Detection and clinical outcome of urinary bladder cancer with 5-aminolevulinic acid-induced fluorescence cystoscopy: A multicenter randomized, double-blind, placebo-controlled trial

Stenzl A, Penkoff H, Dajc-Sommerer E, Zumbraegel A, Hoeltl L, Scholz M, Riedl C, Bugelnig J, Hobisch A, Burger M, Mikuz G, Pichlmeier U

Medical Center of Eberhard Karls University, Department of Urology, Tübingen, Germany

Cancer. 2011 Mar 1;117(5):938-47. doi: 10.1002/cncr.25523. Epub 2010 Nov 8.

Background: The medical community lacks results from prospective controlled multicenter studies of the diagnostic efficacy of 5-aminolevulinic acid (5-ALA) cystoscopy on tumor recurrence in patients with superficial bladder tumors.

Methods: A prospective randomized, double-blind, placebo-controlled study was conducted in 370 patients with nonmuscle-invasive urinary bladder carcinoma who received either 5-ALA (n = 187) or a placebo (n = 183) intravesically before cystoscopy. Each group underwent cystoscopy under visible white light and under fluorescent light followed by transurethral tumor resection. The primary study objective was to evaluate the 12-month recurrence-free survival.

Results: Slightly more patients with tumors were detected by using 5-ALA than by using the placebo (88.5% vs 84.7%). The mean numbers of tumor specimens per patient were 1.8 (5-ALA) and 1.6 (placebo). Intrapatient comparison of fluorescent light versus white light cystoscopy in patients randomized to receive 5-ALA showed a higher tumor detection rate with fluorescent light than with white light cystoscopy. In patients receiving 5-ALA cystoscopy, the percentage of lesions that would not have been detected in these patients by white light cystoscopy ranged between 10.9% (pT1) and 55.9% (atypia). Progression-free survival was 89.4% (5-ALA) and 89.0% (placebo) (P = .9101), and recurrence-free survival 12 months after tumor resection was 64.0% (5-ALA) and 72.8% (placebo) (P = .2216).

Conclusions: In comparison to the placebo, 5-ALA cystoscopy did not increase the rates of recurrence-free or progression-free survival 12 months after tumor resection. Although more tumors per patient were detected in the 5-ALA group, the higher detection rate did not translate into differences in long-term outcome.

Editorial Comment

Fluorescence-guided diagnosis or resection of bladder cancer is a widely used tool and certainly even more widely disputed among urologists worldwide. Therefore, an independent assessment of its value is highly desirable.

This trial was the first double-blind, placebo-controlled, prospective randomized study and therefore the results are worth reading. In short, the mean number of tumor specimens per patient was higher with 5-ALA cystoscopy (1.8) than with placebo arm cystoscopy (1.6). The difference was not significant (P = .1178). Slightly more tumors were detected with 5-ALA cystoscopy than with placebo arm cystoscopy (88.5% vs 84.7%). In contrast to previous studies with 5-ALA the percentages of diagnoses with isolated CIS were rather low (5-ALA 1.6%; placebo arm 1.7%); those with concomitant CIS were 10.8% (5-ALA) and 12.0% (placebo arm). Interestingly, recurrence-free survival rates at 12 months were 64.0% (5-ALA cystoscopy) and 72.8% (placebo arm cystoscopy) (not significant).

In conclusion, this multicenter trial had different results than previous single center trials with dedicated interest in 5-ALA resection. Further multicentric, blinded trials are needed to establish the real value of this potentially helpful adjunct to urologic surgery.

Dr. Andreas Bohle
Professor of Urology
HELIOS Agnes Karll Hospital
Bad Schwartau, Germany
E-mail: boehle@urologie-bad-schwartau.de