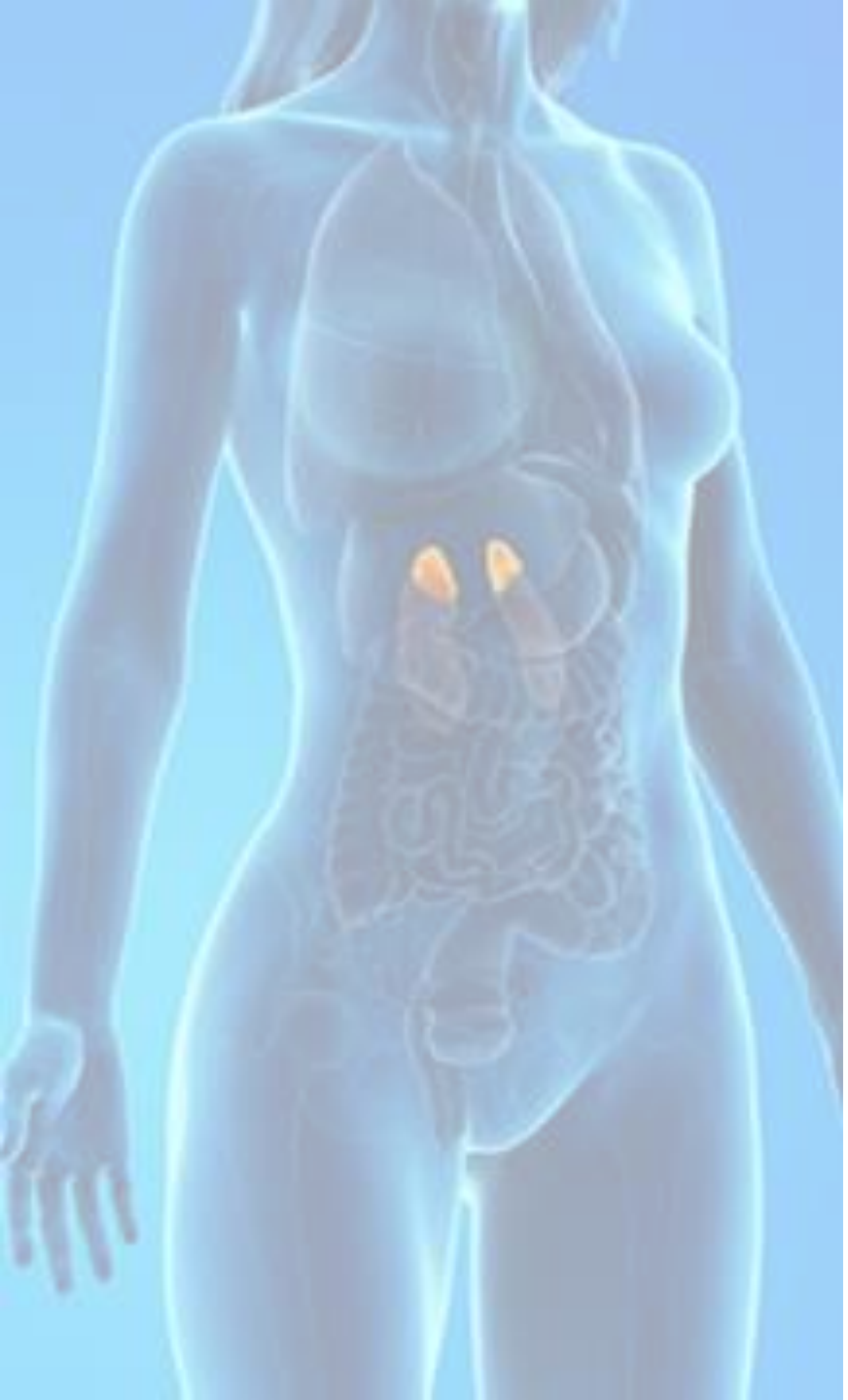


Annika Auranen

- Postoperative Therapy In Endometrial Cancer - Endocrine Therapy

NSGO

Disclosures

- Consultancy, Advisory Board: GSK, MSD
- Participation as investigator in clinical trials: MSD, Roche, GSK, Tesaro, Mersana, Incyte
- NSGO-CTU Foundation Board member

The role of endocrine therapy in EC management - what do the guidelines say?

Joint statement

ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma

Nicole Concin ,[1,2] Xavier Matias-Guiu,[3,4] Ignace Vergote,[5] David Cibula,[6] Mansoor Raza Mirza,[7] Simone Marnitz,[8] Jonathan Ledermann ,[9] Tjalling Bosse,[10] Cyrus Chargari,[11] Anna Fagotti,[12] Christina Fotopoulou ,[13] Antonio Gonzalez Martin,[14] Sigurd Lax,[15,16] Domenica Lorusso,[12] Christian Marth,[17] Philippe Morice,[18] Remi A Nout,[19] Dearbhaile O'Donnell,[20] Denis Querleu ,[12,21] Maria Rosaria Raspollini,[22] Jalid Sehouli,[23] Alina Sturdza,[24] Alexandra Taylor,[25] Anneke Westermann,[26] Pauline Wimberger,[27] Nicoletta Colombo,[28] François Planchamp,[29] Carien L Creutzberg[30]

The role of endocrine therapy in EC management - what do the guidelines say?

- Hormone receptor status is not a feature in molecular classification
- In pathological guideline:

> ► Required ancillary techniques (IHC for p53, MSH-6 and PMS-2, complemented with MLH-1 and MSH-2, MLH-1 promoter methylation analysis in cases of MLH-1/PMS-2 decrease expression). Additional immunohistochemical markers may be important for pathologic diagnosis (PTEN, p16, ER, Napsin A, Racemase, Pax8, E-Cadherin) or prognosis (L1CAM).

When is endocrine therapy indicated/potentially useful?

Systemic treatment for recurrent disease

Hormonal treatment results in a response rate of up to 55% in advanced/recurrent endometrial carcinoma.[394] Low-grade, slowly progressing, hormone receptor-positive tumors appear to gain the greatest benefit from treatment; however, clinical benefit has also been observed in patients with hormone receptor-negative tumors.[395] Progestogens are generally recommended.[395] Alternative options include aromatases inhibitors, tamoxifen, and fulvestrant. In the PARAGON trial a response rate of 7% and a clinical

What kind of endocrine therapy?

Recommendations

- Hormone therapy is the preferred front-line systemic therapy for patients with low-grade carcinomas without rapidly progressive disease (II, A).
- Progestogens (medroxyprogesterone acetate 200 (–300) mg and megestrol acetate 160 mg) are recommended (III, A).
- Alternative options for hormonal therapies include aromatases inhibitors, tamoxifen, fulvestrant (III, C).

A randomized phase II trial of everolimus and letrozole or hormonal therapy in women with advanced, persistent or recurrent endometrial carcinoma: A GOG Foundation study

Brian M. Slomovitz [a,*], Virginia L. Filiaci [b], Joan L. Walker [c], Michael C. Taub [d], Karen A. Finkelstein [e], John W. Moroney [f], Aimee C. Fleury [g], Carolyn Y. Muller [h], Laura L. Holman [c], Larry J. Copeland [i], David S. Miller [j], Robert L. Coleman [k]

Gynecologic Oncology 164 (2022) 481–491

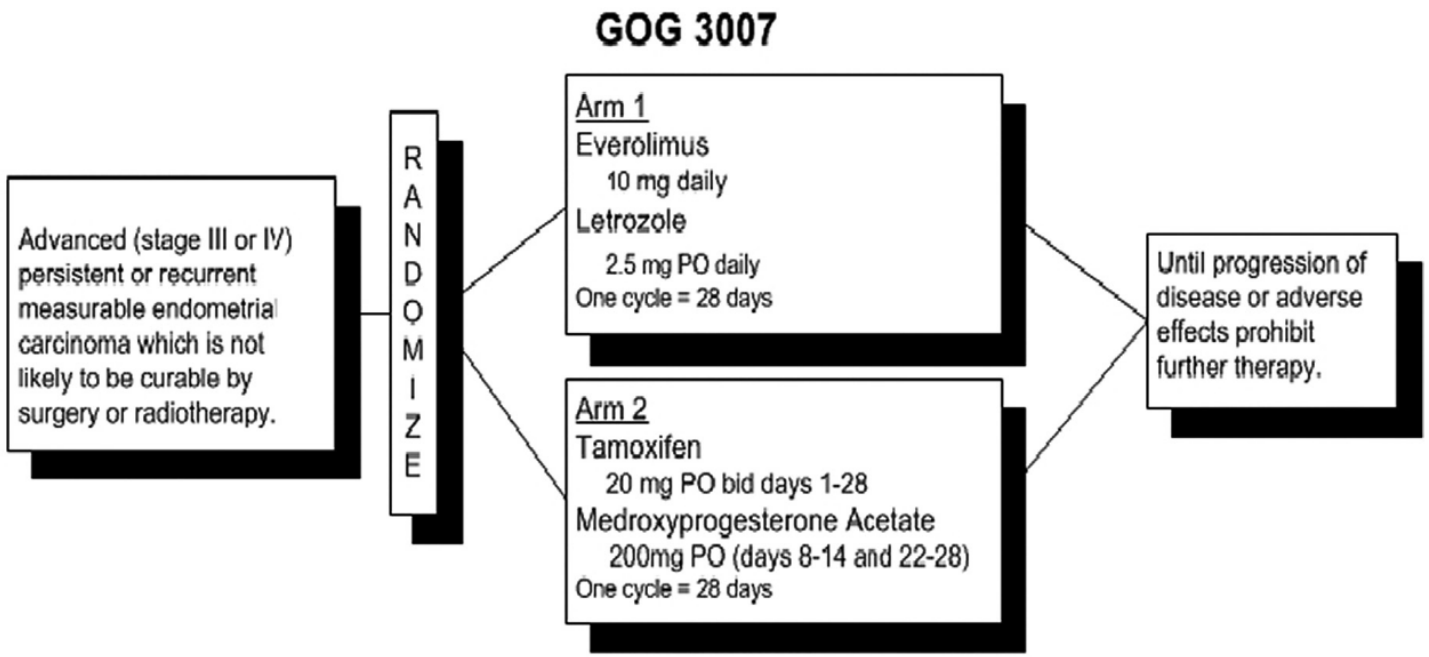


Fig. 1. Schema.

Histology/Grade						
Endometrioid, grade 1	13	35.1	4	10.8	17	23.0
Endometrioid, grade 2	7	18.9	13	35.1	20	27.0
Endometrioid, grade 3	7	18.9	5	13.5	12	16.2
Serous	4	10.8	6	16.2	10	13.5
Clear Cell	1	2.7	2	5.4	3	4.1
Adenosquamous	1	2.7	3	8.1	4	5.4
Mixed Epithelial	0	0	1	2.7	1	1.4
Adenocarcinoma, nos	4	10.8	3	8.1	7	9.5
Stratum						
Prior Chemotherapy or Chemoradiation	22	59.5	22	59.5	44	59.5
No Prior Chemotherapy or Chemoradiation	15	40.5	15	40.5	30	40.5
Total	37	50.0	37	50.0	74	100.0

Principal finding:

In patients without prior chemotherapy, the response rate of everolimus+letrozole was 47 % and median PFD 28 months

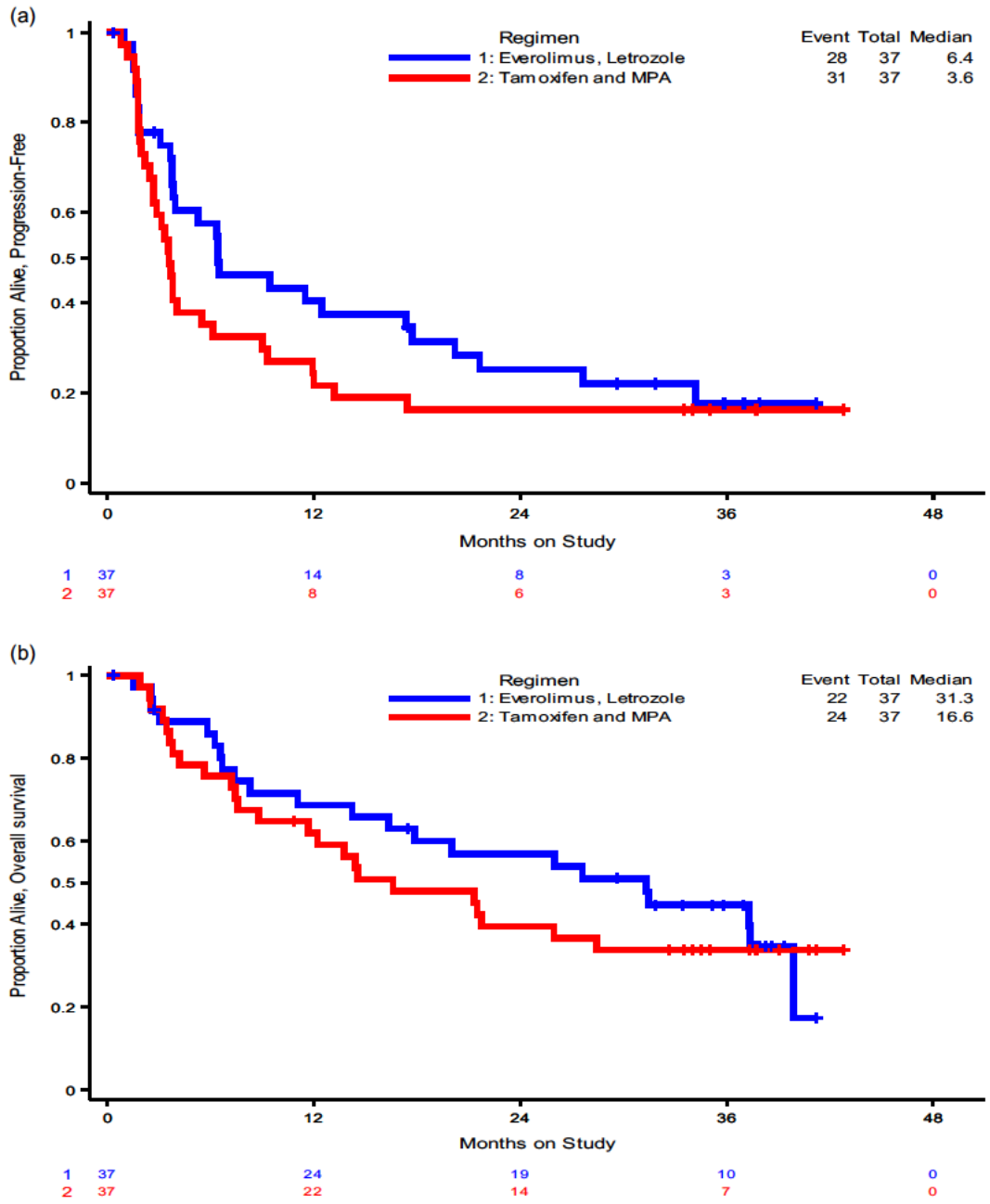
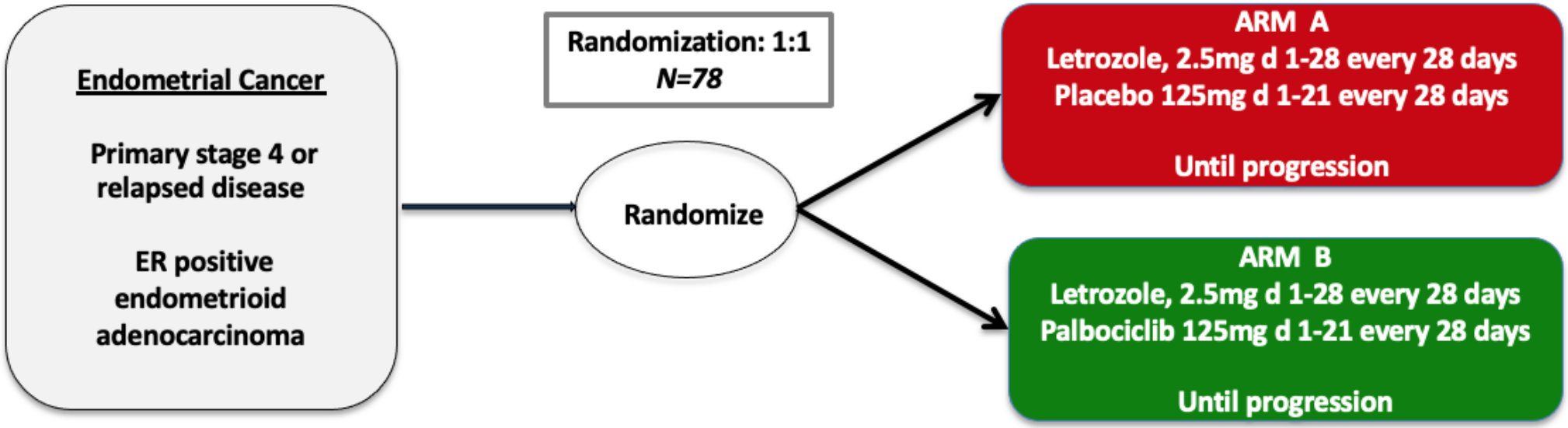


Fig. 3. a - Progression-free survival by regimen. b - Overall survival

ENGOT-EN3/NSGO-PALEO



PFS Median 8.3 vs 3.0 months

DCR at 24 weeks: 64% vs 38 %

What do we know about the role of endocrine therapy as relapse prevention?

- The main target group would be stage I-II EC without high risk features (NSMP)
- However, the relapse rate of these cancers is so low and 5-year survival rate so good (90-95%), that very large studies would be needed to show a possible survival effect

A Randomized Trial of Adjuvant Progestagen in Early Endometrial Cancer

IGNACE VERGOTE, MD, KJELL KJØRSTAD, MD, PHD, VERA ABELER, MD, AND PER KOLSTAD, MD, PHD

Cancer 64:1011–1016, 1989.

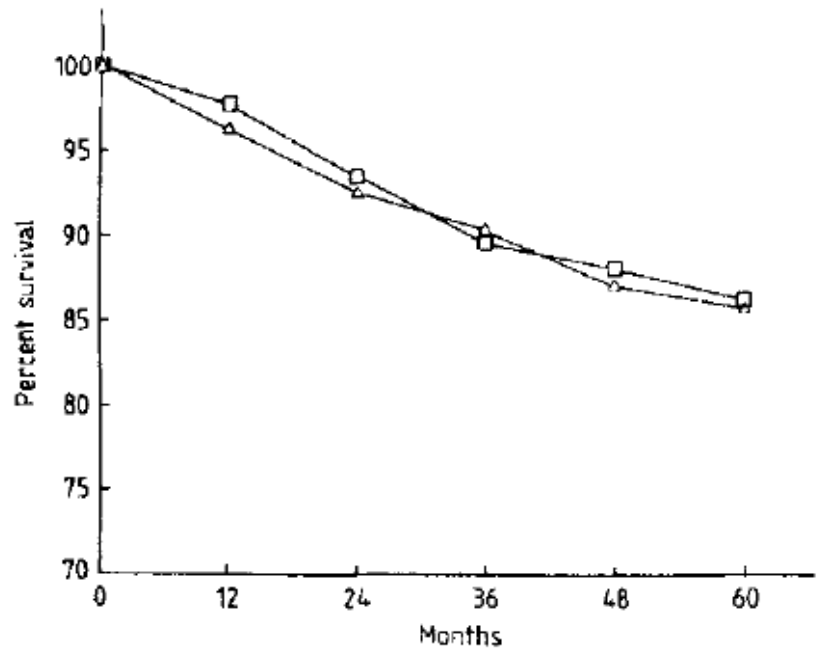


FIG 1. Actuarial crude survival in 553 patients receiving 1-year adjuvant hydroxyprogesterone caproate as compared with 531 control patients.[12] △: Controls; □: treatment group.

PERGAMON

European Journal of Cancer 38 (2002) 2265–2271

European Journal of Cancer

www.ejconline.com

Adjuvant endocrine treatment with medroxyprogesterone acetate or tamoxifen in stage I and II endometrial cancer—a multicentre, open, controlled, prospectively randomised trial

G. von Minckwitz[a], S. Loibl[a], K. Brunnert[b], R. Kreienberg[c], F. Melchert[d], R. Mösch[e], M. Neises[d], J. Schermann[f], R. Seufert[g], R. Stiglmayer[h], U. Stosiek[i], M. Kaufmann,[a,*] for the South West German Gynecologic Oncology Group (SWGGOG)

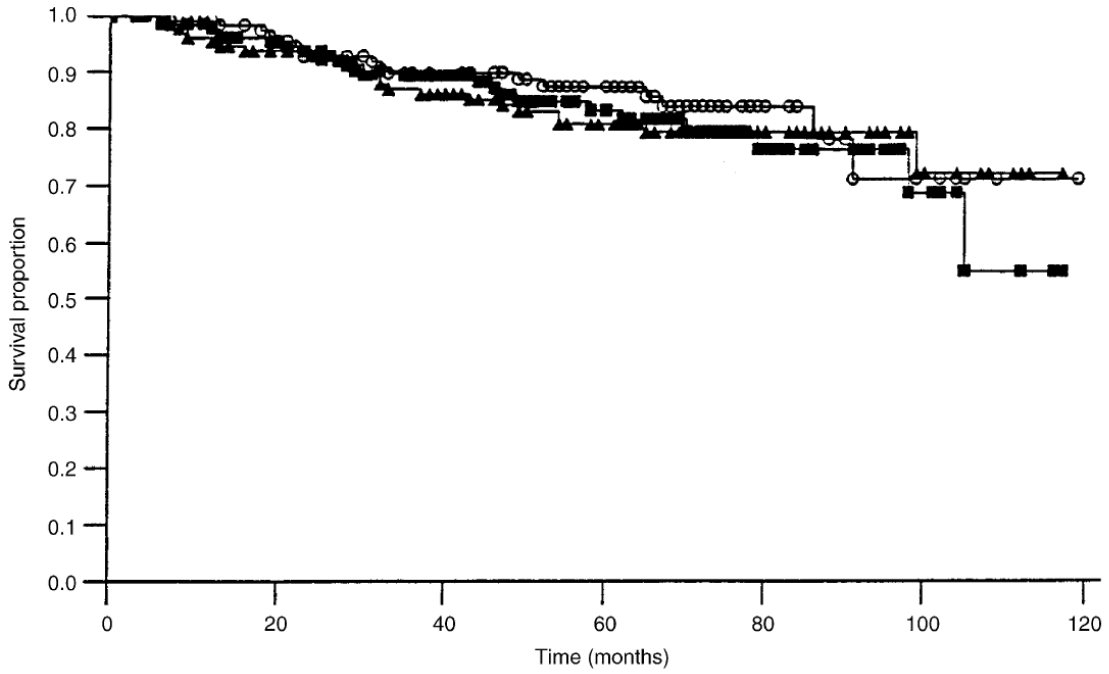


Fig. 1. Acturial analysis of overall survival in 388 patients with surgically pretreated endometrial cancer stages I and II (Kaplan–Meier; log rank; $P = 0.7$). (■) Control group (23/134); (○) tamoxifen treatment (18/121); (▲) MPA treatment (23/133).

MPA = 133

Tamoxifen= 122

Controls = 134

Take home message

- Endocrine therapy has definitely a role in the management of women with slowly progressing low grade EC - there are good possibilites for response, and the treatment is well tolerated
- Combinations including targeted drugs (such as CK4/6 inhibitors or PI3K/Akt/mTOR pathway inhibitors) + endocrine therapy might further improve response rates in treatment of recurrent disease
- There is no evidence, that adjuvant treatment for relapse prevention with hormonal treatments would be beneficial