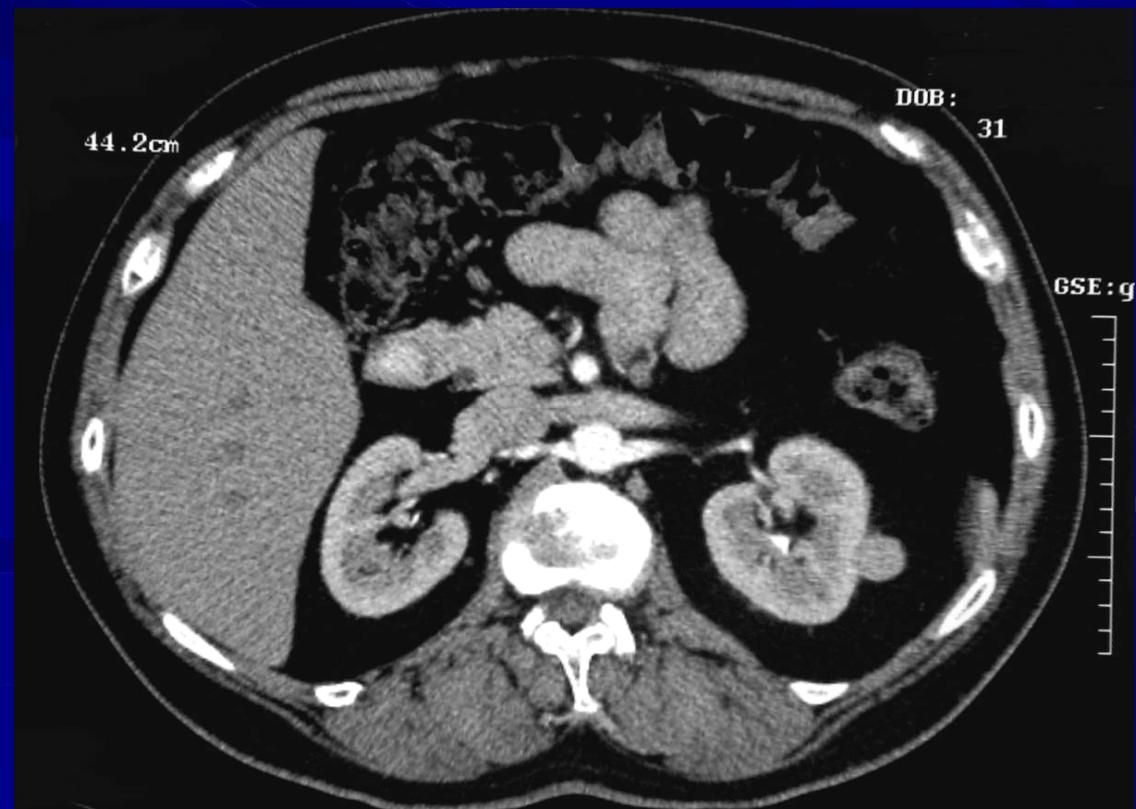


Renal Hücreli Ca Klinik olgular

Prof.Dr.Atif Akdaş

Olgu 1

- 64 yaşında sağlıklı erkek hasta
- Rastlantısal saptanan sol renal kitle



Yaklaşım

- Biyopsi
- Gözleyerek izlem
- Nefron Koruyucu Cerrahi
 - Laparoskopik
 - Açık
- Minimal invazif tedaviler
 - Cryo
 - HIFU
 - RFA
- Radikal nefrektomi

Diagnosis of Renal Tumors on Needle Biopsy Specimens by Histological and Molecular Analysis

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Purpose: We diagnosed the subtypes of renal cell carcinoma on needle core biopsies using a combination of histopathology and a molecular diagnostic algorithm.

Materials and Methods: Core biopsies were taken of renal tumors following nephrectomy. RNA was extracted and quantitative real-time polymerase chain reaction was performed for 4 gene products to differentiate among renal cell carcinoma subtypes. Histopathological diagnosis was achieved on a second core before and after obtaining the molecular diagnostic algorithm results.

Results: Based on the nephrectomy diagnosis 6 of 77 renal masses were nonneoplastic and 71 were tumors, including 65 renal cell carcinoma/oncocytomas. The overall diagnostic accuracy using histology and our molecular diagnostic algorithm combined was 90.0% (70 of 77). Side by side comparison of histology vs molecular diagnostic algorithm was feasible for 60 classifiable renal cell carcinoma/oncocytomas (31 clear cell, 14 papillary renal cell carcinoma, 6 chromophobe renal cell carcinoma, 2 mucinous tubular and spindle cell carcinoma, and 7 oncocytoma). In this group histology correctly predicted the final histological subtype in 83.3% (50 of 60) of cores. Addition of the molecular diagnostic algorithm to histology improved the subtyping accuracy to 95% (57 of 60), whereas the molecular diagnostic algorithm alone was accurate in 50 of 60 cases (83.3%). Dividing these 60 specimens into clear cell and nonclear cell neoplasms, the addition of the molecular diagnostic algorithm improved the sensitivity for the diagnosis of clear cell carcinoma from 87.1% (27 of 31) to 100% and the negative predictive value from 87.5% to 100%.

Conclusions: Core biopsies of renal tumors provide adequate material for diagnosing and subtyping renal cell carcinoma. The addition of our molecular diagnostic algorithm to histology improved the diagnostic accuracy of core biopsies of renal masses.

Study	Number of masses ^a	Average tumor size (cm)	Average follow-up (months)	Average tumor growth (cm/year)	Masses eventually surgically removed (%)	Histologically confirmed RCC (%)
Bosniak <i>et al.</i> [40]	40	1.73	39	0.36	26 (65%)	22/26 (85%)
Volpe <i>et al.</i> [42]	32	2.48	27.9	0.1	9 (28%)	8/9 (89%)
Kassouf <i>et al.</i> [43]	24	3.27	31.6	0.09	4 (17%)	4/4 (100%)
Kato <i>et al.</i> [44]	18	1.98	22.5	0.42	18 (100%)	18/18 (100%)
Wehle <i>et al.</i> [45]	29	1.83	32	0.12	4 (14%)	3/4 (75%)
Sowery and Siemens[46]	22	4.08	26	0.86	2 (9%)	2/2 (100%)
Chawla <i>et al.</i> [47]	61	2.97	36	0.20	21 (34%)	17/21 (81%)

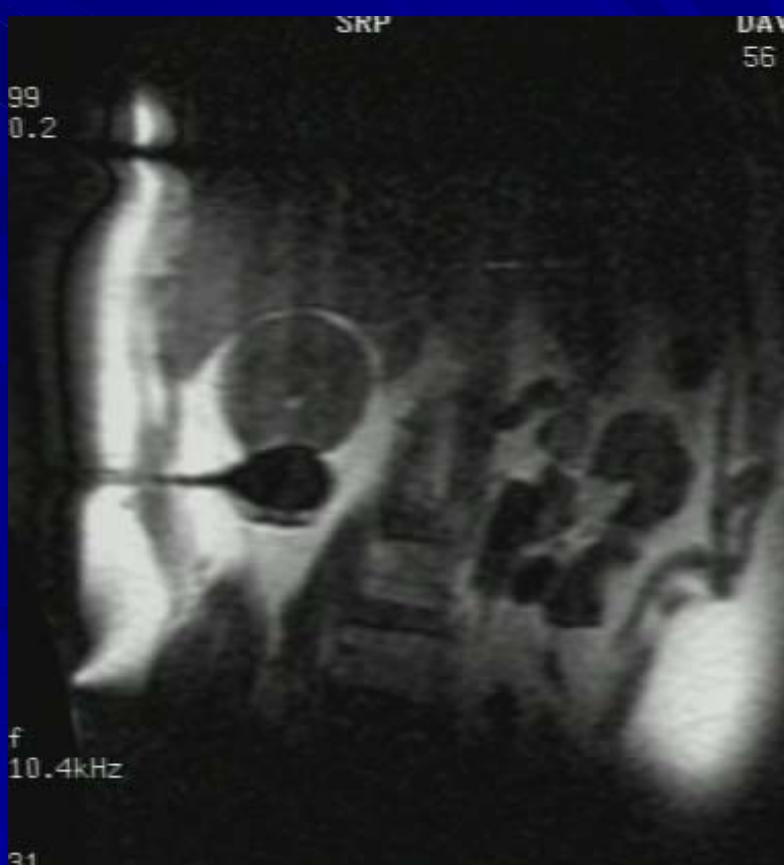
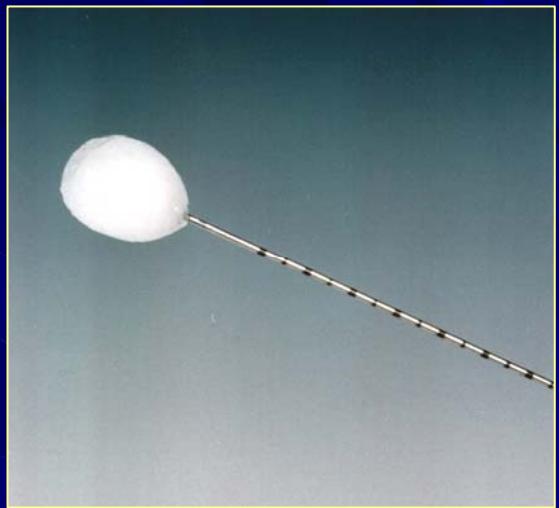
Laparoscopic vs. open partial nephrectomy

	OPEN	LAPARO	P value
Duration of surgery	<u>3.9 h</u>	3h	
Blood loss	250 ml	125 ml	<0.001
Warm ischemia	17.5 min	<u>27.8 min</u>	<0.001
Postoperative recovery	6 weeks	4 weeks	
Postoperative creatinine	1.2	1.1	<0.001
Positive surgical margin	0%	<u>3%</u>	0.1
Intra-operative complications	0%	<u>5%</u>	0.02
Renal/urological complications	2%	<u>11%</u>	0.01

K. Beasley et al, J Urol 2004
S. Matin et al, J Urol 2002

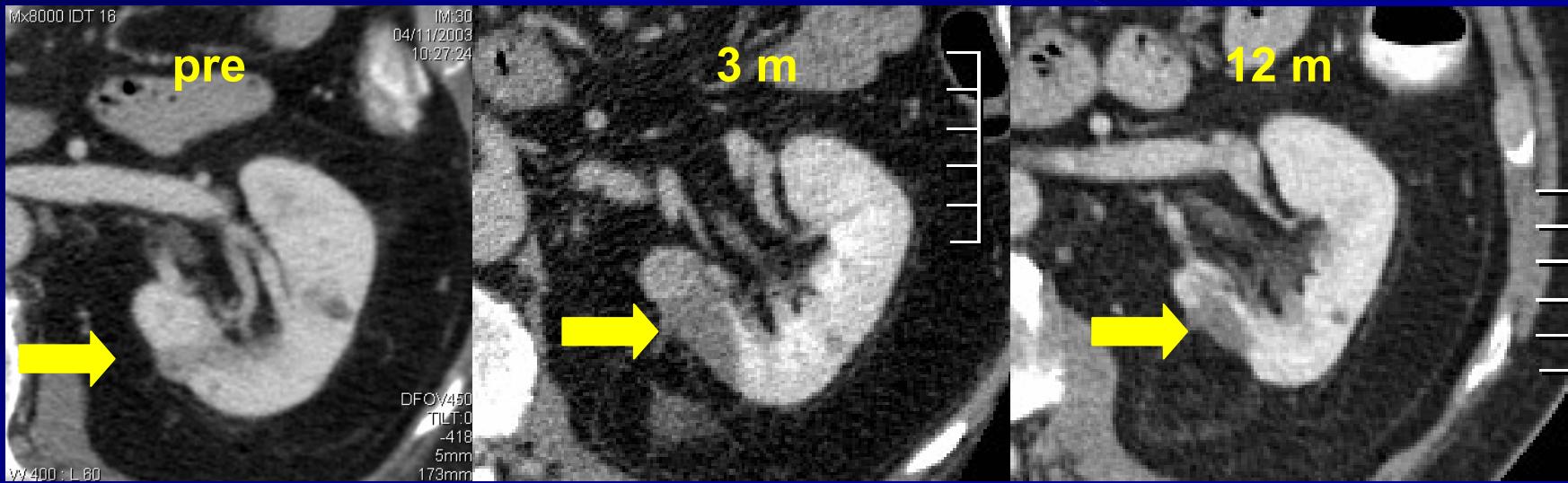
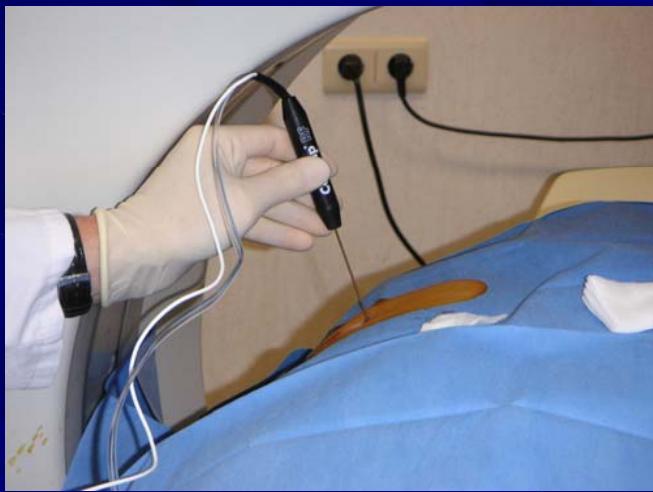
NKC

- Açık NKC standard tedavi
- Laparoskopik NKC
 - Usta ellerde başarılı
 - Deneyim istiyor
 - Kanama, uzun iskemi zamanı
 - Tümör-normal doku ayrimı zor
 - Uzun dönem onkolojik sonuçları yok



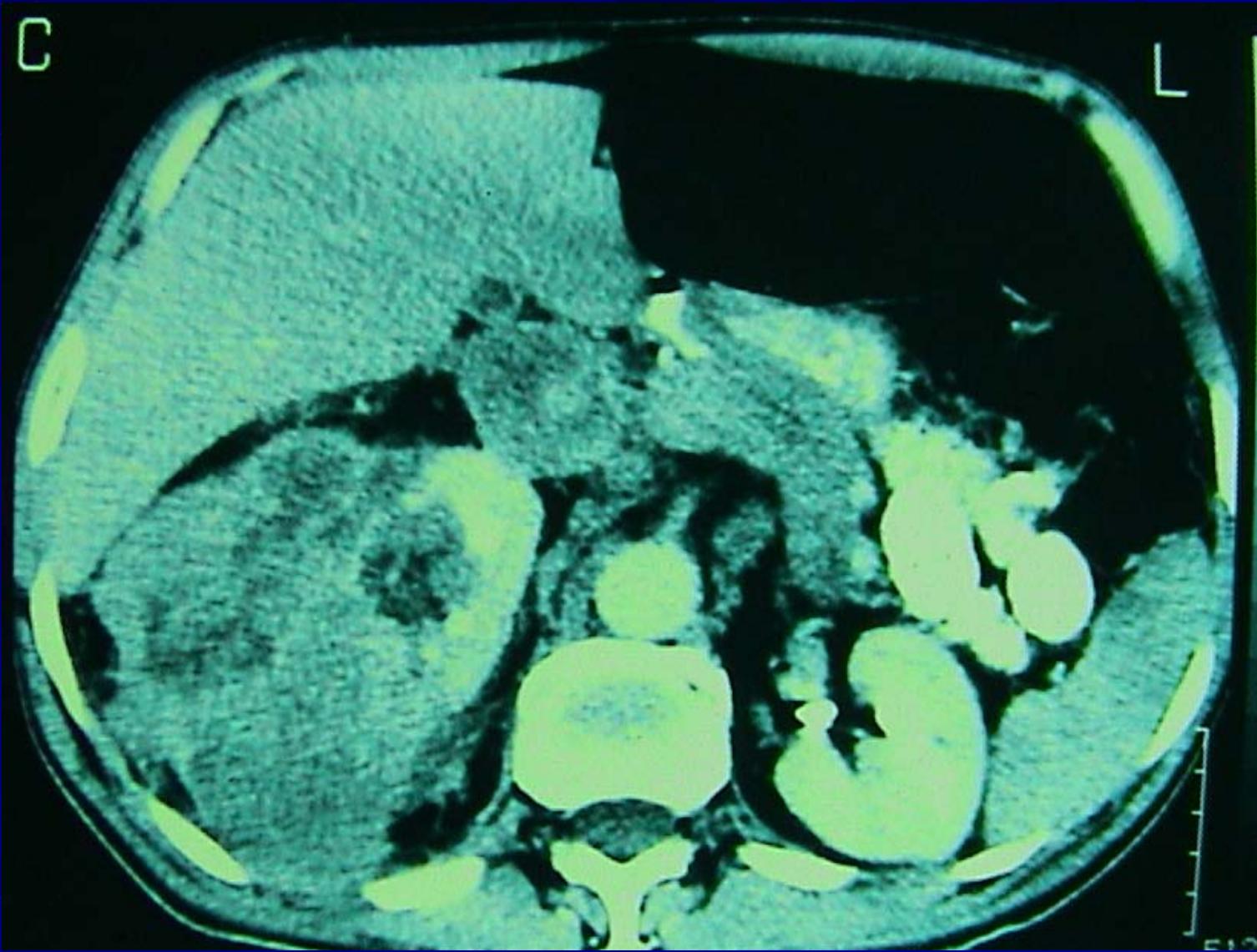
	<i>Approach</i>	<i>Tumors</i>	<i>Size (cm)</i>	<i>Probe (mm)</i>	<i>O. T. (min)</i>	<i>FU (month)</i>	<i>Rec. / Pers.</i>
<i>Rukstalis, 2001</i>	open	29	2.2	3 – 8-		16	1
<i>Lee, 2003</i>	lap	20	2.6	4.8	305	14	1
<i>Nadler, 2003</i>	lap	15	2.15	4.8	260	15	2
<i>Shingleton, 2004</i>	MRI	111	3	3	79	30	8%
<i>Cestari, 2004</i>	lap	37	2.6	3.2	194	20.5	1
<i>Ankem, 2005</i>	lap	22	2.6	2.4 - 5	188	10.4	0
<i>Gill, 2005</i>	lap	60	2.3	4.8	180	> 3years	5.3%

RFA



Olgı 3

- 56 yaşında erkek hasta
- Bel ağrısı nedeni ile incelenirken sağ böbrekte kitle saptanıyor
- 3 ay önce 2 kez hematüri tanımlıyor



İleri görüntüleme – Evreleme

- MRG
- Anjiografi
- Vena cavografi
- Transösefagial ultrasonografi
- Akciğer grafisi



- Sağ radikal nefrektomi + IVC trombüs eksizyonu
- Patoloji: Şeffaf hücreli cRHK
- pT3b + Gerota fasyası invaze
- 14 lenf nodu (-)
- Ne yaparsınız?

Adjuvant Trials in RCC

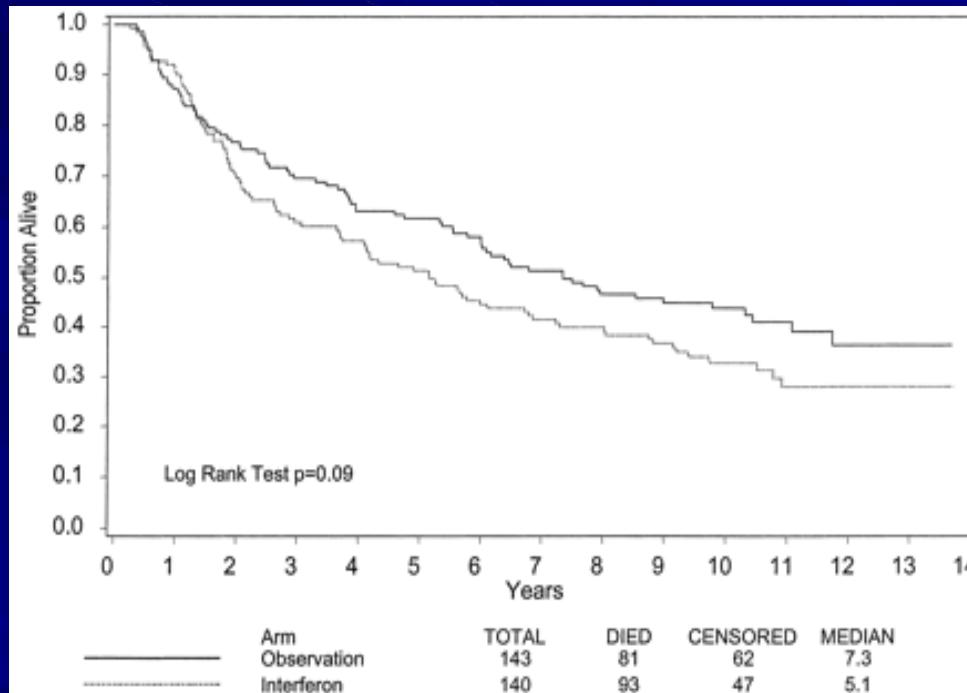
Author / year	Adjuvant Tx	Patients (n)
Atzpodien 2005	IL-2 + IFN- α + 5-FU	203
Jocham 2004	Reniale®	553
Clark 2003	Interleukin-2	69
Messing 2003	Interferon-NL	283
Pizzocaro 2001	Interferon- α	247
Galligioni 1996	Vaccine	120
Delta p Grp 1992	Interferon- α	270
Pizzocaro 1987	MPA	120
Kjaer 1987	Radiation	65

Adjuvant Trials in RCC

Side Effects

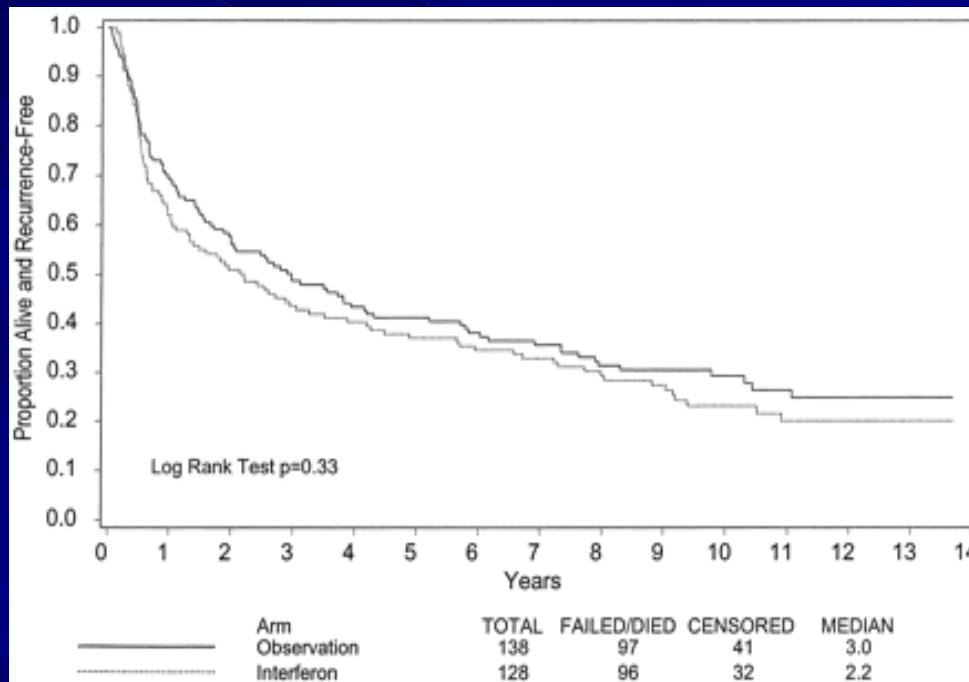
Author/year	Adjuvant Tx	Side Effect
Atzpodien 2005	IL-2+ IFN-a+5FU	-
Jocham 2004	Reniale-Vaccine	1.1%
Clark 2003	IL-2	88% Grade 3/4
Messing 2003	IFN-NL	30% W/D
Pizzocaro 2001	IFN-a	28% W/D
Galligioni 1996	Vaccine	“no relevant”
Pizzocaro 1987	MPA	5.2% W/D
Kjaer 1987	Radiation	5x death/44 % s.e.

RCC adjuvant Interferon Alfa-NL Overall survival



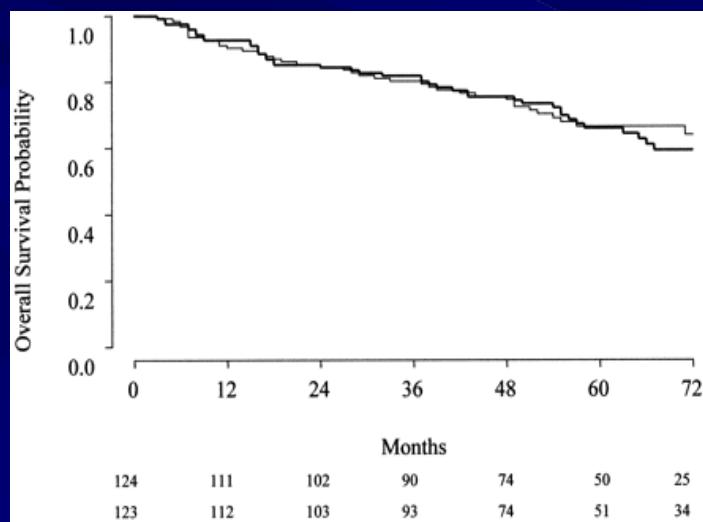
Messing E et al. JCO 2003;21:1214

RCC adjuvant Interferon Alfa-NL Recurrence free survival

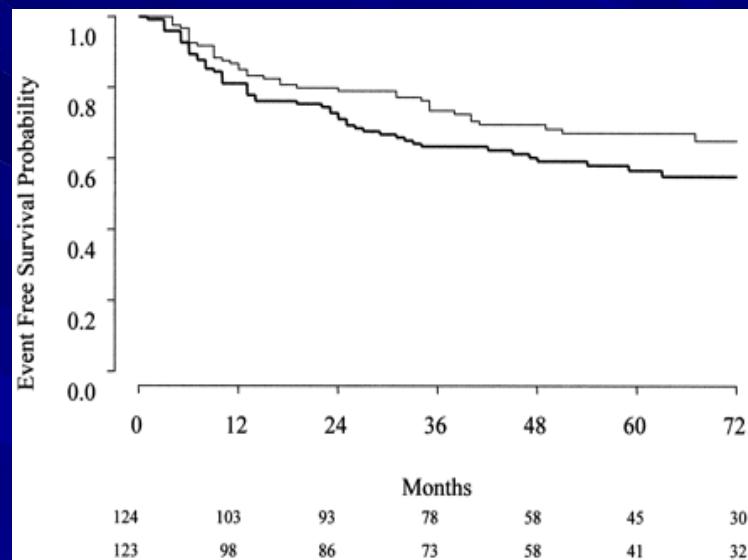


Messing E et al. JCO 2003;21:1214

RCC adjuvant Interferon alpha



Overall survival



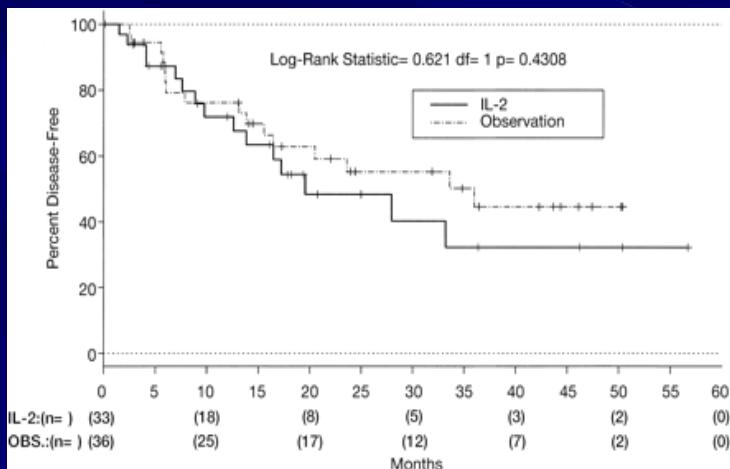
Event free survival

Pizzocaro et al . JCO 2001;19:425

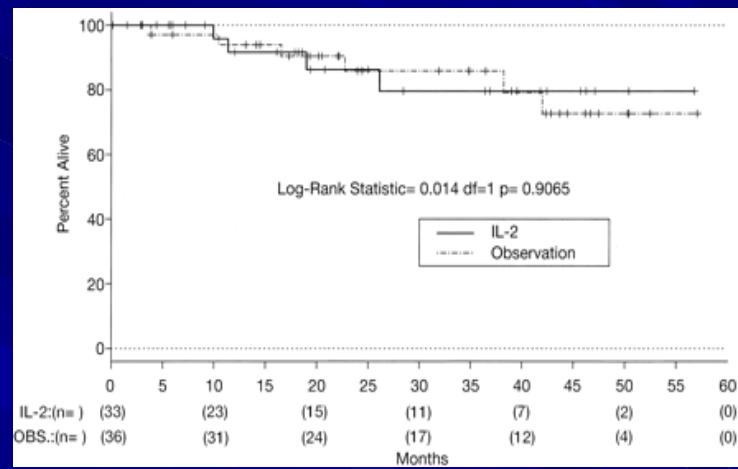
RCC adjuvant High dose bolus IL-2

- Randomized study
- T3b-c,4, N1-3, resectable M+
- N=69
 - 33 IL-2
 - 36 obs

RCC adjuvant High dose bolus IL-2



DF survival



Overall survival

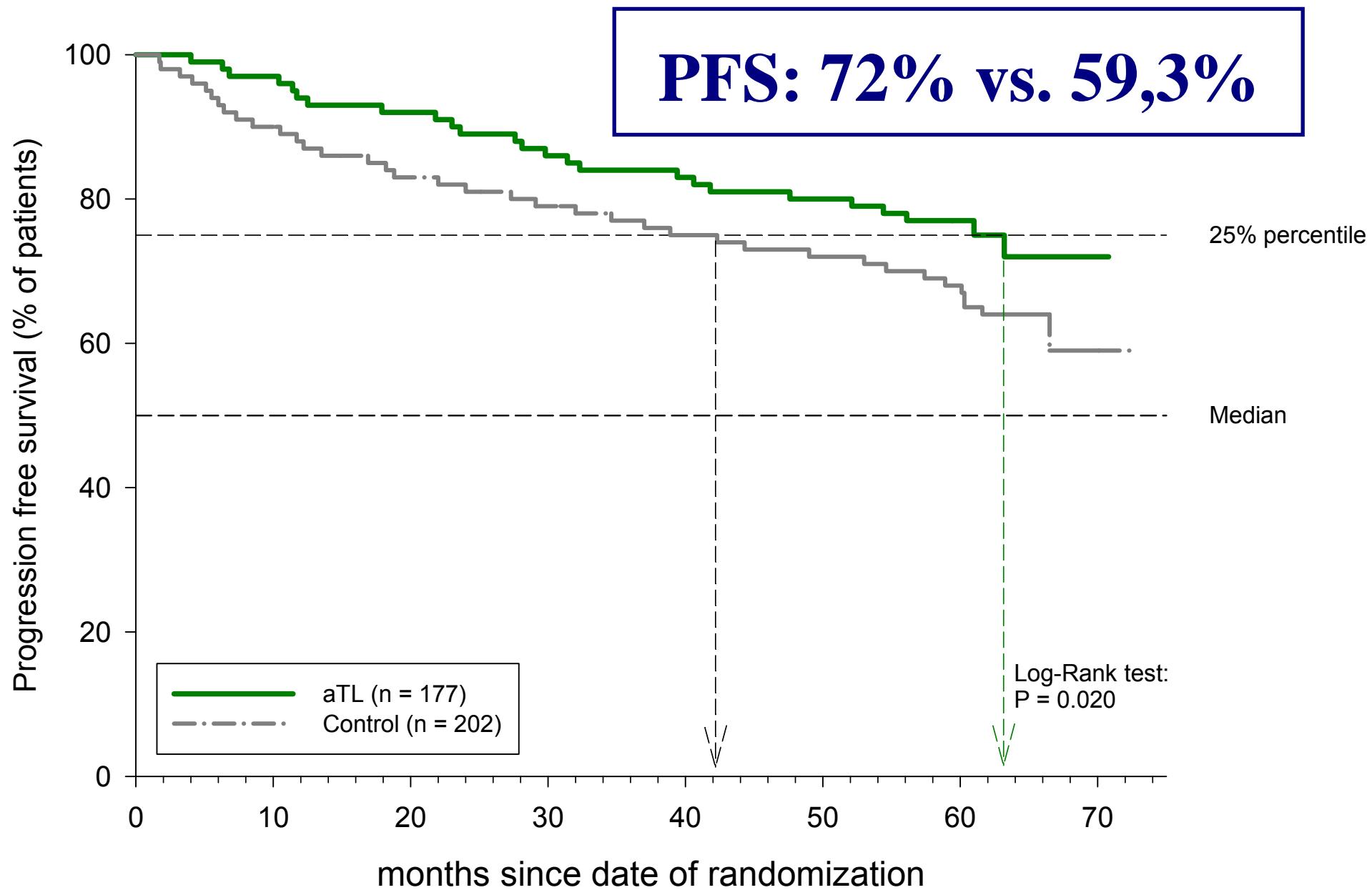
Clark J et al JCO 2003;21:3133

RCC adjuvant Autologous tumour vaccine

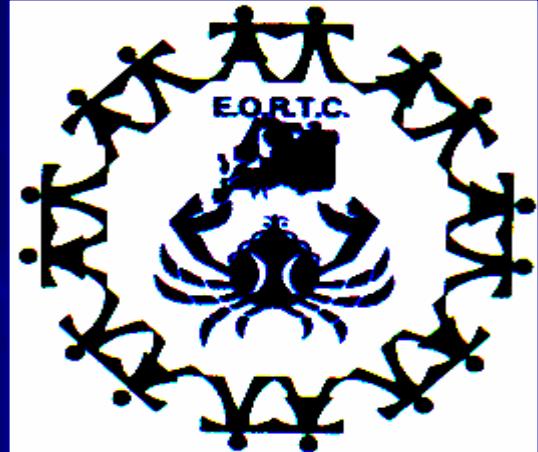
- Randomized study
- N= 558
 - 553 included
 - 276 vaccine group
 - 177 treated (PT2-3b, N0-3,M0).
 - 277 control group
 - 202

Jocham D et al. Lancet 2004;363:594

Time to progression
Intention-to-treat population



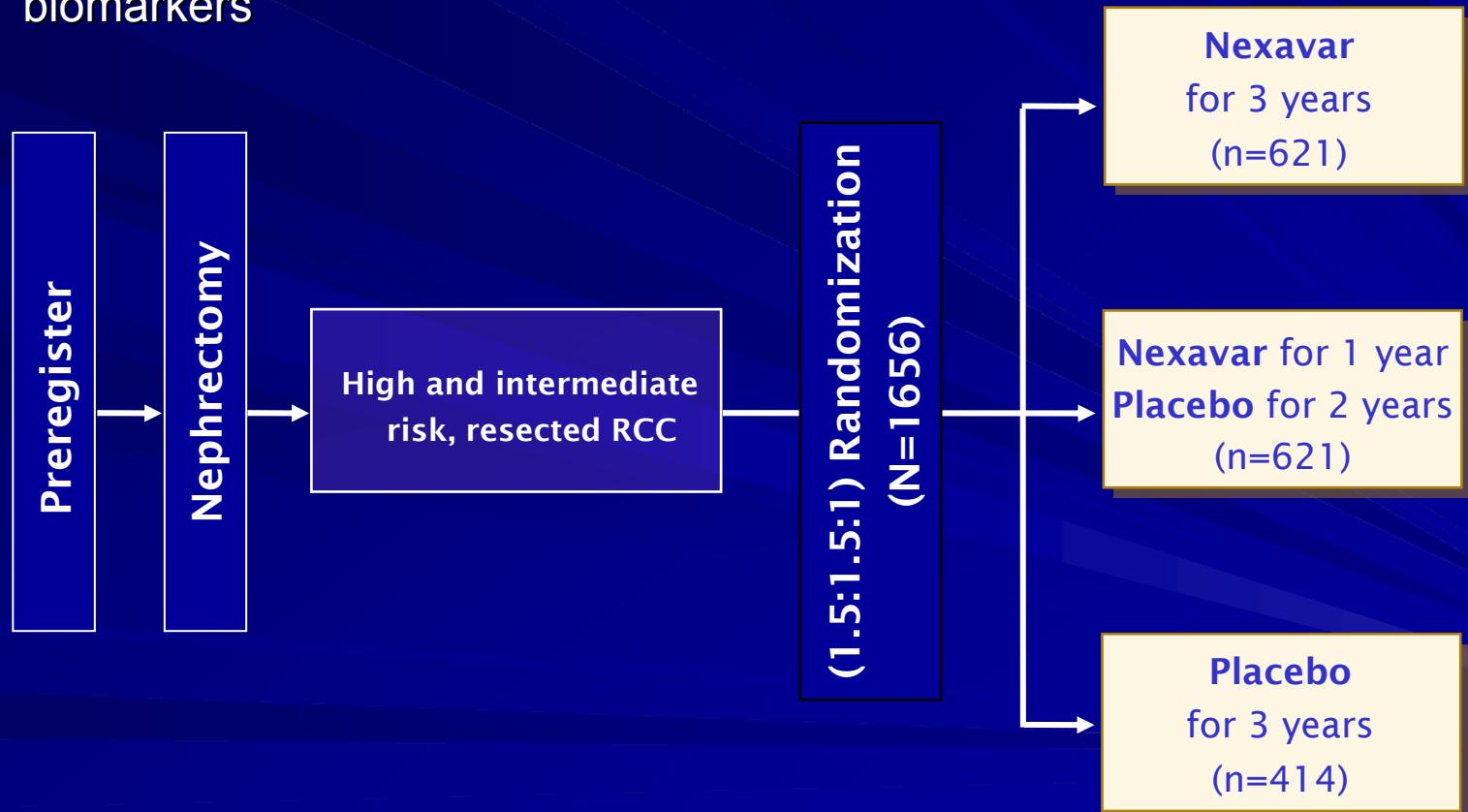
EORTC GU / CRC Protocol 30955



- Randomised trial of IL-2 / IFN-alpha2a / 5FU vs observation in pts with high risk of relapse post nephrectomy
- Stage T3b-c T4, pN1-2, positive margins, microscopic vascular invasion

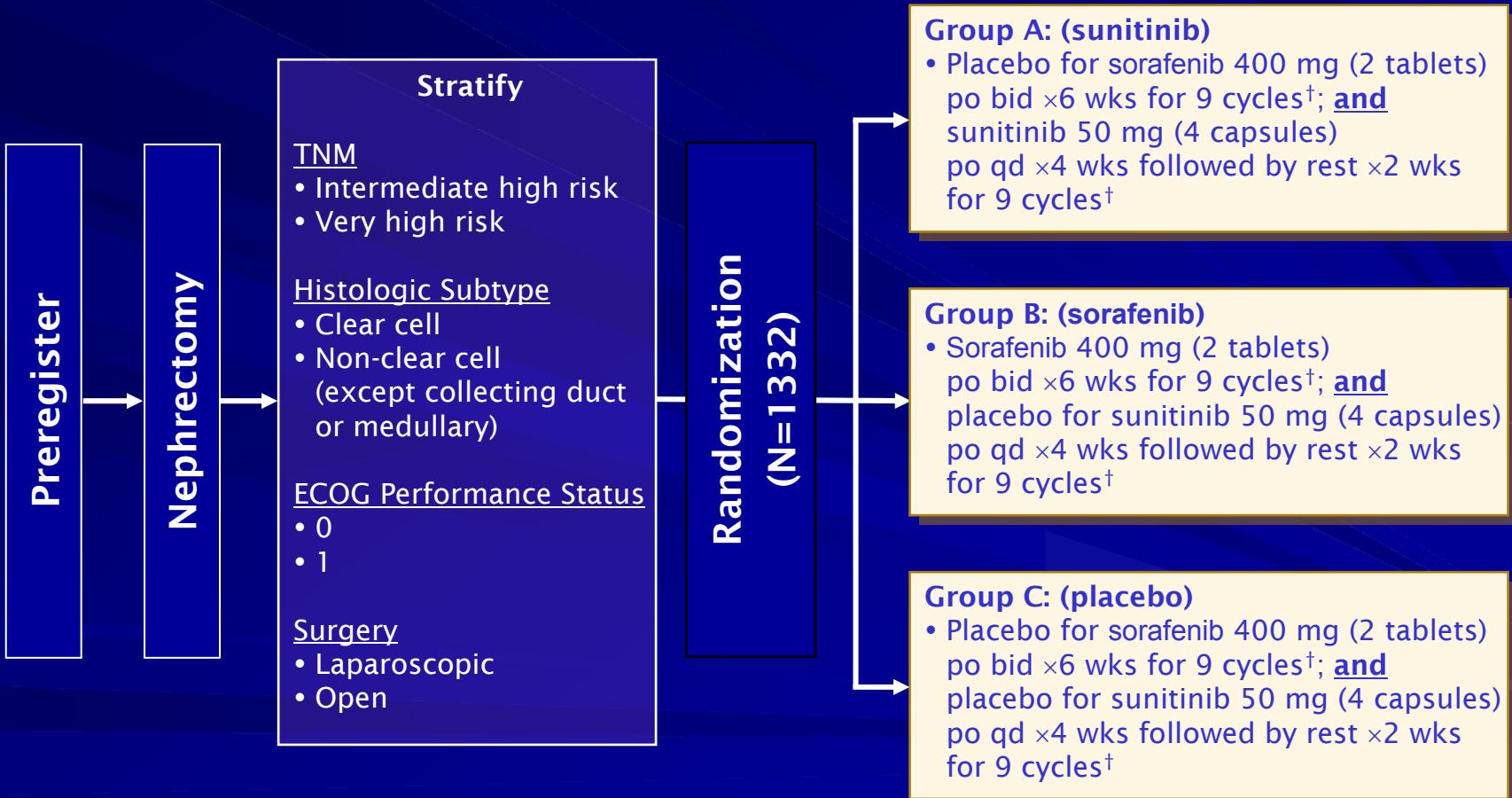
MRC SORCE Phase III Trial

- 1° end point: Disease-free survival
- 2° end points: RCC-specific survival time, toxicity, QOL, and biomarkers



ECOG ASSURE Phase III Trial

- 1° end point: Disease-free survival (DFS)



RCC - Adjuvan Tedavi - Sonuç

- RCC de adjuvan tedavinin yaşamı uzattığına dair kanıt yok
- Hangi tedavi? Ne süre?
- Risk grupları önemli
- Çalışmalara gereksinim var

■ Hastada 6 ay sonra akciğer sağ alt lobda 2 tane metastaz saptanıyor

■ Tedavi yaklaşımınız ne olurdu?

- Gözleyerek izlem
- Cerrahi eksizyon + izlem
- Cerrahi eksizyon + tedavi (IF- α , IL-2, kombine tedaviler)
- Cerrahi eksizyon + tedavi (sorafenib / sunitinib / temsirolimus)
- Immunoterapi + yanıtla göre cerrahi
- AI ile tedavi + yanıtla göre cerrahi

- 3 ay sonra akciğer ve kemik metastazları
- IF + IL + 5FU 2 kür sonrası yanıt yok
- Sorafenib 2 X 400 mg başlandı
- Akciğer metastazları geriledi, kemiğe radyoterapi alıyor