

by RNA sequencing of five distinct intrinsic molecular subtypes (luminal papillary, luminal infiltrated, luminal, basal squamous, and neuronal) closely resembling luminal and basal subclassifications of breast cancers. These bladder TCGA findings have led to clinical trial designs enriching for patients with specific gene mutation profiles as well as interrogation of candidate biomarkers according to intrinsic molecular subtypes.

■ STAGING AND OUTCOMES BY STAGE

The staging of bladder cancer is dependent on the depth of invasion within the bladder wall, involvement of lymph nodes, and spread to surrounding and distant organs as depicted in [Fig. 86-2](#).

Approximately 75% of bladder cancer presents with non–muscle-invasive bladder cancer (NMIBC), 18% with disease invading into or through the muscular wall of the bladder, and only 3% presenting with metastatic spread to distant organs. NMIBC is defined by tumors that involve only the immediate epithelial layer of cells (carcinoma in situ [CIS] and Ta) or that only penetrate into the connective tissue below the urothelium (T1) but not into the muscular layer known as the *muscularis propria*. Muscle-invasive bladder cancer (MIBC) is defined by tumors that invade into the muscularis propria (T2), through the muscularis propria to involve the surrounding serosa (T3), or into immediately adjacent pelvic organs such as the rectum, prostate, vagina, or cervix (T4). Lymph node staging is classified according to involvement of a solitary node within the true pelvis (N1), two nodes involved in the true pelvis (N2), or involvement of the common iliac nodes (N3). Any disease that has spread beyond the common iliac nodes is considered metastatic (M1). The staging of bladder cancer is driven primarily by the T stage of the tumor, with stages 0a–II defined entirely by the T stage in the absence of nodal or metastatic disease. Involvement of regional lymph nodes in the true pelvis or along the common iliac artery qualifies as stage III disease, whereas involvement of any distant metastases qualifies as stage IV disease. Clinical outcomes of patients with bladder cancer correlate closely with staging at diagnosis with 5-year overall survival rates of 70–90% for disease confined to the bladder (stage I–II), 36–50% for disease that