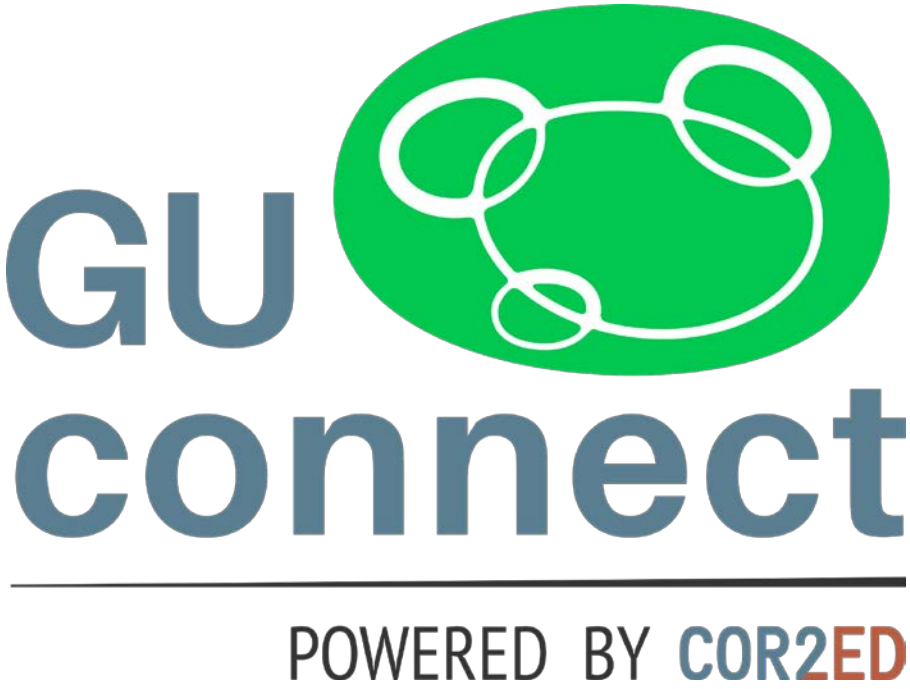
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MEETING SUMMARY
ASCO GU 2019, San Francisco, USA

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KIDNEY CANCER UPDATE

DISCLAIMER

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PEMBROLIZUMAB PLUS AXITINIB VERSUS SUNITINIB AS 1ST-LINE THERAPY FOR LOCALLY ADVANCED OR mRCC: PHASE III KEYNOTE-426 STUDY

Powles T, et al. Abstract #543

mRCC, metastatic renal cell carcinoma

KEYNOTE-426: STUDY DESIGN

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Eligibility:
- Histologically confirmed clear-cell mRCC
- No prior systemic therapy
- KPS ⩾ 70% within 10 days of randomisation
- Measurable disease per RECIST 1.1

Stratification:
- IMDC risk group
- Geographic region

RANDOMISED 1:1

Pembrolizumab 200 mg IV Q3W + Axitinib 5 mg BID (N=432)

Sunitinib 50 mg QD (N=429)

Outcome Measures

Primary:
- OS
- PFS per RECIST 1.1, as assessed by BICR

Secondary:
- ORR per RECIST 1.1, as assessed by BICR
- DCR per RECIST 1.1, as assessed by BICR
- Adverse Events
- DOR per RECIST 1.1, as assessed by BICR

Clinical trial identification: NCT02853331

861 PATIENTS RANDOMISED
Treatment until PD, intolerable toxicity, or patient/investigator decision

BICR, blinded independent central review; BID, twice-a-day; DCR, disease control rate; DOR, duration of response; IMDC, international metastatic renal cell carcinoma database consortium; KPS, karnofsky performance status; mRCC, metastatic renal cell carcinoma; ORR, objective response rate; OS, overall survival; PD, peritoneal dialysis; PFS, progression free survival; Q3W, every three weeks; QD, once-a-day; RECIST, response evaluation criteria in solid tumours.

Powles T, et al. Presented at ASCO GU 2019, Abstract number 543

KEYNOTE-426: FIRST INTERIM ANALYSIS

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	Pembrolizumab + Axitinib (N=432)	Sunitinib (N=429)
Overall Survival, % (12 months)	**89.9**	**78.3**
Benefit vs. Sunitinib Hazards ratio (95% CI) *P* value	0.53 (0.38 – 0.74) <0.0001	
Median Progression Free Survival (Months)	**15.1**	**11.1**
Benefit vs. Sunitinib Hazards ratio (95% CI) *P* value	0.69 (0.57 – 0.84) =0.0001	
Objective Response Rate	**59.3**	**35.7**
P value	<0.0001	
Median duration of response (Months)	**Not reached**	**15.2**

Grade 3-5 toxicities were similar for both drugs.

CI, confidence interval

Powles T, et al. Presented at ASCO GU 2019, Abstract number 543

KEYNOTE-426: CONCLUSIONS

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- Pembrolizumab + Axitinib provided **superior OS, PFS, and ORR** compared to Sunitinib
- **Manageable safety** in patients with previously untreated, advanced, or metastatic ccRCC
- Pembrolizumab + Axitinib **benefit was observed in all subgroups** tested (includes all IMDC risk and PD-L1 expression subgroups)
- **Pembrolizumab + Axitinib can be considered as one of the standard of care options** in this patient demographic

ccRCC, clear cell renal cell carcinoma; IMDC, international metastatic renal cell carcinoma database consortium; OS, overall survival; ORR, objective response rate; PD-L1, programmed death-ligand 1; PFS, progression free survival

Powles T, et al. Presented at ASCO GU 2019, Abstract number 543

SUBGROUP ANALYSIS FROM JAVELIN RENAL 101: OUTCOMES FOR AVELUMAB PLUS AXITINIB VERSUS SUNITINIB IN aRCC

Choueiri TK, et al. Abstract #544

aRCC, advanced renal cell carcinoma

JAVELIN 101: STUDY DESIGN

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Eligibility:
- Histologically confirmed clear cell aRCC
- No prior systemic therapy
- ECOG PS 0 or 1
- Measurable disease per RECIST 1.1
- Availability of FFPE from primary tumor

Stratification:
- ECOG PS (0 vs 1)
- Geographic region

RANDOMISED 1:1

Avelumab 10 mg/kg Q2W + Axitinib 5 mg BID (N=442)

Sunitinib 50 mg QD (N=444)

Outcome Measures

Primary:
- Overall Survival (OS) in PD-L1 positive patients
- Progression Free Survival (PFS) in PD-L1 positive patients

Secondary:
- OS in unselected patients
- PFS in unselected patients
- Objective Response Rate (ORR)
- Disease Control Rate (DCR)
- Time to Tumour Response (TTR)
- Duration of Response (DOR)

Clinical trial identification: NCT02684006

886 PATIENTS RANDOMISED
Treatment until PD, intolerable toxicity, or patient/investigator decision

aRCC, advanced renal cell carcinoma; BID, twice-a-day; ECOG, Eastern Cooperative Oncology Group; FFPE, formalin-fixed paraffin-embedded; mRCC, metastatic renal cell carcinoma; PD, peritoneal dialysis; PD-L1, programmed death-ligand 1; PS,performance status; Q2W, every 2 weeks; QD, once-a-day; RECIST, response evaluation criteria in solid tumours. Choueiri TK, et al. Presented at ASCO GU 2019, Abstract number 544; Motzer RJ, et al. NEJM 2019, DOI:10.1056/NEJMoa1816047

JAVELIN 101: RESULTS

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	PD-L1+ group (N=560)		Overall population (=886)	
	Avelumab + Axitinib (N=270)	Sunitinib (N=290)	Avelumab + Axitinib (N=442)	Sunitinib (N=444)
PFS per IRC*				
Median, months	13.8	7.2	13.8	8.4
95% CI	11.1 – NE	5.7 – 9.7	11.1 – NE	6.9 – 11.1
Benefit vs sunitinib (HR; P value)	0.61; *P*<0.0001	–	0.69; *P*<0.0001	–
ORR per IRC, %	55.2	25.5	51.4	25.7
95% CI	49.0 – 61.2	20.6 – 30.9	46.6 – 56.1	21.7 – 30.0
PFS per investigator assessment				
Median, months	13.3	8.2	12.5	8.4
95% CI	9.8 – NE	6.9 – 8.5	11.1 – 15.2	8.2 – 9.7
Benefit vs sunitinib (HR; P value)	0.51; *P*<0.0001	–	0.64; *P*<0.0001	–
ORR per investigator assessment, %	61.9	29.7	55.9	30.2
95% CI	55.8 – 67.7	24.5 – 35.3	51.1 – 60.6	25.9 – 34.7

Median follow up was 12.0 months (avelumab +axitinib) vs 11.5 months (sunitinib)

* PFS benefit per IRC was observed in patients regardless of PD-L1 status and in all prognostic risk groups. Grade 3–4 toxicities were similar for both drugs.

CI, confidence interval; HR, hazard ratio; IRC, independent review committee; NE, non-estimable; ORR, objective response rate; PD-L1, programmed death-ligand 1; PFS, progression free survival

Choueiri TK, et al. Presented at ASCO GU 2019, Abstract number 544 ; Motzer RJ, et al. NEJM 2019, DOI:10.1056/NEJMoa1816047

JAVELIN 101: CONCLUSIONS

- Avelumab + Axitinib demonstrated **PFS, and ORR benefit** across all MSKCC and IMDC prognostic risk groups and PD-L1 positive and negative subgroups versus Sunitinib in aRCC

aRCC, advanced renal cell carcinoma; IMDC, international metastatic renal cell carinoma Database Consortium; MSKCC, Memorial Sloan Kettering Cancer Center; ORR, objective response rate; PD-L1, programme death-ligand 1; PFS, progression free survival

Choueiri TK, et al. Presented at ASCO GU 2019, Abstract number 544 ; Motzer RJ, et al. NEJM 2019, DOI:10.1056/NEJMoa1816047

1ST-LINE PEMBROLIZUMAB MONOTHERAPY FOR ADVANCED nccRCC: RESULTS FROM KEYNOTE-427 COHORT B

McDermott DF, et al. Abstract #546

nccRCC, non-clear cell renal cell carcinoma

KEYNOTE-427: STUDY DESIGN

Eligibility (Cohort B):

- Histologically confirmed non-clear cell RCC
- Newly diagnosed Stage IV RCC
- No prior systemic therapy
- KPS ⩾ 70% within 10 days prior to treatment
- Measurable disease per RECIST 1.1

Pembrolizumab 200 mg IV Q3W x35 cycles (~2 yrs) (N=165)

165 PATIENTS (Cohort B)
Treatment until PD, intolerable toxicity, or patient/investigator decision

Outcome Measures

Primary:

- Objective Response Rate (ORR) per RECIST 1.1 , as assessed by BICR

Secondary:

- Duration of Response (DOR) per RECIST 1.1, as assessed by BICR
- Disease Control Rate (DCR) per RECIST 1.1, as assessed by BICR
- Progression Free Survival (PFS) per RECIST 1.1, as assessed by BICR
- Overall Survival (OS)
- Adverse Events (AE)

Clinical trial identification: NCT02853344

BICR, blinded independent central review; KPS, Karnofsky performance status; peritoneal dialysis; Q3W, every three weeks; RCC, renal cell carcinoma; RECIST, response evaluation criteria in solid tumours.

McDermott DF, et al. Presented at ASCO GU 2019, Abstract number 546

KEYNOTE-427: PATIENT DEMOGRAPHICS

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Patient Demographics	N=165
aRCC Classification	**N (%)**
Papillary	118 (72%)
Chromophobe	21 (13%)
Unclassified	26 (16%)
IMDC Risk Group	
Favorable	32%
Intermediate/Poor	68%
PD-L1	
Negative	38%
Positive	62%

aRCC, advanced renal cell carcinoma; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium, PD-L1, programme death-ligand 1

McDermott DF, et al. Presented at ASCO GU 2019, Abstract number 546

KEYNOTE-427: RESULTS

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	Pembrolizumab N=165
Overall Objective Response Rate, % (95% CI)	**24.8% (18.5 – 32.2)**
Complete Response, N (%)	8 (4.8%)
Partial Response, N (%)	33 (20%)
ORR by nccRCC subtype (95% CI)	
Papillary	25.4% (17.9 – 34.3)
Chromophobe	9.5% (1.2 – 30.4)
Unclassified	34.6% (17.2 – 55.7)
ORR by IMDC Risk Group (95% CI)	
Favorable	28.3% (16.8 – 42.3)
Intermediate/Poor	23.2% (15.8 – 32.1)
ORR by PD-L1+ [CPS≥1] (95% CI)	
CPS≥1	33.3% (24.3 – 43.4)
CPS<1	10.3% (3.9 – 21.2)
Median duration of response (Months)	**Not Reached**

aRCC, advanced renal cell carcinoma; CI, confidence interval; CPS, combined positive score; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; nccRCC, non-clear cell renal cell carcinoma; ORR, objective response rate; PD-L1, programme death-ligand 1

McDermott DF, et al. Presented at ASCO GU 2019, Abstract number 546

KEYNOTE-427: CONCLUSIONS

- Single agent Pembrolizumab showed **encouraging activity in nccRCC,** especially in papillary or unclassified histologies

- Safety was as expected

aRCC, advanced renal cell carcinoma; nccRCC, non-clear cell carcinoma

McDermott DF, et al. Presented at ASCO GU 2019, Abstract number 546

THANK YOU!

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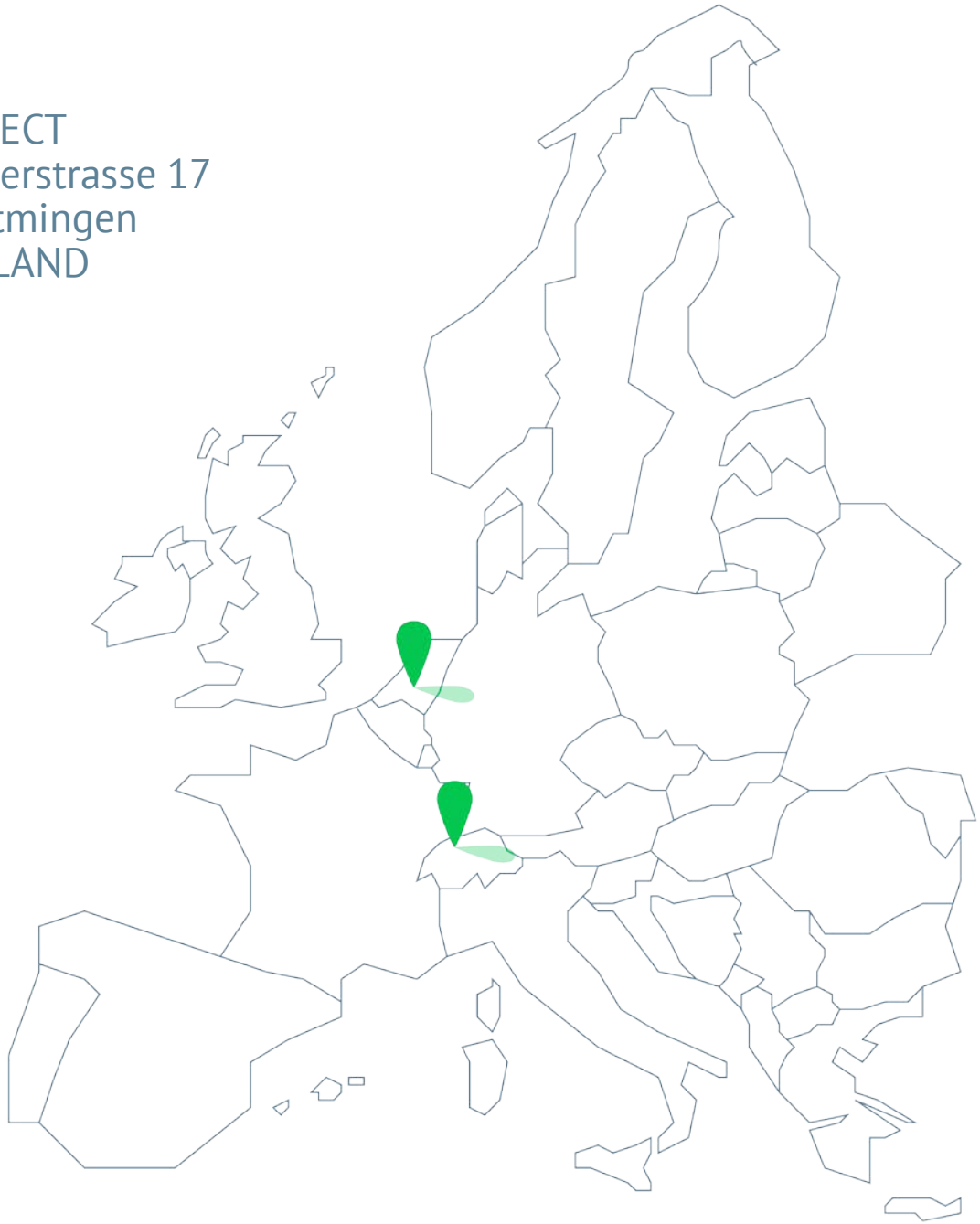

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