IMDC score		**RMH score**		**MDACC score**	
Factor	Poor prognostic factor	Factor	Poor prognostic factor	Factor	Poor prognostic factor
HGB	< LLN	Albumin	< 3.5 g/dL	Albumin	< 3.5 g/dL
Plts	> ULN	LDH	> ULN	LDH	> ULN
ANC	> ULN	Metastatic sites	≥ 3 sites	Metastatic sites	≥ 3 sites
KPS	< 80%	-	-	ECOG PS	≥ 1
Corrected calcium	> ULN	-	-	Primary tumor site	Gastrointestinal
Dx to systemic tx	< 1 year				
IMDC risk group definitions					
Favorable	0 factors				
Intermediate	1-2 factors				
Poor	≥ 3 factors				

Supplemental Table 1: Definitions of the IMDC, RMH, and MDACC prognostic scores
Supplemental Table 1 Legend: HGB = hemoglobin, LLN = lower limit of normal, g = grams, dL = deciliter, Plts = platelets, ULN = upper limit of normal, LDH = lactate dehydrogenase, ANC = absolute neutrophil count, ECOG = Eastern Cooperative Oncology Group, PS = performance status, KPS = Karnofsky performance status, Dx = diagnosis, tx = treatment

Mechanism of action
Anti-CSF1R + PD-1 checkpoint inhibitor
Arginase inhibitor
BET inhibitor
CCR-4 inhibitor
Coenzyme Q10 + gemcitabine
CTLA-4 inhibitor + TLR9 agonist
Exportin inhibitor + PD-1 checkpoint inhibitor
EZH2 inhibitor + CTLA-4 checkpoint inhibitor
Glutaminase inhibitor
Glutaminase inhibitor + mTOR inhibitor
Glutaminase inhibitor + multi-target angiogenesis TKI
Glutaminase inhibitor + PARP inhibitor
Glutaminase inhibitor + PD-1 checkpoint inhibitor
ICOS monoclonal antibody
IDO-1 inhibitor + JAK inhibitor
MDM2 inhibitor
mTOR inhibitor + carboplatin + paclitaxel
Multi-target angiogenesis TKI
Multi-target TKI + mTOR inhibitor
Nanoparticle drug conjugate + VEGF targeted therapy
PARP inhibitor
PARP inhibitor + ATM inhibitor + cisplatin
PD-1 checkpoint inhibitor
PD-1 checkpoint inhibitor + CTLA-4 checkpoint inhibitor
PD-1 checkpoint inhibitor + cyclophosphamide
PD-1 checkpoint inhibitor + enterococcus
PD-1 checkpoint inhibitor + LAG-3 checkpoint inhibitor
PD-L1 checkpoint inhibitor + 4-1BB agonist + OX40 inhibitor
Pegylated IL-10 + PD-1 checkpoint inhibitor
PI3K inhibitor
Proteasome inhibitor + VEGF targeted therapy
Proteasome inhibitor + HDAC inhibitor
STING pathway agonist

Supplemental Table 2: Mechanisms of action of agents in phase 1 trials enrolling patients in the present study

Supplemental Table 2 Legend: TKI = tyrosine kinase inhibitor

Study	Population	Treatment(s)	OS	PFS	ORR
Ko, et al[18]	IMDC, second-line	VEGF or mTOR inhibitor	12.5 m	3.9 m	N/A
Wells, et al[20]	IMDC, third-line	VEGF or mTOR inhibitor	12.4 m	3.9 m	10.4%
METEOR[25]	mccRCC after ≥ 1 prior VEGF TT	Cabozantinib vs. everolimus	21.4 vs. 16.5 m	7.4 vs. 3.9 m	17% vs. 3%
CheckMate 025[26]	mccRCC after 1-3 prior lines	Nivolumab vs. everolimus	25.0 vs. 19.6 m	4.6 vs. 4.4 m	25% vs. 5%
Hahn, et al	MDACC, median third-line*	Phase 1 clinical trial	31.2 m	5.9 m	22%

Supplemental Table 3: Clinical outcomes for second-line or later treatment of metastatic renal cell carcinoma from select population-based studies and clinical trials.
Supplemental Table 3 Legend: OS = overall survival, PFS = progression-free survival, ORR = objective response rate, IMDC = International Metastatic RCC Database Consortium, VEGF = vascular endothelial growth factor, mTOR = mammalian target of Rapamycin, * = median third-line, but range from 0-9 prior lines of treatment.