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2022 ASCO ANNUAL MEETING
ADVANCING EQUITABLE CANCER CARE THROUGH INNOVATION

ASC0' 22 ASCO Sessions:

RECOMMENDED ABSTRACTS in RENAL CANCERS

These recommended abstracts from ASCO22 Annual meeting have been selected by Robert A. Figlin, MD, *Editor-in- Chief* of the Kidney Cancer Journal. The chosen abstracts provided here highlight some of the most important trends in ongoing trials and reflect the foremost research and strategies from latest clinical trials that impact the current standard of care in renal cancer.

Abstract Titles

ABSTRACT LBA4500:

EVEREST: Everolimus for renal cancer ensuing surgical therapy—A phase III study (SWOG S0931, NCT01120249).

- Access Full Abstract

ABSTRACT 4501:

Association between depth of response (DepOR) and clinical outcomes: Exploratory analysis in patients with previously untreated advanced renal cell carcinoma (aRCC) in CheckMate 9ER.

ABSTRACT 4501 :

Characterizing IMDC prognostic groups in contemporary first-line combination therapies for metastatic renal cell carcinoma (mRCC).

- Access Full Abstract

ABSTRACT 4502 :

The relationship between health-related quality of life (HRQoL) and clinical outcomes in patients with advanced renal cell carcinoma (aRCC) in CheckMate (CM) 214.

- Access Full Abstract

ABSTRACT LBA4503 :

CALYPSO: A three-arm randomized phase II study of durvalumab alone or with savolitinib or tremelimumab in previously treated advanced clear cell renal cancer.

- Access Full Abstract

ABSTRACT 4509:

Phase 1 LITESPARK-001 (MK-6482-001) study of belzutifan in advanced solid tumors: Update of the clear cell renal cell carcinoma (ccRCC) cohort with more than 3 years of total follow-up.

- Access Full Abstract

ABSTRACT 4511 :

A phase 1b/2 study of batiraxcept (AVB-S6-500) in combination with cabozantinib in patients with advanced or metastatic clear cell renal cell (ccRCC) carcinoma who have received front-line treatment (NCT04300140).

- **Access Full Abstract**

ABSTRACT 4512 :

Adjuvant pembrolizumab for postnephrectomy renal cell carcinoma (RCC): Expanded efficacy analyses from KEYNOTE-564.

- **Access Full Abstract**

ABSTRACT 4513 :

Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Analysis of progression after first subsequent therapy in KEYNOTE-426.

- **Access Full Abstract**

ABSTRACT 4514 :

Impact of subsequent therapies in patients (pts) with advanced renal cell carcinoma (aRCC) receiving lenvatinib plus pembrolizumab (LEN + PEMBRO) or sunitinib (SUN) in the CLEAR study.

- **Access Full Abstract**

FURTHER DETAILS - All in One Page

ABSTRACT LBA4500:

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/207883**

EVEREST: Everolimus for renal cancer ensuing surgical therapy—A phase III study (SWOG S0931, NCT01120249)..

- Citation: J Clin Oncol 40, 2022 (suppl 17; abstr LBA4500)

Meeting:
2022 ASCO Annual Meeting

Session Type:
Oral Abstract Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
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Clinical Trial Registration Number:
NCT01120249

Citation:
J Clin Oncol 40, 2022 (suppl 17; abstr LBA4500)

DOI:
10.1200/JCO.2022.40.17_suppl.LBA4500

Abstract #:
LBA4500

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Organizations

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Abstract Disclosures

Research Funding

U.S. National Institutes of Health
Other Foundation, Pharmaceutical/Biotech Company

Background:

Patients (pts) who undergo resection of renal cell carcinoma (RCC) with curative intent remain at risk for disease relapse. We conducted a phase III, double-blind, placebo (PB)-controlled, intergroup study to determine the effect of adjuvant treatment with the mTOR inhibitor everolimus (EVE) on recurrence-free survival (RFS).

Methods:

Pts with treatment-naïve, non-metastatic, fully-resected RCC at intermediate high- (pT1 G3-4 N0 to pT3a G1-2 N0) or very high-risk (pT3a G3-4 to pT4 G-any or N+) for recurrence were randomized 1:1 to EVE 10 mg PO daily x 54 weeks or PB within 12 weeks of radical or partial nephrectomy. Randomization was stratified by risk group, histology (clear vs. non-clear cell), and performance status (0 vs. 1). RFS was the

primary end point; secondary endpoints included overall survival (OS) and adverse events (AEs). The study was designed to detect an 18% reduction in the risk of RFS with EVE compared to PB, corresponding to an improvement of median RFS from 6.75 (based on E2805 ASSURE) to 8.23 years. Final analysis, using a stratified logrank test, was to occur after 804 total events or by 3/2022, whichever occurred first.

Results:

Between 4/2011 and 9/2016, 1545 pts were randomized to EVE (n = 775) or PB (n = 770). Overall pt characteristics included: intermediate high-/very high-risk 45%/55%; clear cell/non-clear cell 83%/17%. The DSMC recommended study continuation after each of 4 pre-specified interim analyses. 556 DFS events among 1499 eligible pts occurred by the time of final study analysis on 2/23/2022. The median follow-up was 76 months. RFS was improved with EVE vs. PB (HR 0.85, 95% CI, 0.72 – 1.00; $P_{1\text{-}sided}$= 0.0246), narrowly missing the pre-specified, one-sided significance level of 0.022 which accounted for interim analyses. Median RFS was not reached; the 6-year RFS estimate was 64% for EVE and 61% for PB. RFS improvement with EVE vs. PB was observed in the very high-risk group (HR 0.79, 95% 0.65-0.97; $P_{1\text{-}sided}$= 0.011) but not in the intermediate high-risk group (HR 0.99, 95% CI 0.73-1.35, $P_{1\text{-}sided}$= 0.48) (P for interaction = 0.22). With 290 deaths, OS was similar between arms (HR 0.90, 95% CI, 0.71 – 1.13; $P_{1\text{-}sided}$= 0.178). Fewer pts completed all 54 weeks of study treatment in the EVE group (45% v 69%). In the EVE group, 37% withdrew due to AEs (vs 5% in PB). Grade 3-4 AEs occurred in 46% of pts treated with EVE and 11% with PB. The most common grade 3-4 AEs were mucositis (14% v 0%), hypertriglyceridemia (11% vs. 2%), and hyperglycemia (5% vs. 0%).

Conclusions:

Adjuvant EVE improved RFS in RCC pts after nephrectomy, but the nominal significance level was narrowly missed. The RFS improvement was seen despite a high rate of early treatment discontinuation. A 21% improvement in RFS with EVE was observed in pts with very high-risk disease, a group for whom adjuvant therapy may be most relevant. Clinical trial information: NCT01120249.

ABSTRACT 4501:

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/207895**

Association between depth of response (DepOR) and clinical outcomes: Exploratory analysis in patients with previously untreated advanced renal cell carcinoma (aRCC) in CheckMate 9ER.

- Citation: J Clin Oncol 40, 2022 (suppl 16; abstr 4501)

Meeting:
2022 ASCO Annual Meeting

Session Type:
Oral Abstract Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
Genitourinary Cancer—Kidney and Bladder

Clinical Trial Registration Number:
NCT03141177

Citation:
J Clin Oncol 40, 2022 (suppl 16; abstr 4501)

DOI:
10.1200/JCO.2022.40.16_suppl.4501

Abstract #:
4501

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Organizations

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Abstract Disclosures

Research Funding

Pharmaceutical/Biotech Company

Background:

Among patients (pts) with untreated aRCC in the CheckMate 9ER trial, superior progression-free survival (PFS; hazard ratio [HR], 0.56) and overall survival (OS; HR, 0.70) were maintained, and objective response and complete response (CR) rates were doubled for nivolumab plus cabozantinib (N+C) vs sunitinib (SUN) with extended 25.4 mo minimum (32.9 mo median) follow-up. This exploratory analysis evaluated the relationship between DepOR and clinical outcomes in CheckMate 9ER.

Methods:

Eligible pts received N (240 mg) every 2 weeks plus C (40 mg) once daily or SUN (50 mg once daily; 4 weeks of each 6-week cycle). In this analysis, DepOR subgroups were based on best overall response (blinded independent central review [BICR] per RECIST v1.1) and best tumor reduction threshold, as follows: CR; partial response subdivided by a tumor reduction of ≥80%–<100% (PR1); ≥60%–<80% (PR2); or ≥30%–<60% (PR3); stable disease (SD); and progressive disease (PD). PFS (per BICR) and OS by DepOR subgroups were analyzed after a 6-mo post-randomization landmark. Treatment-related adverse events (TRAEs) were assessed in DepOR subgroups.

Results:

Of 323 and 328 pts randomized to N+C or SUN, 236 and 157 pts were progression-free and alive and 293 and 253 pts were alive at the 6-mo landmark and were categorized by DepOR subgroup. Overall, greater proportions of pts receiving N+C had deeper responses vs SUN (CR, PR1, PR2; Table). Deeper responses with N+C were associated with improved 12-mo PFS rate vs SUN for CR (94.9% vs 82.4%), PR1 (81.3% vs 37.5%), and PR2 (72.1% vs 53.2%). In both arms, increasingly deeper response led to better OS outcome; yet OS rates and medians were comparable between arms for CR, PR1, PR2, and PR3 (Table). No meaningful patterns for overall TRAE rates by DepOR subgroup were identified in either arm.

Conclusions:

In CheckMate 9ER, more pts receiving N+C achieved deeper responses vs SUN. Deeper responses were generally associated with improved PFS and OS. Clinical trial information: NCT03141177.

	N+C						SUN					
	PFS[a] N = 236			OS[a] N = 293			PFS[a] N = 157			OS[a] N = 253		
DepOR	n	12 morate, %[b,c]	Median (95% CI), mo	n	18 morate, %[c]	Median (95% CI), mo	n	12 morate, %[b,c]	Median (95% CI), mo	n	18 morate, %[c]	Median (95% CI), mo
CR	40	94.9	NR (26.0–NE)	40	97.5	NR (NE–NE)	17	82.4	NR (15.9–NE)	17	100	NR (30.2–NE)
PR1	32	81.3	24.3 (17.0–NE)	33	97.0	NR (28.9–NE)	8	37.5	6.5 (0.9–NE)	9	100	NR (19.7–NE)
PR2	37	72.1	24.8 (13.4–NE)	38	83.5	NR (31.7–NE)	18	53.2	12.0 (7.9–NE)	18	88.2	NR (NE–NE)
PR3	62	46.7	10.4 (5.5–14.0)	69	78.3	NR (30.5–NE)	45	57.0	15.9 (6.8–21.6)	49	75.3	NR (25.1–NE)
SD	65	33.5	6.3 (4.0–10.6)	99	59.6	28.7 (17.8–NE)	69	22.6	5.2 (3.7–6.7)	123	68.0	NR (24.6–NE)
PD	0	–	–	14	35.7	10.1 (4.8–25.1)	0	–	–	37	39.1	13.7 (6.4–18.6)

[a]At the 6 mo landmark. [b]12 mo PFS rate is presented due to low patient numbers at later timepoints. [c]12 mo and 18 mo rates are from 6 mo landmark.CI, confidence interval; NE, not evaluable; NR, not reached.

ABSTRACT 4501 :

- **ASCO Link - https://meetinglibrary.asco.org/record/205607/abstract**

Characterizing IMDC prognostic groups in contemporary first-line combination therapies for metastatic renal cell carcinoma (mRCC).

Authors:

Matthew Scott Ernst, Vishal Navani, J Connor Wells, Frede Donskov, Naveen S. Basappa, Chris Labaki, Sumanta K. Pal, Luis A Meza, Lori Wood, D. Scott Ernst, Bernadett Szabados, Rana R. McKay, Francis Parnis, Cristina Suárez, Takeshi Yuasa, Anil Kapoor, Ajjai Shivaram Alva, Georg A. Bjarnason, Toni K. Choueiri, Daniel Yick Chin Heng

Abstract Disclosures

Research Funding:

Background:

The combination of immuno-oncology agents (IO) ipilimumab and nivolumab (IPI-NIVO) and combinations of IO with vascular endothelial growth factor targeted therapies (IOVE) have demonstrated efficacy in clinical trials for the first-line treatment of mRCC. This study seeks to establish real-world clinical benchmarks based on the International mRCC Database Consortium (IMDC) criteria using vascular endothelial growth factor targeted therapy (VEGF-TT) treated patients for context.

Methods:

The IMDC database (IMDConline.com) was used to identify patients with mRCC who received first-line IPI-NIVO, IOVE (axitinib/pembrolizumab, lenvatinib/pembrolizumab, cabozantinib/nivolumab, or axitinib/avelumab) and VEGF-TT (sunitinib or pazopanib) from 2002-2021. The primary endpoint was overall survival (OS) and was calculated from time of initiation of first-line therapy to death or last follow up. Log-rank tests were conducted to compare favorable, intermediate, and poor risk OS outcomes within treatment groups. Overall response rates (ORR) and complete response (CR) rates were calculated based on physician

First Author:	Matthew Scott Ernst, MD
Meeting:	2022 ASCO Genitourinary Cancers Symposium
Session Type:	Poster Session
Session Title:	Poster Session C: Renal Cell Cancer; Adrenal, Penile, Urethral, and Testicular Cancers
Track:	Renal Cell Cancer
Subtrack:	Quality of Care/Quality Improvement and Real-World Evidence
Abstract #:	308
Citation:	J Clin Oncol 40, 2022 (suppl 6; abstr 308)
DOI:	10.1200/JCO.20

assessment of best clinical response.

22.40.6_suppl.3
08

Results:
In total, 692 patients received IPI-NIVO, 244 received IOVE, and 7152 received VEGF-TT. Baseline characteristics for IPI-NIVO, IOVE, and VEGF-TT, respectively, were as follows: median age (interquartile range) 63 (56-69), 64 (57-70), and 63 (56-70); male 72%, 74%, and 72% (p=0.74); non-clear cell histology 15%, 10%, and 13% (p=0.15); sarcomatoid features 24%, 15%, and 13% (p<0.0001); brain metastasis 8%, 4%, and 8% (p=0.04); liver metastasis 18%, 14%, and 18% (p=0.17); underwent nephrectomy 61%, 79% and 80% (p<0.0001). OS and ORR are reported in the table. P-values (log rank) for OS between risk groups were significant for IPI-NIVO (p<0.0001), IOVE (p=0.0005), and VEGF-TT (p<0.0001).

Conclusions:
These findings provide real-world survival and response benchmarks for contemporary first-line mRCC treatments and could be helpful for patient counselling. In addition, these findings mirror the efficacy of combination therapies established in clinical trials against VEGF-TT monotherapy. IMDC criteria continue to risk stratify patients in these novel combination therapies.

	IPI-NIVO n=692			IOVE n=244			VEGF-TT n=7152	
IMDC Risk	**Favorable***	**Intermediate**	**Poor**	**Favorable**	**Intermediate**	**Poor**	**Favorable**	**Intermediate**
n	66	399	227	81	117	46	1290	3977
(%)	(10)	(58)	(33)	(33)	(48)	(19)	(18)	(56)
12-month OS	94%	84%	60%	98%	91%	82%	92%	75%
18-month OS	90%	77%	49%	94%	85%	75%	84%	64%
CR (%)	4/55	16/342	4/186	5/72	4/100	0/39	39/1160	121/3446
	(7)	(5)	(2)	(7)	(4)	(0)	(3)	(4)
ORR (%)	24/55	139/342	61/186	44/72	59/100	17/39	456/1160	1156/3446
	(44)	(41)	(33)	(61)	(59)	(44)	(39)	(34)

*IPI-NIVO is not indicated in favorable risk patients and must be interpreted with caution.

ABSTRACT 4502 :

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/207896**

The relationship between health-related quality of life (HRQoL) and clinical outcomes in patients with advanced renal cell carcinoma (aRCC) in CheckMate (CM) 214.

Meeting:
2022 ASCO Annual Meeting

Session Type:
Oral Abstract Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
Genitourinary Cancer—Kidney and Bladder

Clinical Trial Registration Number:
NCT02231749

Citation:
J Clin Oncol 40, 2022 (suppl 16; abstr 4502)

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Abstract #:

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Organizations
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Abstract Disclosures

Research Funding
Pharmaceutical/Biotech Company

Background:
In CM 214, when compared to sunitinib (S), nivolumab plus ipilimumab (N+I) was associated with both clinical benefit and improved HRQoL as first-line treatment for intermediate/poor (I/P)-risk patients (pts). This analysis investigates the direct

association between HRQoL and clinical outcomes in aRCC pts.

Methods:

I/P-risk population included 425 and 422 pts in the N+I and S arms, respectively. HRQoL was assessed using the FKSI-19 (Total Score and Disease Related Symptoms [DRS]). Three separate analyses (A, B, and C) were conducted. A: Changes in individual item scores from baseline to last assessment prior to progression were descriptively assessed. B: For each FKSI-19 score, multivariable Cox regression, adjusted for treatment and stratification factors, was used to evaluate the prognostic significance of baseline and time-dependent HRQoL scores in separate models. Hazard ratios (HR) were calculated based on the risk of death per improvement in HRQoL scores, defined using the clinically meaningful change threshold (5 points for FKSI-19 Total and 3 points for DRS). Pts with overall survival (OS) events were censored if their survival event was not within 12 weeks of the last available HRQoL assessment. C: The association between HRQoL change status (ie, improvement or maintenance vs. worsening from baseline in the FKSI-19 Total Score), irrespective of treatment arm, and OS was further assessed using a landmark analysis at the month 6 (mo-6) landmark. Additional landmark time points were explored in sensitivity analysis.

Results:

Items related to fatigue and perceived bother of the side-effects of treatment had the largest percentage of pts worsening prior to progression. In both baseline and time-dependent HRQoL analyses, OS was independently associated with both HRQoL measures. Higher (better) baseline scores were associated with significantly reduced risk of death (HR [95% CI] for FKSI-19 Total Score and DRS was 0.83 [0.80-0.87] and 0.80 [0.76-0.84], respectively). Every 5-point increase (improvement) in FKSI-19 Total Score and 3-point increase in DRS was associated with a 31% decreased risk of death (P< 0.01). At mo-6, 301 pts showed improvement or maintenance in HRQoL. Pts with improved/stable HRQoL had a 52% reduction in risk of death compared to pts who had worsened (HR 0.48 [95% CI: 0.39-0.59]).

Conclusions:

Results demonstrate there is an association between HRQoL and clinical outcomes in CM 214. Baseline HRQoL scores are a potential predictor for survival in aRCC, and HRQoL changes are informative for pts' expected survival. HRQoL change status at mo-6 was significantly and positively associated with subsequent survival. Thus, patient-reported outcomes may be useful for both describing pt experience in clinical trials and providing valuable clinical insights during routine practice. Clinical trial information: NCT02231749.

- DOI: 10.1200/JCO.2022.40.16_suppl.4502

ABSTRACT LBA4503 :

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/209130**

CALYPSO: A three-arm randomized phase II study of durvalumab alone or with savolitinib or tremelimumab in previously treated advanced clear cell renal cancer.

Meeting:
2022 ASCO Annual Meeting

Session Type:
Oral Abstract Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
Genitourinary Cancer—Kidney and Bladder

Clinical Trial Registration Number:
NCT02819596

Citation:
J Clin Oncol 40, 2022 (suppl 17; abstr LBA4503)

DOI:
10.1200/JCO.2022.40.17_suppl.LBA4503

Abstract #:
LBA4503

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Organizations

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Abstract Disclosures

Research Funding

Pharmaceutical/Biotech Company

Background:

New drug combinations are required in advanced clear cell renal cancer (RCC). These potentially include MET inhibition with savolitinib (S) or CTLA-4 inhibition with tremelimumab (T). In this study these agents were given alone or in combination with the PD-L1 inhibitor durvalumab (D).

Methods:

A multinational open-label randomised phase II study assigning patients to one of D, S, DT or DS was performed. Patients with RCC, who had previously received VEGF targeted therapy but not immune checkpoint inhibitors or MET inhibitors were included. Confirmed response rate (cRR) was the primary endpoint. A response rate of at least 50% was required for further exploration. The S arm was closed early due to a lack of efficacy. DNA alterations were measured using Foundation One and PD-L1 analysis was performed with SP263. This abstract details the pre-planned 12-month interim analyses after the cohort completed randomisation.

Results:

Between 2017 and 2021, 139 patients were randomised (D N=39, S N=22, DT N=39, DS N=39). The median age was 62 years (range: 28 – 85). cRRs for the 4 arms were D=10%, S=5%, DT=28%, DS=13%, which did not meet the primary objective. cRRs in the MET-driven patients (N=17) were D=0% (0/7), S=0% (0/2), DT=50% (1/2), DS=17% (1/6). cRRs in PD-L1+ves for DT and D were 14% (1/7) and 33% (2/6) respectively. 12-month progression-free survival (PFS) rates were D=26% (80% confidence interval [CI]: 17% - 36%), S=21% (80% CI: 10% - 35%), DT=33% (80% CI: 24% - 43%), DS=17% (80% CI: 10% - 26%). Median overall survival for D=26.1 (80% CI: 16.2 – 32.0) months, S=23.1 (80% CI: 20.6 – 29.7) months, DT=21.9 (80% CI: 16.3 – 31.5) months, DS=16.1 (80% CI: 10.3 – 18.8) months. There was 1 treatment related death in the DT arm. Of the 136 patients who received treatment, grade 3 or more treatment related adverse events occurred in D=10% (4/39), S=26% (5/19), DT=23% (9/39), DS=23% (9/39).

ABSTRACT 4509:

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/207892**

Phase 1 LITESPARK-001 (MK-6482-001) study of belzutifan in advanced solid tumors: Update of the clear cell renal cell carcinoma (ccRCC) cohort with more than 3 years of total follow-up. Add to Collection

Authors:

Stuthi Perimbeti, Changchuan Jiang, Lei Deng, Arya Roy, Keerthy Gopalakrishnan, Gurkamal S. Chatta, Saby George, Dharmesh Gopalakrishnan

Abstract Disclosures

Research Funding:

Background:

The advent of ICIs has dramatically changed the treatment paradigm in mRCC. Although CN was demonstrated to improve survival in combination with cytokine-based therapies, its role is not well-defined in the ICI era. We aimed to compare survival outcomes of patients treated with ICIs, based on their CN status.

Methods:

The National Cancer Database was queried to identify all patients older than 18 years with mRCC who received ICIs from 2015 to 2018. Chi-Square and Mann-Whitney U tests were used to compare frequency distributions. Cox proportional hazards regression was employed for multivariate analysis of factors associated with overall survival (OS).

Results:

A total of 4,369 patients were identified- 36.4% (n=1589) had undergone CN. Among patients who got CN, 85.3% were treated with upfront surgery while 13.8% received prior systemic therapy (P = 0.001). The study population was predominantly Caucasian (89.2%) and male (70.6%). Patients who underwent CN were younger (median age 61 vs. 65 years, P = <0.001). Large primary tumors and clinically node-negative status were associated with higher odds of CN (T4 disease - odds ratio (OR) for 1.49, 95% CI 1.13-3.44, P = 0.03; cN0 disease - OR 1.56, 95% CI 1.23-4.56, P = 0.04). OS after 1 year was significantly higher in patients who underwent CN (66.8% vs 33.2%. P <0.001). On multivariate analysis, CN was independently predictive of improved OS with a hazard ratio (HR) of 0.53 and 95% CI 0.41-0.68, P <0.001.

Conclusions:

In this large retrospective analysis, CN was associated with improved OS among patients with mRCC receiving ICI-based therapies. Our findings suggest that despite recent advances in systemic therapies for mRCC, CN retains an important role in carefully selected patients.

Variable	Univariate HR for mortality (95% CI)	p-value	Multivariate HR for mortality (95% CI)	p-value
ICI + CN vs.	0.42 (0.36-	0.001	0.53 (0.41-	<0.001

First Author:	Stuthi Perimbeti, MD, MPH
Meeting:	2022 ASCO Genitourinary Cancers Symposium
Session Type:	Poster Session
Session Title:	Poster Session C: Renal Cell Cancer; Adrenal, Penile, Urethral, and Testicular Cancers
Track:	Renal Cell Cancer
Subtrack:	Therapeutics
Abstract #:	359
Citation:	J Clin Oncol 40, 2022 (suppl 6; abstr 359)
DOI:	10.1200/JCO.2022.40.6_suppl.359

ICI alone	0.47)		0.68)	
Age group (51-65 vs. 18-35y)	0.47 (0.31-0.72)	0.001	0.61 (0.40-0.90)	<0.001
AA vs. White	1.45 (1.19-1.76)	0.001	1.24 (1.01-1.52)	0.03
=2 vs. 0 comorbidities	1.30 (1.15-1.52)	0.001	1.24 (1.06-1.46)	0.0001
Median annual income <$30,000 vs. >$46,000	1.44 (1.20-1.72)	0.001	1.30 (1.08-1.57)	0.004

- DOI: 10.1200/JCO.2022.40.16_suppl.4509

ABSTRACT 4511 :

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/207886**

A phase 1b/2 study of batiraxcept (AVB-S6-500) in combination with cabozantinib in patients with advanced or metastatic clear cell renal cell (ccRCC) carcinoma who have received front-line treatment (NCT04300140).

Meeting:
2022 ASCO Annual Meeting

Session Type:
Poster Discussion Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
Genitourinary Cancer—Kidney and Bladder

Clinical Trial Registration Number:
NCT04300140

Citation:
J Clin Oncol 40, 2022 (suppl 16; abstr 4511)

DOI:
10.1200/JCO.2022.40.16_suppl.4511

Abstract #:
4511

Poster #:
3

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Abstract Disclosures

Research Funding

Pharmaceutical/Biotech Company

Background:

AXL is up-regulated by hypoxia-inducible factor-1 signaling in both VHL-deficient and hypoxic tumor cells and plays a critical role in the metastatic phenotype of ccRCC. Batiraxcept is a recombinant fusion protein containing an extracellular region of human AXL combined with the human immunoglobulin G1 heavy chain (Fc), demonstrating highly potent, specific AXL inhibition.

Methods:

Batiraxcept at doses of 15 and 20 mg/kg, plus cabozantinib 60 mg daily, was evaluated using a 3+3 dose escalation study design. The primary objective was safety; secondary and exploratory objectives included identification of the recommended phase 2 dose (RP2D), overall response rate (ORR), and duration of response (DOR). Correlation of serum soluble AXL (sAXL)/GAS6 with ORR was evaluated. Key eligibility criteria include previously treated (2L+) ccRCC patients; prior treatment with cabozantanib was not allowed. sAXL/GAS6 was evaluated at baseline.

Results:

Data as of 4-February-2022, Phase 1b enrolled 26 patients, 16 patients treated with 15 mg/kg and 10 patients with 20 mg/kg dose of batiraxcept. Baseline characteristics: median age 60 (40-81); male 22 (85%); median prior line of therapy 1 (1-5); IMDC risk group of favorable 6 (23%); prior VEGF inhibitor 15 (58%); 100% with prior immunotherapy. At median follow up of 4.9 months, 92% (n=24) patients remained on the study. No dose limiting toxicities were observed at either 15 mg/kg or 20 mg/kg dose. Batiraxcept and cabozantinib related adverse events (AEs) occurred in 17 subjects (65%). Most common related AE include decreased appetite 31% (n=8), diarrhea and fatigue 23% (n=6). Grade 3 related AEs occurred in 4 patients (15%) including diarrhea, thromboembolism, hypertension, small bowel obstruction, and thrombocytopenia (n=1, 4% each) being most common. No grade 4 or 5 related AEs were observed. The ORR was 46% (n=12, partial response [PR]; Table). No patients had primary progressive disease. Among the patients who had baseline sAXL/GAS6 ratio of ≥ 2.3, the ORR was 67% (12/18). Regardless of baseline sAXL/GAS6 ratio, 3-month

DOR was 100%; and 6-month progression free survival was 79%. Batiraxcept PK levels were similar across both doses and GAS6 levels suppressed through the dosing period.

Conclusions:

Batiraxcept plus cabozantinib is well tolerated. The RP2D of batiraxcept was identified as 15 mg/kg. Early efficacy signals were observed including 100% DOR at 3 months. Baseline sAXL/GAS6 may serve as a potential biomarker to enrich the population. Clinical trial information: NCT04300140.

	Entire cohort	Batiraxcept 15 mg/kg cohort	Batiraxcept 20 mg/kg cohort
	N=26 (%)	N=16 (%)	N=10 (%)
ORR (confirmed + unconfirmed)	12 PR (46)	9 PR (56)	3 PR (30)
DOR (3-month)	26 (100)	26 (100)	Not reached
Any grade-related AEs	17 (65)	11 (69)	6 (60)
Grade ≥3 related AEs	4 (15)	2 (13)	2 (20)

- DOI: 10.1200/JCO.2022.40.16_suppl.4511

ABSTRACT 4512 :

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/207894**
- DOI: 10.1200/JCO.2022.40.16_suppl.4513

Adjuvant pembrolizumab for postnephrectomy renal cell carcinoma (RCC): Expanded efficacy analyses from KEYNOTE-564.

Meeting:
2022 ASCO Annual Meeting

Session Type:
Poster Discussion Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
Genitourinary Cancer—Kidney and Bladder

Clinical Trial Registration Number:
NCT03142334

Citation:
J Clin Oncol 40, 2022 (suppl 16; abstr 4512)

DOI:
10.1200/JCO.2022.40.16_suppl.4512

Abstract #:
4512

Poster #:
4

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Abstract Disclosures

Research Funding

Pharmaceutical/Biotech Company

Background:

The randomized, double-blind, phase 3 KEYNOTE-564 study (NCT03142334) met its primary end point of disease-free survival with adjuvant pembrolizumab versus placebo after nephrectomy in patients with localized RCC who are at increased risk for recurrence. Extended follow-up (30-month median follow-up) continued to support the benefit of adjuvant pembrolizumab. We describe additional efficacy analyses of time to first subsequent drug treatment or any-cause death (TFST) and time from randomization to progression on next line of therapy or any-cause death (PFS2).

Methods:

Patients with histologically confirmed clear cell RCC, with intermediate-high or high risk for recurrence (pT2, grade 4 or sarcomatoid, N0, M0; or pT3-4, any grade, N0 M0; or pT any stage, any grade, N+ M0) after nephrectomy, or after nephrectomy and resection of metastatic lesions (M1 NED), were randomly assigned 1:1 to receive pembrolizumab 200 mg IV or placebo Q3W for up to 17 cycles (1 y). Exploratory analyses of TFST and PFS2 were conducted. The Kaplan-Meier method was used to estimate TFST and PFS2. Hazard ratios (HRs) were estimated using a Cox regression

model.

Results:

Of 994 patients, 496 were randomly assigned to receive pembrolizumab and 498 to placebo. Median time from randomization to the data cutoff date (June 14, 2021) was 30.1 months (range, 20.8-47.5). Overall, 67 patients (13.5%) in the pembrolizumab group and 99 patients (19.9%) in the placebo group received ≥1 line of subsequent anticancer drug therapy. Of patients who received ≥1 line of subsequent drug therapy, most in the pembrolizumab group (90.0% [60/67]) and placebo group (85.9% [85/99]) received a VEGF/VEGFR-targeted therapy; 23.9% of patients (16/67) in the pembrolizumab group and 59.6% (59/99) in the placebo group received an anti–PD-1/PD-L1 agent. Seventy-seven TFST events were observed in the pembrolizumab group; 110, in the placebo group. Compared with placebo, adjuvant treatment with pembrolizumab delayed TFST (HR, 0.67; 95% CI, 0.50-0.90; medians not reached). A total of 108 PFS2 events were observed, 40 (8.1%; 12 death events and 28 progression events) in the pembrolizumab group and 68 (13.7%; 14 death events and 54 progression events) in the placebo group. PFS2 was also delayed with pembrolizumab compared with placebo (HR, 0.57; 95% CI, 0.39-0.85; medians not reached).

Conclusions:

Treatment with adjuvant pembrolizumab reduced risk for TFST and PFS2 compared with placebo. Results of this exploratory analyses suggest sustained clinical benefit of adjuvant pembrolizumab and support the use of adjuvant pembrolizumab after nephrectomy as standard of care for patients with localized RCC at increased risk for recurrence. Clinical trial information: NCT03142334.

- DOI: 10.1200/JCO.2022.40.16_suppl.4512

ABSTRACT 4513 :

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/207891**

Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Analysis of progression after first subsequent therapy in KEYNOTE-426.

Meeting:
2022 ASCO Annual Meeting

Session Type:
Poster Discussion Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
Genitourinary Cancer—Kidney and Bladder

Clinical Trial Registration Number:
NCT02853331

Citation:
J Clin Oncol 40, 2022 (suppl 16; abstr 4513)

DOI:
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Abstract #:
4513

Poster #:
5

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Abstract Disclosures

Research Funding

Pharmaceutical/Biotech Company

Background:

The randomized, open-label, phase 3 KEYNOTE-426 study (NCT02853331) met its primary and key secondary end points of improved OS, PFS, and ORR with pembro + axi versus sunitinib as first-line treatment for patients with advanced ccRCC. Extended follow-up (42.8-mo median follow-up) continued to show the superior efficacy of pembro + axi versus sunitinib in this patient population. We describe the results of PFS2 for all randomly assigned patients and across IMDC risk categories.

Methods:

Treatment-naive patients with advanced ccRCC, Karnofsky Performance Status Scale score ≥70% and measurable disease per RECIST v1.1 were randomly assigned 1:1 to receive pembro 200 mg IV every 3 weeks for up to 35 doses (2 y) + axi 5 mg orally twice daily or sunitinib 50 mg orally once daily on a 4-wk on/2-wk off schedule. The end point of this exploratory analysis was PFS2, defined as time from randomization to progression after first subsequent therapy or any-cause death. The Kaplan-Meier method was used to estimate PFS2 and hazard ratios were estimated using a Cox regression model.

Results:

Of 861 patients, 432 were assigned to receive pembro + axi; 429, to sunitinib. Median time from randomization to the database cutoff date (January 11, 2021) was 42.8 mo (range, 35.6-50.6). Overall, 47.2% of patients (204/432) in the pembro + axi arm and 65.5% of patients (281/429) in the sunitinib arm received ≥1 line of subsequent anticancer therapy. For patients who received subsequent therapy, anti–PD-1/PD-L1 agents were the first subsequent treatment for 11.3% of patients (23/204) in the pembro + axi arm and 54.8% of patients (154/281) in the sunitinib arm. In the pembro + axi arm, 82.8% of patients (169/204) received a VEGF/VEGFR inhibitor as first subsequent therapy, as did 43.4% (122/281) in the sunitinib arm. PFS2 results are displayed in the Table.

Conclusions:

In this exploratory analysis, PFS2 was longer for patients randomized to pembro + axi compared to sunitinib. Results were consistent across IMDC risk groups. These data support use of pembro + axi for the first-line treatment of patients with advanced ccRCC. Clinical trial information: NCT02853331.

	ITT		IMDC favorable risk		IMDC intermediate/poor risk	
	Pembro + axi N = 432	Sunitinib N = 429	Pembro + axi n = 138	Sunitinib n = 131	Pembro + axi n = 294	Sunitinib n = 298
Received ≥1 line of subsequent anticancer therapy, n (%)	204 (47.2)	281 (65.5)	64 (46.4)	87 (66.4)	140 (47.6)	194 (65.1)
Median (95% CI) PFS2, mo	40.1 (34.9–43.8)	27.7 (23.1–29.9)	46.0 (43.8 to NR)	39.9 (33.5 to NR)	32.1 (27.9–39.3)	20.1 (15.9–25.1)
HR (95% CI)	0.63 (0.53–0.75)		0.68 (0.47–0.98)		0.62 (0.51–0.76)	

- DOI: 10.1200/JCO.2022.40.16_suppl.4513

ABSTRACT 4514 :

- **ASCO Link - https://meetings.asco.org/abstracts-presentations/209127**

Impact of subsequent therapies in patients (pts) with advanced renal cell carcinoma (aRCC) receiving lenvatinib plus pembrolizumab (LEN + PEMBRO) or sunitinib (SUN) in the CLEAR study.

- DOI: 10.1200/JCO.2022.40.16_suppl.4514

2022 ASCO Annual Meeting

Session Type:
Poster Discussion Session

Session Title:
Genitourinary Cancer—Kidney and Bladder

Track:
Genitourinary Cancer—Kidney and Bladder

Sub Track:
Genitourinary Cancer—Kidney and Bladder

Clinical Trial Registration Number:
NCT02811861

Citation:
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Abstract Disclosures

Research Funding

Pharmaceutical/Biotech Company

Abstract #:
4514

Poster #:
6

Background:

In the open-label, randomized, phase 3 CLEAR study, LEN + PEMBRO had significant PFS (primary endpoint) and OS (key secondary endpoint) benefits over SUN among pts with aRCC in the 1L setting (Motzer 2021, *NEJM*). We evaluated PFS on next-line therapy ("PFS2") and explored the effect of subsequent anticancer therapy on OS in the LEN + PEMBRO and SUN treatment arms of CLEAR.

Methods:

PFS2 was defined as time from randomization to disease progression (as assessed by investigator) on next-line treatment or death from any cause (whichever occurred first). PFS2 was evaluated in all pts randomly assigned to LEN 20 mg orally QD + PEMBRO 200 mg IV Q3W (n=355) or SUN 50 mg orally QD (4 wks on/2 wks off) (n=357) using Kaplan-Meier estimates, and compared between treatment arms via a log-rank test stratified by geographic region and MSKCC prognostic groups. The HR and corresponding CI were estimated using the Cox regression model with Efron's method for ties, using the same stratification factors. A post hoc analysis accounting for the effect of subsequent anticancer therapy on OS (time from randomization to death from any cause) in the LEN + PEMBRO and SUN arms using 2-stage estimation was conducted.

Results:

Among pts who received subsequent anticancer therapy in the LEN + PEMBRO (n=117 pts) and SUN (n=206 pts) arms (Table), median time to next-line therapy was 12.2 mos (range 1.45–37.36) and 6.4 mos (range 0.39–28.52), respectively. Median duration of first subsequent anticancer therapy was 5.2 mos (range 0.10–30.23) in the LEN + PEMBRO arm and 6.8 mos (range 0.03–30.72) in the SUN arm. Among all pts, PFS2 was longer with LEN + PEMBRO than with SUN (median not reached vs 28.7 mos; HR, 0.50; 95% CI 0.39–0.65; nominal *P*<0.0001); PFS2 rates at 24 and 36 mos are in the Table. The unadjusted OS HR for LEN + PEMBRO vs SUN (from the primary analysis [Motzer 2021, *NEJM*]) was 0.66 (95% CI 0.49–0.88); the HR for OS adjusted for subsequent therapy was 0.54 (bootstrap 95% CI 0.39–0.72).

Conclusions:

LEN + PEMBRO had a statistically significant and clinically meaningful benefit over SUN in the CLEAR study. These findings remained consistent after accounting for subsequent therapies, as evidenced by prolonged PFS2 and adjusted OS. Results further support LEN + PEMBRO as a standard of care in 1L aRCC. Clinical trial information: NCT02811861.

Parameter	LEN + PEMBRO (n=355)	SUN (n=357)
Pts receiving any subsequent systemic anticancer therapy[a], n (%)	117 (33.0)	206 (57.7)
Anti-VEGF	108 (30.4)	120 (33.6)
PD-1/PD-L1 checkpoint inhibitor	29 (8.2)	154 (43.1)
MTOR Inhibitor	6 (1.7)	17 (4.8)
CTLA-4 Inhibitor	6 (1.7)	18 (5.0)
Other	12 (3.4)	20 (5.6)
PFS2, median (95% CI)	Not reached (NE–NE)	28.7 mos (23.0–NE)
PFS2 HR (95% CI)	0.50 (0.39–0.65)	
Nominal *P* value	<0.0001	
PFS2 rate at 24/36 mos, % (95% CI)	72.7 (67.3, 77.4) / 61.9 (53.7, 69.0)	54.2 (48.4, 59.6) / 42.9 (32.8, 52.5)

[a]Monotherapy or in combination. NE, not estimable.

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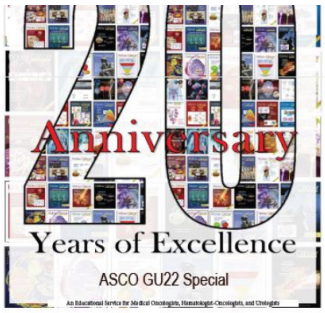

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