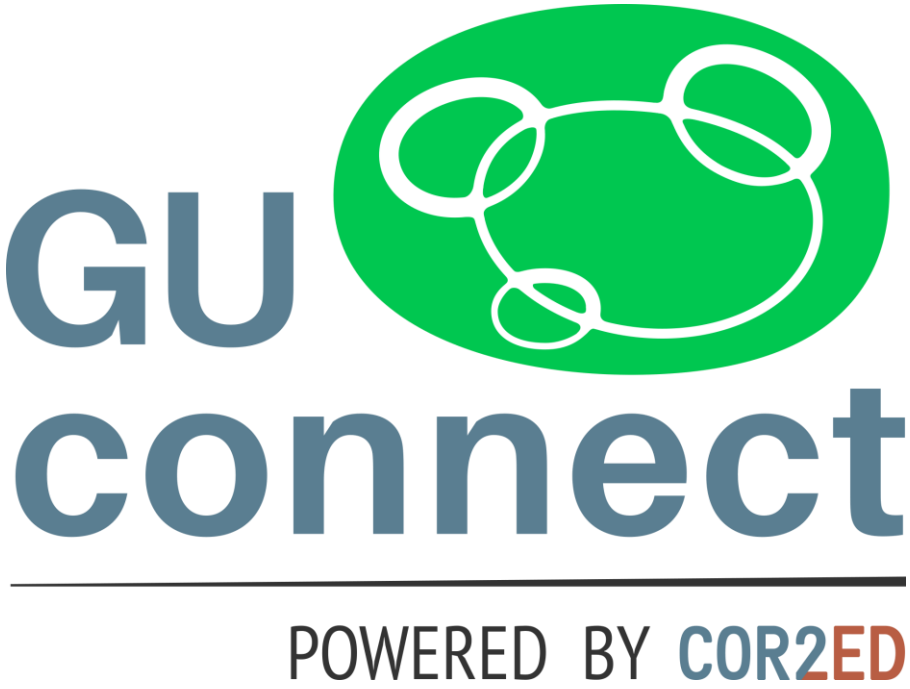
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ADJUVANT THERAPY IN mRCC

By

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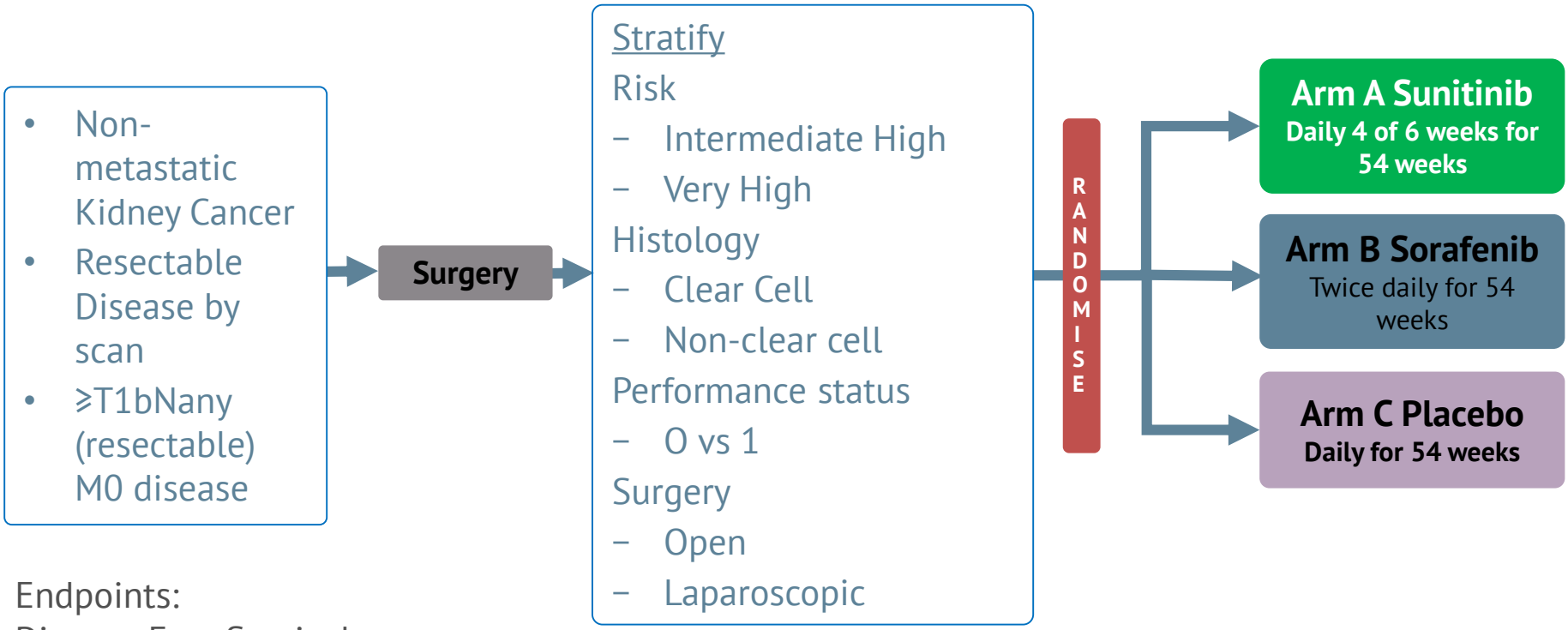
ASSURE TRIAL



Endpoints:
Disease-Free Survival
Overall Survival
Side Effects
(Including Cardiac, Fatigue)
Correlatives

Starting Dose	Sunitinib	Sorafenib
Original	50 mg/day	400 mg twice daily
Revised	35 mg/day	400 mg/day

Presented at ASCO GU 2015 by Naomi B. Haas

ASSURE TRIAL

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Study Population:

	Sunitinib N=647	Sorafenib N=649	Placebo N=647
Male sex	66%	67%	68%
Median age (years)	56	55	57
Race			
Non-Hispanic	89%	87%	87%
Hispanic	5%	6%	6%
Other	6%	7%	7%
ECOG Performance Status			
0	79%	79%	79%
1	21%	21%	21%
UCLA International Staging System risk stratification			
Intermediate high	50%	50%	50%
Very high	50%	50%	50%
Histology			
Clear cell	79%	80%	79%
Non-clear cell	21%	20%	21%

Haas NB et al, Lancet 2016; 387: 2008–16

ASSURE TRIAL

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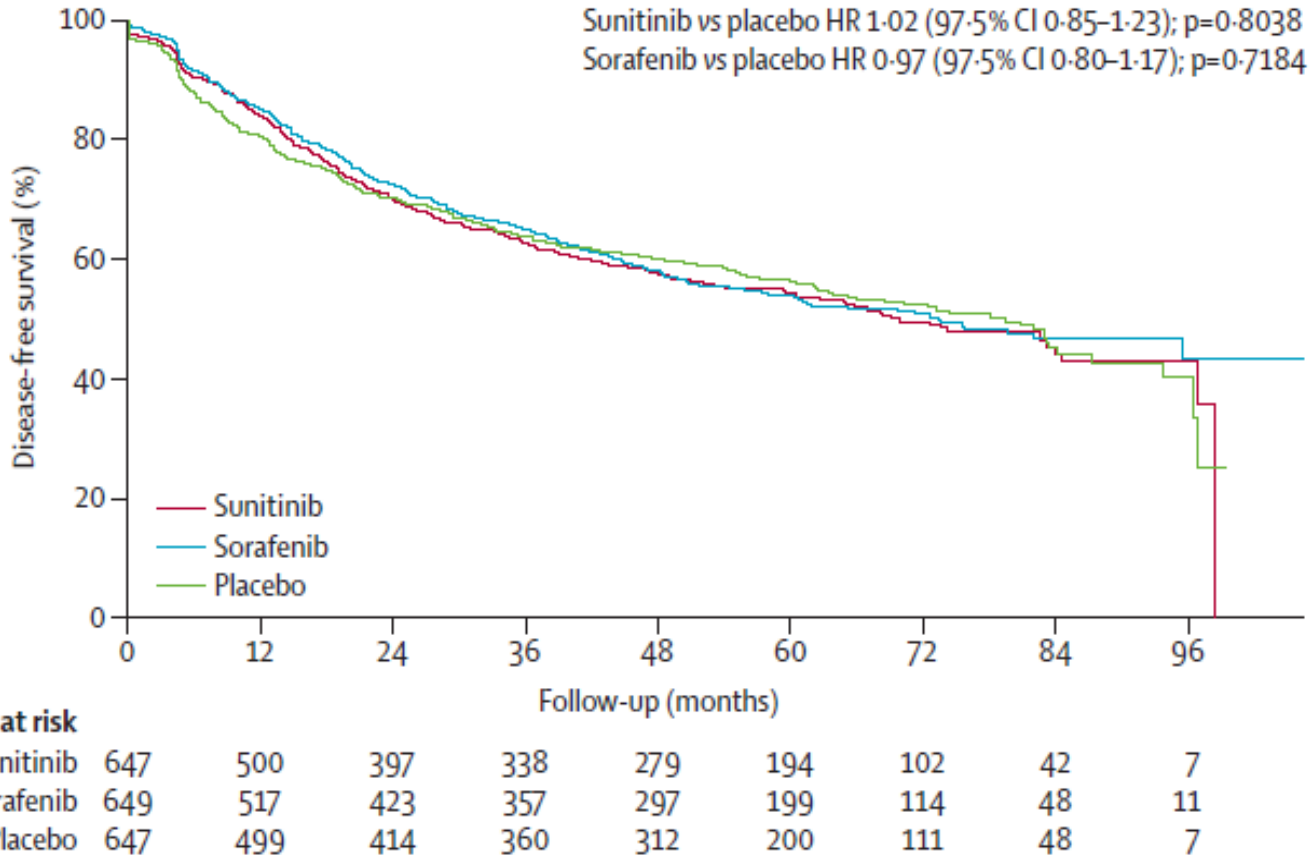
Disease Free Survival:
(primary endpoint)

Therapy	Median DFS (years)
Sunitinib	5.8
Sorafenib	6.1
Placebo	6.6

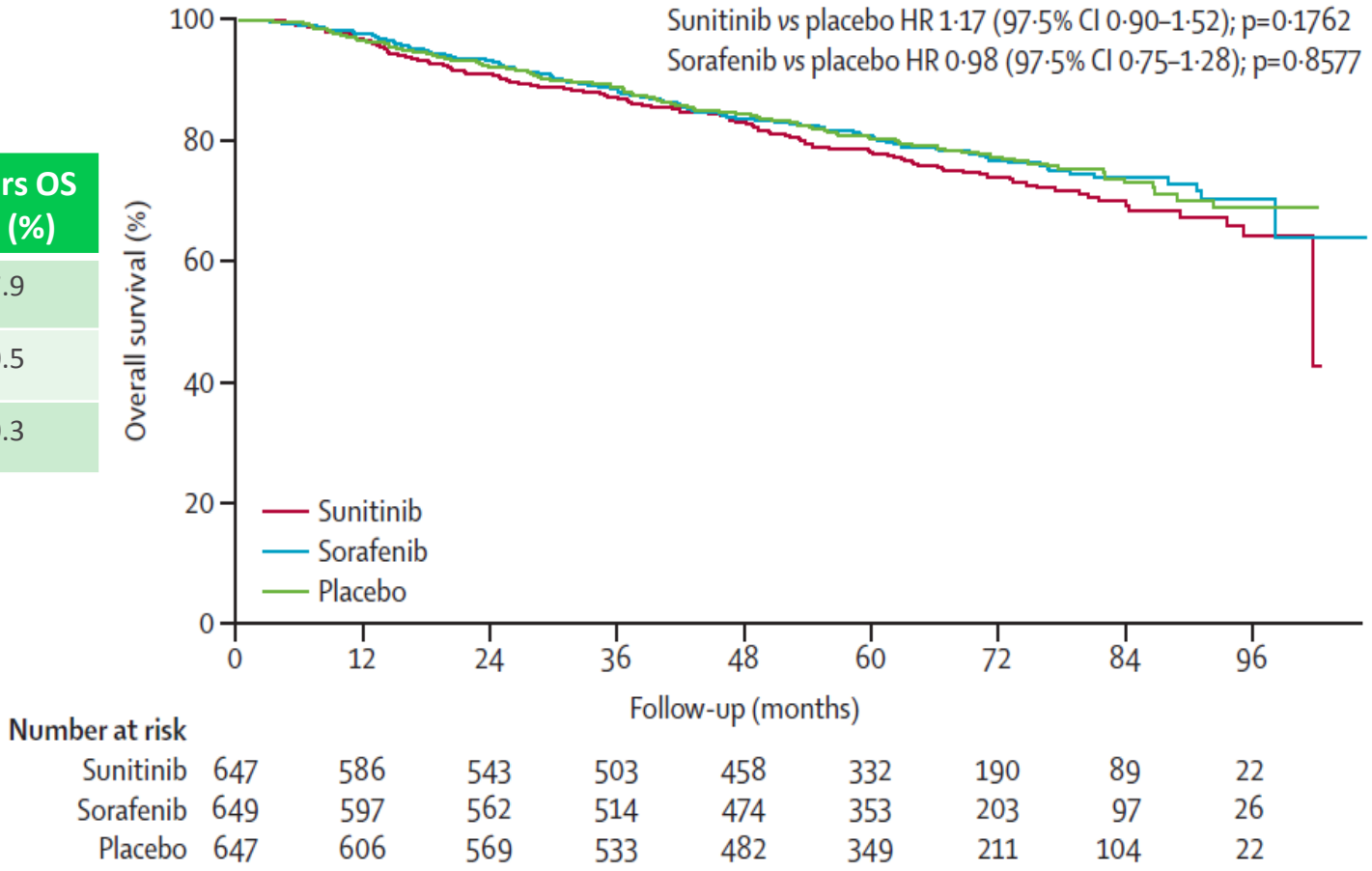


Haas NB et al, Lancet 2016; 387: 2008–16

ASSURE TRIAL

Overall Survival:
(secondary endpoint)

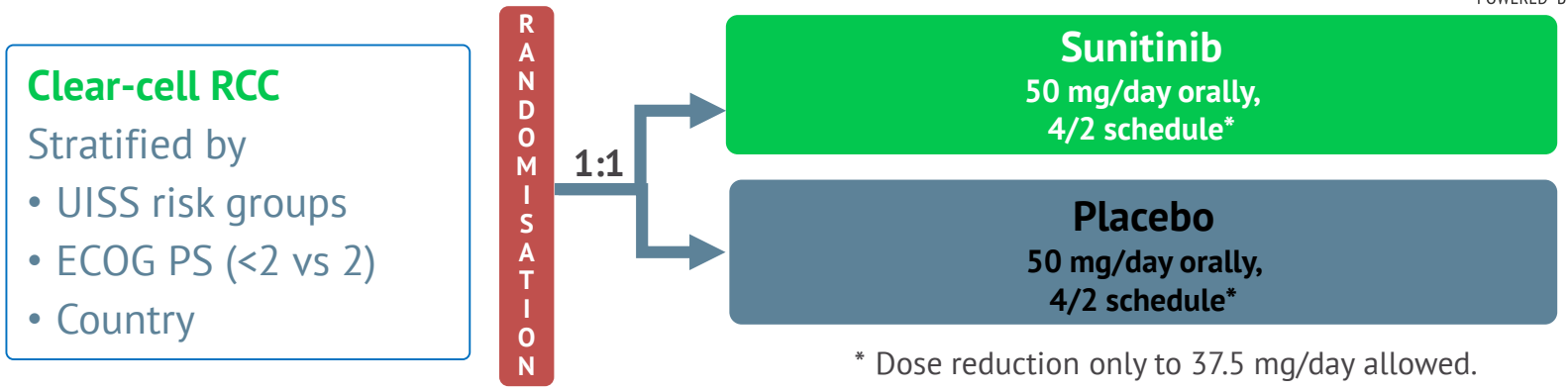
Therapy	5-years OS rate (%)
Sunitinib	77.9
Sorafenib	80.5
Placebo	80.3



Haas NB et al, Lancet 2016; 387: 2008–16

S-TRAC TRIAL

Study Design:



* Dose reduction only to 37.5 mg/day allowed.

N=615 pts enrolled

- Key Eligibility Criteria
  - Clear cell, loco-regional (≥T3 and/or N+) RCC
  - Systemic treatment-naïve
  - ECOG PS 0–2 pre-nephrectomy
  - Lack of metastasis, confirmed by blinded independent central review
- Patients received treatment for 1 year, until recurrence, second cancer, significant toxicity, or consent withdrawal
- Diagnosis of recurrence was based on centrally confirmed imaging and/or histology findings

Ravaud A et al, N Engl J Med. 2016; 375: 2246-2254.

S-TRAC TRIAL

Study Population:

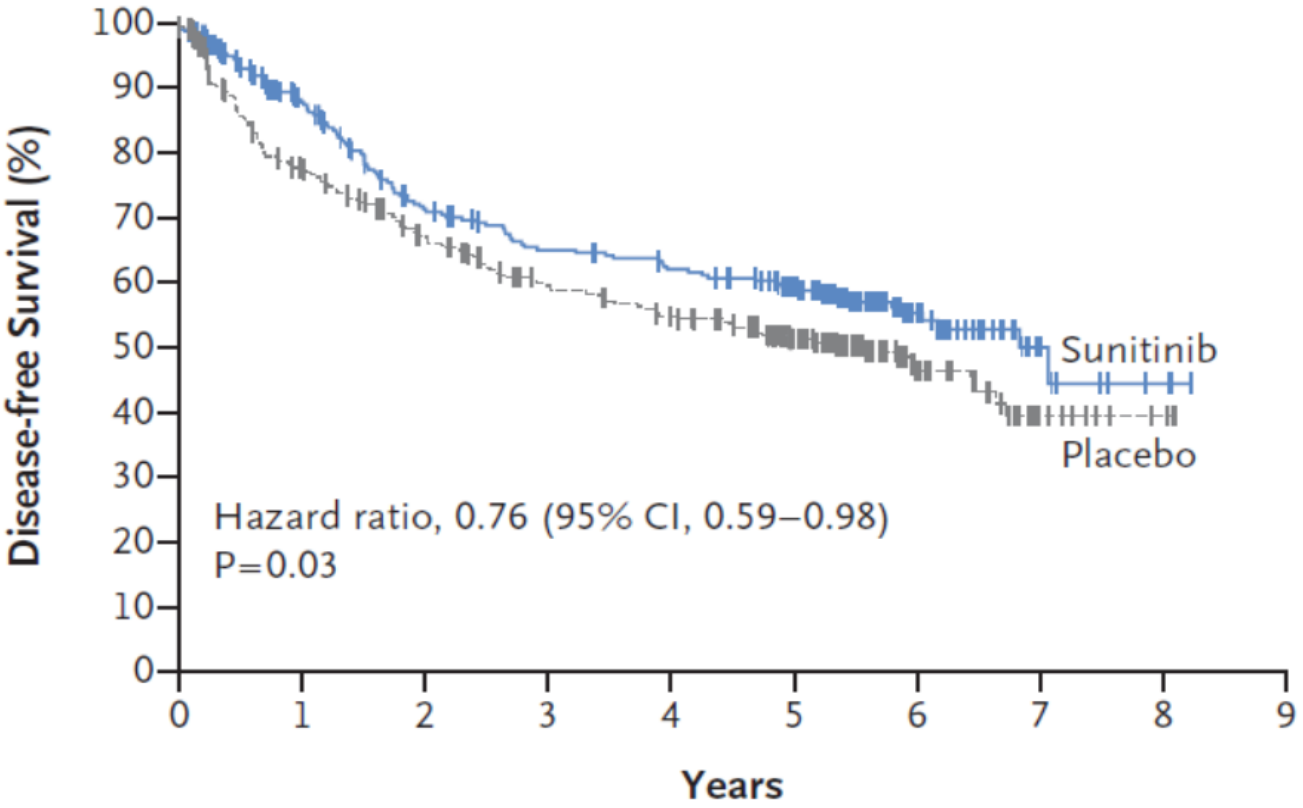
	Sunitinib N=309	Placebo N=306
Male sex	72%	75%
Median age (years)	57	50
Race		
White	82.2	85.9
Black	1.0	0.3
Asian	13.9	13.8
ECOG		
0	73.8%	71.9
1	25.6%	27.5
≥2	0.3%	0
UCLA stage risk		
A	90.6	90.8
B	1.3	1.3
C	8.1	7.8
Histology		
Clear cell	100%	100%

Ravaud A et al, N Engl J Med. 2016; 375: 2246-2254.

S-TRAC TRIAL

Disease Free Survival:
(primary endpoint)

Therapy	Median DFS (years)
Sunitinib	6.8
Placebo	5.6



No. at Risk

Sunitinib	309	225	173	153	144	119	53	10	3	0
Placebo	306	220	181	150	135	102	37	10	2	0

Ravaud A et al, N Engl J Med. 2016; 375: 2246-2254.

S-TRAC TRIAL

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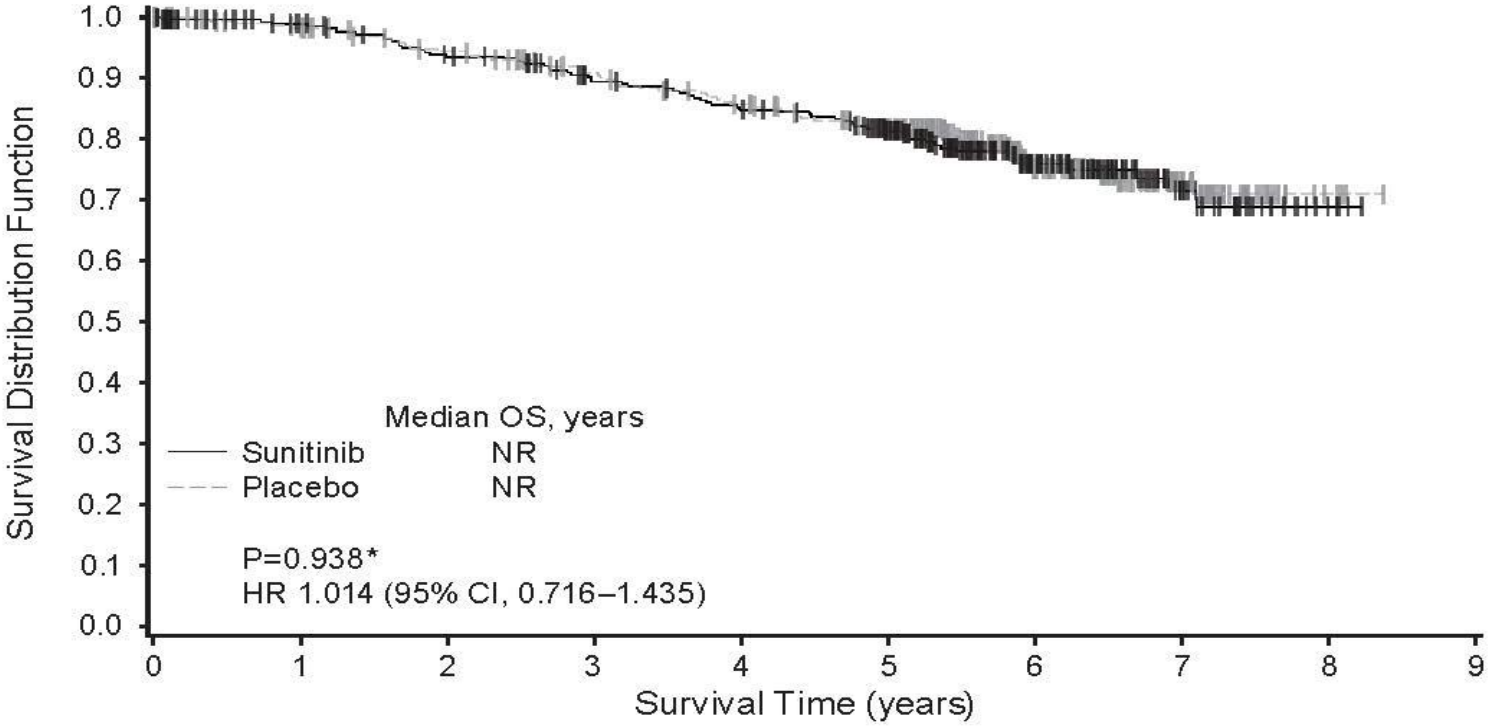
Overall Survival:
(secondary endpoint)

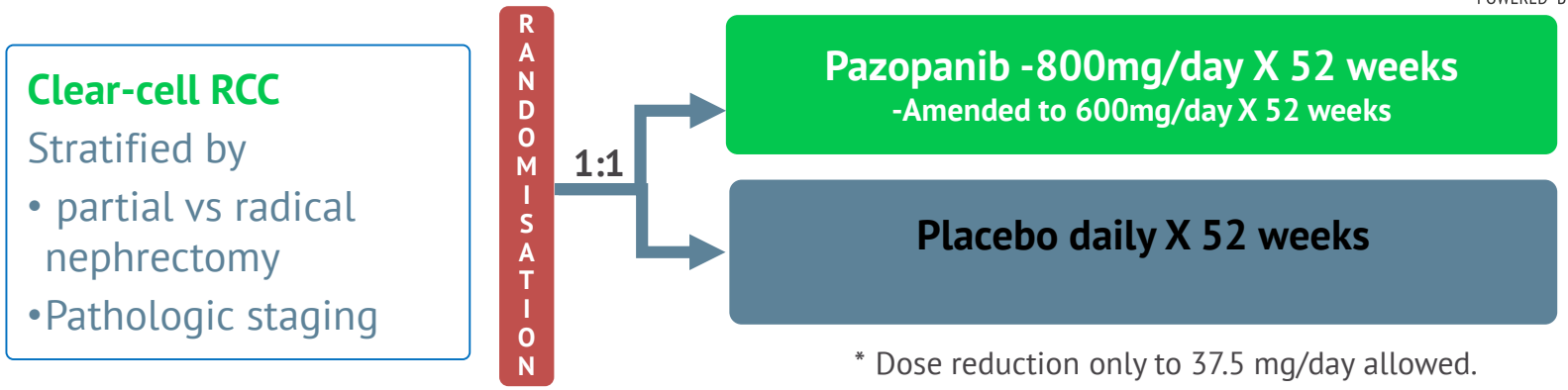


No. at risk										
Sunitinib	309	278	258	236	222	196	98	31	4	0
Placebo	306	289	269	250	231	197	96	40	4	0

Ravaud A et al, N Engl J Med. 2016; 375: 2246-2254

PROTECT trial

Study Design:



* Dose reduction only to 37.5 mg/day allowed.

N= 1538 pts enrolled

- Key Inclusion Criteria
  - pT2 G3 or G4 No
  - pT3 Gany N0
  - pT4 Gany N0
  - pTany Gany N1
  - Lack of metastasis, confirmed by blinded independent central review
- Diagnosis of recurrence was based on centrally confirmed imaging and/or histology findings

PROTECT- RESULTS

	ITT 600mg		ITT 800mg	
	Pazopanib N=571	Placebo N=564	Pazopanib N=198	Placebo N=205
DFS, Primary analysis * HR (95% CI)	0.86 (0.70, 1.06)		0.69 (0.51, 0.94)	
DFS, Follow up analysis ** HR (95% CI)	0.94 (0.77, 1.14)		0.66 (0.49, 0.90)	

CONCLUSION: Pazopanib @ 600mg did not prolong DFS which was the primary endpoint

*Primary analysis- data cut off Oct 2015
**Follow up analysis Oct 2016

TRIALS ABOUT ADJUVANT THERAPY IN KIDNEY CANCER

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Study	Type of Drug	Duration	Primary Endpoint	Patient Population	Status (www.CT.gov)
ASSURE	VEGFR TKI (Sunitinib, sorafenib)	1 year	DFS	High & Int Risk N=1923	Negative[1]
S-TRAC	VEGFR TKI (Sunitinib)	1 year	DFS	High Risk N=720[a]	Positive[2]
PROTECT	VEGFR TKI (Pazopanib)	1 year	DFS	High & Int Risk N=1500	Negative
ATLAS	VEGFR TKI (Axitinib)	3 years	DFS	High Risk N=700	Awaiting results
SORCE	VEGFR TKI (Sorafenib)	3 years	DFS	High & Int Risk N=1656	Awaiting results
EVEREST	mTOR (Everolimus)	1 year	RFS	High & Int Risk N=1218	Awaiting results
IMmotion 010	Anti-PD-L1 antibody (Atezolizumab)	1 year	DFS	High Risk N=664	Recruiting

Legend:
DFS: disease free survival
RFS: relapse free survival
VEGFR: vascular endothelial growth factor receptor
TKI: tyrosine kinase inhibitor
mTOR: mammalian target of rapamycin inhibitor

1-Haas NB et al, Lancet 2016; 387: 2008–16
2-Ravaud A et al, N Engl J Med. 2016; 375: 2246-2254

CONCLUSIONS

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- In the ASSURE trial, adjuvant treatment with the VEGF receptor tyrosine kinase inhibitors sorafenib or sunitinib showed no survival benefit relative to placebo
- The S-TRAC trial reported increased DFS in favor of adjuvant sunitinib over placebo in patients with high risk of relapse
- The S-TRAC trial did not report increased OS in favor of adjuvant sunitinib over placebo in patients with high risk of relapse
- Major differences between these two studies are the dose of drugs at beginning and the centralized radiological evaluation of the imaging performed in the S-TRAC but not in the ASSURE trial
- Recently reported PROTECT trial with pazopanib did not improve DFS compared to placebo
- Further studies are ongoing with other targeted agents and immunotherapy and results are awaited in the next years

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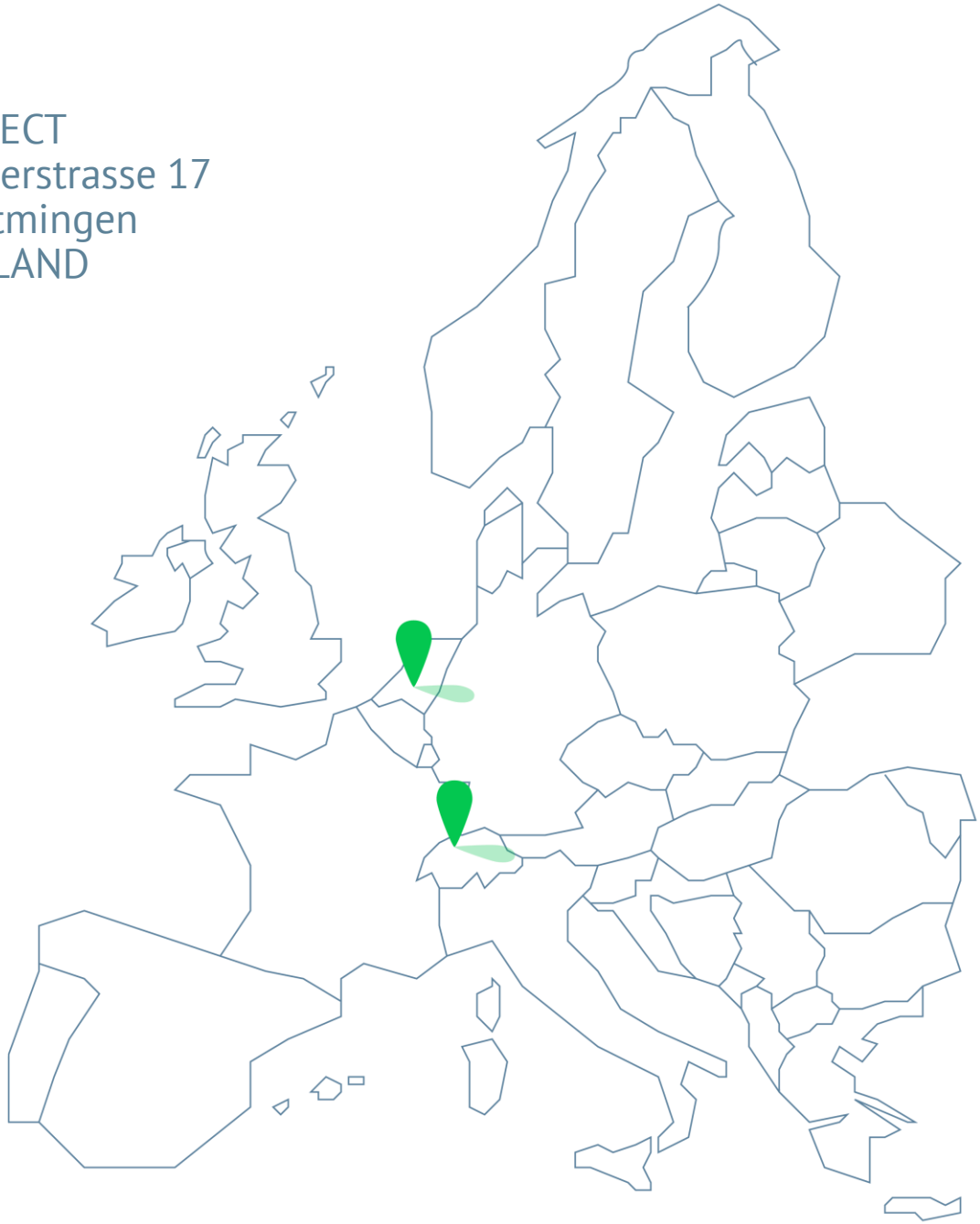

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