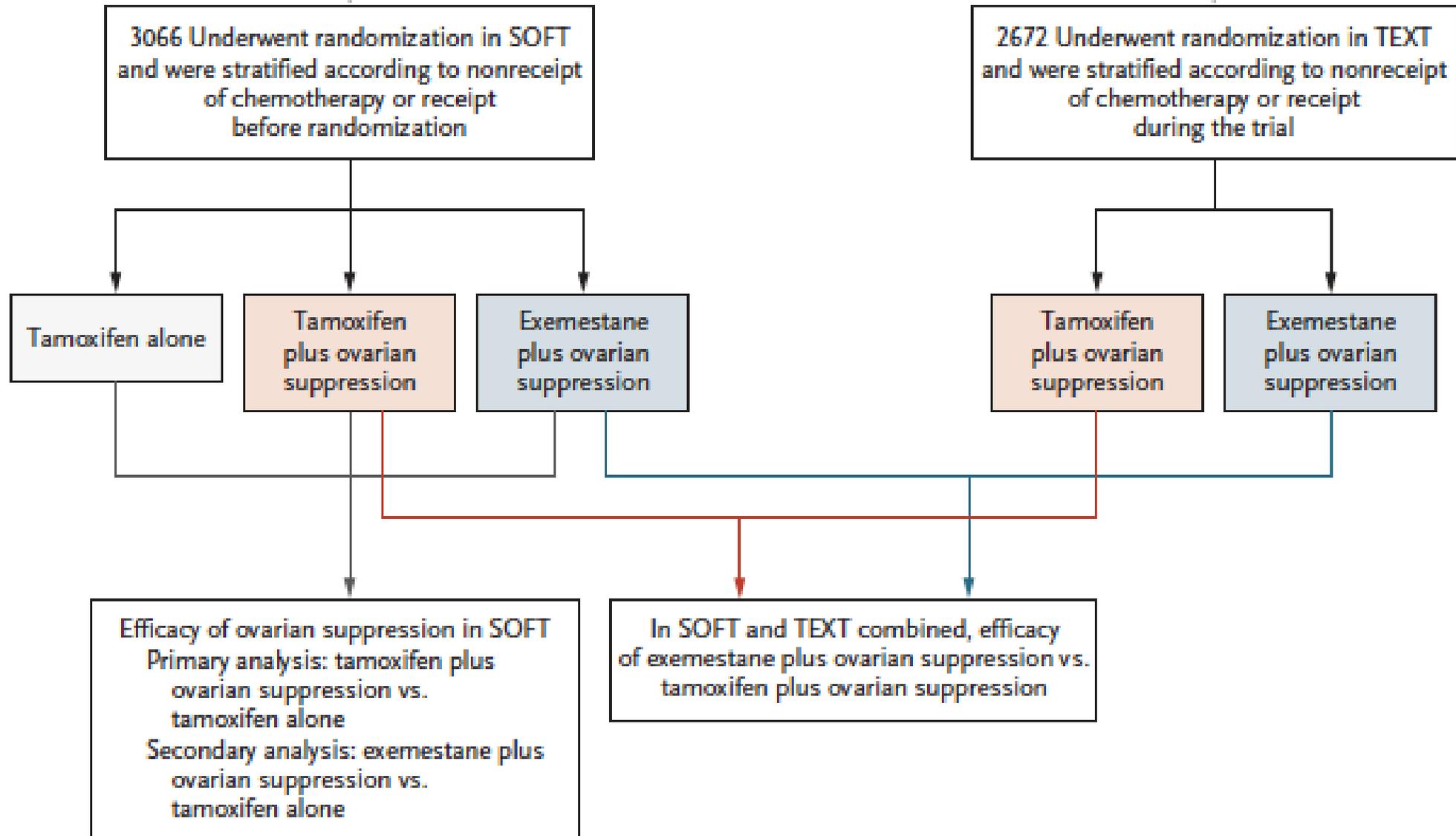
C=ET+Chemo



Stage I ER+, HER2- Breast CA Adjuvant Chemo. Which regimen?

- ▶ CA x 4 = CMFx6-8 ~ TC x4 ~ weekly Pac x12
“Easier” regimens. Blue=no anthracycline
- ▶ CA>Tax, CA>doc, dd CA>Tax4, ddCA>Tax12, CAF, TAC, FEC, TCx6, carbo/pac. These mostly have RCT evidence of superiority to one of the above
- ▶ The superiority of the second group is ~3-10% absolute reduction in relapse rate.

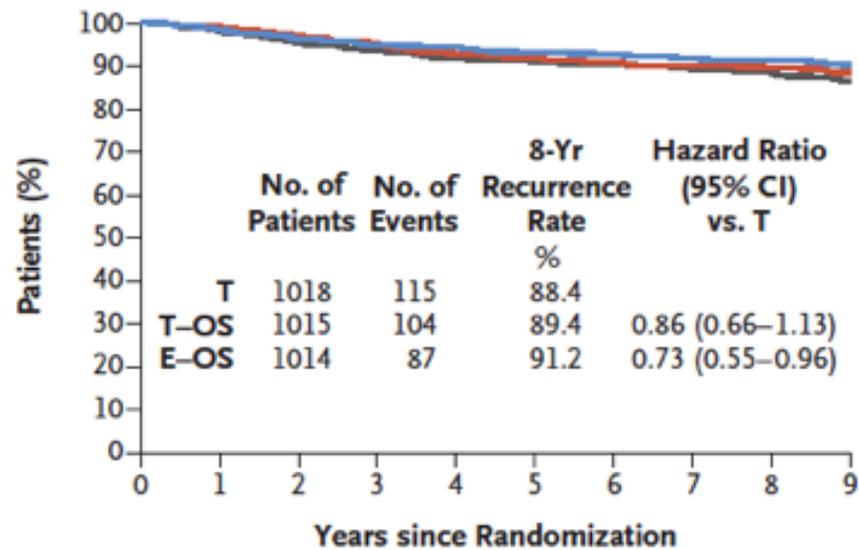
After adjuvant chemo add adjuvant hormonal. Which ET? SOFT and TEXT trials: 5738 pts



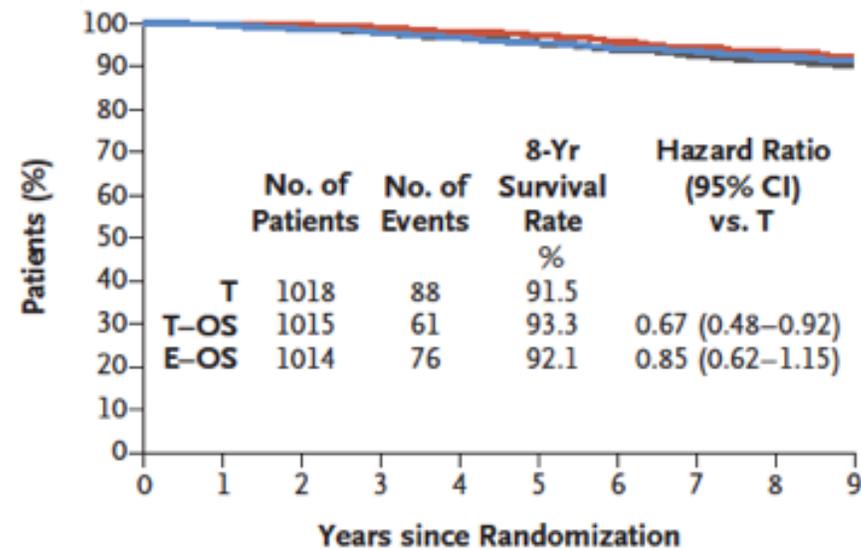


— Tamoxifen alone (T) — Tamoxifen plus ovarian suppression (T-OS) — Exemestane plus ovarian suppression (E-OS)

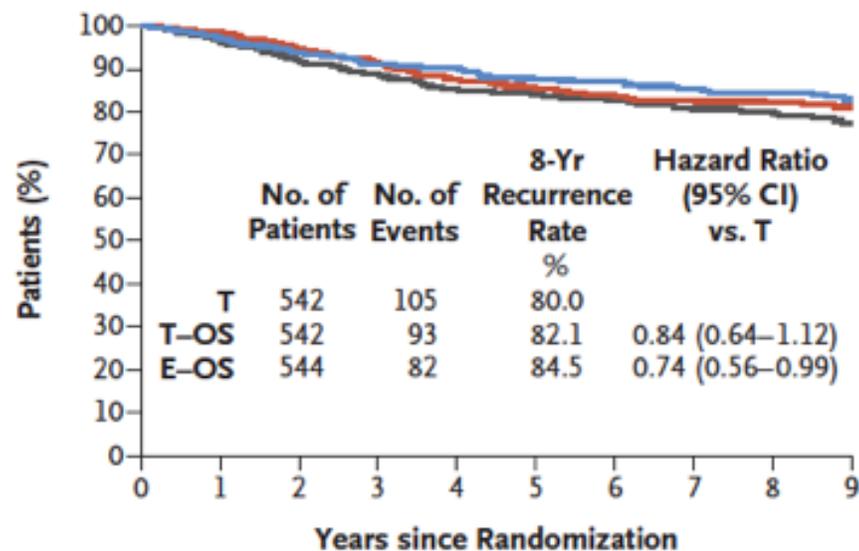
A Freedom from Distant Recurrence



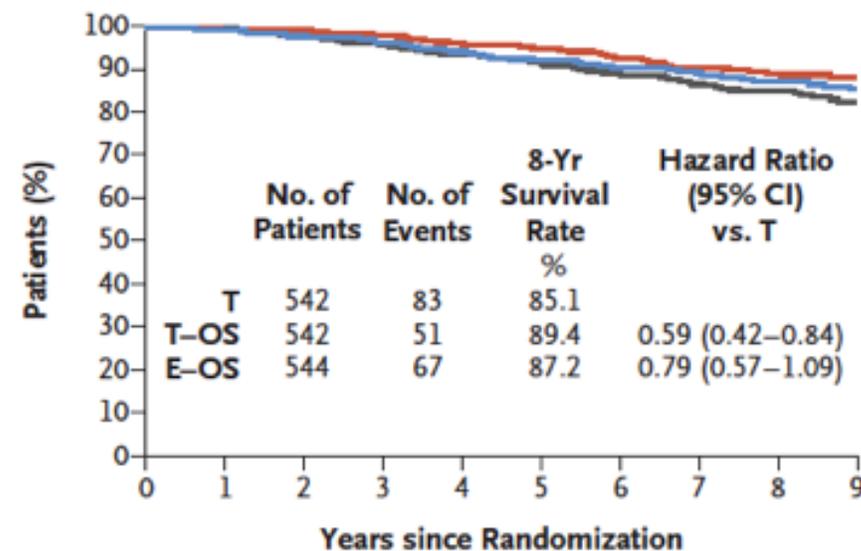
B Overall Survival



C Freedom from Distant Recurrence in Patients with Previous Chemotherapy



D Overall Survival in Patients with Previous Chemotherapy



Targeted Adverse Events during Treatment.

Adverse Event	Tamoxifen (N = 1005)		Tamoxifen plus Ovarian Suppression (N = 2326)		Exemestane plus Ovarian Suppression (N = 2317)	
	Any Event	Grade 3 or 4 Event	Any Event	Grade 3 or 4 Event	Any Event	Grade 3 or 4 Event
	<i>number of patients (percent)</i>					
Any targeted adverse event	962 (95.7)	247 (24.6)	2295 (98.7)	721 (31.0)	2288 (98.7)	748 (32.3)
Allergic reaction or hypersensitivity	35 (3.5)	2 (0.2)	110 (4.7)	9 (0.4)	122 (5.3)	12 (0.5)
Injection-site reaction	4 (0.4)	0	189 (8.1)	1 (<0.1)	174 (7.5)	1 (<0.1)
Hot flushes	808 (80.4)	78 (7.8)	2175 (93.5)	284 (12.2)	2141 (92.4)	234 (10.1)
Depression	476 (47.4)	41 (4.1)	1195 (51.4)	108 (4.6)	1197 (51.7)	95 (4.1)
Sweating	492 (49.0)	NA	1391 (59.8)	NA	1286 (55.5)	NA
Insomnia	470 (46.8)	30 (3.0)	1383 (59.5)	105 (4.5)	1375 (59.3)	89 (3.8)
Fatigue	612 (60.9)	34 (3.4)	1496 (64.3)	70 (3.0)	1450 (62.6)	75 (3.2)
Hypertension	181 (18.0)	57 (5.7)	550 (23.6)	188 (8.1)	564 (24.3)	168 (7.3)
Cardiac ischemia or infarction†	5 (0.5)	4 (0.4)	10 (0.4)	6 (0.3)	17 (0.7)	7 (0.3)
Thrombosis or embolism	22 (2.2)	17 (1.7)	53 (2.3)	47 (2.0)	27 (1.2)	20 (0.9)
Nausea	241 (24.0)	0	692 (29.8)	14 (0.6)	747 (32.2)	17 (0.7)
Musculoskeletal symptom	703 (70.0)	67 (6.7)	1809 (77.8)	132 (5.7)	2082 (89.9)	263 (11.4)
Osteoporosis	138 (13.7)	1 (0.1)	648 (27.9)	7 (0.3)	977 (42.2)	10 (0.4)
Fracture	53 (5.3)	8 (0.8)	140 (6.0)	23 (1.0)	179 (7.7)	37 (1.6)
Vaginal dryness	426 (42.4)	NA	1144 (49.2)	NA	1245 (53.7)	NA
Decreased libido	434 (43.2)	NA	981 (42.2)	NA	1056 (45.6)	NA
Dyspareunia	242 (24.1)	16 (1.6)	636 (27.3)	35 (1.5)	733 (31.6)	56 (2.4)
Urinary incontinence	166 (16.5)	6 (0.6)	433 (18.6)	9 (0.4)	317 (13.7)	9 (0.4)
CNS cerebrovascular ischemia	6 (0.6)	4 (0.4)	10 (0.4)	7 (0.3)	6 (0.3)	5 (0.2)
CNS hemorrhage	15 (1.5)	0	26 (1.1)	2 (0.1)	19 (0.8)	1 (<0.1)
Glucose intolerance‡	18 (1.8)	4 (0.4)	68 (2.9)	23 (1.0)	63 (2.7)	15 (0.6)
Hyperglycemia‡	20 (2.0)	1 (0.1)	92 (4.0)	20 (0.9)	71 (3.1)	14 (0.6)



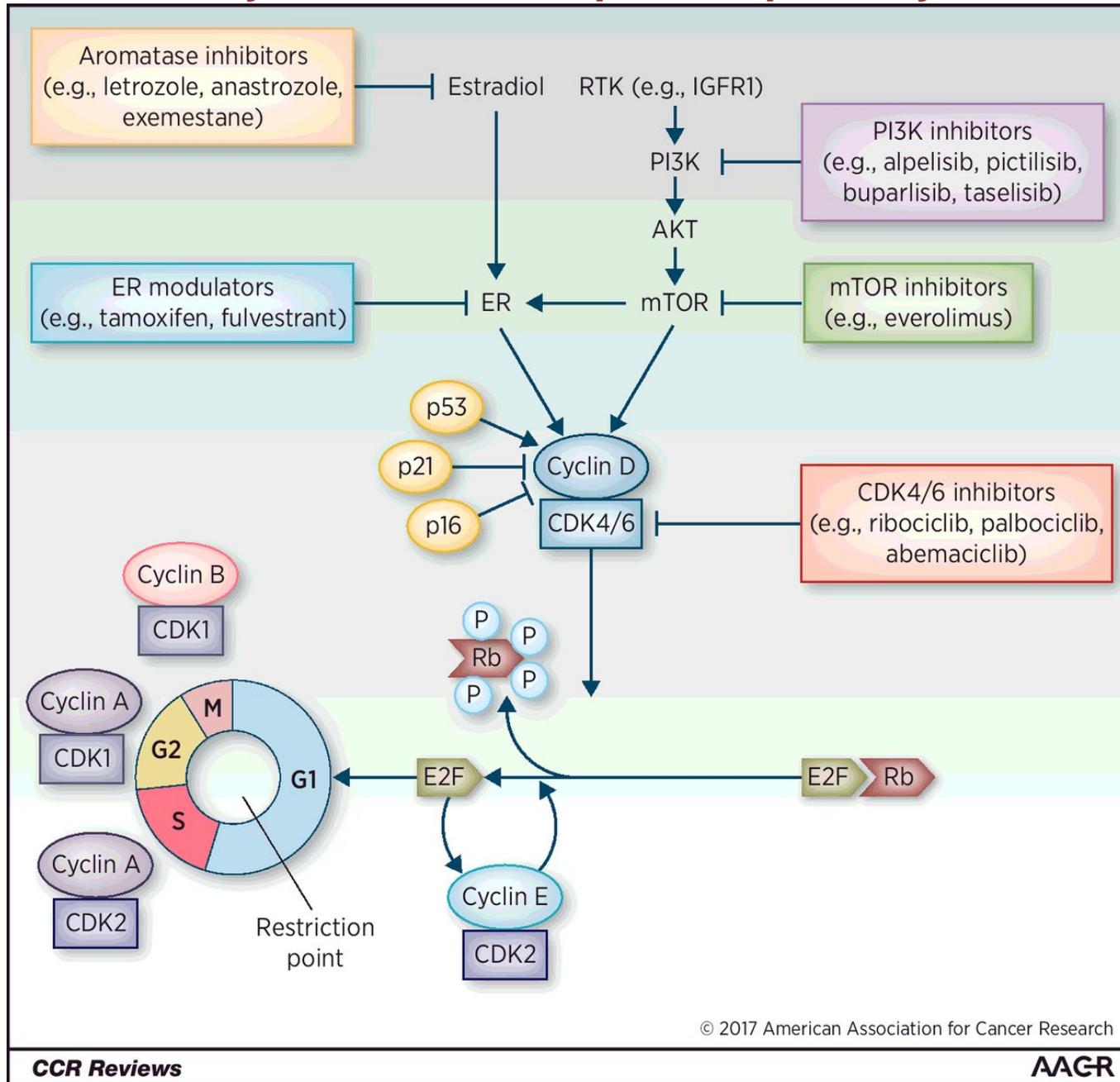
The NEW ENGLAND
JOURNAL of MEDICINE

WHAT NOW ? Relapse at 2 years

Liver and skin metastases

- ▶ *Re-biopsy.* Prove mets, more aggressive histology, loss of ER/PR
Obtain material for possible NGS
- ▶ Chemo vs second line hormonal therapy?
Previously it was accepted that symptomatic rapid growth or visceral disease was indication for chemo.
- ▶ If used for above reason, combination chemo is indicated for higher response rate. Other reasons combination might be considered over single agent: early line tx; young pt w/ good PS; high tumor burden; TNBC; with platinum agents.
- ▶ Single agent sequential treatment is also an option; and becomes increasingly appropriate in subsequent lines of therapy
- ▶ CHEMO: multiple options; avoid anthracyclines for now.
- ▶ A taxane-containing combination would be logical initial tx

Hormonal Options and the cyclin D–CDK4/6–p16–Rb pathway in the cell cycle.

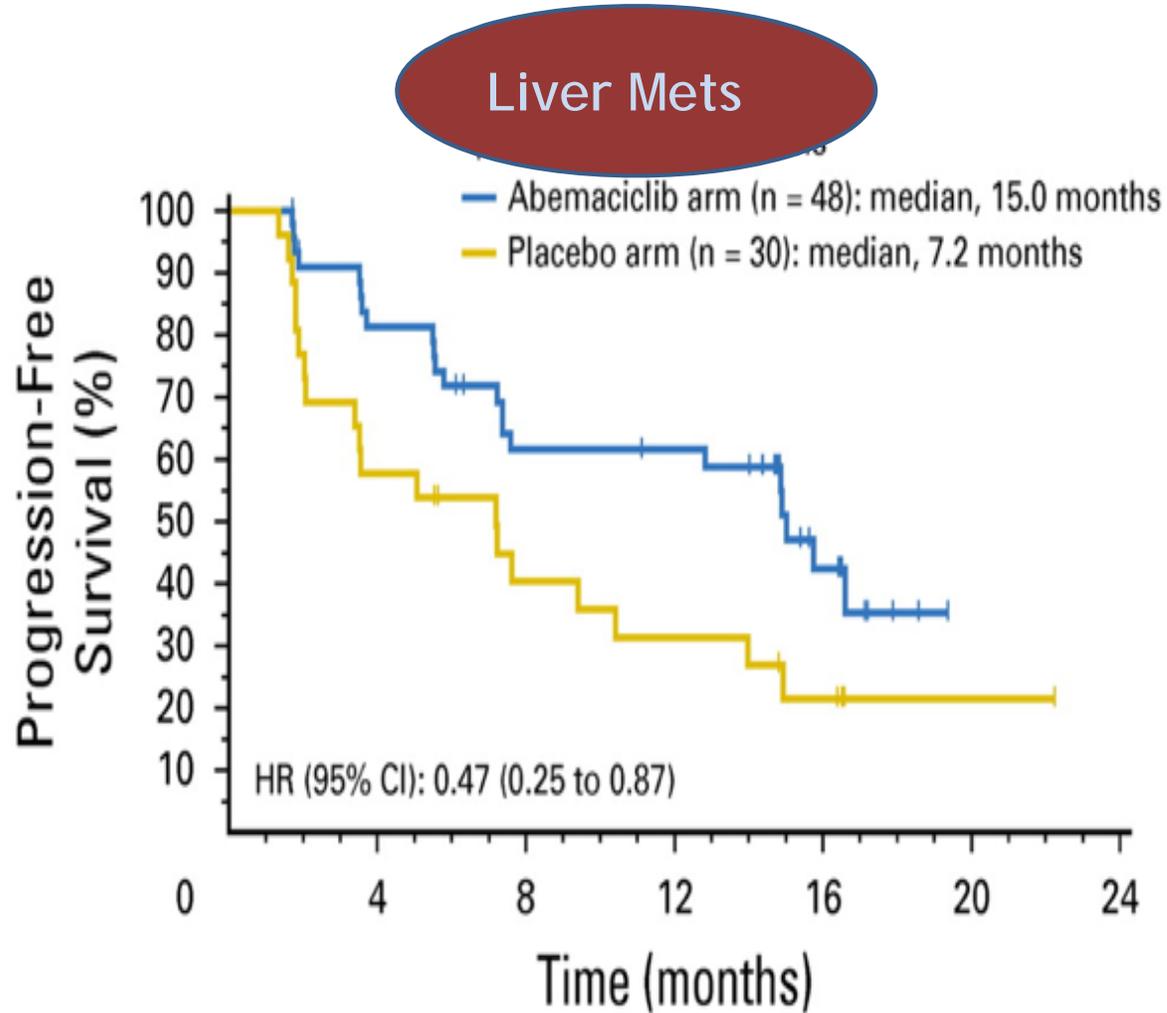


Hormonal Therapy: CDK4/6 Inhibitors

- ▶ **Palbociclib / Ribociclib / Abemaciclib** – Use with AI, fulvestrant, TAM. They all improve DFS +/- OS compared to ET alone
- ▶ **Abemaciclib** more potent affinity for CDK4/6; advantages over the other two:
 - works as single agent (MONARCH 1)
 - works in hormone resistant dz (MONARCH2)
 - works with *liver mets*

Abemaciclib plus AI (Anastrozole or letrozole) as first line tx in metastatic tx with or without liver mets

E



F

