JAMA | Original Investigation

Effect of Intravesical Instillation of Gemcitabine vs Saline Immediately Following Resection of Suspected Low-Grade Non–Muscle-Invasive Bladder Cancer on Tumor Recurrence
SWOG S0337 Randomized Clinical Trial

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RobotReviewer report

Risk of bias table

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Ca Vescica Instillazione Gemcitabina	RCT	406	+	?	+	+

Characteristics of studies

Messing EM, 2018

Population	1. Patients with suspected low-grade non‚Äìmuscle-invasive urothelial cancer based on cystoscopic appearance without any high-grade or without more than 2 low-grade urothelial cancer episodes within 18 months before index TURBT were enrolled between January 23, 2008, and August 14, 2012, and followed up every 3 months with cystoscopy and cytology for 2 years and then semiannually for 2 years. 2. Patients with previous or concurrent upper urinary tract or prostatic urethral urothelial cancer, previous pelvic radiotherapy for any malignancy, or prior treatment for any malignancy within 5 years other than nonmelanoma skin cancer or non‚Äìmuscle-invasive bladder urothelial cancer were not eligible . 3. The SWOG S0337 randomized clinical trial was developed to determine the efficacy of a single intravesical instillation of gemcitabine immediately after TURBT to prevent recurrence of low-grade (grade 1 and grade 2 based on the 1973 World Health Organization classification 15), stage Ta or T1 urothelial cancer of the bladder.
Intervention	1. INTERVENTIONS Participants were randomly assigned to receive intravesical instillation of gemcitabine (2 g in 100 mL of saline) 2. The SWOG S0337 randomized clinical trial was developed to determine the efficacy of a single intravesical instillation of gemcitabine immediately after TURBT to prevent recurrence of low-grade (grade 1 and grade 2 based on the 1973 World Health Organization classification 15), stage Ta or T1 urothelial cancer of the bladder. 3. Similarly, if on the index TURBT no cancer was found or if high-grade urothelial

	cancer, nonurothelial bladder cancer, or muscleinvasive cancer was diagnosed, management was based on physician discretion but follow-up for disease progression to Key Points Question Does a single intravesical instillation of gemcitabine reduce risk of recurrence after resection of low-grade non‚Äìmuscle-invasive urothelial cancer?
Outcomes	1. The primary outcome was time to recurrence of cancer. 2. The primary end point was time to recurrence, where death or cystectomy without recurrence were managed as competing risks in a cumulative incidence analysis. 3. The SWOG S0337 randomized clinical trial was developed to determine the efficacy of a single intravesical instillation of gemcitabine immediately after TURBT to prevent recurrence of low-grade (grade 1 and grade 2 based on the 1973 World Health Organization classification 15), stage Ta or T1 urothelial cancer of the bladder.

Bias	Judgement	Support for judgement
Random sequence generation	low	1. 18 Patients were randomized in a blinded 1:1 fashion to receive gemcitabine or saline with dynamic balancing for 2 stratification factors: disease status (newly diagnosed vs recurrent) and number of lesions (single vs multiple). 2. INTERVENTIONS Participants were randomly assigned to receive intravesical instillation of gemcitabine (2 g in 100 mL of saline) 3. The SWOG S0337 randomized clinical trial was developed to determine the efficacy of a single intravesical instillation of gemcitabine immediately after TURBT to prevent recurrence of low-grade (grade 1 and grade 2 based on the 1973 World Health Organization classification 15), stage Ta or T1 urothelial cancer of the bladder.
Allocation concealment	high/unclear	1. Patients and physicians were blinded to treatment assignment. 2. 18 Patients were randomized in a blinded 1:1 fashion to receive gemcitabine or saline with dynamic balancing for 2 stratification factors: disease status (newly diagnosed vs recurrent) and number of lesions (single vs multiple). 3. INTERVENTIONS Participants were randomly assigned to receive intravesical instillation of gemcitabine (2 g in 100 mL of saline)
Blinding of participants and personnel	low	1. Patients and physicians were blinded to treatment assignment. 2. DESIGN, SETTING, AND PARTICIPANTS Randomized double-blind clinical trial conducted at 23 US centers. 3. 18 Patients were randomized in a blinded 1:1 fashion to receive gemcitabine or saline with dynamic balancing for 2 stratification factors: disease status (newly diagnosed vs recurrent) and number of lesions (single vs multiple).
Blinding of outcome assessment	low	1. Eli Lilly had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; or decision to submit the manuscript for publication. 2. Author Contributions: Drs Messing and Tangen had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. 3. 18 Patients were randomized in a blinded 1:1 fashion to receive gemcitabine or saline with dynamic balancing for 2 stratification factors: disease status (newly diagnosed vs recurrent) and number of lesions (single vs multipl