Update on Immunotherapy in metastatic Bladder Cancer

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Disclosures

- Speaker Bureau: Pfizer, J&J, Sanofi, Novartis, MSD
- Advisory Board/ Consultant: GSK, Novartis, Bayer, J&J, Mundipharma, Astellas, MSD, BMS
- Research support: Sanofi, J&J, Astellas

Outline

- Current standard
- Immunotherapy in mBC
- Clinical Trials
- Summary (Come Monday)

Current Standard

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2017
Bladder Cancer

NCCN Guidelines Index
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Discussion

PRINCIPLES OF SYSTEMIC THERAPY

First-line chemotherapy for locally advanced or metastatic disease

	Standard regimens	Alternate regimens for select patients
Cisplatin eligible	• Gemcitabine and cisplatin[4] (category 1) • DDMVAC with growth factor support (category 1)[2,8]	
Cisplatin ineligible	• Gemcitabine and carboplatin[11] • Atezolizumab[12]	• Gemcitabine[13] • Gemcitabine and paclitaxel[14] • Ifosfamide, doxorubicin, and gemcitabine[15] (for patients with good kidney function and good PS)

- The presence of both visceral metastases and ECOG performance score ≥2 strongly predict poor outcome with chemotherapy. Patients without these adverse prognostic factors have the greatest benefit from chemotherapy.
- For most patients, the risks of adding paclitaxel to gemcitabine and cisplatin outweigh the limited benefit seen in the randomized trial.[16]
- A substantial proportion of patients cannot receive cisplatin-based chemotherapy due to renal impairment or other comorbidities.
  - Participation in clinical trials of new or more tolerable therapy is recommended.

Subsequent systemic therapy for locally advanced or metastatic disease

- Participation in clinical trials of new agents is recommended.

Standard regimens	Alternate regimens for select patients
• Pembrolizumab (category 1)[17] • Atezolizumab[18] • Nivolumab[19] • Durvalumab[20]	• Nab-paclitaxel[23] • Ifosfamide[24] • Methotrexate • Ifosfamide, doxorubicin, and gemcitabine[15]
• Paclitaxel or docetaxel[21] • Gemcitabine[13] • Pemetrexed[22]	• Gemcitabine and paclitaxel[14] • Gemcitabine and cisplatin[4] • DDMVAC[2]

Continued on BL-G 3 of 4
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IMvigor 210, a Phase II trial of Atezolizumab (MPDL3280A) in Platinum-treated Locally Advanced or Metastatic Urothelial Carcinoma (mUC)

Jean Hoffman-Censits,[1] Petros Grivas,[2] Michiel S. van der Heijden,[3] Robert Dreicer,[4] Yohann Loriot,[5] Margitta Retz,[6] Nicholas J. Vogelzang,[7] Jose Luis Perez-Gracia,[8] Arash Rezazadeh Kalebasty,[9] Sergio Bracarda,[10] Evan Y. Yu,[11] Christopher Hoimes,[12] Joaquim Bellmunt,[13] David I. Quinn,[14] Daniel P. Petrylak,[15] Syed A. Hussain,[16] Na Cui,[17] Sanjeev Mariathasan,[17] Oyewale Abidoye,[17] Jonathan E. Rosenberg[18]

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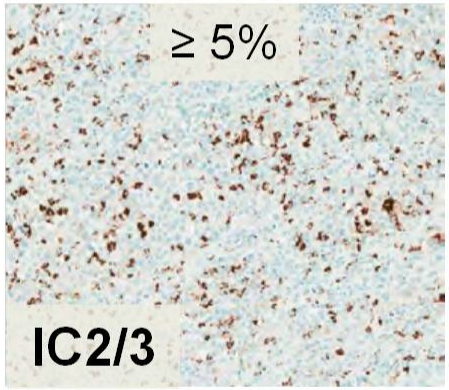
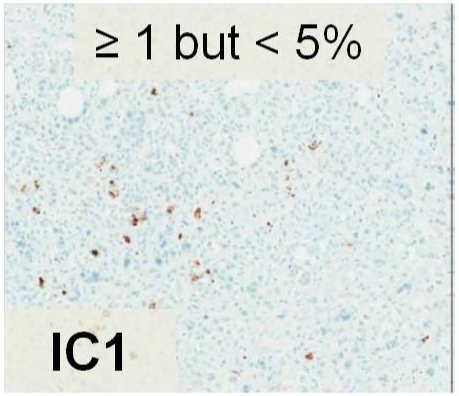
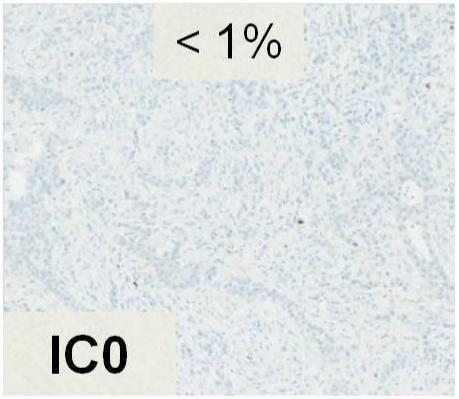
Presented By Jean Hoffman-Censits at Genitourinary Cancers Symposium 2016

IMvigor 210: PD-L1 Immune Cell Expression (IHC)

- PD-L1 expression on IC was evaluated with the VENTANA SP142 IHC assay based on 3 scoring levels: IC2/3 (≥ 5%), IC1 (≥ 1 but < 5%), IC0 (< 1%)[1]







Images at 10x magnification.

Reference: 1. Rosenberg JE, et al. ECC 2015 [abstract 21LBA].

Presented By Jean Hoffman-Censits at Genitourinary Cancers Symposium 2016

IMvigor 210: Responses to Atezolizumab

	IC2/3 (n = 100)	IC1/2/3 (n = 207)	All (N = 310)	IC1 (n = 107)	IC0 (n = 103)
ORR (95% CI) per confirmed IRF RECIST v1.1	26% (18, 36)	18% (13, 24)	15% (11, 19)	10% (5, 18)	8% (3, 15)
ORR (95% CI) per investigator mRECIST	27% (19, 37)	22% (16, 28)	19% (15, 24)	17% (10, 25)	13% (7, 21)
Complete response (CR) per confirmed IRF RECIST v1.1	11%	6%	5%	2%	2%

- Higher ORR was associated with higher PD-L1 IHC status, but responses were seen in all PD-L1 subgroups

Objective response evaluable population: all treated patients had measurable disease at baseline per investigator-assessed RECIST v1.1.
Data cutoff: September 14, 2015.

Presented By Jean Hoffman-Censits at Genitourinary Cancers Symposium 2016

IMvigor 210: Phase II Atezolizumab in mUC Conclusions

- This primary analysis of cohort 2 demonstrated that atezolizumab has the potential to change the standard of care in mUC:
  - ORRs represented clinical improvements over a historical 10% ORR
    - Higher PD-L1 IC status was associated with higher ORR, but low expression did not preclude response
    - mDOR was not reached in any pre-defined PD-L1 or poor prognostic subgroup
  - mOS was 11.4 months in IC2/3 patients and 6.7 months in IC0/1 patients
  - Atezolizumab was well tolerated with a low rate of treatment-related Grade 3-4 toxicities and no treatment-related Grade 5 AEs
- Ongoing studies in the atezolizumab UC clinical development program include:
  - 2 randomized Ph III studies in adjuvant MIBC (NCT02450331) and mUC (NCT02302807)
  - An expanded access study (NCT02589717) for patients with mUC who experience disease progression post platinum chemotherapy

IMvigor 210: Outline

- Current standard
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Accelerated approval Atezolizumab

- Azetolizumab (Tecentriq) approved to treat patients with urothelial carcinoma whose disease has worsened during or following platinum-containing chemotherapy, or within 12 months of receiving platinum containing chemotherapy, either before or after surgical treatment.

- PII single arm (n=310) with locally advanced or metastatic urothelial carcinoma. ORR 15%. ORR PD-L1+ 29%, PD-L1- 10%

- Approved with Ventana PD-L1 assay to detect PD-L1 IC staining

Accelerated approval for Nivolumab

News & Perspective > Medscape Medical News > FDA Approvals

FDA Approves Nivolumab for Bladder Cancer

Nick Mulcahy

DISCLOSURES | February 02, 2017

The US Food and Drug Administration (FDA) today approved nivolumab (*Opdivo*, Bristol-Myers Squibb) for the treatment of patients with locally advanced or metastatic urothelial carcinoma whose disease has progressed during a period of up to 1 year after first-line platinum-containing chemotherapy.

The accelerated approval makes nivolumab, which is a programmed cell death receptor–1 inhibitor, the second immunotherapy approved in this setting in the past year. The agency approved atezolizumab (*Tecentriq*, Genentech/Roche), which acts as a programmed cell death ligand–1 inhibitor, in May 2016.

Both nivolumab and atezolizumab received an accelerated approval on the basis of response rates; data on other outcomes, including survival, are awaited.

Accelerated approval for Durvalumab

FDA Approves Imfinzi (Durvalumab) for Bladder Cancer

May 2, 2017

The US Food and Drug Administration (FDA) has approved the immunotherapy drug Imfinzi (durvalumab) to treat people with advanced urothelial carcinoma, the most common type of bladder cancer. The new drug is approved for use in people who have already had chemotherapy.

Imfinzi is part of a new class of immunotherapy drugs called checkpoint inhibitors. It's the third checkpoint inhibitor to be approved for bladder cancer. This drug, given as an infusion, targets the PD-L1 protein, which some cancer cells use to evade the immune system. By blocking PD-L1, it helps immune cells recognize and attack cancer cells.

The FDA also approved a test to check for levels of the PD-L1 protein.

Accelerated approval for Avelumab

Avelumab: Another Immunotherapy for Bladder Cancer

Zosia Chustecka
May 09, 2017

Another immunotherapy has been approved for use in urothelial cancer, the most common type of bladder cancer, in the United States.

Avelumab (*Bavencio*, EMD Serono INc), which is a programmed cell death ligand–1 (PD L1) inhibitor, has been approved for second-line use in patients with locally advanced or metastatic urothelial carcinoma whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Avelumab was recently approved for the first time worldwide for use in the treatment of Merkel cell carcinoma, a rare and aggressive type of skin cancer.

The new drug joins three similar immunotherapies already approved for similar indications, and experts have said that immunotherapy is already "altering the landscape" for the treatment of bladder cancer.

Is it really making a difference?

FDA

DRUG INFO ROUNDS

ACCELERATED APPROVAL PROGRAM

Was the accelerated approval too early?

Atezolizumab Falls Short in Phase III Bladder Cancer Trial

Jason M. Broderick @jasoncology
Published Online: Wednesday, May 10, 2017

Sandra Horning, MD

Atezolizumab (Tecentriq) missed the phase III IMvigor211 trial's primary endpoint of improving overall survival (OS) in the second-line setting for patients with locally advanced or metastatic urothelial carcinoma (mUC), according to Genentech, the manufacturer of the PD-L1 inhibitor.

The IMvigor211 study was intended to confirm the findings of the phase II IMvigor210 study, on which the FDA based its May 2016 accelerated approval of atezolizumab as a treatment for patients with locally

Keynote 045

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ORIGINAL ARTICLE

Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma

Joaquim Bellmunt, M.D., Ph.D., Ronald de Wit, M.D., Ph.D., David J. Vaughn, M.D., Yves Fradet, M.D., Jae-Lyun Lee, M.D., Ph.D., Lawrence Fong, M.D., Nicholas J. Vogelzang, M.D., Miguel A. Climent, M.D., Daniel P. Petrylak, M.D., Toni K. Choueiri, M.D., Andrea Necchi, M.D., Winald Gerritsen, M.D., Ph.D., Howard Gurney, M.D., David I. Quinn, M.D., Ph.D., Stéphane Culine, M.D., Ph.D., Cora N. Sternberg, M.D., Yabing Mai, Ph.D., Christian H. Poehlein, M.D., Rodolfo F. Perini, M.D., and Dean F. Bajorin, M.D., for the KEYNOTE-045 Investigators*

N Engl J Med 2017; 376:1015-1026 | March 16, 2017 | DOI: 10.1056/NEJMoa1613683

KEYNOTE-045: Study Design

Key Eligibility Criteria

- Urothelial carcinoma of the renal pelvis, ureter, bladder, or urethra
- Transitional cell predominant
- PD after platinum-based chemo for advanced disease or recurrence within 12 mo of perioperative platinum-based therapy for localized muscle-invasive disease
- ECOG PS 0-2
- Provision of tumor sample for biomarker assessment

Stratification Factors

- ECOG PS (0/2 vs 2)
- Hemoglobin level (<10 vs ≥10 g/dL)
- Liver metastases (yes vs no)
- Time from last chemotherapy dose (<3 vs ≥3 mo)

R (1:1)
N=542

n=270

Pembrolizumab
200 mg IV Q3W
For 2 years

n=272

Paclitaxel 175 g/m^2 Q3W
OR
Docetaxel 75 mg/m^2 Q3W
OR
Vinflunine 320 mg/m^2 Q3W

Key End Points

Primary: OS and PFS in total and PD-L1 CPS ≥10% populations

Secondary: OR and DOR in total and PD-L1 CPS ≥10% populations; safety in total population

CPS = combined positive score; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; IV = intravenous; OS = overall survival; PD = progressive disease; PD-L1 = programmed death ligand 1; PFS = progression-free survival; PS = performance status; Q3W – every 3 weeks; R = randomization.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-045: Baseline Characteristics

Characteristic	Pembrolizumab Group (N=270)	Chemotherapy Group (N=272)
Age — yr		
Median	67	65
Range	29–88	26–84
Male sex — no. (%)	200 (74.1)	202 (74.3)
ECOG performance-status score — no. (%)†		
0	119 (44.1)	106 (39.0)
1	143 (53.0)	158 (58.1)
2	2 (0.7)	4 (1.5)
Missing data	6 (2.2)	4 (1.5)
Current or former smoker — no./total no. (%)	165/269 (61.3)	186/269 (69.1)
Pure transitional-cell features in histologic testing — no./total no. (%)	186/270 (68.9)	197/270 (73.0)
Tumor PD-L1 combined positive score ≥10% — no./total no. (%)‡	74/260 (28.5)	90/266 (33.8)
Site of primary tumor in bladder or urethra — no./total no. (%)	232/270 (85.9)	234/271 (86.3)
Visceral disease — no./total no. (%)	240/269 (89.2)	233/271 (86.0)
Liver metastases — no./total no. (%)	91/270 (33.7)	95/271 (35.1)
Hemoglobin concentration <10 g/dl — no./total no. (%)	43/262 (16.4)	44/267 (16.5)
No. of risk factors — no. (%)§		
0	54 (20.0)	44 (16.2)
1	96 (35.6)	97 (35.7)
2	66 (24.4)	80 (29.4)
3 or 4	45 (16.7)	45 (16.5)
Missing data	9 (3.3)	6 (2.2)
Completion or discontinuation of most recent therapy <3 mo previously — no./total no. (%)	103/269 (38.3)	104/271 (38.4)

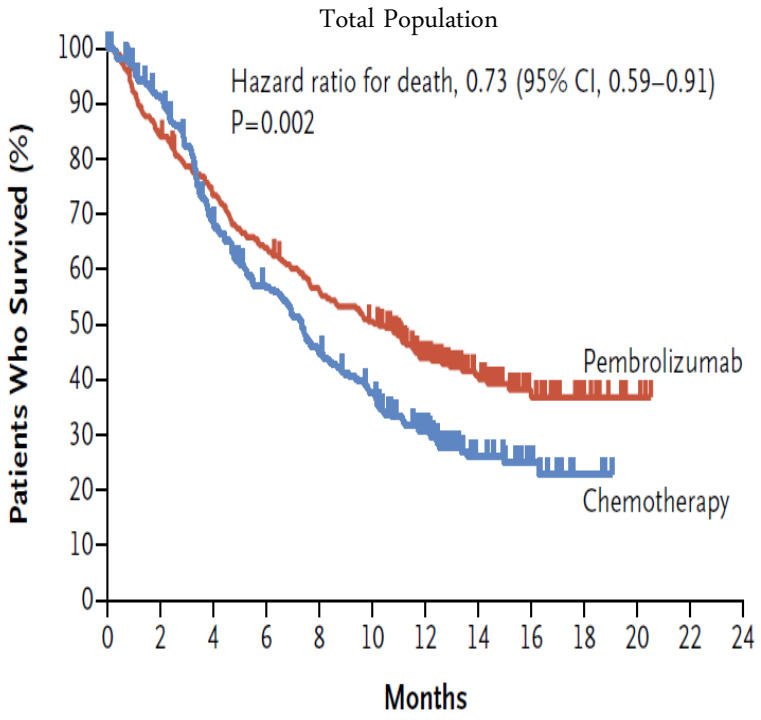
† ECOG PS scores range from 0 to 5, with 0 indicating no symptoms and higher scores indicating greater disability.
‡ PD-L1 CPS: the percentage of tumor and infiltrating immune cells with PD-L1 expression out of the total number of tumor cells.
§ Risk factors include the Bellmunt risk factors: ECOG PS score >0; hemoglobin concentration <10 g/dL; presence of liver metastases,[2] plus time since the completion/discontinuation of previous therapy <3 mo.[3]
CPS = combined positive score; ECOG = Eastern Cooperative Oncology Group; PD-L1 = programmed death ligand 1; PS = performance status.
1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print]; 2. Bellmunt J, et al. *J Clin Oncol*. 2010;28:1850-1855; 3. Sonpavde G, et al. *Eur Urol*. 2013;63:717-723.

KEYNOTE-045: Baseline Characteristics (contd.)

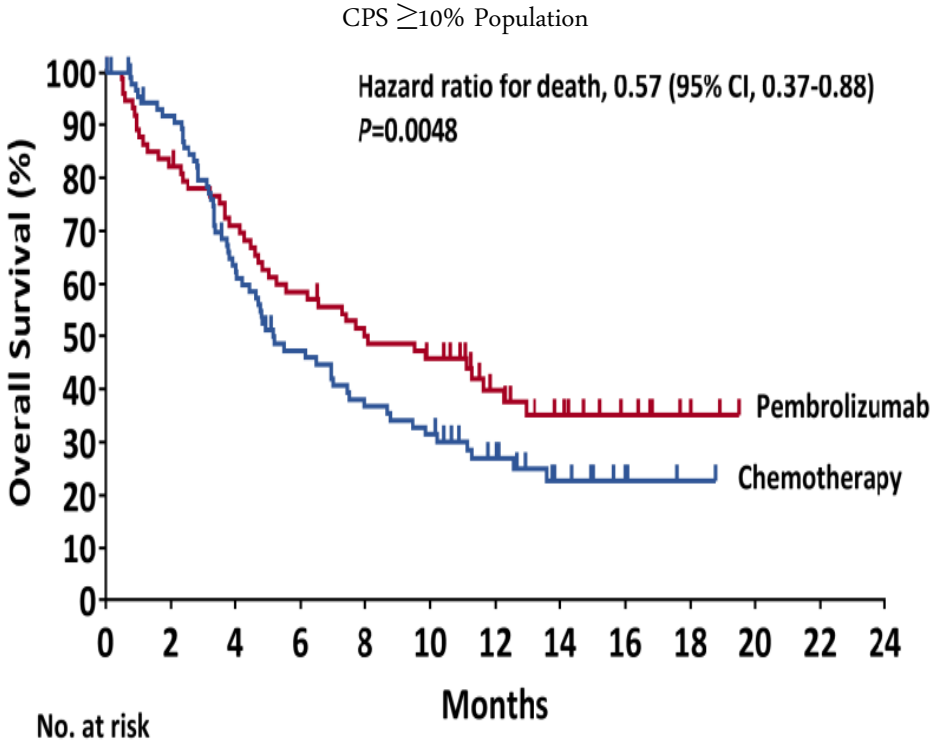
	Pembrolizumab Group (N=270)	Chemotherapy Group (N=272)
Setting of most recent prior therapy,‡‡ no. (%)		
Neoadjuvant or adjuvant	31 (11.5)	53 (19.5)
First line	183 (67.8)	157 (57.7)
Second line	55 (20.4)	60 (22.1)
Time since completion or discontinuation of most recent prior therapy,§§ no. (%)		
<3 months	103 (38.1)	104 (38.2)
≥3 months	166 (61.5)	167 (61.4)
Prior platinum,§§ no. (%)		
Cisplatin	198 (73.3)	213 (78.3)
Carboplatin	70 (25.9)	56 (20.6)
Oxaliplatin or nedaplatin	1 (0.4)	2 (0.7)
Prior cystectomy or nephroureterectomy, no. (%)	61 (22.6)	51 (18.8)
Prior Bacillus Calmette–Guérin therapy, no. (%)	32 (11.9)	22 (8.1)

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-045: Overall Survival



No. at Risk													
Pembrolizumab	270	226	194	169	147	131	87	54	27	13	4	0	0
Chemotherapy	272	232	171	138	109	89	55	27	14	3	0	0	0

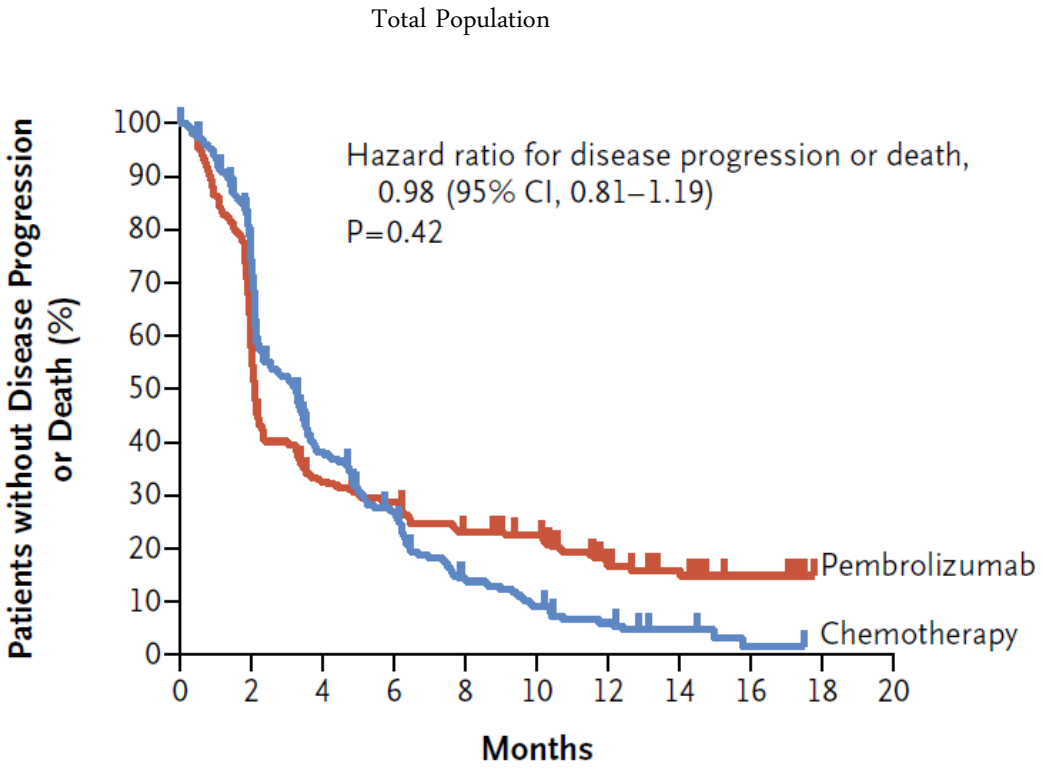


No. at risk													
Pembrolizumab	74	60	51	42	35	31	18	12	7	3	0	0	0
Chemotherapy	90	76	51	36	28	24	16	8	4	1	0	0	0

CI = confidence interval; CPS = combined positive score.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

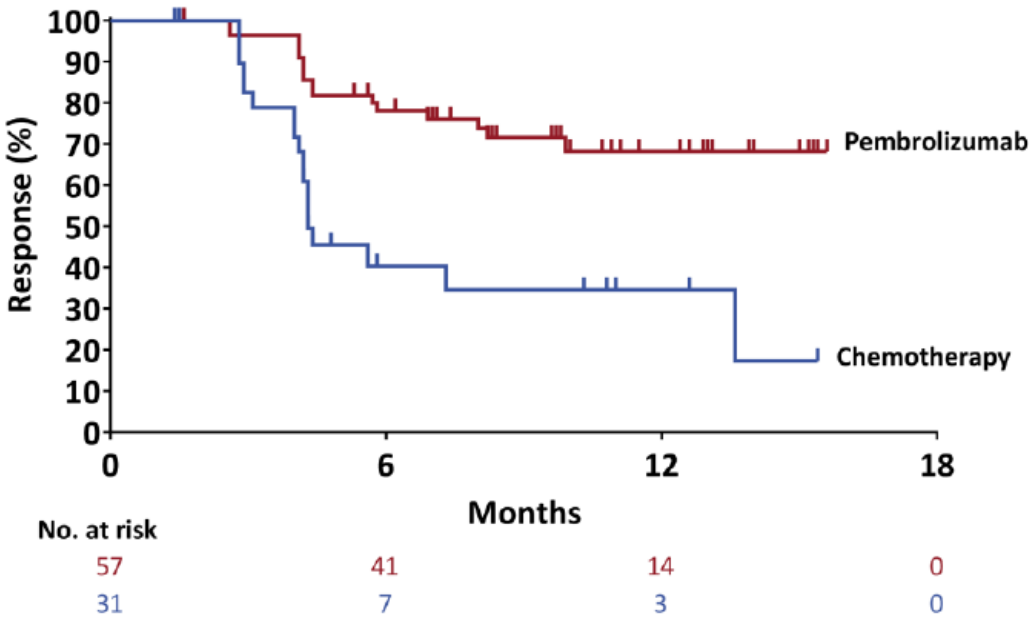
KEYNOTE-045: Progression-Free Survival



CI = confidence interval.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

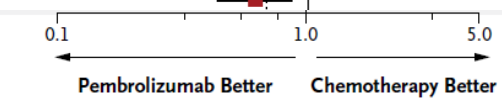
KEYNOTE-045: Duration of Response



1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-045: Overall Survival in Key Subgroups

Subgroup	No. of Deaths/ No. of Patients	Hazard Ratio (95% CI)
Overall	334/542	0.73 (0.59–0.91)
Age		
<65 yr	149/230	0.75 (0.53–1.05)
≥65 yr	185/312	0.76 (0.56–1.02)
Sex		
Male	246/402	0.73 (0.56–0.94)
Female	88/140	0.78 (0.49–1.24)
ECOG performance-status score		
0 or 1	323/526	0.74 (0.59–0.92)
2	5/6	0.43 (0.04–4.20)
Smoking status		
Current	43/67	0.32 (0.15–0.68)
Former	170/284	0.71 (0.52–0.97)
Never	118/187	1.06 (0.72–1.55)
Histologic type		
Transitional cell	240/383	0.80 (0.62–1.04)
Mixed	93/155	0.58 (0.37–0.89)
Tumor PD-L1 combined positive score, 1% cutoff		
<1%	184/298	0.89 (0.66–1.20)
≥1%	142/230	0.61 (0.43–0.86)
Tumor PD-L1 combined positive score, 10% cutoff		
<10%	222/362	0.80 (0.61–1.05)
≥10%	104/164	0.57 (0.37–0.88)
Location of primary tumor		
Upper tract	48/75	0.53 (0.28–1.01)
Lower tract	286/466	0.77 (0.60–0.97)
Location of metastases		
Lymph node only	22/67	0.46 (0.18–1.21)
Visceral disease	312/473	0.75 (0.60–0.95)
Liver metastases		
Yes	145/186	0.85 (0.61–1.20)
No	189/355	0.67 (0.50–0.89)



CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; PD-L1 = programmed death ligand 1.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-045: Exposure, AE Summary, and Treatment-Related AEs With Incidence ≥10%1a

Event	Pembrolizumab Group (N=266)		Chemotherapy Group (N=255)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Treatment-related event†				
Any event	162 (60.9)	40 (15.0)	230 (90.2)	126 (49.4)
Event leading to discontinuation of treatment	15 (5.6)	12 (4.5)	28 (11.0)	16 (6.3)
Event leading to death	4 (1.5)	4 (1.5)	4 (1.6)	4 (1.6)
Event occurring in ≥10% of patients in either group‡				
Pruritus	52 (19.5)	0	7 (2.7)	1 (0.4)
Fatigue	37 (13.9)	3 (1.1)	71 (27.8)	11 (4.3)
Nausea	29 (10.9)	1 (0.4)	62 (24.3)	4 (1.6)
Diarrhea	24 (9.0)	3 (1.1)	33 (12.9)	2 (0.8)
Decreased appetite	23 (8.6)	0	41 (16.1)	3 (1.2)
Asthenia	15 (5.6)	1 (0.4)	36 (14.1)	7 (2.7)
Anemia	9 (3.4)	2 (0.8)	63 (24.7)	20 (7.8)
Constipation	6 (2.3)	0	52 (20.4)	8 (3.1)
Peripheral sensory neuropathy	2 (0.8)	0	28 (11.0)	5 (2.0)
Neutrophil count decreased	1 (0.4)	1 (0.4)	36 (14.1)	31 (12.2)
Peripheral neuropathy	1 (0.4)	0	27 (10.6)	2 (0.8)
Neutropenia	0	0	39 (15.3)	34 (13.3)
Alopecia	0	0	96 (37.6)	2 (0.8)

AE = adverse event.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-045: Safety Events of Interest

Event	Pembrolizumab Group (N = 266)		Chemotherapy Group (N = 255)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Event of interest‖				
Any event	45 (16.9)	12 (4.5)	19 (7.5)	4 (1.6)
Hypothyroidism	17 (6.4)	0	3 (1.2)	0
Hyperthyroidism	10 (3.8)	0	1 (0.4)	0
Pneumonitis	11 (4.1)	6 (2.3)	1 (0.4)	0
Colitis	6 (2.3)	3 (1.1)	1 (0.4)	0
Infusion reaction	2 (0.8)	0	10 (3.9)	0
Nephritis	2 (0.8)	2 (0.8)	0	0
Severe skin reaction	2 (0.8)	1 (0.4)	3 (1.2)	3 (1.2)
Thyroiditis	2 (0.8)	0	0	0
Adrenal insufficiency	1 (0.4)	1 (0.4)	0	0
Myositis	0	0	1 (0.4)	1 (0.4)

AE = adverse event.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-045: Summary

- Pembrolizumab significantly improved OS over chemotherapy in patients with advanced urothelial carcinoma following first-line platinum-based therapy
  - HR 0.73, P=0.0022
  - OS benefit observed in all PD-L1 populations
- No significant difference in PFS between pembrolizumab and chemotherapy (P=0.42)
- ORR significantly higher and responses more durable with pembrolizumab
  - ORR 21.1% with pembrolizumab vs 11.4% with chemotherapy (P=0.001)
- Lower incidence of treatment-related AEs of any grade (60.9% vs 90.2%) and grade 3-5 severity (15.0% vs 49.4%) with pembrolizumab

AE = adverse event; Hr = hazard ratio; OS = overall survival; PD-L1 = programmed death ligand 1.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-045: Conclusions

- Pembrolizumab demonstrated OS improvement compared with chemotherapy in patients with advanced urothelial carcinoma after failure of platinum-based therapy
- Pembrolizumab benefit is observed regardless of PD-L1 expression

OS = overall survival; PD-L1 = programmed death ligand 1.

1. Bellmunt J, et al. *N Engl J Med*. 2017; February 17 [Epub ahead of print].

KEYNOTE-052

Presented at ASCO GU 2017, Poster 284

Baseline Characteristics & Disease Characteristics (N=370)[1]

- Of 541 patients screened, 370 were enrolled and received ≥1 dose of pembrolizumab
  - 307 patients were enrolled for ≥4 months before the data cutoff, and thus had the opportunity for at least 2 postbaseline scans
- Overall, patients were representative of a cisplatin-ineligible population

Characteristic, n (%)	Total Population
Age, median (range), years	74 (34-94)
≥80 years	107 (29)
Male	286 (77)
ECOG performance status†	
0	80 (22)
1	133 (36)
2	156 (42)
Primary tumor location‡	
Upper tract	69 (19)
Lower tract	300 (81)
Metastases location§	
Lymph node only	51 (14)
Visceral disease	315 (85)
Liver metastases	78 (21)
Previous adjuvant/neoadjuvant platinum-based chemotherapy‖	36 (10)
Reasons for cisplatin ineligibility	
ECOG performance status 2	120 (32)
Renal dysfunction††	182 (49)
ECOG performance status 2 and renal dysfunction	35 (10)
Other reasons‡‡	33 (9)

†One patient had an ECOG performance status of 3. ‡Primary tumor location unknown for 1 patient. § Metastases location not reported for 4 patients. ‖Adjuvant platinum-based chemotherapy following radical cystectomy or neoadjuvant platinum-based chemotherapy with recurrence >12 months from completion of therapy was allowed. ††Renal dysfunction defined as creatinine clearance <60 mL/min. ‡‡Other reasons include NYHA Class III heart failure, Grade ≥2 peripheral neuropathy, and Grade ≥2 hearing loss.

ECOG = Eastern Cooperative Oncology Group; NYHA = New York Heart Association.

1. Balar A et al. Presented at: 2017 Genitourinary Cancers Symposium; Feb 16-18, 2017; Orlando, FL. Abstract 284.

Efficacy

- Median follow-up duration was 5 months (range, 0.1–17 months) as of September 1, 2016
- Median duration of response for the total population was not reached (95% confidence interval [CI], 9 months to not reached)
  - Median duration of response for patients enrolled ≥4 months before data cutoff was not reached (95% CI, 9 months to not reached)
- 83% of all responses were ongoing at the data cutoff (median follow-up, 5 months [range, 0.1–17 months])
- Median PFS was 2 months (range, 2–3 months)
- 6-month and 12-month PFS rates were 30% and 19%, respectively
- OS rate was 67% at 6 months

1. Balar A et al. Presented at: 2017 Genitourinary Cancers Symposium; Feb 16-18, 2017; Orlando, FL. Abstract 284.

Conclusions

- First-line pembrolizumab demonstrated clinically meaningful antitumor activity in cisplatin-ineligible patients with advanced urothelial cancer
  - 24% of all patients and 27% of those enrolled ≥4 months before data cutoff responded to treatment
  - The PD-L1 high cut point was determined to be CPS ≥10%. Higher response rates were observed in patients with a CPS ≥10%; ORR was 48% for those with CPS ≥10% enrolled ≥4 months before data cutoff
  - 37% of all patients were still receiving treatment, and 83% of responses were ongoing as of the data cutoff
  - Longer follow-up will further elucidate the durability of antitumor activity and impact of pembrolizumab on patient survival
- No new safety signals for pembrolizumab were identified
- These results support the KEYNOTE-361 Phase 3 trial (ClinicalTrials.gov, NCT02853305), which is currently recruiting and is designed to evaluate the efficacy and safety of first-line pembrolizumab with or without chemotherapy vs chemotherapy alone in cisplatin-eligible and -ineligible patients with advanced urothelial cancer

1. Balar A et al. Presented at: 2017 Genitourinary Cancers Symposium; Feb 16-18, 2017; Orlando, FL. Abstract 284.

Why did Pembrolizumab Succeed?

MAY 11, 2017 @ 09:52 AM 11,166

Has Merck Lucked Into A $10 Billion Drug?

Matthew Herper, FORBES STAFF

I cover science and medicine, and believe this is biology's century. **FULL BIO**

Merck–and its cancer drug Keytruda–had a great day yesterday.

First, rival drug giant Roche revealed that a clinical trial failed to show its Tecentriq, a drug similar to Keytruda, extended the lives of patients with bladder cancer. Keytruda, by contrast, had added a median 3.1 months to patients' lives in a similar study. Then, late last night, Keytruda was approved as a first choice for most patients with non-small cell lung cancer when used in combination with a chemotherapy regimen that includes Eli Lilly's Alimta.

Outline

- Current standard
- Immunotherapy approvals in mBC
- Clinical Trials
- Summary (Come Monday)

Come Monday…..

- We have 5 IO drugs with some data for use in mUC but only one with phase III trial data to support its use (Pembrolizumab)
- Biomarker studies seem to show a relationship but not clear
- Accelerated approval does not guarantee phase 3 trial success
- More IO drugs and combination trials are ongoing
- Cost will play a big role in its usage and access in non reimbursable markets

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Call for Papers	1 Feb – 30 May 2017
Abstract Submission Deadline	30 May 2017
Review Period	1 – 5 June 2017
Announcement of Results	7 June 2017
Confirmation by abstract authors (thru registration)	10 June 2017

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