Title: Efficacy and Safety of Pembrolizumab (MK-3475) in Combination with Bacillus Calmette-Guerin (BCG) in High-Risk Non-Muscle Invasive Bladder Cancer (HR NMIBC) (MK-3475-676/KEYNOTE-676)

Sponsor:
Merck Sharp & Dohme Corp

Brief Summary	This study is designed to assess the antitumor efficacy and safety of pembrolizumab in combination with BCG, compared to BCG monotherapy, in participants with HR NMIBC that is persistent or recurrent following adequate BCG induction. The primary hypothesis is that the combination of pembrolizumab plus BCG has a superior complete response rate (CRR) as assessed by central pathology review compared to BCG in participants with carcinoma in situ (CIS).
Study Type	Interventional
Condition	High-risk Non-muscle Invasive Bladder Cancer
Study Arms	• Experimental: BCG plus Pembrolizumab (Arm 1) Participants receive BCG (Induction and Maintenance), in combination with 200 mg pembrolizumab administered intravenously (IV) every 3 weeks (Q3W) for 35 doses (~2 years). Interventions: ○ Biological: Pembrolizumab ○ Biological: BCG • Experimental: BCG (Arm 2) Participants receive BCG monotherapy (Induction and Maintenance). Intervention: Biological: BCG
Recruitment Status	Recruiting: Contact Alicia Davis to participate in this study at ADavis@urologygeorgia.com or by calling 678-344-8900x696.
Eligibility Criteria	Inclusion Criteria: Has histologically-confirmed diagnosis of non-muscle invasive (T1, high grade Ta and/or CIS) transitional cell carcinoma (TCC) of the bladder Has been treated with one adequate course of BCG induction therapy for the treatment of HR NMIBC Following adequate BCG induction therapy, must have persistent or recurrent HR NMIBC

	Has undergone cystoscopy/ transurethral resection of bladder tumor (TURBT) to remove all resectable disease Has provided tissue for biomarker analysis Has Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2 Has adequate organ function Male participants must agree to use approved contraception during the treatment period and for at least 120 days after the last dose of study treatment and refrain from donating sperm during this period Female participants who are not pregnant, not breastfeeding, and either not a woman of child bearing potential (WOCBP) or are a WOCBP who agrees to use approved contraception during the treatment period and for at least 120 days after the last dose of study treatment Exclusion Criteria: Has persistent T1 disease following an induction course of BCG Has a history of or concurrent muscle invasive (i.e., T2, T3, T4), locally advanced non-resectable or metastatic UC Has concurrent extra-vesical (i.e., urethra, ureter, renal pelvis) non-muscle invasive TCC of the urothelium, concurrent upper tract involvement, or invasive prostatic TCC including T1 or greater disease, or ductal invasion WOCBP who has a positive urine pregnancy test within 72 hours prior to randomization Has received prior therapy with anti-PD-1, anti-PD-L1, or anti-PD-L2 agent or with an agent directed to another co-inhibitory T-cell receptor Has received prior systemic anti-cancer therapy including investigational agents within 4 weeks of start of study treatment Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks of start of study treatment Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy or any other form of immunosuppressive therapy within 7 days of start of study treatment Has a known additional malignancy that is progressing or requires active treatment within the past 3 years Has an active autoimmune disease that has required systemic treatment in past 2 years Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis Has one or more of the following contraindications to BCG: prior BCG sepsis or systemic infection, total bladder incontinence, or an adverse experience to a previous BCG instillation that resulted in treatment discontinuation and precludes retreating with BCG Has an active infection requiring systemic therapy Has a known history of human immunodeficiency virus (HIV) infection Has a known history of Hepatitis B or known active Hepatitis C virus infection Has current active tuberculosis Is pregnant or breastfeeding or expecting to conceive or father children within the projected duration of the trial, starting with the screening visit through 120 days after the last dose of trial treatment

	Has had an allogenic-tissue/solid organ transplant