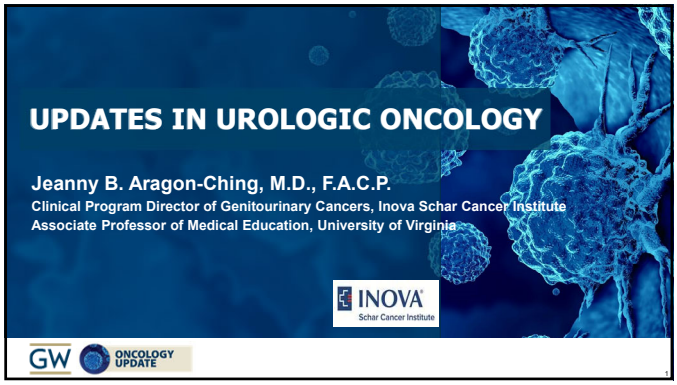


Disclosures

INOVA Schar Cancer Institute

- Has served on advisory board of Dendreon, Janssen/Ortho-Biotech, Algeta/Bayer, Astra Zeneca, Sanofi/Genzyme, EMD Serono/Merck
- Has served on the Speakers Bureau of Bristol Myers Squibb, Janssen, Astellas/Medivation and Astellas/Seattle Genetics

GW ONCOLOGY UPDATE

Learning Objectives

INOVA Schar Cancer Institute

- Understand and discuss recent abstracts and data presented at GU symposium meetings that reflect cutting-edge research reports on the practice of prostate, bladder and kidney cancers
- Understand updates to prostate cancer treatment
- Evaluate results of frontline immunotherapy trials in metastatic urothelial cancer and adjuvant therapy
- Evaluate updates to first-line kidney cancer treatment and adjuvant therapy

GW ONCOLOGY UPDATE

Urologic Oncology: Highlights of GU Oncology 2021

- Prostate cancer
  - Biochemical recurrence
    - Approval of 18F-DCFPyL based on ASCO GU 2020 Abstract 5501 - Impact of PSMA-targeted imaging with 18F-DCFPyL-PET/CT on clinical management of patients (pts) with biochemically recurrent (BCR) prostate cancer (PCa): Results from a phase III, prospective, multicenter study (CONDOR). (Michael Morris, MD)
  - mCRPC treatment
    - ASCO 2021 Plenary - Phase III study of lutetium-177-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION) (Michael Morris, MD)

GW ONCOLOGY UPDATE

Urologic Oncology: Highlights of GU Oncology 2021

- Bladder Cancer
  - Adjuvant therapy for high-risk muscle-invasive bladder cancer
    - ASCO GU abstract: First results from the phase 3 CheckMate 274 trial of adjuvant nivolumab vs placebo in patients who underwent radical surgery for high-risk muscle-invasive urothelial carcinoma (MIUC).
    - ASCO 2020 Abstract 500: IMvigor010: Primary analysis from a phase III randomized study of adjuvant atezolizumab (atezo) versus observation (obs) in high-risk muscle-invasive urothelial carcinoma (MIUC). (Maha Hussain, MD, FASCO)
  - Metastatic urothelial cancer
    - Summary of first-line metastatic urothelial trials: Keynote 361 and Imvigor130
    - ASCO Abstract 4508: First-line pembrolizumab (pembro) in cisplatin-ineligible patients with advanced urothelial cancer (UC): Response and survival results up to five years from the KEYNOTE-052 phase 2 study (Peter O'Donnell, MD)

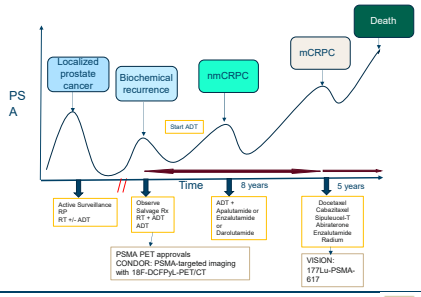
GW ONCOLOGY UPDATE

Urologic Oncology: Highlights of GU Oncology 2021

- Renal
  - Adjuvant Therapy
    - ASCO 2021 Plenary: Pembrolizumab versus placebo as post-nephrectomy adjuvant therapy for patients with renal cell carcinoma: Randomized, double-blind, phase III KEYNOTE-564 study (Toni Choueiri, MD)
  - First line mRCC
    - ASCO GU 2021 Abstract : Phase 3 trial of lenvatinib (LEN) plus pembrolizumab (PEMBRO) or everolimus (EVE) versus sunitinib (SUN) monotherapy as a first-line treatment for patients (pts) with advanced renal cell carcinoma (RCC) (CLEAR study). (Robert Motzer, MD)

GW ONCOLOGY UPDATE

Potential Natural History Prostate Cancer



nmCRPC = non-metastatic castration-resistant prostate cancer; mCRPC = metastatic castration-resistant prostate cancer

GW ONCOLOGY UPDATE

PSMA PET Scan approvals

FDA Approves First PSMA-Targeted PET Imaging Drug for Men with Prostate Cancer

For Immediate Release: December 01, 2020

The FDA granted approval to the University of California, Los Angeles and the University of California, San Francisco.

Today, the U.S. Food and Drug Administration approved Gallium 68 PSMA-11 (Ga 68 PSMA-11) – the first drug for positron emission tomography (PET) imaging of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer.

FDA approves second PSMA-targeted PET imaging drug for men with prostate cancer

Content current as of: 05/27/2021

FDA has approved Pylarify (piflufolastat F 18) – a drug for positron emission tomography (PET) imaging of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer. With the approval of Pylarify, certain men with prostate cancer will have greater access to PSMA-targeted PET imaging that can aid health care providers in assessing prostate cancer.

GW ONCOLOGY UPDATE

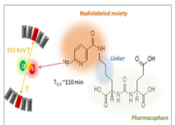
F18 DCFPyL PSMA PET Scan

Diagnostic Performance of ^{18}F-DCFPyL-PET/CT and its Impact on Clinical Management of Patients with Biochemically Recurrent Prostate Cancer: Results from a Phase 3, Prospective, Multicenter Study (CONDOR)

Michael J. Morris*, Peter R. Carroll, Lawrence Saperstein, Frédéric Pouliot, David Josephson, Jeffrey Y.C. Wong, Austin R. Pantel, Steve Y. Cho, Kenneth Gage, Morand Piert, Andrei Iagaru, Janet H. Pollard, Vivien Wong, Jessica Donato Jensen, Nancy Stambler, Michael A. Gorin, Barry A. Siegel

^{18}F-DCFPyL

- Lysine-linked, urea-based small molecule
- Targets the extracellular domain of PSMA
- High specific activity
- 9 (±20%) mCi administered intravenously as bolus injection
- Imaging performed 1-2 hours following administration



Chen et al. Clin Cancer Res 2011; laboratory of Martin G. Pomper, MD, PhD

GW ONCOLOGY UPDATE

F18 DCFPyL PSMA PET Scan

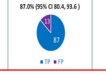
Select Baseline Characteristics, N=208

Patients Screened/Consented (N)	217
Patients dosed (N)	208
Age (years): Median (range)	68 (43, 91)
Months from Prostate Cancer Diagnosis: Median (range)	71 (3, 356)
Prior Prostate Cancer Therapies, N (%)	
RP only	103 (49.5)
RP and RT	74 (35.6)
RT only	31 (14.9)
At least 1 prior systemic therapy	58 (27.9)
Total Gleason Score, N (%)	
< 8	153 (73.6)
≥ 8	55 (26.4)

PSA: Median (range) ng/mL	0.8 (0.17, 98.45)
PSA Group (N=202), N (%)	
<2.0 ng/mL	139 (68.8)
<0.5 ng/mL	69 (34.2)
0.5 to <1.0 ng/mL	37 (18.3)
1.0 to <2.0 ng/mL	33 (16.3)
≥2.0 ng/mL	63 (31.2)
2.0 to <5.0 ng/mL	33 (16.3)
≥5.0 ng/mL	30 (14.9)

Diagnostic Performance of ^{18}F-DCFPyL PET/CT in Biochemical Recurrence: Correct Localization Rate

	All subjects (N=208)		
	Reader 1	Reader 2	Reader 3
Positive ^{18}F-DCFPyL Scan on Subject Level (Detection Rate)	137 (65.9%)	124 (59.6%)	123 (59.1%)
Unevaluable*	33	24	24
CLR (TP/(TP+FP))	89/104 85.6% (95% CI 78.8, 92.3)	87/100 87.0% (95% CI 80.4, 93.6)	84/99 84.8 (95% CI 77.8, 91.9)

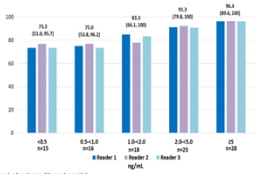


*NOT not submitted or false-negative at the lesion level

- Correct Localization Rate met the primary endpoint, as the lower limit of the 95% CI for exceeded 20% by all 3 readers

F18 DCFPyL PSMA PET Scan

Correct Localization Rate by PSA



Median values for each group of three readers provided

PYLARIFY® (piflufolastat F 18) Injection

Indication

PYLARIFY® (piflufolastat F 18) Injection is a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer:

- with suspected metastasis who are candidates for initial definitive therapy.
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level.

- 63.9% of evaluable subjects had a change in intended management after ^{18}F-DCFPyL-PET/CT

Increasing detection with sensitive imaging

Table 1. Summary of Mechanism and Diagnostic Efficacy of the Different Available PET Radiotracers

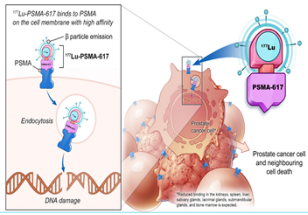
PET Tracer	Mechanism	Sensitivity (%)	Specificity (%)	Advantages	Disadvantages
PSMA Ligands ^{68}Ga-PSMA, ^{18}F-DCFBC	PSMA analog	Diagnosis: 49-92 Staging: 56-61 Recurrence: 77-100	Diagnosis: 84-92 Staging: 90-97 Recurrence: 50-99	High sensitivity and specificity at low PSA levels	(68)Ga ligands more common, but they require considerable expenditure
Choline ^{11}C and ^{18}F	Cell membrane synthesis	Diagnosis: 66 Staging: 49 Recurrence: 47-72	Diagnosis: 92 Staging: 95 Recurrence: 92	Minimal bladder excretion	Poor discrimination between PCa and BPH Variable sensitivity and specificity for BCR, especially at lower PSA levels
^{11}C- Acetate	Lipid synthesis	Diagnosis: 73-81 Staging: 38-90 Recurrence: 59-92	Diagnosis: 29-41 Staging: 89-96 Recurrence: 50-96	Minimal bladder excretion	Short half-life requiring in-site cyclotron Sensitivity for BCR drops to 50% when PSA < 1 ng/mL
^{18}F-NaF	Chemisorption in bone matrix	87-89	80-91	Superior sensitivity compared to (99m)Tc bone scans Faster acquisition time compared to conventional bone scans Extensively Validated	Not tumor specific High false positive rate Not reimbursed by Medicare
Fluciclovine ^{18}F-FACBC	Amino acid transport	Diagnosis: 67 Staging: 55-86 Recurrence: 67-89	Diagnosis: 73 Staging: 87-97 Recurrence: 40-67	Superior sensitivity at low PSA values Slow urinary excretion improving signal	Moderate specificity Data based on small sample studies

Abbreviations: PET: positron emission tomography, PSMA: prostate-specific membrane antigen, Pca: prostate cancer, BPH: Benign Prostatic Hyperplasia

Correa A and Smaldone M. ESHI Nov 2016

Role of Lutetium

^{177}Lu-PSMA-617 targeted radioligand therapy



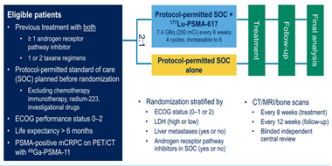
Clinical Trials with Radioligand therapy targeting PSMA:

- LuPARP trial - ^{177}Lu-PSMA-617 with Olaparib (NCT03874884)
- PRINCE trial – ^{177}Lu-PSMA-617 with pembrolizumab (NCT03658447)
- Antibody with small molecular combination - ^{177}Lu-PSMA-617 with ^{177}Lu-J591 (NCT03545165)
- Lu-PSMA trial - Radiometabolic ^{177}Lu-PSMA-617 (NCT03454750)
- Fractionated ^{177}Lu-PSMA-617 trial (NCT03042468)

Sartor O et al., TPS5099 J Clin Oncol 2019 37, no. 15_suppl; Yu E. Urotoday. Accessed May 2020 link

VISION: Phase III trial lutetium vs SOC mCRPC

Open-label study of protocol-permitted standard of care ± ^{177}Lu-PSMA-617 in adults with PSMA-positive mCRPC



Prespecified endpoints: alternate primary, key secondary and other secondary

Alternate primary endpoints	Key secondary endpoints	Other secondary endpoints
Radiographic progression-free survival (rPFS) per PCWG3	Time to first symptomatic skeletal event (SSE)	Safety and tolerability
Overall survival (OS)	RECIST v1.1 overall response rate	Biomarkers including PSA
	RECIST v1.1 disease control rate	Health-related quality of life and pain

Sartor O et al., *NEJM* 2021; Morris et., ASCO Annual Meeting 2021

VISION: Phase III trial lutetium vs SOC mCRPC

Baseline characteristics were well balanced across treatment arms and the two analysis sets

	rPFS analysis set (n = 581)		All randomized (N = 831)	
	^{177}Lu-PSMA-617 + SOC (n = 385)	SOC alone (n = 196)	^{177}Lu-PSMA-617 + SOC (n = 551)	SOC alone (n = 280)
Age, median (range)	71.0 (52–94)	72.0 (51–89)	70.0 (48–94)	71.5 (40–89)
Race, n (%)				
White	336 (87.3)	166 (84.7)	486 (88.2)	235 (83.9)
Black/African-American	29 (7.5)	14 (7.1)	34 (6.2)	21 (7.5)
Asian	6 (1.6)	9 (4.6)	9 (1.6)	11 (3.9)
ECOG status, n (%)				
0 or 1	352 (91.4)	179 (91.3)	510 (92.6)	258 (92.1)
2	33 (8.6)	17 (8.7)	41 (7.4)	22 (7.9)
Site of disease, n (%)				
Lung	35 (9.1)	20 (10.2)	49 (8.9)	28 (10.0)
Liver	47 (12.2)	26 (13.3)	63 (11.4)	38 (13.6)
Lymph node	193 (50.1)	99 (50.5)	274 (49.7)	141 (50.4)
Bone	351 (91.2)	179 (91.3)	504 (91.5)	256 (91.4)

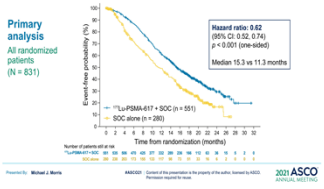
Previous cancer treatments were well balanced across treatment arms and the two analysis sets

	rPFS analysis set (n = 581)		All randomized (N = 831)	
	^{177}Lu-PSMA-617 + SOC (n = 385)	SOC alone (n = 196)	^{177}Lu-PSMA-617 + SOC (n = 551)	SOC alone (n = 280)
Number received, median (range)				
Androgen receptor pathway inhibitor	1.0 (1–5)	1.5 (1–4)	1.0 (1–5)	2.0 (1–4)
Taxane regimen	1.0 (1–3)	1.0 (1–3)	1.0 (1–3)	1.0 (1–3)
Patients who received more than one, n (%)				
Androgen receptor pathway inhibitor	172 (44.7)	98 (50.0)	253 (45.9)	152 (54.3)
Taxane regimen	178 (46.2)	94 (48.0)	226 (41.0)	124 (44.3)

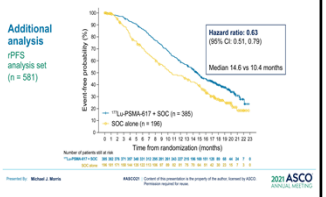
Sartor O et al., *NEJM* 2021; Morris et., ASCO Annual Meeting 2021

VISION: Phase III trial lutetium vs SOC mCRPC

Primary endpoints: ^{177}Lu-PSMA-617 prolonged OS



^{177}Lu-PSMA-617 prolonged OS in the rPFS analysis set

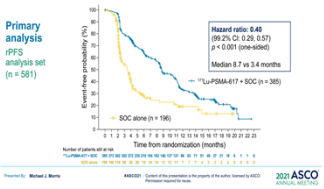


Sartor O et al., NEJM 2021; Morris et., ASCO Annual Meeting 2021

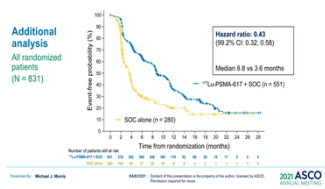
GW ONCOLOGY UPDATE

VISION: Phase III trial lutetium vs SOC mCRPC

Primary endpoints: ^{177}Lu-PSMA-617 improved rPFS



^{177}Lu-PSMA-617 improved rPFS in the OS analysis set



Sartor O et al., NEJM 2021; Morris et., ASCO Annual Meeting 2021

GW ONCOLOGY UPDATE

VISION: Phase III trial lutetium vs SOC mCRPC

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

GW ONCOLOGY UPDATE

Conclusions in Prostate Cancer

- Use of PSMA tracers are here to stay
  - Cost and availability of tracers and facilities
  - Disease state applicability: biochemical recurrence, high-risk prostate cancer
  - Trials show changes in treatment decisions, but not in survival yet
- Use of lutetium-PSMA is very promising, results of VISION trial likely will lead to regulatory approval
  - Likely in the post-AR failure and chemotherapy failure
  - SOC arm have not yet seen cabazitaxel or radium, both agents known to improve survival

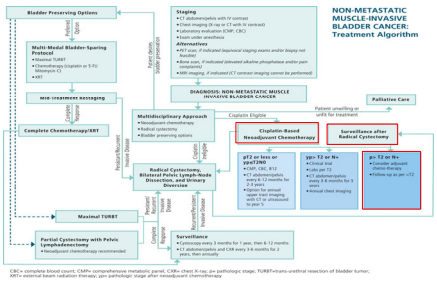
GW ONCOLOGY UPDATE

Bladder Cancer

- **Bladder**
  - Adjuvant therapy for high-risk bladder cancer
    - ASCO GU abstract: First results from the phase 3 CheckMate 274 trial of adjuvant nivolumab vs placebo in patients who underwent radical surgery for high-risk muscle-invasive urothelial carcinoma (MIUC).
    - ASCO 2020 Abstract 500: IMvigor010: Primary analysis from a phase III randomized study of adjuvant atezolizumab (atezo) versus observation (obs) in high-risk muscle-invasive urothelial carcinoma (MIUC). (Maha Hussain, MD, FASCO)
  - Metastatic urothelial cancer
    - Summary of first-line metastatic urothelial trials: Keynote 361 and Imvigor130 and Javelin Bladder 100 subgroups
    - ASCO Abstract 4508: First-line pembrolizumab (pembro) in cisplatin-ineligible patients with advanced urothelial cancer (UC): Response and survival results up to five years from the KEYNOTE-052 phase 2 study (Peter O'Donnell, MD)

GW ONCOLOGY UPDATE

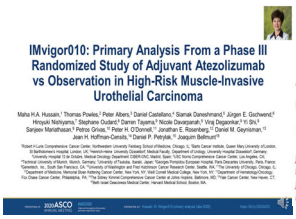
Standard of care Muscle-invasive bladder cancer (MIBC)



The Journal of Urology 2017 198, 552-559DOI: (10.1016/j.juro.2017.04.086)

GW ONCOLOGY UPDATE

IMvigor010: Adjuvant atezolizumab vs Observation



IMvigor010: Primary Analysis From a Phase III Randomized Study of Adjuvant Atezolizumab vs Observation in High-Risk Muscle-Invasive Urothelial Carcinoma

THE LANCET Oncology

Published: March 12, 2021

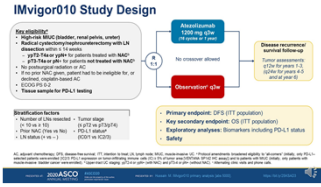
Adjuvant atezolizumab versus observation in muscle-invasive urothelial carcinoma (IMvigor010): a multicentre, open-label, randomised, phase 3 trial

Joaquim Bellmunt, Maha Hussain, Jürgen E Gschwend, Peter Albers, Stephane Oudard, Daniel Castellano, Siamak Daneshmand, Hiroyuki Nishiyama, Martin Majchrowicz, Vinaj Degaonkar, Yi Shi, Sanjeev Mariathasan, Petros Grivas, Alexandra Drakaki, Peter H O'Donnell, Jonathan E Rosenberg, Daniel M Geynisman, Daniel P Petrylak, Jean Hoffman-Censits, Jens Bedke, Arash Rezazadeh Kalebasty, Yousef Zakharia, Michiel S van der Heijden, Cora N Sternberg, Nicole N Davarpanah, Thomas Powles, *for the IMvigor010 Study Group**

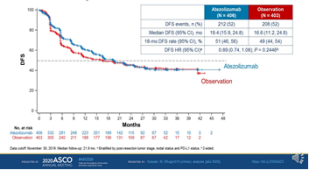
GW ONCOLOGY UPDATE

IMvigor010: Adjuvant atezolizumab

IMvigor010 Study Design



DFS in ITT Population



- Ten (3%) patients in the atezolizumab group and one (<1%) patients in the observation group had an adverse event of special interest requiring systemic corticosteroids
- 35 pts in observation group vs 15 pts in atezolizumab withdrew

GW ONCOLOGY UPDATE

Checkmate 274: Adjuvant nivolumab vs placebo

ASCO Genitourinary Cancers Symposium

First results from the phase 3 CheckMate 274 trial of adjuvant nivolumab versus placebo in patients who underwent radical surgery for high-risk muscle-invasive urothelial carcinoma

Dean F. Bajorin,[1] Johannes Alfred Witjes,[2] Jürgen E. Gschwend,[3] Michael Schenker,[4] Begoña R. Valderrama,[5] Yoshihiko Tomita,[6] Aristotelis Bamias,[7] Thierry Lebret,[8] Shahrokh F. Shariat,[9] Se Hoon Park,[10] Dingwei Ye,[11] Mads Agerbæk,[12] Sandra Collette,[13] Reziban Unsal-Kacmaz,[13] Dimitrios Zardavas,[13] Henry B. Koon,[13] Matthew D. Galsky[14]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]Radboud University, Nijmegen, the Netherlands; [3]Technical University Munich, Munich, Germany; [4]Vectarde Oncology Center, Craiova, Romania; [5]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [6]Kitasato University Graduate School of Medical and Dental Sciences, Kitgata, Japan; [7]National and Kapodistrian University of Athens, Athens, Greece; [8]Urology Department Hospital Foch, Paris-Saclay University UVSQ, Versailles, France; [9]Medical University of Vienna, Vienna General Hospital, Vienna, Austria; [10]Samsung Medical Center, Seoul, South Korea; [11]Fudan University Shanghai Cancer Center, Shanghai, China; [12]Aarhus University Hospital, Aarhus, Denmark; [13]Bristol Myers Squibb, Princeton, NJ; [14]Icahn School of Medicine at Mount Sinai, New York, NY

Abstract Number: 391

Presented By: Dean Bajorin at 2021 Genitourinary Cancers Symposium

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

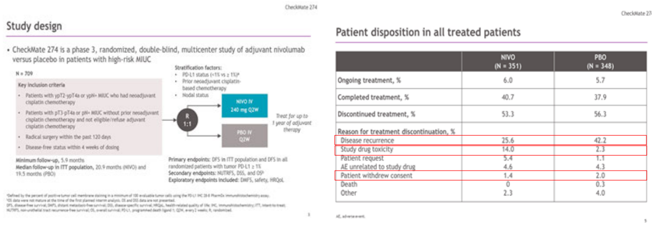
Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma

D.F. Bajorin, J.A. Witjes, J.E. Gschwend, M. Schenker, B.P. Valderrama, Y. Tomita, A. Bamias, T. Lebret, S.F. Shariat, S.H. Park, D. Ye, M. Agerbaek, D. Enting, R. McDermott, P. Gajate, A. Peer, M.I. Milowsky, A. Nosov, J. Neif Antonio, Jr., K. Tupikowski, L. Toms, B.S. Fischer, A. Qureshi, S. Collette, K. Unsal-Kacmaz, E. Broughton, D. Zardavas, H.B. Koon, and M.D. Galsky

Bajorin D et al., ASCO GU Cancers Symposium 2021; NEJM 2021

GW ONCOLOGY UPDATE

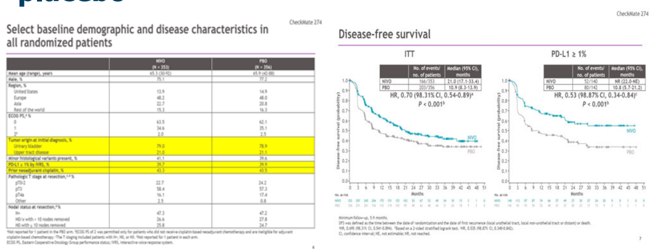
Checkmate 274: Adjuvant nivolumab vs placebo



Bajorin D et al., ASCO GU Cancers Symposium 2021; NEJM 2021

GW ONCOLOGY UPDATE

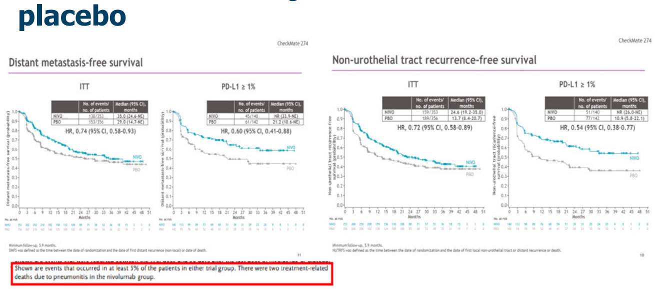
Checkmate 274: Adjuvant nivolumab vs placebo



Bajorin D et al., ASCO GU Cancers Symposium 2021; NEJM 2021

GW ONCOLOGY UPDATE

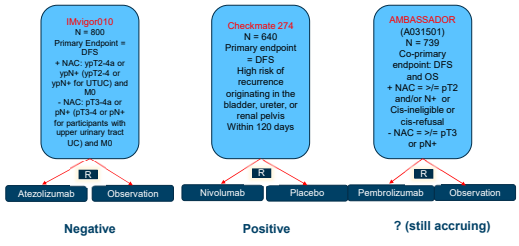
Checkmate 274: Adjuvant nivolumab vs placebo



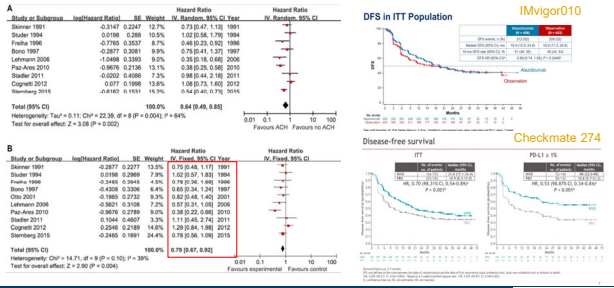
Bajorin D et al., ASCO GU Cancers Symposium 2021; NEJM 2021

GW ONCOLOGY UPDATE

Adjuvant trials MIBC >/= pT2 or N+



Adjuvant Chemotherapy Studies



Kim H et al., *Oncotarget.* 2017 Oct 6; 8(46): 81204–81214.

Adjuvant Immunotherapy Conclusions

- Very promising results
  - Await regulatory approval for widespread use
- Impact of one-year of therapy when the goal remains non-curative in intent – delay of metastasis = surrogate for survival
- Is this early vs late initiation of treatment
- Relevance of different checkpoint inhibitor trial results – difference in biology vs study design; ie., observation resulted in fall-out of subjects vs placebo-controlled
- Concerns regarding clinicians and patients favoring adjuvant immunotherapy over offering neoadjuvant cisplatin-based chemotherapy to those who are eligible

Metastatic Urothelial Cancer

- 2020 – 2021 brought about multiple landmark trial results and developments in urothelial cancer
- Javelin Bladder 100 established switch maintenance immunotherapy with avelumab is the current standard of care
- First-line chemotherapy with immunotherapy Keynote-361 and IMvigor130 had disappointing results
- FDA accelerated approval granted 4/2020 for Sacituzumab govitecan for treatment beyond chemotherapy and immune checkpoint inhibitor failure
  - Adds to another ADC – Enfortumab vedotin (regular approval July 2021)
- Voluntary withdrawal of durvalumab and atezolizumab in the 2nd line space

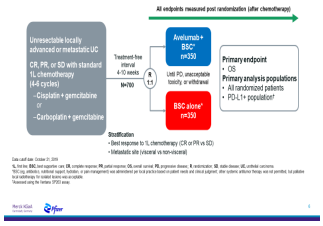
GW ONCOLOGY UPDATE

Javelin Bladder 100 updated subgroups

Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (UC): analysis of clinical and genomic subgroups from the JAVELIN Bladder 100 trial

T. Powles,[1] D. P. Petrylak,[2] S. H. Park,[3] S. S Sridhar,[4] C. Caserta,[5] A. Thiery-Vuillemin,[6] H. J. Lee,[7] J. Bellmunt,[8] Y. Yamamoto,[9] J. B. Aragon-Ching,[10] B. Huang,[11] K. Ching,[11] C. Davis,[11] A. Di Pietro,[11] Y. Loriot,[12] P. Grivas[13]

Figure 1. JAVELIN Bladder 100 phase 3 study design



JAVELIN Bladder 100

Powles T et al., ASCO Annual Meeting 2021

GW ONCOLOGY UPDATE

Javelin Bladder 100 updated subgroups

Figure 3. OS (A) and PFS (B) in patients with PD-L1+ tumors who received 1L gemcitabine + carboplatin

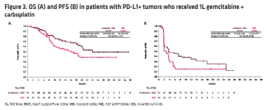
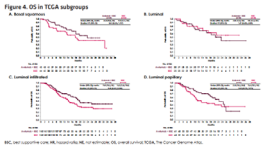


Figure 4. OS in TCGA subgroups

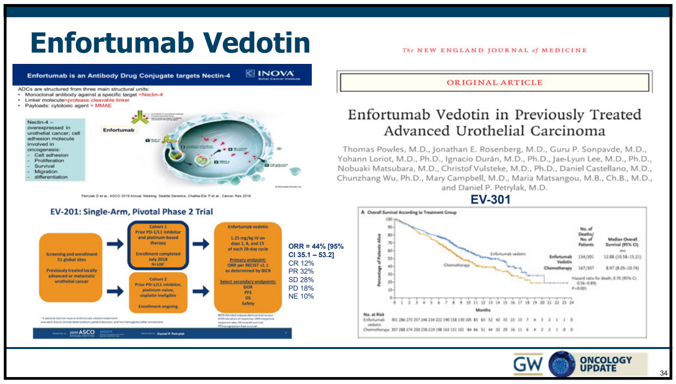


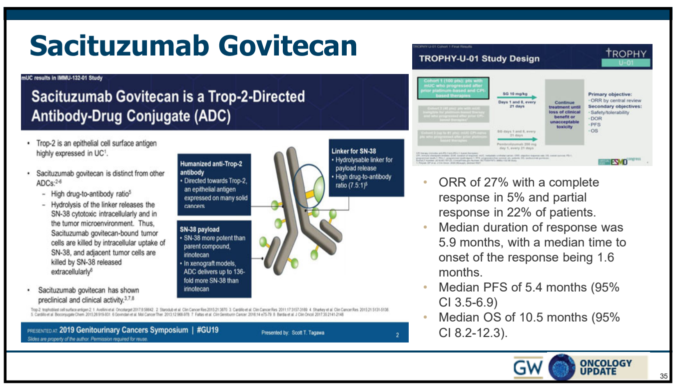
CONCLUSIONS

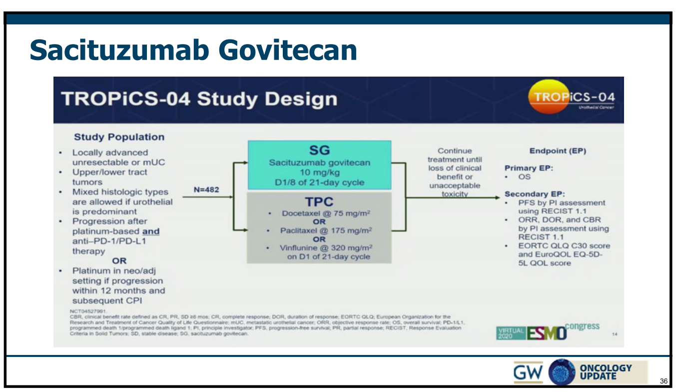
- An OS and PFS benefit was seen with avelumab 1L maintenance + BSC vs BSC alone across several subgroups of interest, including patients with:
  - Upper or lower tract disease
  - Metastatic disease, unresectable locally advanced (LA) disease, or lymph node–only disease
  - PD-L1+ tumors who received 1L gemcitabine + carboplatin
  - Tumor genomic subtypes defined by The Cancer Genome Atlas (TCGA),[1] except luminal
- Analysis of key immune biomarkers by TCGA subtype did not predict benefit with avelumab 1L maintenance
- These data further support avelumab 1L maintenance as a standard of care for patients with advanced UC that has not progressed with 1L platinum-containing chemotherapy

Powles T et al., ASCO Annual Meeting 2021

GW ONCOLOGY UPDATE







Voluntary withdrawal Durvalumab and Atezolizumab

Durvalumab FDA indication for bladder cancer voluntarily withdrawn

Urology Times

February 22, 2021
Jason M. Broderick

The withdrawal comes after the

AstraZeneca has voluntarily wit
locally advanced or metastatic

Durvalumab received an accele
an FDA accelerated approval is
DANUBE trial exploring durvalu

Atezolizumab FDA indication for pretreated bladder cancer voluntarily withdrawn

March 8, 2021
Jason M. Broderick

The withdrawal comes after the confirmatory phase 3 IMvigor211 study missed its primary end point.

Roche (Genentech) has voluntarily withdrawn the FDA indication for the PD-L1 inhibitor atezolizumab (Tecentriq) for use in patients with locally advanced or metastatic urothelial carcinoma (mUC) previously treated with platinum-based chemotherapy.[1]

Atezolizumab received an accelerated approval from the FDA for this indication in May 2016 based on cohort data from the phase 2 IMvigor210 study.[2] However, an FDA accelerated approval is contingent upon the results of a confirmatory trial, and in May 2017, Roche reported that the phase 3 IMvigor211 study exploring atezolizumab in the second-line setting for patients with locally advanced or (mUC) missed its primary end point of improving overall survival (OS).[3]

GW ONCOLOGY UPDATE

Potential landscape: First-line phase III Metastatic trials

IMvigor 130[1]
- Gemcitabine/Platinum
- Atezolizumab*
- Gem/Platinum + Atezolizumab

Improvement in PFS 8.2 vs 6.3 mos; HR 0.82; P=0.007
OS = 16 vs 13.4 mos HR=0.83; p=0·027

Javelin Bladder 100[2]
- Gem/Platinum -> Avelumab
- BSC

Improvement in OS = 21.4 vs 14.3 HR = 0.69; P=0.001

Keynote 361[3]
- Gemcitabine/Platinum
- Pembrolizumab*
- Gem/Platinum + Pembrolizumab

Did not meet dual primary endpoints of OS and PFS**

DANUBE[4]
- Gemcitabine/Platinum
- Durvalumab
- Durvalumab + tremelimumab

Failed to improve OS

Checkmate 901[5]
- Gemcitabine/Platinum
- Gem/Platinum + Nivolumab
- Nivolumab + Ipilimumab

Pending results

EV302[6]
- Enfortumab + pembrolizumab
- Gem/platinum

Pending results

[1]Galsky M et al., Lancet May 2020, Pages 1547-1557; [2]Powles T et al, ASCO 2020; [3]Keynote-361: Clinicaltrials.gov NCT02853305; [4]AstraZeneca update on Phase III DANUBE trial. Clinicaltrials.gov NCT02516241 [5]Checkmate 901 clinicaltrials.gov NCT03036098; [6]EV302: Clinicaltrials.gov NCT04223856; [*Access https://www.fda.gov/drugs/resources-information-approved-drugs/fda-limits-use-tecentriq-and-bavencio-some-urothelial-cancer-patients **Access https://investors.merck.com/news/press-release-details/2020/Merck-Provides-Update-on-Phase-3-KEYNOTE-361-Trial-Evaluating-KEYTRUDA-pembrolizumab-as-Monotherapy-and-in-Combination-with-Chemotherapy-in-Patients-with-Advanced-or-Metastatic-Urothelial-Carcinoma/default.aspx

GW ONCOLOGY UPDATE

First-line pembrolizumab and atezolizumab retained indication

Check for updates

nature reviews urology

NEWS & VIEWS

BLADDER CANCER

Pembrolizumab use in bladder cancer: a tale of two trials

Jeanny B. Aragon-Ching

pembrolizumab plus chemotherapy cohort compared with chemotherapy alone. Efficacy of the treatments was assessed in the total population and the PDL1+ population, defined as those patients with a CPS of ≥10% in the intention-to-treat group. The study used a hierarchical sequential statistical testing strategy in which a dual primary end point of PFS, as determined by blinded independent cen-

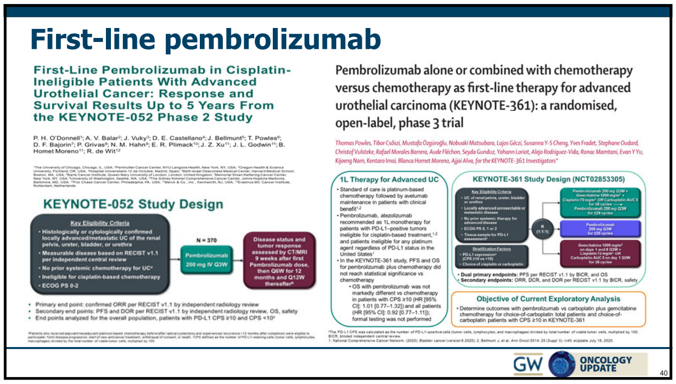
FDA ODAC Votes in Favor of Retaining Accelerated Approval for Bladder Cancer Treatments

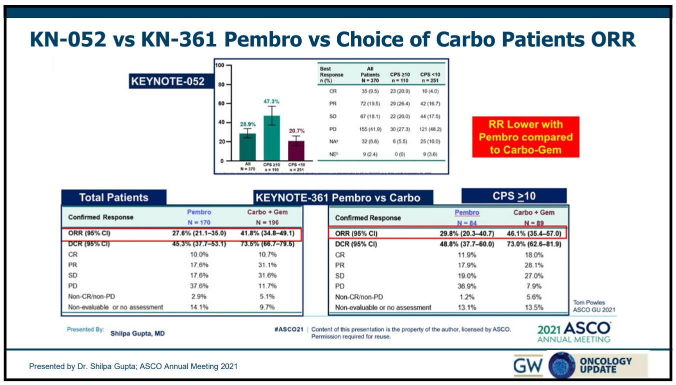
By The ASCO Post Staff

Roche has announced that the U.S. Food and Drug Administration (FDA) Oncologic Drugs Advisory Committee (ODAC) voted no to 1 in favor of maintaining the accelerated approval of atezolizumab for the treatment of adults with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin–containing chemotherapy and whose tumors express high levels of PD-L1 (IC 2–stained tumor–infiltrating immune cells covering ≥ 5% of the tumor area) as determined by an FDA–approved test or are not eligible for any platinum–containing chemotherapy regardless of PD–L1 status.

In addition, according to a report in pharmaphorum, the panel voted 5 to 3 to maintain the accelerated approval of pembrolizumab as first–line treatment for patients with cisplatin– and carboplatin–ineligible locally advanced or metastatic urothelial carcinoma.

GW ONCOLOGY UPDATE


First-line pembrolizumab
First-Line Pembrolizumab in Cisplatin-Ineligible Patients With Advanced Urothelial Cancer: Response and Survival Results Up to 5 Years From the KEYNOTE-052 Phase 2 Study
P. H. O'Donnell; A. V. Balar; J. Vuky; D. E. Castellano; J. Bellmunt; T. Powles; D. F. Bajorin; P. Grivas; N. M. Hahn; E. R. Plimack; J. Z. Xu; J. L. Godwin; B. Homet Moreno; R. de Wit
KEYNOTE-052 Study Design
Key Eligibility Criteria
• Histologically or cytologically confirmed locally advanced/metastatic UC of the renal pelvis, ureter, bladder, or urethra
• Measurable disease based on RECIST v1.1 per independent central review
• No prior systemic chemotherapy for UC
• Ineligible for cisplatin-based chemotherapy
• ECOG PS 0-2
N = 370
Pembrolizumab 200 mg IV Q3W
Disease status and tumor response assessed by CT/MRI 9 weeks after first Pembrolizumab dose, then Q6W for 12 months and Q12W thereafter
• Primary end point: confirmed ORR per RECIST v1.1 by independent radiology review
• Secondary end points: PFS and DOR per RECIST v1.1 by independent radiology review, OS, safety
• End points analyzed for the overall population, patients with PD-L1 CPS ≥10 and CPS <10
Pembrolizumab alone or combined with chemotherapy versus chemotherapy as first-line therapy for advanced urothelial carcinoma (KEYNOTE-361): a randomised, open-label, phase 3 trial
Thomas Powles, Tibor Csőszi, Mustafa Özgüroğlu, Nobuaki Matsubara, Lajos Géczi, Susanna Y-S Cheng, Yves Fradet, Stephane Oudard, Christof Vulsteke, Rafael Morales Barrera, Aude Fléchon, Seyda Gunduz, Yohann Loriot, Alejo Rodriguez-Vida, Ronac Mamtani, Evan Y Yu, Kijoeng Nam, Kentaro Imai, Blanca Homet Moreno, Ajjai Alva, for the KEYNOTE-361 Investigators
1L Therapy for Advanced UC
• Standard of care is platinum-based chemotherapy followed by avelumab maintenance in patients with clinical benefit
• Pembrolizumab, atezolizumab recommended as 1L monotherapy for patients with PD-L1–positive tumors ineligible for cisplatin-based treatment, and patients ineligible for any platinum agent regardless of PD-L1 status in the United States
• In the KEYNOTE-361 study, PFS and OS for pembrolizumab plus chemotherapy did not reach statistical significance vs chemotherapy
• OS with pembrolizumab was not markedly different vs chemotherapy in patients with CPS ≥10 (HR [95% CI]: 1.01 [0.77–1.32]) and all patients (HR [95% CI]: 0.92 [0.77–1.11]); formal testing was not performed
KEYNOTE-361 Study Design (NCT02853305)
R (1:1:1)
• Dual primary endpoints: PFS per RECIST v1.1 by BICR, and OS
• Secondary endpoints: ORR, DCR, and DOR per RECIST v1.1 by BICR, safety
Objective of Current Exploratory Analysis
• Determine outcomes with pembrolizumab vs carboplatin plus gemcitabine chemotherapy for choice-of-carboplatin total patients and choice-of-carboplatin patients with CPS ≥10 in KEYNOTE-361
GW ONCOLOGY UPDATE
40


KN-052 vs KN-361 Pembro vs Choice of Carbo Patients ORR
KEYNOTE-052
28.9%
47.3%
20.7%
All N = 370
CPS ≥10 n = 110
CPS <10 n = 251
RR Lower with Pembro compared to Carbo-Gem
Total Patients
KEYNOTE-361 Pembro vs Carbo
CPS ≥10
Tom Powles ASCO GU 2021
Presented By: Shilpa Gupta, MD
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2021 ASCO ANNUAL MEETING
Presented by Dr. Shilpa Gupta; ASCO Annual Meeting 2021
GW ONCOLOGY UPDATE

Best Response n (%)	All Patients N = 370	CPS ≥10 n = 110	CPS <10 n = 251
CR	35 (9.5)	23 (20.9)	10 (4.0)
PR	72 (19.5)	29 (26.4)	42 (16.7)
SD	67 (18.1)	22 (20.0)	44 (17.5)
PD	155 (41.9)	30 (27.3)	121 (48.2)
NA[a]	32 (8.6)	6 (5.5)	25 (10.0)
NE[b]	9 (2.4)	0 (0)	9 (3.6)

Confirmed Response	Pembro N = 170	Carbo + Gem N = 196
ORR (95% CI)	27.6% (21.1–35.0)	41.8% (34.8–49.1)
DCR (95% CI)	45.3% (37.7–53.1)	73.5% (66.7–79.5)
CR	10.0%	10.7%
PR	17.6%	31.1%
SD	17.6%	31.6%
PD	37.6%	11.7%
Non-CR/non-PD	2.9%	5.1%
Non-evaluable or no assessment	14.1%	9.7%

Confirmed Response	Pembro N = 84	Carbo + Gem N = 89
ORR (95% CI)	29.8% (20.3–40.7)	46.1% (35.4–57.0)
DCR (95% CI)	48.8% (37.7–60.0)	73.0% (62.6–81.9)
CR	11.9%	18.0%
PR	17.9%	28.1%
SD	19.0%	27.0%
PD	36.9%	7.9%
Non-CR/non-PD	1.2%	5.6%
Non-evaluable or no assessment	13.1%	13.5%

Metastatic Urothelial Cancer conclusions

- First-line cisplatin-based chemotherapy for those who are cis-eligible then transition to avelumab maintenance whenever appropriate
- Platinum-eligible patients should remain to get chemotherapy then transition to avelumab maintenance whenever appropriate
- Pembrolizumab monotherapy should be limited to a select group of patients who are platinum-ineligible and those who are PD-L1 positive

GW ONCOLOGY UPDATE

Renal Cell Carcinoma

- **Renal**
  - Adjuvant Therapy
    - ASCO 2021 Plenary: Pembrolizumab versus placebo as post-nephrectomy adjuvant therapy for patients with renal cell carcinoma: Randomized, double-blind, phase III KEYNOTE-564 study (Toni Choueiri, MD)
  - First line mRCC
    - ASCO GU 2021 Abstract : Phase 3 trial of lenvatinib (LEN) plus pembrolizumab (PEMBRO) or everolimus (EVE) versus sunitinib (SUN) monotherapy as a first-line treatment for patients (pts) with advanced renal cell carcinoma (RCC) (CLEAR study). (Robert Motzer, MD)

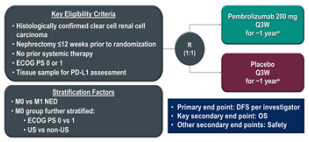
GW ONCOLOGY UPDATE

Keynote 564: Adjuvant pembrolizumab in high-risk RCC

Pembrolizumab vs Placebo as Post Nephrectomy Adjuvant Therapy for Patients with Renal Cell Carcinoma: Randomized, Double-Blind, Phase 3 KEYNOTE-564 Study

Toni K. Choueiri[1]; Piotr Tomczak[2]; Se Hoon Park[3]; Balaji Venugopal[4]; Thomas Ferguson[5]; Yen-Hwa Chang[6]; Jaroslav Hajek[7]; Stefan Symeonides[8]; Jae Lyun Lee[9]; Naveed Sarwar[10]; Antoine Thiery-Vuillemin[11]; Marine Gross-Goupil[12]; Mauricio Maha[13]; Noomi Haas[14]; Piotr Sawrycki[15]; Rodolfo F. Perini[16]; Pingyu Zhang[16]; Jaqueline Willemann-Rogerio[16]; Kentaro Imai[16]; David Quinn[17]; Thomas Powles[18]; on behalf of the KEYNOTE-564 investigators.

KEYNOTE-564 Study Design



GW ONCOLOGY UPDATE

Keynote 564: Adjuvant pembrolizumab in high-risk RCC

Prespecified Disease Risk Categories

Intermediate-High Risk		High Risk		M1 NED
pT2	pT3	pT4	Any pT	NED after resection of oligometastatic sites ≤1 year from nephrectomy
Grade 4 or sarcomatoid	Any grade	Any grade	Any grade	
N0	N0	N0	N+	
M0	M0	M0	M0	

Baseline Characteristics

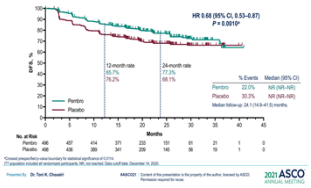
Characteristic, n (%)	Pembro N = 496	Placebo N = 498
Age, median (range), yrs	60 (27–81)	60 (25–84)
Male	347 (70.0)	359 (72.1)
ECOG PS		
0	421 (84.9)	426 (85.5)
1	75 (15.1)	72 (14.5)
Disease risk category		
M0 intermediate-high risk	427 (86.1)[a]	433 (86.9)
M0 high risk	40 (8.1)	36 (7.2)
M1 NED	29 (5.8)	29 (5.8)

Characteristic, n (%)	Pembro N = 496	Placebo N = 498
Geographic location		
North America	113 (26.8)	125 (25.1)
European Union	188 (37.9)	187 (37.6)
Rest of the world	175 (35.3)	186 (37.3)
PD-L1 status[b]		
CPS <1	124 (25.0)	113 (22.7)
CPS ≥1	365 (73.6)	383 (76.9)
Missing	7 (1.4)	2 (0.4)
Sarcomatoid features		
Present	52 (10.5)	59 (11.8)
Absent	417 (84.1)	415 (83.3)
Unknown	27 (5.4)	24 (4.8)

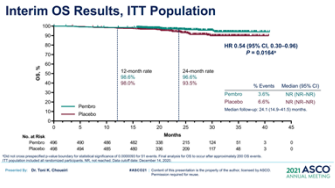
GW ONCOLOGY UPDATE

Keynote 564: Adjuvant pembrolizumab in high-risk RCC

DFS by Investigator, ITT Population



Interim OS Results, ITT Population



2021 ASCO ANNUAL MEETING

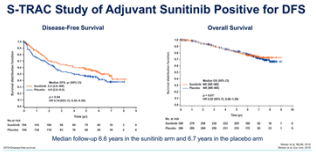
GW ONCOLOGY UPDATE

Adjuvant therapy has been negative except for sunitinib in the S-TRAC trial

Adjuvant Targeted Therapy with Mixed Results

Trial	Arms	Years	N	Primary Endpoint	Clear Cell Only	Eligibility	Hazard Ratio Confidence Interval
ASSURE	Sunitinib vs. Sorafenib vs. Placebo*	1	1943	DFS	No	pT1bG3-4N0, pT2-4N+M0, TxGxN+	Sunitinib – 1.02 (97.5% CI 0.85-1.23) Sorafenib – 0.97 (97.5% CI 0.80-1.17)
STRAC	Sunitinib vs. Placebo	1	615	DFS	Yes	pT3-4bN0M0 x TxG4N1-2	0.70 (95% CI 0.59-0.98)
PROTECT	Pazopanib vs. Placebo*	1	1538	DFS	Yes	p12G3-4N0, pT3-4N0, pTxN1	0.96 (95% CI 0.70-1.06)
ATLAS	Axitinib vs. Placebo	1-3	724	DFS	Yes	pT2-4GxN0, pTxN1	0.870 (95% CI 0.66-1.147)
SORCE	Sorafenib vs. Placebo*	1-3	1711	DFS	No	Leibovich score 3-11	1.01 (95% CI 0.83-1.23)
EVEREST	Everolimus vs. Placebo	1	1545	RFS	No	pT1bG3-4N0, pT2-4N1	Pending

S-TRAC Study of Adjuvant Sunitinib Positive for DFS



FDA approves sunitinib malate for adjuvant treatment of renal cell carcinoma

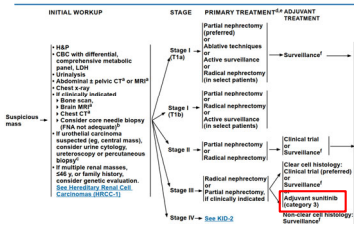
Presented by Dr. Rana McKay; ASCO Annual Meeting 2021

GW ONCOLOGY UPDATE

Conclusions: Adjuvant therapy for Renal Cell Cancer

- Adjuvant therapy is very promising
  - Met primary endpoint of DFS; overall survival not met (though not primary endpoint)
  - M1 NED population – E2810 adjuvant pazopanib negative*
  - Await regulatory approval for widespread use

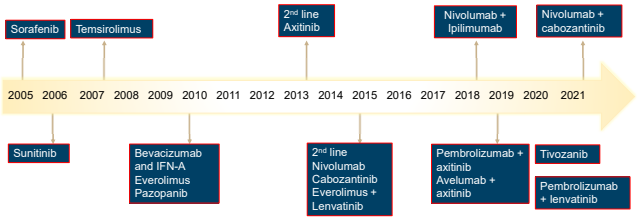
NCCN Guidelines Version 1.2022
Kidney Cancer



*Appleman L et al., *J Clin Oncol* 2019: 37, no. 15_suppl : 4502-4502.

GW ONCOLOGY UPDATE

Evolving Landscape of mRCC Treatment



www.eau2021.org

European Association of Urology

Presented by: Jeanny B. Aragon-Ching, MD, FACP

EAU21 VIRTUAL 8-12 July

GW ONCOLOGY UPDATE

Results for IO/TKI combination

ORIGINAL ARTICLE

Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

T.K. Choueiri, T. Powles, M. Burotto, B. Escudier, M.T. Bourlon, B. Zurawski, V.M. Oyervides Juárez, J.J. Hsieh, U. Basso, A.Y. Shah, C. Suárez, A. Hamzaj, J.C. Goh, C. Barrios, M. Richardet, C. Porta, R. Kowalyszyn, J.P. Feregrino, J. Zolnierek, D. Pook, E.R. Kessler, Y. Tomita, R. Mizuno, J. Bedke, J. Zhang, M.A. Maurer, B. Simsek, F. Ejzykowicz, G.M. Schwab, A.B. Apolo, and R.J. Motzer, for the CheckMate 9ER Investigators*

FDA approves nivolumab plus cabozantinib for advanced renal cell carcinoma

January 22, 2021

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 8, 2021 VOL. 384 NO. 14

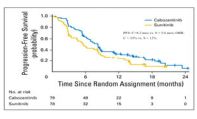
Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma

R. Motzer, B. Alekseev, S.-Y. Rha, C. Porta, M. Eto, T. Powles, V. Grünwald, T.E. Hutson, E. Kopyltsov, M.J. Méndez-Vidal, V. Kozlov, A. Alyasova, S.-H. Hong, A. Kapoor, T. Alonso Gordoa, J.R. Merchan, E. Winquist, P. Maroto, J.C. Goh, M. Kim, H. Gurney, V. Patel, A. Peer, G. Procopio, T. Takagi, B. Melichar, F. Rolland, U. De Giorgi, S. Wong, J. Bedke, M. Schmidinger, C.E. Dutcus, A.D. Smith, L. Dutta, K. Mody, R.F. Perini, D. Xing, and T.K. Choueiri, for the CLEAR Trial Investigators*

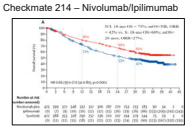
GW ONCOLOGY UPDATE

Results from 1st line mRCC trials

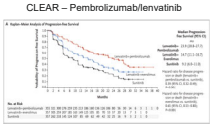
CABOSUN - Cabozantinib



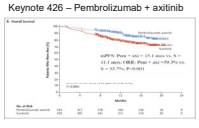
Checkmate 214 – Nivolumab/Ipilimumab



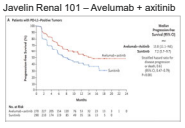
CLEAR – Pembrolizumab/lenvatinib



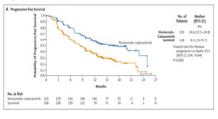
Keynote 426 – Pembrolizumab + axitinib



Javelin Renal 101 – Avelumab + axitinib



Checkmate 9ER – Nivolumab + cabozantinib



Choueiri T et al., *J Clin Oncol* 35:591-597; Motzer R et al., *Lancet Oncol* 2019: 1370–85; Motzer R et al., *N Engl J Med* 2021;384:1289-300; Rini B et al., *N Engl J Med* 2019;380:1116-27; Motzer R et al., *N Engl J Med* 2019;380:1103-15; Choueiri T et al., *N Engl J Med* 2021;384:829-41

Presented by: Jeanny B. Aragon-Ching, MD, FACP

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Efficacy of first line mRCC trials

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Trial	Phase of trial/MOA	Arms of therapy (n) Primary endpoint	Overall Responses (ORR) in active arm	Endpoints/ Responses	Comments
CABOSUN	Phase II/ TKI	Cabozantinib vs Sunitinib (n = 157) PFS primary endpoint	33%	PFS: C=8.2 mos vs. S = 5.6 mos;	US FDA-approved 12/19/17 for first-line advanced RCC
Checkmate 214	Phase III/ PD-L1 and CTLA-4 inhibitor	Nivolumab + Ipilimumab then Nivolumab vs. sunitinib (n =1096) Int/Poor risk OS	41.9%	N/I: 18-mo OS = 75%; mOS=NR; ORR = 42% vs. S: 18-mo OS=60%; mOS= 26 mos; ORR=27%;	US FDA approved on 4/16/18 for intermediate and poor-risk
JAVELIN Renal 101	Phase III/ PD-L1 + TKI	Avelumab + Axitinib vs. sunitinib (n = 886) PFS in PD-L1 +	55.2%	mPFS: Ave + axi = 13.8 mos vs. S = 7.2 mos	FDA approved on 5/14/19 for front-line treatment advanced RCC
Checkmate 9ER	Phase III/ PD-L1 + VEGF TKI	Nivolumab + cabozantinib vs sunitinib (n=651) PFS	55.7%	mPFS N/C = 16.6 mos vs S = 8.3 mos	FDA approved on 1/20/21 for advanced RCC
KEYNOTE-426	Phase III/ PD-1 + TKI	Pembrolizumab + axitinib vs. sunitinib (n = 840) PFS, OS	59.3%	mPFS: Pem + axi = 15.1 mos vs. S = 11.1 mos;	FDA approved on 4/19/19 for first-line treatment advanced RCC
KEYNOTE-581/ CLEAR	Phase III/ PD-1 + TKI	Pembrolizumab + lenvatinib vs. everolimus + lenvatinib vs. sunitinib (n = 735) PFS	Len + Pembro: 71.0%; Len + Eve: 53.5%	PFS: Len + P = 23.9 mos vs S = 9.2 mos; Len + eve = 14.7 mos vs. S = 9.2 mos; OS = Len + P vs S HR = 0.66;	Not FDA approved yet

VEGF = vascular endothelial growth factor; TKI = tyrosine kinase inhibitor; PD-1 = programmed cell death protein 1; PD-L1 = programmed death-ligand 1; n = number; q = every; BID = twice a day; ORR = objective response rate; OS = Overall survival; PFS = progression-free survival; mPFS = median PFS; mOS = median OS; ITT = intention-to-treat population; mos = months; AE = adverse event; DCR = disease control rate; Ave = avelumab; Axi = axitinib; BICR = Blinded Independent central review; S = sunitinib; N = Nivolumab; I = ipilimumab; C = cabozantinib; Len = Lenvatinib; Pem = pembrolizumab; eve = everolimus; Abeza = atezolizumab;

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Common toxicities from first line mRCC trials

	mRCC first line trials									
	Checkmate 214: Nivolumab + Ipilimumab (N=547)		Checkmate 9ER: Nivolumab + cabozantinib (N=320)		CLEAR: Lenvatinib + pembrolizumab (N=355)		Keynote 426: Pembrolizumab + Axitinib (N=426)		Javelin Renal 101: Avelumab + Axitinib (N=434)	
All TRAEs, %	All grades	Grade 3-4	All grades	Grade 3-4	All grades	Grade 3-4	All grades	Grade 3-4	All grades	Grade 3-4
Fatigue	37.8%	4.4%	32.2%	3.4%	40.1%	4.3%	38.5%	2.8%	36%	3 (0)
Increased ALT	6.0%	4.0%	28.1%	5.3%	NR	NR	26.8%	13.3%	13%	4 (1)
Hand-foot syndrome	<1%	<1%	40.0%	7.5%	28.7%	4.0%	28.0%	5.1%	33%	6 (0)
Nausea	20.1%	1.5%	26.6%	0.6%	25.8%	2.6%	27.7%	0.9%	25%	1 (0)
Diarrhea	24.0%	4.0%	63.8%	6.9%	61.4%	9.7%	54.3%	9.1%	54%	5 (0)
Decreased appetite	13.9%	1.3%	13.9%	1.3%	40.3%	4.0%	29.6%	2.8%	20%	2 (0)
TRAEs leading to discontinuation (d/c) of Treatment	22%		19.7%; Nivo: 6.6%; Cabo : 7.5%; Nivo +Cabo: 5.6%		37.2%; Len: 25.6%; Pembro: 28.7%; Len + Pembro: 13.4%		d/c of either drug: 30.5%; d/c both drugs = 10.7%;		4.0%	
TRAEs leading to death	1%		<1%		n = 15		2.6%		1.0%	

Presented by: Jeanny B. Aragon-Ching, MD, FACP

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HRQoL Summary of Randomized Phase 3 First-Line Combination Studies in cc Renal Cell Carcinoma

	CHECKMATE-214[1]		KEYNOTE-426[2]		CHECKMATE-9ER[3]		CLEAR[4]			
	N=847		N=861		N=651		N=1069			
HRQoL Tools	Nivolumab + Ipilimumab	vs. Sunitinib	Axitinib + Pembrolizumab	vs. Sunitinib	Cabozantinib + Nivolumab	vs. Sunitinib	Lenvatinib + Pembrolizumab	vs. Sunitinib	Lenvatinib + Everolimus	vs. Sunitinib
	Intermediate and Poor Risk Only		All Risk Groups		*All Risk Groups		All Risk Groups			
FKSI-19	✓				✓					
FKSI-DRS			=				=		=	
EORTC QLQ-C30			=				=		=	
FACT-G	✓									
EQ-5D-3L	✓		=		✓		=		=	

Andrea B. Apolo, MD @apolo_andrea

1. *Lancet Oncol* 2019; 20: 297–310; 2. Bedke J. et al., 35th Annual EAU Congress -July 2020 (via https://www.urotoday.com) 3. Cella D et al., *JCO* 39, no. 6_suppl (February 20, 2021) 285; 4. Motzer R et al., *JCO* 39, 2021 (suppl 15; abstr 4502).

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Conclusions: metastatic Renal Cell Cancer

- First-line metastatic RCC treatment is rapidly evolving
- Determination of IMDC risk groups that would dictate choice of first-line therapy
- Choice remains to be IO/IO or IO/TKI combinations

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NCCN Guidelines Version 1.2022
Kidney Cancer

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PRINCIPLES OF SYSTEMIC THERAPY FOR RELAPSE OR STAGE IV DISEASE

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)

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Thank you!

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