GONORTE
Grupo Oncológico

REUNIÓN POST CONGRESO DE LA
SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2023

Presentaciones más destacadas en cáncer renal

Javier Puente, MD, PhD
GU Cancer Unit
Medical Oncology Department
Hospital Clínico Universitario San Carlos, Madrid, Spain
Associate Professor of Medicine
Complutense University of Madrid, Spain

@docjavip

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Disclosures

- **Advisory Boards:**
  - MSD, BMS, Roche-Genentech, Janssen, Novartis, Bayer, Astellas
- **Research Funding:**
  - Roche-Genentech, Astellas, Pfizer
- **Travel expenses:**
  - Janssen, Merck, IPSEN, Pfizer
- **Clinical Trials:**
  - BMS, Roche-Genentech, Merck, EISAI, MSD, Gilead, Exelixis
- **Lectures:**
  - Astellas, Astra Zeneca, Janssen, MSD, Bayer, Pfizer, Eisai, Ipsen, Sanofi, Roche, BMS, Pierre Fabre, Merck

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Current treatment landscape mRCC

1st line

FIRST-LINE THERAPY FOR CLEAR CELL HISTOLOGY			
Risk	**Preferred Regimens**	**Other Recommended Regimens**	**Useful in Certain Circumstances**
Favorable[a]	• Axitinib + pembrolizumab[b] (category 1) • Cabozantinib + nivolumab[b] (category 1) • Lenvatinib + pembrolizumab[b] (category 1)	• Axitinib + avelumab[b] • Cabozantinib (category 2B) • Ipilimumab + nivolumab[b] • Pazopanib • Sunitinib	• Active surveillance[c] • Axitinib (category 2B) • High-dose IL-2[d] (category 2B)
Poor/ intermediate[a]	• Axitinib + pembrolizumab[b] (category 1) • Cabozantinib + nivolumab[b] (category 1) • Ipilimumab + nivolumab[b] (category 1) • Lenvatinib + pembrolizumab[b] (category 1) • Cabozantinib	• Axitinib + avelumab[b] • Pazopanib • Sunitinib	• Axitinib (category 2B) • High-dose IL-2[d] (category 3) • Temsirolimus[e] (category 3)

More lines

SUBSEQUENT THERAPY FOR CLEAR CELL HISTOLOGY (IN ALPHABETICAL ORDER BY CATEGORY)			
Immuno-oncology (IO) Therapy History Status	**Preferred Regimens**	**Other Recommended Regimens**	**Useful in Certain Circumstances**
IO Therapy Naïve	• None	• Axitinib + pembrolizumab[b] • Cabozantinib • Cabozantinib + nivolumab[b] • Ipilimumab + nivolumab[b] • Lenvatinib + everolimus • Lenvatinib + pembrolizumab[b] • Nivolumab[b]	• Axitinib • Everolimus • Pazopanib • Sunitinib • Tivozanib[f] • Belzutifan (category 2B) • Bevacizumab[g] (category 2B) • High-dose IL-2 for selected patients[d] (category 2B) • Temsirolimus[e] (category 2B) • Axitinib + avelumab[b] (category 3)
Prior IO Therapy	• None	• Axitinib • Cabozantinib • Lenvatinib + everolimus • Tivozanib[f]	• Axitinib + pembrolizumab[b] • Cabozantinib + nivolumab[b] • Everolimus • Ipilimumab + nivolumab[b] • Lenvatinib + pembrolizumab[b] • Pazopanib • Sunitinib • Belzutifan (category 2B) • Bevacizumab[g] (category 2B) • High-dose IL-2 for selected patients[d] (category 2B) • Temsirolimus[e] (category 2B) • Axitinib + avelumab[b] (category 3)

5 abstracts de Cáncer Renal que no te puedes perder en ESMO 23

GRUPO CENTRO DE TUMORES GENITOURINARIOS

https://grupocentrogu.com

@CentroGU

Belzutifan versus everolimus in participants (pts) with previously treated advanced clear cell renal cell carcinoma (ccRCC): randomized open-label phase 3 LITESPARK-005 study. Presented by L.Albiges.

Phase 2 LITESPARK-003 Study of Belzutifan in Combination With Cabozantinib for Advanced Clear Cell Renal Cell Carcinoma (ccRCC)
Presented by T.Choueiri.

Phase II study of avelumab (Ave) plus intermittent axitinib (Axi) in previously untreated patients (pts) with metastatic renal cell carcinoma (mRCC): The TIDE-A study. Presented by R. Iacovelli

Tumor response by baseline metastases in patients (pts) with renal cell carcinoma (RCC) treated with lenvatinib (L) plus pembrolizumab (P) vs sunitinib (S): Post hoc analysis of the CLEAR trial Presented by Viktor Grünwald

MEDI5752 (volrustomig), a novel PD-1/CTLA-4 bispecific antibody, in the first line (1L) treatment of 65 patients (pts) with advanced clear cell renal cell carcinoma (aRCC). Presented by M.Voss.

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Abstract selection ESMO 2023 RCC

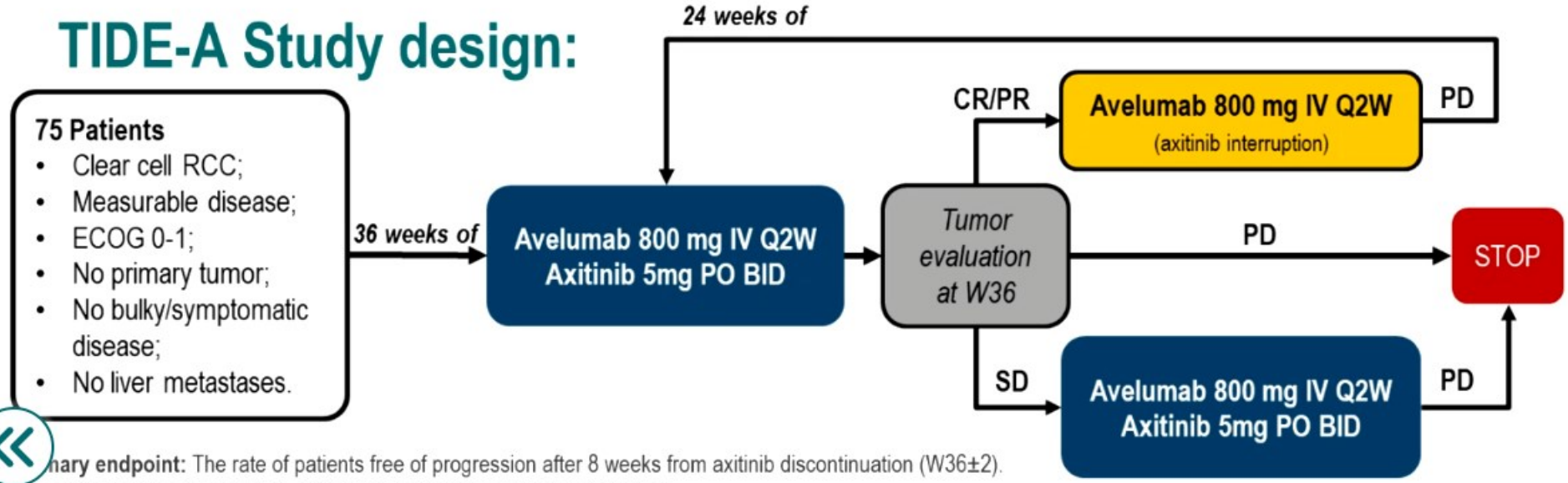
1st line

Phase II study of avelumab (Ave) plus intermittent axitinib (Axi) in previously untreated patients (pts) with metastatic renal cell carcinoma (mRCC): The TIDE-A study. Presented by R. Iacovelli

More lines

TIDE-A Study

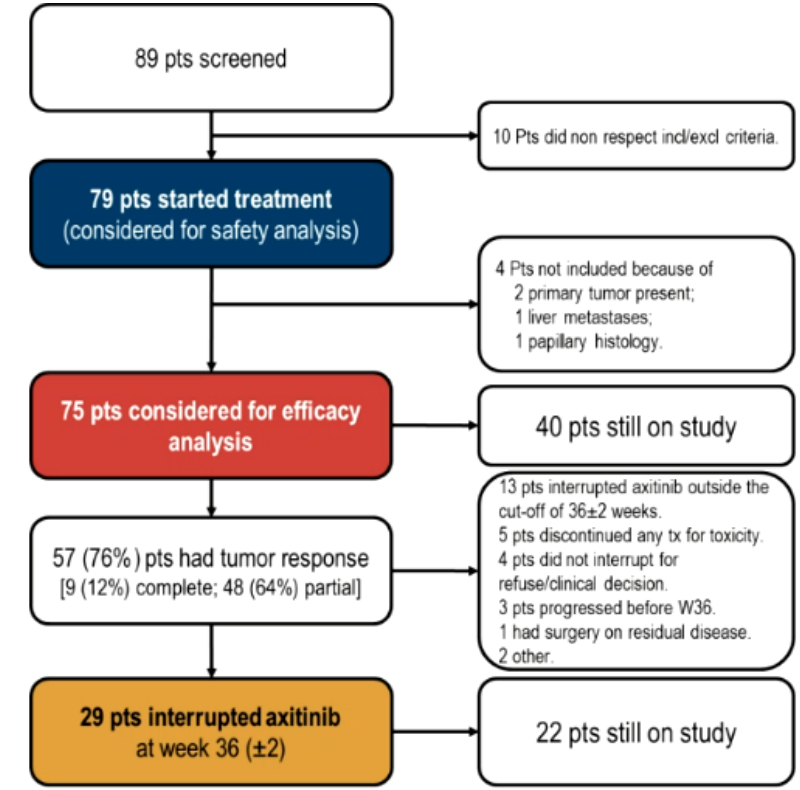
TIDE-A Study design:



nary 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.

Lacovelli R, et al. ESMO 2023

TIDE-A Study



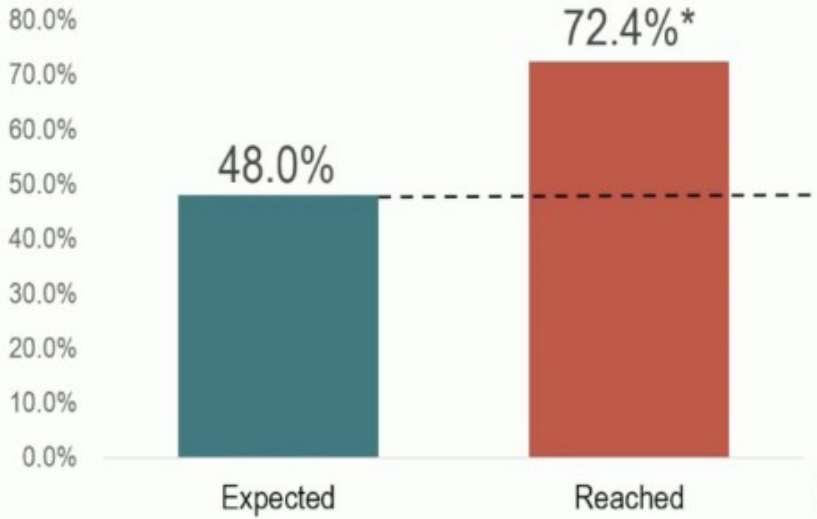
Baseline characteristics	Patients N=75 (%)
Median age (min-max)	64 (42-84)
Male sex	49 (65.3%)
Nephrectomy	75 (100%)
Interval from Nx to Tx <1y	31 (41.3%)
Sites of metastases	
Lung	43 (57.3%)
Lymph nodes	31 (41.3%)
Pancreas	16 (21.3%)
Bone	11 (14.7%)
Kidney bed	11 (14.7%)
Soft tissue	11 (14.7%)
IMDC prognostic class	
Favorable	30 (40.0%)
Intermediate	43 (57.3%)
Poor	2 (2.7%)
ECOG performance status	
0	60 (80.0%)
1	15 (20.0%)

Lacovelli R, et al. ESMO 2023

TIDE-A Study

Primary endpoint:

Rate of patients free of progression after 8 weeks from 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 discontinuati
* Evaluated in all 29 patients who interrupted axitinib at week 36.

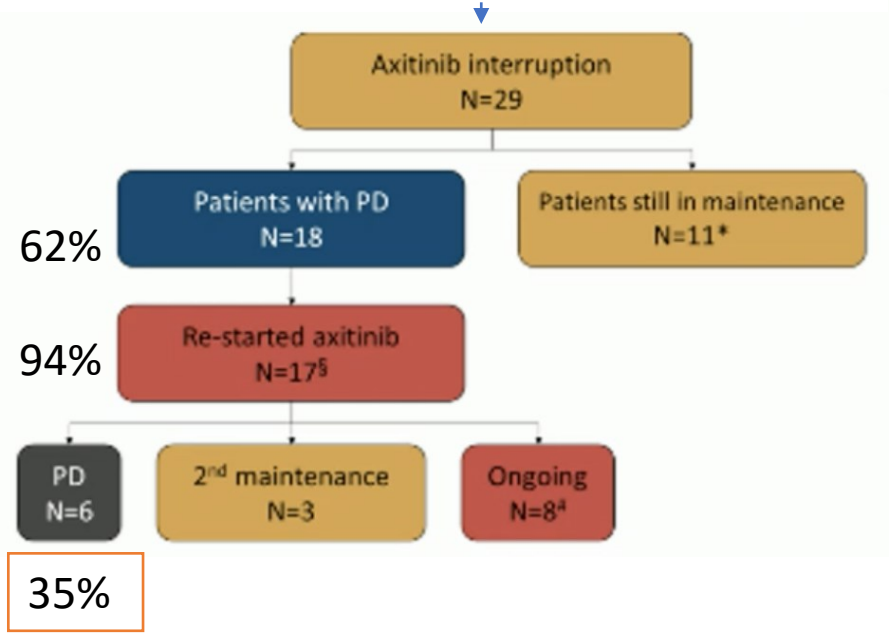
Content of this presentation is copyright and responsibility of the author. Permission is required for re-

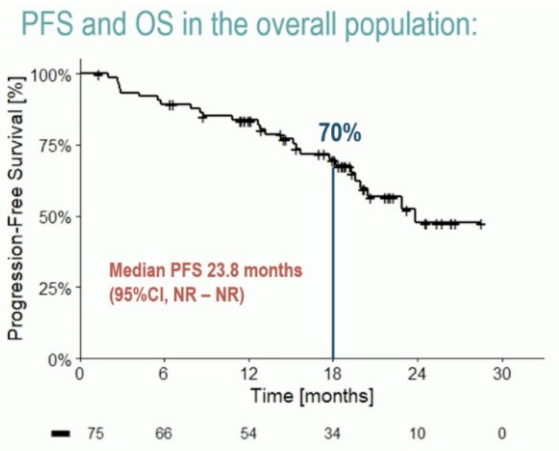
Lacovelli R, et al. ESMO 2023

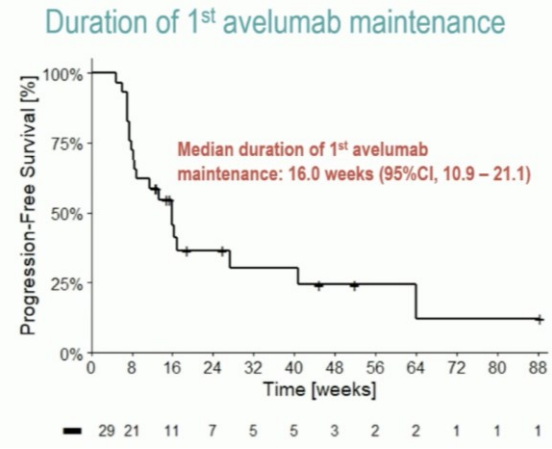
Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

TIDE-A Study

59 patients CR/PR







Lacovelli R, et al. ESMO 2023

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Abstract selection ESMO 2023 RCC

1st line

Phase II study of avelumab (Ave) plus intermittent axitinib (Axi) in previously untreated patients (pts) with metastatic renal cell carcinoma (mRCC): The TIDE-A study. Presented by R. Iacovelli

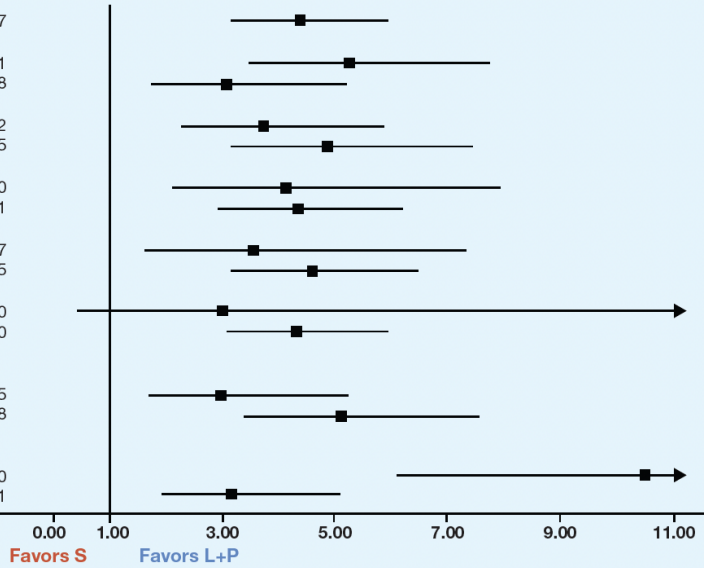
Tumor response by baseline metastases in patients (pts) with renal cell carcinoma (RCC) treated with lenvatinib (L) plus pembrolizumab (P) vs sunitinib (S): Post hoc analysis of the CLEAR trial Presented by Viktor Grünwald

More lines

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Update CLEAR study: post-hoc analysis

	Responders/Patients		ORR, %		Odds ratio[a] (95% CI)	Median DOR, mos (95% CI)[b]	
	L+P	S	L+P	S		L+P	S
Overall	253/355	131/357	71.3	36.7	4.31 (3.14–5.92)	26.7 (22.8–34.6)	14.7 (9.4–18.2)
Baseline Lung Metastasis							
Yes	184/252	80/228	73.0	35.1	5.19 (3.48–7.72)	25.8 (21.4–31.7)	11.1 (9.2–16.5)
No	69/103	51/128	67.0	39.8	3.02 (1.75–5.20)	39.2 (22.0–NE)	19.0 (9.3–35.1)
Baseline Lymph Node Metastasis							
Yes	110/162	58/156	67.9	37.2	3.66 (2.28–5.88)	25.9 (20.4–36.6)	9.5 (7.4–16.7)
No	143/193	73/200	74.1	36.5	4.83 (3.14–7.43)	27.9 (22.4–36.4)	15.8 (10.9–24.0)
Baseline Bone Metastasis							
Yes	48/80	24/89	60.0	27.0	4.09 (2.11–7.94)	22.0 (12.5–27.2)	16.6 (3.7–35.5)
No	205/275	107/267	74.5	40.1	4.30 (2.97–6.20)	30.5 (24.1–36.6)	13.1 (9.3–18.4)
Baseline Liver Metastasis							
Yes	35/63	18/70	55.6	25.7	3.51 (1.68–7.30)	20.1 (8.5–NE)	9.2 (3.7–20.3)
No	218/292	113/286	74.7	39.5	4.53 (3.17–6.47)	27.9 (25.5–36.4)	14.8 (9.5–18.4)
Baseline Brain Metastasis[c]							
Yes	4/6	3/10	66.7	30.0	3.00 (0.43–20.72)	12.9 (3.3–NE)	13.7 (9.2–NE)
No	249/349	128/346	71.3	37.0	4.29 (3.11–5.92)	27.1 (23.4–34.7)	14.7 (9.4–18.4)
No. of Metastatic Organs/ Sites Involved							
1	86/119	53/114	72.3	46.5	2.98 (1.71–5.21)	39.2 (27.1–46.7)	29.5 (11.1–NE)
≥ 2	162/231	75/236	70.1	31.8	5.06 (3.40–7.53)	23.4 (19.6–27.2)	9.5 (8.1–16.5)
Baseline Sums of Diameters of Target Lesions							
≥ 60 mm	117/162	37/161	72.2	23.0	10.50 (6.08–18.13)	25.7 (20.3–34.6)	9.5 (6.2–18.4)
< 60 mm	124/160	93/175	77.5	53.1	3.14 (1.94–5.07)	29.2 (22.2–37.3)	14.8 (9.4–20.3)

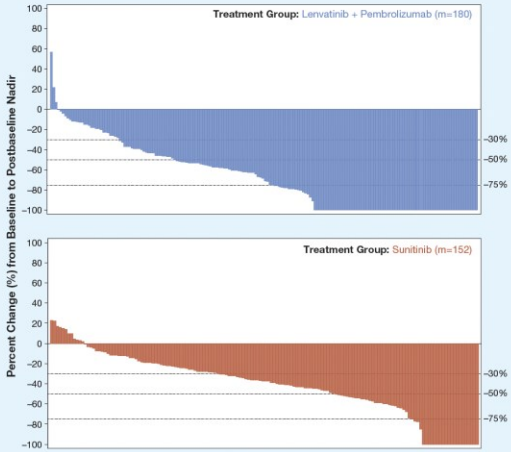


Grünwald V, et al. ESMO 2023

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

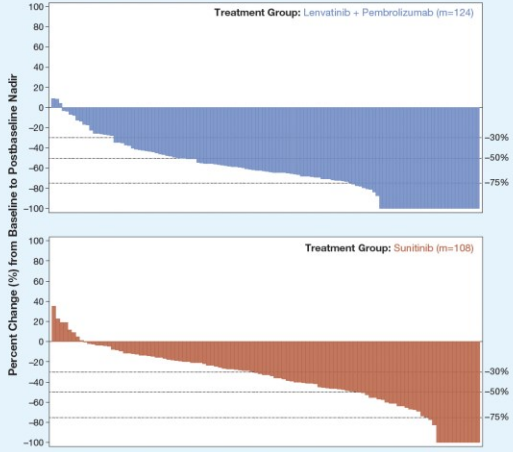
Update CLEAR study: post-hoc analysis

Figure 4. Percentage change in sum of diameters of target lesions in lung from baseline to postbaseline nadir.



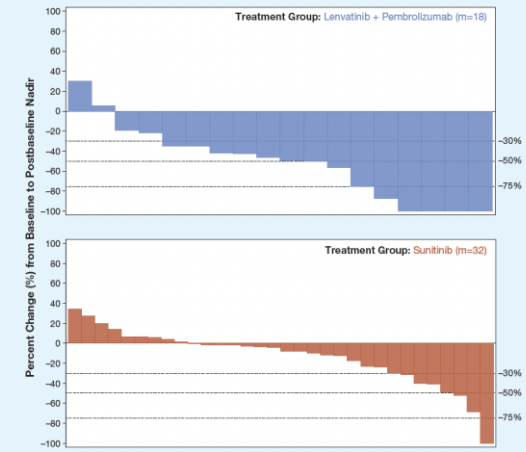
This figure includes patients (m) with both baseline and at least 1 postbaseline target lesion assessment in the lung per independent image review.

Figure 5. Percentage change in sum of diameters of target lesions in lymph nodes from baseline to postbaseline nadir.



This figure includes patients (m) with both baseline and at least 1 postbaseline target lesion assessment in the lymph nodes per independent image review.

Figure 7. Percentage change in sum of diameters of target lesions in bone from baseline to postbaseline nadir.



This figure includes patients (m) with both baseline and at least 1 postbaseline target lesion assessment in the bone per independent image review.

Grünwald V, et al. ESMO 2023

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Abstract selection ESMO 2023 RCC

1st line

Phase II study of avelumab (Ave) plus intermittent axitinib (Axi) in previously untreated patients (pts) with metastatic renal cell carcinoma (mRCC): The TIDE-A study. Presented by R. Iacovelli

Tumor response by baseline metastases in patients (pts) with renal cell carcinoma (RCC) treated with lenvatinib (L) plus pembrolizumab (P) vs sunitinib (S): Post hoc analysis of the CLEAR trial Presented by Viktor Grünwald

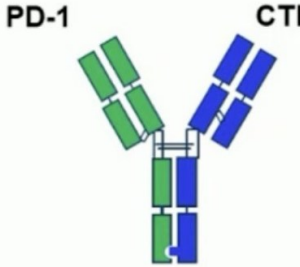
MEDI5752 (volrustomig), a novel PD-1/CTLA-4 bispecific antibody, in the first line (1L) treatment of 65 patients (pts) with advanced clear cell renal cell carcinoma (aRCC). Presented by M.Voss.

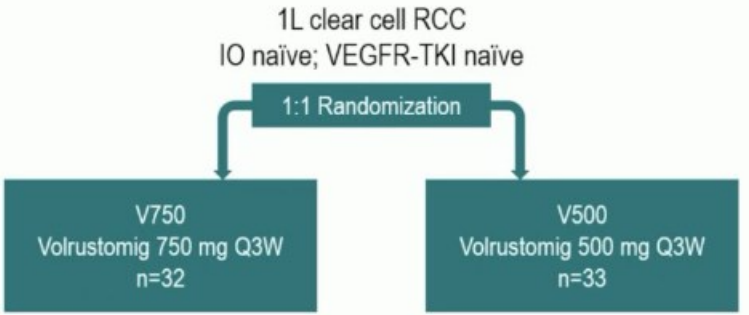
More lines

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

MEDI5752 (Volrustomig)

MEDI5752: A monovalent bispecific antibody





DCO 25 Aug 2023

Primary objective: antitumor activity (ORR based on RECIST v1.1)
Key secondary objectives: pharmacokinetics, immunogenicity

	V750 (N=32)	V500 (N=33)
Median age (range), years	59 (36–78)	64 (47–86)
Female / male, n (%)	10 (31.3) / 22 (68.8)	6 (18.2) / 27 (81.8)
ECOG performance status 0 / 1, n (%)	21 (65.6) / 11 (34.4)	21 (63.6) / 12 (36.4)
Prior nephrectomy, n (%)	17 (53.1)	22 (66.7)
IMDC category*		
Favorable risk, n (%)	8 (25.0)	12 (36.4)
Intermediate/Poor risk, n (%)	23 (71.9)	21 (63.6)
PD-L1 expression (SP263), n (%)		
<1%	21 (65.6)	26 (78.8)
≥1%	6 (18.8)	3 (9.1)
NE†	5 (15.6)	4 (12.1)

Voss M, et al. ESMO 2023

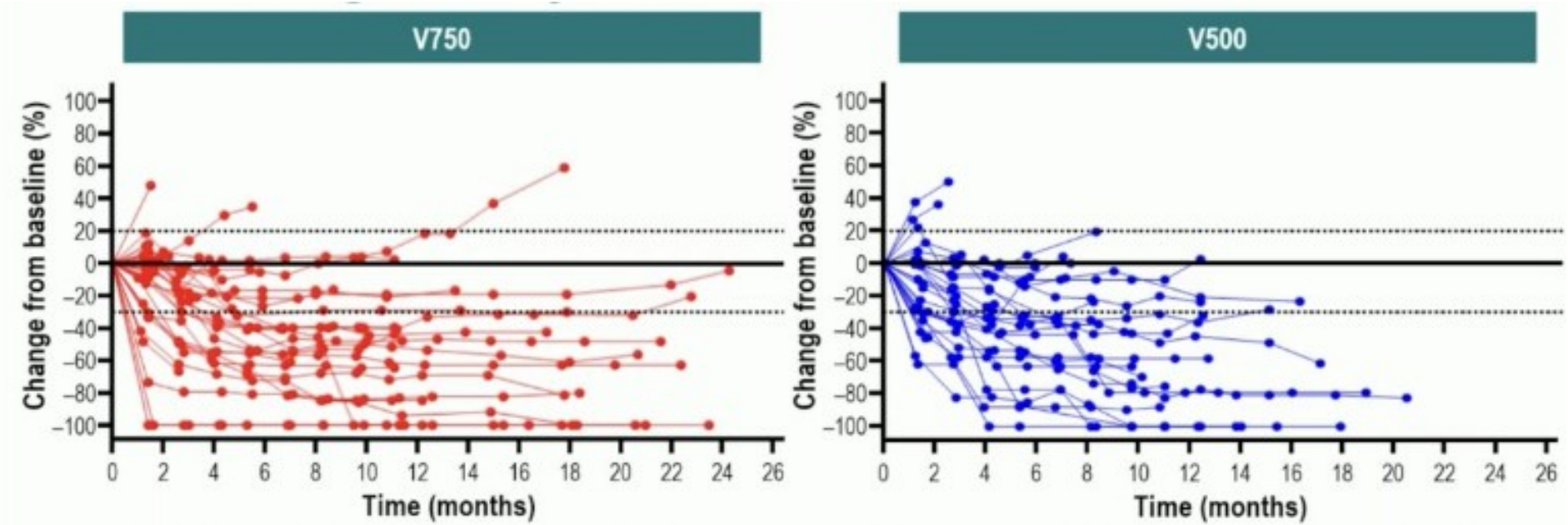
MEDI5752 (Volrustomig)

	V750 (N=32)		V500 (N=33)	
Response-evaluable, N	**31***		**33**	
Median follow-up, months (range)	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, months (95% CI)†	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, months (95% CI)	15.4 (8.4–NE)	NR (NE–NE)	8.4 (2.9–NE)	NR (2.8–NE)

Voss M, et al. ESMO 2023

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

MEDI5752 (Volrustomig)



Median DoR, months (95% CI)	17.0 (9.8-NE)
Median PFS, months (95% CI)	12.3 (8.1-22.8)
PFS-12 (%)	51.7

Median DoR, months (95% CI)	11.5 (5.8–NE)
Median PFS, months (95% CI)	9.7 (3.9-NE)
PFS-12 (%)	43.8

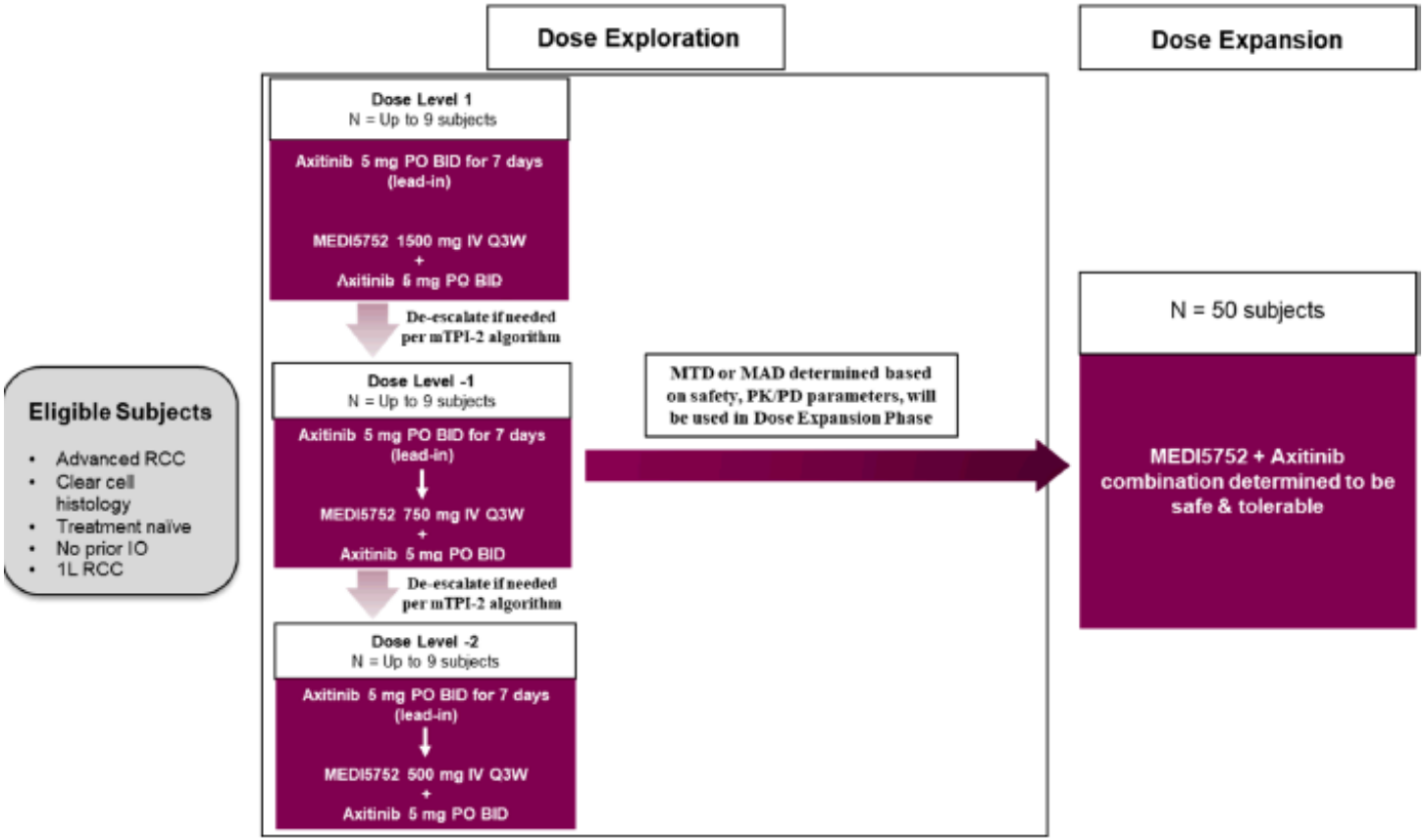
Voss M, et al. ESMO 2023

MEDI5752 (Volrustomig)

	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
Treatment-related AE, 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)*	
Select TRAEs, n (%)	**All**	**Grade 3/4**	**All**	**Grade 3/4**
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
Diarrhea	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

Voss M, et al. ESMO 2023

MEDI5752 (Volrustomig)



Voss M, et al. ESMO 2023

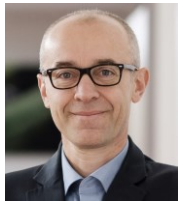
Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Abstract selection ESMO 2023 RCC

1st line

Phase II study of avelumab (Ave) plus intermittent axitinib (Axi) in previously untreated patients (pts) with metastatic renal cell carcinoma (mRCC): The TIDE-A study. Presented by R. Iacovelli

Tumor response by baseline metastases in patients (pts) with renal cell carcinoma (RCC) treated with lenvatinib (L) plus pembrolizumab (P) vs sunitinib (S): Post hoc analysis of the CLEAR trial Presented by Viktor Grünwald

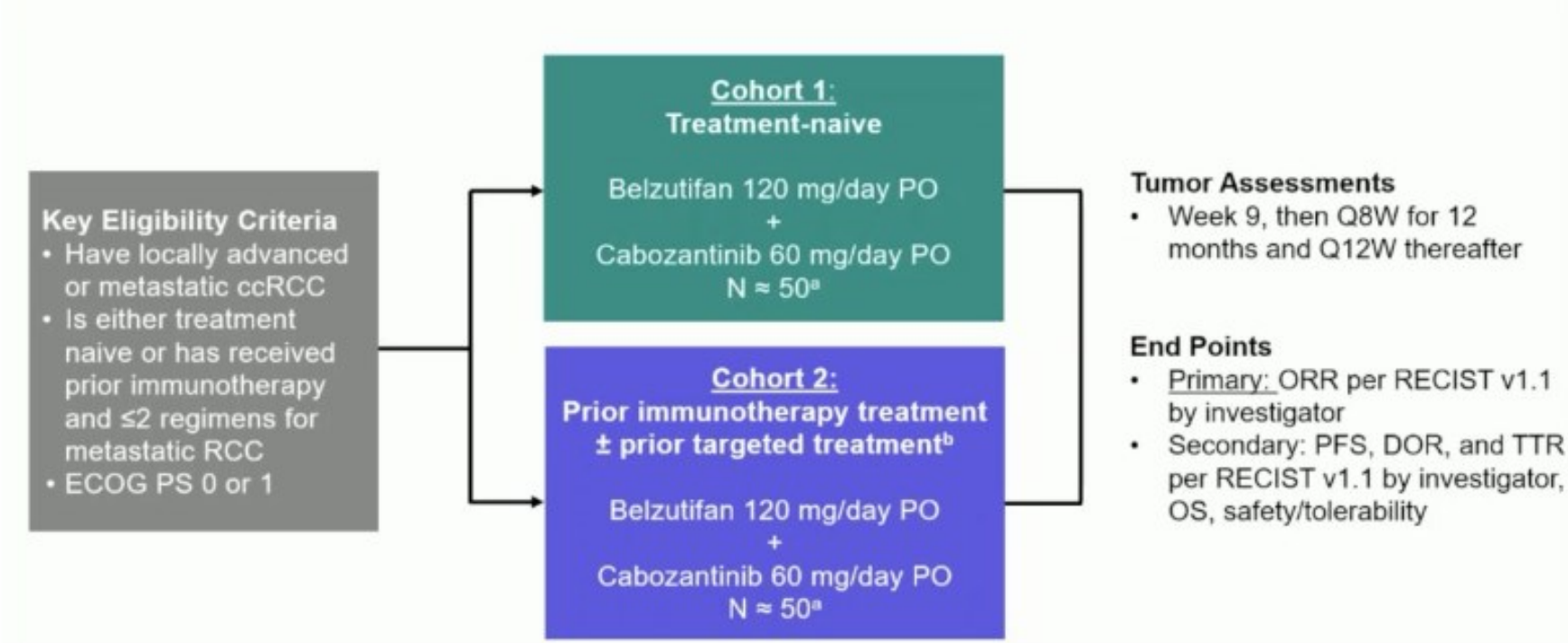


MEDI5752 (volrustomig), a novel PD-1/CTLA-4 bispecific antibody, in the first line (1L) treatment of 65 patients (pts) with advanced clear cell renal cell carcinoma (aRCC). Presented by M.Voss.

More lines

Phase 2 LITESPARK-003 Study of Belzutifan in Combination With Cabozantinib for Advanced Clear Cell Renal Cell Carcinoma (ccRCC)
Presented by T.Choueiri.

LITESPARK-003



Cohort	ORR
Cohort 1 (median follow-up, 14.0 months)	57%[a,3]
Cohort 2 (median follow-up, 24.6 months)	31%[4]

Choueiri T, et al. ESMO 2023

Baseline Characteristics

	Cohort 1 N = 50	Cohort 2 N = 52
Age, median (range), years	64.0 (33-89)	63.0 (43-79)
≥65 years	23 (46)	24 (46)
Male	40 (80)	38 (73)
ECOG performance status 0/1, n (%)	33 (66)/17 (34)	23 (44)/29 (56)
IMDC risk group		
Favorable	28 (56)	11 (21)
Intermediate/poor	22 (44)	41 (79)
Prior nephrectomy	40 (80)	42 (81)
Number of prior lines of anticancer therapy		
1	0 (0)	29 (56)
2	0 (0)	23 (44)
Prior type of anticancer therapy		
Immunotherapy[a]	0 (0)	28 (54)
Immunotherapy + anti-VEGF/VEGFR therapy[b]	0 (0)	24 (46)

Choueiri T, et al. ESMO 2023

ORR by Investigator in All Patients and by IMDC Risk

	Cohort 1			Cohort 2		
	Overall N = 50	IMDC risk category		Overall N = 52	IMDC risk category	
		Favorable n = 28	Intermediate/ poor n = 22		Favorable 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)

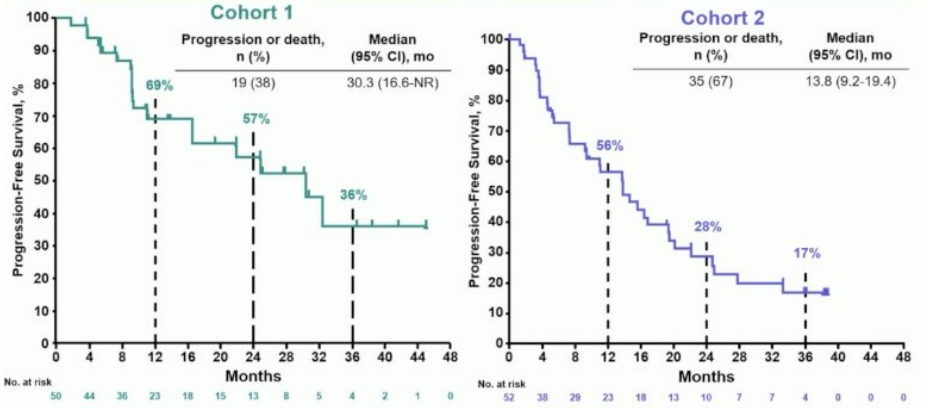
Choueiri T, et al. ESMO 2023

ORR by Prior Anticancer Therapy: Cohort 2

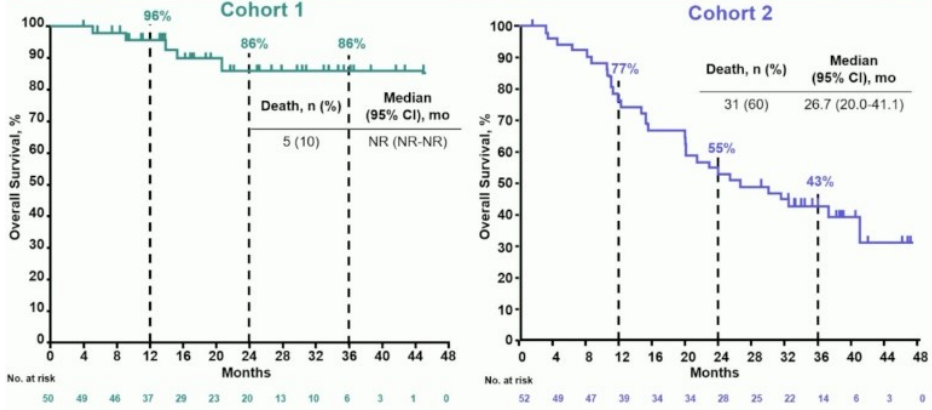
	Overall N = 52	Prior anticancer therapy		Line of prior anticancer therapy	
		Immunotherapy only[a] n = 28	Immunotherapy/ anti-VEGF therapy[b] n = 24	1 line of prior therapy n = 29	2 lines of prior therapy n = 23
ORR (CR + PR)	**16 (31)**	9 (32)	7 (29)	9 (31)	7 (30)
DCR (CR + PR + SD)	48 (92)	26 (93)	22 (92)	27 (93)	21 (91)
Best response					
CR	2 (4)	1 (4)	1 (4)	1 (3)	1 (4)
PR	14 (27)	8 (29)	6 (25)	8 (28)	6 (26)
SD	32 (62)	17 (61)	15 (63)	18 (62)	14 (61)
PD	3 (6)	1 (4)	2 (8)	2 (7)	1 (4)
Not available[c]	1 (2)	1 (4)	0 (0)	0 (0)	1 (4)

Choueiri T, et al. ESMO 2023

Progression-Free Survival by Investigator



Overall Survival



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)

Choueiri T, et al. ESMO 2023

Hospital Clínico San Carlos
SaludMadrid Instituto de Oncología
Comunidad de Madrid

Abstract selection ESMO 2023 RCC

1st line

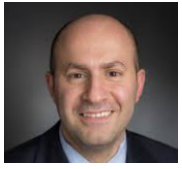
Phase II study of avelumab (Ave) plus intermittent axitinib (Axi) in previously untreated patients (pts) with metastatic renal cell carcinoma (mRCC): The TIDE-A study. Presented by R. Iacovelli

Tumor response by baseline metastases in patients (pts) with renal cell carcinoma (RCC) treated with lenvatinib (L) plus pembrolizumab (P) vs sunitinib (S): Post hoc analysis of the CLEAR trial Presented by Viktor Grünwald

MEDI5752 (volrustomig), a novel PD-1/CTLA-4 bispecific antibody, in the first line (1L) treatment of 65 patients (pts) with advanced clear cell renal cell carcinoma (aRCC). Presented by M.Voss.

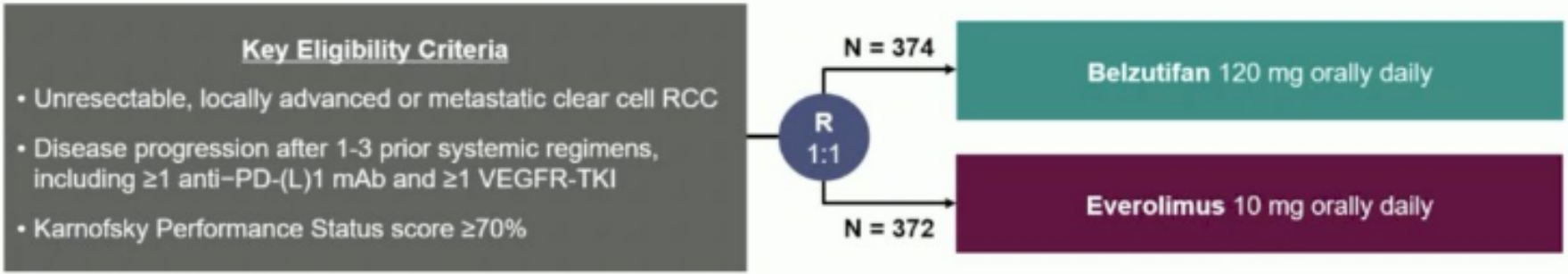
More lines

Phase 2 LITESPARK-003 Study of Belzutifan in Combination With Cabozantinib for Advanced Clear Cell Renal Cell Carcinoma (ccRCC)
Presented by T.Choueiri.



Belzutifan versus everolimus in participants (pts) with previously treated advanced clear cell renal cell carcinoma (ccRCC): randomized open-label phase 3 LITESPARK-005 study. Presented by L.Albiges.

LITESPARK-005



Stratification Factors
- IMDC prognostic score[a]: 0 vs 1-2 vs 3-6
- Prior VEGF/VEGFR-targeted therapies: 1 vs 2-3

Dual Primary Endpoints:
- PFS per RECIST 1.1 by BICR
- OS

Key Secondary Endpoint:
- ORR per RECIST 1.1 by BICR

Other Secondary Endpoints Include:
- DOR per RECIST 1.1 by BICR
- Safety
- Time to deterioration in FKSI-DRS and EORTC QLQ-C30 GHS/QoL

Planned analysis	Planned timing	Planned analysis	Data cutoff date
Interim analysis 1 (IA1)	• ~563 PFS events[b], AND • ~7 months after last participant randomized	Interim PFS Interim OS Final ORR	Nov 1, 2022
Interim analysis 2 (IA2)	• ~410 OS events, AND • ~17 months after last participant randomized	Interim OS Final PFS	Jun 13, 2023
Final	• ~483 OS events, AND • ~27 months after last participant randomized	Final OS	

Albbiges L, et al. ESMO 2023

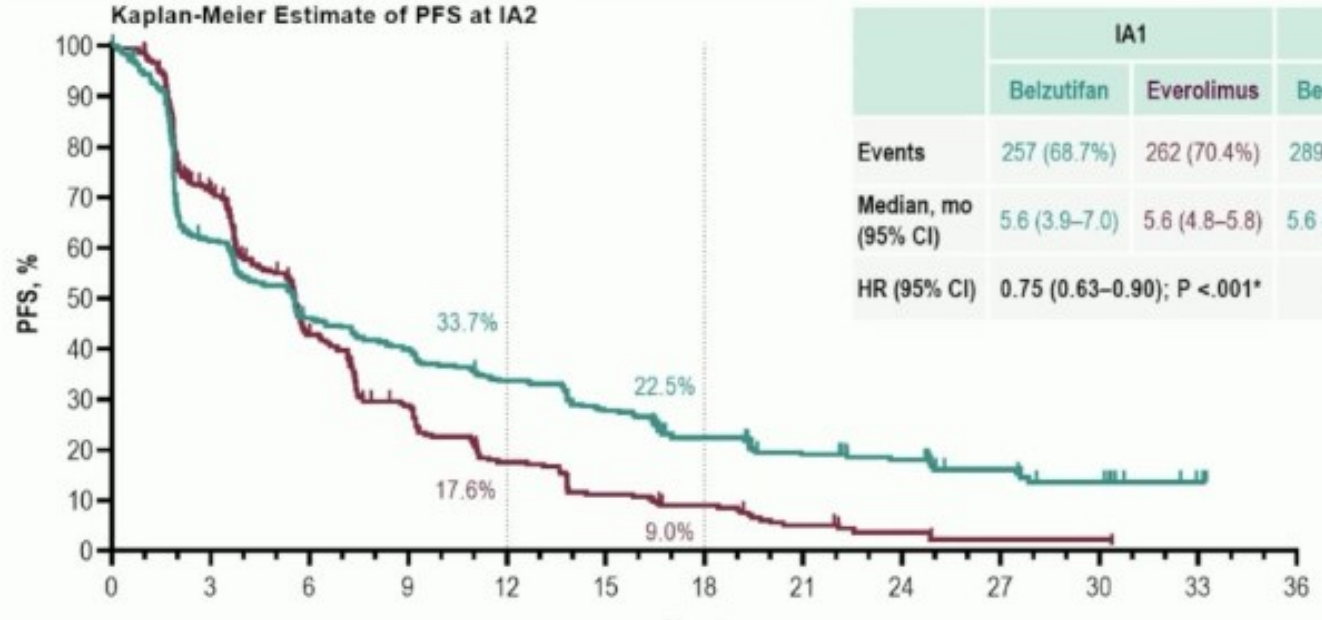
LITESPARK-005

	Belzutifan (N = 374)	Everolimus (N = 372)
Age, median (range), yrs	62 (22–90)	63 (33–87)
Male	79.4%	76.3%
KPS score[a]		
90/100	63.6%	64.5%
70/80	36.1%	35.2%
IMDC risk categories		
Favorable	21.1%	22.3%
Intermediate	66.6%	65.6%
Poor	12.3%	12.1%
Sarcomatoid features		
Yes	11.2%	8.3%
No/Unknown/Missing	88.8%	91.7%
Prior nephrectomy	69.8%	69.6%
# Prior VEGF/VEGFR-TKIs		
1	50.0%	51.1%
2-3	50.0%	48.9%
# Prior lines of therapy[b]		
1	12.3%	14.0%
2	42.0%	44.6%
3	45.2%	40.3%

Albbiges L, et al. ESMO 2023

LITESPARK-005

Primary Endpoint: PFS per RECIST 1.1 by BICR

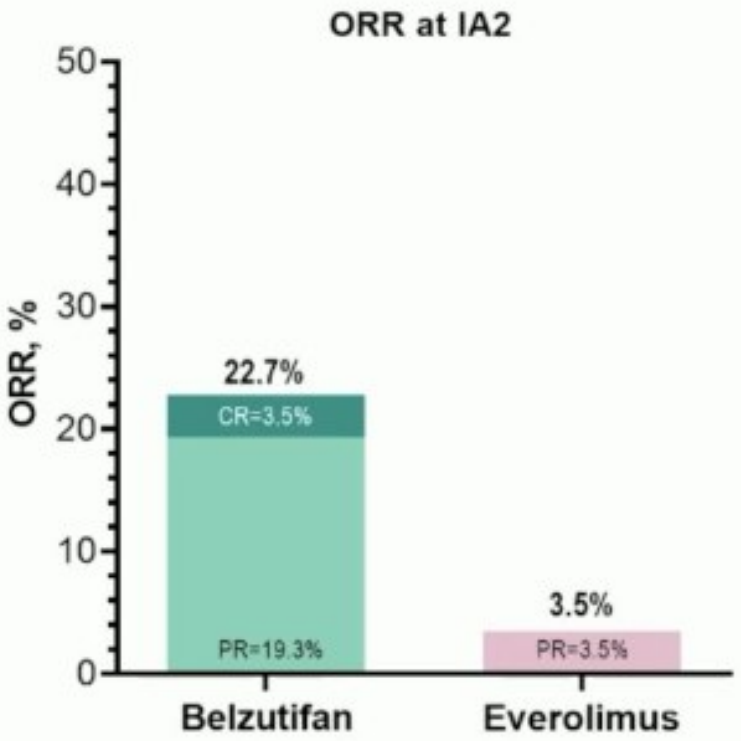


	IA1		IA2	
	Belzutifan	Everolimus	Belzutifan	Everolimus
Events	257 (68.7%)	262 (70.4%)	289 (77.3%)	276 (74.2%)
Median, mo (95% CI)	5.6 (3.9–7.0)	5.6 (4.8–5.8)	5.6 (3.8–6.5)	5.6 (4.8–5.8)
HR (95% CI)	0.75 (0.63–0.90); P <.001*		0.74 (0.63–0.88)	

Albbiges L, et al. ESMO 2023

LITESPARK-005

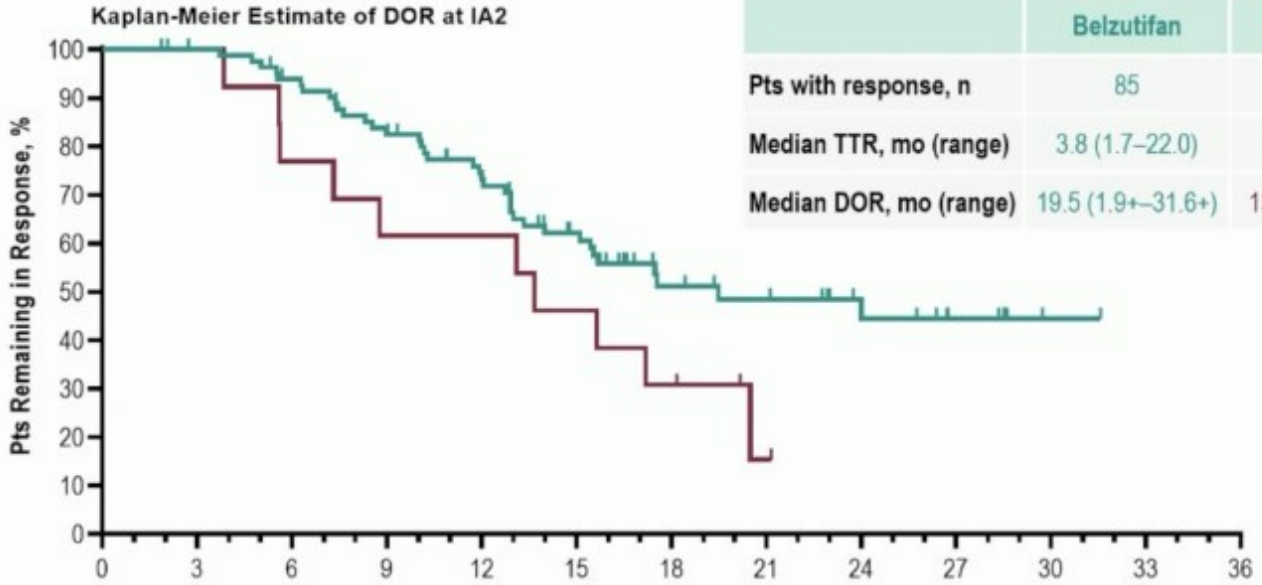
	Belzutifan (N = 374)	Everolimus (N = 372)
	IA1	
ORR, % (95% CI)	**21.9% (17.8–26.5)**	**3.5% (1.9–5.9)**
Estimated difference in % (95% CI)	**18.4 (14.0–23.2); P <.00001***	
CR	2.7%	0
PR	19.3%	3.5%
SD	39.3%	65.9%
PD	33.7%	21.5%
Non-evaluable[a]	1.3%	2.2%
No assessment[b]	3.7%	7.0%
	IA2	
ORR, % (95% CI)	**22.7% (18.6–27.3)**	**3.5% (1.9–5.9)**
Estimated difference in % (95% CI)	**19.2 (14.8–24.0)**	



Albbiges L, et al. ESMO 2023

LITESPARK-005

DOR per RECIST 1.1 by BICR

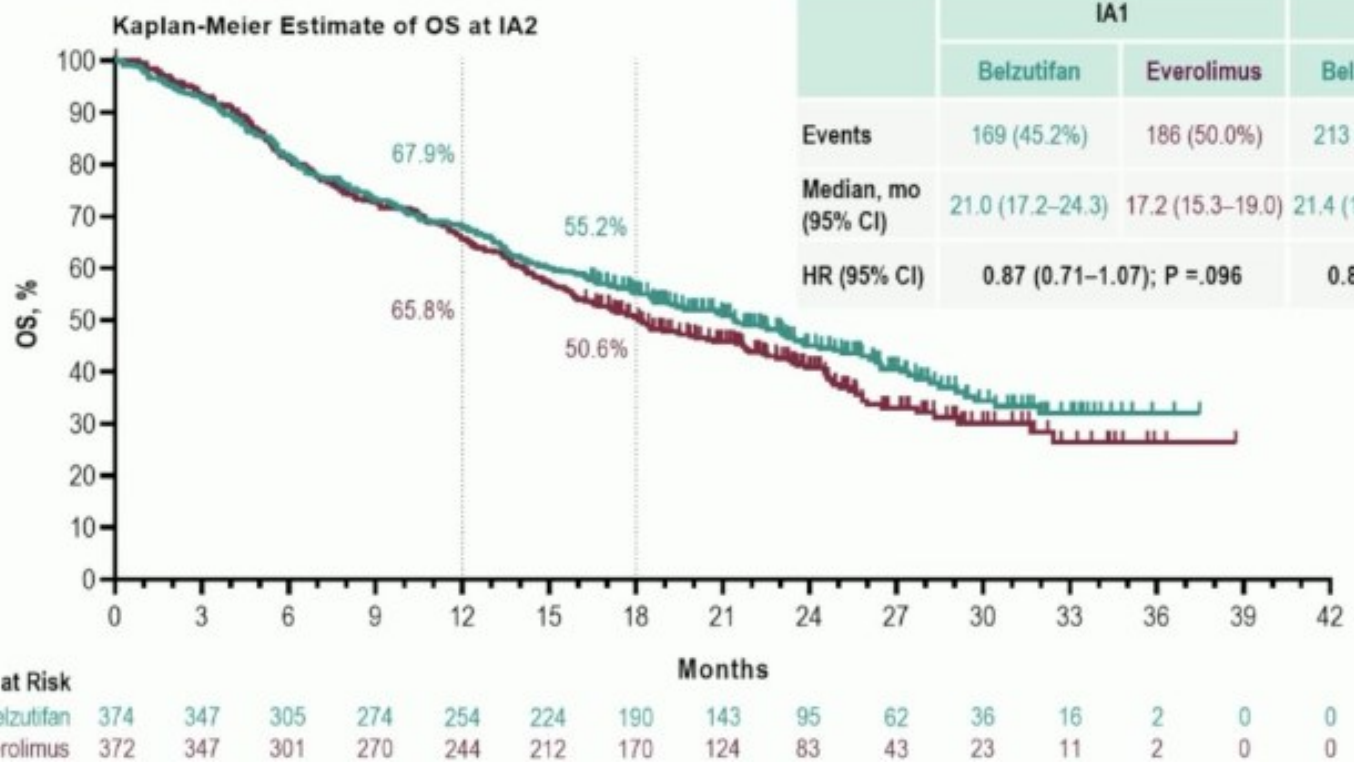


	Belzutifan	Everolimus
Pts with response, n	85	13
Median TTR, mo (range)	3.8 (1.7–22.0)	3.7 (1.8–5.4)
Median DOR, mo (range)	19.5 (1.9+–31.6+)	13.7 (3.8–21.2+)

No. at Risk													
Belzutifan	85	82	75	65	54	40	21	18	12	6	1	0	0
Everolimus	13	13	10	8	8	6	4	1	0	0	0	0	0

Albbiges L, et al. ESMO 2023

Primary Endpoint: OS

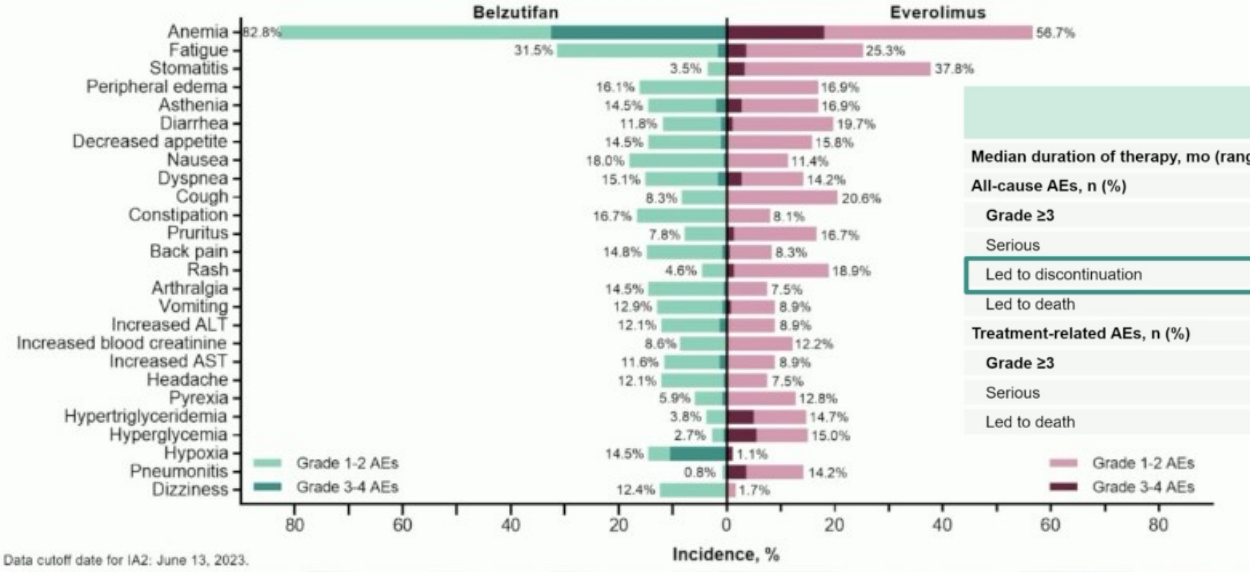


	IA1		IA2	
	Belzutifan	Everolimus	Belzutifan	Everolimus
Events	169 (45.2%)	186 (50.0%)	213 (57.0%)	228 (61.3%)
Median, mo (95% CI)	21.0 (17.2–24.3)	17.2 (15.3–19.0)	21.4 (18.2–24.3)	18.1 (15.8–21.8)
HR (95% CI)	0.87 (0.71–1.07); P =.096		0.88 (0.73–1.07); *P* =.099	

Albbiges L, et al. ESMO 2023

LITESPARK-005

All-Cause AEs in ≥10% of Patients in Either Arm



Data cutoff date for IA2: June 13, 2023.

	Belzutifan (N = 372)	Everolimus (N = 360)
Median duration of therapy, mo (range)	7.6 (0.1–35.8)	3.9 (0.0–33.2)
All-cause AEs, n (%)	369 (99.2%)	357 (99.2%)
Grade ≥3	230 (61.8%)	225 (62.5%)
Serious	157 (42.2%)	137 (38.1%)
Led to discontinuation	22 (5.9%)	53 (14.7%)
Led to death	13 (3.5%)	19 (5.3%)
Treatment-related AEs, n (%)	331 (89.0%)	322 (89.4%)
Grade ≥3	144 (38.7%)	142 (39.4%)
Serious	49 (13.2%)	47 (13.1%)
Led to death	1 (0.3%)[a]	2 (0.6%)[b]

Albbiges L, et al. ESMO 2023

LITESPARK-005

PROs	CONs
RESPONSE RATE: 22,7% (CR 3.5%) vs 3.5%	PD: 33.7 vs 21%
DURATION of RESPONSE: 19.5 vs 13.5 m	mPFS: 5.6 vs 5.6 m
LONG TERM SURVIVALS 18 m: 22 vs 8%	PENDING OS
TOXICITY: Aes G3-4: 61.8 vs 62.5%	SAEs: 42 vs 38%
DISCONTINUATION RATE: 5.9 vs 14.7%	COMPARATOR: EVEROLIMUS

Conclusions

- Belzutifan is the new actor in RCC paradigm.
- Combination between Belzutifan and cabozantinib is a promising strategy in all RCC settings
- De-escalation strategies in IO-TKI combinations in still on research
- Novel strategies are being under research in kidney cancer: new immunotherapies, novel TKIs, etc.

GONORTE
Grupo Oncológico

REUNIÓN POST CONGRESO DE LA
SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2023

Javier Puente, MD, PhD
GU Cancer Unit
Medical Oncology Department
Hospital Clínico Universitario San Carlos, Madrid, Spain
Associate Professor of Medicine
Complutense University of Madrid, Spain
@docjavip