Immunotherapy-based combinations for advanced/metastatic renal cell carcinoma: What have we learned from ASCO GU 2023?

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Agenda

ICI-based combinations in the treatment of advanced/metastatic RCC: What do the latest efficacy and safety data show?

What is the potential role of biomarkers in predicting response to ICI-based combinations in patients with advanced/metastatic RCC?

How might the latest data for ICI-based combinations for advanced/metastatic RCC be implemented in clinical practice?

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ICI-based combinations in the treatment of advanced/metastatic RCC: What do the latest efficacy and safety data show?

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Overview of the developing RCC therapeutic landscape[1*]

Approved therapies 2005–2014

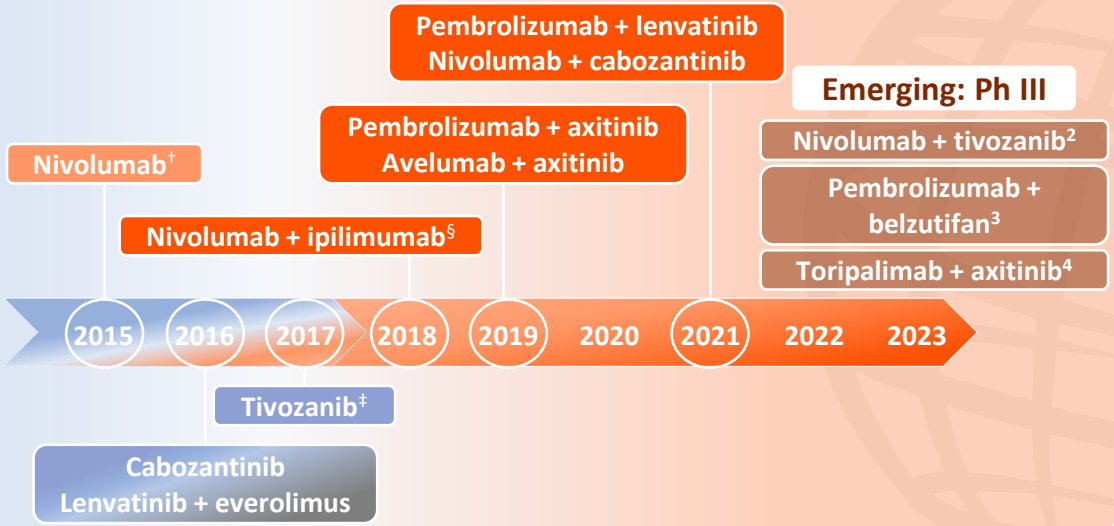
VEGF-signalling inhibitors

- Sorafenib
- Sunitinib
- Bevacizumab + IFN-α
- Pazopanib
- Axitinib

mTOR pathway inhibitors

- Temsirolimus
- Everolimus

Approved and emerging combination and single-agent therapies 2015–2023



With the emergence of new therapies for metastatic RCC, mOS has increased from <1 year in the 1990s to >4 years in some trials with combination therapies. Combination therapies in the first-line are now SoC for almost all patients[5]

*First approval date (either EMA or FDA) indicated; differences between two regions are footnoted; †EMA, 2016; ‡FDA, 2021; §EMA, 2019. EMA, European Medicines Agency; FDA, US Food and Drug Administration; IFN, interferon; mOS, median overall survival; mTOR, mammalian target of rapamycin; Ph, phase; RCC, renal cell carcinoma; SoC, standard of care; VEGF, vascular endothelial growth factor. Adapted from 1. Hsieh JJ, et al. *Nat Rev Dis Primers*. 2017;3:17009; 2. NCT04987203; 3. NCT05239728; 4. NCT04394975; 5. Tran J, et al. *JCO Oncol Pract*. 2021;18:187–96. Clinical trials are available at: ClinicalTrials.gov using the study identifier (accessed 15 March 2023); FDA. History of approval for all drugs. Available at: www.fda.gov/drugs; EMA. History of approval for all drugs. Available at www.ema.europa.eu (accessed 15 March 2023).

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Phase III trials: Developments in combination regimens

Treatment	Patients; risk*	Design	Study (completion†)
Triplet vs doublet combination	N=840; Intermediate or poor risk	Nivolumab + ipilimumab + cabozantinib *vs* Nivolumab + ipilimumab + placebo	**COSMIC-313** NCT03937219 (March 2025)
Combination vs monotherapy	N=437; Intermediate or poor risk	Nivolumab + ipilimumab *vs* nivolumab	**CheckMate CA209-8Y8** NCT03873402 (March 2025)
Drug sequencing	N=1,046; Intermediate or poor risk	Nivolumab + ipilimumab **followed by** nivolumab + cabozantinib *vs* Nivolumab + ipilimumab **followed by** nivolumab	**PDIGREE** NCT03793166 (September 2023)
Drug sequencing	N=523; Evaluable IMDC risk score	Atezolizumab + cabozantinib **following ICI in the metastatic setting** *vs* cabozantinib	**CONTACT-03** NCT04338269 (December 2024)

*IMDC risk score; †Estimated completion dates.
ICI, immune checkpoint inhibitor; IMDC, International mRCC Database Consortium.
Clinical trials are available at: ClinicalTrials.gov using the study identifier (accessed 15 March 2023).

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Abstr. 603: Nivolumab plus cabozantinib vs sunitinib for first-line treatment of advanced RCC: 3-year follow-up from the phase 3 CheckMate 9ER trial

Burotto M, et al.

- 3-year follow-up comparing first-line nivolumab + cabozantinib (N+C) vs sunitinib (S) in patients with advanced RCC

N=651

- Randomization 1:1 to N+C or S
- Stratified by IMDC risk score, PD-L1 expression, and geographical region

- N (240 mg IV Q2W) + C (40 mg PO QD)
- S (50 mg PO QD)
- 4 weeks on/2 weeks off

Primary endpoint:

- PFS (by BICR*)

Secondary endpoints:

- OS
- ORR (by BICR*)
- Safety

Treatment until disease progression or unacceptable toxicity (maximum nivolumab treatment of 2 years)

*Per RECIST 1.1.
BICR, blinded independent central review; C, cabozantinib; IMDC, International Metastatic RCC Database Consortium; IV, intravenous; N, nivolumab; ORR, objective response rate; OS, overall survival; PD-L1, programmed death cell ligand 1; PFS, progression-free survival; PO, per os/oral administration; Q2W, every 2 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumours.
Burotto M, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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Abstr. 603: Nivolumab plus cabozantinib vs sunitinib for first-line treatment of advanced RCC: 3-year follow-up from the phase 3 CheckMate 9ER trial

Burotto M, et al.

Efficacy

- Median follow-up for OS: 44.0 months
- Median PFS and CR rates consistently higher with N+C vs S across prespecified IMDC risk groups

	N+C (n=323)	S (n=328)
Median PFS (95% CI), mo	16.6 (12.8–19.8)	8.4 (7.0–9.7)
Median OS (95% CI), mo	49.5 (40.3–NE)	35.5 (29.2–42.3)
ORR (95% CI), %	55.7 (50.1–61.2)	28.4 (23.5–33.6)
CR, %	12.4	5.2
PR, %	43.3	23.2
SD, %	32.5	40.9
PD, %	6.2	13.7
Median DoR (95% CI), mo	23.1 (20.2–27.9)	15.2 (9.9–20.7)

Safety*

	N+C (n=320)	S (n=320)
TRAEs (any grade) %	97	93
TRAEs (≥grade 3), %	67	55
TRAEs (any grade leading to discontinuation), %	27.5	10.6

- No new safety signals emerged with N+C or S

At 44 months, N+C survival and response benefits were maintained and were consistent with those in previous follow-up periods

*Safety population vs ITT population for efficacy analysis.
CI, confidence interval; CR, complete response; DoR, duration of response; IMDC, International Metastatic RCC Database Consortium; mo, months; N+C, nivolumab + cabozantinib; NE, not estimable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RCC, renal cell carcinoma; S, sunitinib; SD, stable disease; TRAE, treatment-related adverse event.
Burotto M, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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Abstr. 605: Outcomes by IMDC risk in the COSMIC-313 phase 3 trial evaluating cabozantinib plus nivolumab and ipilimumab in first-line advanced RCC of IMDC intermediate or poor risk

Powles T, et al.

- Outcomes analysis by IMDC risk group (poor or intermediate)

N=855

- Patients with advanced ccRCC and IMDC risk (poor or intermediate)
- Stratified by IMDC risk and region

- **Randomization 1:1** to C (40 mg QD) or P
- **Both groups:** N (3 mg/kg Q3W) + I (1 mg/kg Q3W) (4 cycles), then N (480 mg Q4W)

Primary endpoint:

- PFS (by BICR*); first 550 patients

Secondary endpoints:

- OS (all patients)
- ORR
- DoR
- Safety

Treatment until loss of clinical benefit or intolerable toxicity; nivolumab treatment for a maximum of 2 years

*Per RECIST 1.1.
BICR, blinded independent central review; C, cabozantinib; ccRCC, clear cell RCC; DoR, duration of response; I, ipilimumab; IMDC, International Metastatic RCC Database Consortium; N, nivolumab; ORR, objective response rate; OS, overall survival; P, placebo; PFS, progression-free survival; Q3W, every three weeks; Q4W, every 4 weeks; QD, once daily; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria in Solid Tumours.
Powles T, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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Abstr. 605: Outcomes by IMDC risk in the COSMIC-313 phase 3 trial evaluating cabozantinib plus nivolumab and ipilimumab in first-line advanced RCC of IMDC intermediate or poor risk

Powles T, et al.

Efficacy

	Intermediate risk*		Poor risk*	
	C+N+I (n=321)	P+N+I (n=321)	C+N+I (n=107)	P+N+I (n=106)
PFS, mo (95% CI)	17.9 (14.1–NE)	11.3 (8.4–15.3)	9.5 (8.3–15.8)	11.2 (6.0–14.2)
HR-PFS (95% CI)	0.68 (0.54–0.86)		0.93 (0.64–1.35)	
ORR, %	45	36	36	38
CR, %	3	4	2	0

Safety

	Intermediate risk*		Poor risk*	
	C+N+I (n=321)	P+N+I (n=320)	C+N+I (n=105)	P+N+I (n=104)
TRAEs (≥grade 3), %	74	42	67	38
IMAEs (≥grade 3), %	52	25	48	18
TRAEs leading to discontinuation, %	14	5	5	4

PFS benefit for C+N+I versus P+N+I was maintained at follow-up in the overall population and in IMDC intermediate-risk patients

*ITT population.
AE, adverse event; C+N+I, cabozantinib + nivolumab + ipilimumab; CI, confidence interval; CR, complete response; HR, hazard ratio; IMAE, immune-mediated AE; IMDC, International Metastatic RCC Database Consortium; ITT, intention to treat; mo, month; NE, not estimable; ORR, objective response rate; PFS, progression-free survival; P+N+I, placebo + nivolumab + ipilimumab; RCC, renal cell carcinoma; TRAE, treatment-related AE.
Powles T, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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Abstr. 606: CaboPoint: Interim results from a phase 2 study of cabozantinib after checkpoint inhibitor therapy in patients with advanced RCC

Albiges L, et al.

- Prospective, phase II, multicentre, open-label study of cabozantinib (C) in advanced ccRCC

N=88

- Adults with unresectable, locally advanced or metastatic ccRCC who progressed on first-line ICI-based therapy
- No prior treatment with cabozantinib

- **Cohort A:** C (60 mg QD) post N+I
- **Cohort B:** C (60 mg QD) post ICI+VEGFR TKI

Primary endpoint:

- ORR* (by ICR; cohort A [n=60])

Secondary endpoints:

- ORR (by ICR; cohort B [n=28])
- ORR (by local IR; both cohorts)

Pre-planned interim analysis of ORR when 80% of patients in cohort A reached ≥3 months of treatment

*Per RECIST 1.1.
ccRCC, clear cell RCC; ICI, immune checkpoint inhibitor; ICR, independent central review; IR, investigator review; N+I, nivolumab + ipilimumab; ORR, objective response rate; QD, every day; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria in Solid Tumours; TKI, tyrosine kinase inhibitor; VEGFR, vascular endothelial growth factor receptor.
Albiges L, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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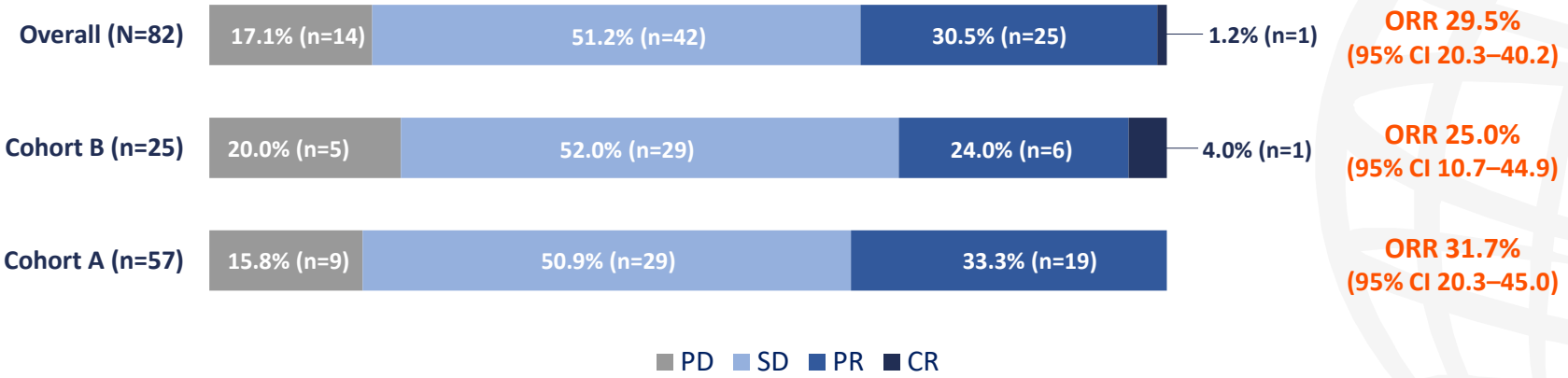
Abstr. 606: CaboPoint: Interim results from a phase 2 study of cabozantinib after checkpoint inhibitor therapy in patients with advanced RCC

Albiges L, et al.

Interim efficacy (3-month analysis)*



In patients with advanced ccRCC post-first-line therapy, cabozantinib showed preliminary efficacy, regardless of the first-line regimen used

*Percentages of best response were calculated based on the number of patients with non-missing values.
ccRCC, clear cell RCC; CI, confidence interval; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease.
Albiges L, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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What is the potential role of biomarkers in predicting response to ICI-based combinations in patients with advanced/metastatic RCC?

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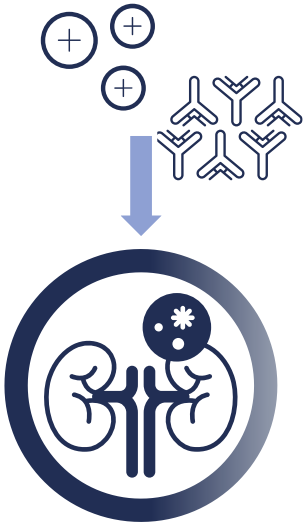
Potential predictors for response to immunotherapy in mRCC[1,2]



PD-L1 expression	• Associated with a higher tumour stage and poorer prognosis
TME/genomic signatures	• Heterogeneous tumour-infiltrating immune cells (e.g. CD8+, Tregs) • Genomic signatures indicative of immune system activation
Circulating biomarkers	• Non-invasive, with numerous promising potential biomarkers (CTCs, ctDNA, non-coding RNA, proteins, extracellular vesicles)
TMB	• High TMB may indicate increased production of surface neoantigens • RCC tends to have a low TMB
irAEs	• Possible association between the occurrence of irAEs and increased benefit in terms of survival from ICIs

CD, cluster of differentiation; CTC, circulating tumour cell; ctDNA, circulating tumour DNA; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; mRCC, metastatic RCC; PD-L1, programmed death cell ligand 1; RCC, renal cell carcinoma; TMB, tumour mutation burden; TME, tumour microenvironment; Treg, regulatory T cell.

1. Raimondi A, et al. *Front Oncol.* 2020;10:1644; 2. Cinque A, et al. *Biomedicines*. 2022;10:90.

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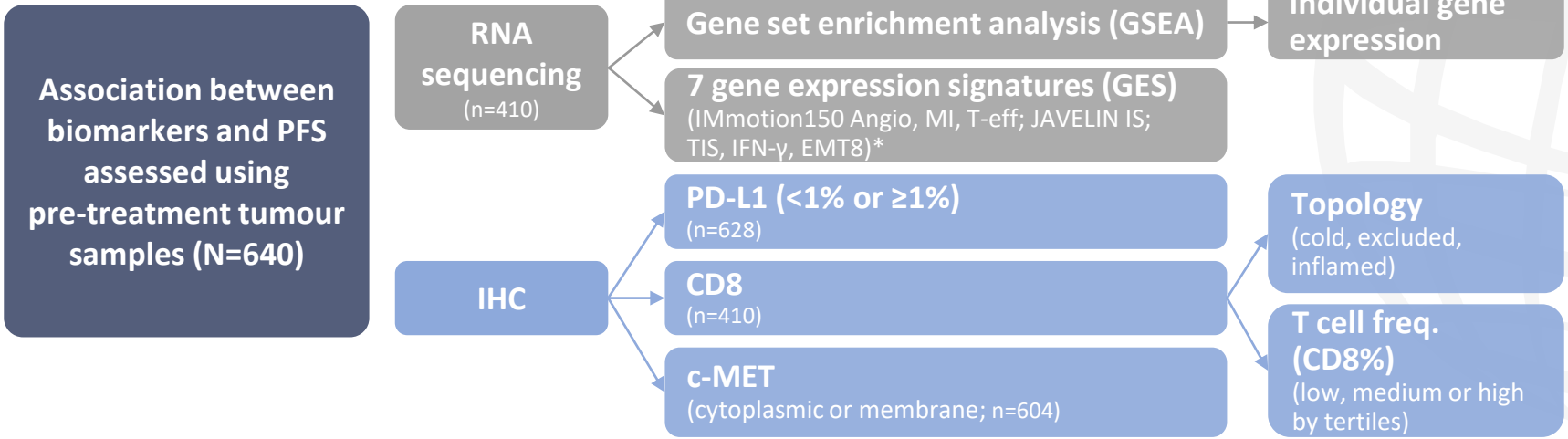
Abstr. 608: Biomarker analysis from the phase 3 CheckMate 9ER trial of nivolumab + cabozantinib versus sunitinib for advanced RCC

Choueiri TK, et al.

- Exploratory, post hoc analysis of efficacy biomarkers for nivolumab (anti-PD-1) + cabozantinib (anti-VEGF) vs sunitinib in the CheckMate 9ER phase III trial



*Previously published gene expression signatures.
CD, cluster of differentiation; c-MET, c-mesenchymal-epithelial transition factor; EMT8, epithelial mesenchymal transition-8; freq., frequency; GES, gene expression signature; GSEA, gene set enrichment analysis; IFN-γ, interferon-gamma; IHC, immunohistochemistry; IS, immuno-signature; MI, myeloid inflammation; PD-1, programmed cell death protein 1; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; RCC, renal cell carcinoma; T-eff, T-effector; TIS, tumour inflammation signature; VEGF, vascular endothelial growth factor.

Choueiri TK, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

Abstr. 608: Biomarker analysis from the phase 3 CheckMate 9ER trial of nivolumab + cabozantinib versus sunitinib for advanced RCC

Choueiri TK, et al.

	Nivolumab + cabozantinib vs sunitinib arm*		
Biomarker	**Associated with PFS**	**Prognostic**	**Predictive**
GSEA	✓	✓	✗
GES	✗	✗	✗
PD-L1	✗†	✗	✗
CD8 typology	✓‡	✗	✗
T cell freq. (CD8%)	✓‡	✗	✗
Cytoplasmic c-MET	✓	✓	✗
Membrane c-MET	✗	✗	✗

Biomarkers previously associated with anti-PD-L1 + anti-VEGF therapy outcomes were not consistently associated with survival outcomes of anti-PD-1 + anti-VEGF therapies in patients with advanced RCC

*Findings reported after a median follow-up of 44 months. †Associated with worse PFS in the sunitinib arm only; ‡Kaplan–Meier analysis only (Cox proportional hazards model analysis showed no significant association with survival outcomes). CD, cluster of differentiation; c-MET, c-mesenchymal-epithelial transition factor; freq., frequency; GES, gene expression signature; GSEA, gene set enrichment analysis; PD-1, programmed cell death protein 1; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; RCC, renal cell carcinoma; VEGF, vascular endothelial growth factor. Choueiri TK, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

Abstr. 704: Dynamic and immunocytochemistry analysis of circulation tumor cells in blood samples from patients with advanced ccRCC starting first-line treatment in a Brazilian Cancer Center

Tariki MS, et al.

- Evaluation of CTC counts in serial blood samples in patients with advanced ccRCC starting first-line therapy (N=12)

10-mL blood sample collected at BL and 30 and 60 days

Samples diluted with buffer

Filtration to collect and isolate CTCs

Analysis: CTC count, CTC kinetics, protein expression*

CTC count: BL, Day 30 and Day 60

CTC kinetics: Day 30

Protein expression (PBRM1, BAP1, PD-L1 and CD133): BL

*Evaluated using immunocytochemistry.
BAP1, BRCA1 associated protein 1; BL, baseline; ccRCC, clear cell renal cell carcinoma; CD, cluster of differentiation; CTC, circulating tumour cell; PBRM1, polybromo-1; PD-L1, programmed cell death-ligand 1.
Tariki MS, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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Abstr. 704: Dynamic and immunocytochemistry analysis of circulation tumor cells in blood samples from patients with advanced ccRCC starting first-line treatment in a Brazilian Cancer Center

Tariki MS, et al.

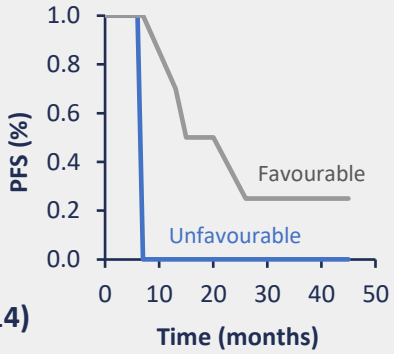
CTC count

- Detectable CTCs at baseline in all patients (Median: **1.5 CTCs/mL**)
- Patients with CTCs >1.5 CTCs/mL had **≥2 metastatic sites** (p=0.015) and **worse PFS** vs patients with CTCs <1.5 CTCs/mL (19.7 vs 31.1 months; p=0.35)

CTC kinetics*

Median follow-up: 36.4 months

Patients with favourable CTC kinetics at Day 30 had a better PFS vs those with unfavourable kinetics **(24.8 vs 6.7 months; p=0.014)**



Protein expression

Expression of **PBRM1, BAP-1**, **PD-L1** and **CD133** did not significantly associate with OS

CTC counts were feasible in patients with advanced ccRCC starting first-line treatment and favourable kinetics at Day 30 were associated with improved PFS

*Data estimated from visual representation.
BAP1, BRCA1 associated protein 1; ccRCC, clear cell renal cell carcinoma; CD, cluster of differentiation; CTC, circulating tumour cell; OS, overall survival; PBRM1, polybromo-1; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival.
Tariki MS, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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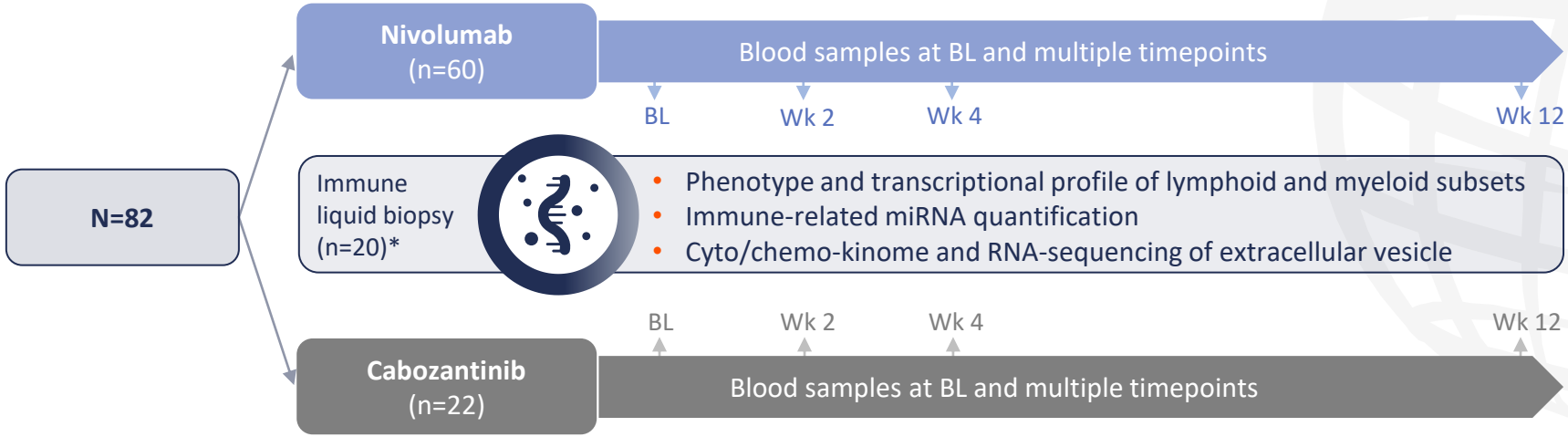
Abstr. 712: A platform for high resolution immune liquid biopsy analysis to predict response in RCC patients treated with nivolumab or cabozantinib: Preliminary data from I-RENE trial (Meet-URO 8 study)

Verzoni E, et al.

- Prospective study of real-world patients with mRCC treated with nivolumab or cabozantinib after anti-VEGFR agent failure, using 'immune liquid biopsy' to identify biomarkers predictive of clinical benefit of PD-1 blockade



*Patients selected based on best and worst response.
BL, baseline; miRNA, microRNA; mRCC, metastatic RCC; PD-1, programmed cell death protein 1; RCC, renal cell carcinoma; VEGFR, vascular endothelial growth factor receptor; Wk, week.
Verzoni E, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

Abstr. 712: A platform for high resolution immune liquid biopsy analysis to predict response in RCC patients treated with nivolumab or cabozantinib: Preliminary data from I-RENE trial (Meet-URO 8 study)

Verzoni E, et al.

Monocytes and monocytic MDSCs*

Responders: Stable

Non-responders: Increases

T cells†

Overall: $CD8^+PD\text{-}1^+$ increases

Responders: Effector T cells and Ki67 expressing T cells increase

Multiplex cyto-chemokine analysis

IL-6, IL-10 and CXCL10

- Differences in plasma levels associated with response/ non-response

IL-8

- No association with response

MDSC-miRNA‡

miRNAs

- Modulated by treatment

Non-responders: miRNA 125b decreases

Early data suggest that blood offers a promising source of dynamic biomarkers for the development of algorithms predicting response to PD-1 blockade

*$CD14^+$, $CD14^+HLA\text{–}DR^-$ and $CD14^+PD\text{-}L1^+$; †$CD8^+PD\text{-}L1^+$, effector T cells ($CD8^+$, $CD45RA^+$, and $CCR7^-$) and Ki67 expressing $CD8^+$ T cells;
‡miRNA: 99b, 100, 125a, 125b, 7e, 146a, 146b, 155.
CD, cluster of differentiation; CXCL10, C-X-C motif chemokine ligand 10; HLA–DR, human leukocyte antigen–DR isotype; IL, interleukin; MDSC, myeloid-derived suppressor cells; miRNA, microRNA; PD-1, programmed cell death protein 1; PD-L1, programmed cell death-ligand 1; RCC, renal cell carcinoma.
Verzoni E, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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How might the latest data for ICI-based combinations for advanced/metastatic RCC be implemented in clinical practice?

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Guideline recommendations: First-line advanced RCC

Preferred

NCCN (2023)[1]*

Ordered per guidelines

Favourable risk†
- Axitinib + pembrolizumab
- Cabozantinib + nivolumab
- Lenvatinib + pembrolizumab

Intermediate or poor risk†
- Axitinib + pembrolizumab
- Cabozantinib + nivolumab
- Ipilimumab + nivolumab
- Lenvatinib + pembrolizumab
- Cabozantinib

Recommended

ESMO (2021)[2,3]*

Ordered per guidelines

Favourable risk‡
- Lenvatinib + pembrolizumab
- Axitinib + pembrolizumab
- Cabozantinib + nivolumab

Intermediate or poor risk‡
- Ipilimumab + nivolumab
- Lenvatinib + pembrolizumab
- Axitinib + pembrolizumab
- Cabozantinib + nivolumab

Other regimens

Favourable risk†
- Axitinib + avelumab
- Cabozantinib
- Ipilimumab + nivolumab
- Pazopanib
- Sunitinib

Intermediate or poor risk†
- Axitinib + avelumab
- Pazopanib
- Sunitinib

Alternative§

Favourable risk‡
- Sunitinib
- Pazopanib
- Tivozanib

Intermediate or poor risk‡
- Sunitinib
- Pazopanib
- Cabozantinib‖

*Order of agents is as per guidelines; †IMDC criteria or MSKCC prognostic model; ‡IMDC; §Where recommended treatment is not available or is contraindicated;
‖In patients who cannot receive first-line PD-1 inhibitor-based therapy.
ESMO, European Society for Medical Oncology; IMDC, International Metastatic RCC Database Consortium; MSKCC, Memorial Sloan Kettering Cancer Center;
NCCN, The National Comprehensive Cancer Network; RCC, renal cell carcinoma.

1. NCCN guidelines. Kidney Cancer. Version 4.2023. Available at: www.nccn.org/professionals/physician_gls/pdf/kidney.pdf (accessed 15 March 2023);
2. Powles T, et al. *Ann Oncol*. 2021;1511–9; 3. Powles T, et al. *Ann Oncol*. 2021;32:422–3.

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Beyond RCTs: Overview of some topics of studies presented at ASCO GU 2023 that have relevance for daily clinical practice

Real-world experience

- CARINA: treatment sequencing/outcomes in aRCC
- Non-interventional, retrospective study of pts with aRCC or mRCC
- Observational study of pts with aRCC treated with avelumab + axitinib (UK)
- Outcomes for pts with mRCC treated with different regimens
- Outcomes for pts with aRCC treated with pembrolizumab + axitinib

Special groups and combination therapies

- Outcomes for pts with RCC and associated BM, treated with first-line therapies
- Impact of ethnicity on outcomes in pts with mRCC treated with nivolumab + ipilimumab
- Impact of sarcomatoid features on outcomes in pts with mRCC
- Clinical outcomes in pts with chromophobe RCC

Treatment variations

- Treatment discontinuation electively or due to toxicities in pts with mRCC
- Outcomes with intermittent therapy

aRCC, advanced RCC; BM, brain metastases; mRCC, metastatic RCC; pts, patients; RCC, renal cell carcinoma; RCT, randomized clinical trial.
For further details see ASCO GU 2023, Abstracts and Posters. Available at: https://conferences.asco.org/gu/abstracts-posters (accessed 15 March 2023).

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Abstr. 604: Treatment-free survival outcomes from the phase II study of nivolumab and salvage nivolumab + ipilimumab in advanced ccRCC (HCRN GU16-260-Cohort A)

Atkins MB, et al.

- Analysis of TFS in phase II trial investigating nivolumab (N) and salvage N + ipilimumab (I) in advanced RCC

N=128

- Patients with advanced ccRCC treated with first-line N monotherapy

- **PR or CR at 12 weeks:** N monotherapy (up to 96 weeks)
- **PD or SD at 48 weeks:** salvage N+I then N monotherapy (up to 48 weeks)

Study point of interest:
- TFS*

Study point of interest:
- Time on or off treatment with ≥grade 3 TRAEs

TFS began when treatment stopped for TRAEs, PD or treatment completion

*Defined as the area between Kaplan–Meier curves for (1) time from registration to therapy cessation; and (2) time from registration to subsequent therapy initiation or death, estimated from 36-month mean times.
ccRCC, clear cell RCC; CR, complete response; PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease; TFS, treatment-free survival; TRAE, treatment-related adverse event.
Atkins MB, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

Abstr. 604: Treatment-free survival outcomes from the phase II study of nivolumab and salvage nivolumab + ipilimumab in advanced ccRCC (HCRN GU16-260-Cohort A)

Atkins MB, et al.

	Mean number of months (% of 36-month period)		
	FAV (n=38)	I/P (n=90)	Overall (N=128)
OS	35.7 (99)	27.4 (76)	29.9 (83)
Survival after subsequent treatment initiation	6.9 (19)	9.8 (27)	8.9 (25)
TFS (95% CI; % of 36 months)	12.9 (9.7–16.1; 36)	8.0 (5.8–10.2; 22)	9.4 (7.6–11.3; 26)
TFS without TRAEs ≥grade 3	11.4 (32)	7.0 (19)	8.2 (23)
TFS with TRAEs ≥grade 3	1.5 (4)	1.0 (3)	1.2 (3)
Time on protocol treatment	16.0 (44)	9.6 (27)	11.5 (32)
Time on protocol treatment without TRAEs ≥grade 3	15.0 (42)	9.2 (26)	
Time on protocol treatment with TRAEs ≥grade 3	1.0 (2)	0.4 (1)	

At 36 months, **68.3%** patients were alive

- **96.8%** of IMDC FAV patients
- **56.6%** of IMDC I/P patients

Nivolumab monotherapy with salvage nivolumab + ipilimumab was associated with substantial TFS and toxicity-free TFS

ccRCC, clear cell RCC; CI, confidence interval; FAV, favourable risk; I/P, intermediate/poor risk; IMDC, International Metastatic RCC Database Consortium; OS, overall survival; RCC, renal cell carcinoma; TFS, treatment-free survival; TRAE, treatment-related adverse event.

Atkins MB, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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Abstr. 625: Clinical outcomes of patients with metastatic RCC who discontinued nivolumab +/- ipilimumab therapy electively or due to toxicity

Yoo JH, et al.

- Retrospective, single-centre study evaluating durability of treatment response in patients with metastatic RCC who discontinued nivolumab +/- ipilimumab (N +/- I) therapy

N=53

- Patients who responded to N +/- I then discontinued electively or due to toxicity
- Exclusion if discontinued due to PD or death*

Endpoints:

- OS
- EFS†

*Within 3 months of last immune checkpoint inhibitor dose; †Defined as survival without next-line treatment.
EFS, event-free survival; OS, overall survival; PD, progressive disease; RCC, renal cell carcinoma.
Yoo JH, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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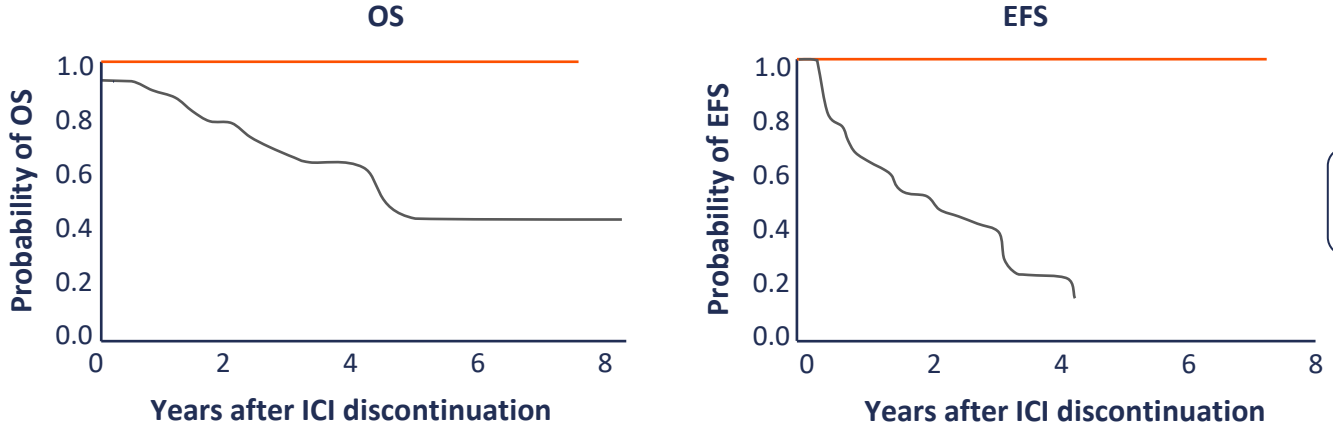
Abstr. 625: Clinical outcomes of patients with metastatic RCC who discontinued nivolumab +/- ipilimumab therapy electively or due to toxicity

Yoo JH, et al.

Survival outcomes stratified by best response



Patients who achieved CR as a best response prior to ICI discontinuation had good survival outcomes

CR, complete response; EFS, event-free survival; ICI, immune checkpoint inhibitor; OS, overall survival; RCC, renal cell carcinoma.

Yoo JH, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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Abstr. 672: Phase II trial of intermittent therapy in patients with metastatic RCC treated with front-line ipilimumab and nivolumab

George L, et al.

- Phase II trial of intermittent ipilimumab + nivolumab (I+N) with re-induction at progression

N=9

- Treatment-naïve mRCC
- Intermediate or poor IMDC risk score

- Induction I+N and up to 24 weeks N

- Patients included if they had experienced a CR or PR following initial I+N treatment

Study objectives:

- Estimate success rate of observation in patients who achieve CR/PR*
- Assess toxicity in patients undergoing re-induction

If there was no PD, patients remained off treatment;
they were re-challenged with 2 doses of I+N every 3 weeks† upon PD

*Success rate defined by 50% of CR/PR patients with a treatment-free interval ≥9 months; †Additional 1 or 2 doses at physician discretion.
CR, complete response; IMDC, International Metastatic RCC Database Consortium; mRCC, metastatic RCC; PD, disease progression; PR, partial response; RCC, renal cell carcinoma.

George L, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

Abstr. 672: Phase II trial of intermittent therapy in patients with metastatic RCC treated with front-line ipilimumab and nivolumab

George L, et al.

Patient characteristics

- Clear cell histology: 66.7%
- KPS: ≥80%
- IMDC intermediate risk: 77.8%
- Response to I+N and N maintenance: **CR**: 33.3%; **PR**: 66.7%

Findings

- Median treatment-free interval in patients with radiographic response to I+N: 30.6 months (range 8.7–41.8 months)
- Re-induction with I+N after progression did not result in a radiographic response in two patients
- No grade 3/4 irAEs observed

Patients with radiographic response to I+N can have prolonged treatment-free intervals
Duration of therapy and prospective identification of patients who can benefit from treatment-free intervals is important to reduce the burden of extended treatment

CR, complete response; I+N, ipilimumab + nivolumab; IMDC, International Metastatic RCC Database Consortium; irAE, immune-related adverse event; KPS, Karnofsky Performance Status; PR, partial response.
George L, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

Abstr. 654: Characterization of clinical outcomes among patients with advanced chromophobe RCC treated with first-line immunotherapy-based regimens

Labaki C, et al.

- Real-world, retrospective analysis of patients with advanced ChRCC receiving first-line IO-based therapies derived from the IMDC database

ChRCC N=31
ccRCC N=856

- Patients with advanced ChRCC who received IO-based regimens, including dual IO or IO + VEGF-targeted therapies
- Additional patients with ccRCC included for comparison

Primary endpoint:

- OS

Secondary endpoints:

- TTF
- ORR

OS and TTF were evaluated between RCC subtypes (ChRCC vs ccRCC) adjusting for age and IMDC risk group; association between odds of achieving a response to 1L therapy and RCC subtype was also evaluated

1L, first-line; ccRCC, clear cell RCC; ChRCC, chromophobe RCC; IMDC, International Metastatic RCC Database Consortium; IO, immuno-oncology; ORR, objective response rate; OS, overall survival; RCC, renal cell carcinoma; TTF, time to treatment failure; VEGF, vascular endothelial growth factor.
Labaki C, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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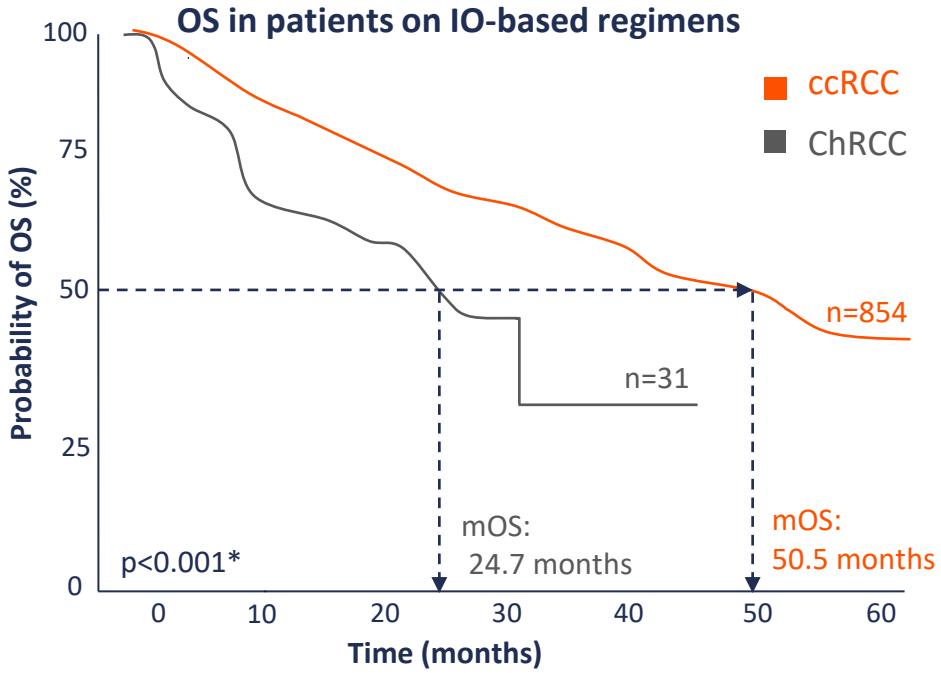
Abstr. 654: Characterization of clinical outcomes among patients with advanced chromophobe RCC treated with first-line immunotherapy-based regimens

Labaki C, et al.



- TTF was lower in patients with ChRCC vs ccRCC (4.5 vs 11.0 months; p<0.001†)
- ORR was lower in patients with ChRCC vs ccRCC (12.0 vs 47.1%; p<0.001†)

Real-world data suggest patients with advanced ChRCC have poor clinical outcomes compared with patients with ccRCC when on IO-based regimens

*Cox regression; †Logistic regression.
ccRCC, clear cell RCC; ChRCC, chromophobe RCC; IO, immuno-oncology; mOS, median OS; ORR, objective response rate; OS, overall survival; RCC, renal cell carcinoma; TTF, time to treatment failure.
Labaki C, et al. Presented at: ASCO GU 2023, San Francisco, CA, USA. 16–18 February 2023.

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