Neue AGO-LeitlinieEndometriumkarzinom

CTempfer

Universitätsfrauenklinik der Ruhr Universität Bochum

Marienhospital Herne

Endometriumkarzinom- Fakten

- 11 300 Neuerkrankungen/Jahr in D
- 2,7% krebsbedingte Todesfälle - Platz 9
- **Lebenszeitrisiko 1,7%**
- Typ I -endometrioidesAdeno-Ca(90%)
- Typ II - G3, serös-papillär,Klarzell(10%)

LL 2013 - Statements

1. Die Diagnose einesEndometriumkarzinomsund seiner Vorstufen soll durch die Gewinnung einer Histologie gesichert werden.

2. **Jede Blutung in der Postmenopause soll unabhängig von dersonographischenEndometriumdickehistologisch abgeklärt werden.**

3. Die therapieresistente atypische Blutung in derPerimenopausesoll histologisch abgeklärt werden.

4. Die atypische Blutung unter Hormonersatztherapie soll histologisch abgeklärt werden.

5. **Unter Tamoxifen-Einnahme soll nur eine Blutung histologisch abgeklärt werden.**

Ein Screening bei asymptomatischen Frauen ohne Risikofaktoren soll nicht durchgeführt werden.

- Ziel Screening = Mortalität ≠ Detektion
- **NNS=1038**(Gerber 2000, Fung 2003)
- 9112 Frauen; 13 FIGO I, 6/13 mit PMB:**NNS=701**(Kurjak1994, Karlsson 1996,Vuento1999,Ciatto1995)
- **keineoutcome-relevanten Studien**
- AGO, ACOG, RCOG: keine Empfehlung f. Screening

Eine radikale Hysterektomie soll beimEndometriumkarzinomStadium II nicht durchgeführt werden.

Eine**‚fraktionierte‘Abrasio**ist nicht mehr notwendig.

Signorelli 2009: n=520,stageI,rad. HE (PiverII) vs.PiverI, RCT

70mosmedian follow-up, 51deaths

5-Y-DSF (87,7 vs. 89,7%) und 5-Y-OS (88,9 vs. 92,2%)n.s.

Fazit: kein sign. Überlebensvorteil

Table 5. Prognostic Factors of Subjected Cases

Clinicopathologic Factors	*P*	Odds Ratio	95% Confidence Interval
Age (older than 65 compared with 65 or younger)	.032	6.231	1.171–33.165
Pelvic lymph node metastasis	.033	3.736	1.109–12.589
Peritoneal cytology	.148	2.469	0.726–8.396
Ovarian metastasis	.067	3.739	0.912–15.336
PRMS	.233	2.177	0.607–7.808

PRMS, parametrial spread.
Value was calculated by logistic regression test.

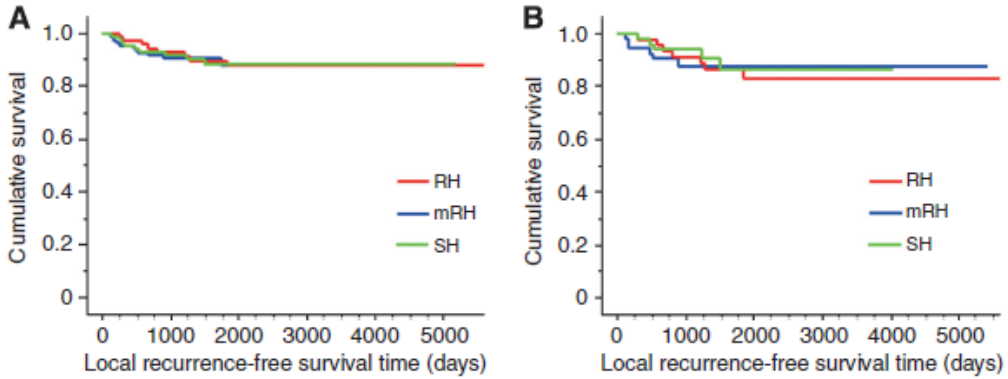


Figure 1. (**A**) Local recurrence-free curves of all patients according to the type of hysterectomy. There was no significant difference among three groups. Five-year survival rates were 88.0% in RH, 89.6% in mRH, and 87.9% in SH group, respectively. There was no significant difference among three groups. (**B**) Local recurrence-free curves of the patients that had pathological cervical stromal involvement according to the type of hysterectomy. There was no significant difference in OS among three groups. Five-year survival rates were 86.4% in RH, 87.9% in mRH, and 86.5% in SH group, respectively. There was no significant difference among three groups.

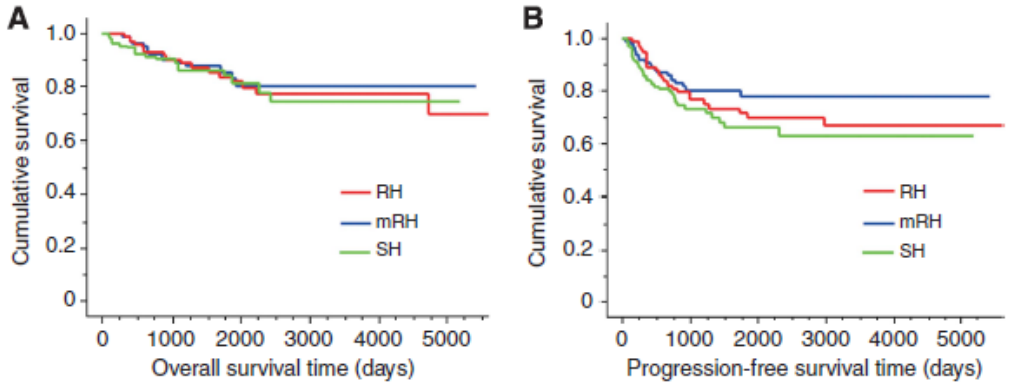


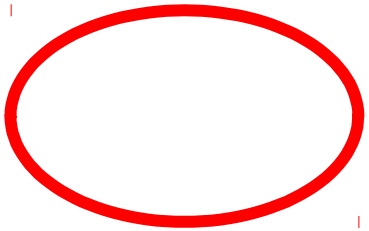
Figure 2. (**A**) Overall survival curves of all cases according to the type of hysterectomy. Five-year overall survival rates were 83.6% in RH, 85.6% in mRH, and 84% in SH group, respectively. There was no significant difference in OS among three groups. (**B**) PFS curves of all patients according to the type of hysterectomy. Five-year PFS rates were 71.6% in RH, 77.7% in mRH, and 66.4% in SH group, respectively. There was no significant difference in PFS among three groups.

Table 4. Adverse effects according to surgical procedures

Variables	RH ($n=74$)	mRH ($n=112$)	SH ($n=114$)	*P*-value
Perioperative adverse effects				
Operative time (minutes)				0.058[a] <0.01[b]
Median Range	292 174–677	282 187–475	184 81–288	
Blood loss (g)				<0.01[a]
Median Range	1162 320–6000	855 120–4060	355 30–3140	<0.01[b]
Blood transfusion				<0.01
Yes No	43 31	47 65	18 96	
Deep vein thrombosis, or pulmonary embolism (grade ⩾2)				0.25
Yes No	2 72	2 110	0 114	
Ileus (grade ⩾2)				0.87
Yes No	2 72	3 109	2 112	
Late adverse effects [c]				
Lymphedema (grade ⩾2)				0.18
Yes No	9 65	7 105	6 108	
Urinary retention (grade ⩾2)				<0.01
Yes No	11 63	1 111	0 114	

Bei**Typ I**-Karzinomendes Stadiums**pT1A**(FIGO 2010)sollbei intraoperativ makroskopisch unauffälligen Lymphknoten eineLymphonodektomie**nicht durchgeführt werden**.

Tumor Stage	Number (n)	Percent (%)
I	5730	74.8
II	871	11.4
III	818	10.7
IV	2272.9	
No Stage	170.2	
Total	7663100.0	



Benedetti-Panici2008: n=514, FIGOstageI,pelLNDvs.nopelLND

49mosmedian follow-up, 78events

5-Y-DSF (81,0 vs. 81,7%) und 5-Y-OS (85,9 vs. 90,0%)n.s.

Fazit: kein sign. Überlebensvorteil

MRC-ASTEC Trial 2009; n=1408, FIGOstageI

Bei Betrachtung der kurzfristigen postoperativen Morbidität ist das**laparoskopische**Vorgehen dem offen-chirurgischen**überlegen**. Die langfristige Morbidität ist**identisch**.

Laparoscopy versus laparotomy for the management of early stage endometrial cancer (Review)

Galaal K, Bryant A, Fisher AD, Al-Khaduri M, Kew F, Lopes AD

THE COCHRANE COLLABORATION®

8 RCTs, n=3644, n=359 FIGOstageI

kein Unterschied:death,recurrence, intraoperativecomplications

lessbloodloss, LSK sign.longer

Figure 2. Forest plot of comparison: 1 Primary outcomes, outcome: 1.1 Overall survival.

Study or Subgroup	log[Hazard Ratio]	SE	Laparoscopy Total	Laparotomy Total	Weight	Hazard Ratio IV, Random, 95% CI
Malzoni 2009	-0.59	0.59	81	78	26.9%	0.55 [0.17, 1.76]
Tozzi 2005	0.45	0.46	63	59	43.3%	1.57 [0.64, 3.86]
Zullo 2009	0.32	0.56	40	38	29.8%	1.38 [0.46, 4.13]
Total (95% CI)			**184**	**175**	**100.0%**	**1.14 [0.62, 2.10]**

Heterogeneity: Tau² = 0.01; Chi² = 2.09, df = 2 (P = 0.35); I² = 4%
Test for overall effect: Z = 0.42 (P = 0.67)

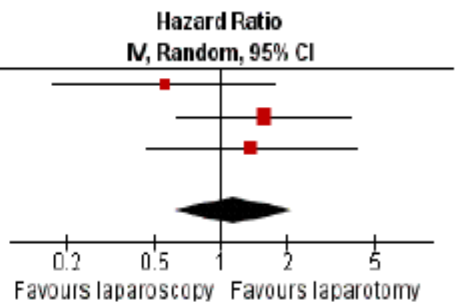


Figure 3. Forest plot of comparison: 1 Primary outcomes, outcome: 1.2 Recurrence-free survival.

Study or Subgroup	log[Hazard Ratio]	SE	Laparoscopy Total	Laparotomy Total	Weight	Hazard Ratio IV, Random, 95% CI
Malzoni 2009	-0.54	0.5	81	78	5.4%	0.58 [0.22, 1.55]
Tozzi 2005	0.56	0.57	63	59	4.2%	1.75 [0.57, 5.35]
Walker 2012	0.13	0.126	1696	920	85.4%	1.14 [0.89, 1.46]
Zullo 2009	0.34	0.52	40	38	5.0%	1.40 [0.51, 3.89]
Total (95% CI)			**1880**	**1095**	**100.0%**	**1.13 [0.90, 1.42]**

Heterogeneity: Tau² = 0.00; Chi² = 2.52, df = 3 (P = 0.47); I² = 0%
Test for overall effect: Z = 1.05 (P = 0.29)

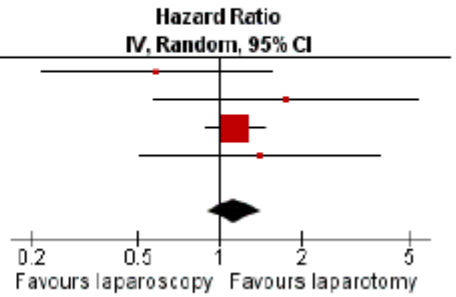
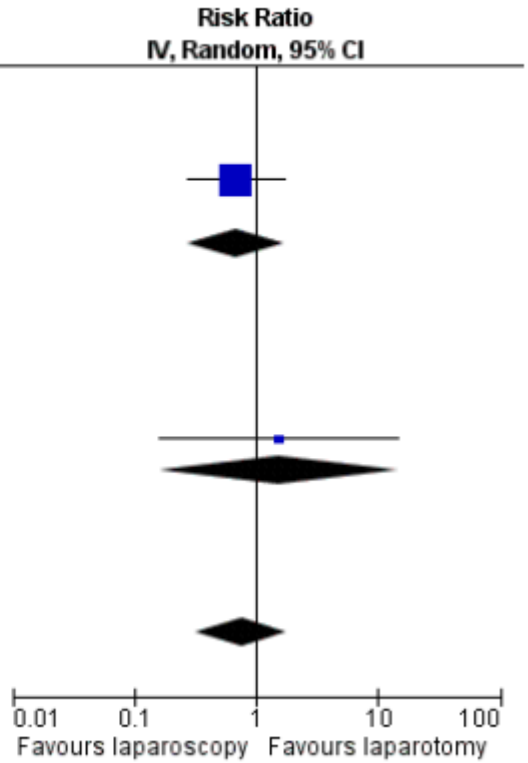


Figure 4. Forest plot of comparison: 2 Secondary outcomes, outcome: 2.1 Peri-operative death.

Study or Subgroup	Laparoscopy Events	Laparoscopy Total	Laparotomy Events	Laparotomy Total	Weight	Risk Ratio IV, Random, 95% CI
2.1.1 Within 30 days						
Malzoni 2009	0	81	0	78		Not estimable
Tozzi 2005	0	63	0	59		Not estimable
Walker 2012	10	1682	8	909	85.5%	0.68 [0.27, 1.71]
Zullo 2009	0	40	0	38		Not estimable
Subtotal (95% CI)		**1866**		**1084**	**85.5%**	**0.68 [0.27, 1.71]**
Total events	10		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.83 (P = 0.41)						
2.1.2 Within 6 weeks						
Mourits 2010	3	187	1	96	14.5%	1.54 [0.16, 14.61]
Subtotal (95% CI)		**187**		**96**	**14.5%**	**1.54 [0.16, 14.61]**
Total events	3		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.71)						
Total (95% CI)		**2053**		**1180**	**100.0%**	**0.76 [0.32, 1.79]**
Total events	13		9			
Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 1 (P = 0.51); I² = 0%						
Test for overall effect: Z = 0.62 (P = 0.53)						
Test for subgroup differences: Chi² = 0.44, df = 1 (P = 0.51), I² = 0%						



Obermair2012, LACE, n=760, RCT, FIGOstageI

kein Unterschied: intraoperativecomplications

lessbloodloss,lessseverepostoperativecomplications, LSK sign.longer

Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for stage I endometrial cancer (LACE): a randomised trial

Monika Janda, Val Gebski, Alison Brand, Russel Hogg, Thomas W Jobling, Russel Land, Tom Manolitsas, Anthony McCartney, Marcelo Nascimento, Deborah Neesham, James L Nicklin, Martin K Oehler, Geoff Otton, Lewis Perrin, Stuart Salfinger, Ian Hammond, Yee Leung, Tom Walsh, Peter Sykes, Hextan Ngan, Andrea Garrett, Michael Laney, Tong Yow Ng, Karfai Tam, Karen Chan, C David H Wrede, Selvan Pather, Bryony Simcock, Rhonda Farrell, Andreas Obermair

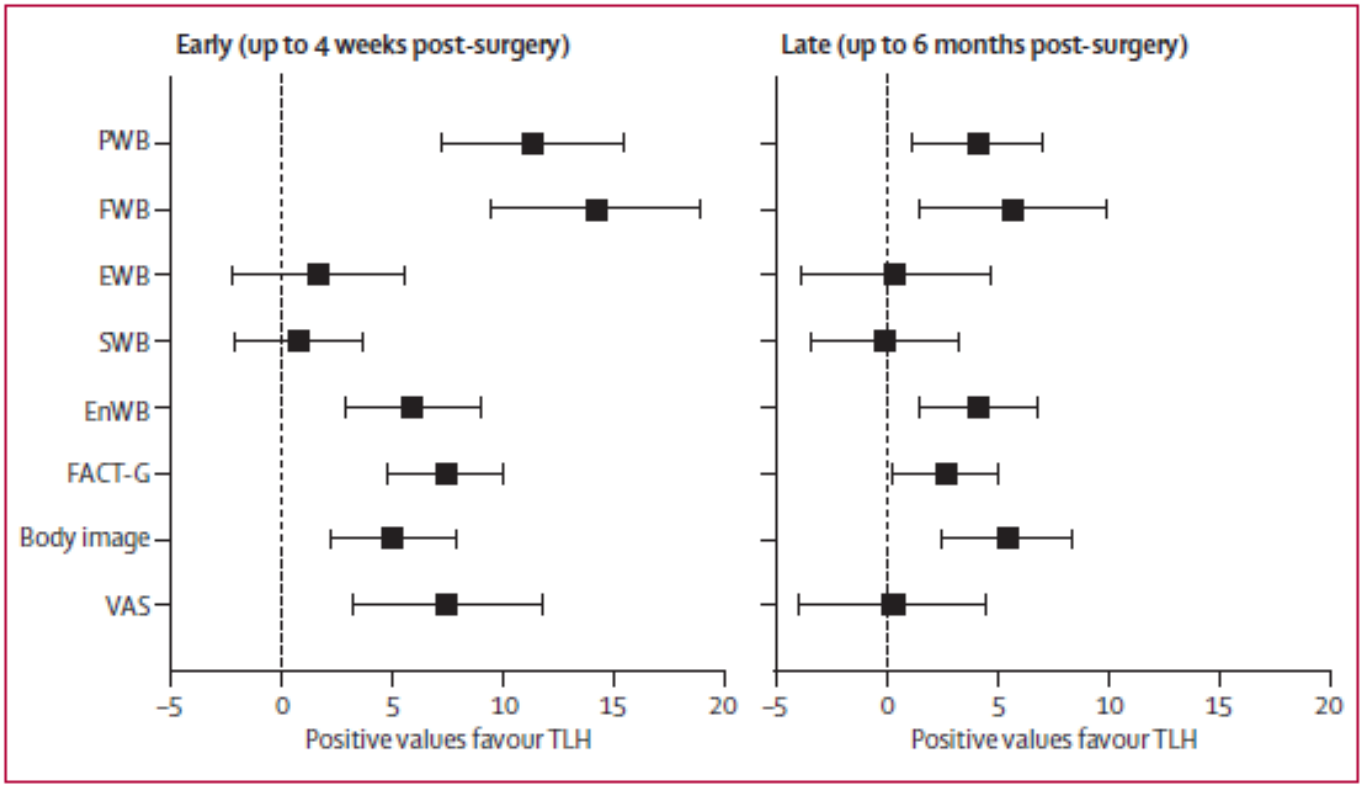


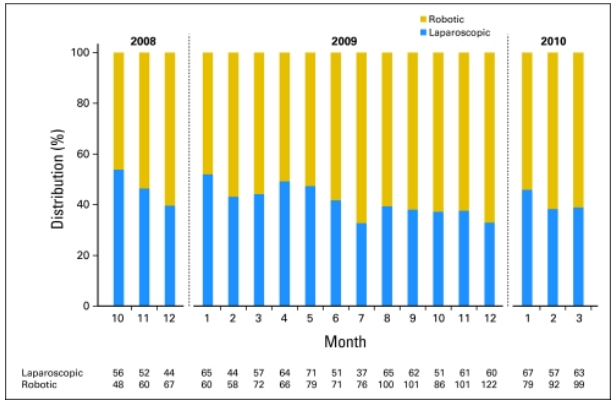
***Figure 3*: Forest plot of mean difference (95% CI) in QoL improvement from baseline between TLH and TAH groups**

QoL=quality of life. TLH=total laparoscopic hysterectomy. TAH=total abdominal hysterectomy. PWB=physical wellbeing. FWB=functional wellbeing. EWB=emotional wellbeing. SWB=social wellbeing. EnWB=endometrial wellbeing. FACT-G=Functional Assessment of Cancer Therapy-General. VAS=single-item visual analogue scale.

Wright 2012; n=2464, LSK (n=1027) vs.Robotic(n=1437); USA,nation-wide,retrospective

kein Unterschied: intraoperativecomplications(9,8 vs. 8,1%), Gesamtmorbidität,prolongedhospitalization

sign. höhere Kosten, sign. längere OP-Dauer



BeiTyp II-Karzinomen (Stadium≥pT1B, G3, serös-pap.,klarzellig)sollte die**pelvineundparaaortaleLymphonodektomie**bis zum Nierenstiel durchgeführt werden.

Depth of Inv.	G1 (n=180)	G2 (n=288)	G3 (n=153)
Endometrium	0 (0%)	1 (3%)	0 (0%)
Inner Third	1 (1%)	5 (4%)	2 (4%)
Middle Third	1 (5%)	0 (0%)	0 (0%)
Outer Third	1 (6%)	8 (14%)	15 (23%)

Creasmanet al. 1987

SEPAL Study;Todo2010; retrospektive Kohorte; n=671, alle Stadien,pelLNDoderpelLND+paraLND

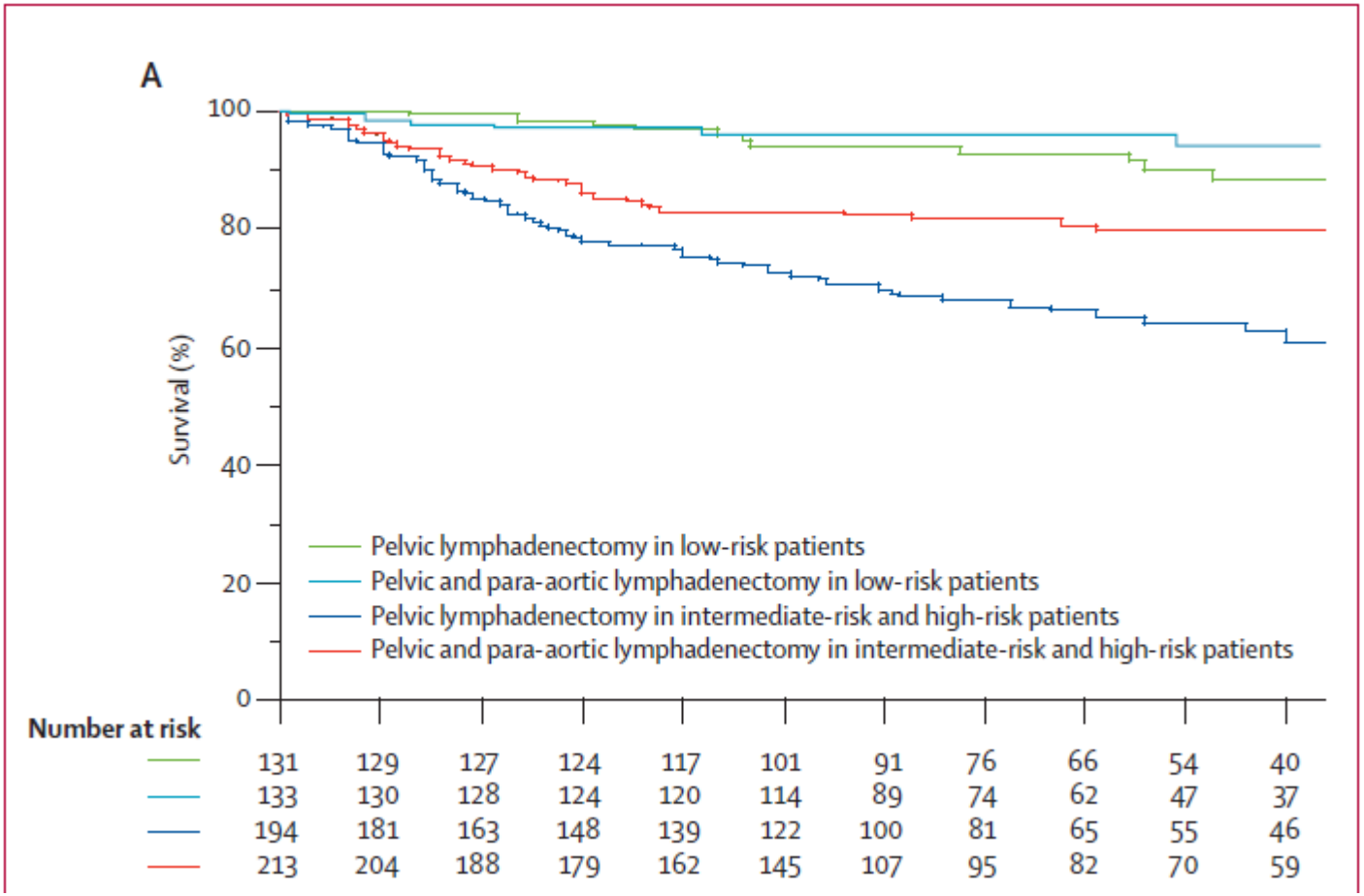
Ergebnis: 8Y-DSF besser high-risk(84 vs. 69%), nichtlow-risk(94 vs. 93%)

max.Benefit: G3

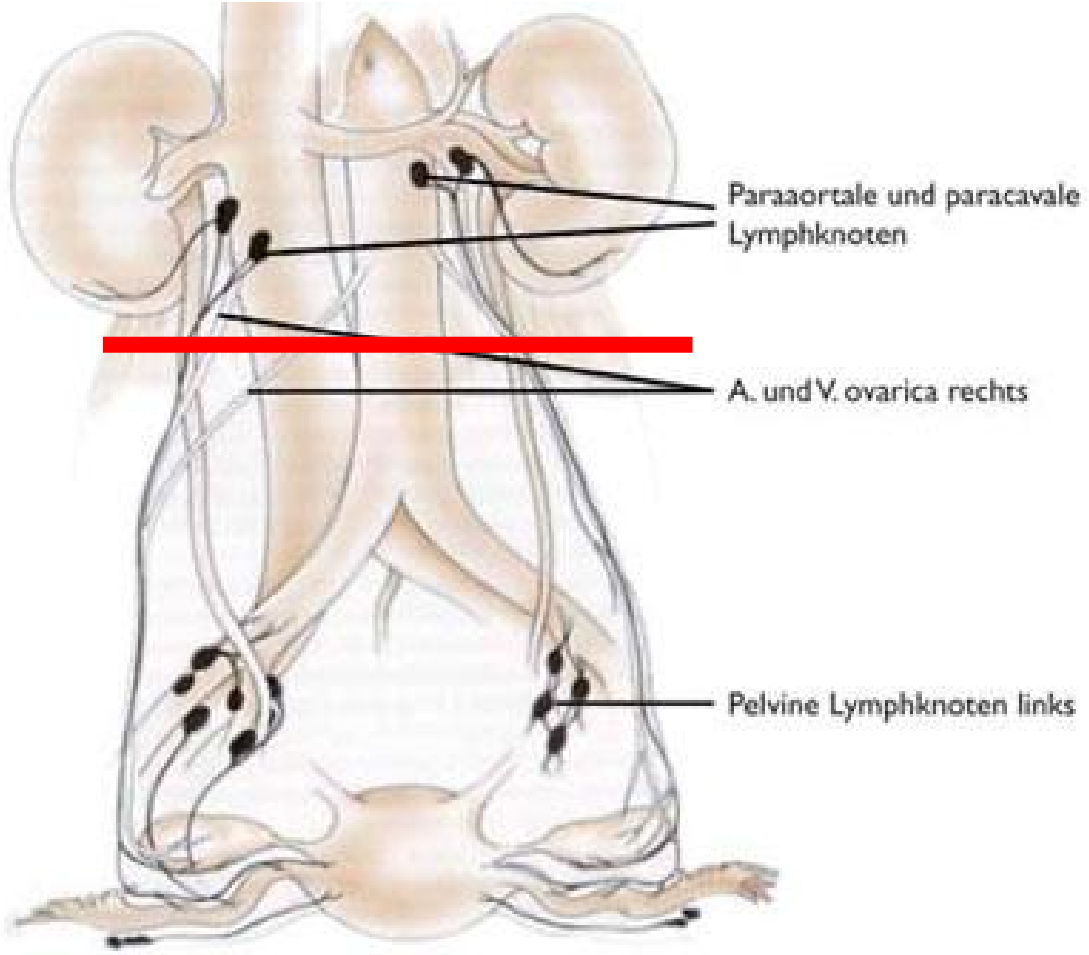
AGO-OK UTERUS:**ECLAT-Studie ab 2014**

Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis

Yukiharu Todo, Hidenori Kato, Masanori Kaneuchi, Hidemichi Watari, Mahito Takeda, Noriaki Sakuragi



LAP stageI-IIA



O er, 8%

Bei Typ II-Karzinomen [Stadium ≥ pT1b, G3, serös-pap.,klarzellig] sollte diepelvineundparaaortaleLymphonodektomiebis zum Nierenstiel durchgeführt werden.

Empfehlung AGO: Laparotomie

BeiTyp II-Karzinomen (Stadium≥pT1B, G3, serös-pap.,klarzellig)sollteeine**adjuvanteChemotherapie**durchgeführtwerden.

Die meisten Daten liegen für platin-haltige Schemata vor, z.B.Carboplatin/Paclitaxel.

Kein Screening

Invasive Abklärung PMB, nichtsonogr. EM-Auffälligkeiten

Keine fraktionierteAbrasio

Keine radikale HE im Stadium FIGO II

Typ I: HE (TLH) ohneLnn

Keine EmpfehlungRobotics

Typ II:Abd. HE +pelv. +paraaort.Lnn(LAP), CHXT

Japan; Multicenter;Nagao2013; retrospektive Analyse; n=262, Z. n. platin-CHXT; Rezidiv

Frage: Response platinsensibel?

Response: 25, 38, 61, 65%

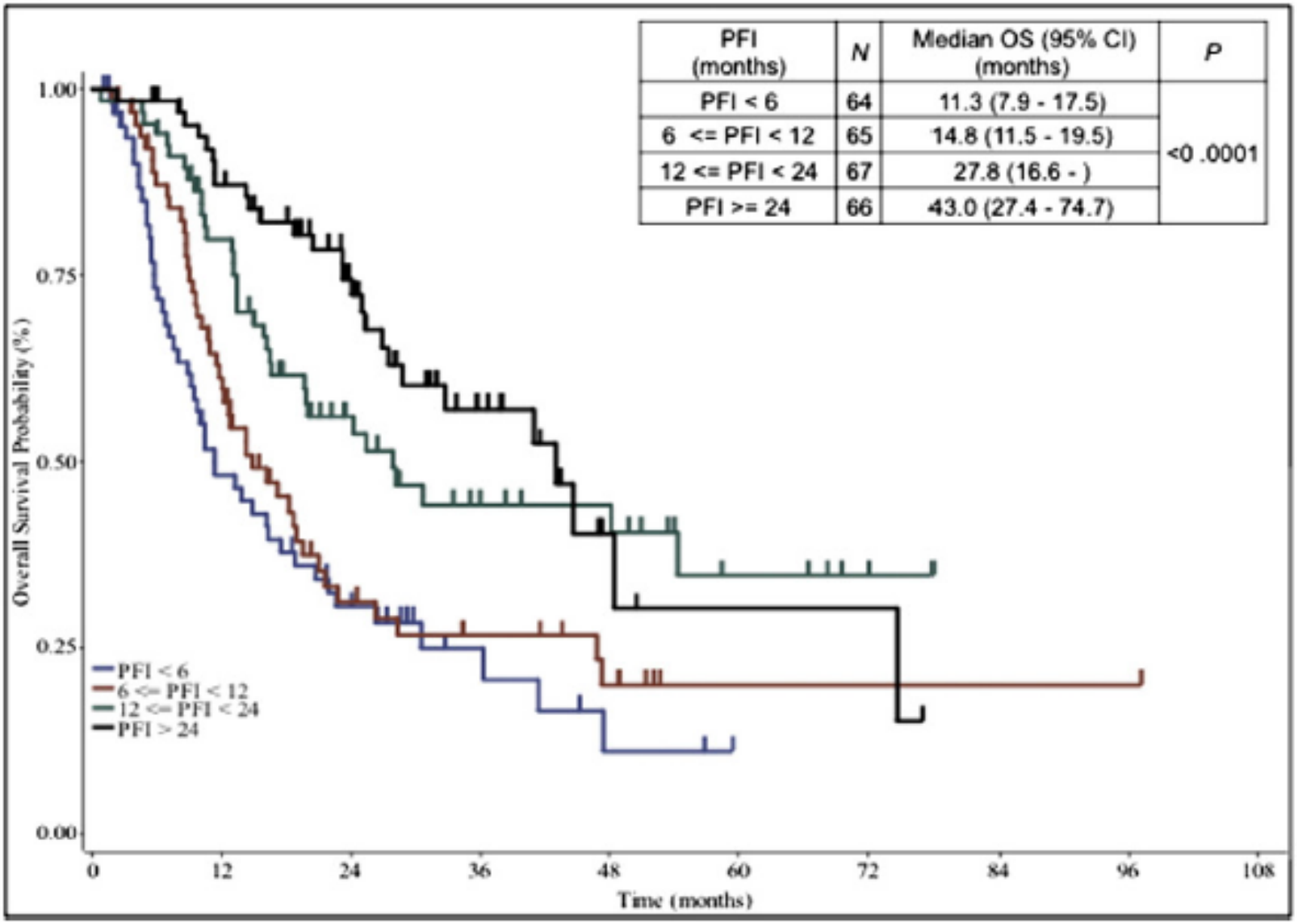
Intervall: <6, <12, <24, >24mos

Fazit:**Konzept ‚platinsensitivity‘**

LL 2013 - Neues

B

PFI (months)	N	Median OS (95% CI) (months)	P
PFI < 6	64	11.3 (7.9 - 17.5)	<0 .0001
6 <= PFI < 12	65	14.8 (11.5 - 19.5)	
12 <= PFI < 24	67	27.8 (16.6 -)	
PFI >= 24	66	43.0 (27.4 - 74.7)	



S3 - Leitlinie 2015!

Vielen Dank für Ihre Aufmerksamkeit!