Intravesical gemcitabine for non-muscle invasive bladder cancer: A Cochrane Review

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OBJECTIVE

To assess the comparative effectiveness and toxicity of intravesical gemcitabine instillation for non-muscle invasive bladder cancer.

METHODS

Based on published protocol in Cochrane Library. Comprehensive search of multiple databases for published and unpublished studies. Exclusion criteria: previous or concurrent upper urinary tract or prostatic urethral urothelial cancer. Other cancer rather than bladder. Previous systemic treatment or radiotherapy for any cancer. Primary outcomes: time to recurrence, time to progression, Grade III to V AEs. Secondary outcomes: time to death from bladder cancer, time to death from any cause, Grade I to II AEs. GRADE approach for certainty of evidence (CoE).

RESULTS

Table 1: Gemcitabine vs. saline for primary and recurrent NMIBC (single instillation after TUR)

Table 2: Gemcitabine vs. mitomycin for recurrent NMIBC (relapsed after BCG or BCG ineligible; induction and maintenance therapy for 1 year)

Table 3: Gemcitabine versus BCG for recurrent (1 course BCG failure) high risk NMIBC (induction and maintenance therapy for 1 year).

DISCUSSION

Key findings: Compared to saline, gemcitabine may reduce the risk of recurrence over time although the confidence interval includes the possibility of no effect (low CoE). Compared to mitomycin, gemcitabine may reduce the risk of recurrence over time (low CoE). Compared to BCG, gemcitabine may reduce the risk of recurrence and progression over time in patients who recurred after BCG treatment (low CoE). We are uncertain about the effect of gemcitabine on CTCAE grade III-V adverse events (Very low CoE). Comparison with other studies: In contrast to the previous version of this Cochrane review, we provide measures of treatment effect and rate the CoE using the GRADE approach. Strengths and limitations: First rigorous systematic review focused on the effect of gemcitabine in patients with primary and recurrent NMIBC. Studies were of limited quality; limitations raise concerns about performance and detection bias. Except one study which compared gemcitabine to saline, most studies had small sample sizes. Implications for practice and research: May offer recurrence reduction benefit in primary and recurrent NMIBC. Need for studies investigate QoL with active controls.

CONCLUSIONS

Gemcitabine appears superior in terms of recurrence over time in primary and recurrent NMIBC compared to saline and mitomycin. In patients who have recurred after BCG treatment, it may be superior in terms of risk of recurrence and progression over time. The underlying low and very low certainty evidence indicates that our confidence in these results is limited; therefore, better quality studies are needed.