

Overall survival improvement in metastatic clear-cell renal cell carcinoma patients from 2000 to 2020

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Disclosure

- I have no financial interests or relationships to disclose



- Retrospective study: all consecutively treated m-ccRCC
- All patients who started systemic treatment between 01/2000 and 10/2020
 - IFNa
 - VEGFR-TKI
 - ICI
 - mTOR inhibitors
- Objective: evaluate impact of introduction of new treatments on overall survival

Overall survival data of recent phase 3 studies

Study	Agent	PFS (months)	OS (months)
NCT00073307	Sorafenib v placebo	5,5 v 2,8 HR 0,44 (0,35-0,55) p<0,01	19,3 v 15,9 HR 0,77 (0,63-0,95) p=0,02
NCT00083889	Sunitinib v INFα	11 v 5 HR 0,42 (0,32-0,54) p<0,001	26,4 v 21,8 0,821 (0,673-1,001) p= 0,051
VEG105192	Pazopanib v placebo	9,2 v 4,2 HR 0,46 (0,34-0,62) P<0,0001)	22,9 v 20,5 HR 0,91 (0,71-1,16) P=0,224
RECORD-I	Everolimus v placebo	4,9 v 1,9 HR 0,33 (0,25-0,43) P<0,001	14,8 v 14,4 HR 0,87 (0,65-1,15) P=0,162
AXIS	Axitinib v sorafenib	6,7 v 4,7 HR 0,665 (0,544-0,812) p<0,0001	20,1 v 19,2 HR 0,969 (0,800-1,174) P= 0,3744
METEOR	Cabozantinib v everolimus	7,4 v 3,8 HR 0,58 (0,45-0,75) P<0,001	21,4 v 16,5 HR 0,66 (0,53-0,83) P=0,00026
CheckMate 025	Nivolumab v everolimus	4,6 v 4,4 HR 0,88 (0,75-1,03) P=0,11	25 v 19,6 HR 0,73 (0,57-0,93) P=0,002
CheckMate 214	Ipilimumab-nivolumab v sunitinib	11,6 v 8,4 HR 0,82 (0,64 -1,05) p= 0,03	NR v 26 HR 0,63 (0,44-0,89) P<0,001

RESULTS

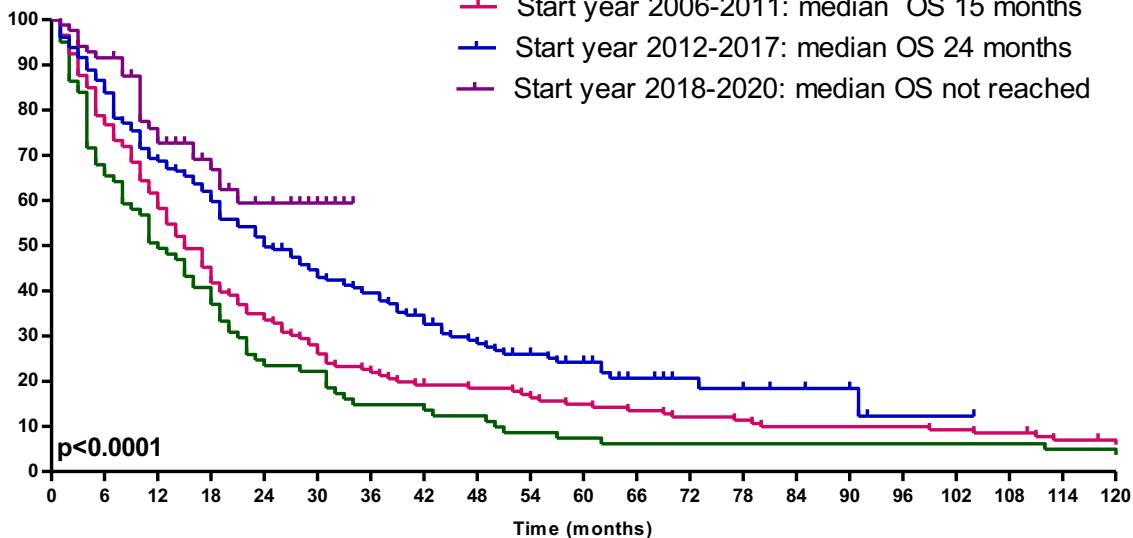
- 500 patients were included
- Patients were divided in two different ways
 - Start year of first line therapy
 - 2000 until 2005: 88 patients
 - 2006 until 2011: 146 patients
 - 2012 until 2017: 180 patients
 - 2018 until 2020: 86 patients
 - Type of first line therapy
 - IFNa: 92 patients
 - VEGFR-TKI: 330 patients
 - ICI: 57 patients
 - mTOR-I: 21 patients



OVERALL SURVIVAL DEPENDING ON START YEAR

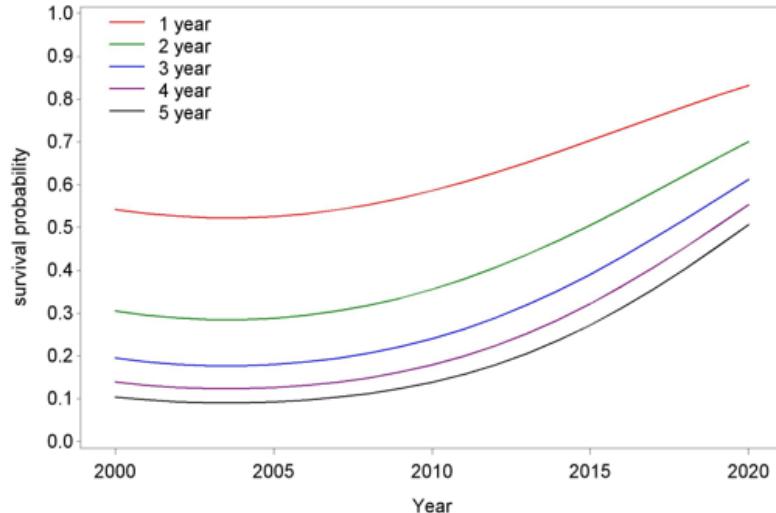
OS (%)

- Start year 2000-2005: median OS 12 months
- Start year 2006-2011: median OS 15 months
- Start year 2012-2017: median OS 24 months
- Start year 2018-2020: median OS not reached



Months	0	12	24	36	48	60	72	84	96
2000-2005	81	41	20	12	10	6	5	5	5
2006-2011	146	90	51	33	26	21	17	14	14
2012-2017	179	124	93	67	39	25	9	7	1
2018-2020	86	47	15	-	-	-	-	-	-

1 to 5-year survival probabilities depending on start year



Variable	Test	Hazard Ratio (95% CI)	P-value
UNIVARIABLE ANALYSIS			
Year (linear)	+1 year	0.947 (0.930;0.965)	<.0001
Year (nonlinear)	Quadratic effect		0.0092
	2001 vs 2000	1.029 (0.964;1.097)	0.3942
	2006 vs 2005	0.982 (0.950;1.015)	0.2789
	2011 vs 2010	0.937 (0.918;0.957)	<.0001
	2016 vs 2015	0.895 (0.853;0.938)	<.0001

HR: hazard ratio, CI: confidence interval
 Binary variables/pairwise tests: HR>(<)1: higher (lower) risk for first category HR<(>)1 means lower (higher) risk for a later start of therapy

In the non-linear model (both univariable and multivariable), the indicated HR do not compare two single treatment years but give an indication of the globe slope of the curve at different time points.

MULTIVARIABLE ANALYSIS (NON-LINEAR)

IMDC	Global test	<.0001
	GOOD vs INTERMEDIATE	0.585 (0.407;0.841) 0.0038
	GOOD vs POOR	0.340 (0.231;0.501) <.0001
	INTERMEDIATE vs POOR	0.581 (0.459;0.736) <.0001
CRP	>5mg/l vs <=5mg/l	2.213 (1.691;2.897) <.0001
Bone meta	Present vs Absent	1.072 (0.864;1.331) 0.5276
Brain meta	Present vs Absent	2.441 (1.668;3.573) <.0001
Year (nonlinear)	Quadratic effect	0.0104
	2001 vs 2000	1.039 (0.965;1.118) 0.3141
	2006 vs 2005	0.987 (0.950;1.025) 0.5031
	2011 vs 2010	0.938 (0.917;0.959) <.0001
	2016 vs 2015	0.892 (0.848;0.938) <.0001

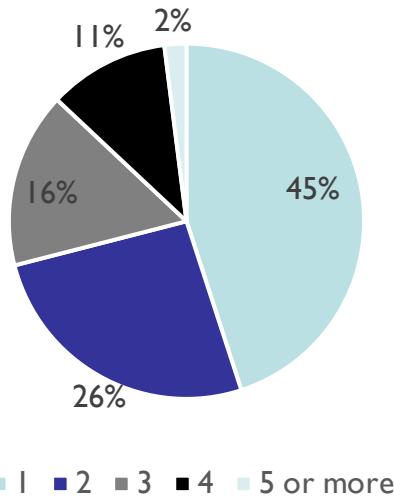
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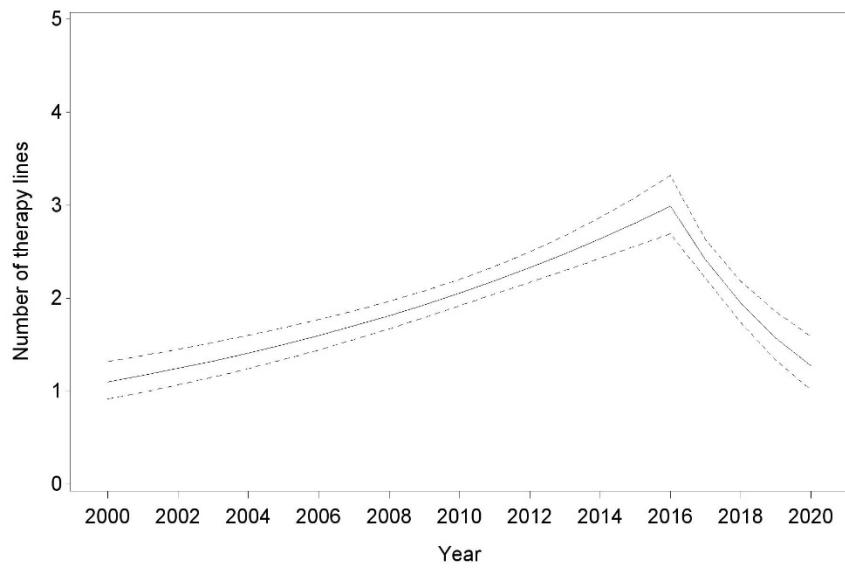
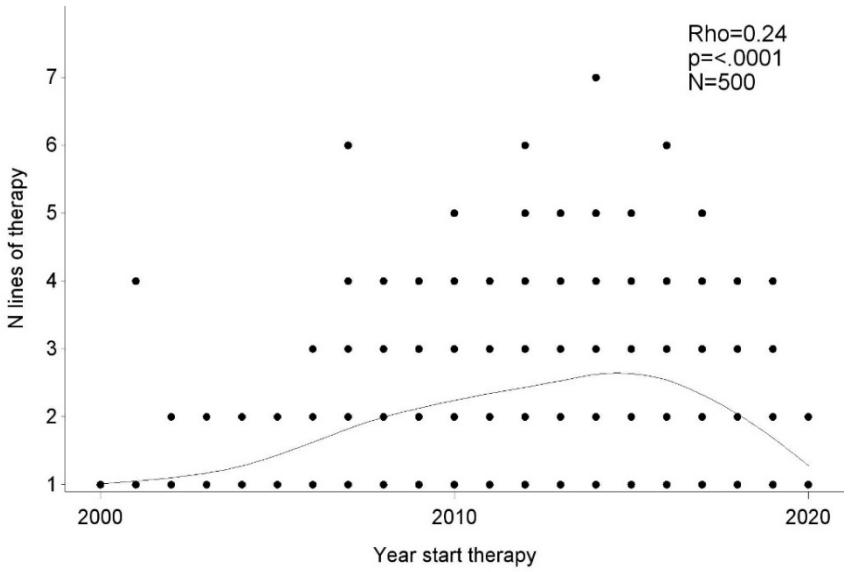
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NUMBER OF THERAPY LINES DURING THE PERIOD 2000-2020

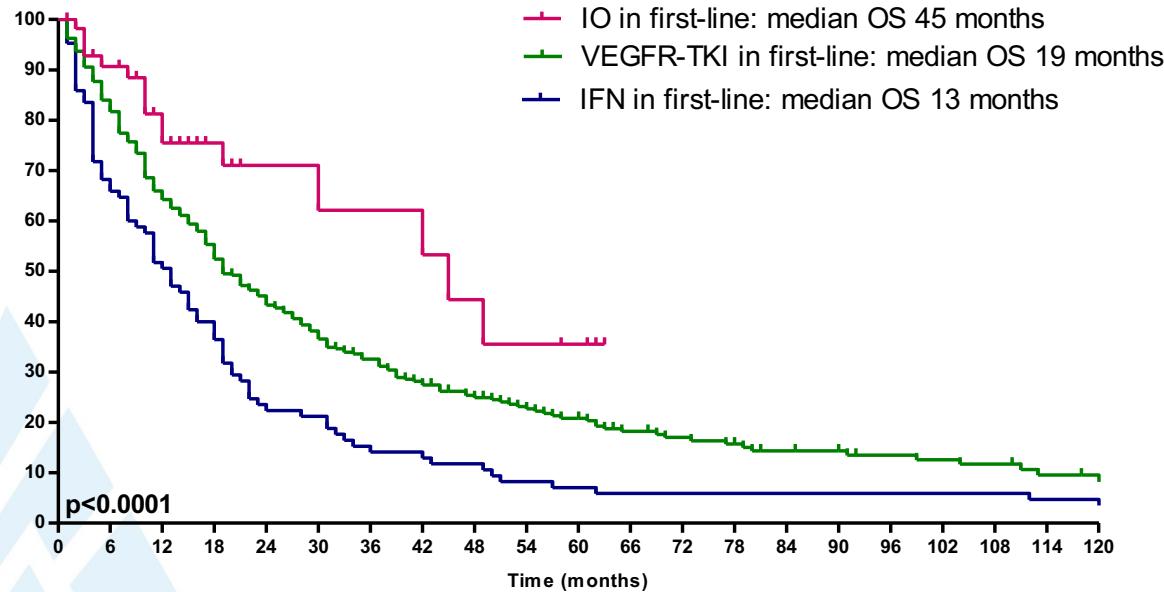
Number of therapy lines





OVERALL SURVIVAL DEPENDING ON TYPE OF FIRST-LINE OF THERAPY

OS (%)



Months	0	12	24	36	48	60	72	84	96
IFN	85	44	20	13	10	6	5	5	5
VEGFR-TKI	350	230	151	92	60	43	26	20	16
IO	57	28	8	7	5	3	-	-	-

Conclusions



Significant improvement in overall survival the last 15 years



Plausible that this improvement is brought by the arrival of the VEGFR-TKI and immune checkpoint inhibitors



If a single therapy would not be associated with a significant OS benefit, with sequentially new therapies, there will be a significant OS benefit