Bladder Cancer

DISEASE

Key risk factors

6th most common cancer in the US

>90% of bladder cancers are urothelial carcinoma

≈12% of patients have **locally advanced or metastatic** bladder cancer at diagnosis

5-year relative **survival rate**

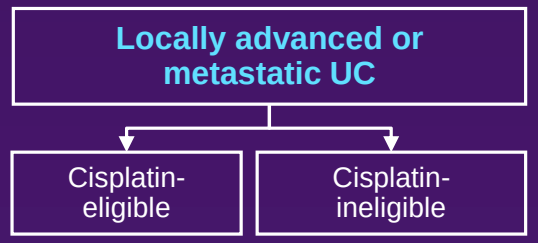
≈6.4% for metastatic disease at diagnosis

≈37.5% for locally advanced disease at diagnosis

≈35-45% of **tumors** express PD-L1

TREATMENT

1L treatment of locally advanced or metastatic disease is guided by **cisplatin eligibility**



40-60% of patients with metastatic UC do not receive any treatment in real-world studies

Outcomes with 1L platinum-containing chemotherapy for locally advanced or metastatic UC

≈65-79% disease control rate

≈4-9.5 mo median PFS

≈8-15 mo median OS

30-40% of patients receive **2L treatment** after 1L chemotherapy for metastatic UC in real-world studies

EMD Serono Pfizer Medical Affairs

May 2022
US-NONO-00281

Bladder Cancer: Key Risk Factors

INTRINSIC RISK FACTORS FOR BLADDER CANCER

Age

- **>90% of cases** occur in individuals aged ≥55 years[1]

Sex

- **≈75% of cases** occur in men[2]

Race/ethnicity

- Occurrence is **twice as likely** in Whites than in African-Americans and Hispanics[1]

Genetics

- Family history of bladder cancer
- Genetic changes that affect the breakdown of toxins and mutations in known tumor suppressors[1]

Chronic infections

- Urinary infections, kidney and bladder stones, and schistosomiasis infections[1]

ENVIRONMENTAL RISK FACTORS FOR BLADDER CANCER

Smoking

- **>3-fold** increased risk[1]

Chemicals

- Exposure to specific chemicals in the workplace[1]

Certain medicines or herbal supplements

Low fluid intake

1. American Cancer Society. Bladder cancer risk factors. https://www.cancer.org/cancer/bladder-cancer/causes-risks-prevention/risk-factors.html. Accessed January 5, 2022. 2. Richters A, et al. World J Urol 2020;38:1895-904.

Bladder Cancer: Key US and Global Statistics

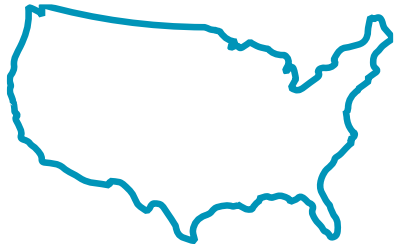
10th most common cancer globally[1]

Estimated new cases in 2020[1]

573,278

Estimated deaths in 2020[1]

212,536



6th Most common cancer in the US[2]

Estimated new cases in 2021[2]

83,730

Estimated deaths in 2021[2]

17,200

Median age at diagnosis[2]

73 y

ESTIMATED NEW CASES OF BLADDER CANCER IN THE US IN 2021[3]

- **Breast,** 284,200
- **Prostate,** 248,530
- **Lung & bronchus,** 235,760
- **Melanoma of the skin,** 106,110
- **Colon,** 104,270
- **Urinary bladder,** 83,730
- **Non-Hodgkin lymphoma,** 81,560
- **Kidney & renal pelvis,** 76,080
- **Uterine corpus,** 66,570
- **Pancreas,** 60,430
- **Rectum,** 45,230
- **Thyroid,** 44,280
- **Liver & intrahepatic bile duct,** 42,230
- **Myeloma,** 34,920
- **Stomach,** 26,560
- **All other cancers,** 357,700

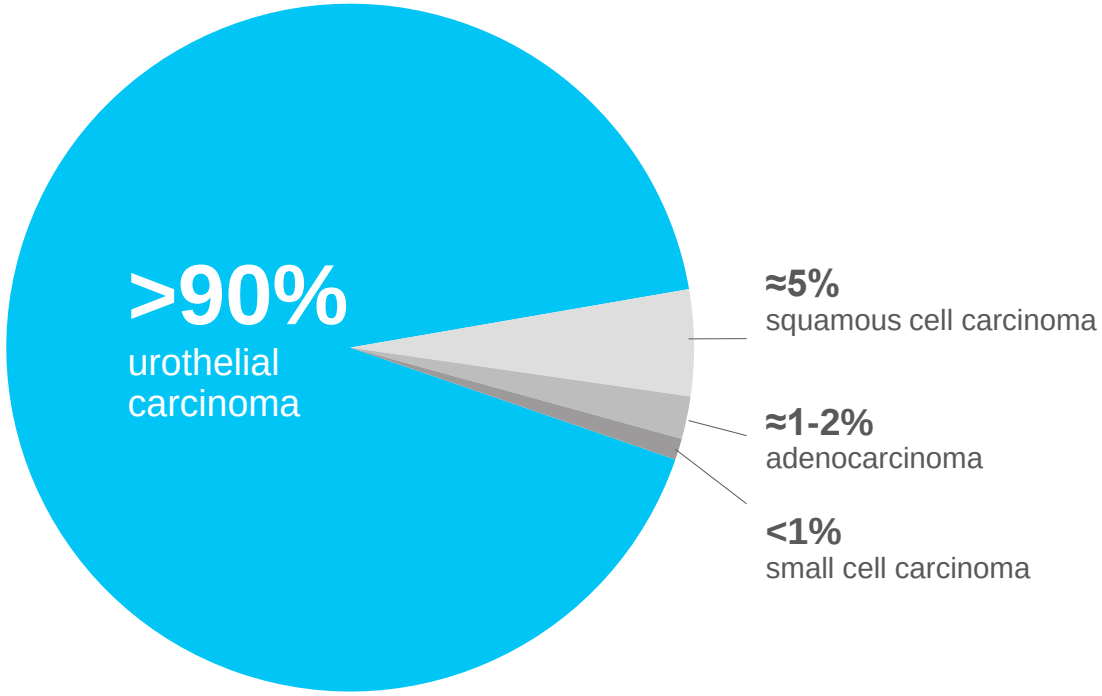
ESTIMATED DEATHS FROM BLADDER CANCER IN THE US IN 2021[3]

- **Lung & bronchus,** 131,880
- **Colon,** 52,980
- **Pancreas,** 48,220
- **Breast,** 44,130
- **Prostate,** 34,130
- **Liver & intrahepatic bile duct,** 30,230
- **Non-Hodgkin lymphoma,** 20,720
- **Brain and other nervous system,** 18,600
- **Urinary bladder,** 17,200
- **Esophagus,** 15,530
- **Kidney & renal pelvis,** 13,780
- **Ovary,** 13,770
- **Uterine corpus,** 12,940
- **Myeloma,** 12,410
- **Acute myeloid leukemia,** 11,400
- **All other cancers,** 130,650

1. Sung H, et al. CA Cancer J Clin 2021;71:209-49. 2. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. Available from https://seer.cancer.gov/explorer/. Accessed February 11, 2022. 3. Siegel RL, et al. CA Cancer J Clin 2021;71:7-33.

Bladder Cancer

BLADDER CANCER HISTOLOGIES[1-4]



ADDITIONAL INFORMATION ON DIFFERENT TYPES OF BLADDER CANCER[2,3]

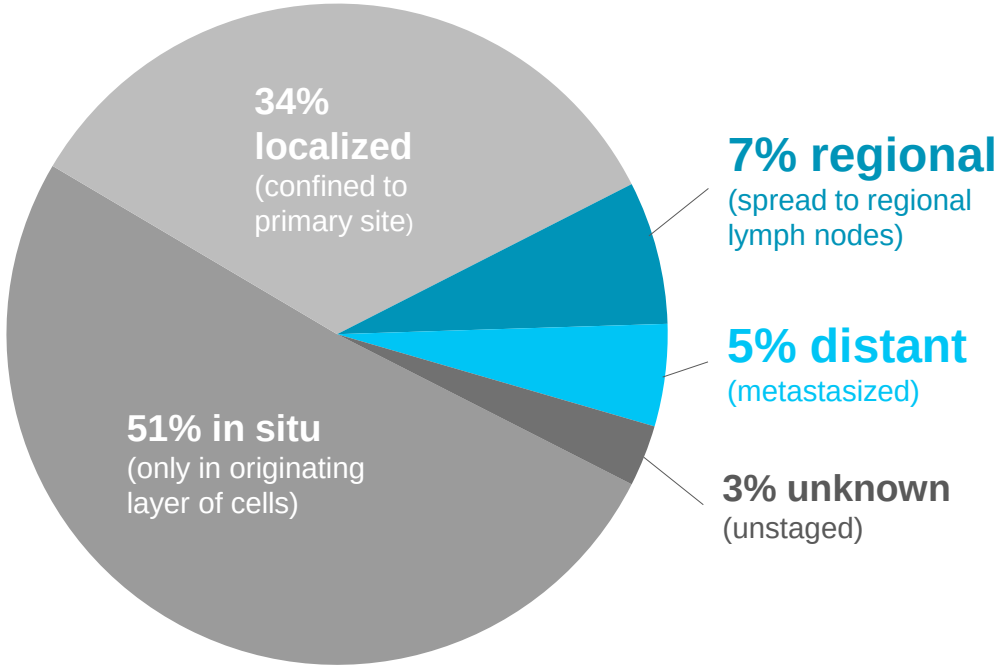
Urothelial carcinoma	• Also called transitional cell carcinoma • 90% of UC originates in the urothelial cells that line the inside of the bladder[1] • May also originate in the renal pelvis, ureters, or urethra
Squamous cell carcinoma	• More common in developing countries • Most cases are invasive
Adenocarcinoma	• Develops from mucus-producing cells • Usually invasive
Small cell carcinoma	• Originates in neuroendocrine cells • Standard treatment is similar to small cell carcinoma of the lung

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.6.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed December 18, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. 2. American Cancer Society. About bladder cancer. https://www.cancer.org/cancer/bladder-cancer/about/what-is-bladder-cancer.html. Accessed July 5, 2021. 3. Cancer Research UK. Bladder cancer. https://www.cancerresearchuk.org/about-cancer/bladder-cancer/types-stages-grades/types. Accessed July 5, 2021.4. Yousef PG, Gabril MY. Pathol Res Pract 2018;214:1-6.

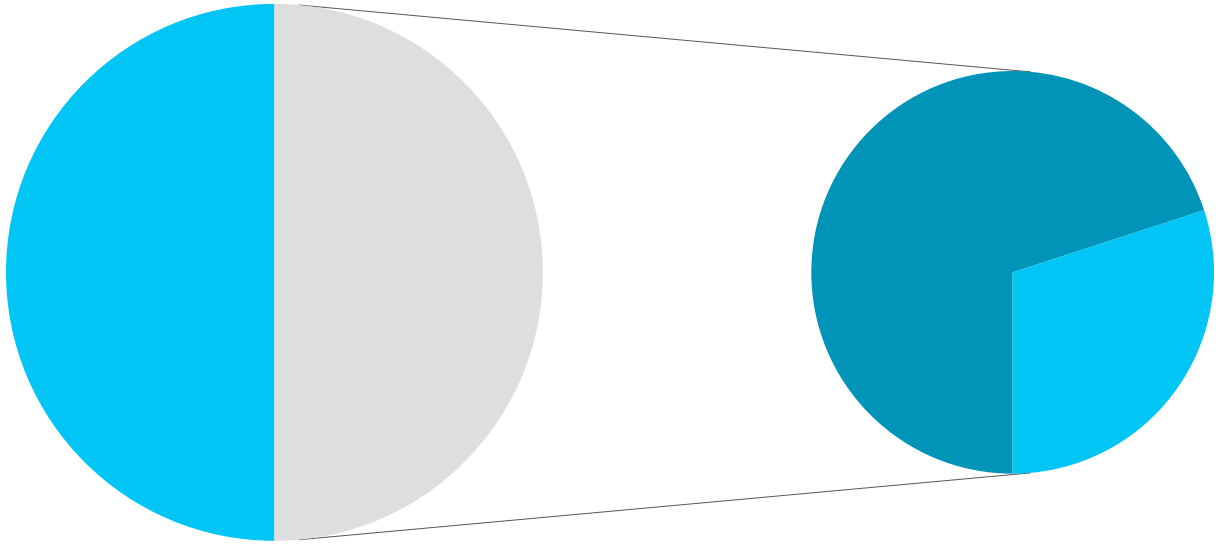
Bladder Cancer: Metastatic Disease

- Approximately 5% of patients have metastatic bladder cancer at diagnosis[1]
- Relapse occurs after cystectomy in approximately half of patients, with distant metastasis accounting for 70-90% of relapses[2]

PERCENTAGE OF BLADDER CANCER CASES BY STAGE AT DIAGNOSIS[1]



RELAPSE AFTER CYSTECTOMY IN BLADDER CANCER[2]



≈50%
of patients have relapse after cystectomy

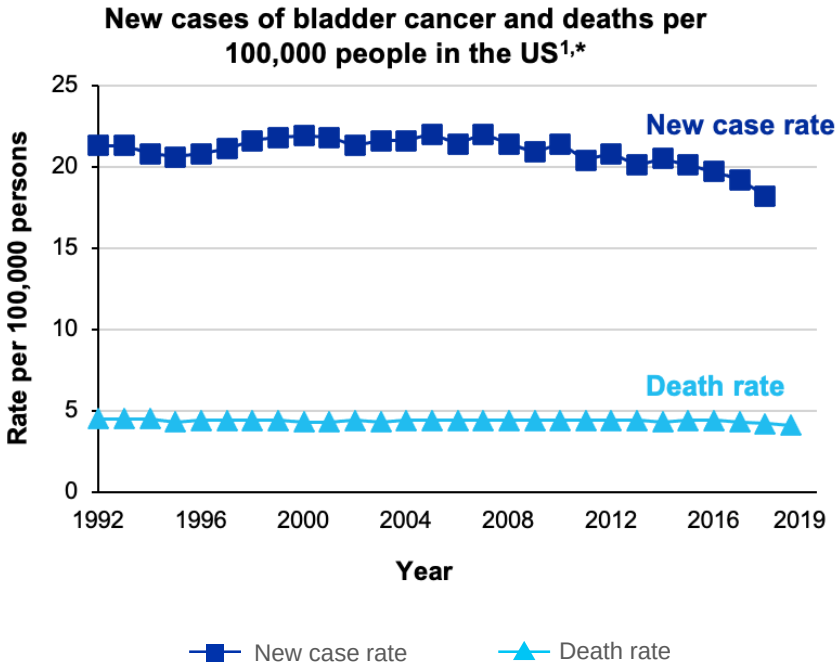
≈70-90%
of patients relapse with distant metastases

1. National Cancer Institute, Surveillance Research Program. SEER*Explorer: An interactive website for SEER cancer statistics. Accessed November 5, 2021. https://seer.cancer.gov/explorer/. 2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.6.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed December 18, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Bladder Cancer: US Survival

- In the last 20 years, the death rate from bladder cancer has remained relatively unchanged
- Metastatic disease has a 5-year relative survival rate of ≈6.4%

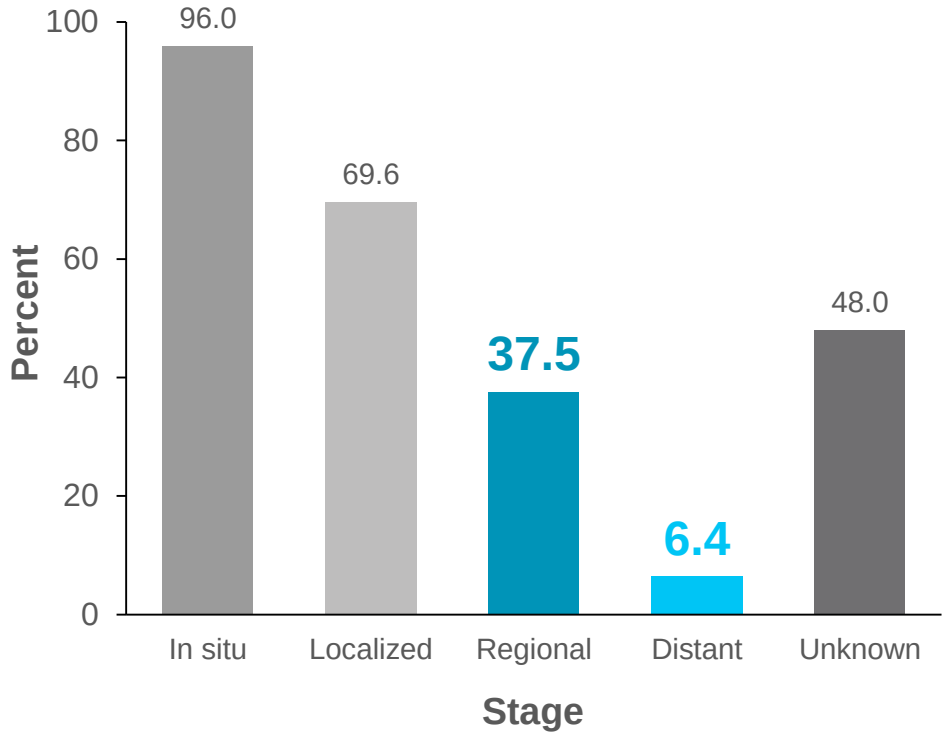
NEW CASES OF BLADDER CANCER AND DEATHS PER 100,000 PEOPLE IN THE US*



19.7
per 100,000 people
per year (2014-2018*)

4.2
per 100,000 people
per year (2015-2019*)

5-YEAR SURVIVAL BY BLADDER CANCER STAGE AT DIAGNOSIS

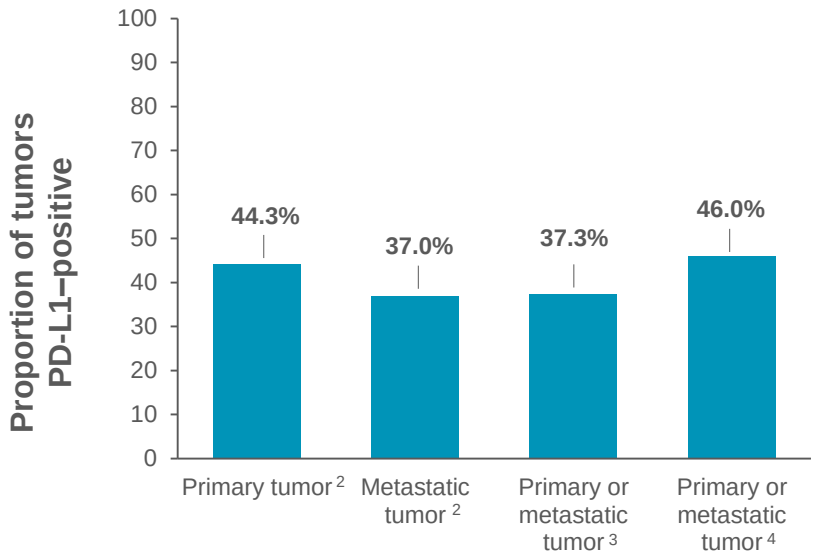


* Age-adjusted observed data.
National Cancer Institute, Surveillance Research Program. SEER*Explorer: An interactive website for SEER cancer statistics. Accessed November 5, 2021. https://seer.cancer.gov/explorer/.

Urothelial Carcinoma: Biology

- UC is characterized by a high tumor mutational burden and genomic instability[1]
- UC tumors are characterized by PD-L1 expression (≈35-45% of tumors), which can downregulate antitumor immune responses by binding to PD-1 on T cells[2-7]
- Prominent base pair substitutions in UC have been grouped into four mutational signatures detected in UC[1]

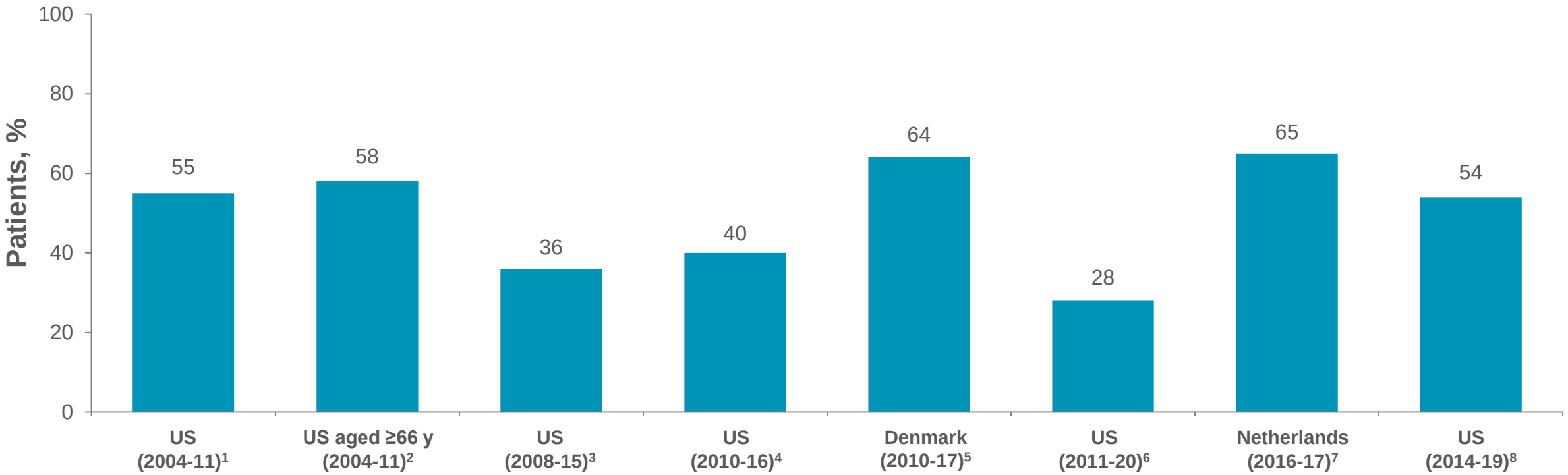
PD-L1 EXPRESSION IN UC TUMORS



1. Alexandrov LB, et al. Nature 2013;500:415-21. 2. Pichler R, et al. Oncotarget 2017;8:66849-64. 3. Sharma P, et al. Lancet Oncol 2016;17:1590-8. 4. Sharma P, et al. Lancet Oncol 2017;18:312-22. 5. Cheng W, et al. Oncogenesis 2018;7:2. 6. Kim JW, et al. Curr Opin Oncol 2015;27:191-200. 7. Dudley JC, et al. Clin Cancer Res 2016;22:813-20.

Metastatic UC: Patients Not Receiving Treatment

Across several real-world studies, **≈40-60%** of patients presenting with locally advanced or metastatic UC did not receive any 1L drug therapy[1-8]

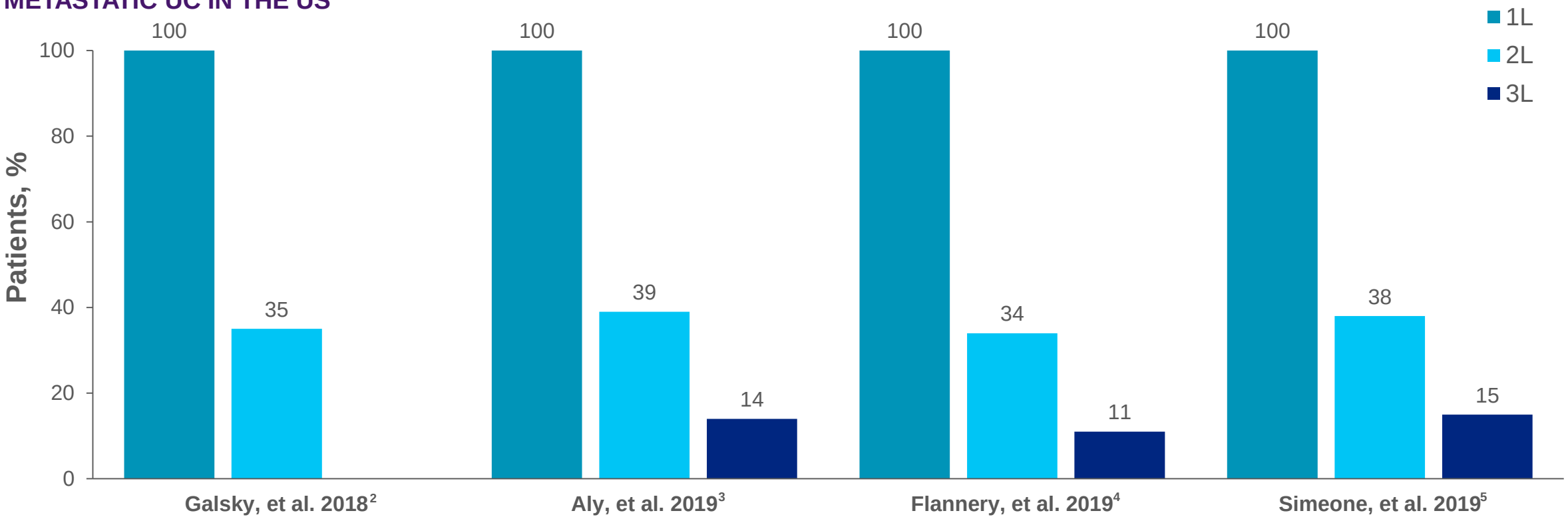


1. Aly A, et al. J Med Econ 2019;22:662-70. 2. Galsky MD, et al. Bladder Cancer 2018;4:227-38. 3. Fisher MD, et al. Clin Genitourin Cancer 2018; 16:e1171-9. 4. Flannery K, et al. Future Oncol 2019;15:1323-34. 5. Jensen JB, et al. Ann Oncol 2021. Abstract 707P (poster presentation). 6. Geynisman DM, et al. J Clin Oncol. 2021;39:(suppl 15): Abstract 4538 (poster presentation). 7. Richters A, et al. Cancer Treat Res Commun 2020;25:100266. 8. Bilen M, et al. Ann Oncol 2021. Abstract 701P (poster presentation).

Urothelial Carcinoma: Unmet Need After 1L Treatment for Metastatic Disease

Data from real-world studies show that 34-39% of patients who received 1L chemotherapy for metastatic UC received 2L treatment[1]

PATIENT ATTRITION BETWEEN 1L AND LATER LINES OF THERAPY IN REAL-WORLD STUDIES OF PATIENTS WITH METASTATIC UC IN THE US



1L, first line; 2L, second line; UC, urothelial cancer.

1. Grivas P, et al. Cancer Treat Rev. 2021;97. doi:10.1016/j.ctrv.2021.102187. 2. Galsky MC, et al. Bladder Cancer. 2018;4:227-38. doi:10.3233/blc-170149. 3. Aly A, et al. J Med Econ. 2019;22:662-70. doi:10.1080/13696998.2019.1591424. 4. Flannery K, et al. Future Oncol. 2019;15:1323-34. doi:10.2217/fon-2018-0564. 5. Simeon JC, et al. Cancer Epidemiol. 2019;60:121-7. doi:10.1016/j.canep.2019.03.013.