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MEETING SUMMARY
RENAL CANCER HIGHLIGHTS FROM ESMO 2023

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DEVELOPED BY GU CONNECT

This programme is developed by GU CONNECT, an international group of experts in the field of genitourinary oncology.

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CLINICAL TAKEAWAYS

- **LITESPARK-003/005/013:** belzutifan plus cabozantinib appears to improve outcomes in first and subsequent-line settings. Belzutifan monotherapy improves outcomes after IO or VEGFR TKI therapies in previously treated mRCC
- **MEDI5752:** volrustomig monotherapy is active in treatment-naïve aRCC and has the potential to improve outcomes
- **TIDE-A:** shows that VEGFR-TKI discontinuation is safe for selected mRCC pts with evidence of response to VEGFR-TKI+IO combinations in first line
- **RENOTORCH:** As a significant number of RCC patients live in China, the RENOTORCH trial is expected to be practice-changing for a large population of patients with advanced RCC worldwide

IO, immuno-oncology; (a/m)RCC, (advanced/metastatic) renal cell carcinoma; VEGFR-TKI, vascular endothelial growth factor receptor-tyrosine kinase inhibitor

EDUCATIONAL OBJECTIVES

- Help physicians translate the latest renal cell carcinoma data from ESMO 2023 into clinical practice

LITESPARK PROGRAM STUDIES 003/005/013 BELZUTIFAN

003: Choueiri T, et al. ESMO 2023. Abstract #LBA87

005: Albiges L, et al. ESMO 2023. Abstract #LBA88

013: Agarwal N, et al. ESMO 2023. Abstract #1881O

LITESPARK: BACKGROUND

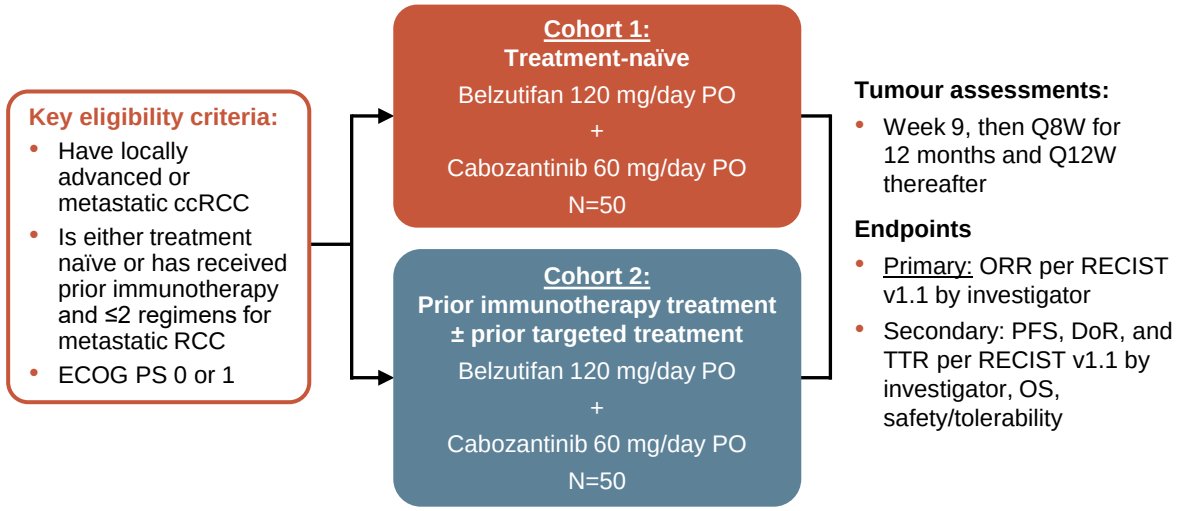
- Belzutifan is a first-in-class oral hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor[1-3]
- Belzutifan is approved in the US for patients with VHL disease-associated RCC and CNS hemangioblastomas, and pNETs[4] – and has anti-tumour activity in previously treated ccRCC[2]
- Three studies from the belzutifan LITESPARK program were presented at ESMO 2023:
  - **LITESPARK-003** – phase 2 study of belzutifan in combination with cabozantinib for advanced ccRCC[5]
  - **LITESPARK-005** – randomised, open-label, phase 3 study comparing belzutifan vs everolimus in previously treated advanced ccRCC[6]
  - **LITESPARK-013** – phase 2 study investigating the safety and efficacy of two doses of belzutifan in patients with advanced RCC[7]

(cc)RCC, (clear cell) renal cell carcinoma; CNS, central nervous system; pNET, pancreatic neuroendocrine tumour; US, United States; VHL, Von Hippel-Lindau

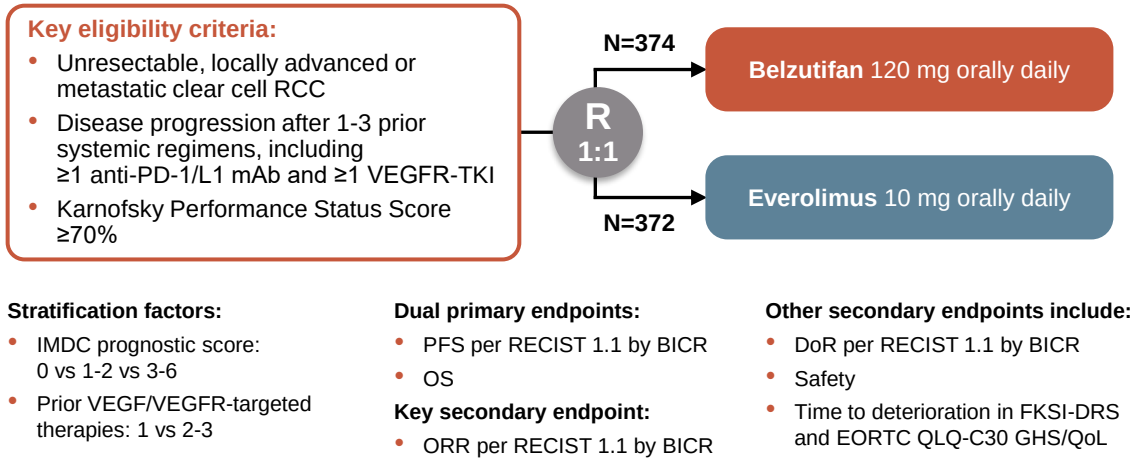
1. Welireg (belzutifan) [Prescribing Information]. Rahway, New Jersey, USA. Merck Sharp & Dohme LLC; 2. Choueiri T, et al. Nat Med. 2021;27: 802-805; 3. Choueiri T, et al. Lancet Oncol. 2023; 24: 553-562; 4. Fallah J, et al. Clin Cancer Res. 2022;28:4843-4848; 5. Choueiri T, et al. Annals of Oncology 2023; Vol. 34: Supplement S1328–S1329; 6. Albiges L, et al. Annals of Oncology 2023; Vol. 34: Supplement S1329–S1330; 7. Agarwal N, et al. Annals of Oncology 2023; Vol. 34: Supplement S1011

LITESPARK STUDY DESIGNS

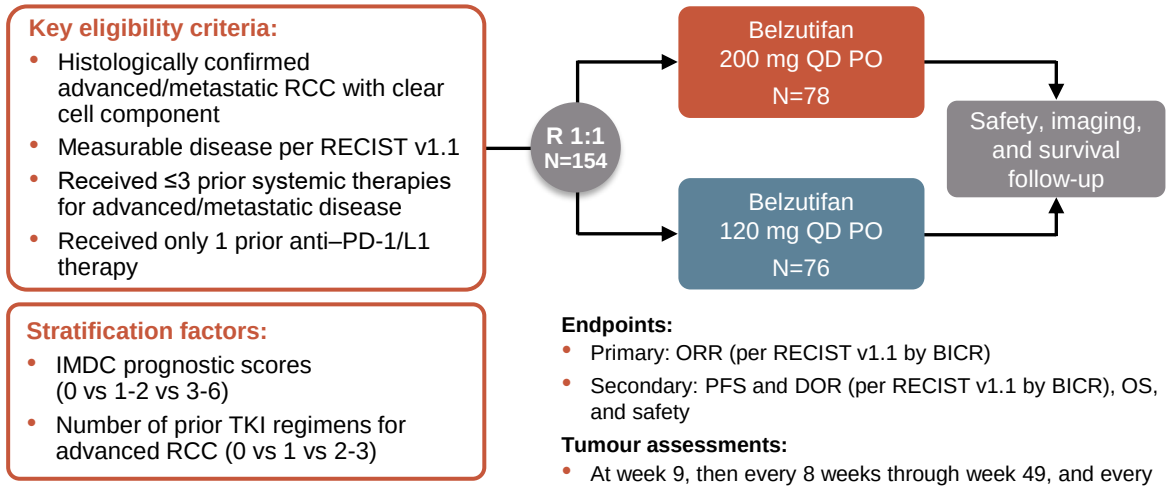
Study Design of LITESPARK-003 (NCT03634540) (Phase 2)[1]



LITESPARK-005 Study (NCT04195750) (Phase 3)[3]



LITESPARK-013 (NCT04489771) (Phase 2)[2]



BICR, blinded independent central review; (cc)RCC, (clear cell) renal cell carcinoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC QLC-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; FKSI-DRS, Functional Assessment of Cancer Therapy Kidney Cancer Symptom Index - Disease Related Symptoms; GHS, global health status; IMDC, International Metastatic RCC Database Consortium; mAb, monoclonal antibody; ORR, overall response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-1/L1, programmed death-ligand 1; PFS, progression-free survival; PO, orally; Q8/12W, every 8/12 weeks; QD, every day; QoL, quality of life; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; TKI, tyrosine kinase inhibitor; TTR, time to response; VEGF(R), vascular endothelial growth factor (receptor)

1. Choueiri T, et al. ESMO 2023. Abstract #LBA87 (oral presentation);
2. Agarwal N, et al. ESMO 2023, #1881O (oral presentation);
3. Albiges L, et al. ESMO 2023. Abstract #LBA88 (oral presentation)

LITESPARK-003: RESULTS

- Median follow-up was 24.3 mo (range, 4.1-48.2) in cohort 1 and 39.8 mo (range, 33.1-55.0) in cohort 2
- Median DoR was 28.6 mo (range, 1.9+ to 35.8) in cohort 1 and 31.5 mo (range, 4.2+ to 36.8) in cohort 2
  - ~ 57% of all responders in cohort 1 and 51% in cohort 2 remained in response for ≥24 mo
- Median PFS was 30.3 mo (95% CI, 16.6-NR) in cohort 1 and 13.8 mo (95% CI, 9.2-19.4) in cohort 2
- Median OS was NR (95% CI, NR-NR) in cohort 1 and 26.7 mo (95% CI, 20.0-41.1) in cohort 2

ORR by investigator in all patients and by IMDC risk

	Cohort 1			Cohort 2		
		IMDC risk category			IMDC risk category	
	Overall N=50	Favourable n=28	Intermediate/ poor n=22	Overall N=52	Favourable n=11	Intermediate/ poor n=41
ORR (CR + PR)	**35 (70)**	22 (79)	13 (59)	**16 (31)**	3 (27)	13 (32)
DCR (CR + PR + SD)	49 (98)	28 (100)	21 (96)	48 (92)	11 (100)	37 (90)
Best response						
CR	4 (8)	3 (11)	1 (5)	2 (4)	0	2 (5)
PR	31 (62)	19 (68)	12 (55)	14 (27)	3 (27)	11 (27)
SD	14 (28)	6 (21)	8 (36)	32 (62)	8 (73)	24 (59)
PD	1 (2)	0 (0)	1 (5)	3 (6)	0 (0)	3 (7)
Not available[a]	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)

All values are n (%). Data cutoff date: May 15, 2023
[a] 1 patient in cohort 2 did not have postbaseline assessment at the data cut-off date

Summary of treatment-related adverse events

	Cohort 1 N=50	Cohort 2 N=52
Any-grade treatment-related AE	50 (100)	51 (98)
Grade ≥3 treatment-related AE	23 (46)	33 (64)
Grade 5 treatment-related AE	0 (0)	1 (2)[a]
Discontinued any drug because of a treatment-related AE	7 (14)	11 (21)
Serious treatment-related AE	7 (14)	16 (31)
Dose reduction because of a treatment-related AE	38 (76)	37 (71)

All values are n (%). Data cut-off date: May 15, 2023
[a] Due to respiratory failure

AE, adverse event; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; IMDC, International Metastatic renal cell carcinoma Database Consortium; mo, months; NR, not reached; ORR, overall response rate; OS, overall survival; PR, partial response; PD, progressive disease; PFS, progression-free survival; SD, stable disease

Choueiri T, et al. ESMO 2023. Abstract #LBA87 (oral presentation); Choueiri T, et al. Annals of Oncology 2023; Vol. 34: Supplement S1328–S1329

LITESPARK-005: RESULTS

- Median follow up at: IA1 18.4 mo (range 9.4–31.7), IA2 25.7 mo (range 16.8–39.1)
- Complete responses occurred in 13 (3.5%) vs 0 pts with belzutifan vs everolimus. More pts remained progression-free with belzutifan vs everolimus at 12 mo (PFS rate 33.7% vs 17.6%) and 18 mo (22.5% vs 9.0%)

	IA1		IA2	
	Belzutifan (n=374)	Everolimus (n=372)	Belzutifan (n=374)	Everolimus (n=372)
Median PFS, mo	5.6	5.6	5.6	5.6
HR (95% CI)	0.75 (0.63–0.90)		0.74 (0.63–0.88)	
p value	<0.001*		Not applicable	
Median OS, mo	21.0	17.2	21.4	18.1
HR (95% CI)	0.87 (0.71–1.07)		0.88 (0.73–1.07)	
p value	0.09583		0.09941	
ORR, % (95% CI)	21.9 (17.8–26.5)	3.5 (1.9–5.9)	22.7 (18.6–27.3)	3.5 (1.9–5.9)
p value	<0.00001		Not applicable	

- 22.6% vs 5.0% of pts had ongoing treatment; 5.9% vs 14.7% of pts discontinued study therapy due to any AE
- Grade 3-5 TRAEs occurred in 38.7% vs 39.4% of pts

AE, adverse event; CI, confidence interval; HR, hazard ratio; IA, interim analysis; mo, months; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; pts, patients; TRAE, treatment-related adverse events

Albiges L, et al. ESMO 2023. Abstract #LBA88 (oral presentation); Albiges L, et al. Annals of Oncology 2023; Vol. 34: Supplement S1329–S1330

LITESPARK-013: RESULTS

EFFICACY

	Belzutifan 200 mg N=78	Belzutifan 120 mg N=76
ORR (CR + PR) n (%)	18 (23.1)	18 (23.7)
Estimated difference (95% CI), %[a]	−0.5 (−14.0 to 12.9); One-sided p=0.5312	
DCR (CR + PR + SD), n (%)	61 (78.2)	57 (75.0)
Best response, n (%)		
CR	4 (5.1)	0 (0)
PR	14 (17.9)	18 (23.7)
SD	43 (55.1)	39 (51.3)
PD	12 (15.4)	15 (19.7)
No assessment[b]	5 (6.4)	4 (5.3)
PFS, median (95% CI), mo	9.1 (5.5-12.0)	7.3 (5.6-9.5)
HR (95% CI)	0.94 (0.63-1.4)	
OS, median (95% CI) mo	Not reached (20.6-NR)	Not reached (22.0-NR)
HR (95% CI)	1.11 (0.65-1.90)	

[a] Based on Miettinen and Nurminen method stratified by IMDC risk group (favourable vs intermediate or poor. [b] Includes patients without postbaseline assessment on the data cut-off date. Data cut-off date: February 10, 2023

SAFETY

- 142 pts had a TRAE; 70 (92.1%) with 120 mg; 72 (92.3%) with 200 mg
- Two pts (2.6%) in the 120 mg arm and 7 (9.0%) in the 200 mg arm discontinued treatment due to a TRAE
- Treatment-related anemia (75.0% with 120 mg and 80.8% with 200 mg) and hypoxia (23.7% with 120 mg and 26.9% with 200 mg) was similar between arms

- Median follow-up was 20.1 months (range 14.8-28.4)

CI, confidence interval; CR, complete response; DCR, disease control rate; HR, hazard ratio; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; mo, months; NR, not reached; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TRAE, treatment-related adverse event

Agarwal N, et al. ESMO 2023. Abstract #1881O (oral presentation); Agarwal N, et al. Annals of Oncology 2023; Vol. 34: Supplement S1011

LITESPARK: SUMMARY

- **LITESPARK-003** – belzutifan plus cabozantinib showed durable anti-tumour activity and a safety profile consistent with prior observations. These results further support the combination of an HIF-2α inhibitor and VEGFR-TKI as a potential treatment option for advanced ccRCC in both the first- and subsequent-line settings[1]
- **LITESPARK-005** – belzutifan was associated with a statistically significant improvement in PFS and ORR vs everolimus for pts with advanced ccRCC after immune checkpoint and anti-angiogenic therapies. The safety profile of belzutifan was consistent with prior reports with no new safety signals[2]
- **LITESPARK-013** – the efficacy of belzutifan was similar between the RP2D of 120-mg dose and the 200-mg dose and was consistent with prior reports of anti-tumour activity in ccRCC. Safety at both doses was consistent with the known safety profile of belzutifan. These results further support 120 mg QD as the preferred dose for belzutifan[3]

Clinical Perspective

- **Belzutifan is the first HIF-2α inhibitor to demonstrate activity in heavily pre-treated advanced ccRCC**

ccRCC, clear cell renal cell carcinoma; HIF-2α, hypoxia-inducible factor-2 alpha ORR overall response rate; PFS, progression-free survival; pts, patients; QD, every day; RP2D, recommended phase 2 dose; VEGFR-TKI, vascular endothelial growth factor receptor-tyrosine kinase inhibitor

1. Choueiri T, et al. Annals of Oncology 2023; Vol. 34: Supplement S1328–S1329; 2. Albiges L, et al. Annals of Oncology 2023; Vol. 34: Supplement S1329–S1330; 3. Agarwal N, et al. Annals of Oncology 2023; Vol. 34: Supplement S1011

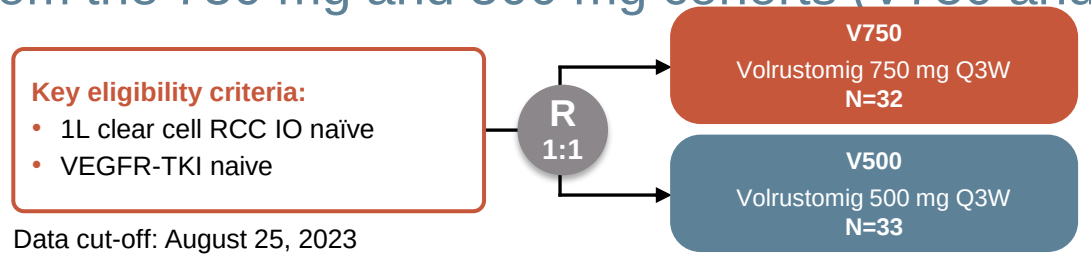
MEDI5752 (VOLRUSTOMIG), A NOVEL PD-1/CTLA-4 BISPECIFIC ANTIBODY, IN THE 1L TREATMENT OF 65 PTS WITH aRCC (FIH STUDY)

Voss M, et al. ESMO 2023. Abstract #1883MO

1L, first-line; aRCC, advanced clear cell renal cell carcinoma; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; PD-1, programmed cell death protein 1; pts, patients

FIH: BACKGROUND AND STUDY DESIGN

- PD-1/CTLA-4 inhibition has improved survival in aRCC, especially in intermediate/poor risk subgroups, but maximising the potential benefit of CTLA-4 inhibition is limited by toxicity[1-3]
- Volrustomig is designed to fully inhibit PD-1 while preferentially inhibiting CTLA-4 on activated PD-1+ T cells[3]
- This first-time-in-human trial showed encouraging activity with volrustomig 1500 mg in 1L aRCC[4]
- We present data from the 750 mg and 500 mg cohorts (V750 and V500)[4,5]



Data cut-off: August 25, 2023

Primary objective: Anti-tumour activity (ORR based on RECIST v1.1)

Key secondary endpoint: Pharmacokinetics, immunogenicity

1L, first-line; (a)RCC, (advanced) renal cell carcinoma; CTLA-4, cytotoxic T lymphocyte antigen 4; IO, immuno-oncology; ORR, overall response rate; PD-1, programmed cell death protein 1; Q3W, every 3 weeks; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; VEGFR-TKI, vascular endothelial growth factor receptor-tyrosine kinase inhibitor

1. Motzer et al. Lancet Oncol. 2019 Oct;20:1370-1385; 2. Albiges L, et al. J Clin Oncol. 2022;40(16_suppl):107; 3. Tran B, et al. Cancer Res 2022;82(12_Supplement):CT016; 4. Voss M, et al. ESMO 2023. Abstract #1883MO (oral presentation); 5. Voss M, et al. Annals of Oncology 2023; Vol. 34: Supplement S1012

FIH: RESULTS

- IMDC I/P risk at baseline
  - V750 (n=32), 71.9%
  - V500 (n=33), 63.6%

EFFICACY

	V750 N=32		V500 N=33	
Response-evaluable, N	**31**[a]		**33**	
Median follow-up (range), months	22.7 (2.2-27.4)		14.9 (1.6-21.7)	
ORR, n (%)	15 (48.4)		15 (45.5)	
CR, n (%)	3 (9.7)		2 (6.1)	
PD, n (%)	3 (9.7)		8 (24.2)	
Disease control rate, n (%)	28 (90.3)		23 (69.7)	
Median duration of response[b] (95% CI), months	17.0 (9.8-NE)		11.5 (5.8-NE)	
IMDC risk group	**I/P**	**F**	**I/P**	**F**
ORR, n/N (%)	13/23 (56.5)	2/8 (25.0)	8/21 (38.1)	7/12 (58.3)
Median duration of response (95% CI), months	15.4 (8.4-NE)	NR (NE-NE)	8.4 (2.9-NE)	NR (2.8-NE)

[a] one ineligible patient is included; [b] median DoR in subjects who discontinued due to AE

SAFETY

	V750 (N=32)		V500 (N=33)	
Median duration of exposure, months (range)	5.52 (0.7-23.4)		5.98 (0.7-20.0)	
	All	**Grade 3/4**	**All**	**Grade 3/4**
TRAE, n (%)	31 (96.9)	20 (62.5)	31 (93.9)	14 (42.4)
TRAE leading to treatment discontinuation, n (%)	15 (46.9)		13 (39.4)	
Treatment-related deaths, n (%)	0		1 (3.0)[a]	
Select TRAEs, n (%)	**All**	**Grade 3/4**	**All**	**Grade ¾**
Pruritus	16 (50)	0	13 (39.4)	0
Hyperthyroidism	11 (34.4)	1 (3.1)	7 (21.2)	0
Hypothyroidism	9 (28.1)	0	6 (18.2)	0
Rash maculo-papular	9 (28.1)	2 (6.3)	2 (6.1)	0
Diarrhoea	8 (25)	1 (3.1)	7 (21.2)	2 (6.1)
Aspartate aminotransferase increase	8 (25)	2 (6.3)	4 (12.1)	2 (6.1)
Alanine aminotransferase increase	6 (18.8)	3 (9.4)	4 (12.1)	2 (6.1)
Infusion-related reaction	5 (15.6)	0	1 (3)	0
Pneumonitis	1 (3.1)	0	2 (6.1)	0
Colitis	0	0	2 (6.1)	0

[a] Cause of death: Bronchopulmonary aspergillosis with immune neutropenia

1L, first line; AE, adverse event; CI, confidence interval; CR, complete response; DoR, duration of response; F, favourable; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; I/P, intermediate/poor; NE, not estimable; NR, not reached; ORR, overall response rate; PD, progressive disease

TRAE, treatment-related adverse event; V500/750, volrustomig 500/750 mg

Voss M, et al. ESMO 2023. Abstract #1883MO (oral presentation); Voss M, et al. Annals of Oncology 2023; Vol. 34: Supplement S1012

FIH: SUMMARY

- Volrustomig is a novel bispecific antibody with high degree of efficacy in 1L aRCC and across IMDC risk groups, with a low rate of upfront treatment failure
- The safety profile is consistent with dual checkpoint inhibition.
- Volrustomig with lenvatinib is also being evaluated in 1L aRCC (NCT04522323)

Clinical Perspective

- **Volrustomig monotherapy is active in treatment-naïve aRCC and has the potential to improve outcomes**

1L, first line; aRCC, advanced renal cell carcinoma; IMDC, International Metastatic RCC Database Consortium

Voss M, et al. Annals of Oncology 2023; Vol. 34: Supplement S1012

PHASE 2 STUDY OF AVE PLUS INTERMITTENT AXI IN PREVIOUSLY UNTREATED PTS WITH mRCC. THE TIDE-A STUDY

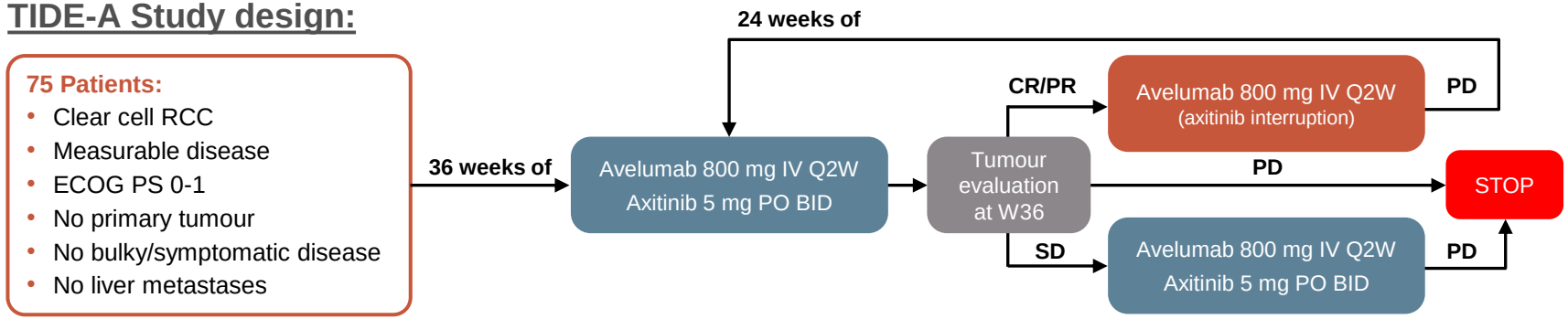
Iacovelli R, et al. ESMO 2023. Abstract #1884MO

AVE, avelumab; AXI, axitinib; mRCC, metastatic renal cell carcinoma; pts, patients

TIDE-A: BACKGROUND AND STUDY DESIGN

- Combinations of VEGFR-TKI plus anti-PD-1/L1 immunotherapy are the standard of care for first-line therapy of mRCC pts due to increased response rate, prolonged progression-free (PFS) and overall (OS) survivals compared to VEGFR TKI alone[1]
- It is well recognised that the majority of toxicities of the combinations are due to the VEGFR TKI[2,3]
- Previous studies have suggested a TKI treatment break may not impact outcomes in RCC patients receiving first-line treatment with IO-VEGFR TKI[4,5]
- The TIDE-A study investigated whether continuation of avelumab alone to manage TKI-related toxicity is feasible in RCC patients who have achieved a tumour response with axitinib plus avelumab[6,7]

TIDE-A Study design:



Primary endpoint: The rate of patients free of progression after 8 weeks from axitinib discontinuation (W36±2)
Secondary endpoints: mPFS, mOS, ORR and safety by local evaluation

BID, two times a day; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; IO, immuno-oncology; IV, intravenous; mOS, median overall survival; mPFS, median progression-free survival; (m)RCC, (metastatic) renal cell cancer; ORR, overall response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PO, orally; PR, partial response; pts, patients; Q2W, every 2 weeks; SD, stable disease; TKI, tyrosine kinase inhibitor; W, week; VEGFR, vascular endothelial growth factor receptor

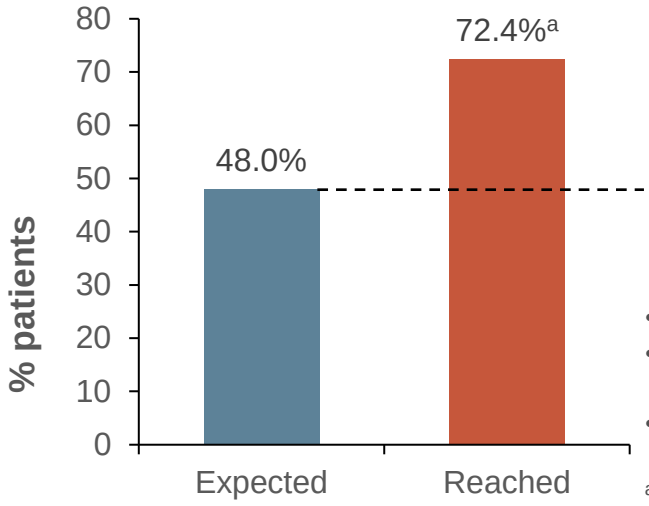
1. Powles T; ESMO Guidelines Committee. Ann Oncol. 2021;32:422-423; 2. Motzer R, et al. N Engl J Med. 2019; 380: 1103-1115; 3. Motzer R, et al. N Engl J Med. 2021; 384: 1289-1300; 4. Brown JE, et al. Lancet Oncol. 2023; 24: 213-227; 5. Ornstein MC, et al. J Clin Oncol. 2017; 35: 1764-1769; 6. Iacovelli R, et al. ESMO 2023. Abstract #1884MO (oral presentation);
7. Iacovelli R, et al. Annals of Oncology 2023; Vol. 34: Supplement S1013

TIDE-A: RESULTS

- 79 pts were enrolled and 75 evaluated for efficacy (IMDC risk: 40.0% favourable, 57.3% intermediate, 2.7% poor)
- 29 (38.2%) of 75 pts discontinued axitinib at 36W; the rate of these pts FoP after 8W was 72.4%

PRIMARY ENDPOINT

Rate of patients free of progression 8 weeks after axitinib interruption:



Considering the first 22 patients who discontinued axitinib, 14 patients were free from PD at week 8

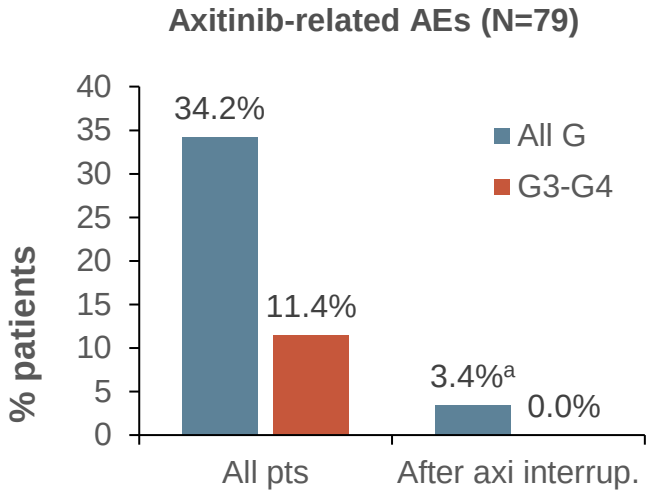
The primary endpoint was met

- Patients enrolled (full criteria): 75
- Patients who interrupted axitinib at week 36 (±2): 29 (38.2%)
- Patients with progression within 8 weeks from axitinib discontinuation: 8

[a] Evaluated in all 29 patients who interrupted axitinib at week 36

SECONDARY ENDPOINT

Safety:



[a] The only pt with axi-related toxicity after the treatment interruption had G1 hand-foot syndrome subsequently recovered

- Median PFS 23.8 months (95% CI: NR-NR)
- Median OS not reached (18-mo OS was 94%)

- Safety: 96.2% of pts had at least one AE and 40.5% had G3-G4 AEs with no treatment-related death

AE, adverse event; axi, axitinib; CI, confidence interval; FoP, freedom of progression; G, grade; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; mo, months; NR, not reached; OS, overall survival; PD, progressive disease; PFS, progression-free survival; pts, patients; W, week

Iacovelli R, et al. ESMO 2023. Abstract #1884MO (oral presentation); Iacovelli R, et al. Annals of Oncology 2023; Vol. 34: Supplement S1013

TIDE-A: SUMMARY

- The TIDE-A study shows that VEGFR-TKI discontinuation is safe for selected mRCC pts with evidence of response to VEGFR-TKI+IO combinations in first line
- Axitinib discontinuation allows decreasing of toxicity, while maintaining the possibility of axitinib benefit in case of its reintroduction

Clinical Perspective

- **TIDE-A shows that VEGFR-TKI de-escalation strategies have the potential to spare toxicity for RCC patients and cost**

IO, immuno-oncology; (m)RCC, (metastatic) renal cell carcinoma; VEGFR-TKI, vascular endothelial growth factor receptor-tyrosine kinase inhibitor

Iacovelli R, et al. ESMO 2023. Abstract #1884MO (oral presentation); Iacovelli R, et al. Annals of Oncology 2023; Vol. 34: Supplement S1013

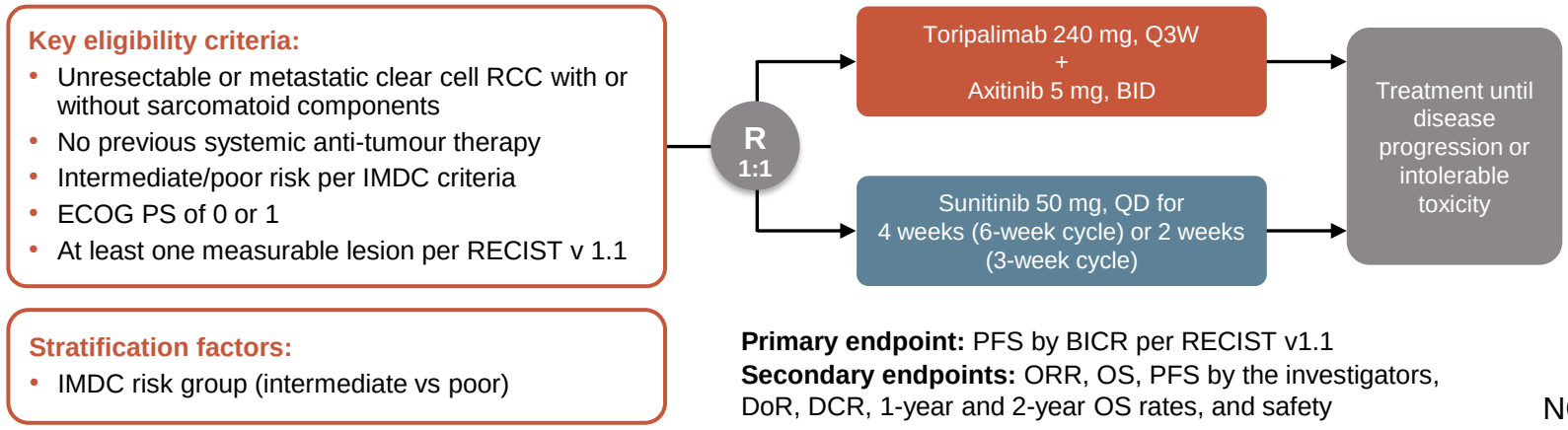
RENOTORCH: TORIPALIMAB COMBINED WITH AXITINIB VERSUS SUNITINIB IN FIRST-LINE TREATMENT OF aRCC: A RANDOMISED, OPEN-LABEL, PHASE 3 STUDY

Sheng X, et al. ESMO 2023. Abstract #1882O

aRCC, advanced renal cell carcinoma

RENOTORCH: BACKGROUND AND STUDY DESIGN

- Anti-PD-1 antibody plus antiangiogenic therapy can play a synergistic anti-tumour role in the treatment of advanced renal cancer, especially in patients with intermediate or poor IMDC risk
- Toripalimab is a humanised monoclonal antibody against PD-1
- RENOTORCH is a randomised, open label, phase 3 trial comparing toripalimab plus axitinib with sunitinib as first-line treatment for advanced RCC patients



Primary endpoint: PFS by BICR per RECIST v1.1
Secondary endpoints: ORR, OS, PFS by the investigators, DoR, DCR, 1-year and 2-year OS rates, and safety

NCT04394975

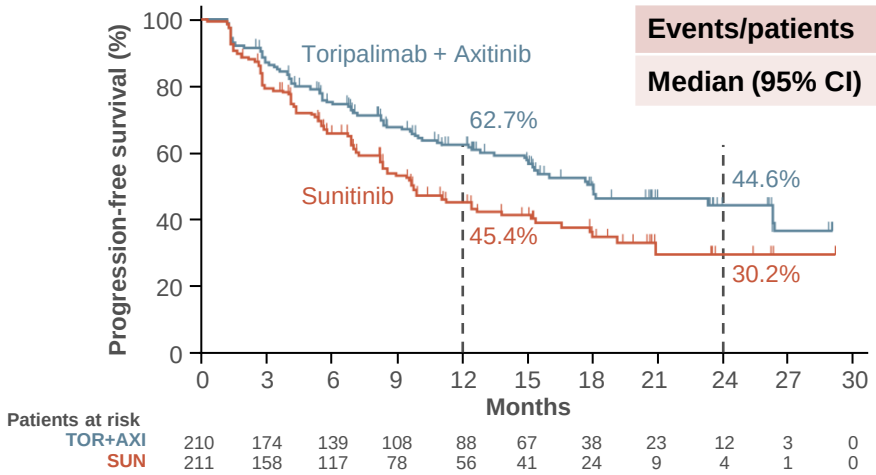
BICR, blinded independent review; BID, two times a day; DCR, disease control rate; DoR, duration of response; ECOG-PS, Eastern Cooperative Oncology Group performance status; IMDC, International Metastatic RCC Database Consortium; ORR, overall response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; Q3W, every 3 weeks; QD, every day; R, randomisation; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria in Solid Tumours

Sheng X, et al. ESMO 2023. Abstract #1882O (oral presentation); Sheng X, et al. Annals of Oncology 2023; Vol. 34: Supplement S1011–S101

RENOTORCH: RESULTS

PFS BY BICR PER RECIST v1.1

Interim PFS analysis data cut-off date: March 31, 2023, with a median follow-up time of 14.6 months



	TOR+AXI	SUN
Events/patients	88/210	109/211
Median (95% CI)	18.0 (15.0, NE)	9.8 (8.3, 13.8)

Stratified HR for disease progression or death:
0.65 (95% CI, 0.49, 0.86)
P=0.0028

Stratified Cox proportions hazard model, stratification factor: IMDC level at randomisation

	TOR+AXI N=210	SUN N=211
PFS (Investigator assessed)		
No. of events, n	92	122
Median PFS (95% CI), mo	18.0 (14.9, 20.4)	10.4 (8.4, 12.4)
Objective response rate (BICR)		
ORR (%) (95% CI), %	56.7 (49.7-63.5)	30.8 (24.6-37.5)
p value	P<0.0001	
Overall survival (descriptive)		
No. of events, n	38	57
Median OS (95% CI), mo	NE (NE, NE)	26.8 (24.5, NE)
HR (95% CI) p value	0.61 (0.40, 0.92) P=0.0186	

- Toripalimab plus axitinib consistently outperformed sunitinib across all evaluated subgroups
- The incidence of Grade ≥3 AEs (71.2% vs 67.1%), AEs leading to discontinuation of treatment (14.4% vs 8.1%), and fatal AEs (1.0% vs 1.0%) were similar between respective TOR+AXI and SUN arms

AE, adverse events; AXI, axitinib; BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; mo, months; NE, not evaluable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; SUN, sunitinib; TOR, toripalimab

Sheng X, et al. ESMO 2023. Abstract #1882O (oral presentation); Sheng X, et al. Annals of Oncology 2023; Vol. 34: Supplement S1011–S101

RENOTORCH: SUMMARY

- Treatment with toripalimab plus axitinib resulted in significantly longer PFS, as well as a higher ORR, than treatment with sunitinib in patients with previously untreated advanced RCC[1,2]
- The combination of toripalimab and axitinib was generally well-tolerated with a safety profile consistent with each individual agent[1,2]
- These results support the use of toripalimab with axitinib as a first-line treatment for advanced RCC[1,2]

Clinical Perspective

- **Toripalimab plus axitinib combination is approved in China for patients with advanced RCC**
- **As many patients with RCC patients live in China, the RENOTORCH trial is expected to be practice-changing for a large population of patients with advanced RCC worldwide**

ORR, overall response rate; PFS, progression-free survival; RCC, renal cell carcinoma

1. Sheng X, et al. ESMO 2023. Abstract #1882O (oral presentation); 2. Sheng X, et al. Annals of Oncology 2023; Vol. 34: Supplement S1011–S101; 3. van der Veldt A. ESMO 2023. Invited Discussant, abstract #1882O (oral presentation)

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