Falke J, Lammers RJ, Arentsen HC, Ravic M, Pozzi R, Cornel EB, Vergunst H, de Reijke TM, Witjes JA (2013). Results of a phase 1 dose escalation study of intravesical TMX-101 in patients with nonmuscle invasive bladder cancer. *J Urol*.; 189(6):2077-82.

PURPOSE:
Imiquimod, a toll like receptor 7 (TLR-7) agonist, is effective as a topical treatment for skin malignancies. TMX-101 is a liquid formulation of imiquimod. In this study we establish a safety profile of TMX-101 in patients with nonmuscle invasive bladder cancer.
MATERIALS AND METHODS:
We conducted a multicenter phase 1 dose escalation study in patients with nonmuscle invasive bladder cancer. Patients were included in 1 of 4 dose groups (0.05%, 0.1%, 0.2% or 0.4%) and treated with 6 weekly instillations of TMX-101, starting 2 weeks after transurethral resection of bladder tumor. Patients were evaluated weekly, and pharmacokinetic and pharmacodynamic parameters were measured.
RESULTS:
A total of 16 patients were included in the study with 4 per dose group. Two patients dropped out after instillation 2 in dose groups 1 and 2. Overall, 88 instillations were administered without serious adverse events. There were 118 adverse events, of which 84 were related to the study drug. All adverse events were mild or moderate and number or severity was not correlated with dose group. Of the related adverse events 70% were confined to the genitourinary tract and resolved without intervention. There was a dose dependent systemic uptake with low plasma levels up to dose group 3 (0.2%, 100 mg). Maximum plasma concentration in dose group 4 (0.4%, 200 mg) was 71.7 ng/ml. This is below plasma concentrations of 123 and 128 ng/ml without significant side effects measured in healthy volunteers after subcutaneous (30 mg) or oral intake (100 mg) of imiquimod, respectively.
CONCLUSIONS:
Intravesical treatment with TMX-101 is safe. The side effects are common but mild and mostly limited to the genitourinary tract. There is a low systemic uptake