Metastatik Renal Kanserlerinde Birinci Basamak Tedavi Seçenekleri

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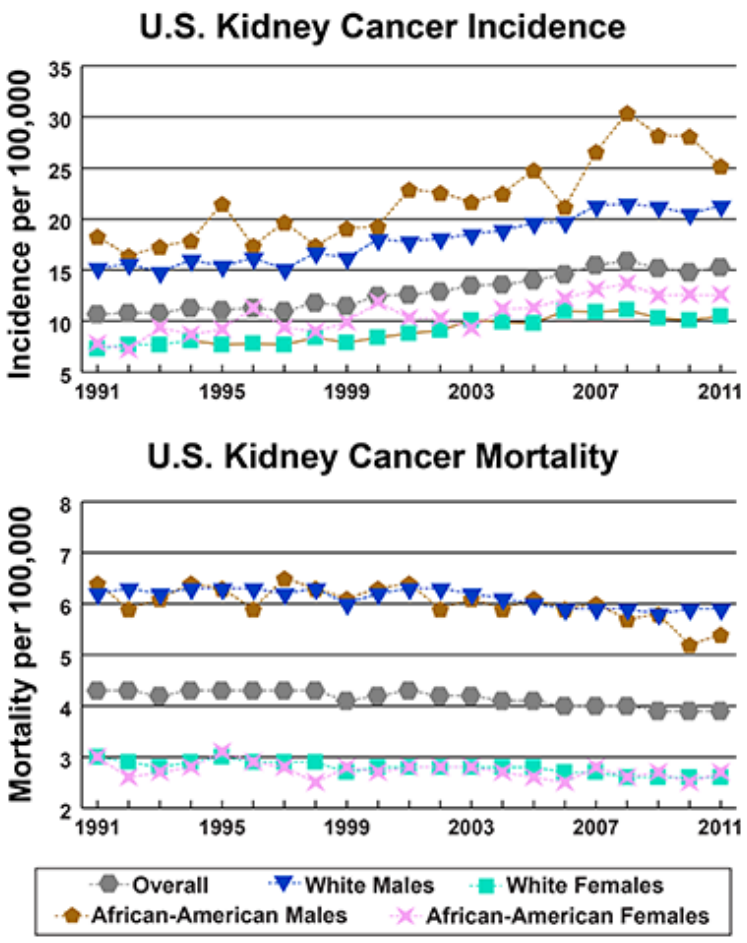
İnsidans ve Epidemiyoloji

- Nearly 66 000 cases of cancers of the kidney and renal pelvis in the USA in 2014[1]
- 13 600 deaths

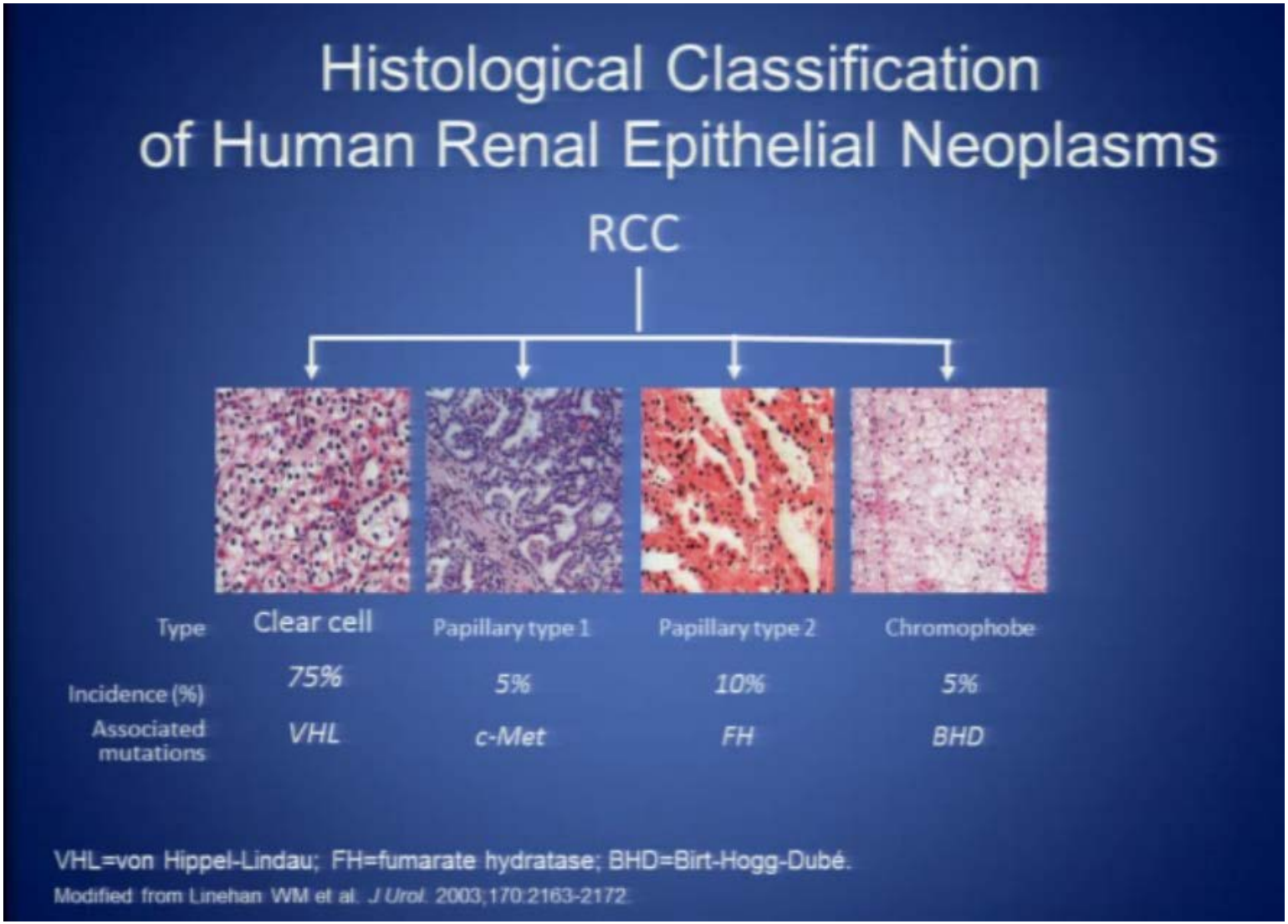
1: Jemal CA Cancer Journal 2014

İnsidans ve Epidemiyoloji



Source: Surveillance, Epidemiology, and End Results (SEER) Program and the National Center for Health Statistics. Additional statistics and charts are available at the SEER Web site.

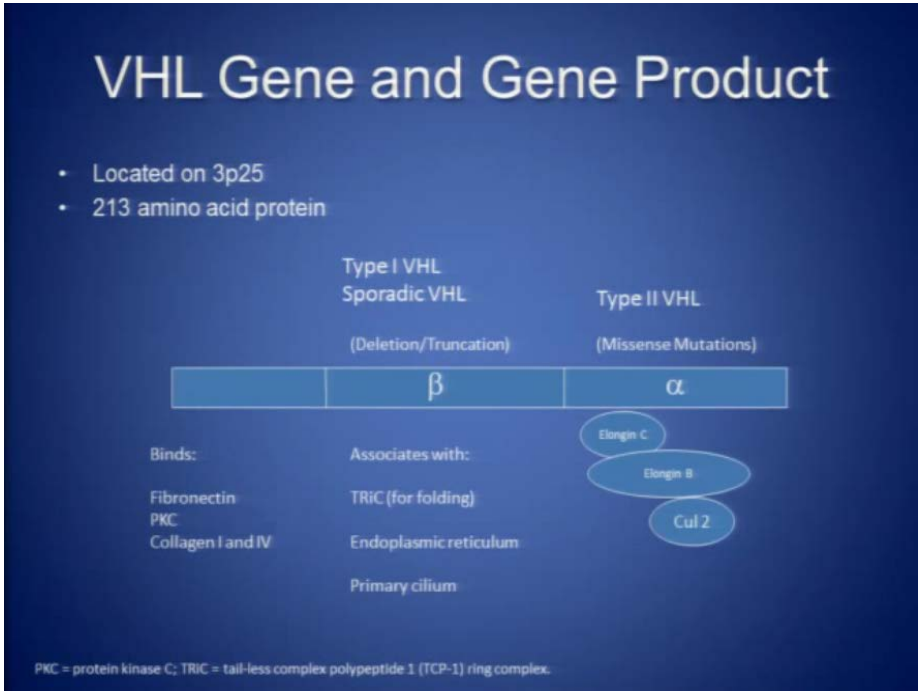
Histolojik Alt Gruplar

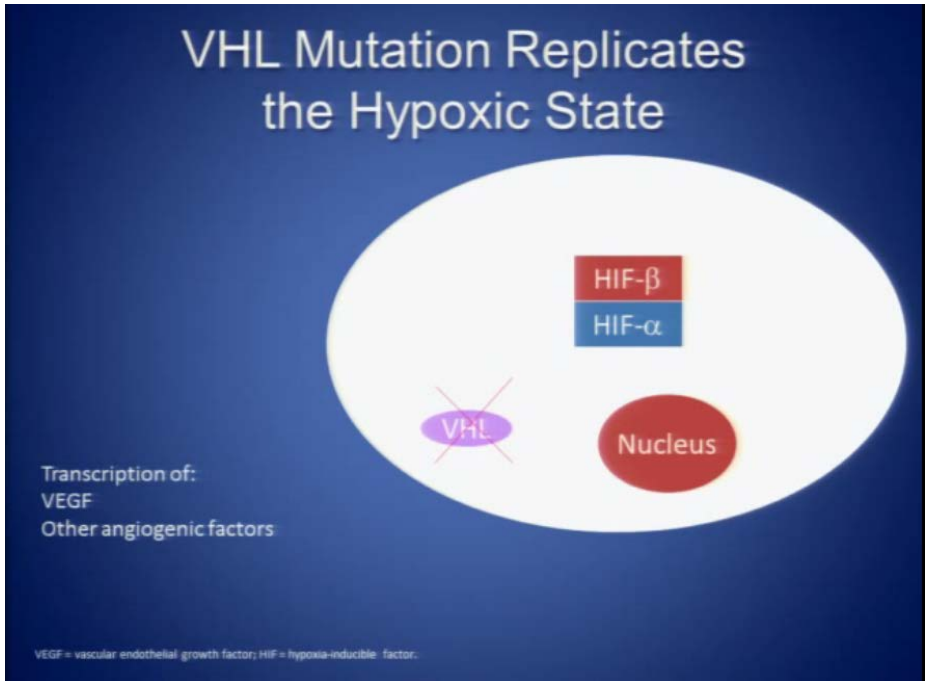


Histolojik Alt Gruplar

Histology	Mutation	Other Key Characteristics
Clear Cell Histology	VHL	• 80% sporadic RCC has somatic VHL mutations • Hemangioblastomas, pheos
Papillary RCC	*c-MET* activating mutation	• Type 1 papillary RCC
RCC with hereditary leimyomatosis	Fumarate hydratase	• Type 2 papillary RCC • Uterine and cutaneous leimomymas
Chromophobe/ Oncocytic RCC	*FLCN* gene (Birt-Hogg-Dubè Syndrome)	Spontaneous pneumothorax

Histolojik Alt Gruplar



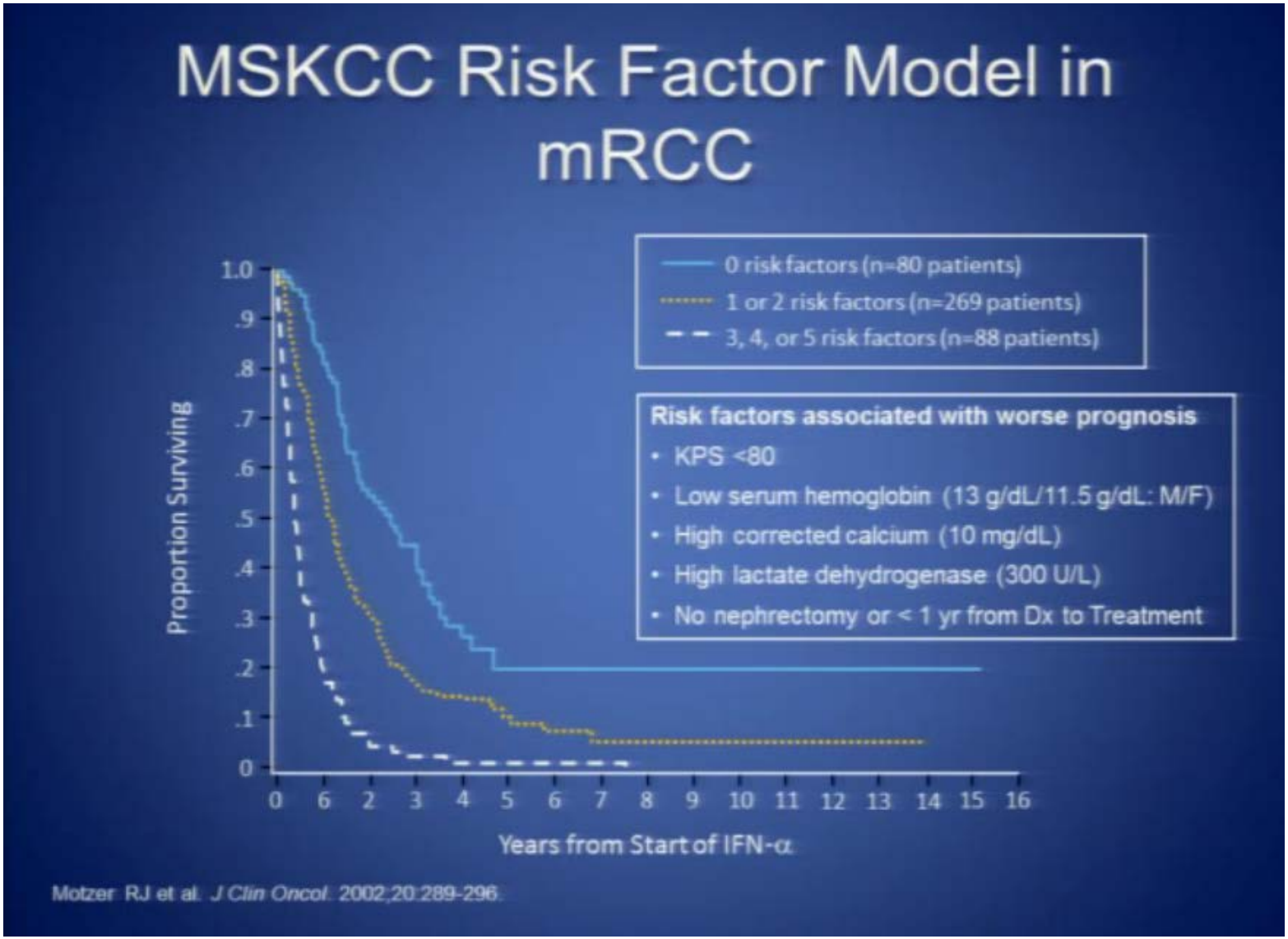


Evreye Göre Sağkalım

American Joint Committee on Cancer (AJCC) 2010 Clinical Staging System

Stage	Description	5-Year Survival (%)
Stage I	T1, N0, M0	95
Stage II	T2, N0, M0	88
Stage III	T1-2, N1 or T3, N0-1	59
Stage IV	T4 (any N or M) or N2 (any T or M) or M1	20

Risk Faktörlerine Göre Sağkalım



Risk Faktörlerine Göre Sağkalım

VOLUME 27 · NUMBER 34 · DECEMBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prognostic Factors for Overall Survival in Patients With Metastatic Renal Cell Carcinoma Treated With Vascular Endothelial Growth Factor–Targeted Agents: Results From a Large, Multicenter Study

Daniel Y.C. Heng, Wanling Xie, Meredith M. Regan, Mark A. Warren, Ali Reza Golshayan, Chakshu Sahi, Bernhard J. Eigl, J. Dean Ruether, Tina Cheng, Scott North, Peter Venner, Jennifer J. Knox, Kim N. Chi, Christian Kollmannsberger, David F. McDermott, William K. Oh, Michael B. Atkins, Ronald M. Bukowski, Brian I. Rini, and Toni K. Choueiri

From the Tom Baker Cancer Center, Calgary; Cross Cancer Institute, Edmonton, Alberta; Princess Margaret Hospital, Toronto, Ontario; British Columbia Cancer Agency, Vancouver, British Columbia, Canada; Harvard School of Public Health; Dana-Farber/Harvard Cancer Center Renal Cancer Program, Dana-Farber Cancer Institute, Beth Israel Deaconess Medical Center, Boston, MA; Medical University of South Carolina, Charleston, SC; and Cleveland Clinic Taussig Cancer Institute, Cleveland, OH.

Submitted December 9, 2008; accepted June 18, 2009; published online ahead of print at www.jco.org on October 13, 2009.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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The Appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF version (via Adobe® Reader®).

A B S T R A C T

Purpose
There are no robust data on prognostic factors for overall survival (OS) in patients with metastatic renal cell carcinoma (RCC) treated with vascular endothelial growth factor (VEGF) –targeted therapy.

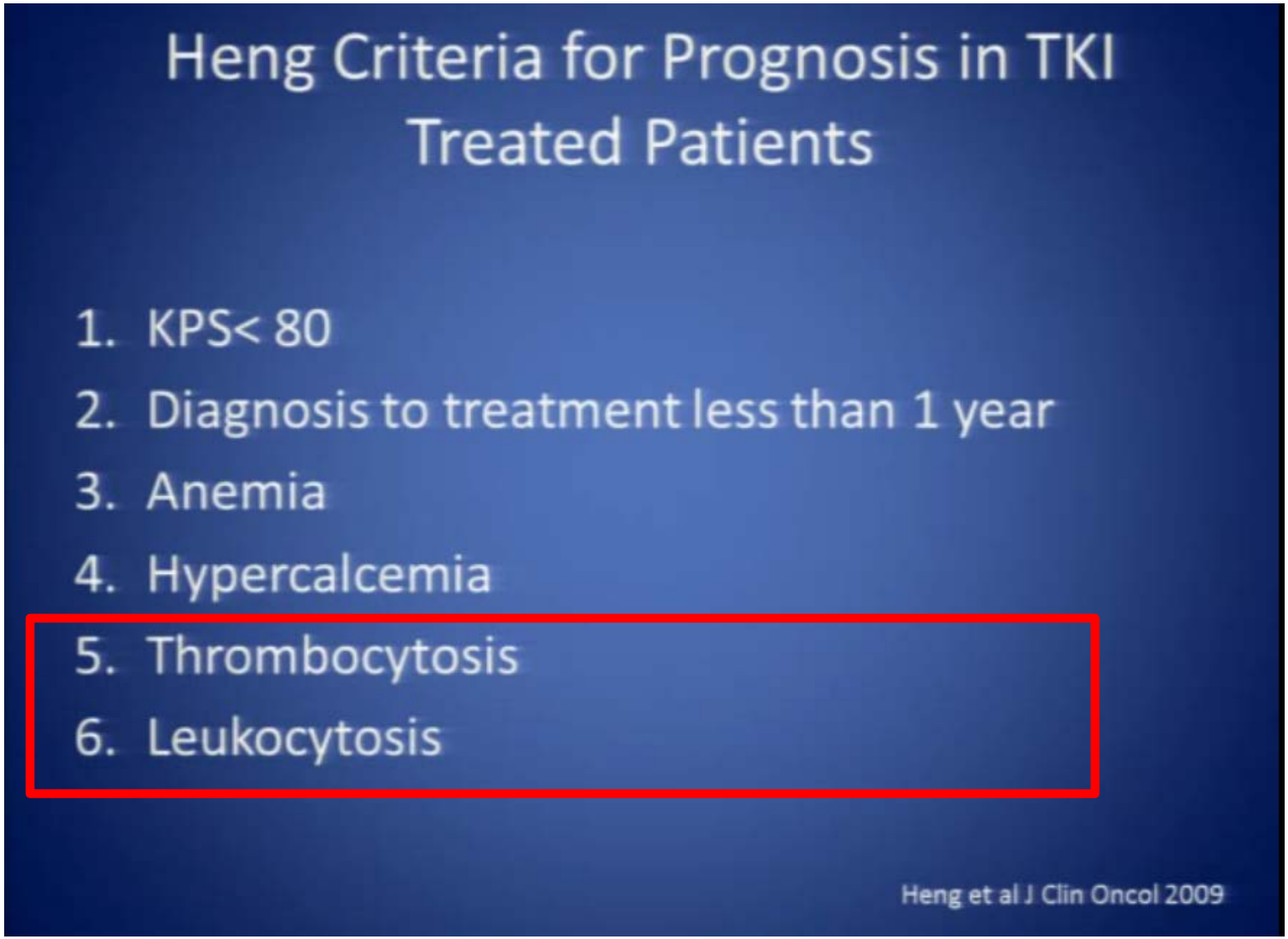
Methods
Baseline characteristics and outcomes on 645 patients with anti-VEGF therapy–naïve metastatic RCC were collected from three US and four Canadian cancer centers. Cox proportional hazards regression, followed by bootstrap validation, was used to identify independent prognostic factors for OS.

Results
The median OS for the whole cohort was 22 months (95% CI, 20.2 to 26.5 months), and the median follow-up was 24.5 months. Overall, 396, 200, and 49 patients were treated with sunitinib, sorafenib, and bevacizumab, respectively. Four of the five adverse prognostic factors according to the Memorial Sloan-Kettering Cancer Center (MSKCC) were independent predictors of short survival: hemoglobin less than the lower limit of normal ($P < .0001$), corrected calcium greater than the upper limit of normal (ULN; $P = .0006$), Karnofsky performance status less than 80% ($P < .0001$), and time from diagnosis to treatment of less than 1 year ($P = .01$). In addition, neutrophils greater than the ULN ($P < .0001$) and platelets greater than the ULN ($P = .01$) were independent adverse prognostic factors. Patients were segregated into three risk categories: the favorable-risk group (no prognostic factors; n = 133), in which median OS (mOS) was not reached and 2-year OS (2y OS) was 75%; the intermediate-risk group (one or two prognostic factors; n = 301), in which mOS was 27 months and 2y OS was 53%; and the poor-risk group (three to six prognostic factors; n = 152), in which mOS was 8.8 months and 2y OS was 7% (log-rank $P < .0001$). The C-index was 0.73.

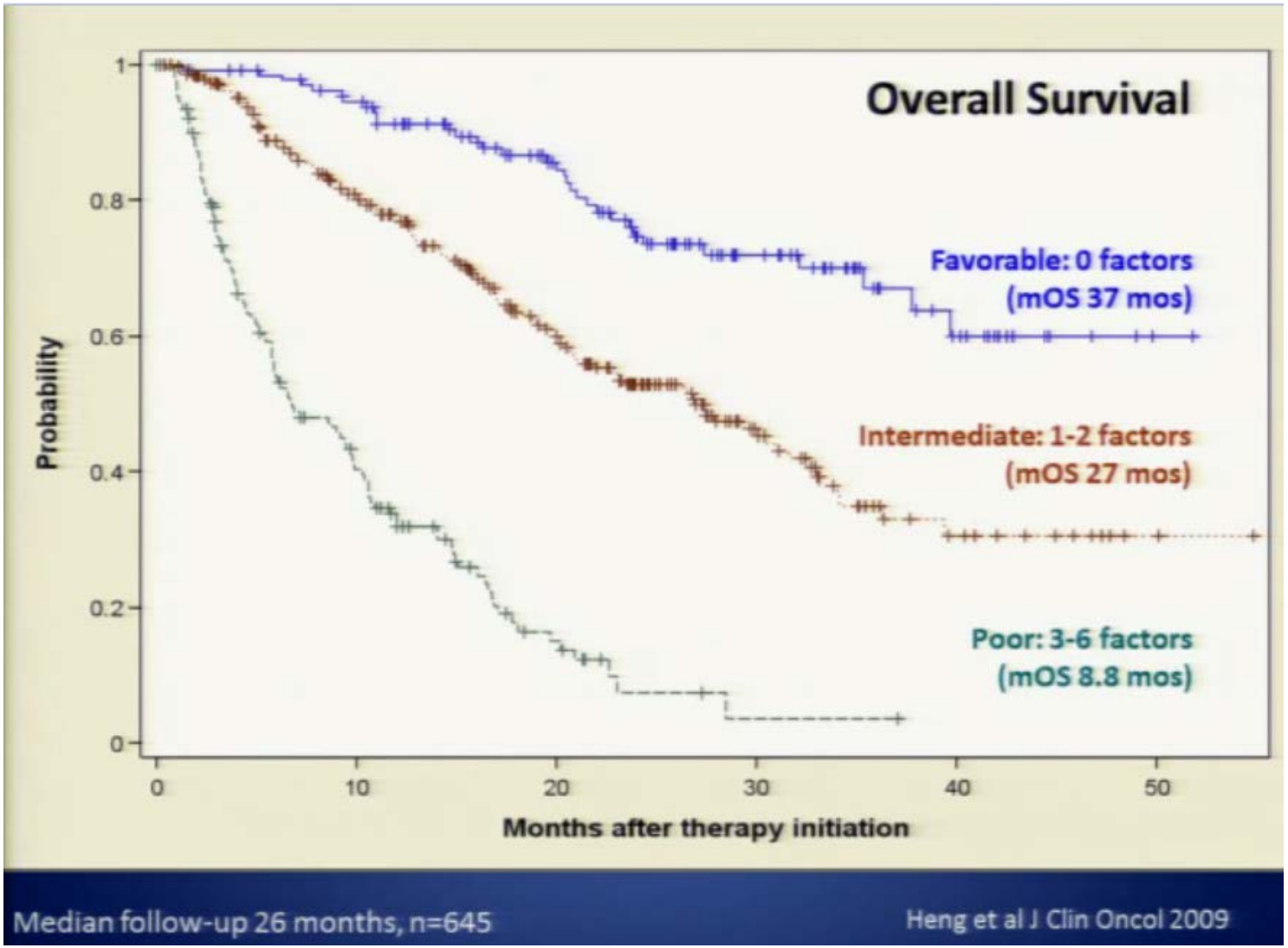
Conclusion
This model validates components of the MSKCC model with the addition of platelet and neutrophil counts and can be incorporated into patient care and into clinical trials that use VEGF-targeted agents.

J Clin Oncol 27:5794-5799. © 2009 by American Society of Clinical Oncology

Risk Faktörlerine Göre Sağkalım



Risk Faktörlerine Göre Sağkalım



Sağ yan ağrısı ile başvuran kadın hasta

- 48 yaşında, kadın hasta, ev hanımı
- Sağ yan ağrısı ile başvurdu
- Bilinen hastalık öyküsü yok
- Aile öyküsünde bilinen özelik yok
- Sigara, alkol alışkanlığı yok
- Sürekli kullandığı ilaç yok
- 3. doğum sezaryen ile yapılmış

Toraks-Batın BT

- Akciğerde en büyüğü 18x14 mm olan multiple nodüler metastaz
- Sağ böbrekte 136X129X103 mm RCC ile uyumlu kitle
- Vena kava inferiorda kalbe uzanım gösteren trombüs

Metastatik Papiller Tip 2 Renal cell ca, Akciğer Metastazı

- Vena kava inferior da trombus ve operasyonun mortalitesi nedeniyle nefrektomi yapılmadı
- Tru-cut bx: Papiler tip 2 renal cell karsinom ile uyumlu olarak geldi.

Metastatik Papiller Tip 2 Renal Karsinom, Akciğer Metastazı

- Sol yan ağrısı dışında semptom yok(ECOG PS 1)
- Karaciğer enzimleri; yalnız ALP 2 kat artmış olarak saptandı.
- WBC; 9.2X10^3 , Plt; 245X10^3, Hgb; 10.4 mg/dl, Htc; 31
- Albumin: 3.8, Ca++: 10.1, LDH: 212
- Üre : 23, kreatin 1.12, elektrolit imbalansı yok
  Boy; 1.73, Ağırlığı; 78 kg olarak saptandı.
- GFR: 60.8 ml/dak.

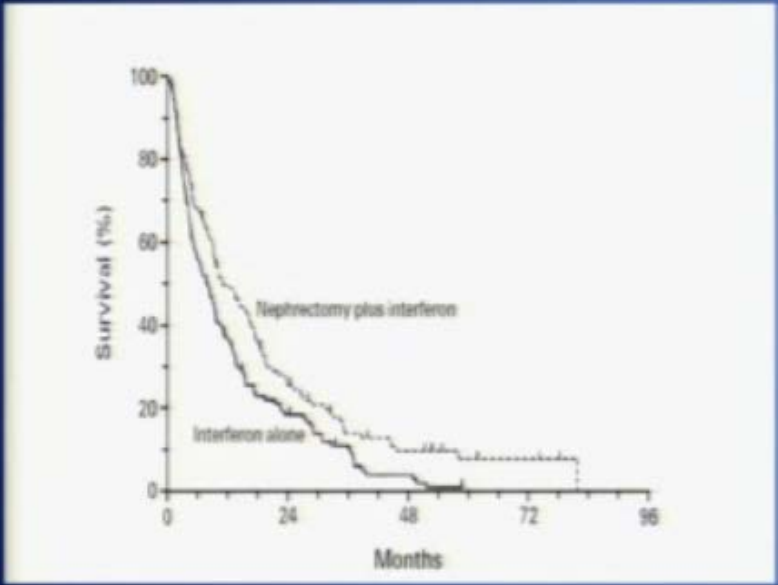
MSKCC=1 RİSK FAKTÖRÜ ORTA RİSK GURUBU

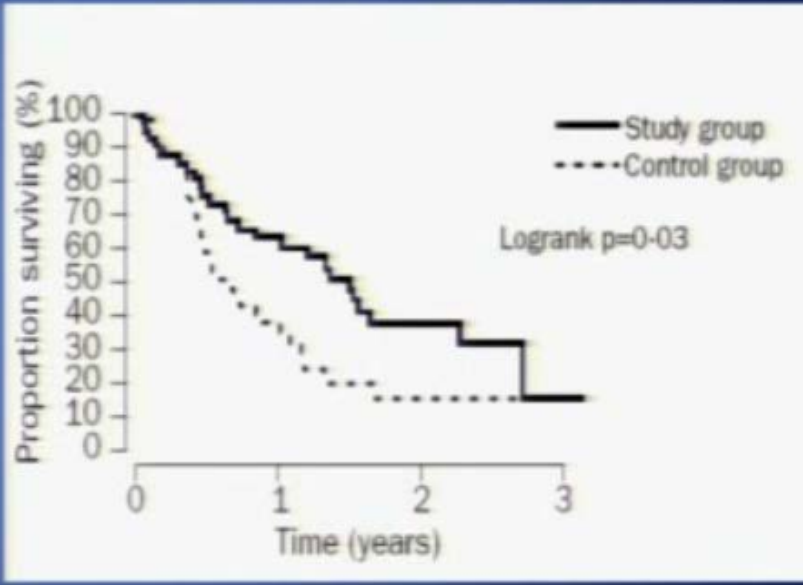
Metastatik Papiller Tip 2 Renal Karsinom, Akciğer Metastazı

- Nefrektomi ?
- Hangi Tedavi; TKİ? mTOR, Bevacizumab+ İFN? kemoterapi?, Erlotinib?, Klinik Çalışma?
- TKİ başlanacaksa, Hangi TKİ? mTOR başlanacaksa hangi mTOR?

Metastatik Renal cell ca, Nefrektomi?

Nephrectomy Followed by Interferon Alpha Improves Survival





Flanigan *et al*, NEJM 345, 23: 1655-9.

Mickisch *et al*, Lancet 2001; 358: 966–70

Metastatik Renal cell ca, Nefrektomi?

Absolute Benefit Diminishes in Poor Risk Groups

TABLE 2. SURVIVAL IN SUBGROUPS DEFINED ACCORDING TO STRATIFICATION FACTORS.

CATEGORY	MEDIAN SURVIVAL		1-YR SURVIVAL		P VALUE*
	INTERFERON ALONE	NEPHREC-TOMY PLUS INTERFERON	INTERFERON ALONE	NEPHREC-TOMY PLUS INTERFERON	
	mo		%		
Not stratified	8.1	11.1	36.8	49.7	0.012
Stratification factor					
Measurable disease					0.010
Yes	7.8	10.3	34.7	46.6	
No	11.2	16.4	43.1	63.6	
Performance status†					0.080
0	11.7	17.4	49.2	63.6	
1	4.8	6.9	28.2	32.5	
Type of metastases					0.008
Lung only	10.3	14.3	41.5	58.5	
Other	6.3	10.2	34.6	45.1	

*P values for the comparison of median survival between groups were derived with the log-rank test.

Flanigan *et al*, NEJM 345, 23: 1655-9.

Metastatik Renal cell ca, Nefrektomi?

Table 1 Phase III trials of IFN-α with nephrectomy

Trial	No. patients	Median survival (months)			Response to therapy (%)			Unable to receive post-surgery immunotherapy *n* (%)	Operative Mortality no. (%)
		IFN alone	Surgery + IFN	*P*	IFN alone	Surgery + IFN	*P*		
SWOG 8949[6]	241	8.1	11.1	0.05	3.3	3.6	NS	NR	1 (0.8)
EORTC 30957[7]	85	7	17	0.03	12	19	0.38	NR	1 (2.4)
Combined analysis[26]	331	7.8	13.6	0.002	5.7	6.9	0.60	9 (5.6)	2 (1.4)

EORTC, European Organization for the Research and Treatment of Cancer; IFN, interferon; NR, not reported; NS, not significant; SWOG, Southwest Oncology Group.

Anthony J Polcari , et al, International Journal of Urology 2009

Metastatik Renal cel ca Kanserler, Nefrektomi?

J Urol. 2011 Jan;185(1):60-6. doi: 10.1016/j.juro.2010.09.012. Epub 2010 Nov 12.

The impact of cytoreductive nephrectomy on survival of patients with metastatic renal cell carcinoma receiving vascular endothelial growth factor targeted therapy.

Choueiri TK[1], Xie W, Kollmannsberger C, North S, Knox JJ, Lampard JG, McDermott DF, Rini BI, Heng DY.

⊕ Author information

Abstract

PURPOSE: Vascular endothelial growth factor targeted therapy is a standard of care in patients with metastatic renal cell carcinoma. The role of cytoreductive nephrectomy in the era of novel agents remains poorly defined.

MATERIALS AND METHODS: We retrospectively reviewed baseline characteristics and outcomes of 314 patients with anti-vascular endothelial growth factor therapy naïve, metastatic renal cell carcinoma from United States and Canadian cancer centers to study the impact of cytoreductive nephrectomy on overall survival.

RESULTS: Patients who underwent cytoreductive nephrectomy (201) were younger ($p < 0.01$), and more likely to have a better Karnofsky performance status ($p < 0.01$), more than 1 site of metastasis ($p = 0.04$) and lower corrected calcium levels ($p < 0.01$) compared to those who did not undergo cytoreductive nephrectomy (113). On univariable analysis cytoreductive nephrectomy was associated with a median overall survival of 19.8 months compared to 9.4 months for patients who did not undergo cytoreductive nephrectomy (HR 0.44; 95% CI 0.32, 0.59; $p < 0.01$). On multivariable analysis and adjusting for established prognostic risk factors the overall survival difference persisted (adjusted HR 0.68; 95% CI 0.46, 0.99; $p = 0.04$) in favor of the cytoreductive nephrectomy group. In subgroup analyses stratified for favorable/intermediate/poor risk criteria, patients in the poor risk group had a marginal benefit ($p = 0.06$). Similarly patients with Karnofsky performance status less than 80% also had a marginal survival benefit ($p = 0.08$).

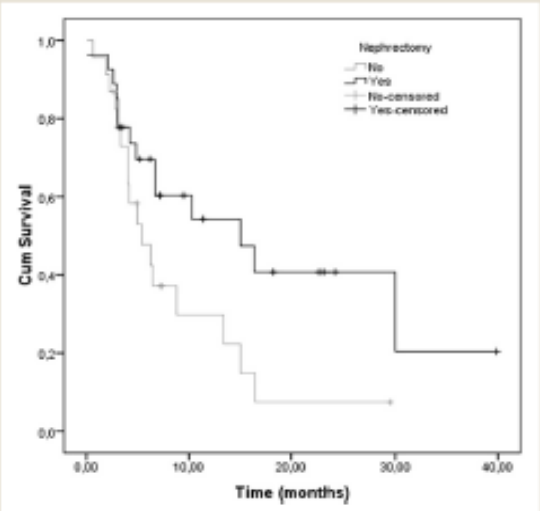
CONCLUSIONS: In this retrospective study cytoreductive nephrectomy was independently associated with a prolonged overall survival of patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor targeted agents, although the benefit is marginal in those patients with poor risk features.

Metastatik Renal cel ca Kanserler, Nefrektomi?

Original Study

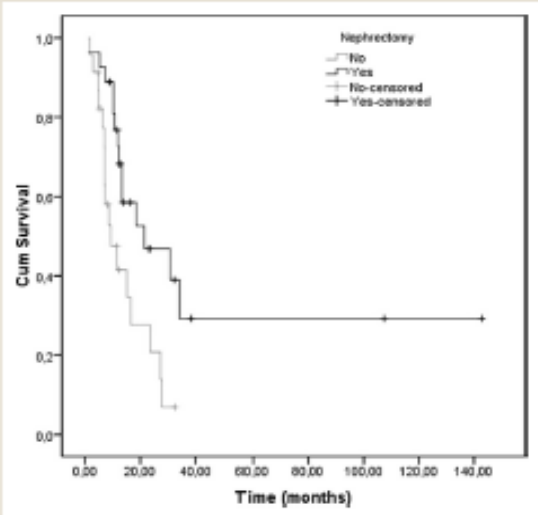
The Necessity of Cytoreductive Nephrectomy in Patients With Metastatic Renal Cell Carcinoma Using Antiangiogenic Targeted Therapy After Interferon Alfa-2b

Figure 2 Overall Survival Curves From the Date of Starting TKI for CRN (+) and (−) Groups (P = .034)



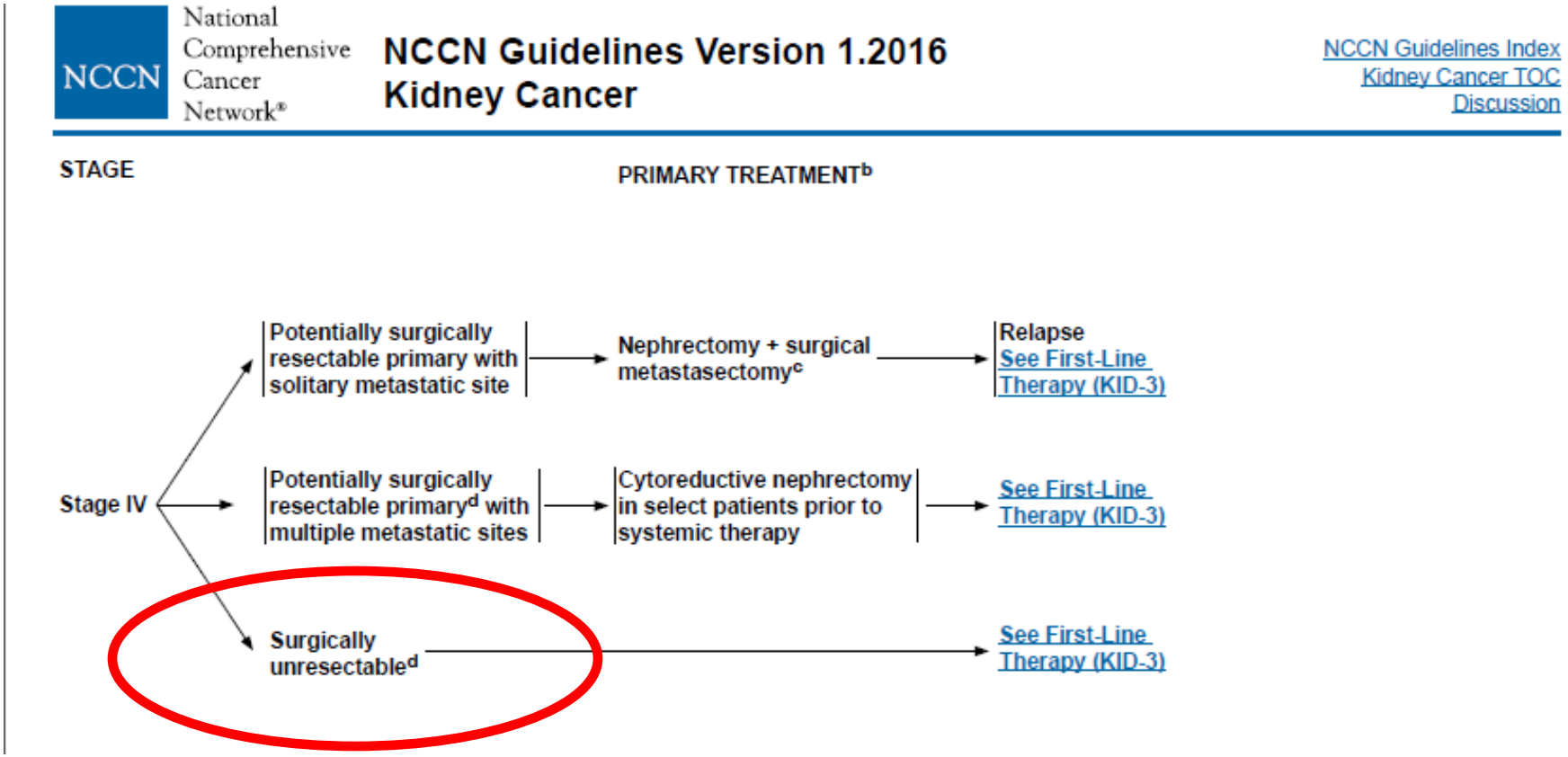
Abbreviations: CRN — Cytoreductive Nephrectomy; Cum — Cumulative; TKI — Tyrosine Kinase Inhibitors.

Figure 4 Overall Survival Curves From Diagnosis for CRN (+) and (−) Groups (P = .008)

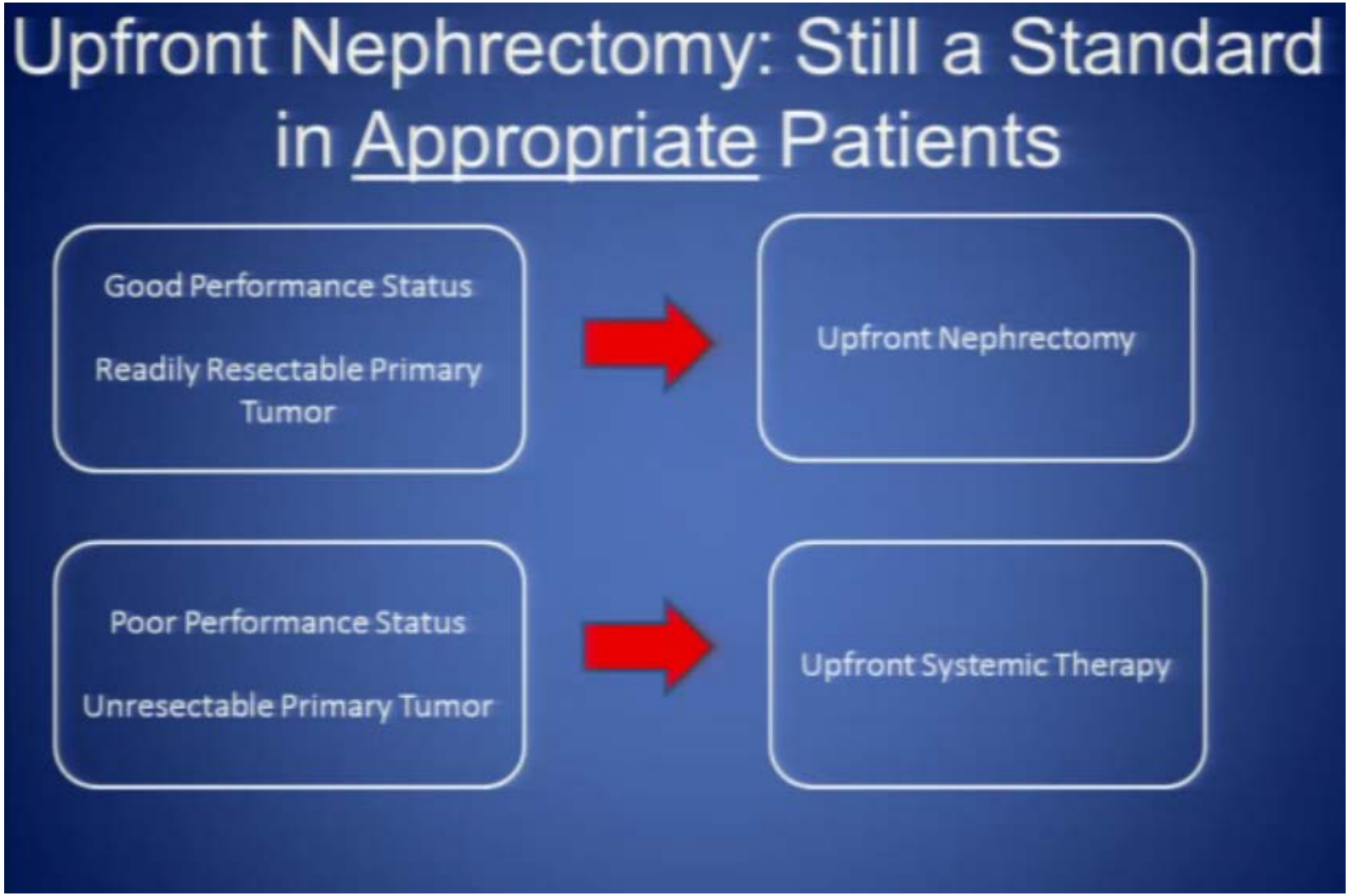


Abbreviations: CRN — Cytoreductive nephrectomy; Cum — Cumulative.

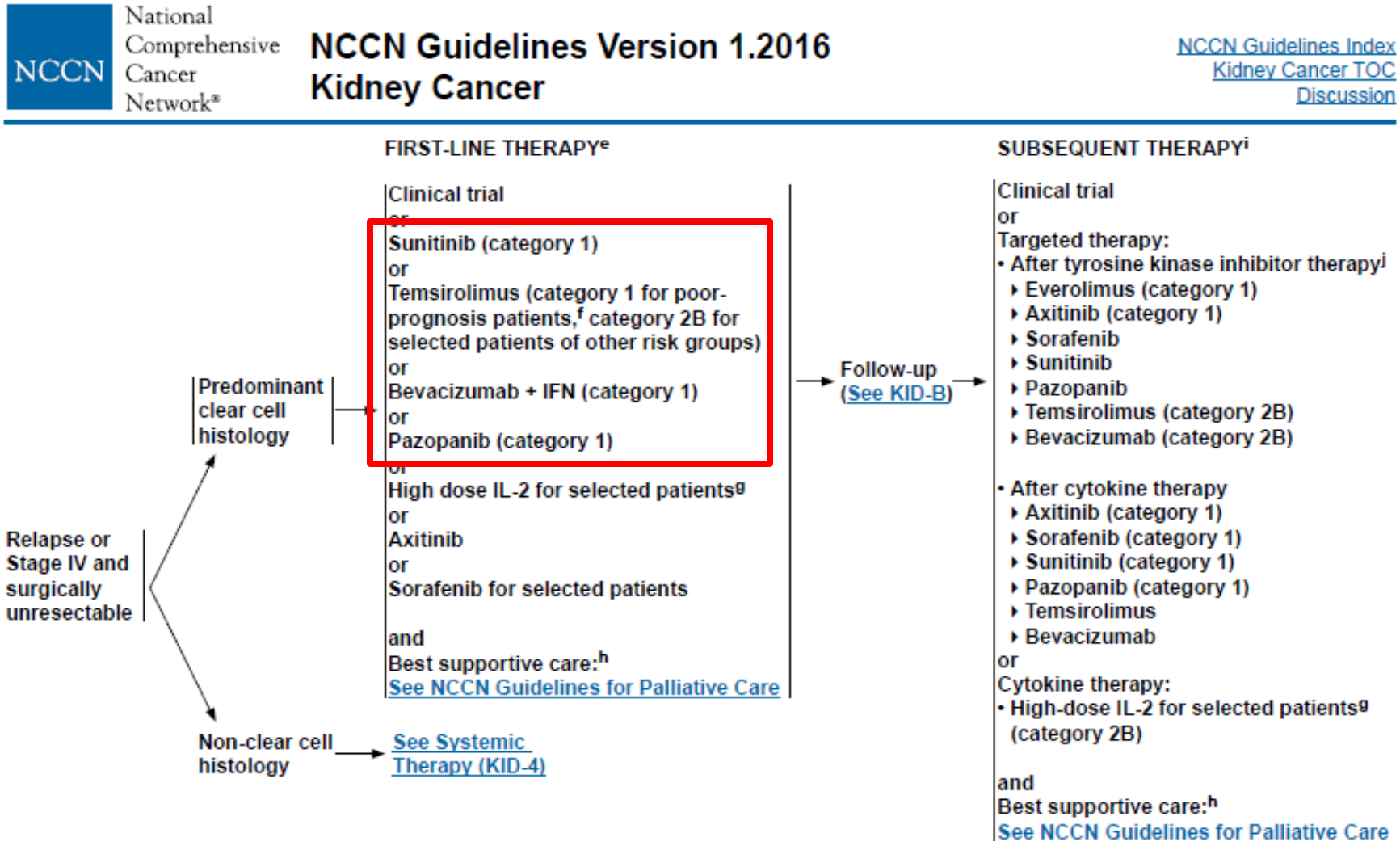
Metastatik Renal cell ca, Nefrektomi?



Metastatik Renal Kanserler, Nefrektomi?



Metastatik Renal cell ca, Tedavi Seçenekleri



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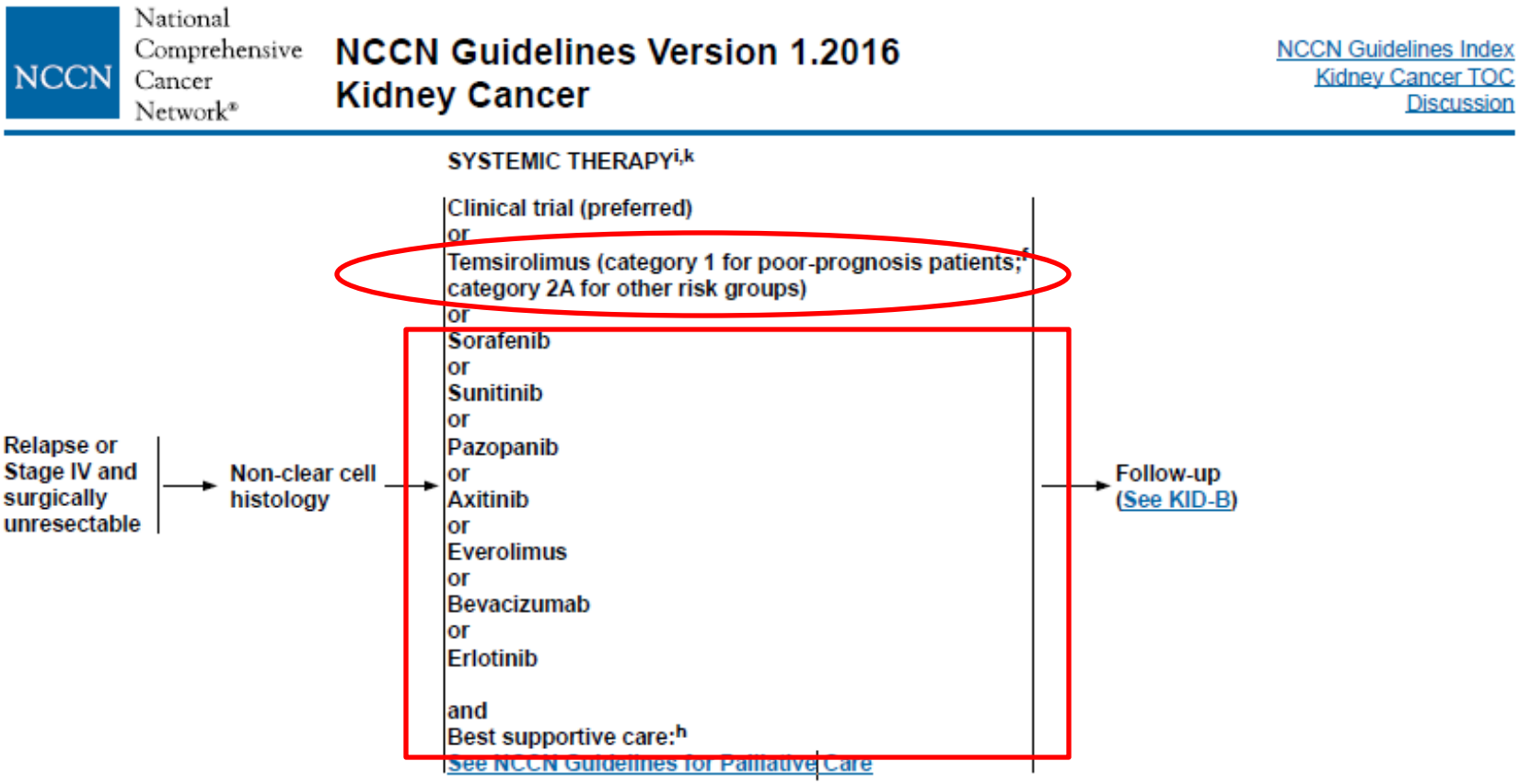


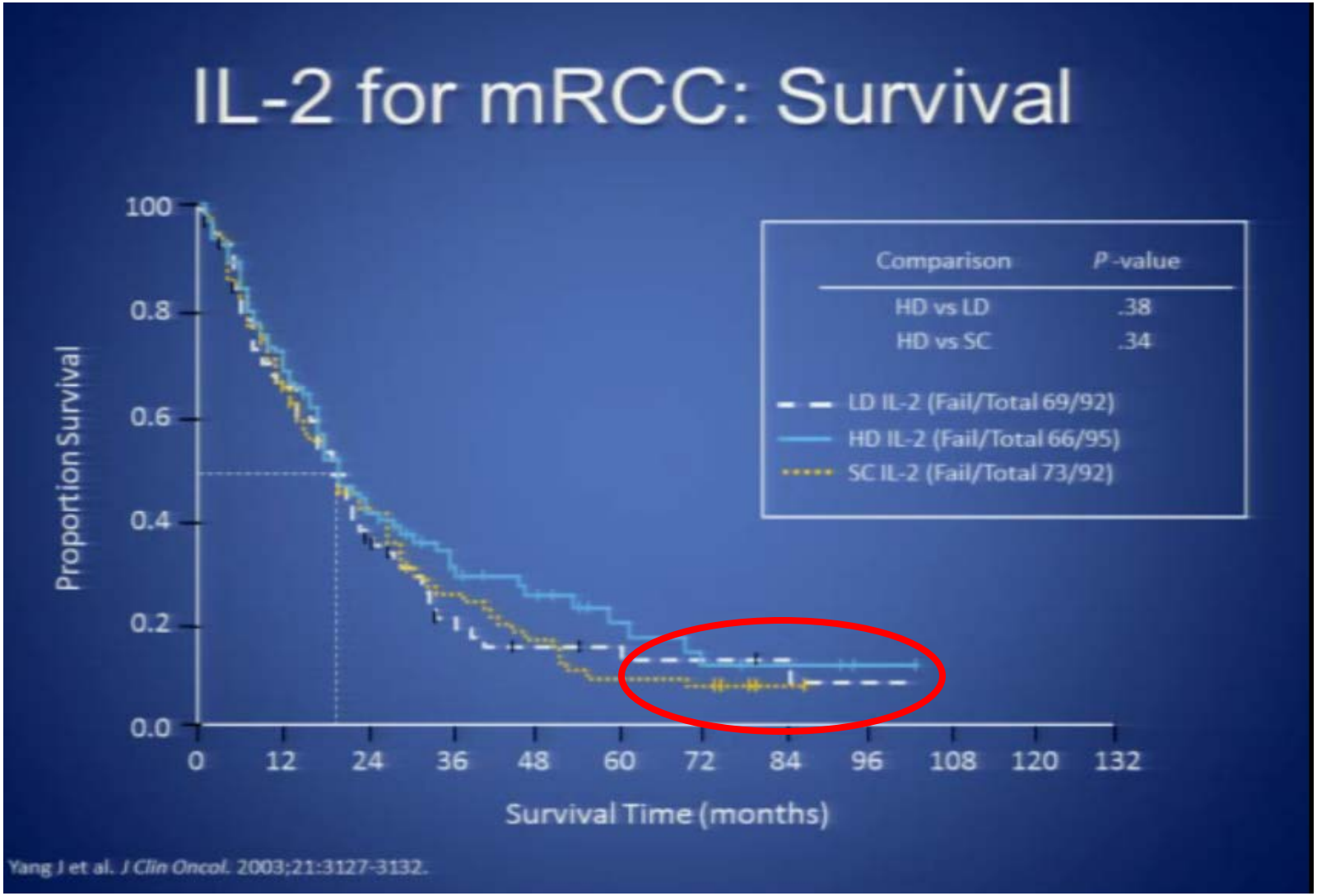
Metastatik Renal cell ca, Tedavi Seçenekleri

IL-2 for mRCC: Response

	HD IL-2 (720,000 IU/kg)	LD IL-2 (72,000 IU/kg)	SC IL-2 (250,000 IU/kg d1-5, 125,000 IU/kg 5x/wk)
Evaluable (n)	155	149	93
CR	6%	1%	2%
PR	14%	9%	8%
Major RR	**21%**	13%	**10%**

Yang J et al. *J Clin Oncol.* 2003;21:3127-3132.

Metastatik Renal Kanserler, Tedavi Seçenekleri



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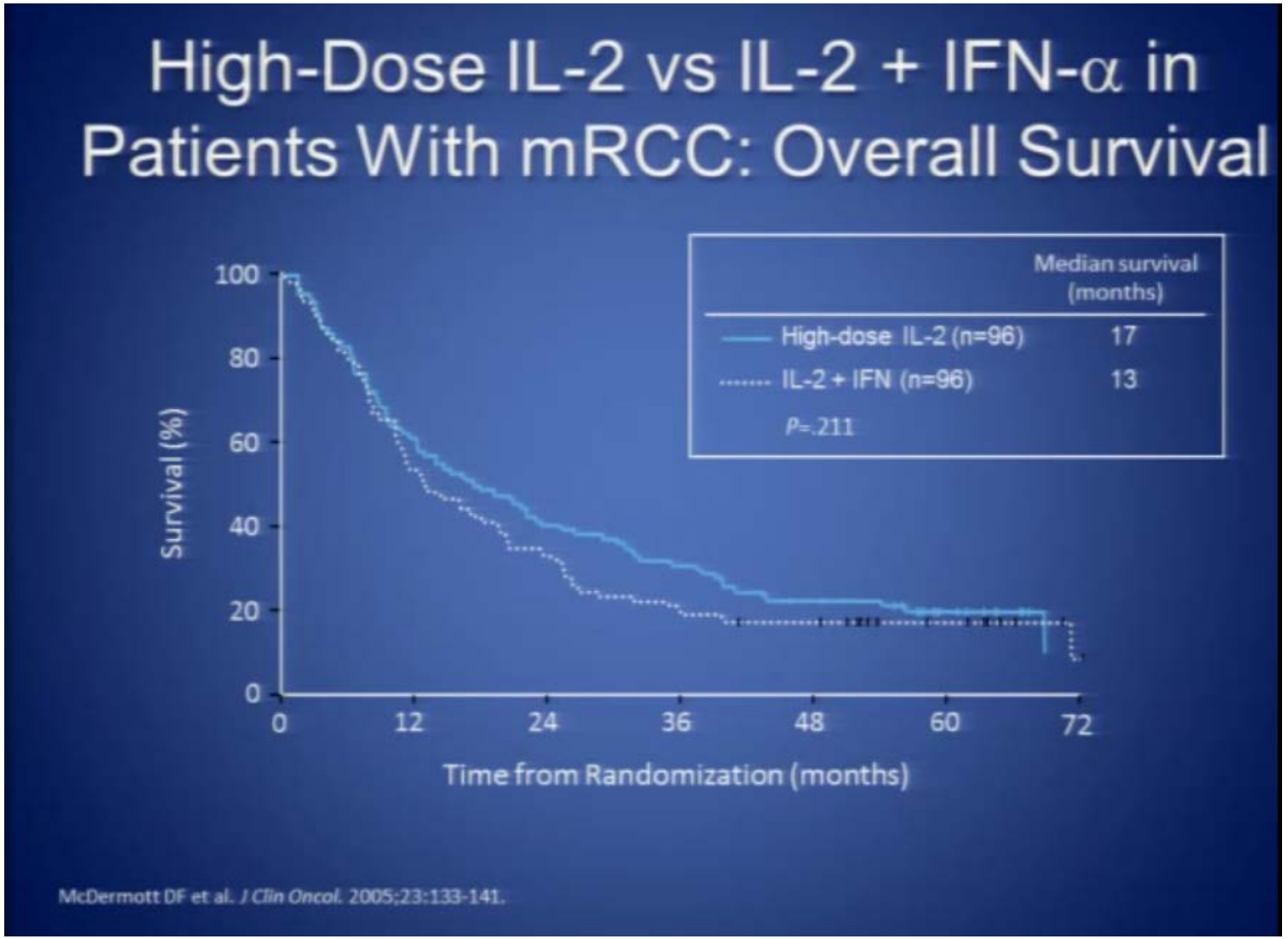


Metastatik Renal Kanserler, Tedavi Seçenekleri

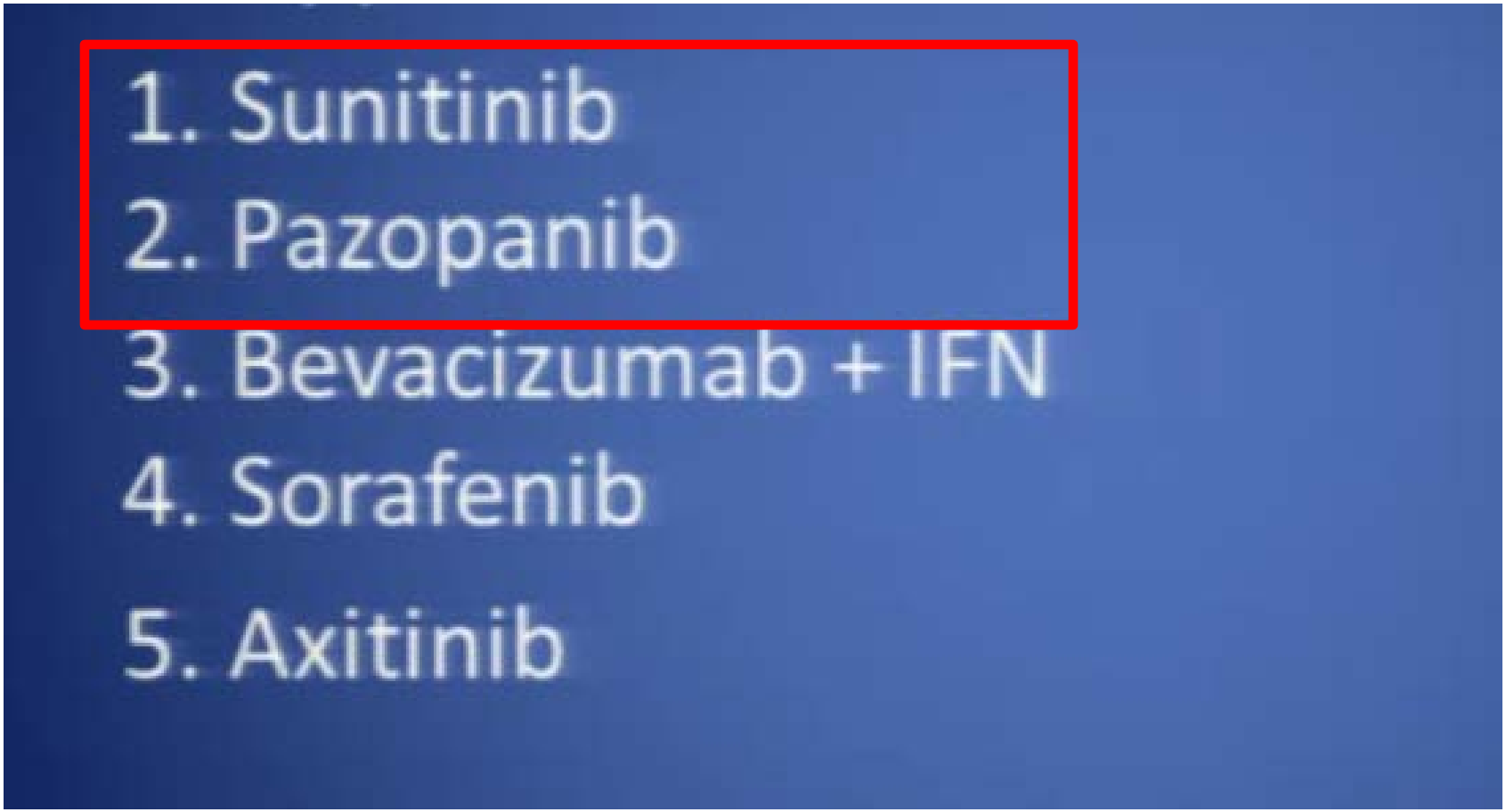
Cytokine Therapy for RCC: Summary

HD IL-2

- 15% ORR in stage IV patients, with 5% CR[3]
- No OS improvement likely due to small number who truly benefit.
- Remains a choice for fit patients with good performance status, clear cell RCC, minimal disease burden.

1. Krown SE. *Cancer*. 1987;59:647-651.
2. Muss HB. *Semin Oncol*. 1988;15:30-34.
3. Rosenberg SA et al. *JAMA*. 1994;271:907-913.

Metastatik Renal Kanserler, Tedavi Seçenekleri
VEGF Yollağı İnhibitörleri

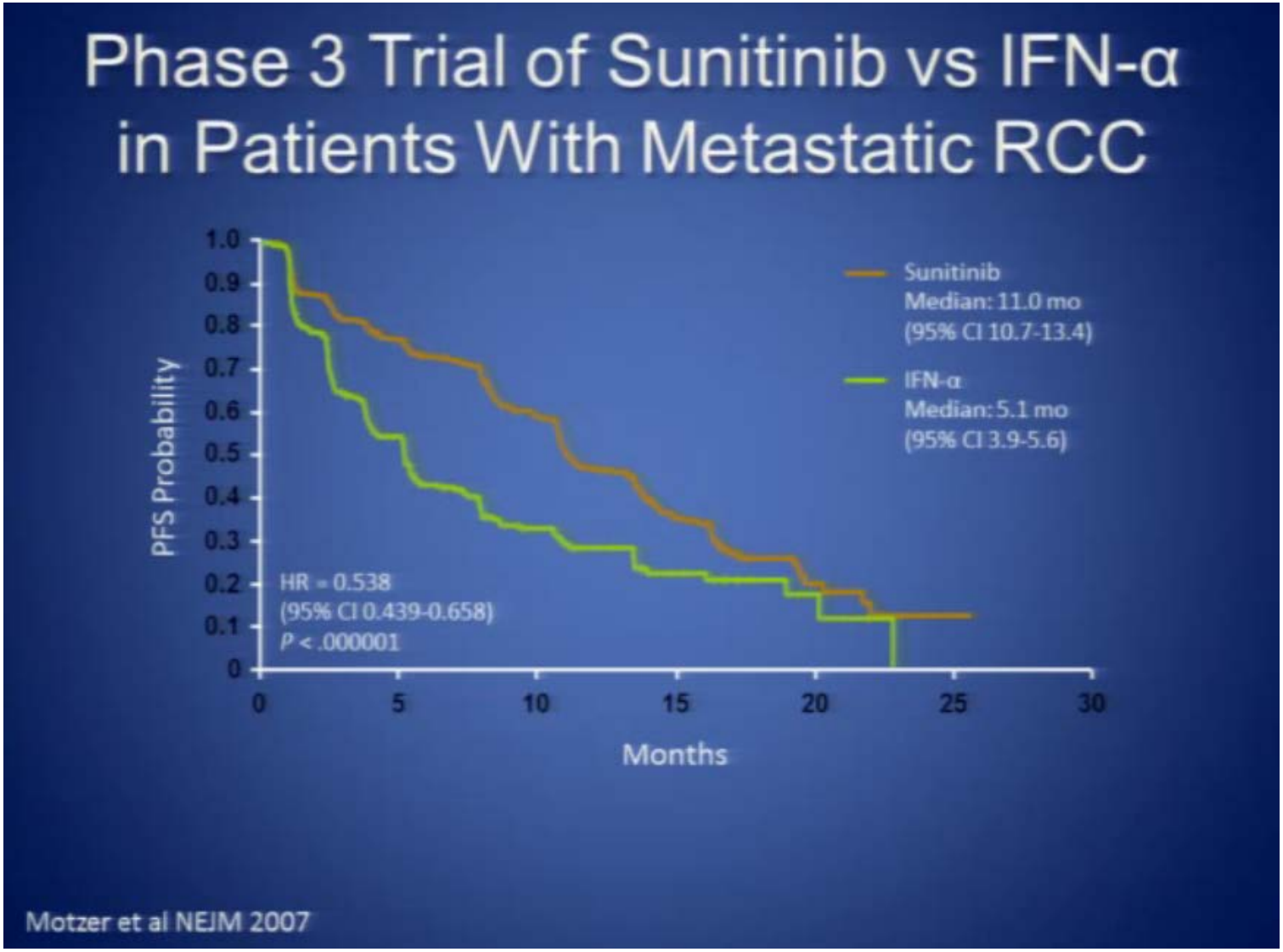


Metastatik Renal Kanserler, Tedavi Seçenekleri

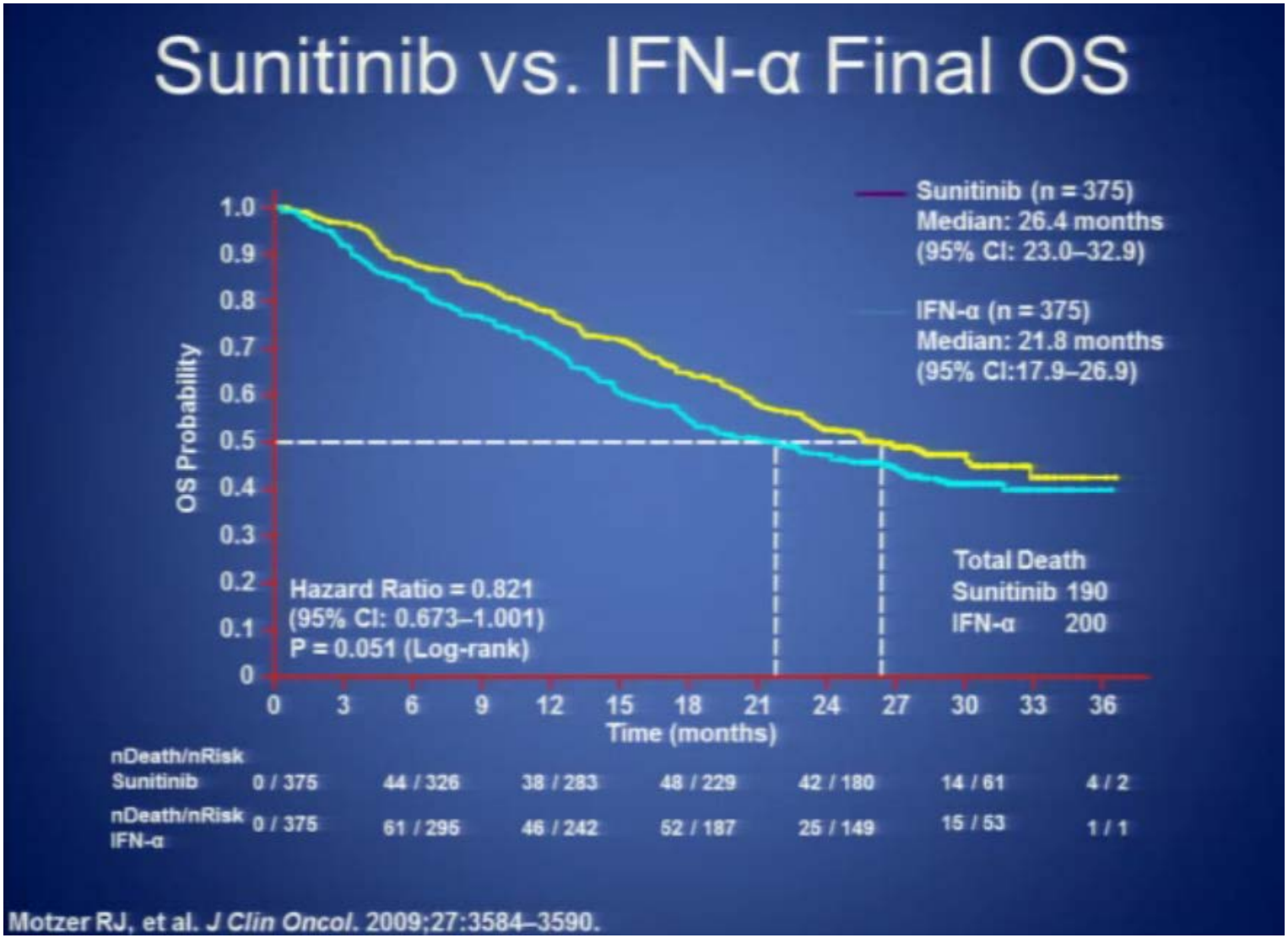
Sunitinib

- Oral, small molecule inhibitor of VEGFR, PDGFR, and other receptor tyrosine kinases.
- Administered 50mg PO daily, four weeks on, two off.
- FDA approved for advanced RCC January 2006.

Metastatik Renal cell ca, Tedavi Seçenekleri



Metastatik Renal cell ca, Tedavi Seçenekleri



Metastatik Renal cell ca, Tedavi Seçenekleri

Table 3. Results of an Analysis of OS by Individual Baseline Factors

Factor	OS		
	HR	95% CI	*P*
Treatment (sunitinib *v* IFN-α)	0.764	0.623 to 0.936	.0096
ECOG PS (0 *v* 1)	0.515	0.417 to 0.636	< .0001
Hemoglobin (≥ *v* < LLN)	0.504	0.401 to 0.634	< .0001
Time from diagnosis to treatment (≥ *v* < 1 year)	0.574	0.461 to 0.715	< .0001
Corrected calcium (≤ *v* > 10 mg/dL)	0.466	0.327 to 0.664	< .0001
Alkaline phosphatase (≤ *v* > ULN)	0.676	0.542 to 0.844	.0005
Lactate dehydrogenase (≤ *v* > 1.5× ULN)	0.500	0.337 to 0.742	.0006
No. of metastatic sites (1 *v* ≥ 2)	0.664	0.503 to 0.876	.0037

Abbreviations: OS, overall survival; HR, hazard ratio; IFN-α, interferon alfa; ECOG PS, Eastern Cooperative Oncology Group performance status; LLN, lower limit of normal; ULN, upper limit of normal.

Table 4. Poststudy Cancer Treatment

Treatment	Sunitinib (n = 323)		IFN-α (n = 359)*	
	No. of Patients	%	No. of Patients	%
Any poststudy treatment	182	56	213	59
Sunitinib†	36	11	117	33
Other VEGF inhibitors	106	33	115	32
Cytokines	63	20	47	13
mTOR inhibitors	28	9	16	4
Chemotherapy	21	6	20	6

Abbreviations: IFN-α, interferon alfa; VEGF, vascular endothelial growth factor; mTOR, mammalian target of rapamycin.
*Includes patients who crossed over to sunitinib on study before discontinuation.
†$P < .001$ for the comparison between the sunitinib group and the IFN-α group.

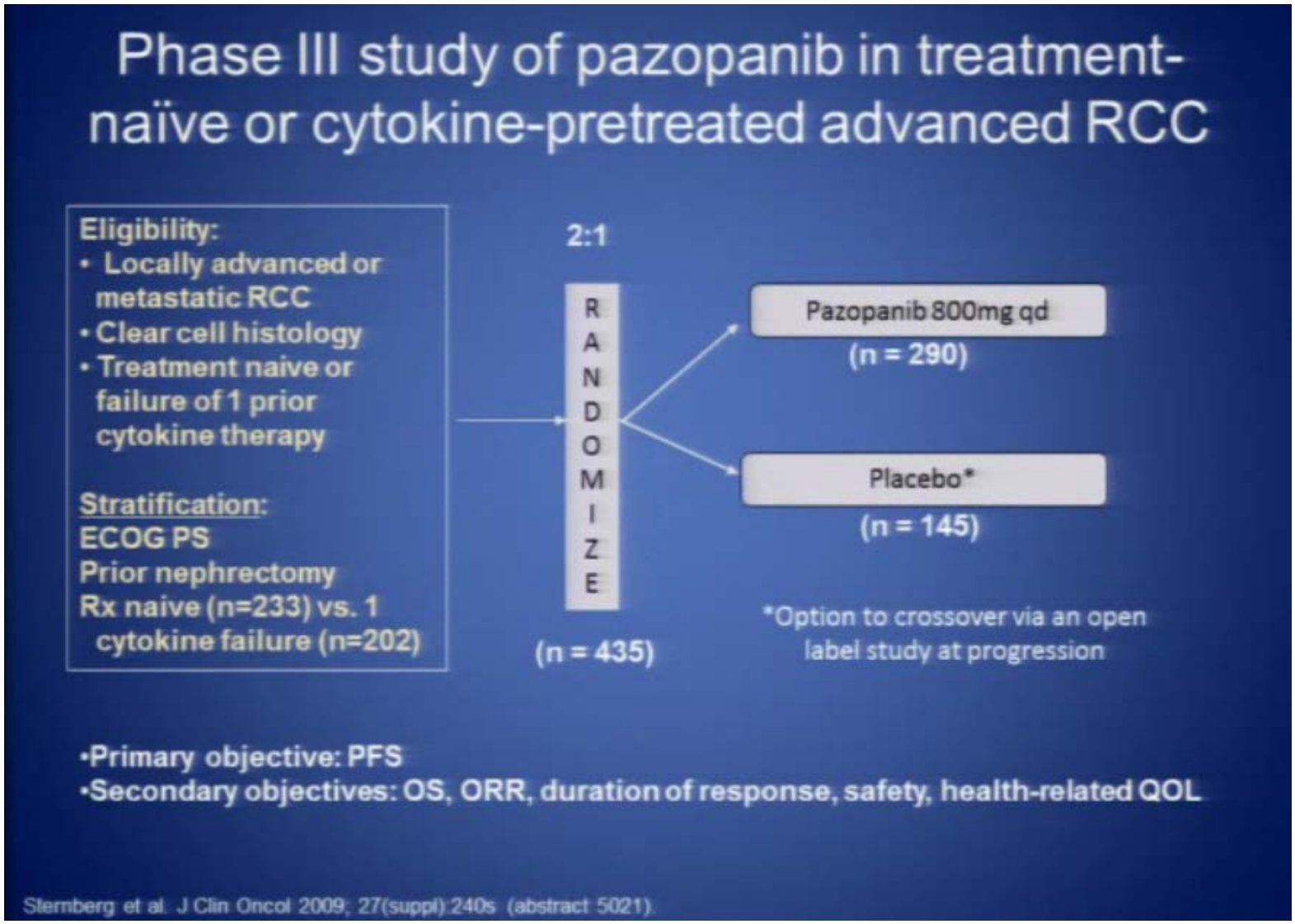
Robert J. Motzer, et al, JCO 2009

Metastatik Renal cell ca, Tedavi Seçenekleri

Pazopanib

- Oral, small molecule inhibitor of VEGFR, PDGFR, and other receptor tyrosine kinases.
- Administered 800mg PO daily, continuous.
- FDA approved for advanced RCC October 2009.

Metastatik Renal cell ca, Tedavi Seçenekleri



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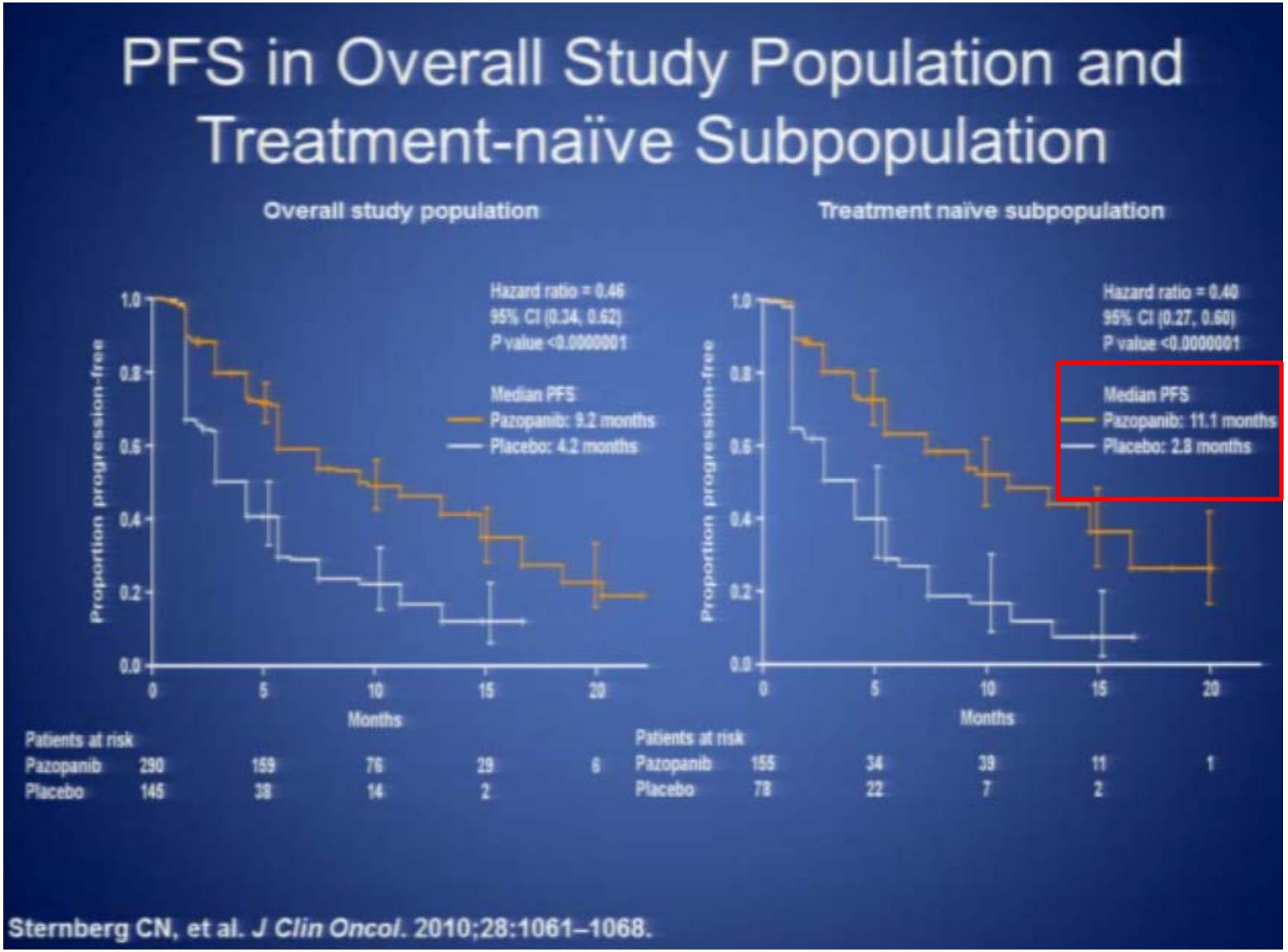


Metastatik Renal cell ca, Tedavi Seçenekleri

Phase III study of pazopanib in treatment-naïve or cytokine-pretreated advanced RCC: Efficacy

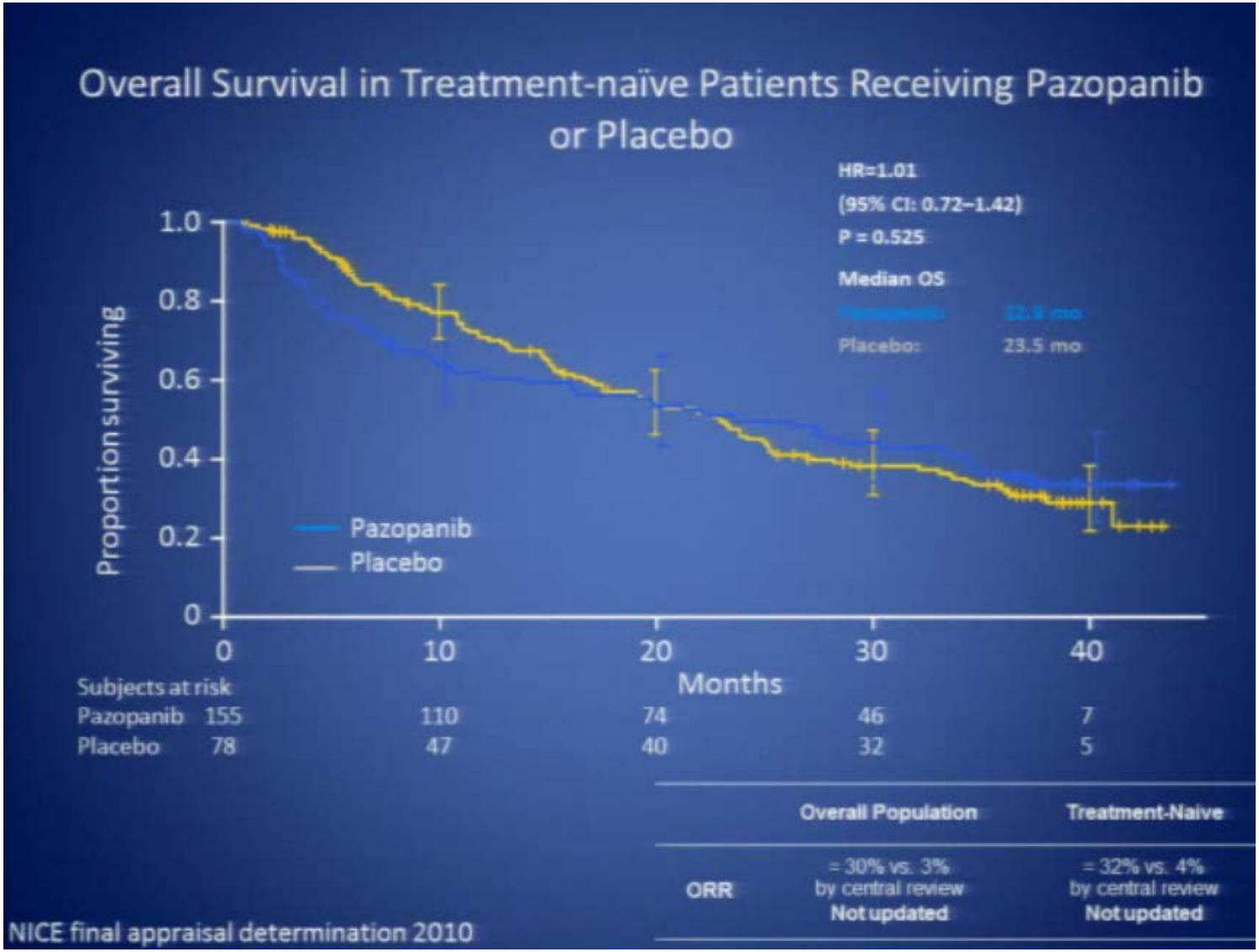
Patient population	placebo (n=145)	pazopanib (n=290)	HR	*P* Value
ORR (%)				
Overall population	3	30	NR	NR
Treatment-naïve*	4	32	NR	NR
Cytokine-pretreated†	3	29	NR	NR
Median PFS (months)				
Overall population	4.2	9.2	0.46 (0.34-0.62)	<.0000001
Treatment-naïve*	2.8	11.1	0.40 (0.27-0.60)	<.0000001
Cytokine-pretreated†	4.2	7.4	0.54 (0.35-0.84)	<.001
Median OS (months)	18.7	21.1	0.73 (0.47-1.12)	.02‡

* n = 78 for placebo and 155 for pazopanib; † n = 67 for placebo and 135 for pazopanib
‡ one-sided *P* value

- **48% of patients on placebo arm received pazopanib at disease progression**

Sternberg et al. J Clin Oncol 2009; 27(suppl):240s (abstract 5021).

Metastatik Renal cell ca, Tedavi Seçenekleri



Metastatik Renal Kanserler, Tedavi Seçenekleri

COMPARZ

COMParing the, s**A**fety and tole**R**ability
of
pa**Z**opanib vs sunitinb

22 Ağustos 2013

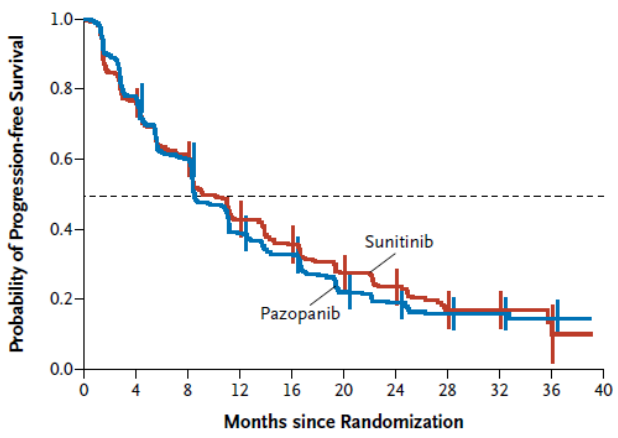
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pazopanib versus Sunitinib in Metastatic Renal-Cell Carcinoma

Robert J. Motzer, M.D., Thomas E. Hutson, D.O., David Cella, Ph.D., James Reeves, M.D., Robert Hawkins, M.B., B.S., Ph.D., Jun Guo, Ph.D., Paul Nathan, M.B., B.S., Ph.D., Michael Staehler, M.D., Paul de Souza, M.B., B.S., Ph.D., Jaime R. Merchan, M.D., Ekaterini Boleti, M.D., Ph.D., Kate Fife, M.D., Jie Jin, M.D., Robert Jones, Ph.D., Hirotsugu Uemura, M.D., Ph.D., Ugo De Giorgi, M.D.,

Metastatik Renal cell ca, Tedavi Seçenekleri

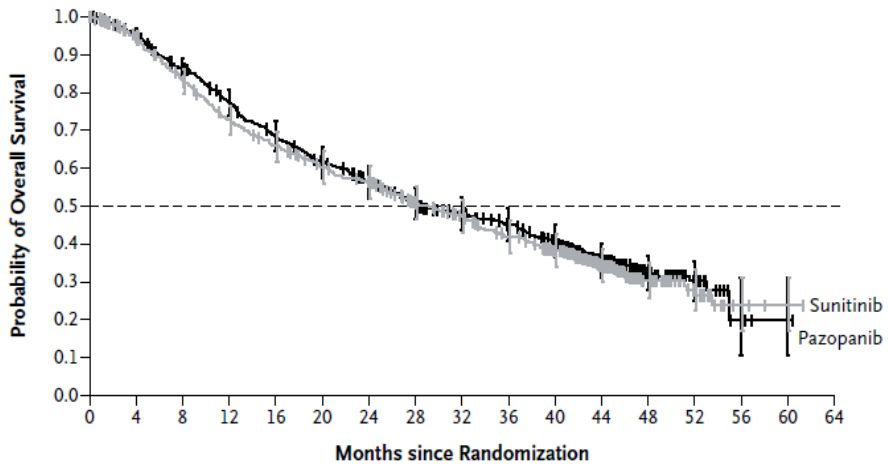


No. at Risk

Pazopanib	557	361	245	136	105	61	46	19	13	1
Sunitinib	553	351	249	147	111	69	48	18	10	3

Figure 1. Kaplan–Meier Estimates of Progression-free Survival According to Independent Review.

The median progression-free survival was 8.4 months with pazopanib (95% CI, 8.3 to 10.9) and 9.5 months with sunitinib (95% CI, 8.3 to 11.1). The dotted line represents the median (0.5), and vertical lines represent 95% confidence intervals.



No. at Risk

Pazopanib	557	521	462	409	360	320	284	243	221	197	169	99	51	21	4	1	0
Sunitinib	553	501	435	377	339	304	281	237	211	180	153	100	45	20	4	1	0

Figure 1. Kaplan–Meier Curves for Overall Survival in the Intention-to-Treat Population.

The dashed line represents the median (0.5), and vertical lines represent 95% confidence intervals.

Metastatik Renal cell ca, Tedavi Seçenekleri

COMPARZ: En sık görülen advers olaylar (≥% 30)[1]

Advers Olay,* %	Pazopanib (n=554)		Sunitinib (n=548)	
	Grade 1-4	Grade 3-4	Grade 1-4	Grade 3-4
Herhangi olay†	>99	59/15	>99	57/17
Diyare	63	9/0	57	7/<1
Bitkinlik	55	10/<1	63	17/<1
Hipertansiyon	46	15/<1	41	15/<1
Mide bulantısı	45	2/0	46	2/0
İştah kesilmesi	37	1/0	37	3/0
ALT düzeyinin artması	31	10/2	18	2/<1
Saç rengi değişikliği	30	0/0	10	<1/0
El-ayak sendromu	29	6/0	50	11/<1
Tat değişimi	26	<1/0	36	0/0
Trombositopeni	10	2/<1	34	12/4

1. Motzer R, *et al.* ESMO 2012 oral presentation; abstract LBA8_PR.

Metastatik Renal cell ca, Tedavi Seçenekleri

PISCES Çalışması

Pazopan**I**b versus **S**unitinib patient preferen**CE** **S**tudy in treatment naïve advanced or metastatic renal cell carcinoma

(Tedaviye dirençli ilerlemiş veya metastatik renal hücreli karsinom tedavisinde hasta tercih çalışması Pazopanib ile Sunitinib karşılaştırılması)

(Randomize, çift kör, çapraz geçişli tedaviye dirençli ilerlemiş veya metastatik renal hücreli karsinom

VOLUME 32 · NUMBER 14 · MAY 10 2014

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized, Controlled, Double-Blind, Cross-Over Trial Assessing Treatment Preference for Pazopanib Versus Sunitinib in Patients With Metastatic Renal Cell Carcinoma: PISCES Study

Bernard Escudier, Camillo Porta, Petri Bono, Thomas Powles, Tim Eisen, Cora N. Sternberg, Jürgen E. Gschwend, Ugo De Giorgi, Omi Parikh, Robert Hawkins, Emmanuel Sevin, Sylvie Négrier, Sadya Khan, Jose Diaz, Suman Redhu, Faisal Mehmud, and David Cella

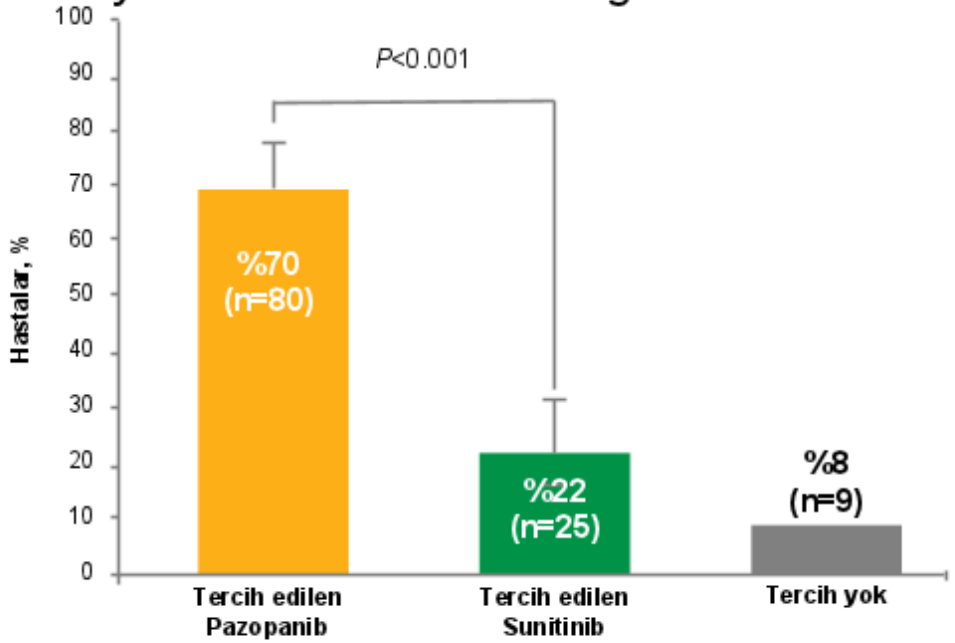
See accompanying editorial on page 1392

Bernard Escudier, Institut Gustave Roussy, Villejuif; Emmanuel Sevin, Centre François Baclesse, Caen; Sylvie Négrier, Leon Berard Cancer Center, Lyon, France; Camillo Porta, Fondazione

Metastatik Renal cell ca, Tedavi Seçenekleri

PISCES: Anlamlı Olarak Daha Fazla Hasta Sunitinibe karşı Pazopanibi Tercih Etmiştir

- Hasta tercihi çalışmanın sonunda anketle değerlendirilmiştir
- Hastalardan periyot 1 veya periyot 2'de ilaçla tedaviye devam etmeyi tercih ettiklerini ya da bir tercihleri olmadığını belirtmeleri istenmiştir



Metastatik Renal cell ca, Tedavi Seçenekleri

PISCES İkincil Sonlanım Noktası: HRQoL

Hasta tarafından bildirilen çeşitli QoL ölçümlerinde Pazopanib Sunitinibe karşı üstünlük göstermiştir

QoL Ölçümü	Pazopanib		Sunitinib		Tedavi Farkı[a]	*P* değeri
	Ortalama Skor[b]	Hasta Sayısı	Ortalama Skor	Hasta Sayısı		
FACIT-F[c]	38.1	131	35.6	131	2.49	0.002
SQLQ						
En kötü ağız ve boğaz ağrısı	0.40	131	0.78	131	–0.38	<0.001
En kötü el ağrısı	0.21	131	0.29	131	–0.08	0.026
En kötü ayak ağrısı	0.36	129	0.52	129	–0.16	0.005
SQLQ kısıtlanma skorları						
Ağız ve boğaz ağrısı	14.32	126	13.72	126	0.60	<0.001
Ayak ağrısı	13.82	129	13.24	129	0.58	0.003

[a] Hesaplanmış tedavi farkı CI ve P değeri varyans analizi modelindeki periyot ve sekans etkileri açısından düzeltilmiştir.
[b] Ortalama skor tüm hastalar için periyotlara göre ortalaması alınmış her bir periyot içindeki ortalama başlangıç sonrası skor olarak hesaplanmıştır; daha yüksek skorlar daha iyi sağlığa işaret etmiştir.
[c] Hastaların analize dahil edilmek için her iki tedavi periyodunda da değerlendirmeleri tamamlaması gerekmiştir.

Escudier B et al. *J Clin Oncol*. 2014;32(14):1412-1418.

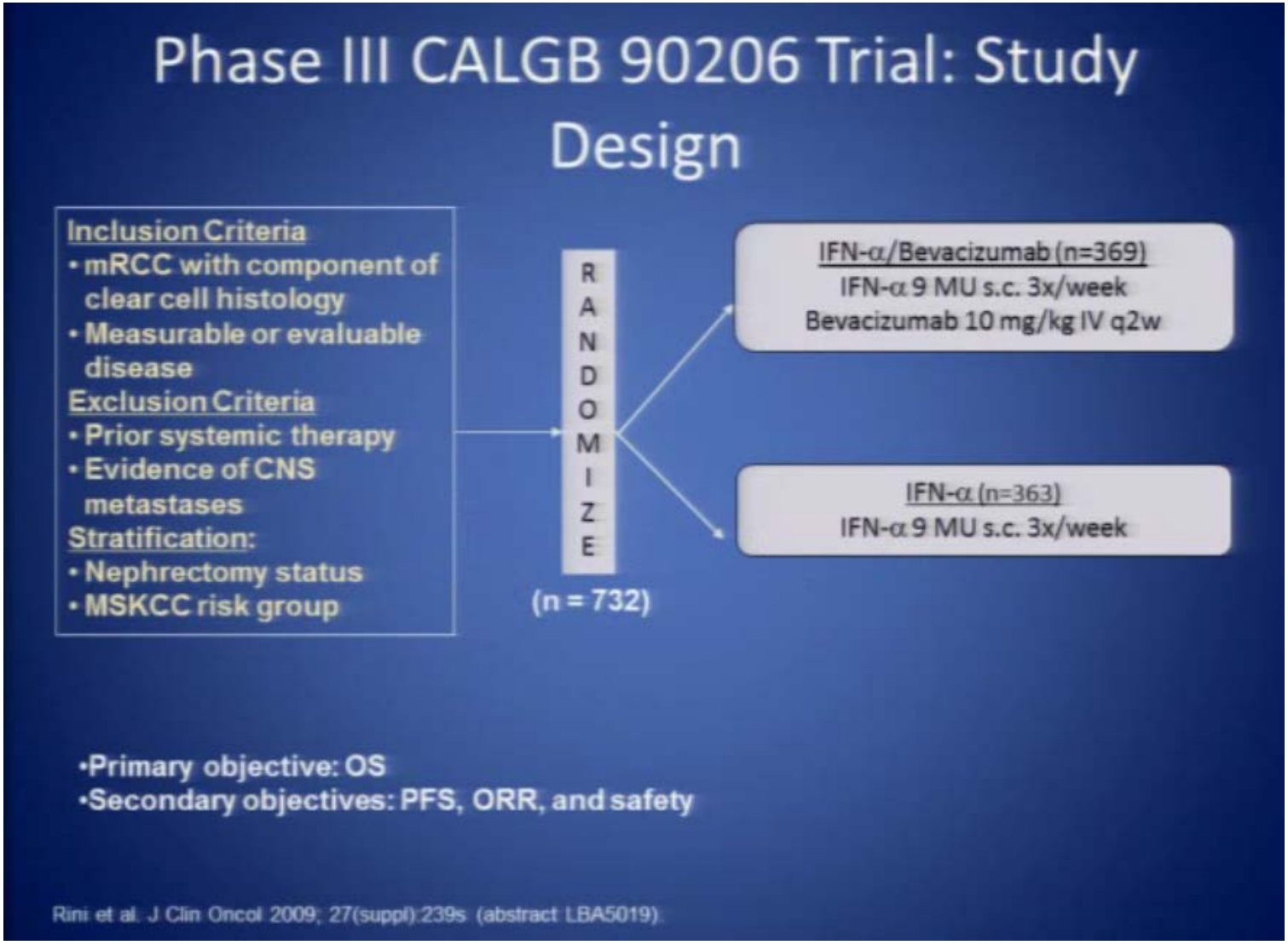
Metastatik Renal cell ca, Tedavi Seçenekleri

Bevacizumab

- Anti-VEGF antibody
- Administered 10mg/kg IV every 14 days

- Was approved for use in advanced RCC in combination with IFN alpha given 10Mu TIW subcutaneously, August 2009.

Metastatik Renal cell ca, Tedavi Seçenekleri



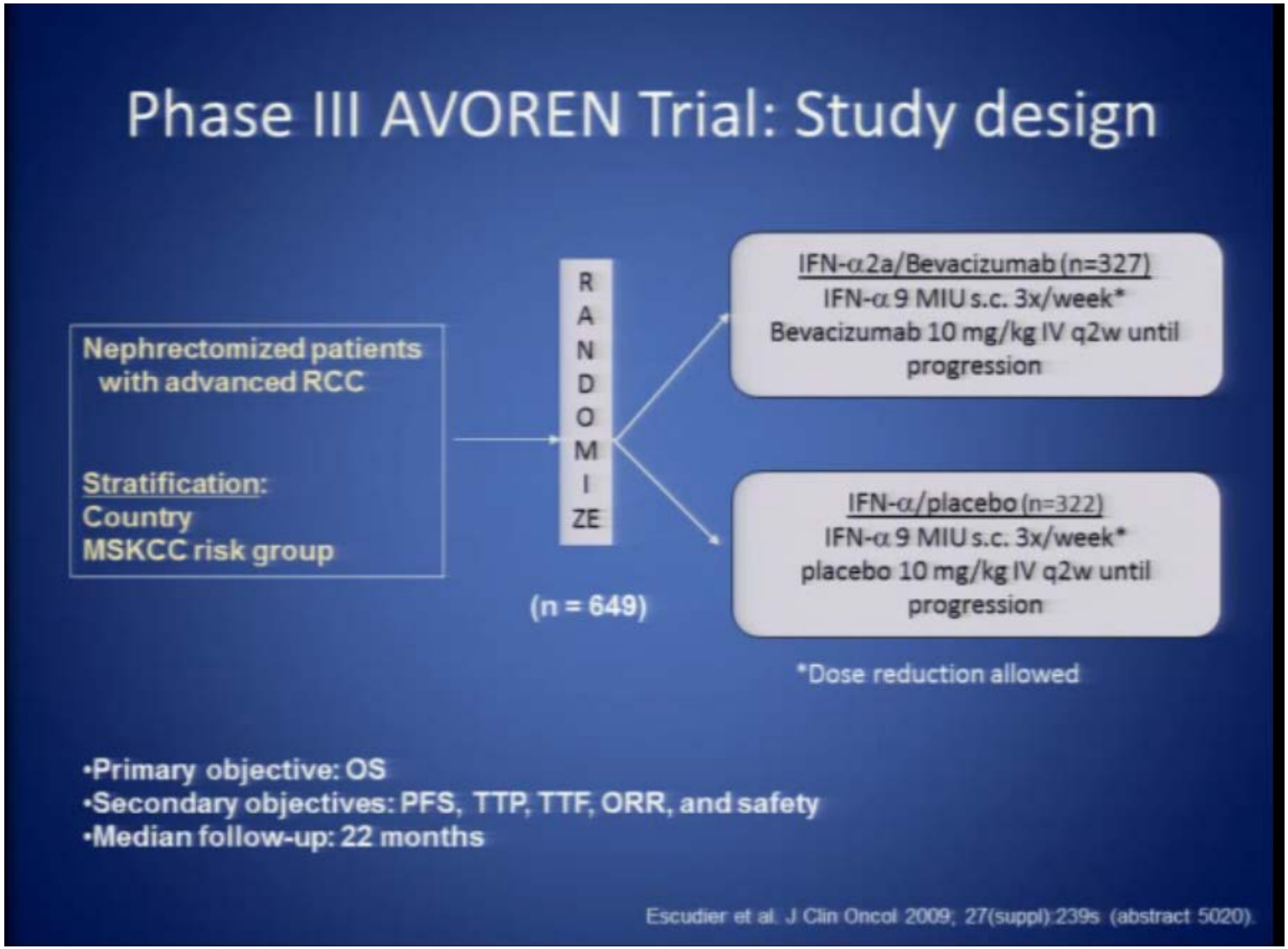
Metastatik Renal cell ca, Tedavi Seçenekleri

Phase III CALGB 90206 trial of first-line interferon alpha +/- bevacizumab in patients with metastatic renal cell carcinoma: Efficacy

	IFN (n=363)	IFN+bev (n=369)	HR	*P* Value
ORR (%)	13 (n = 314)	25.5 (n = 325)	NR	<.0001
Median PFS (months)	4.9	8.4	0.71	<.0001
Median OS (months)	17.4	18.3	NR	.069
Median OS by MSKCC risk group (months)				
Favorable	33.5	32.5	0.89	.524
Intermediate	16.1	17.7	0.87	.174
Poor	5.7	6.6	0.76	.25
Median OS based on receiving 2nd line therapy				
Yes (n = 408)	26.8	31.4	0.80	.055
No (n = 324)	9.1	13.1	0.82	.108

Rini et al. J Clin Oncol 2009; 27(suppl):239s (abstract LBA5019).

Metastatik Renal cell ca, Tedavi Seçenekleri



Metastatik Renal cell ca, Tedavi Seçenekleri

Table 3. Clinical Outcome to Bevacizumab Plus Interferon Alfa According to the Development of Grade ≥ 2 Hypertension

Outcome	Patients With Grade ≥ 2 Hypertension* (n = 75)	Patients Without Grade ≥ 2 Hypertension (n = 291)
ORR, %	13.1	9.0
95% CI	9.7 to 16.7	6.3 to 18.9
P	.95	
PFS, months	13.2	8.0
95% CI	10.6 to 15.5	5.9 to 8.6
P	< .001	
OS, months	41.6	16.2
95% CI	26.3 to 55.1	14.2 to 18.7
P	< .001	

Abbreviations: ORR, objective response rate; PFS, progression-free survival; OS, overall survival.

*Any relation to therapy according to Common Terminology Criteria for Adverse Events (version 3).

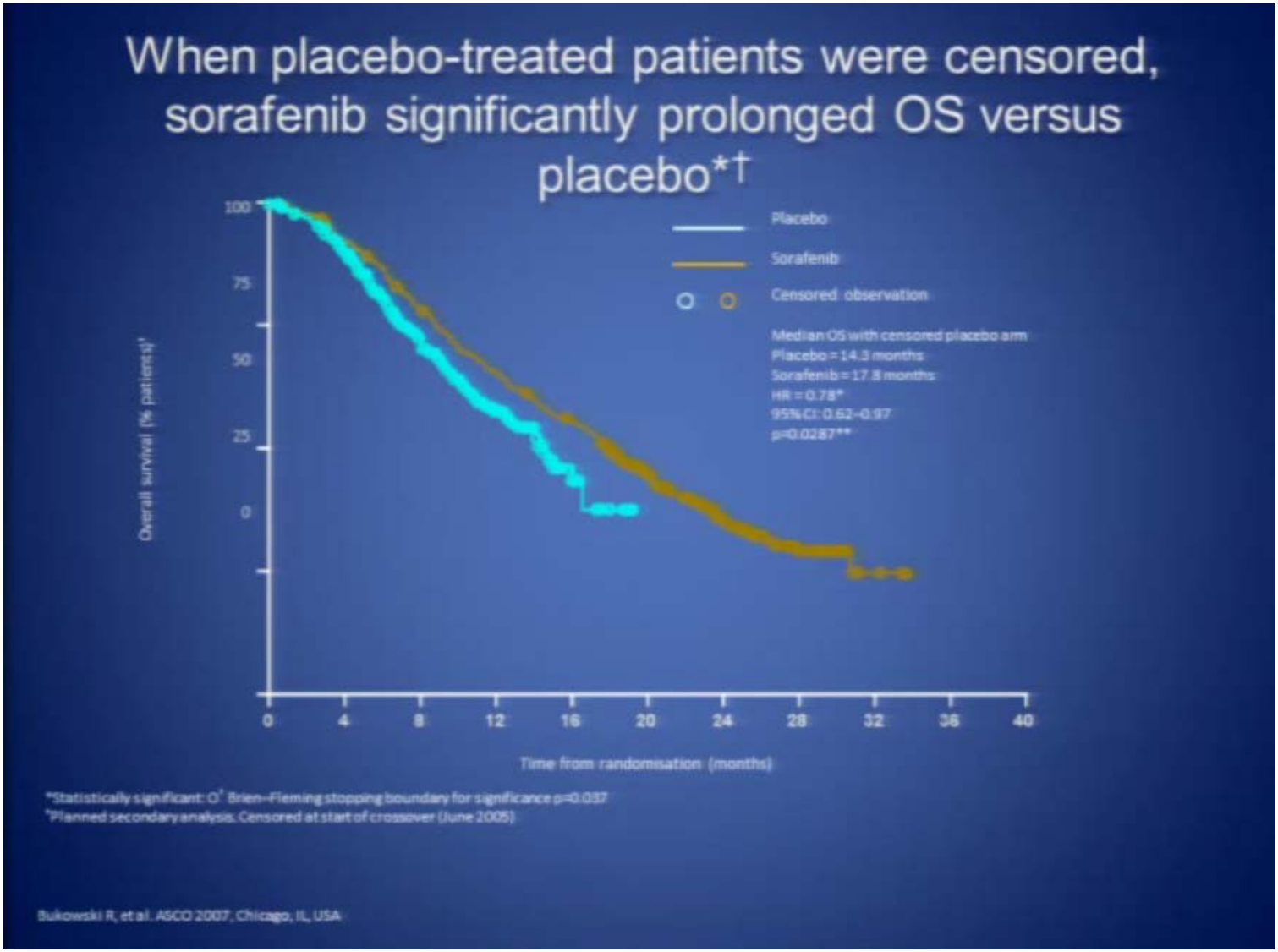
Metastatik Renal cell ca, Tedavi Seçenekleri

Sorafenib

- Oral Agent.
- Dosed 400mg PO BID continuously.
- Blocks VEGFR1-3, PDGFR, Raf, c-Kit, FLT-3.
- FDA approved for advanced RCC December 2005.

Metastatik Renal cell ca, Tedavi Seçenekleri

Metastatik Renal cell ca, Tedavi Seçenekleri



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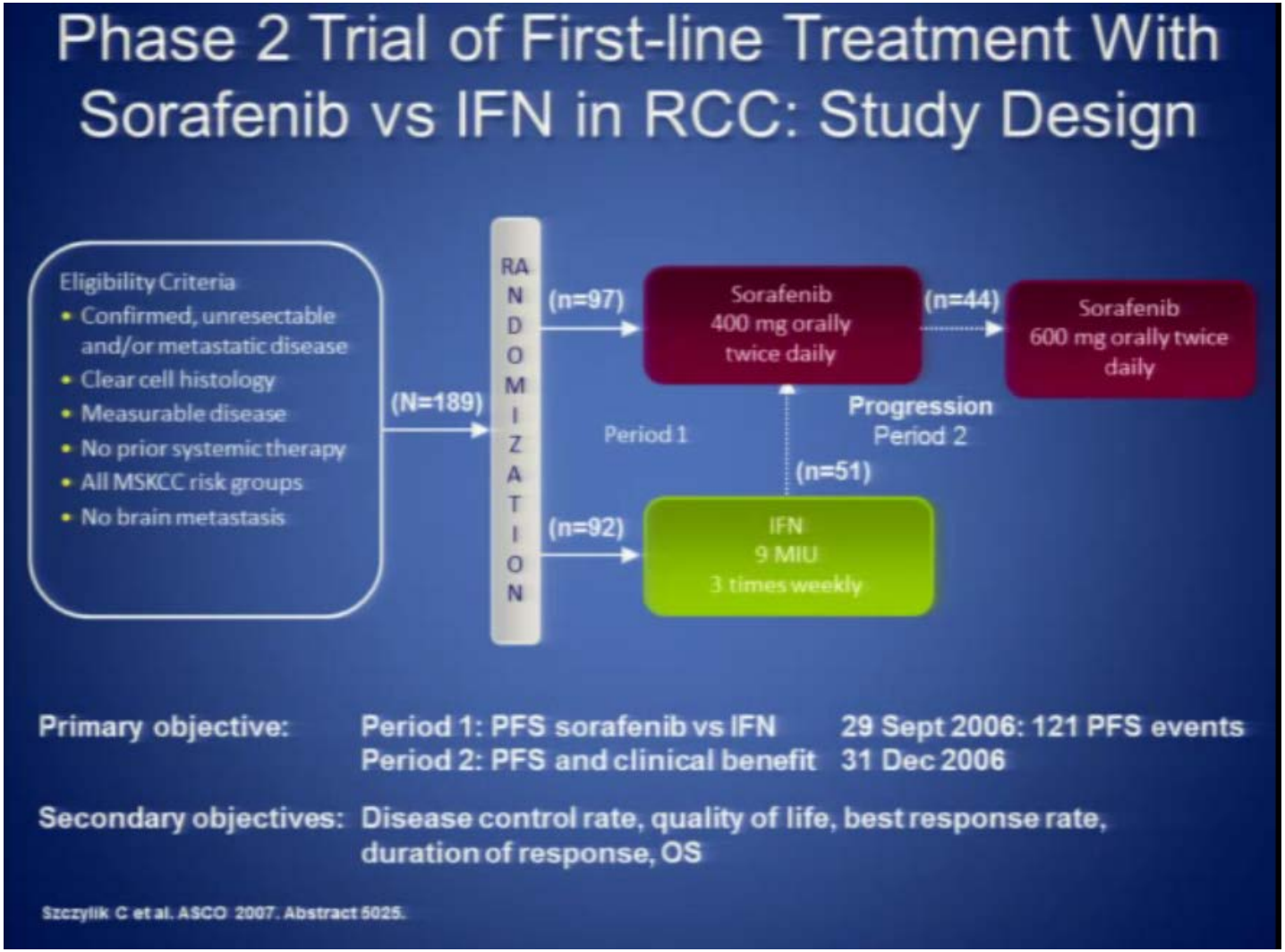
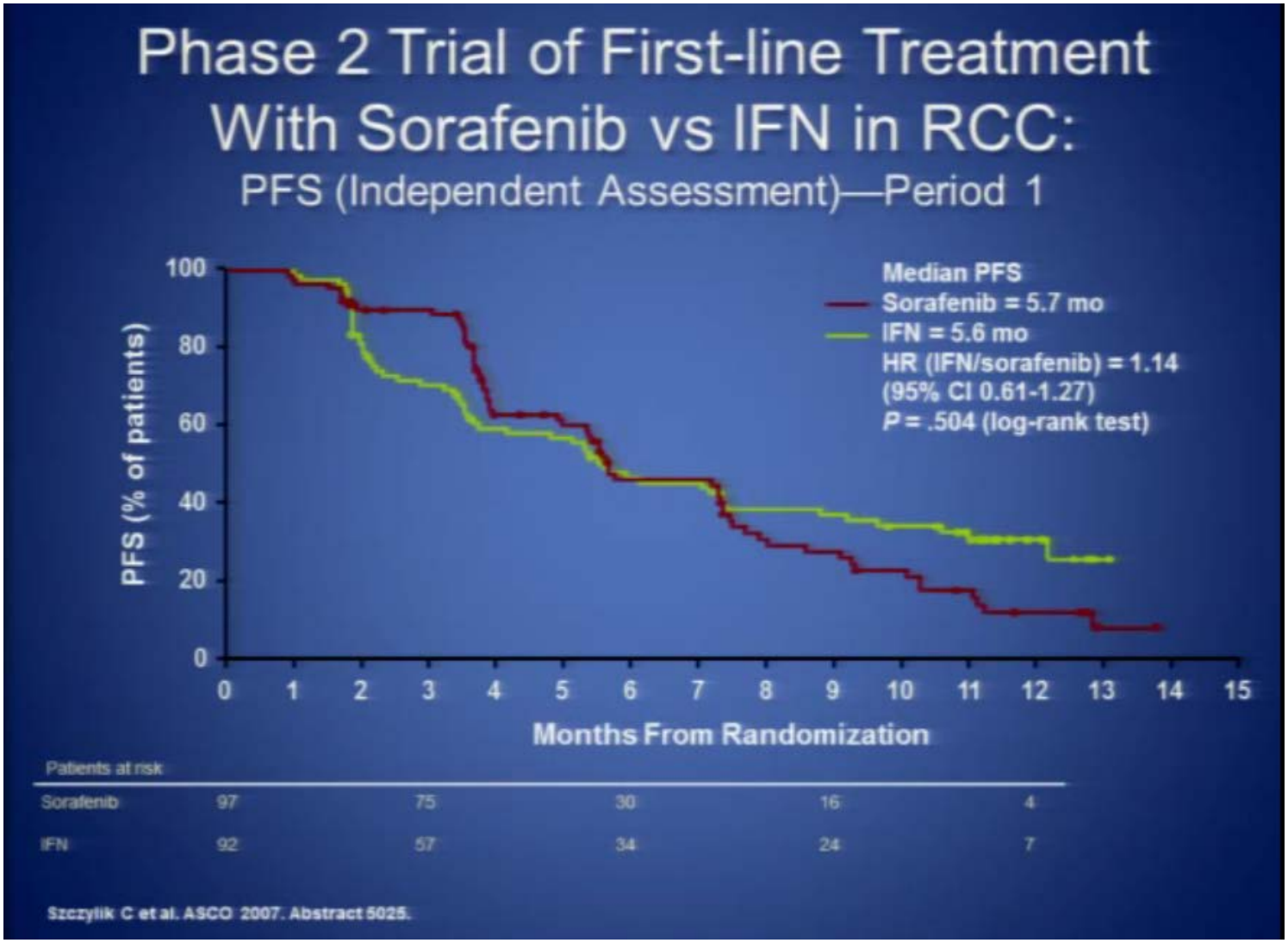


Metastatik Renal cell ca, Tedavi Seçenekleri

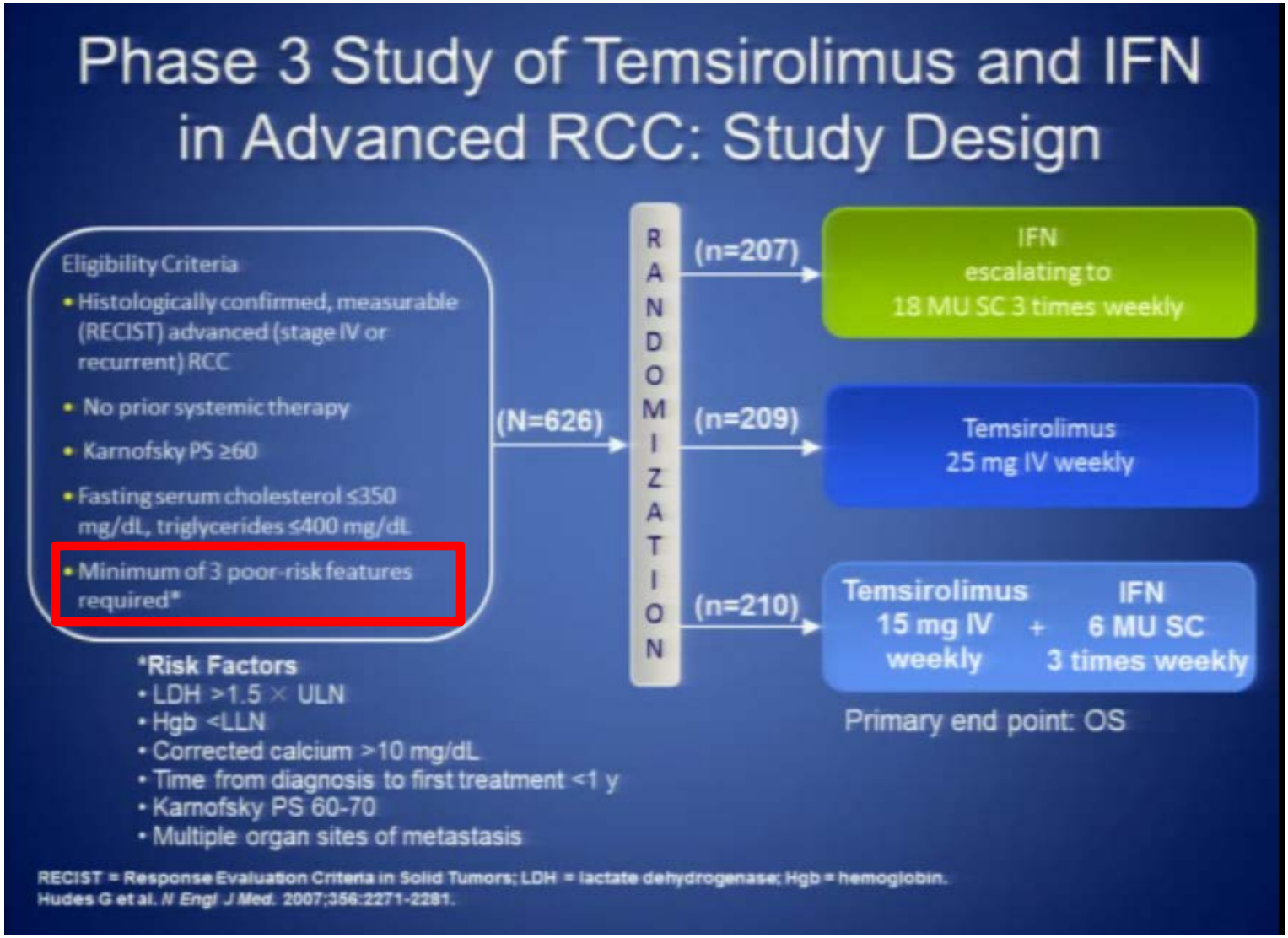


Metastatik Renal cell ca, Tedavi Seçenekleri mTOR İnhibitörleri

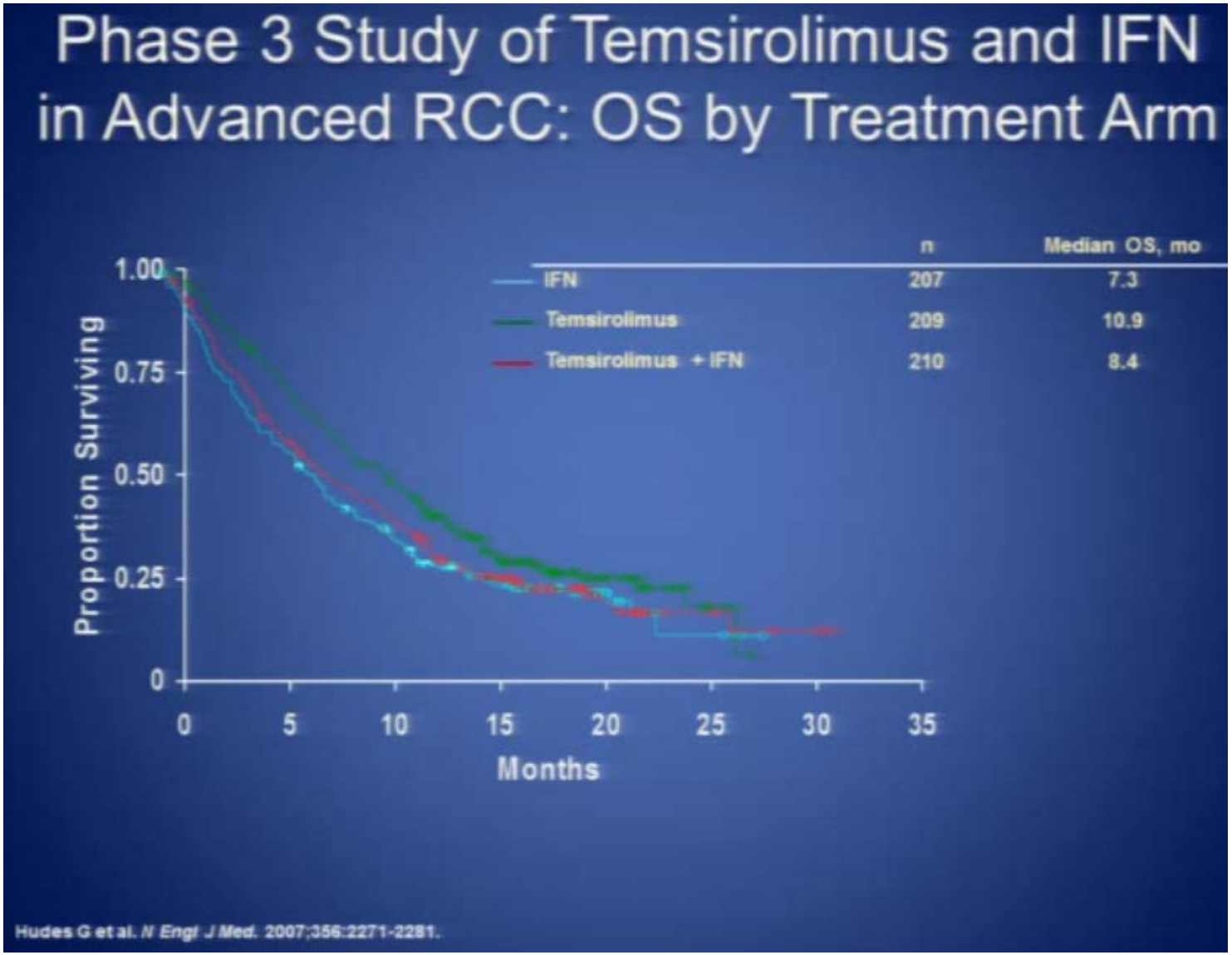
Temsirolimus

- IV small molecule.
- Administered weekly.
- Targets mTOR, an intracellular molecule involved in protein synthesis, survival and possibly HIF regulation.
- FDA approved for advanced RCC in May 2007.

Metastatik Renal cell ca, Tedavi Seçenekleri



Metastatik Renal cell ca, Tedavi Seçenekleri mTOR İnhibitörleri



Metastatik Renal cell ca, Tedavi Seçenekleri
mTOR İnhibitörleri

Temsirolimus Summary

- Improves survival in poor risk patients.
- Relatively well tolerated.
- May be useful in non-clear cell histologies.
- Further studies needed to assess role in good risk populations.

Metastatik Renal cell ca, Tedavi Seçenekleri

Systemic Treatment For Clear Cell RCC

Setting		Phase III	Alternative
1st-Line Therapy	Good or intermediate risk*	Sunitinib Bevacizumab + IFNα Pazopanib	HD IL-2
	Poor risk*	Temsirolimus	Sunitinib
2nd-Line Therapy	Prior cytokine	Axitinib Sorafenib	Sunitinib or bevacizumab
	Prior VEGFR inhibitor	Everolimus Axitinib	Clinical Trials
	Prior mTOR inhibitor	Clinical Trials	

*MSKCC risk status.

Atkins. ASCO 2006 Plenary session; Figlin. *Clin Adv Hematol Oncol*. 2007;5:35; Escudier. *Drugs*. 2007;67:1257; Cho. *Clin Cancer Res*. 2007;13:761s; Atkins. *Clin Cancer Res*. 2005;11:3714.

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Hereditary RCC Syndromes

Syndrome	Gene Location	Gene Name	Manifestations
Von Hippel Lindau Disease	3p25-26	VHL	Hemangioblastomas Clear cell RCC
Hereditary Papillary RCC	7q31	cMet	Bilateral Papillary RCC
Hereditary Leiomyomatosis RCC Syndrome	1q42-43	Fumarate Hydratase (FH)	Uterine Leiomas Solitary Papillary II RCC
Birt Hogg Dube Syndrome	17p11.2	Folliculin	Cutaneous lesions Chromophobe, clear cell RCC
Tuberous Sclerosis	9q34; 16p13	TSC1; TSC2	CNS Tubers Angiomyolipomas of the kidney Clear cell RCC

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Hereditary Type I Papillary RCC

- Autosomal dominant, high penetrance.
- Occurs in later age range.
- Bilateral, multifocal renal cell carcinomas.
- Associated with activating mutations in the *c-MET* oncogene on 7q34, the receptor for HGF/SF (hepatocyte growth factor).
- Metastatic potential.

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Birt Hogg Dube Syndrome

- Very rare disorder first described by Birt *et al* in 1977.
  - Fibrofolliculomas, trichodiscomas, achrocordons.
  - Spontaneous pneumothorax
  - Renal cell carcinoma: chromophobe, clear cell RCC.
  - Kidney cancer occurs in 15-30% of BHD patients.
  - BHD is due to mutation in Folliculin, localized on chromosome 17p11.2.
  - Associated with the nutrient sensing pathway and AMPK which is upstream of TSC and mTOR.

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Leiomyomatosis Renal Cell Carcinoma (HLRCC)/Multiple Cutaneous Leiomyoma (MCL)

- Multiple cutaneous leiomyomas
- Uterine leiomyomata
- Uterine leiomyosarcoma
- Renal carcinoma- typically papillary type 2.

- Mutation in Fumarate hydratase , (FH), located on chromosome 1q42- Krebs cycle enzyme

Berak Hü erlerinde ,

Te
or Both
Gary Hu
Janice
Elzbieta Staro
István Bod
Ingo G.H. Sch
Ti
Laure

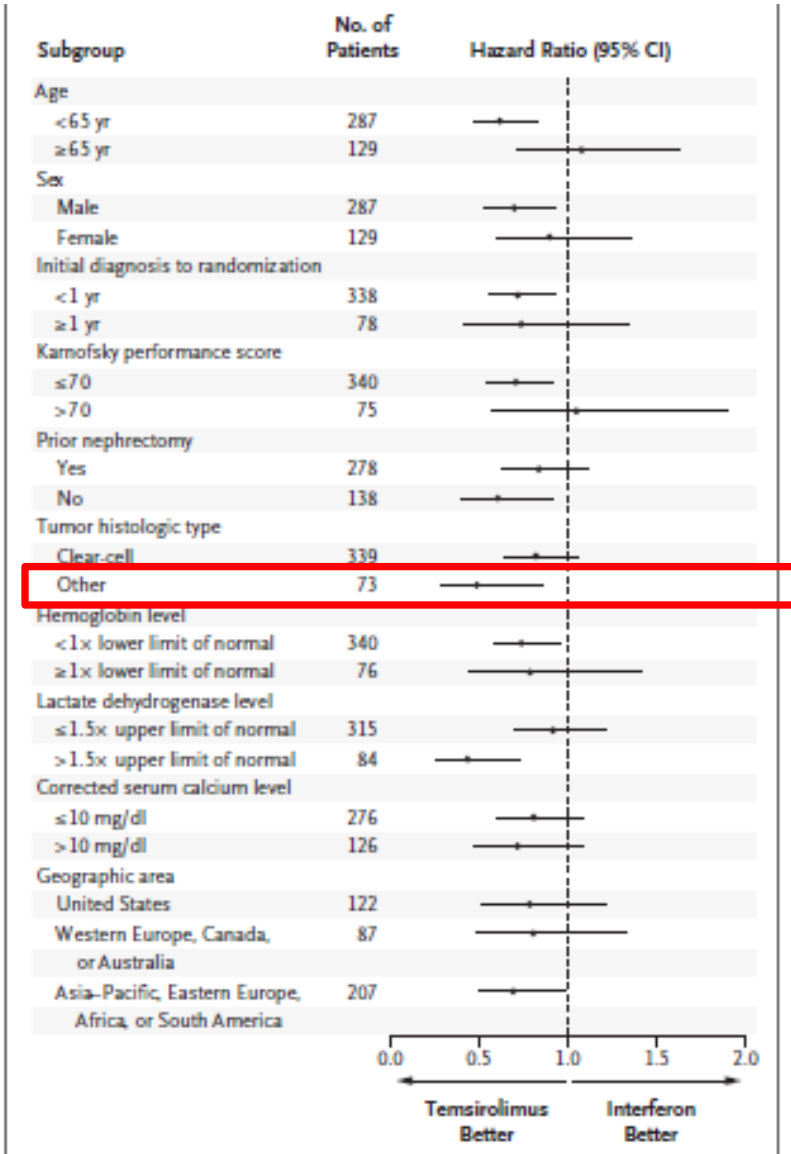


Figure 2. Hazard Ratios for Overall Survival among Subgroups of Patients.

Hazard ratios (indicated by circles) with 95% confidence intervals (indicated by horizontal lines) are shown for subgroups of patients receiving interferon alfa or temsirolimus. Data are missing for the serum lactate dehydrogenase level in 17 patients, the serum calcium level in 14 patients, the tumor histologic type in 4 patients, and the Karnofsky performance score in 1 patient.

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

JOURNAL OF CLINICAL ONCOLOGY

Official Journal of the American Society of Clinical Oncology

Journal of Clinical Oncology, 2012 Genitourinary Cancers Symposium.
Vol 30, No 5_suppl (February 10 Supplement), 2012: 402

Safety and efficacy of everolimus in patients with non-clear cell renal cell carcinoma refractory to VEGF-targeted therapy: Subgroup analysis of REACT.

Christian U. Blank, Petri Bono, James M. G. Larkin, Svetozar Gogov, Ashok Panneerselvam, Carlos A. Garay, Viktor Grünwald and on behalf of the REACT Study Group

The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; Helsinki University Hospital, Helsinki, Finland; Urology Unit, Royal Marsden Hospital, London, United Kingdom; Novartis Pharma AG, Basel, Switzerland; Novartis Pharmaceuticals, Florham Park, NJ; Novartis Pharmaceuticals, East Hanover, NJ; Clinic for Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany

Abstract Disclosures

Table of Contents

This Article

J Clin Oncol (Meeting Abstracts) **February 2012** vol. 30 no. 5_suppl **402**

? Meeting Abstract

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Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Background: Metastatic non-clear cell renal cell carcinoma (mncRCC), which accounts for about 25% of all RCCs, is characterized by resistance to treatment and poor overall survival. Despite recent advances in targeted therapies for patients with mRCC, effective therapies for patients with mncRCC remain limited. The REACT (RAD001 Expanded Access Clinical Trial in RCC) study was initiated to provide patients with mRCC of any histology refractory to VEGF-targeted therapy access to everolimus in advance of regulatory approval.

Methods: REACT, an open-label, international, expanded-access program (Clinicaltrials.gov: NCT00655252) enrolled patients with measurable or nonmeasurable mRCC of any histology who were intolerant of, or progressed while on, VEGFR-TKI therapy in order to evaluate the long-term safety of everolimus 10 mg daily. Overall incidence of grade 3/4 and serious adverse events (AEs) were recorded, as was tumor response to everolimus according to RECIST criteria. A subgroup analysis of safety and efficacy in patients with mncRCC was performed.

Results: Of 1367 patients enrolled, 75 patients (5.5%) had mncRCC. Median everolimus treatment duration in the mncRCC subgroup was 12.14 weeks (range, 0.9–49.0 weeks) and in the overall REACT population it was 14.0 weeks (range, 0.1–83.7 weeks). In the mncRCC subgroup, most commonly reported grade 3/4 AEs were anemia (17.3%), dyspnea (10.7%), pleural effusion (9.3%), fatigue (8.0%), and hyperglycemia (6.6%). Best overall response was similar in the mncRCC subgroup and overall population: respectively, 1.3% and 1.7% had partial response and 49.3% and 51.6% had stable disease.

Conclusions: Although patients with mncRCC had a slightly lower treatment duration than the overall REACT population, approximately 50% of these patients achieved disease control on treatment. In this subgroup, everolimus was well tolerated, no new safety issues were observed, and the AE profile was consistent with that of the overall population. These encouraging results of the safety and efficacy of everolimus in patients with mncRCC support further evaluation of everolimus in these patients.

Abstract presentation from the 2012 Genitourinary Cancers Symposium

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Abstract ▾ Send to: ▾

Ann Oncol. 2012 Aug;23(8):2108-14. doi: 10.1093/annonc/mdr586. Epub 2012 Jan 6.

Multicenter phase II study of sunitinib in patients with non-clear cell renal cell carcinoma.

Lee JL[1], Ahn JH, Lim HY, Park SH, Lee SH, Kim TM, Lee DH, Cho YM, Song C, Hong JH, Kim CS, Ahn H.

⊕ **Author information**

Abstract

BACKGROUND: Retrospective and molecular biologic data suggest that sunitinib may be effective in patients with non-clear cell renal cell carcinoma (nccRCC).

PATIENTS AND METHODS: Eligibility criteria included advanced nccRCC except for collecting duct carcinoma and sarcomatoid carcinoma without identifiable renal cell carcinoma subtypes. Patients were treated with 50 mg/day oral sunitinib for 4 weeks, followed by 2 weeks of rest. The primary end point was overall response rate (RR).

RESULTS: Thirty-one eligible patients were enrolled. Twenty-four patients (77%) had prior nephrectomy. By Memorial Sloan-Kettering Cancer Center criteria, 8 patients (26%) had poor risk and 14 (45%) had intermediate risk. Twenty-two patients had papillary renal cell carcinoma (RCC), and three had chromophobe RCC. Eleven patients had partial response with a RR of 36% (95% confidence interval (CI) 19% to 52%) and an additional 17 patients (55%) had stable disease. Median duration of response was 12.7 months (95% CI 6.3-19.1 months), and median progression-free survival was 6.4 months (95% CI 4.2-8.6 months). At a median follow-up duration of 18.7 months (95% CI 13.7-23.7 months), 13 patients (42%) had died, resulting in an estimated median survival of 25.6 months (95% CI 8.4-42.9 months). Toxicity profiles were commensurate with prior reports.

CONCLUSIONS: Sunitinib has promising activity in patients with nccRCC (NCT01219751).

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

ANTICANCER RESEARCH *34*: 4329-4334 (2014)

Sunitinib for Patients with Metastatic Non-clear Cell Renal Cell Carcinoma: A Multicenter Retrospective Turkish Oncology Group Trial

IBRAHIM YILDIZ[1], MELTEM EKENEL[2], TULAY AKMAN[3], MUHARREM KOCAR[4], MÜKREMIN UYSAL[5], METIN KANITEZ[6], UMUT VAROL[1], IBRAHIM VEDAT BAYOGLU[1], DENIZ TURAL[7], MEHMET ALI KAPLAN[8], NILUFER AVCI[9], ZEKI SÜRMELI[10], İSA DEDE[11], ARIFE ULAŞ[12], OZAN YAZICI[13] and MERT BASARAN[2]

Departments of Medical Oncology at:
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[2]*Institute of Oncology, Istanbul University, Istanbul, Turkey;*
[3]*Izmir Tepecik Training and Research Hospital, Izmir, Turkey;*
[4]*Sanliurfa Education and Research Hospital, Sanliurfa, Turkey;*
[5]*Afyon Kocatepe University, Afyonkarahisar, Turkey;*
[6]*Marmara University Hospital, Istanbul, Turkey;*
[7]*Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, Turkey;*
[8]*Dicle University, Diyarbakir, Turkey;*
[9]*Balikesir State Hospital, Balikesir, Turkey;*
[10]*Ege University, Tulay Aktas Oncology Hospital, Izmir, Turkey;*
[11]*Ankara University Medical Faculty, Ankara, Turkey;*
[12]*Ali Osman Sonmez Oncology Training and Research Hospital, Bursa, Turkey;*
[13]*Ankara Numune Education and Research Hospital, Ankara, Turkey*

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Table I. *Patients' characteristics.*

Characteristic	No. (%) of patients
Gender	
Female	25 (39.3)
Male	38 (60.3)
Age (years)	
Median	63
Range	25-82
Histopathological findings	
Papillary RCC	46 (73.0)
Chromophobe RCC	10 (15.9)
Undifferentiated	7 (11.1)
Sarcomatoid	
Without sarcomatoid	47 (66.1)
With sarcomatoid	24 (33.9)
ECOG PS	
0	12 (19.0)
1	34 (54.0)
≥2	17 (27.0)
Sites of disease	
Lung	38 (60.3)
Liver	15 (23.8)
Bone	23 (36.5)
Brain	11 (17.5)
Laboratory findings	
Hemoglobin	
<LLN	28 (50.9)
≥LLN	27 (49.1)
LDH	
<1.5×ULN	42 (72.4)
≥1.5×ULN	16 (27.6)
Calcium	
<10 mg/dl	36 (78.3)
≥10 mg/dl	10 (21.7)
Treatment	
Prior cytokine-based therapy (interferon)	39 (61.9)
Prior radiotherapy	28 (44.4)
Prior nephrectomy	51 (81.0)
Time from diagnosis/surgery to sunitinib initiation	
<12 months	41 (65.1)
≥12 months	22 (34.9)
No. of cycles	
Median	7
Range	2-86

Table II. *Objective response, clinical benefit and disease control rates.*

Response	No. of patients	%
Objective response	7	11.1
Complete	0	0.0
Partial	7	11.1
Stable disease for ≥3 months	33	52.4
Disease control rate	40	63.5

ANTICANCER RESEARCH *34*: 4329-4334 (2014)

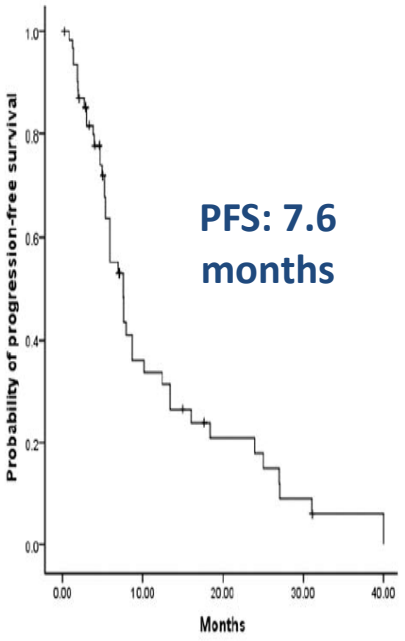

Figure 1. *Progression-free survival in Turkish patients with metastatic non-clear cell renal cell carcinoma.*

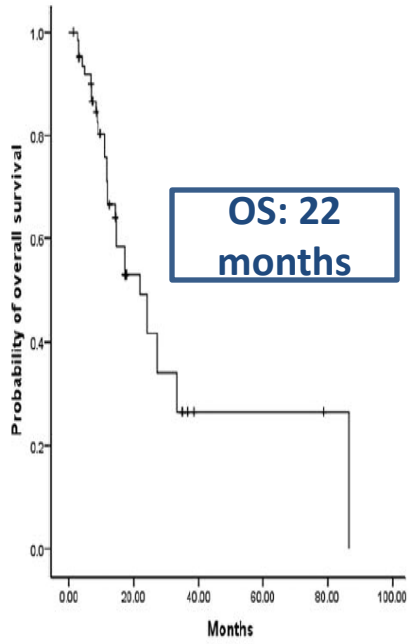

Figure 2. *Overall survival in Turkish patients with metastatic non-clear cell renal cell carcinoma.*

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A Phase II Study of Axitinib in Metastatic Non-clear Cell Renal Cell Carcinoma Patients Previously Treated With Temsirolimus

This study is currently recruiting participants. (see Contacts and Locations)

Verified February 2013 by Seoul National University Hospital

Sponsor:
Seoul National University Hospital

Collaborator:
Pfizer

Information provided by (Responsible Party):
Se-Hoon Lee, Seoul National University Hospital

ClinicalTrials.gov Identifier:
NCT01798446

First received: February 20, 2013
Last updated: May 23, 2014
Last verified: February 2013
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

- 1. There is no standard treatment option for non-clear cell renal cell carcinoma (RCC).
- 2. Patients with non-clear cell RCC is strongly assumed to have benefit from anti-VEGF treatment.
- 3. There is no trial of axitinib for non-clear cell RCC.
- 4. Axitinib is expected to show more potent efficacy over sorafenib or sunitinib in renal cell carcinoma.

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Table. Ongoing Clinical Trials in Papillary Renal Cell Carcinoma (Phases II and III)

Agent	ClinicalTrials.gov Identifier	Inclusion Criteria	Primary Endpoint	Phase	Status
Combination mTOR inhibitors					
MK2206 vs everolimus	NCT01239342	Mixed histology	PFS	II	Ongoing, not recruiting
Everolimus vs sunitinib	NCT01108445	ncc RCC	Antitumor activity	II	Ongoing, not recruiting
Everolimus	NCT01120249	Mixed histology	RFS	III	Recruiting
mAbs (anti-VEGFA)					
Everolimus + bevacizumab	NCT01399918	pRCC	Efficacy (PFS)	II	Recruiting
Bevacizumab + erlotinib	NCT01130519	HLRCC/pRCC	ORR	II	Recruiting
Bevacizumab + TRC105	NCT01727089	Mixed histology	PFS	II	Ongoing, not recruiting
TKIs					
Pazopanib	NCT01767636	ncc RCC	ORR	II	Recruiting
Pazopanib	NCT01538238	ncc RCC	ORR	II	Recruiting
MET inhibitors					
Crizotinib	NCT01524926	pRCC	Antitumor activity	II	Recruiting
Tivantinib	NCT01688973	pRCC or mixed histology with papillary component	RR	II	Ongoing, not recruiting
INC280	NCT02019693	pRCC	ORR	II	Recruiting
Volitinib	NCT02127710	pRCC	ORR	II	Recruiting

HLRCC = hereditary leiomyomatosis and renal cell carcinoma; mAbs = monoclonal antibodies; mTOR = mammalian target of rapamycin; ncc RCC = non–clear-cell renal cell carcinoma; ORR = overall response rate; PFS = progression-free survival; pRCC = papillary renal cell carcinoma; RR = response rate; TKI = tyrosine kinase inhibitor; VEGFA = vascular endothelial growth factor A.

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NCCN Kidney Cancer Panel

- Pazopanib
- Axitinib
- None-clear cell RCC Kategori 2A

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VOLUME 27 · NUMBER 34 · DECEMBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Phase II Study of Erlotinib in Patients With Locally Advanced or Metastatic Papillary Histology Renal Cell Cancer: SWOG S0317

Michael S. Gordon, Michael Hussey, Raymond B. Nagle, Primo N. Lara Jr, Philip C. Mack, Janice Dutcher, Wolfram Samlowski, Joseph I. Clark, David I. Quinn, Chong-Xian Pan, and David Crawford

From Premiere Oncology of Arizona, Scottsdale; Arizona Cancer Center, Tucson, AZ; Southwest Oncology Group Statistical Center, Seattle, WA; University of California at Davis, Sacramento; University of Southern California School of Medicine, Los Angeles, CA; Our Lady of Mercy Medical Center Comprehensive Cancer Center, New York Medical College, Bronx, NY; Nevada Cancer Institute, Las Vegas, NV; Loyola University Stritch School of Medicine, Maywood, IL; and University of Colorado, Denver, CO.

Submitted July 30, 2008; accepted May 15, 2009; published online ahead of print at www.jco.org on November 2, 2009.

Supported in part by Public Health Service Cooperative Agreement Grants

A B S T R A C T

Purpose
Patients with advanced papillary renal cell cancer (pRCC) have poor survival after systemic therapy; the reported median survival time is 7 to 17 months. In this trial, we evaluated the efficacy of erlotinib, an oral epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor in patients with advanced pRCC, a tumor type associated with wild-type von Hippel Lindau gene.

Patients and Methods
Patients with histologically confirmed, advanced, or metastatic pRCC were treated with erlotinib 150 mg orally once daily. A RECIST (Response Evaluation Criteria in Solid Tumors) response rate (RR) of ≥ 20% was considered a promising outcome. Secondary end points included overall survival and 6-month probability of treatment failure.

Results
Of 52 patients registered, 45 were evaluable. The overall RR was 11% (five of 45 patients; 95% CI, 3% to 24%), and the disease control rate was 64% (ie five partial response and 24 stable disease). The median overall survival time was 27 months (95% CI, 13 to 36 months). Probability of freedom from treatment failure at 6 months was 29% (95% CI, 17% to 42%). There was one

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Abstract ▾ Send to: ▾

Cancer. 2004 Oct 1;101(7):1545-51.

Active chemotherapy for sarcomatoid and rapidly progressing renal cell carcinoma.

Nanus DM[1], Garino A, Milowsky MI, Larkin M, Dutcher JP.

⊕ Author information

Abstract

BACKGROUND: Immunotherapy is generally ineffective in patients with sarcomatoid renal cell carcinoma (RCC) and in patients with rapidly progressive metastatic or locally recurrent disease, with a median time to progression of approximately 2 months and a median survival of 4-7 months. Gemcitabine-based regimens have modest antitumor activity, whereas doxorubicin is often used to treat sarcomatoid RCC. Based on the antitumor activity of doxorubicin and gemcitabine in collecting duct carcinoma of the kidney, the authors used this combination to treat selected patients with sarcomatoid or rapidly progressing RCC.

METHODS: Eighteen patients (11 males and 7 females; median age, 53 years; range, 31-81 years) with RCC (56% sarcomatoid; 44% other) were treated at 2 institutions in a collaborative study that was not institutional review board reviewed. Seven patients received previous treatment with interferon or interleukin-2. Sites of metastases included the lung, soft tissue, bone, liver, and brain with 88% of patients having > or = 3 sites of disease. Treatment consisted of doxorubicin (50 mg/m2) and gemcitabine (1500 or 2000 mg/m2) every 2-3 weeks with granulocyte-colony-stimulating factor support.

RESULTS: A median of 5 courses was administered (range, 2-12 cycles). Therapy was well tolerated with no Grade 4 toxicities. Two patients had a complete response, five had a partial response, three had a mixed response, and one had stable disease. The median duration of response was 5 months (range, 2-21+ months).

CONCLUSIONS: These data suggested that the combination of doxorubicin and gemcitabine has antitumor activity in patients with sarcomatoid RCC or with rapidly progressing RCC. A prospective investigation of this combination in RCC is warranted.

PMID: 15378501 [PubMed - indexed for MEDLINE] Free full text

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Abstract

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Med Oncol. 2011 Dec;28(4):1530-3. doi: 10.1007/s12032-010-9649-2. Epub 2010 Aug 18.

Long-term survival of patients with sarcomatoid renal cell cancer treated with chemotherapy.

Dutcher JP[1], Nanus D.

Author information

Abstract

Sarcomatoid renal cell cancer is associated with a very poor prognosis, characterized by rapid progression of advanced disease. We previously reported the outcome of 18 patients with advanced sarcomatoid renal cell cancer treated with a regimen consisting of doxorubicin, 50 mg/m2 and gemcitabine, 1,500-2,000 mg/m2, administered every two weeks with growth factor support (A/G). Among the 18 patients, there were two complete and 5 partial responses and two patients with stable disease of more than 6 months of duration. We now report long-term survival of 4 patients with stage IV sarcomatoid renal cell carcinoma treated with this regimen at the 1,500 mg/m2 dose of gemcitabine, and achieving complete response (2 patients), or rendered complete responders following surgery after maximum response (2 patients). The two complete responders are alive, disease free at 6+ and 8+ years after starting A/G, and the 2 patients rendered CR by surgery survived 3½ and 6 years, respectively. Both died of progressive disease, one with clear cell recurrence, one with sarcomatoid recurrence. In summary, this regimen is associated with a high response rate, overall improvement in progression free survival and occasional meaningful long-term survival in a disease expected to be fatal within one year.

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

Urology. 2007 Nov;70(5):878-82.

Renal medullary carcinoma: the Bronx experience.

Hakimi AA[1], Koi PT, Milhoua PM, Blitman NM, Li M, Hugec V, Dutcher JP, Ghavamian R.

Author information

[1]Department of Urology, Montefiore Medical Center, Bronx, New York 10467, USA. ahakimi@montefiore.org

Abstract

OBJECTIVES: Renal medullary carcinoma (RMC) is a devastating and extremely rare malignancy primarily afflicting young men with sickle cell trait. We present our clinical experience with 9 cases of RMC during a 10-year period and briefly review the published data.

METHODS: A retrospective chart review of 9 cases of RMC during a 10-year period at our institutions was performed. The clinical patient characteristics, presentations, treatments, and outcomes were recorded. The radiographic images and pathologic specimens were reviewed. Applicable studies were selected from a Medline search.

RESULTS: All 9 patients had sickle cell trait, the male/female ratio was 6:3, and the age range was 13 to 31 years. All the patients presented with flank pain, two thirds had hematuria, and 3 of the 9 patients presented with a palpable mass. Eight of the nine tumors were right sided, ranging from 4 to 12 cm in the greatest diameter. Of the 9 patients, 7 underwent radical nephrectomy. One patient was deemed to have unresectable disease by the operating surgeon, and one was given initial chemotherapy after biopsy of a metastatic lesion. The neoadjuvant therapies varied. Overall survival ranged from 4 to 16 months, with 2 patients still living at the last follow-up visit.

CONCLUSIONS: Our urban setting likely explains our relatively large experience with this rare and extremely aggressive tumor. An early diagnosis is critical, and a high index of suspicion should be given to any individual with sickle cell trait and new-onset hematuria, especially in the setting of a right-sided mass. Prospective trials are needed for chemotherapy/immunotherapy, because surgical intervention alone is inadequate.

Berak Hücreli Dışı Böbrek Kanserlerinde , Tedavi Seçenekleri

J Urol. 2007 May;177(5):1698-702.

Prospective multicenter phase II study of gemcitabine plus platinum salt for metastatic collecting duct carcinoma: results of a GETUG (Groupe d'Etudes des Tumeurs Uro-Génitales) study.

Oudard S[1], Banu E, Vieillefond A, Fournier L, Priou F, Medioni J, Banu A, Duclos B, Rolland F, Escudier B, Arakelyan N, Culine S; GETUG (Groupe d'Etudes des Tumeurs Uro-Génitales).

⊕ Author information

Abstract

PURPOSE: Collecting duct carcinoma of the kidney is a rare and aggressive neoplasm of the distal collecting tubules for which there is no established treatment. Since the histology of collecting duct carcinoma is similar to that of urothelial carcinoma, the standard chemotherapy regimen defined by a gemcitabine and platinum salts combination was prospectively investigated in patients with metastatic collecting duct carcinoma.

MATERIALS AND METHODS: A total of 23 patients with metastatic collecting duct carcinoma with no prior systemic chemotherapy were treated with 1,250 mg/m(2) gemcitabine on days 1 and 8 plus 70 mg/m(2) cisplatin or carboplatin (AUC 5) in patients with renal insufficiency on day 1. The drugs were repeated every 21 days for 6 cycles according to toxicity and efficacy. The objective response rate was the primary end point.

RESULTS: There were 1 complete and 5 partial responses for an objective response rate of 26% (95% CI 8 to 44). Median progression-free and overall survival was 7.1 (95% CI 3 to 11.3) and 10.5 months (95% CI 3.8 to 17.1), respectively. Toxicity was mainly hematological with grade 3-4 neutropenia and thrombocytopenia in 52% and 43% of patients, respectively. The severity of granulocytopenia and the number of metastatic sites were associated with overall survival on univariate and multivariate analyses.

CONCLUSIONS: To our knowledge this is the first prospective, multicenter, phase II study showing that the platinum salts combination is an active and safe regimen as first line treatment in patients with metastatic collecting duct carcinoma. This platinum based chemotherapy should be considered the standard regimen in these patients.

Metastatik Papiler Tip 2 Renal Kanser, Akciğer Metastazı

Tedavi

- ❑ Pazopanib 800 mg/gün, başlandı
- ❑ Enteral mama desteği

Metastatik Papiler Tip 2 Renal Kanser, Akciğer Metastazı

- Tedavinin 4 . Ayında ağız içi grad 1-2 mukozit, ishal şikayetleri oldu
- Destek tedavisi ile yan etkiler geriledi
- Tedavi süresince yaklaşık 10 gün ilaç kesilmek zorunda kalındı
- 3 ayda bir kontrole geliyor, klinik yanıt, radyolojik stabil bulgular
- Tedavinin 9 ayında stabil izleniyor