

Ekstremit -dış  Sarkomlar

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- **Retroperitoneal sarkomlar**

- Liposarkom

- **Torasik sarkomlar**

- Pulmoner blastom

- Hemanjioendotelioma

- **Uterin sarkomlar**

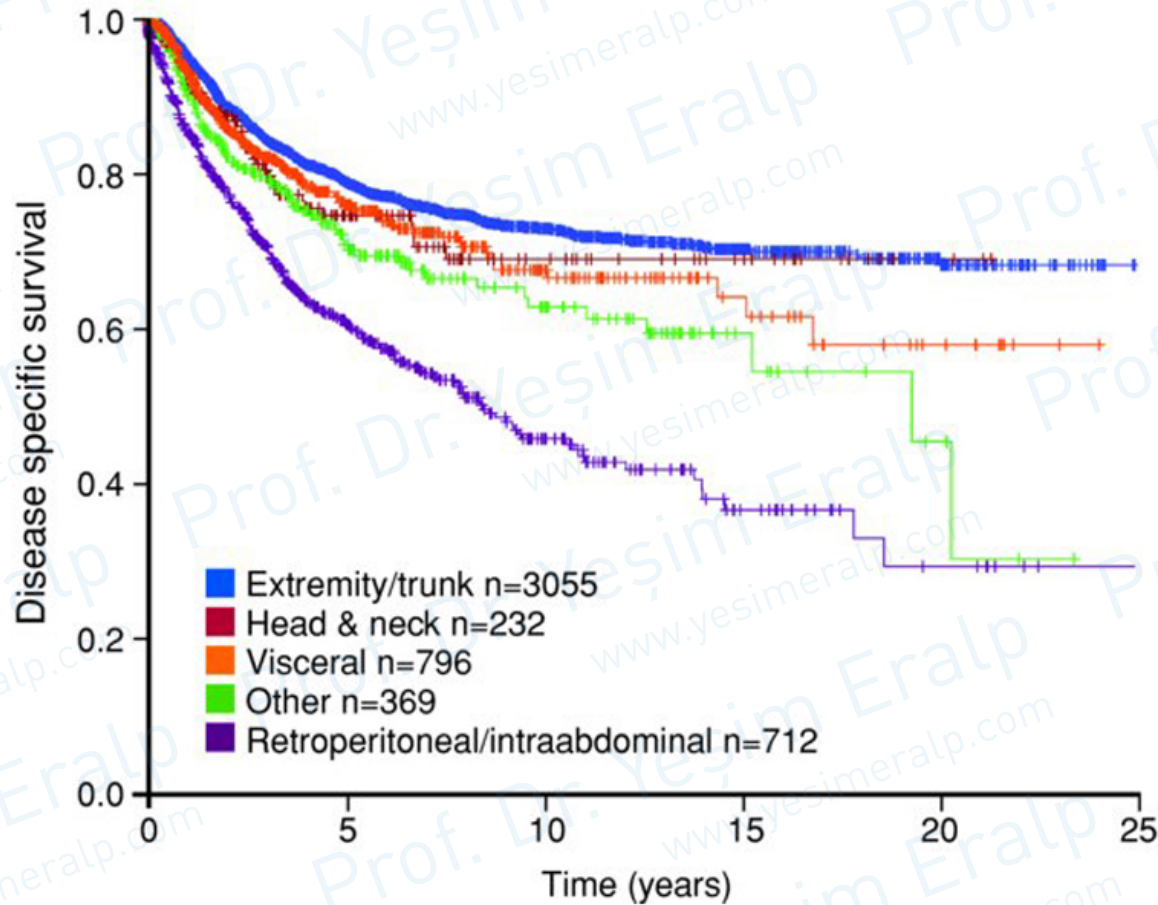
- ESS

- LMS/İndifferansiye sarkom

Tümör Yerleşimi

- %40 Ekstremit (%30 alt)
- %36 intra-abd
- %10 Gövde-yüzeyel
- % 5 Baş-boyun

- prognoz ve yönetimde önemli



Source: DeVita VT, Lawrence TS, Rosenberg SA: *DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology*, 9th Edition: www.lwwoncology.com

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Lokalize Extremitte/Gövde YDS' de Adjuvan Tedavi

- Cerrahi ve RT asıl etkili tedavilerdir
- 15 adjuvan çalışma var, çoğu küçük ve istatistik gücü zayıf çalışmalar, randomize çalışmalar da eski çalışmalar

Goffman T. *Cancer* 1991;67:572.

Sarcoma Meta-analysis Collaboration. *Lancet* 1997;350:1647.

Alvegard TA. *J Clin Oncol* 1989;7:1504.

Bramwell V. *J Clin Oncol* 1994;12:1137.

Frustaci S. *J Clin Oncol* 2001;19:1238.

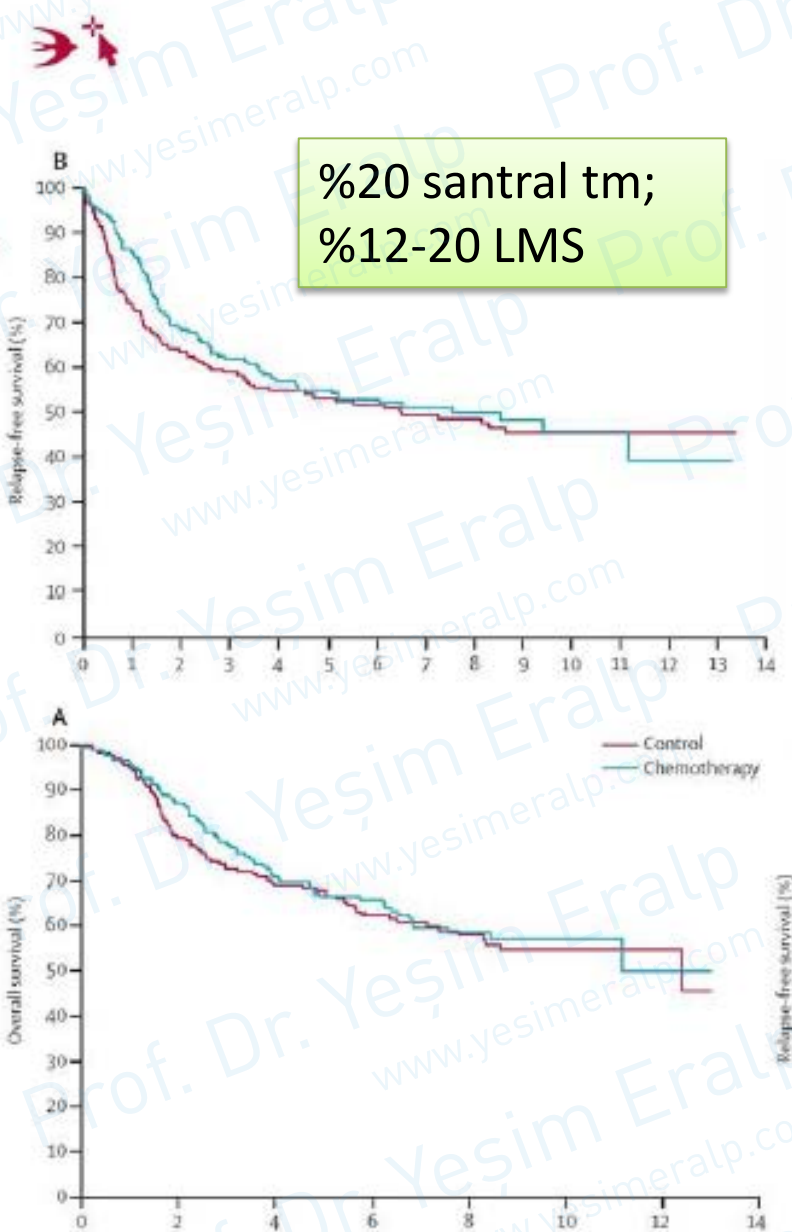
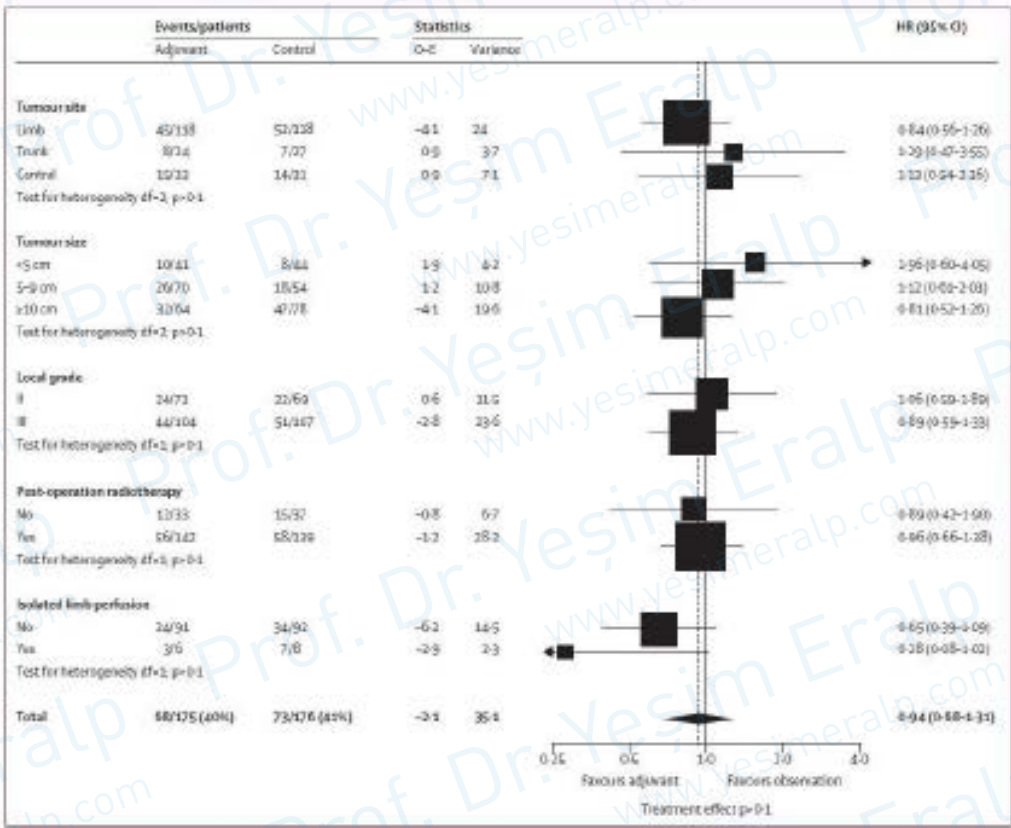
Petrioli R. *Am J Clin Oncol* 2002;25:468.

Gortzak E, Azzarelli A, Buesa J, et al. *Eur J Cancer* 2001;37:1096.

- İskandinav Ç:
 - Adjuvan (60 mg/m² doxo)Tedavi vs Tedavi yok⇒yararı yok
- İtalyan Ç:
 - Adjuvan (epi+ ifos)Tedavi vs tedavi yok⇒yararı yok
- EORTC+NCIC
 - Neoadjuvan (Doxo+ifos)Tedavi vs tedavi yok⇒yararı yok
- Avusturya Ç:
 - Adjuvan (doxo+ifos+DTIC)Tedavi vs tedavi yok⇒yararı yok
- EORTC:
 - Adjuvan (Doxo+ifos)Tedavi vs tedavi yok⇒yararı yok

Adjuvant chemotherapy with doxorubicin, ifosfamide, and lenograstim for resected soft-tissue sarcoma (EORTC 62931): a multicentre randomised controlled trial

Penella J Woll, Peter Reichardt, Axel Le Cesne, Sylvie Bonvalot, Alberto Azzarelli, Harald J Hoekstra, Michael Leahy, Frits Van Coevorden, Jaap Verweij, Poncras CW Hogendoorn, Monica Ouali, Sandrine Mairaud, Vivien H C Bramwell, Peter Hohenberger, for the EORTC Soft Tissue and Bone Sarcoma Group and the NCIC Clinical Trials Group Sarcoma Disease Site Committee



6.3.1. Adjuvant Chemotherapy. The role of adjuvant chemotherapy remains unproven. Although currently not regarded as standard treatment in the UK, there is conflicting evidence, and it may be considered for individual patients with potentially chemosensitive subtypes on the basis that benefit cannot be excluded, even though it has not been proven (Table 4). It may be also considered in situations where local relapse would be untreatable or where adequate radiotherapy could not be administered owing to the sensitivity of adjacent structures, for example, spinal cord. A

Primary, high-grade, superficial	Surgery: wide excision		
Primary, high-grade, deep, ≤5 cm	Surgery: wide excision	Surgery: wide excision + adjuvant radiation therapy OR compartmental resection	
Primary, high-grade, deep, >5 cm	Surgery: wide excision + adjuvant radiation therapy (pre and/OR post)	Surgery: wide excision + adjuvant radiation therapy (pre and/OR post) + Discussion of adjuvant Chemotherapy	Neoadjuvant chemotherapy ± postoperative chemotherapy followed by Wide surgical excision + adjuvant postoperative (or preoperative) radiation therapy
	Compartmental resection	Compartmental resection + Discussion of adjuvant Chemotherapy	

Chemotherapy integral to management

Chemosensitive

- (i) Ewing's sarcoma family tumours
 - (ii) Embryonal and alveolar rhabdomyosarcoma
-

- (i) Synovial sarcoma
 - (ii) Myxoid/round cell liposarcoma
 - (iii) Uterine leiomyosarcoma
-

Moderately chemosensitive

- (i) Pleomorphic liposarcoma
- (ii) Myxofibrosarcoma
- (iii) Epithelioid sarcoma
- (iv) Pleomorphic rhabdomyosarcoma
- (v) Leiomyosarcoma
- (vi) Malignant peripheral nerve sheath tumour
- (vii) Angiosarcoma
- (viii) Desmoplastic small round cell tumour
- (ix) Scalp and face angiosarcoma

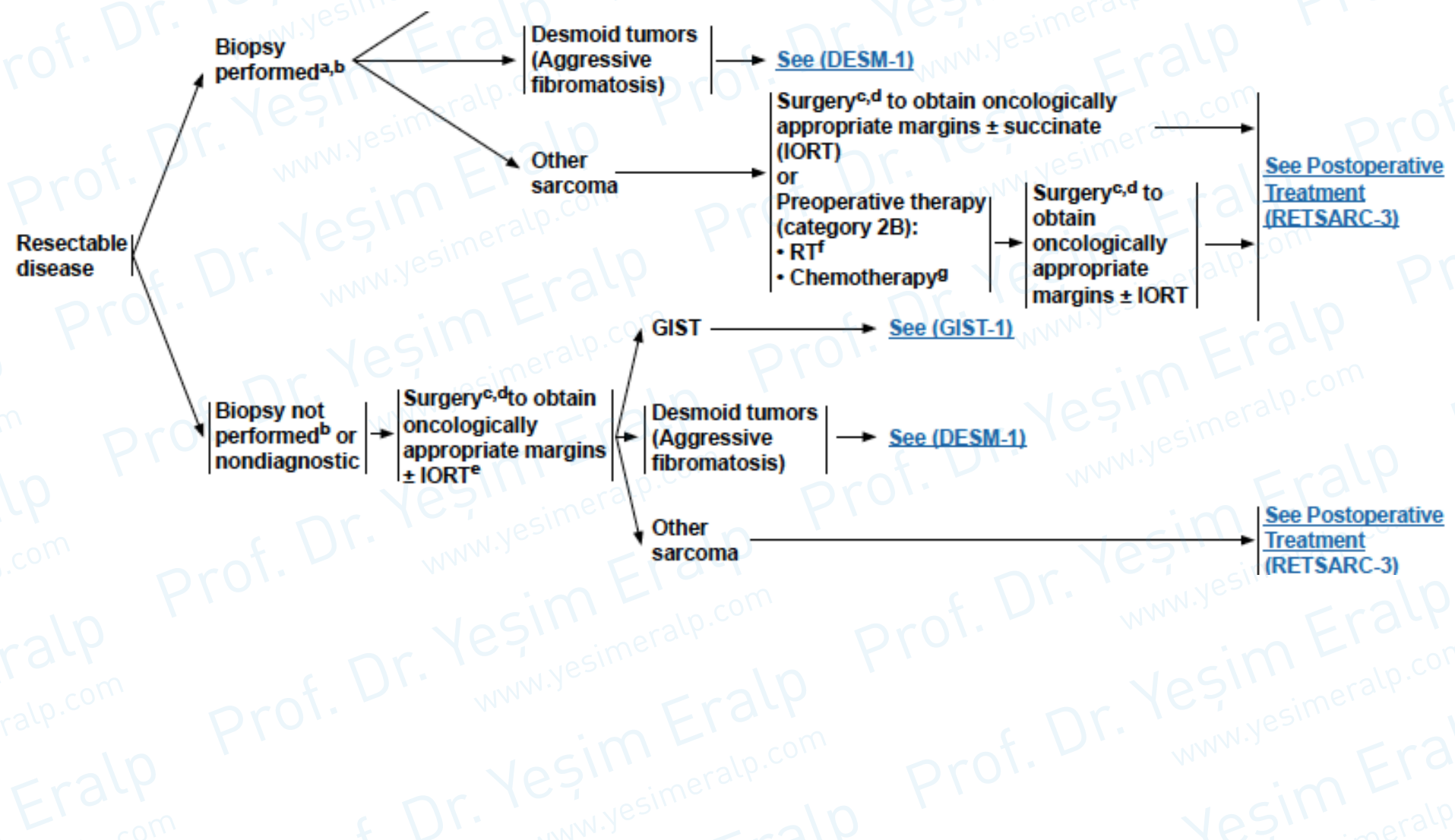
RETROPERITONEAL SARKOMLAR

Liposarcoma Histologic Subtype	Genetic and/or Molecular Aberration	Histologic Features	Anatomic Site	Clinical Behavior	Response to Current Therapy
Well differentiated (WD)	12q13-15 amplification (MDM2, CDK4, <i>etc.</i>)	Adipocytes of varying size, prominent fibrous stroma	Retroperitoneum >extremities, paratesticular areas, trunk	Locoregional recurrence	Poor
Dedifferentiated (DD)	same as WD	Highly-cellular portion (5 or more mitoses/10 HPF) next to WD portion	same as WD	Locoregional recurrence and distant metastasis (10–15%)	Low
Myxoid/Round Cell (MRC)	Translocation (t12;16)(q13;p11) or (t12;22)(q13;q12) leading to FUS-CHOP/DDIT3 or EWS-CHOP/DDITS fusion protein	Abundant extracellular myxoid material; sparse cellular portion w/mature adipocytes, immature lipoblasts, round cells (>5% of tumor)	Proximal lower extremities	Distant metastasis (10–20%) to visceral organ sites, bone, and fat bearing areas	High
Pleomorphic	Complex	Highly cellular resembling MFH; pleomorphic lipoblasts; occassional multinucleated cells	Lower extremities >retroperitoneum; mediastinum	Distant metastasis (30–50%)	Low



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SURGICAL OUTCOMES/CLINICAL PATHOLOGIC FINDINGS^c

POSTOPERATIVE TREATMENT

FOLLOW-UP

TREATMENT FOR RECURRENT DISEASE

R0

Post-op RT should not be administered routinely with the exception of highly selected patients and unless local recurrence would cause undue morbidity.^{f,h}

R1

Post-op RT should not be administered routinely with the exception of highly selected patients and unless local recurrence would cause undue morbidity.^{f,h}
or
Post-op external beam
or
Consider boost (10–16 Gy) if preoperative RT was given

R2

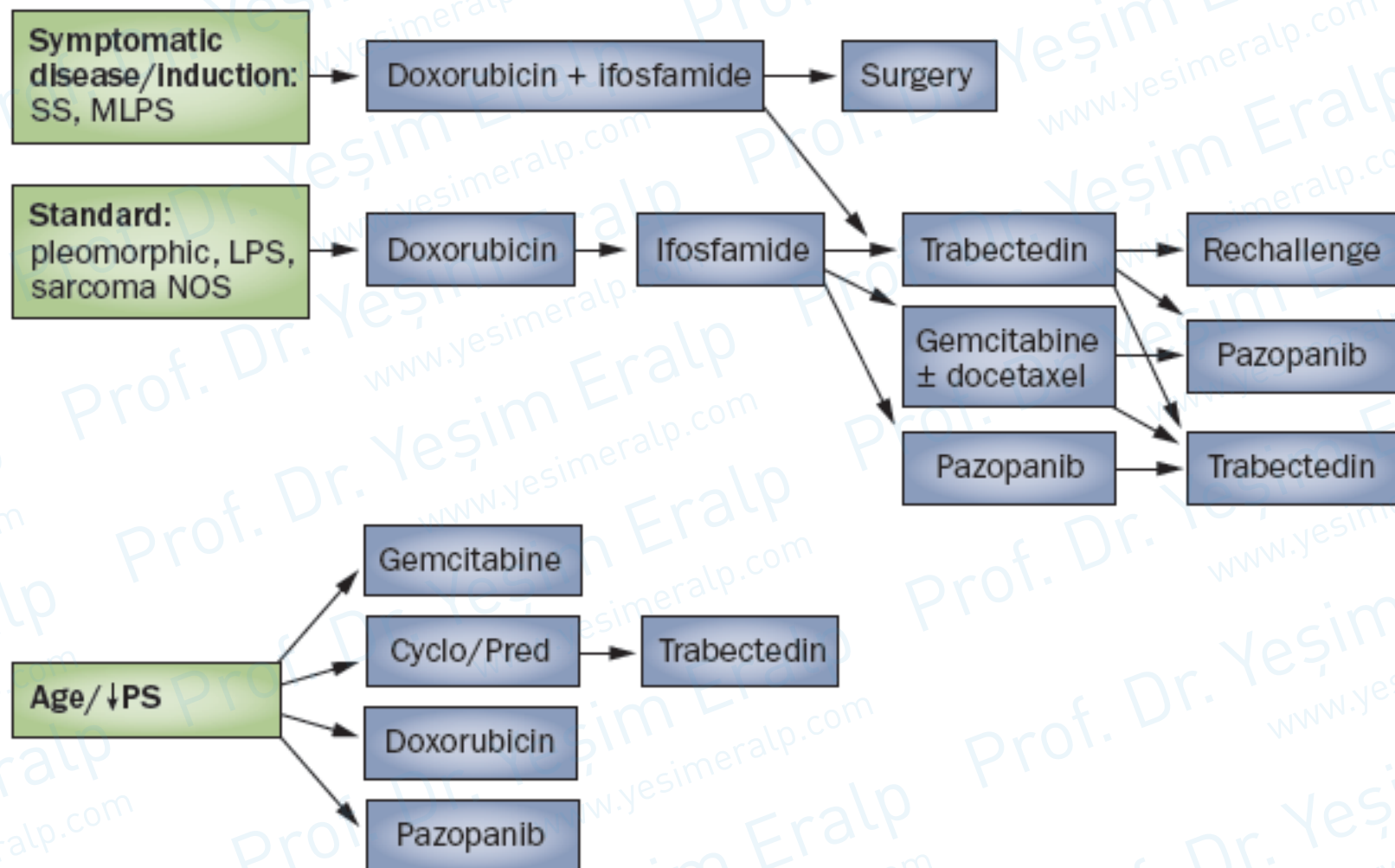
Consider re-resection if technically feasible
or
[See Primary Treatment \(Unresectable\) \(RETSARC-4\)](#)

- Physical exam with imaging (abdominal/pelvic CT) every 3–6 mo for 2–3 y, then every 6 mo for next 2 y, then annually
- Consider chest imaging

Recurrent disease

Unresectable or Stage IV/Metastatic diseaseⁱ
([See RETSARC-4](#))

Resectableⁱ
([See RETSARC-2](#))



cyclophosphamide; LPS, liposarcoma; MLS, myxoid liposarcoma; NOS, not otherwise specified; Pred, prednisolone; PS, performance status; SS, synovial sarcoma.

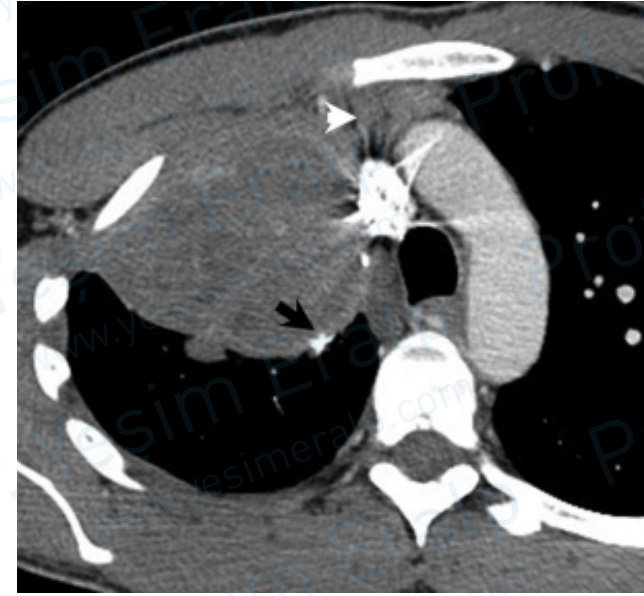
Novel Therapy	Mechanism of Action	Liposarcoma Histologic Subtype	Study Type/Clinical Trial Phase	References^ (n = liposarcoma pts)
Trabectedin	Binding of DNA minor groove; direct interaction w/FUS-CHOP	MRC	Phase II, Retrospective, and Neoadjuvant	Garcia-Cabonero, 2004 (10); Yovine, 2004 (6); Le Cesne, 2005 (10); Grosso, 2007 (51 *); Grosso, 2009 (32 *); Demetri, 2009 (93); Gronchi, 2012 (23 *), Samuels, 2013 (233)
Eribulin	Microtubule inhibitor	DD	Phase II	Schoffski, 2011 (37)
RG7112	MDM2 antagonist	WD/DD	Phase I (Neoadjuvant)	Ray-Coquard, 2012 (20 *)
Flavopiridol	pan-CDK inhibitor, including CDK4	WD/DD	Phase I	Luke, 2012 (16)
PD 0332991	CDK4/6 inhibitor	WD/DD	Phase I	Schwartz, 2012 (7)
Troglitazone, Rosiglitazone, Efatutazone	PPAR-gamma agonist	all	Phase I, II	Debrock, 2003 (12 *); Pishvaian, 2012 (5)
Nelfinavir	SREBP-1 inhibitor	WD/DD	Phase I	Pan, 2012 (20 *)
Pazopanib, Sorafenib, Sunitinib	Tyrosine kinase receptor inhibitor	all	Phase II	Sleijfer, 2009 (19); von Mehren, 2012 (10); Tariq Mahmood, 2011 (17)

INTRA-TORASİK SARKOMLAR

- Pulmoner blastom*
- Sarkomatoid mezotelioma
- Anjiosarkom, hemanjioendothelioma*
- Karsinosarkom (sarkomatoid karsinom, pleomorfik karsinom vb)
- Sinovial sarkom
- Liposarkom
- LMS
- Kondrosarkom, Osteosarkom
- MPNST
- Ewing/p-NET, RMS

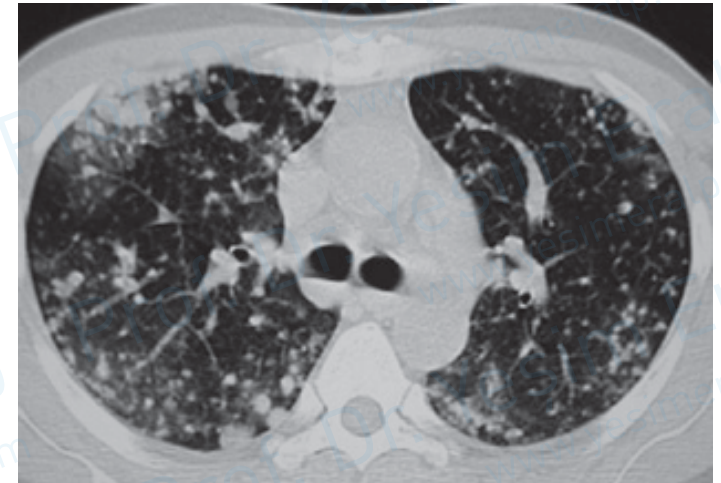
• Pulmoner blastom*

- Erişkinde çok nadir
- Kötü prognozlu; >5 yıl nüksler mümkün
- Lokal nüks; kemik ve beyin met açısından uzun takip
- Tedavi :
 - Operable hastalık: Cerrahi +/- KT +/- RT
 - İn-op hastalık : Neo KT +/- RT—Cerrahi
 - Platin + Etoposid ---VAI



• Hemanjioendothelioma*

- AC de soliter / multipl nodüller
- Kötü prognoz
 - Plevral, ekstensif bronşial tutulum
 - Lenfatik tutulum, organ metastazi
- Kanıtlanmış tedavi yok
- Anti-VEGF ted
 - Carbo+Pac + Bev
 - Sorafenib



Uterin Sarkomlar

Dr. Yeşim ERALP
İÜ Onkoloji Enstitüsü

- LMS %67
- Endometrial stromal sarkom (ESS) %17-25
- Yüksek gradlı (indifferansiye) endometrial sarkom (Yüksek gradlı ESS) %8-17
- Adenosarkom %8
- Karsinosarkom (MMMT)

Uterin Adenosarkom

- Selim epitelyal komponent
- Düşük gradlı & homolog sarkomatöz komponent
- Çoğu post-menapozal
 - Anormal vaginal kanama
 - Karın ağrısı
- Yavaş seyirli
- Nüks oranı: %25-30
- Standart tedavi: TAH±BSO
- Adjuvan tedavi ??



Sarkomatöz “over-growth”

- >%25 sarkom (yüksek grad)
 - Selim glandüler komponent yok
- ### Myometrial invazyon

Myometrial invazyon

- Selim glandüler komponent yok

Uterin Adenosarkom

Variable	No. of patients (%)
Stage	
* I	59 (80)
II	10 (14)
III	3 (4)
IV	2 (3)
Tumor size, median (range)	6.0 cm (0.1–11 cm)
Depth of invasion	
None	19 (26)
* ≤ 50%	24 (32)
> 50%	1 (1)
Unknown	30 (41)
Lymphovascular space invasion	
Present	7 (9)
* Absent	67 (91)
Sarcomatous overgrowth	
Present	31 (42)
* Absent	43 (58)
Heterologous elements	
Present	15 (20)
* Absent	59 (80)
Primary treatment	
Chemotherapy + radiation	1 (1)
* Surgery alone	47 (64)
Surgery + radiation	14 (19)
Surgery + chemotherapy	5 (7)
Surgery + chemotherapy + radiation	3 (4)
Surgery + hormones	4 (5)

Çok-değişkenli Analiz

PFS:	HR
• Sarkmtöz Gr	2.58
• LVI	3.78
• İleri Yaş	1.02
• İleri evre	3-24

DSS:	
• Sarkmtöz Gr	6.75
• LVI	4.25
• Evre III	16.97

OS:	
• Sarkmtöz Gr	2.45
• LVI	3.50

Uterin Adenosarkom

Patient subset	n	Median survival time, mo	p value	Hazard ratio	95% CI
PFS					
Stage I with SO					
Surgery alone	15	29.4	–	Ref	–
Surgery + adjuvant	7	46.7	0.28	0.58	0.22–1.56
All stage I					
Surgery alone	45	67.2	–	Ref	–
Surgery + adjuvant	14	89.2	0.63	0.82	0.37–1.82
DSS					
Stage I with SO					
Surgery alone	15	61.3	–	Ref	–
Surgery + adjuvant	7	97.3	0.46	0.67	0.23–1.96
All stage I					
Surgery alone	45	NR	–	Ref	–
Surgery + adjuvant	14	NR	0.82	1.12	0.42–3.01
OS					
Stage I with SO					
Surgery alone	15	55.4	–	Ref	–
Surgery + adjuvant	7	97.3	0.18	0.45	0.14–1.44
All stage I					
Surgery alone	45	81.6	–	Ref	–
Surgery + adjuvant	14	112.4	0.27	0.61	0.25–1.48

- Yüksek riskli hastalarda adj KT önerilebilir...
 - SO
 - İleri evre.

LMS & ESS: Evreleme

TNM Categories	FIGO Stages	Definition
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the uterus
T1a	IA	Tumor 5 cm or less in greatest dimension
T1b	IB	Tumor more than 5 cm
T2	II	Tumor extends beyond the uterus, within the pelvis
T2a	IIA	Tumor involves adnexa
T2b	IIB	Tumor involves other pelvic issues
T3	III**	Tumor infiltrates abdominal tissues (not just protruding into the abdomen)
T3a	IIIA	One site
T3b	IIIB	More than one site
T4	IVA	Tumor invades bladder or rectum
N1	IIIC	Regional lymph node metastasis
M1	IVB	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

LMS & ESS: Genomik Profil

	Uterine leiomyosarcoma	ESS
PDGFR- α	60–70% (38) ^{32,33}	87% (8) ³²
* PDGFR- β	7–100% (19) ^{33,34}	0–100% (16) ^{32,34}
* KIT	0–100% (150) ^{9-16*, 32, 34, 35, 52}	0–100% (53) ^{10-13*, 15*, 16*, 23*, 32, 36}
EGFR	4% (25) ³³	..
* Oestrogen receptor	18–87% (105) ^{9*, 17-19*, 31}	40–100% (34) ^{19*, 22*, 32, 38}
* Progesterone receptor	18–80% (104) ^{9*, 17-19*, 31}	60–100% (33) ^{19*, 22*, 32, 38}
Aromatase	59% (22) ^{19*}	0–83% (28) ^{19*, 23*}
GnRH receptor	100% (2) ^{30*}	76% (29) ^{24*}
Androgen receptor	40% (25) ³²	36% (14) ³⁸
WT1	76% (38) ³²	47–93% (39) ^{25*, 26*, 51}
ERBB2	0% (10) ³⁹	0% (21) ³⁹

Endometrial Stromal Sarkom

- Düşük gradlı
- %70-90 hormon duyarlı
- Yavaş seyirli
- Lenf nodu tutulumu: %10-45
- 10-20 yıla kadar nüks görülebilir
- Standart tedavi: TAH
 - ±BSO
 - Lenfadenektomi ?
- Adjuvan tedavi ??



Evre I hastalık;

5 yıl OS: %98; 10 yıl OS: %89

Evre III & IV:

5 yıl OS: %66

Endometrial Stromal Sarkom: Prognostik Faktörler

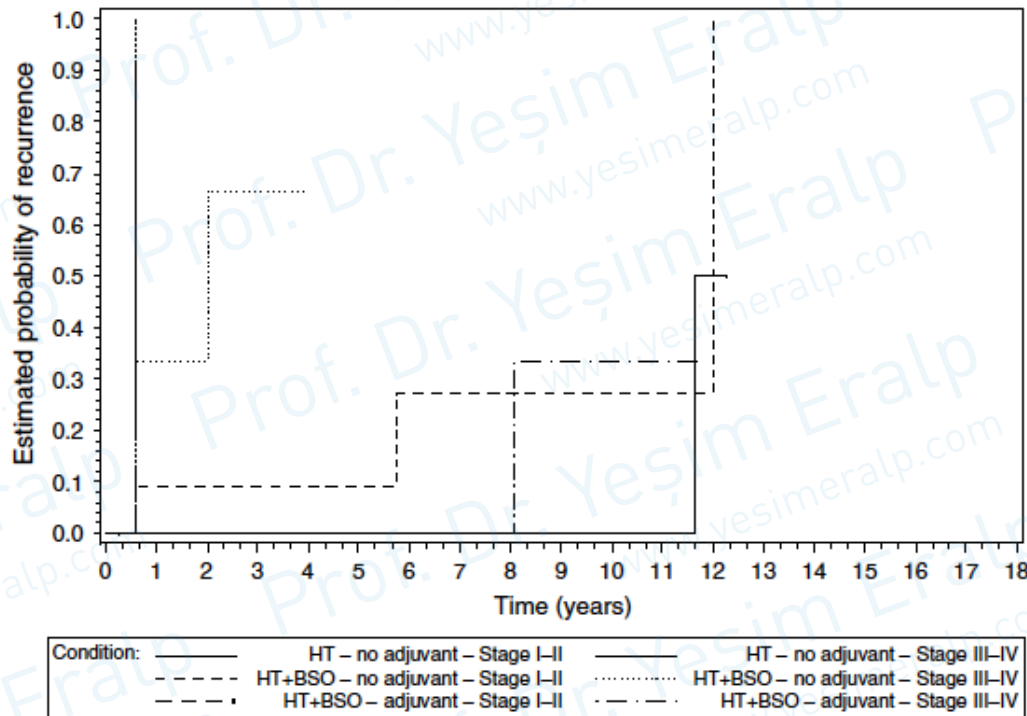
- Yaş (>50)
- Menapoz durumu
- Tm çapı (>5 cm)
- Grad
- Hücresel atipi
- Mitoz
- Rezeksiyon sınırı (R1 rez)
- Lenf nodu tutulumu



Çok Değişkenli Analiz:

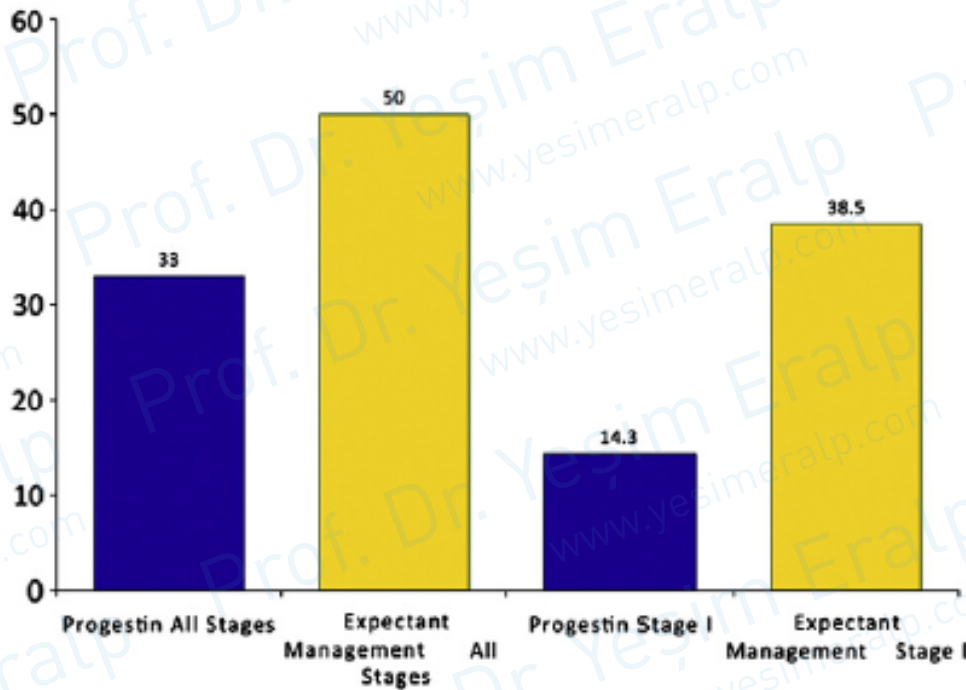
- R0 Rezeksiyon
- Grad
- Tm çapı
- Menapoz durumu

Endometrial Stromal Sarkom: Adjuvan Tedavi



- N:34; 22 hasta evre I
- Evre I:
 - %90: tedavisiz takip
 - %10: adj progestin
- Nüks oranı (evre I-II)
 - Takip: % 20
 - Progestin: % 0
- Nüks oranı (evre III-IV)
 - Takip: % 75
 - Progestin: % 20
- Nüks paterni:
 - Pelvik: %38
 - AC: %25

Endometrial Stromal Sarkom: Adjuvan Tedavi



- N:42; 28 hasta evre I
- Evre I:
 - %65: tedavisiz takip
 - %35: sürekli progestin
- Nüks oranı (evre I)
 - Takip: % 38.5
 - Progestin: % 14.3
- Nüks oranı (evre II-IV)
 - Takip: % 50
 - Progestin: % 33
- Nüks paterni:
 - Pelvik: %44
 - AC: %25

Endometrial Stromal Sarkom: Adjuvan Tedavi

- Evre I & II hastalık  TAH+BSO
 - Yaş <50; küçük tm: ooferektomi gerekmez
 - Lenfadenektominin sağkalımı değiştirdiği gösterilemedi; şüpheli görülen LN varsa yapılabilir
- Evre III & IV hastalık:
 - TAH+BSO + lenfadenektomi
 - Adjuvan Hormon tedavisi
 - Megesterol asetat
 - LHRH analogu
 - Aromataz inhibitörü

TMX & Östrojenik ajan



KONTRENDİKE

KONTRENDİKE

İndifferansiye Sarkom (Yüksek Gradlı ESS)

- Yüksek mitoz oranı, endometrial stromal farklılaşma az veya yok
- Kompleks kromozomal karyotip
- LMS benzeri agresif seyir
 - Nükslerin çoğu ilk 6 ay içinde
 - Ölümlerin çoğu ilk 2 yıl içinde
- Standart tedavi:
 - Evre I & II: TAH+BSO
 - Evre III & IV: TAH+BSO + maksimal sitoredüksiyon
- Adjuvan tedavi: LMS ile paralel



5 yıllık sağkalım:

Evre 1 hastalık % 55

- LVI +: %85

- LVI -: %17

Evre II-IV: %0-25

Evre II-IV: %0-25

- LVI -: %17

- LVI +: %85

Uterin Leiomyosarkom

- Yüksek mitoz oranı, yaygın nükleer atipi
- Vasküler myometriuma lokalize; yüksek sistemik met oranı
- 47-56 yaş arası
- Kanama (%56), kitle (%55), pelvik ağrı (%22)
- Myomlu hastalarda LMS insidansı: %0.13-%0.7
- Standart tedavi:
 - Evre I & II: TAH+BSO
 - Evre III-IVA : TAH+BSO + lenfadenektomi +maksimal sitoredüksiyon



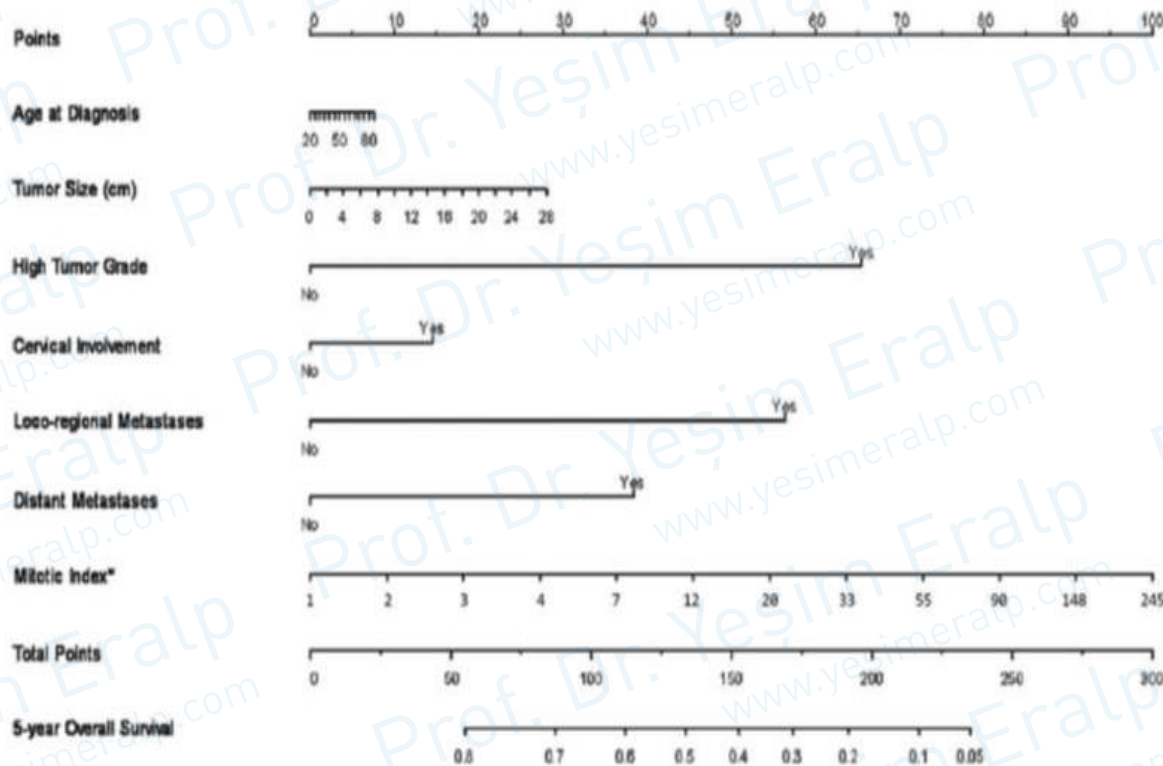
Nüks oranı: %45-80

AC, Karın boşluğu, KC

Nüks sonrası sağkalım: 2 yıl

Nüks sonrası sağkalım: 5 yıl

A Nomogram to Predict Postresection 5-Year Overall Survival for Patients With Uterine Leiomyosarcoma



- 45 yaş: 3 p
- 10 cm tm: 10 p
- Yüksek grad: 65 p
- Mitotik index 3: 18 p
- Yayılım yok: 0 p

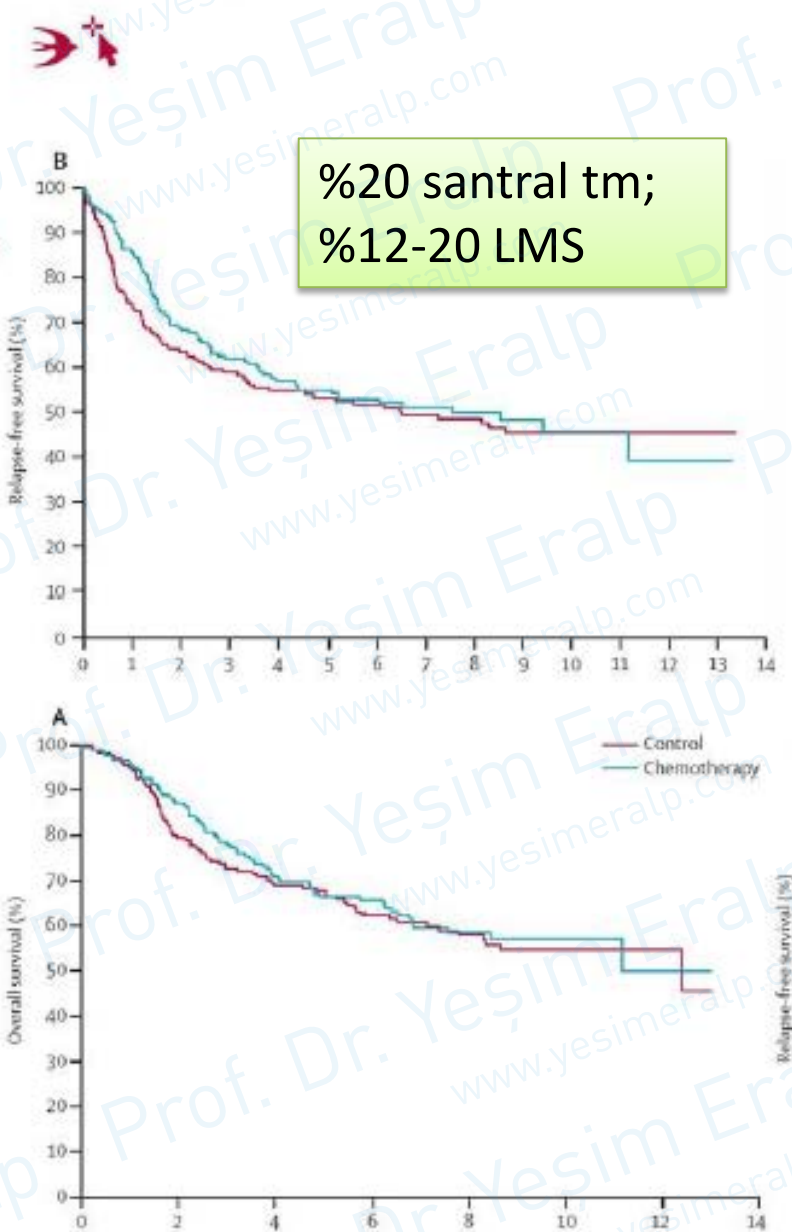
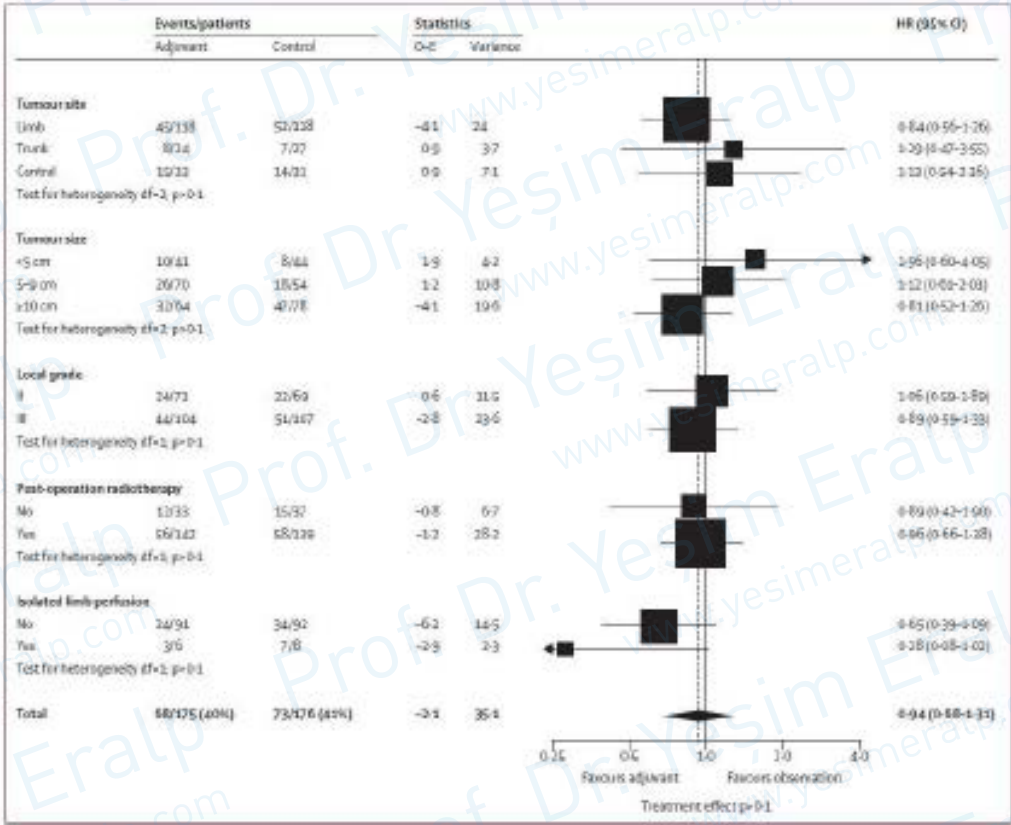
(FIGO Evre I)



5 yıllık OS: %67

Adjuvant chemotherapy with doxorubicin, ifosfamide, and lenograstim for resected soft-tissue sarcoma (EORTC 62931): a multicentre randomised controlled trial

Penella J Woll, Peter Reichardt, Axel Le Cesne, Sylvie Bonvalot, Alberto Azzarelli, Harald J Hoekstra, Michael Leahy, Frits Van Coevorden, Jaap Verweij, Poncras CW Hogendoorn, Monica Quail, Sandrine Mairreud, Vivien H C Bramwell, Peter Hohenberger, for the EORTC Soft Tissue and Bone Sarcoma Group and the NCIC Clinical Trials Group Sarcoma Disease Site Committee



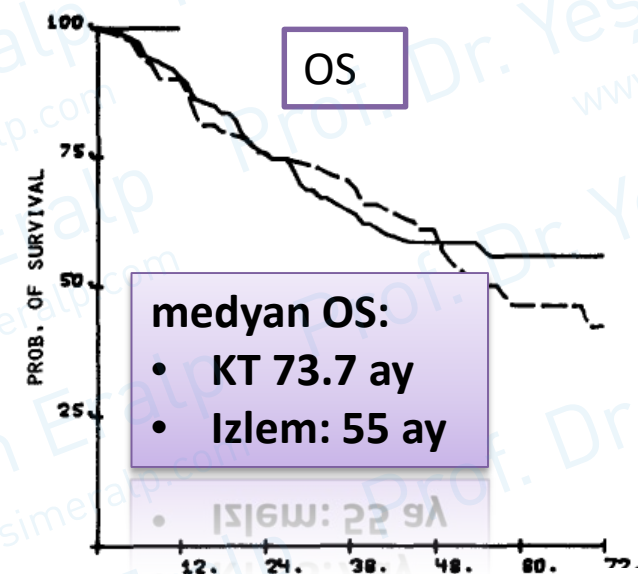
LMS & İNDİFFERANSİYE KARSİNOM:

ADJUVAN KT

ADJUVAN KT

Uterin Sarkomlar: Adj KT & nüks riski

Cell Type	Adriamycin	No Chemotherapy	Total
Leiomyosarcoma	11/25 (44)	14/23 (61)	25/48 (52)
MMS—homologous	10/25 (40)	12/23 (52)	22/48 (46)
MMS—heterologous	7/19 (37)	13/26 (50)	20/45 (44)
Other	3/6 (50)	4/9 (44)	7/15 (47)
Total	31/75 (41)	43/81 (53)	74/156 (47)



medyan OS:

Evre I vs II

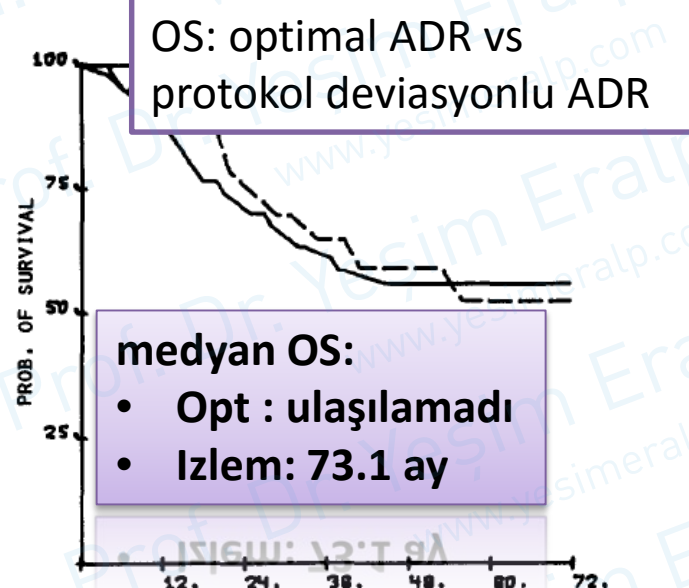
- 67.2 mo

- 32.9 mo

p:0.02

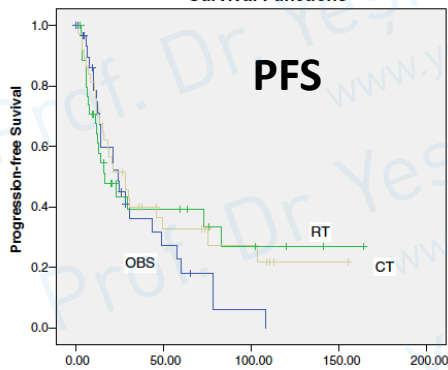
b:0.05

- 35.2 mo

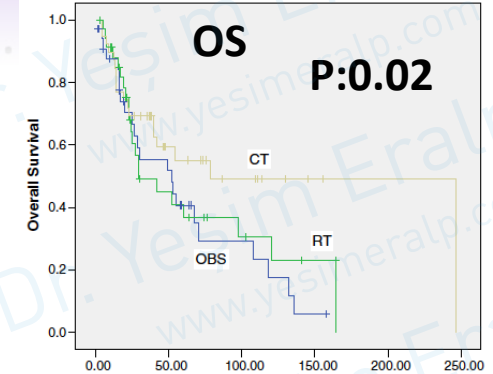


Does adjuvant chemotherapy improve survival for women with early-stage uterine leiomyosarcoma? ☆

- Yüksek gradlı; 104 LMS; %87 evre I, %13 evre II
- Medyan 42 ay takip; Tüm grup medyan OS: 52.6 ay



	Median PFS (mo.)
OBS	24.7
RT	16.8
CT	28.3
Overall	23.3



- KT kolu: %59 hastada: Gemesitabin + Dosetaksel
- Tüm kollar arasında yaş, evre & prognostik faktör dağılımı dengeli
- %70 hastada nüks +; ¾'ü ekstra-pelvik nüks
- KT vs RT kollarına göre nüks oranı farklı değil

Does adjuvant chemotherapy improve survival for women with early-stage uterine leiomyosarcoma? ☆

Recurrence	OBS* (n = 34)	RT* (n = 35)	CT* (n = 39)	All patients (n = 108)
Overall	25 (73.5)	21 (60.0)	28 (71.8)	74 (64.8)
Pelvic	10 (40.0)	* 1 (4.8)	10 (35.7)	21 (25.4)
Extrapelvic	15 (60.0)	20 (95.2)	18 (64.3)	53 (74.6)

*p- Value for adjuvant treatment = 0.413. p-Value for pelvic vs extrapelvic relapses = 0.010 *

- RT pelvik nüksleri engelliyor
- KT sonrası nüks tedavisi daha başarılı; 28 hastanın 21'i izole pelvik nüks...

• Genel Sağkalım Çok-değişkenli analiz:

- Evre HR: 3.53 p<0.001
- Adj KT HR: 0.53 p:0.045

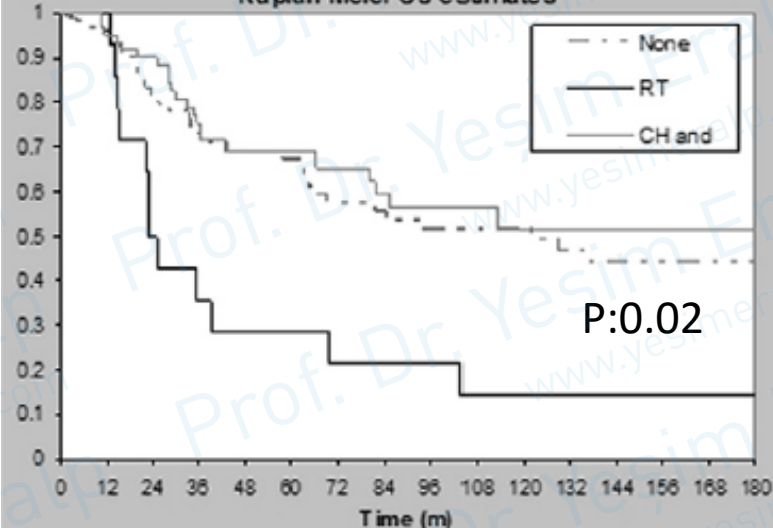
Adjuvant chemotherapy in stage I–II uterine leiomyosarcoma: A multicentric retrospective study of 140 patients

	Overall population (n = 140)	Percentage frequencies
Patients median age (range)	51	21–74
Stage		
• I	125	(89.3%)
• II	15	(10.7%)
Tumor size		
• <5 cm	10	(7.1%)
• >5 cm	68	(48.6%)
• Missing data	62	(44.3%)
No. of mitosis		
• <20	63	(45.0%)
• >20	62	(44.3%)
• Missing data	15	(10.8%)
Post surgical treatment		
• Observation	62	(44.3%)
• EBRT	14	(10.0%)
• Chemo	52	(37.1%)
• Chemo-EBRT	12	(8.6%)

- KT kolu: %8 hastada: Gemsitabin + Dosetaksel; kalanı dokso-bazlı
- RT kolu: daha çok evre II hasta & >20 mitoz içeren tm.ler
- 63 ay takip ; %72 hastada sistemik nüks (+/- lokal nüks)
- 5 yıl DFS: %43; 5 yıl OS: %64

Adjuvant chemotherapy in stage I–II uterine leiomyosarcoma: A multicentric retrospective study of 140 patients

Kaplan Meier OS estimates



Tek değişkenli analiz

	Relapse		Death	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Number of mitosis <20 vs >20	1.66 (0.80–3.43)	0.174	2.26 (1.10–6.65)	0.026
Diameter <5 cm vs >5 cm	1.86 (0.48–7.23)	0.369	7.10 (0.85–59.2)	0.070
Age <60 y vs >60 y	1.71 (0.67–4.42)	0.264	3.21 (1.29–8.00)	0.012
Therapy:				
CHT/CHT-RT vs observation	1.13 (0.55–2.29)	0.743	0.56 (0.27–1.14)	0.112
RT vs observation	4.33 (0.89–21.0)	0.069	6.40 (1.32–31.0)	0.021
CHT/CHT-RT vs RT	0.26 (0.05–1.26)	0.094	0.09 (0.18–0.43)	0.003

• Nüks sonrası sağkalım:

- RT: 8 ay
- KT: 20 ay
- İzlem: 28 ay

• Çok değişkenli analiz:

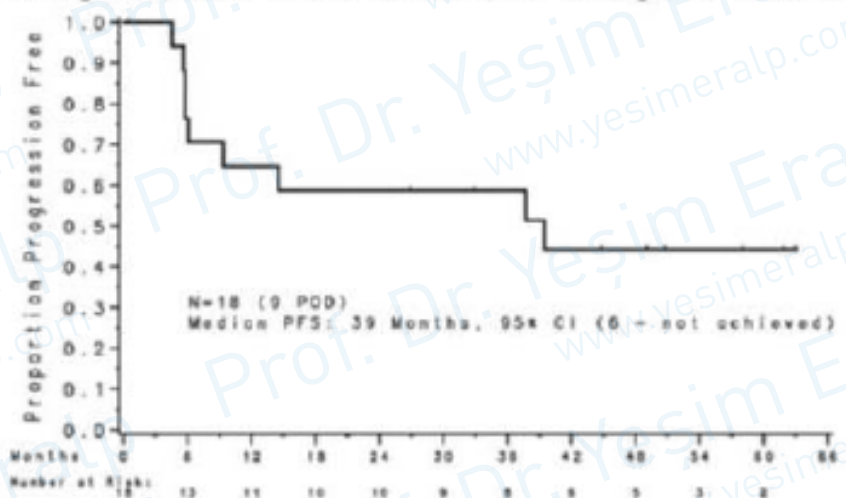
- Mitoz >20 p:0.04
- Yaş p:0.05

Adjuvant gemcitabine plus docetaxel for completely resected stages I–IV high grade uterine leiomyosarcoma: Results of a prospective study☆

Patient and tumor characteristics

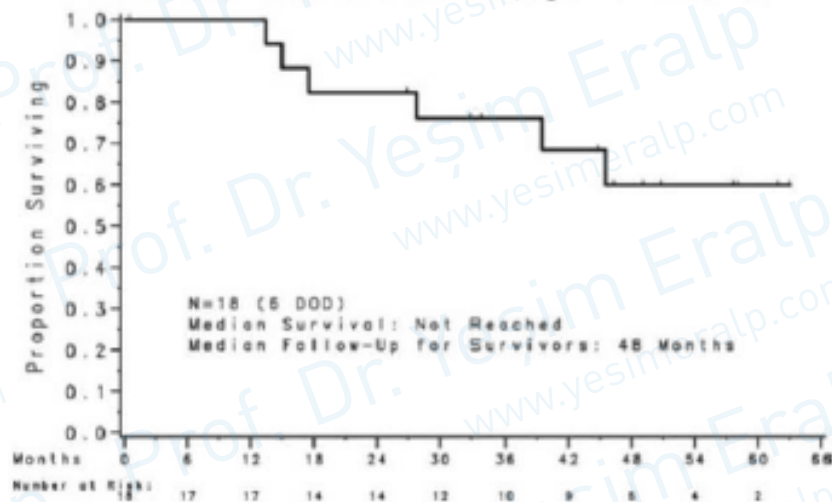
Patient age, years	Median 49	Range 37–73
Stage I (number of patients, percent)	15	65%
Stage II	3	13%
Stage III	1	4%
Stage IV	4	17%
Tumor mitotic rate	Median 20 mitoses/10 high-power fields	Range 5–60 mitoses/10 high-power fields
Tumor size for stages I and II patients (n= 18)	Median 10 cm	Range 6–28 cm

Progression Free Survival Stage 1 and 2



Medyan DFS: 39 ay
2 yılda %60'ı hastalıksız

Overall Survival Stage 1 and 2



Medyan OS: ulaşamadı

SARC005: Schema

Gemcitabine 900 mg/m² over 90 minutes days 1, 8
Docetaxel 75 mg/ m² day 8
q 3 wk x 4 cycles

Repeat CT scan – if disease free, then proceed

Doxorubicin 60 mg/m² q 3 wk x 4

Patient demographics

Age: Median (range), y 53 (37-70)

Menopausal status, no. of women

Postmenopausal 43

Premenopausal 4

Tumor characteristics

Tumor size: Median (range), cm 8 (2.5-30)

Mitotic rate: Median mitoses 18 (5-83)

per10 high-power fields (range)

ER status, n = 38 evaluable 63% Positive

PR status, n = 38 evaluable 50% Positive

Either ER or PR 29% Negative for both

1988 FIGO stage

I 81%

II 15%

III, serosa only 4%

AJCC stage

I 0%

II 13%

III 87%

Yüksek gradlı LMS

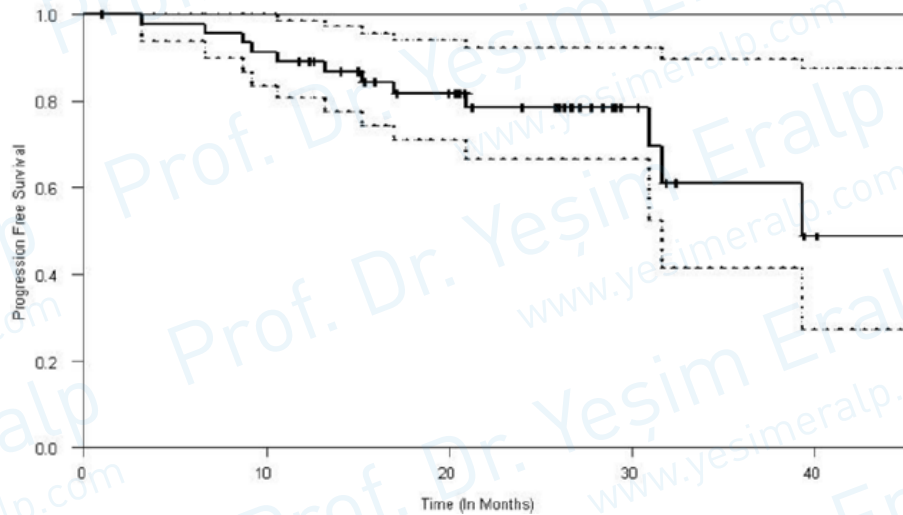
>5 mitoz / 10 BBA

Cerrahi sonrası adj KT:

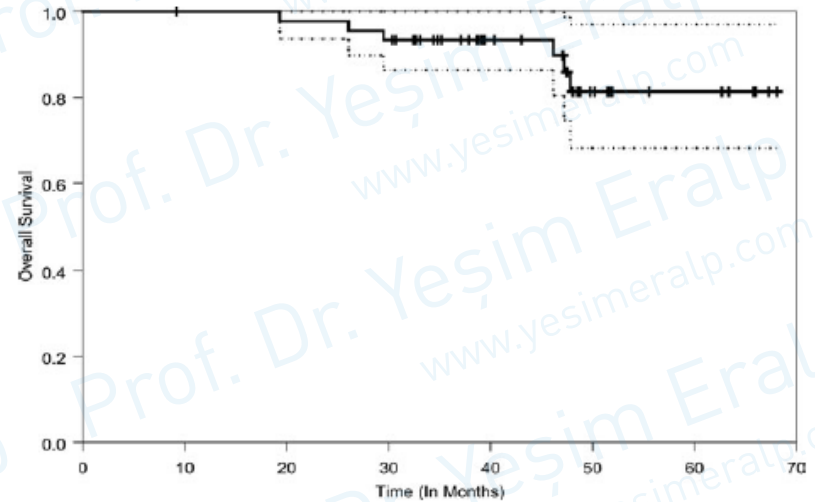
en az :TAH

Adjuvant Therapy for High-Grade, Uterus-Limited Leiomyosarcoma

Results of a Phase 2 Trial (SARC 005)



Medyan DFS: ulařılamadı
2 yılda %75'ı hastalıksız
(historik kontrol: %45-50)



Medyan OS: ulařılamadı

Faz III alıřma devam ediyor



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NCCN Guidelines Version 2.2015

Uterine Sarcoma

- High-grade (undifferentiated) endometrial sarcoma
- Uterine leiomyosarcoma (uLMS)

Stage I

Observe
or
Consider chemotherapy
(category 2B)^f

Stage II, III

Consider chemotherapy^f
and/or
Consider tumor-directed RT^e

Stage IVA

Chemotherapy^f
and/or
RT^e

Stage IVB

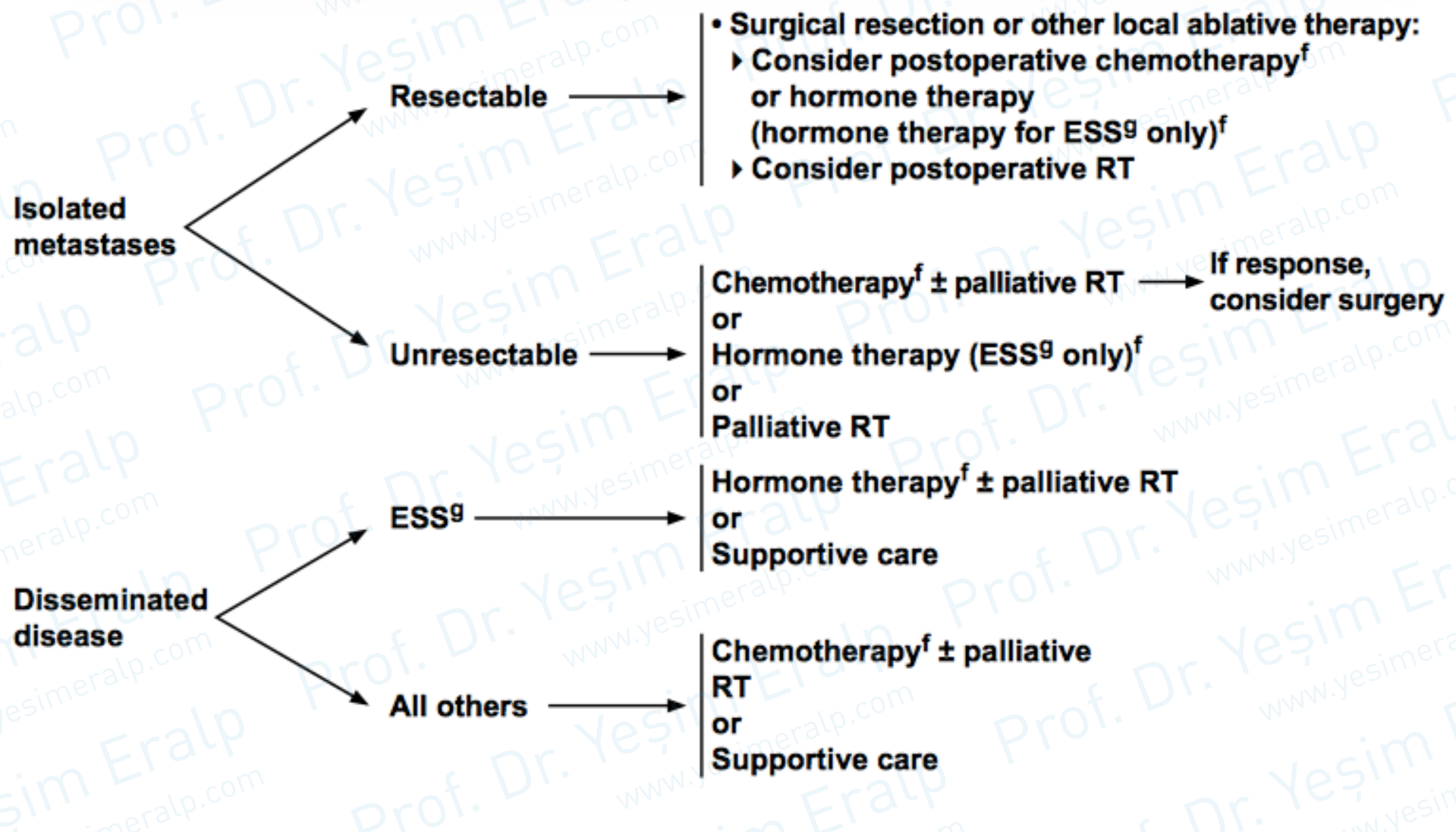
Chemotherapy^f ± palliative RT



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Uterine Sarcoma



NCCN Guidelines Version 2.2015

Uterine Sarcoma

CHEMOTHERAPY REGIMENS¹

(Clinical trials strongly recommended)

- **Combination regimens:**

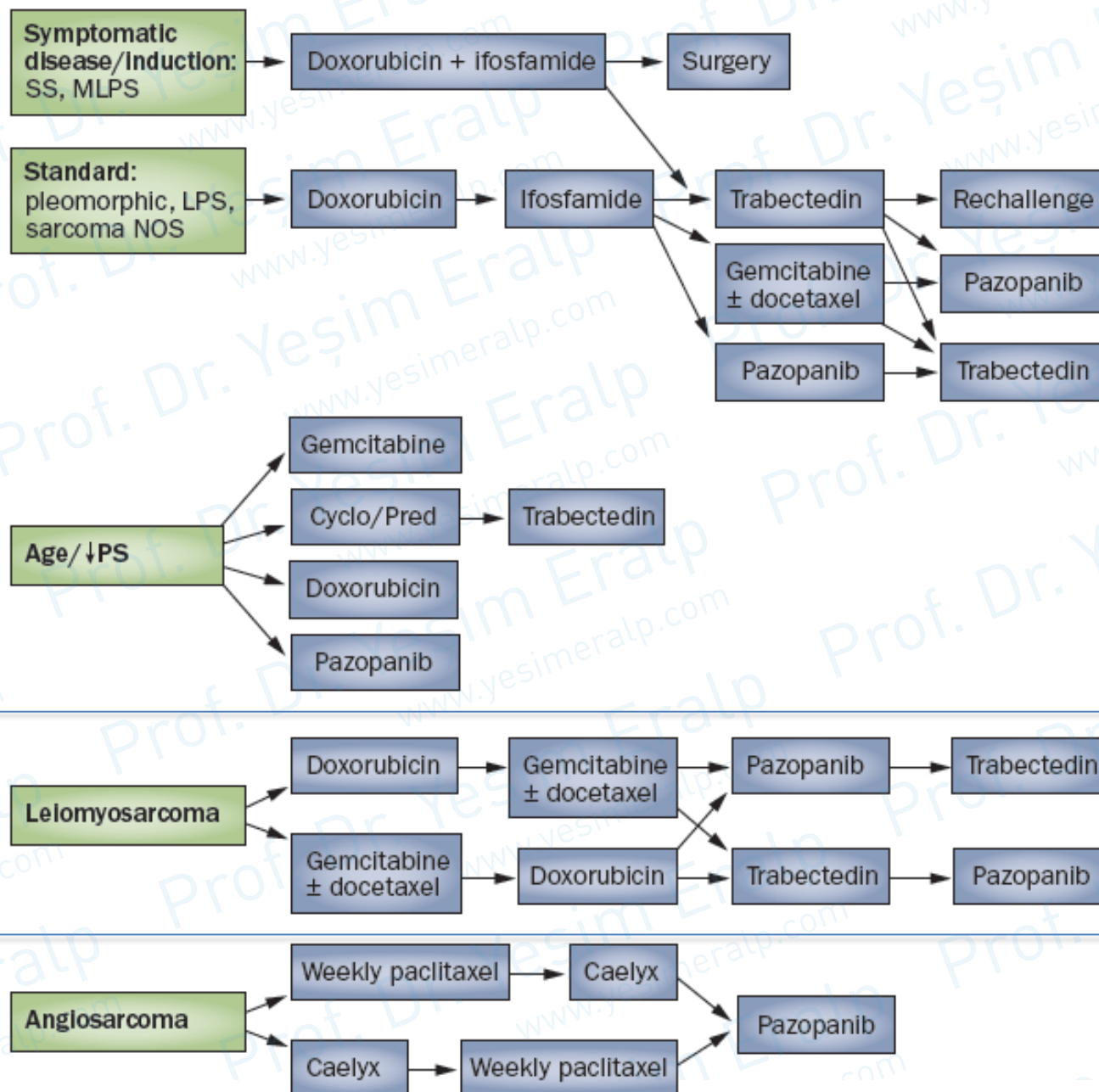
- ▶ Docetaxel/gemcitabine
(preferred for leiomyosarcoma)
- ▶ Doxorubicin/ifosfamide
- ▶ Doxorubicin/dacarbazine
- ▶ Gemcitabine/dacarbazine
- ▶ Gemcitabine/vinorelbine

- **Single-agent options:**

- ▶ Dacarbazine
- ▶ Doxorubicin
- ▶ Epirubicin
- ▶ Gemcitabine
- ▶ Ifosfamide
- ▶ Liposomal doxorubicin
- ▶ Pazopanib
- ▶ Temozolomide
- ▶ Vinorelbine (category 2B)
- ▶ Docetaxel (category 3)

HORMONE THERAPY (ESS only)

- Medroxyprogesterone acetate
- Megestrol acetate
- Aromatase inhibitors²
- GnRH analogs (category 2B)



cyclophosphamide; LPS, liposarcoma; MLS, myxoid liposarcoma; NOS, not otherwise specified; Pred, prednisolone; PS, performance status; SS, synovial sarcoma.