



Kidney Cancer Research Summit **KCRS21**

Real-world outcomes of front-line axitinib plus pembrolizumab versus ipilimumab plus nivolumab for metastatic clear cell renal cell carcinoma: Landmark 18-month survival analysis

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Background

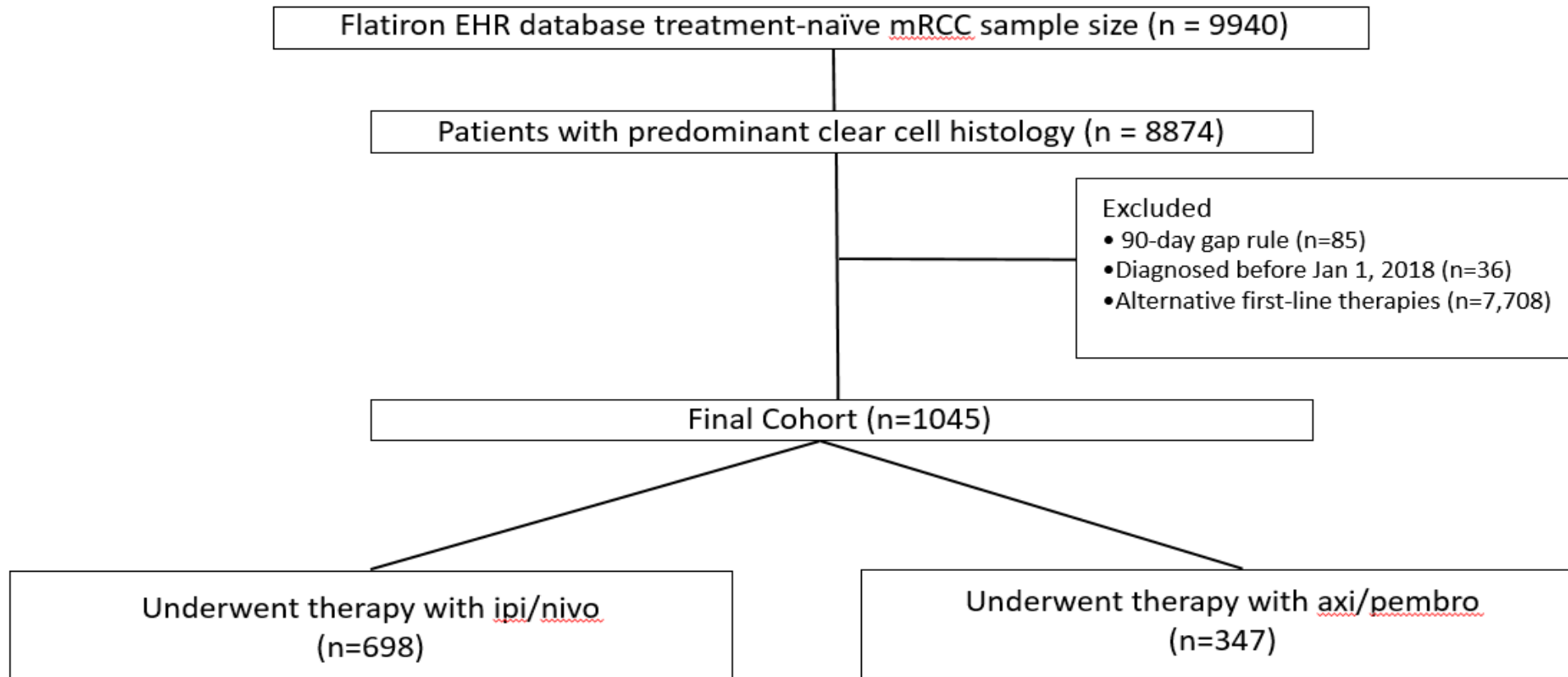
- In the phase 3 **CheckMate-214**¹ trial, Ipilimumab + Nivolumab demonstrated improved OS and ORR's among intermediate- and poor-risk patients with previously untreated advanced renal-cell carcinoma (2018 FDA approval)
- In the phase 3 **KEYNOTE-426**² trial, Axitinib + Pembrolizumab demonstrated longer OS, PFS, and a higher ORR, than treatment with sunitinib (2019 FDA approval)

	Ipilimumab + Nivolumab		Axitinib + Pembrolizumab	
Study	CheckMate-214		KEYNOTE-426	
Sample Size	1,096		861	
Primary Endpoints	OS, ORR, PFS in IMDC I/P risk group		OS, PFS in IMDC all-risk groups in Intention to treat population	
	Ipi/Nivo	Sunitinib	Axi/Pembro	Sunitinib
mPFS, mo (95% CI, p-value) IMDC All-Risk	12.4 (9.9 – 16.5, p = 0.85)	12.3 (9.8 – 15.2)	15.1 (12.6 – 17.7, p < 0.001)	11.1 (8.7 – 12.5)
mPFS, mo (95% CI, p-value) IMDC I/P Risk	11.6 (8.7 – 15.5, p = 0.03)	8.4 (7.0 – 10.8)	12.6 (N/A)	8.2 (N/A)
Landmark 12-month OS, mo (95% CI, p-value) IMDC All-Risk	83% (80 – 86)	77% (74 – 81)	89.9% (N/A)	78.3% (N/A)
ORR, % (95% CI, p-value) IMDC All-Risk	39% (35 – 43, p = 0.02*)	32% (28 – 36)	59.3% (54.5 – 63.9, p < 0.001)	35.7% (31.1 – 40.4)

1) Motzer RJ et al: Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med* 2018, 378(14):1277-1290

2) Rini BI et al: Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med* 2019, 380(12):1116-1127

Methods

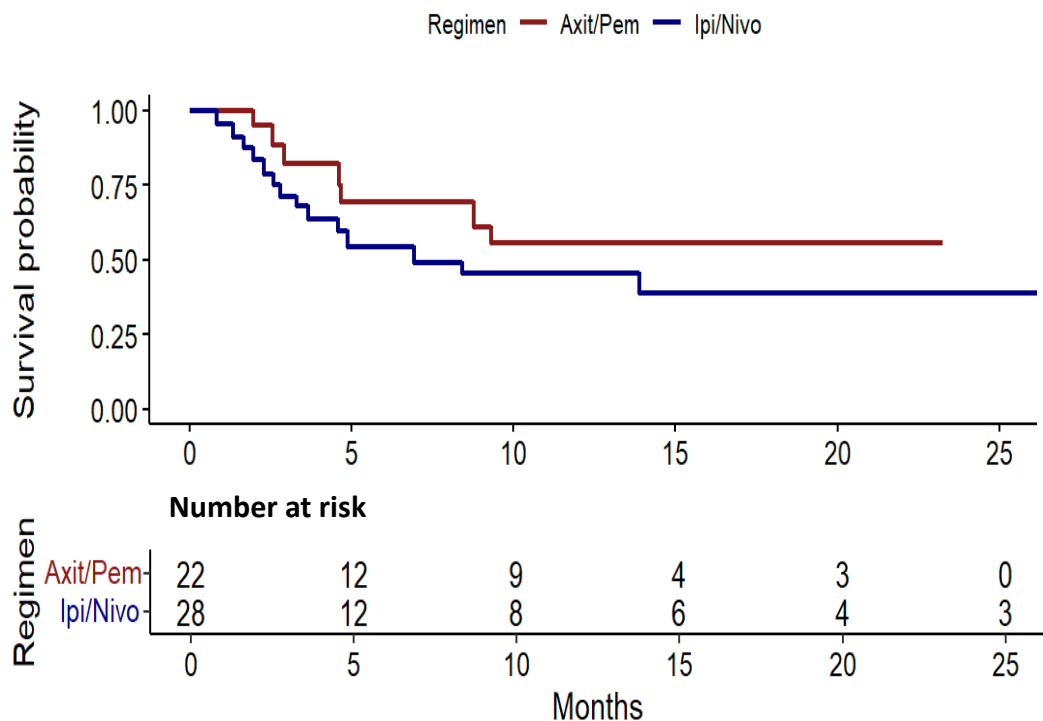


Patient demographic and clinical characteristics

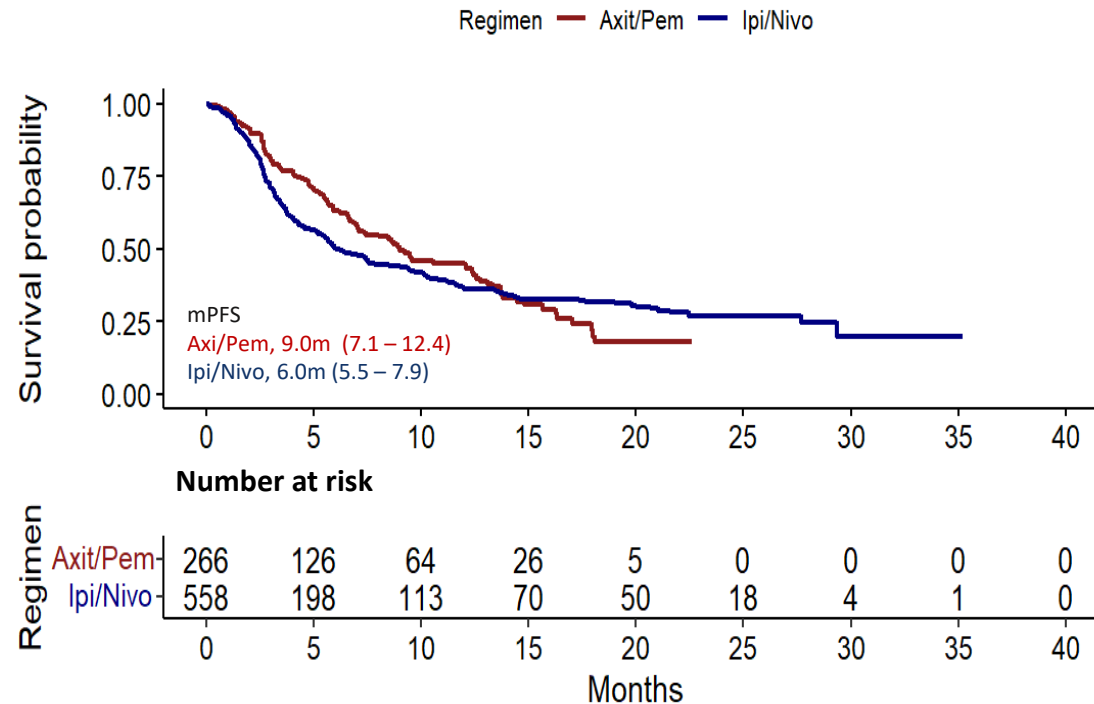
	Axitinib + Pembrolizumab (n=347)	Ipilimumab + Nivolumab (n=698)	p-value
Median age (range), years	68.0 (21-85)	66.0 (29-84)	0.003
Male, n (%)	245 (70.6%)	528 (75.6%)	0.080
Race, n (%)			0.429
White	243 (70.0%)	444 (63.6%)	
Black or AA	15 (4.3%)	41 (5.9%)	
Other or unknown	89 (25.7%)	213 (30.5%)	
IMDC risk group, n (%)			0.238
Favorable	25 (7.2%)	30 (4.3%)	
★ Intermediate/Poor	279 (80.5%)	593 (84.9%)	
Unknown	43 (12.4%)	75 (10.7%)	
Hx of Nephrectomy, n (%)	196 (56.5%)	381 (54.6%)	0.561
Stage at diagnosis, n (%)			0.389
I - III	142 (40.9%)	258 (37.0%)	
IV	195 (56.2%)	423 (60.6%)	
Unknown	10 (2.9%)	17 (2.4%)	
Practice Type, n (%)			0.175
Academic	25 (7.2%)	68 (9.7%)	
★ Community Practice	322 (92.8%)	630 (90.3%)	
Time from diagnosis to treatment (range), months	0.21 (0.003-26.3)	0.17 (0.005-29.1)	0.010
Prescription patterns by year, n (%)			<0.001
2018	7 (2.0%)	226 (32.4%)	
2019	169 (48.7%)	243 (34.8%)	
2020	148 (42.7%)	193 (27.7%)	
2021	23 (6.6%)	36 (5.2%)	

Real-world Progression Free Survival

IMDC Favorable Risk



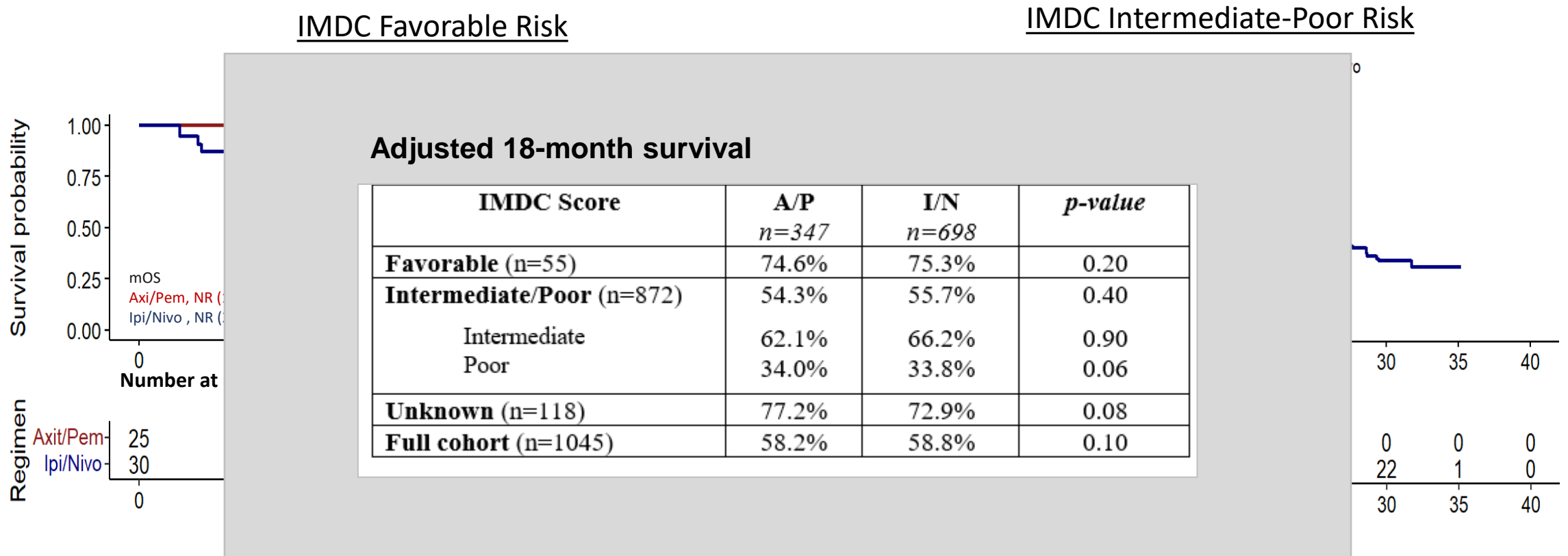
IMDC Intermediate-Poor Risk



rwPFS for the ITT population:
(P=0.20)

Axi/Pembro - 9.0 months
Ipi/Nivo - 6.9 months

Overall Survival



- mOS for the ITT population: **Axi/Pembro** - NR months
(*P*=0.10) **Ipi/Nivo** - 23.7 months

Cross trial comparisons

		Ipilimumab + Nivolumab			Axitinib + Pembrolizumab		
		Real world dataset	CheckMate-214 ¹	CheckMate-214 ² (extended 42-month)	Real world dataset	KEYNOTE-426 ³	KEYNOTE-426 ⁴ (extended 42-month)
Intermediate-Poor Risk	PFS	6.9m	11.6m	11.6m	9.0m	12.6m	15.7m
	OS	22.0m	NR	47.0m	NR	NR	45.7m
ITT	Landmark Survival (18-month)	58.8%	78%	77%	58.2%	82.3%	81.0%

- 1) Motzer RJ et al: Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med* 2018, 378(14):1277-1290
- 2) Motzer RJ et al: Survival outcomes and independent response assessment with nivolumab plus ipilimumab versus sunitinib in patients with advanced renal cell carcinoma: 42-month follow-up of a randomized phase 3 clinical trial. *Journal for ImmunoTherapy of Cancer* 2020
- 3) Rini BI et al: Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med* 2019, 380(12):1116-1127
- 4) Powles T et al: Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2020 Dec;21(12):1563-1573. doi: 10.1016/S1470-2045(20)30436-8. Epub 2020 Oct 23. Erratum in: *Lancet Oncol.* 2020 Dec;21(12):e553. (ACSO 2021)

Conclusions and future directions

- In the absence of prospective studies, retrospective analyses such as this report may provide guidance for clinicians in choosing front-line treatments.
- In the real world setting, 18-month survival was not statistically different between treatment groups irrespective of IMDC risk*
- Longer follow-up time will be necessary to discern any clinically significant difference in survival
- Future studies may include data on newly approved front-line combination therapies, including lenvatinib/pembrolizumab and cabozantinib/nivolumab

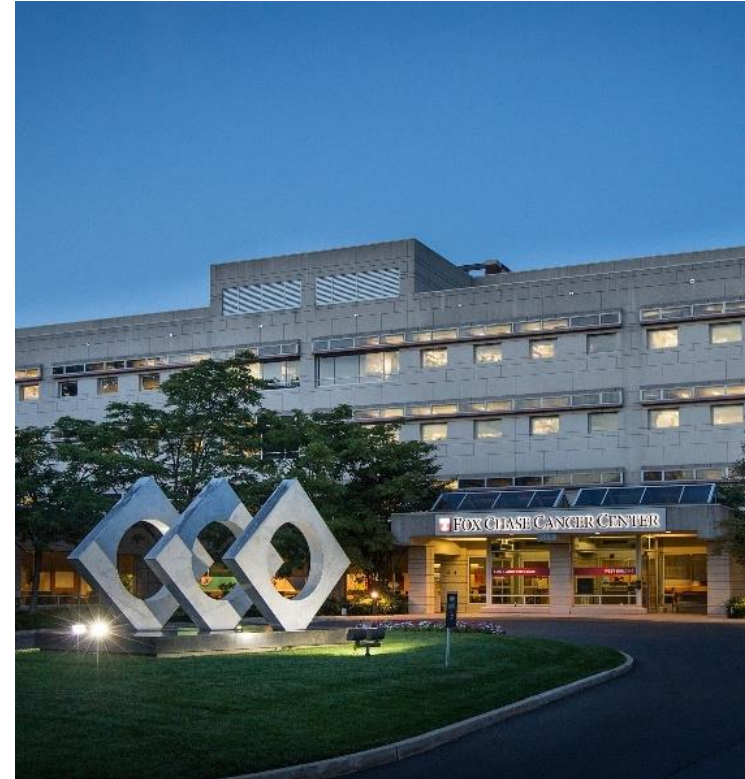
*Gan et al: Outcomes of first-line (1L) immuno-oncology (IO) combination therapies in metastatic renal cell carcinoma (mRCC): Results from the International mRCC Database Consortium (IMDC). Journal of Clinical Oncology 2021 39:6_suppl, 276-276 (ASCO 2021)

Thank you for your attention

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