Abstract No. 4503

Axitinib vs Sorafenib as Second-line Therapy for Metastatic Renal Cell Carcinoma: Results of the Phase 3 AXIS Trial

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Disclosures

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- **Research Funding: Pfizer**

Background

- **Axitinib is a potent and selective second-generation inhibitor of VEGFR-1, 2, 3[1]**

- **Antitumor efficacy observed in previous phase 2 trials:**
  - **Cytokine-refractory RCC[2] 44% ORR; 15.7 mo TTP**
  - **Sorafenib-refractory RCC[3] 23% ORR; 7.4 mo PFS**

- **The standard of care for metastatic RCC patients resistant to initial therapy is not well-defined. No randomized trials have yet compared targeted therapies.**

[1] Hu-Lowe DD, et al. *Clin Cancer Res* 2008;14:7272-83
[2] Rixe O, et al. *Lancet Oncol* 2007;8:975-84
[3] Rini BI, et al. *J Clin Oncol* 2009;27:4462-8

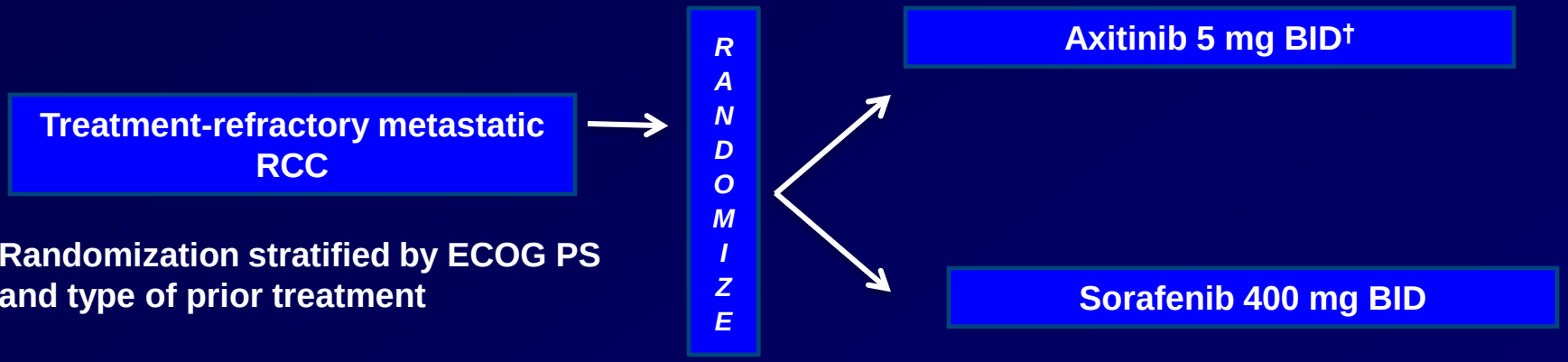
Key Eligibility Criteria

- Metastatic RCC with clear cell histology
- Measurable disease per RECIST criteria[1]
- RECIST-defined progressive disease after one prior sunitinib-, bevacizumab + IFN-α-, temsirolimus-, or cytokine-based regimen
- ECOG Performance Status 0 or 1
- Adequate blood counts and serum chemistry

[1] Therasse P, et al. J Natl Cancer Inst 2000;92:205-16

Study Design & Objectives

Trial design	Primary Objective	Select Secondary Endpoints	Study sites
Randomized, Open-label, Phase 3	Compare PFS in mRCC patients following failure of 1 prior sunitininb-, bevacizumab + IFN-α-, temsirolimus-, or cytokine-based regimen	Secondary: Overall Survival Objective Response Rate (RECIST) Safety and tolerability Duration of response Patient-reported Outcomes (PRO)	Global 191 sites 22 countries



Randomization stratified by ECOG PS and type of prior treatment

†Starting dose 5 mg BID with option for dose titration to 10 mg BID

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Assessments & Analysis

Assessments

- **Tumor assessments at screening, wk 6 and 12, then every 8 wks**
  - **All scans collected for independent central review**
- **Safety assessments included office visits at wk 2 and 4, then every 4 wks; Home BP monitoring**
- **Patient-reported QoL at screening, every 4 wk of therapy, end of study, 28 days after last dose (FKSI and EQ-5D)**

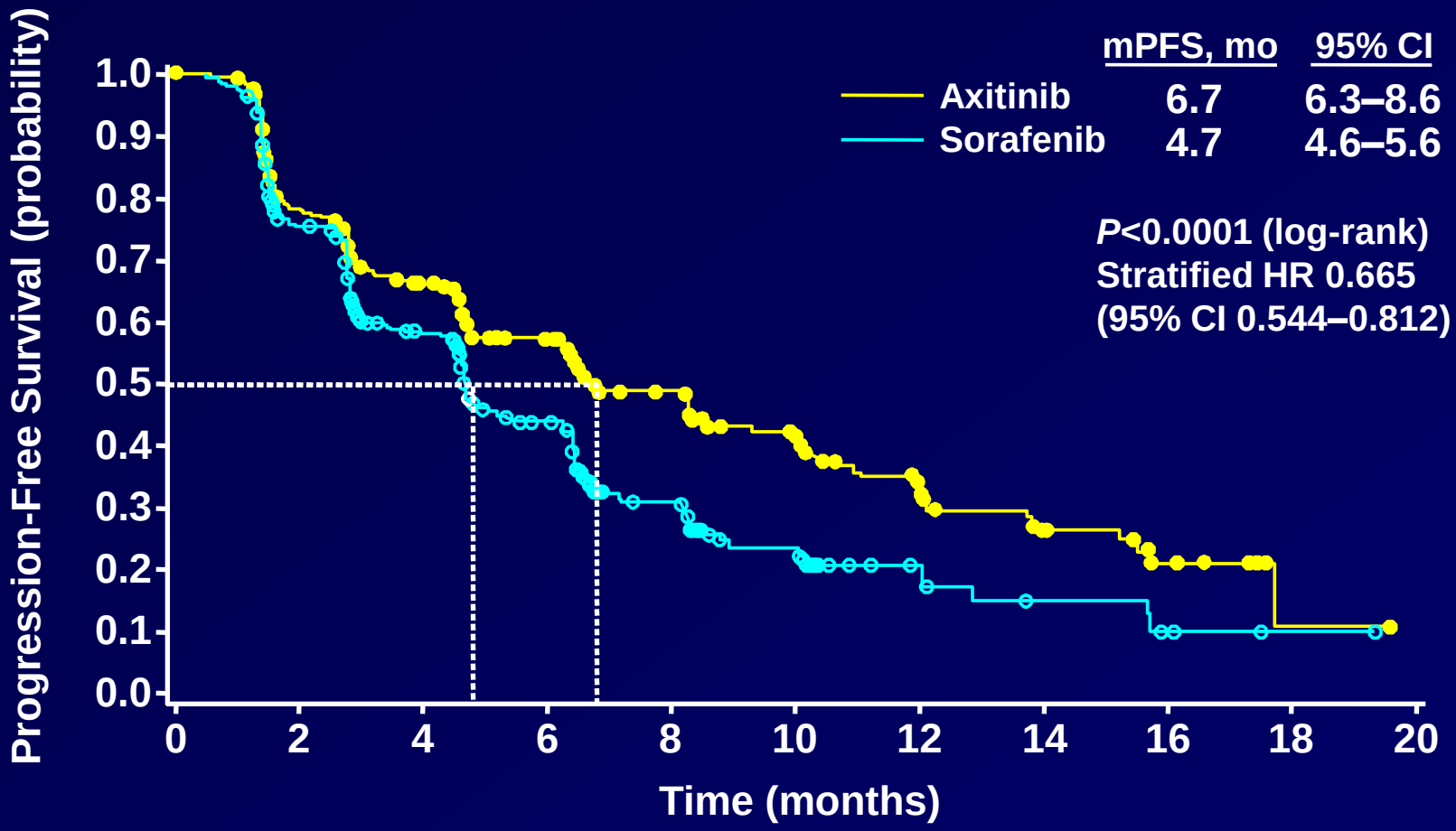
Statistical Analysis

- **PFS: time from randomization to either disease progression (assessed by blinded, independent review committee [IRC]), or death**
  - **90% power to observe a ≥ 40% improvement in median PFS, from 5 months with sorafenib to 7 months with axitinib**

Patient Characteristics

Characteristic	Axitinib (n=361)	Sorafenib (n=362)
Median age, yrs (range)	61 (20-82)	61 (22-80)
Gender		
Male/Female(%)	73/27	71/29
Race (%)		
•Caucasian	77	74
•Black	0	1
•Asian	21	22
•Other	1	2
ECOG PS (%)		
•0	54	55
•1	45	44
Prior nephrectomy, (%)	91	91
Sites of disease involvement (%)		
•Lung	76	81
•Lymph node	58	56
•Bone	33	30
•Liver	28	29
Prior Systemic Therapy (%)		
•Sunitinib	54	54
•Cytokines	35	35
•Bevacizumab	8	8
•Temsirolimus	3	3
MSKCC risk factors[1] (%)		
0 (favorable)	40	40
1-2 (intermediate)	54	54
≥3 (poor)	2	2
Heng et al. risk factors[2] (%)		
•0 (favorable)	18	22
•1-2 (intermediate)	65	62
•≥3 (poor)	10	9

Progression-free Survival
(IRC Assessment)



Subjects at risk, n

Axitinib	361	256	202	145	96	64	38	20	10	1	0
Sorafenib	362	224	157	100	51	28	12	6	3	1	0

IRC = Independent Review Committee

Progression-free Survival

Median PFS, mo	Axitinib (n=361)	Sorafenib (n=362)	HR	P value*
IRC Assessment	6.7	4.7	0.665	<0.0001
Investigator Assessment	8.3	5.6	0.658	<0.0001

*One-sided log-rank test stratified by ECOG PS and prior treatment

PFS by Prior Regimen

Prior Treatment Regimen	Axitinib (n=361)	Sorafenib (n=362)	HR	P value*
Cytokines (n=251)				
IRC	12.1	6.5	0.464	<0.0001
Investigator	12.0	8.3	0.636	0.005
Sunitinib (n=389)				
IRC	4.8	3.4	0.741	0.011
Investigator	6.5	4.5	0.636	0.0002
Temsirolimus (n=24)				
IRC	10.1	5.3	0.511	0.142
Investigator	2.6	5.7	1.210	0.634
Bevacizumab (n=59)				
IRC	4.2	4.7	1.147	0.637
Investigator	6.5	4.5	0.753	0.213

*One-sided log-rank test stratified by ECOG PS

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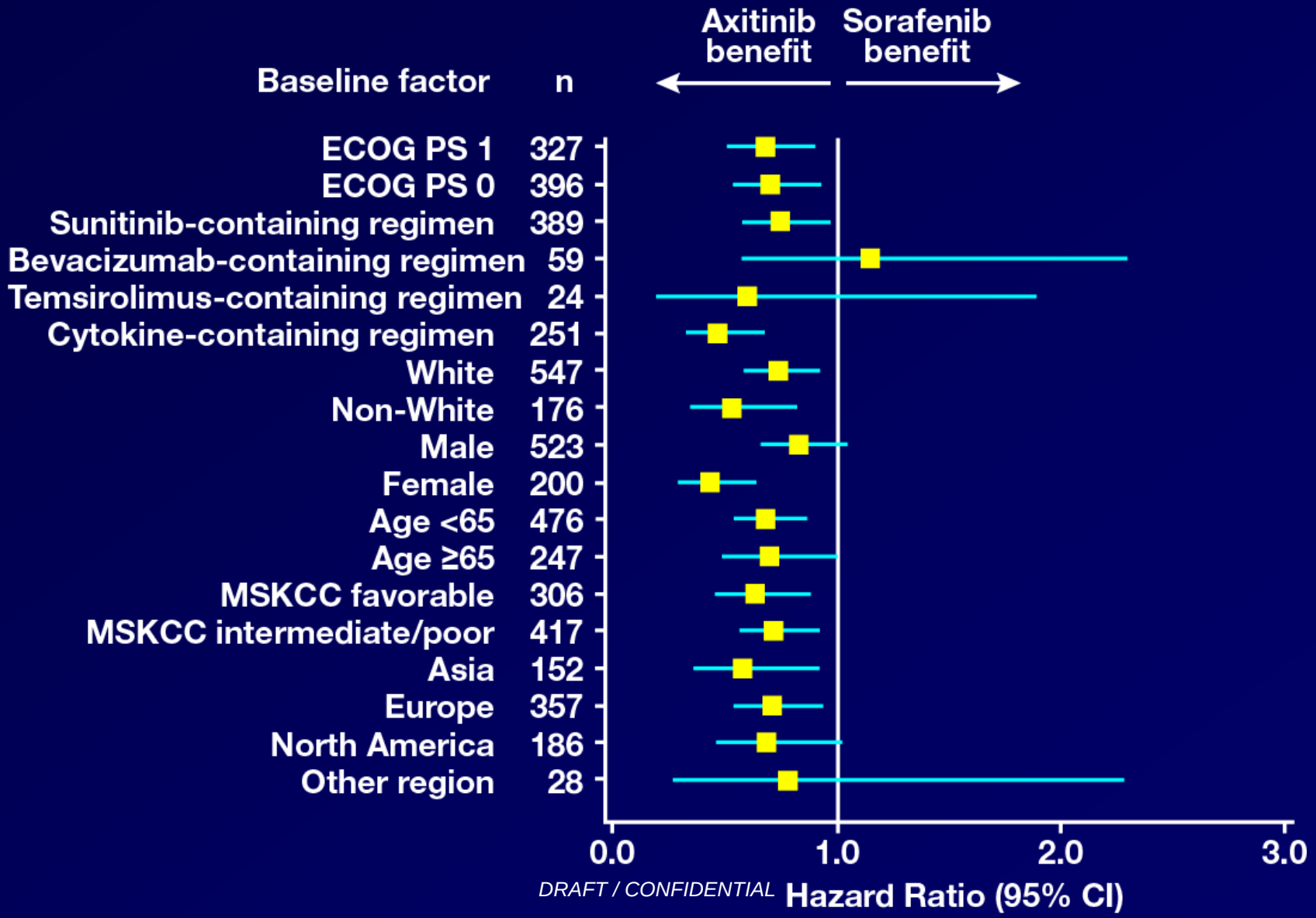
Hazard Ratios for PFS by Prognostic Factors and Baseline Characteristics



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Best Response by RECIST
(IRC Assessment)

Best Overall Response, %	Axitinib	Sorafenib
Partial response*	19.4	9.4
Stable disease	49.9	54.4
Progressive disease	21.6	21.0
Indeterminate	6.1	11.6
Risk ratio (95% CI)	2.1 (1.4–3.0)	

*Axitinib vs. Sorafenib: P = 0.0001

Drug Delivery

	Axitinib (n=359)	Sorafenib (n=355)
Dose interruptions, %	76.9	80.3
Due to AEs, %	54.0	63.1
Patients with dose increase, %	36.8	NA
Patients with dose decrease, %	30.6	52.1
Median relative dose intensity, %	98.6	91.7
Discontinuations due to treatment-related AEs, %*	3.9	8.2

*Adverse events as determined by investigators

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Adverse Events*

Event	Axitinib (%)		Sorafenib (%)	
	All grade	Grade 3/4	All grade	Grade 3/4
Diarrhea	55	11	53	7
Hypertension	40	16	29	11
Fatigue	39	11	32	5
Nausea	32	3	22	1
Vomiting	24	3	17	1
Hypothyroidism	19	<1	8	0
Stomatitis	15	1	12	<1
Hand-foot syndrome	27	5	51	16
Rash	13	<1	32	4
Alopecia	4	0	32	0

*All-causality; highest AEs of interest

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Laboratory Abnormalities*

Event	Axitinib (%)		Sorafenib (%)	
	All grade	Grade 3/4	All grade	Grade 3/4
Neutropenia	6	1	8	1
Anemia	35	<1	52	4
Elevation of Hgb	9	NA	1	NA
Thrombocytopenia	15	<1	14	0
Lymphopenia	33	3	36	4
Hypophosphatemia	13	2	50	16
Hypercalcemia	30	<1	7	0
Hypocalcemia	10	1	28	1
Elevation of Lipase	27	5	46	15

*All-causality; highest AEs of interest

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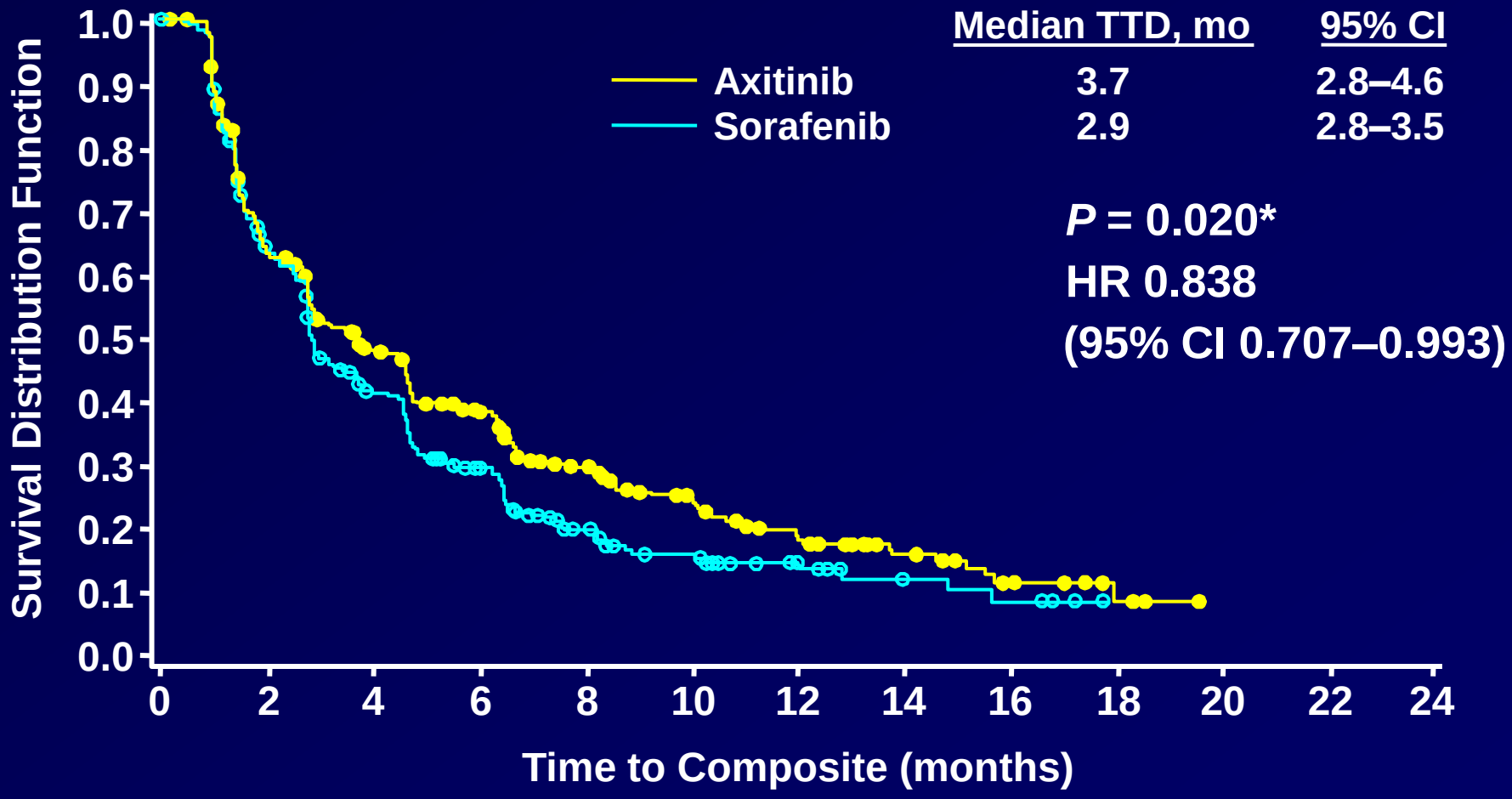
TTD of Composite Endpoint (with FSKI-DRS)



*One-sided *P* value

Conclusions

- **Axitinib treatment led to a statistically significant and clinically meaningful improvement in PFS compared to sorafenib in treatment-refractory RCC**
- **Axitinib had a generally similar safety profile compared to sorafenib with exception of ↑HTN, ↑hypothyroidism, ↓hand-foot syndrome, ↓rash, and ↓alopecia**
- **These data support the hypothesis that more potent biochemical targeting of the VEGF receptor is associated with superior clinical activity in RCC**
- **Axitinib should be considered as the reference standard in second-line treatment of advanced RCC**

Acknowledgments

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