Meeting at the Communications Crossroads: Understanding Treatment Options for Advanced and Metastatic Bladder Cancer – Explore Your Options Activity

Supplement: Terminology Definitions

Members of Your Care Team

- **Medical oncologists (or "med oncs"):** Physicians who specialize in using chemotherapy, targeted therapies, and immunotherapies to treat cancer
- **Oncologists:** Physicians who specialize in diagnosing and treating cancer
- **Oncology nurses:** Nurses with specialized training and expertise in cancer care
- **Oncology pharmacists:** Pharmacists with specialized training and expertise in the safe and effective use of drugs used to treat cancer
- **Oncology physician assistants:** Health care providers with specialized training in treating cancer
- **Pathologists:** Physicians trained in identifying and classifying tumor cells for accurate cancer diagnosis and staging
- **Patient navigators (or "patient advocate"):** Professionals trained in facilitating communication between patients and health care providers as well as helping with financial, legal, and social support
- **Radiation oncologists (or "rad oncs"):** Physicians who specialize in using various forms of radiation therapy to treat cancer
- **Surgical oncologists (or "surg oncs"):** Physicians trained in surgical techniques to diagnose, stage, and treat cancer by removing tumors or organs and tissues affected by cancer
- **Urologists:** Physicians who specialize in treating diseases of the urinary tract
- **Urologic oncologist:** Physicians who specialize in diagnosing and treating cancers of the urinary tract

Medical Terminologies You May Hear and What They Mean

Advanced bladder cancer: Cancer that has grown past the bladder lining through the bladder muscle wall. It may have spread to 1 or more lymph nodes that are near the bladder. Sometimes this is called "Stage III" cancer.

Adverse events (AEs): Medical terminology for side effects caused by treatments. Most common side effects caused by cancer treatments include nausea, diarrhea, fatigue, itch, rash, sore muscles, mouth sores, hair loss, altered taste sensation (called dysgeusia) and decreased appetite. It may also cause nerve damage (called neuropathy), marked by tingling and numbness in the hands and feet, and blood disorders such as high or low levels of red or white blood cells.

Antibody drug conjugate (ADC): A laboratory-engineered antibody (an immune system component) designed to target a particular protein on cancer cells. This is linked with a cancer-killing drug that goes directly into cancer cells. (Also see "Monoclonal antibody".) The ADCs that are approved by the Food and Drug Administration for advanced or metastatic bladder cancer are enfortumab vedotin (EV, or Padcev), and sacituzumab govitecan (SG, or Trodelvy). (Also see "Second-line treatment" and "Third-line treatment")

Best supportive care (BSC): Interventions intended to manage symptoms and provide relief of discomfort caused by the disease itself or by treatment side effects. This can include giving medications to control pain, nausea, and vomiting; managing infections and controlling fever; giving nutritional or hydration support; or using other measures that improve a patient's comfort and quality of life. Although this is also sometimes referred to as "palliative care," best supportive care can be used any time during cancer treatment and is ***not*** just for end-of-life care.

Cisplatin ineligible (or cis-ineligible): This indicates a person who for cannot take cisplatin (most often because of poor overall health, kidney or heart disease, or other health conditions) because they might not be able to tolerate the side effects. Cisplatin in combination with one or more other chemotherapy drug(s) is the preferred treatment for patients who are newly diagnosed with advanced or metastatic bladder cancer. Some cisplatin-ineligible patients can still safely take carboplatin because it has fewer side effects; others will need to receive immunotherapy with one of the immune checkpoint inhibitors instead. (Also see "Initial treatment," "Gem/Cis," "Platinum-based chemotherapy," and "Immune checkpoint inhibitors")

Cycles: A repeated set number of days or weeks in which the patient receives cancer medications. A cycle may be 21 or 28 days long, and is used for chemotherapies and antibody drug conjugates (ADCs). Chemotherapies are usually given once a week for 2 weeks followed by 1 week off. In the next week, the process starts over again. This is a 21-day or 3-week cycle. ADCs are given on certain days (example: day 1 and day 8) in a 21-day or 28-day cycle. (Also see "Antibody drug conjugate," and "Platinum-based chemotherapy")

FGFR: Stands for fibroblast growth factor receptor and consists of a family of 4 genes (FGFR1 to FGFR4). FGFR2 and FGFR3 are involved in cell division, cell maturity, formation of new blood vessels, and wound healing. Changes in these genes (referred to as "mutations," "alterations," or "fusions") are the most commonly seen gene mutations in bladder cancer. People with bladder cancer and FGFR2/FGFR3 mutations are eligible for treatment with an FGFR inhibitor if the cancer comes back after completing chemotherapy. Called erdafitinib (Balversa), this is the only FGFR inhibitor that is approved by the Food and Drug Administration. (Also see "Second-line treatment")

Initial treatment: First drug treatment after diagnosis and surgery. This is also called "first-line" or "frontline" treatment. (Also see "Gem/Cis," and "Cisplatin-ineligible")

Gem/Cis: Refers to the chemotherapy combination of gemcitabine + cisplatin. This is the most commonly prescribed and frequently recommended chemotherapy treatment for patients who are newly diagnosed with advanced or metastatic bladder cancer. (Also see "Initial treatment")

Immune checkpoint inhibitors: These are 4 monoclonal antibody drugs that have been approved by the Food and Drug Administration to treat advanced or metastatic bladder cancer (also see "Immunotherapy"). The names of these drugs are atezolizumab (Tecentriq), avelumab (Bavencio), nivolumab (Opdivo), and pembrolizumab (Keytruda). (Also see "Immunotherapy" and "Maintenance Therapy")

Immunotherapy: Treatment that unleashes the immune system's ability to recognize and destroy cancer cells. In advanced or metastatic bladder cancer, this is achieved with immune checkpoint inhibitors. (Also see "Immune checkpoint inhibitors")

Maintenance therapy: A drug that is started after initial or first-line chemotherapy is finished. This is thought of as an extension of first-line treatment. The only drug approved by the Food and Drug Administration for maintenance therapy for advanced or metastatic bladder cancer is avelumab (Bavencio), which is an immune checkpoint inhibitor. People who cannot take platinum-based treatment and must take an immune checkpoint inhibitor as their initial treatment are not eligible for maintenance therapy with avelumab. (Also see "Initial treatment," "Immune checkpoint inhibitors," and "Cisplatin ineligible")

Metastatic bladder cancer: Cancer that has spread to lymph nodes or other body organs that are far from the bladder. This is also called "Stage IV" cancer.

Monoclonal antibody (mAb): A laboratory-engineered protein derived by cloning a single B-cell (a type of white blood cell used by the immune system to fight disease) in large enough quantities to target many cancer cells simultaneously. These antibodies seek and bind to specific receptors on cancer cells. They can be used alone or to carry drugs or radioactive substances directly into cancer cells to kill them. (Also see "Immune checkpoint inhibitors" and "Antibody drug conjugate")

Platinum-based chemotherapy: A combination of 2 or more chemotherapy drugs that contains either cisplatin or carboplatin. Both of these drugs are derived from platinum and are key to first-line or initial therapy after a diagnosis of advanced or metastatic bladder cancer. Cisplatin is the preferred drug because it is more effective against cancer. Carboplatin has fewer side effects than cisplatin but may not be as effective. It is used for patients who might not be able to tolerate the side effects of cisplatin (mostly those with poor overall wellness, kidney or heart disease, or other conditions). (Also see "Cisplatin ineligible," "Initial treatment," and "Gem/Cis")

Second-line treatment: Drug therapies that can be used if the cancer comes back or gets worse after being on an initial or first-line treatment. (Also see "First-line treatment," "Adjuvant chemotherapy," and "Third-line treatment")

Systemic treatment: Any drug that can travel through the blood stream potentially affecting cells and organs throughout the body.

Third-line treatment: Drug therapies that can be used if the cancer comes back or gets worse after being on two previous kinds of treatments. This is sometimes called "later-line" treatment. (Also see "Initial treatment" and "Second-line treatment")

Urinary tract cancer (UTC): Umbrella term for cancers of the bladder and upper urinary tract. Bladder cancer is the most common UTC location, comprising 95% of all cases. Upper urinary tract cancer includes cancer in the renal pelvis (the part of the kidneys that collect urine) and in the ureters (tubes that carry urine from the kidneys to the bladder).

References

Balar AV, Galsky MD, Rosenberg JE, et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial. *Lancet.* 2017;389:67-76.

Balversa. Package insert. Janssen Products, LP; April 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212018s001lbl.pdf

Bavencio. Package insert. EMD Serono, Inc.; November 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761049s005lbl.pdf.

Bellmunt J, de Wit R, Vaughn DJ, et al. on behalf of the KEYNOTE-045 investigators. Pembrolizumab as second-line therapy for advanced urothelial carcinoma. *N Engl J Med.* 2017;376:1015-1026.

Bladder Cancer Basics Handbook. Bladder Cancer Advocacy Network (BCAN). Accessed December 6, 2021. https://bcan.org/

Bladder Cancer Risk Factors. American Cancer Society. Accessed December 6, 2021. https://www.cancer.org/cancer/bladder-cancer/causes-risks-prevention/risk-factors.html

Cancer Facts and Figures 2021. American Cancer Society. Accessed December 6, 2021. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2021.html

Galsky M, Ma E, Shah-Manek B, et al. Cisplatin ineligibility for patients with metastatic urothelial carcinoma: a survey of clinical practice perspectives among US oncologists. *Bladder Cancer.* 2019;5:281-288.

Immune checkpoint inhibitors. National Cancer Institute (NCI). Accessed December 6, 2021. https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/checkpoint-inhibitors

Keytruda. Package insert. Merck & Co., Inc.; August 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125514s102lbl.pdf

Loriot Y, Necchi A, Park SH, et al. Erdafitinib in locally advanced or metastatic urothelial carcinoma. *N Engl J Med.* 2019;381:338-348.

Liu Y-H, Zang X-Y, Wang J-C, Huang S-S, Xu J, Zhang P. Diagnosis and management of immune related adverse events (irAEs) in cancer immunotherapy. *Biomed Pharmacother.* 2019;120:109437.

Matulewicz RS, Sherman S, Bjurlin MA. Smoking cessation and cancer survivorship. *JAMA.* 2020;324:1475.

National Comprehensive Cancer Network (NCCN). *Guidelines for Patients. Bladder Cancer.* Version 2019. Accessed December 6, 2021. https://www.nccn.org/patients/guidelines/content/PDF/bladder-patient.pdf

Padcev. Package insert. Astellas Pharma US, Inc.; July 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761137s006s008lbl.pdf

Patel MR, Ellerton J, Infante JR, et al. Avelumab in metastatic urothelial carcinoma after platinum failure (JAVELIN Solid Tumor): pooled results from two expansion cohorts of an open-label, phase 1 trial. *Lancet Oncol.* 2018;19:51-64.

Powles T, Park SH, Voog C, et al. Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. *N Engl J Med.* 2020;383:1218-1230.

Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. *N Engl J Med.* 2021;384:1125-1135.

Rosenberg JE, Galsky MD, Balar AV, et al. Atezolizumab monotherapy in cisplatin-ineligible patients with previously untreated metastatic urothelial carcinoma: 5-year response and survival analysis from the phase II IMvigor210 study (cohort 1). ESMO 2021 abstract 699P.

Sharma P, Retz M, Siefker-Radtke A, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 2017;18:312-322.

Surveillance, Epidemiology, and End Results Program (SEER). Cancer Stat Facts: Bladder Cancer. National Cancer Institute. Accessed December 6, 2021. https://seer.cancer.gov/statfacts/html/urinb.html

Tagawa ST, Balar AV, Petrylak, et al. TROPHY-U-01: a phase II open-label study of sacituzumab govitecan in patients with metastatic urothelial carcinoma progressing after platinum-based chemotherapy and checkpoint inhibitors. *J Clin Oncol.* 2021;39:2474-2485.

Tecentriq. Package insert. Genentech, Inc.; April 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761034s041lbl.pdf

Trodelvy. Package insert. Immunomedics, Inc.; April 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761115s009lbl.pdf.

Vuky J, Balar AV, Castellano D, et al. Long-term outcomes in KEYNOTE-052: phase II study investigating first-line pembrolizumab in cisplatin-ineligible patients with locally advanced or metastatic urothelial cancer. *J Clin Oncol.* 2020;38:2658-2666.

Yu EY, Petrylak DP, O'Donnell PH, et al. Enfortumab vedotin after PD-1 or PD-L1 inhibitors in cisplatin-ineligible patients with advanced urothelial carcinoma (EV-201): a multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 2021;22:872-882.

Medications: Generic Name Followed by Trade Name in Parentheses

Atezolizumab (Tecentriq)
Avelumab (Bavencio)
Bacillus Calmette-Guerin (TheraCys or TICE)
Carboplatin (Paraplatin)
Cisplatin (Platinol, or Platinol-AQ)
Enfortumab vedotin (Padcev)
Erdafitinib (Balversa)
Gemcitabine (Gemzar)
Nivolumab (Opdivo)
Pembrolizumab (Keytruda)
Sacituzumab govitecan (Trodelvy)