Supplementary Table S1. Distribution of Baseline Characteristics by schedule at baseline

Characteristic	Traditional schedule	Alternative schedule	*P* value
N=	98	24	
Male	81 (83%)	14 (58%)	0.01
Age, years	59 (34-82)	63.5 (23-77)	0.28
Race			
Caucasian	72 (74%)	18 (75%)	0.85
African-American	6 (6%)	2 (8%)	
Other	20 (20%)	4 (17%)	
ECOG PS			
0	19 (19%)	8 (33%)	0.34
1	59 (60%)	12 (50%)	
≥ 2	20 (21%)	4 (17%)	
Nephrectomy	56 (57%)	10 (42%)	0.25
MSKCC			
Good	4 (4%)	1 (4%)	0.40
Intermediate	46 (47%)	8 (33%)	
Poor	48 (49%)	15 (63%)	
Heng Criteria			
Favorable	10 (10%)	0 (0%)	0.21
Intermediate	60 (61%)	18 (75%)	
Poor	28 (29%)	6 (25%)	
Number of metastases			
Lungs	73 (74%)	15 (63%)	0.30
Bone	25 (26%)	14 (58%)	0.00
Liver	19 (19%)	6 (25%)	0.58
Number of metastases			
1	33 (34%)	3 (13%)	0.08
2	37 (38%)	10 (42%)	
≥ 3	28 (29%)	11 (46%)	
Laboratory abnormalities			
Hgb < LLN	74 (76%)	21 (88%)	1.00
ANC > 7.3 K/uL	31 (32%)	4 (17%)	0.00
Cor. Ca > 10 mg/dL	20 (20%)	7 (29%)	0.72
PLT > 440 K/uL	16 (16%)	10 (42%)	0.40

ECOG PS = Eastern Cooperative Oncology Group performance status; MSKCC = Memorial Sloan-Kettering Cancer Center; Hgb = hemoglobin; LLN = lower limit of normal; ANC = absolute neutrophil count; Cor. Ca = corrected calcium; PLT = platelets

Supplementary Table S2. Multivariable Cox proportional hazards model for progression-free survival at baseline (Total patients = 122, Progression = 106)

Variable	Hazard Ratio	95% CI	*P* value
LDH ≥ 927 (vs. <927)	2.54	1.28 – 5.05	0.008
Albumin ≤ 4 (vs. >4)	1.73	1.08 – 2.78	0.02
Heng Intermediate vs. Favorable	1.18	0.53 – 2.63	0.68
Heng Poor vs. Favorable	1.59	0.66 – 3.85	0.30
AS at treatment baseline (vs. TS)	0.71	0.42 – 1.21	0.21

LDH = lactate dehydrogenase; AS = alternative schedule; TS = traditional schedule

Supplementary Table S3. Multivariable Cox proportional hazards model for progression-free survival for patients treated beyond the median time to schedule change (5.6 mo) (Total patients = 122, Progression = 99)

Variable	Hazard Ratio	95% CI	*P* value
Albumin ≤ 4 (vs. >4)	1.43	0.94 – 2.17	0.06
ECOG PS = 1 (vs. 0)	1.49	0.93 – 2.40	0.09
ECOG PS ≥ 2 (vs. 0)	3.24	1.40 – 4.00	0.003
Heng Intermediate vs. Favorable	1.13	0.66 – 2.02	0.60
Heng Poor vs. Favorable	1.60	0.68 – 3.59	0.02
AS beyond median time to schedule change (vs. TS)	0.59	0.38 – 0.91	0.002

ECOG PS = Eastern Cooperative Oncology Group performance status; AS = alternative schedule; TS = traditional schedule

Supplementary Table S4: Univariate Cox proportional hazards models for overall survival (Total patients=185, Deaths=128)

Variable	Hazard Ratio	95% CI	*P* value
Time to systemic therapy < 1 year	1.84	1.27 – 2.67	0.001
Prior Nephrectomy	0.55	0.39 – 0.79	0.001
AS at treatment discontinuation (vs. TS)	0.48	0.34 – 0.69	0.0001
AS at treatment baseline (vs. TS)*	0.61	0.34 – 1.08	0.09
LDH > ULN	5.45	2.95 – 10.05	<0.0001
Albumin < LLN	2.28	1.58 – 3.29	<0.0001
Corrected calcium	1.23	1.03 – 1.47	0.02
Hemoglobin	0.84	0.78 – 0.91	<0.0001
ECOG PS = 1 (vs.0)	2.11	1.29 – 3.46	0.03
ECOG PS = 2,3 (vs.0)	4.83	2.71 – 8.58	<0.0001
MSKCC Good vs. Poor	0.04	0.005 – 0.27	0.001
MSKCC Intermediate vs. Poor	0.40	0.28 – 0.58	<0.0001
Heng Intermediate Vs Favorable	1.88	0.97 – 3.64	0.06
Heng Poor vs. Favorable	5.52	2.74 – 11.12	<0.0001
Metastases = 2 (vs.1)	1.47	0.96 – 2.28	0.08
Metastases ≥ 3 (vs.1)	2.15	1.35 – 3.42	0.001

*****63 patients were excluded in this model as they did not start with an alternative schedule (Total patients=122, Deaths=92)

AS = alternative schedule; TS = traditional schedule; LDH = lactate dehydrogenase; ULN = upper limit of normal; LLN = lower limit of normal; ECOG PS = Eastern Cooperative Oncology Group performance status; MSKCC = Memorial Sloan-Kettering Cancer Center

Supplementary Table S5. Multivariable Cox proportional hazards model for overall survival at baseline (Total patients=122, Deaths=92)

Variable	Hazard Ratio	95% CI	*P* value
LDH ≥ 927 (vs. <927)	2.99	1.46 – 6.14	0.003
Albumin ≤ 4 (vs. >4)	2.10	1.26 – 3.50	0.005
ECOG PS = 1 (vs. 0)	1.99	1.09 – 3.64	0.03
ECOG PS ≥ 2 (vs. 0)	2.79	1.25 – 6.21	0.01
Heng Intermediate vs. Favorable	2.18	0.77 – 6.17	0.14
Heng Poor vs. Favorable	2.73	0.85 – 8.75	0.09
AS at treatment baseline (vs. TS)	0.72	0.40 – 1.30	0.27

LDH = lactate dehydrogenase; ECOG PS = Eastern Cooperative Oncology Group performance status; AS = alternative schedule; TS = traditional schedule

Supplementary Table S6. Multivariable Cox proportional hazards model for overall survival in patients treated beyond the median time to schedule change (5.6 mo) (Total patients = 122, Deaths = 72)

Variable	Hazard Ratio	95% CI	*P* value
Albumin ≤ 4 (vs. >4)	1.60	0.99 – 2.60	0.05
ECOG PS = 1 (vs. 0)	1.62	1.03 – 3.44	0.03
ECOG PS ≥ 2 (vs. 0)	3.40	1.55 – 7.46	0.002
Heng Intermediate vs. Favorable	0.93	0.45 – 1.93	0.08
Heng Poor vs. Favorable	1.94	0.80 – 4.68	0.01
AS beyond median time to schedule change (vs. TS)	0.93	0.56 – 1.53	0.76

ECOG PS = Eastern Cooperative Oncology Group; AS = alternative schedule; TS = traditional schedule

Supplementary Figure S1A. Kaplan-Meier estimates for progression-free survival by sunitinib dosing schedule at baseline (*N* =122).

Supplementary Figure S1B. Kaplan-Meier estimates for overall survival by sunitinib dosing schedule at baseline (*N* =122).

Supplementary Figure S2A. Kaplan-Meier estimates for progression-free survival by sunitinib dosing schedule in patients treated beyond median time to schedule change (*N* =122).

Supplementary Figure S2B. Kaplan-Meier estimates for overall survival by sunitinib dosing schedule in patients treated beyond median time to schedule change (*N* =122).