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- Cumming, J. A., Kirk, D., Newling, D. W., Hargreave, T. B. and Whelan, P.: A multi-centre phase 2 study of intravesical epirubicin in the treatment of superficial bladder tumour. Eur. Urol., 17: 20, 1990.
- Whelan, P., Cumming, J. A., Garvie, W. H., Hargreave, T. B., Kirk, D., Newling, D. W., Robinson, M. R. and Smith, P. H.: Multi-centre phase II study of low dose intravesical epirubicin in the treatment of superficial bladder cancer. Yorkshire and Scottish Urological Cancer Research Groups. Brit. J. Urol., 67: 600, 1991.
- Herr, H. W., Laudone, V. P. and Whitmore, W. F., Jr.: An overview of intravesical therapy for superficial bladder tumors. J. Urol., 138: 1363, 1987.
- Soloway, M. S.: Intravesical therapy for bladder cancer. Urol. Clin. N. Amer., 15: 661, 1988.
- Smith, G., Elton, R. A., Beynon, L. L., Newsam, J. E., Chisholm, G. D. and Hargreave, T. B.: Prognostic significance of biopsy results of normal-looking mucosa in cases of superficial bladder cancer. Brit. J. Urol., 55: 665, 1983.
- 14. Oosterlinck, W., Kurth, K. H., Schröder, F., Bultinck, J., Hammond, B., Sylvester, R. and Members of the European Organization for Research and Treatment of Cancer Genitourinary Group: A prospective European Organization for Research and Treatment of Cancer Genitourinary Group randomized trial comparing transurethral resection followed by a single intravesical instillation of epirubicin or water in single stage Ta, T1 papillary carcinoma of the bladder. J. Urol., 149: 749, 1993.
- Melekos, M. D., Chionis, H. S., Paranychianakis, G. S. and Dauaher, H. H.: Intravesical 4'-epi-doxorubicin (epirubicin) versus bacillus Calmette-Guérin. A controlled prospective study on the prophylaxis of superficial bladder cancer. Cancer, 72: 1749, 1993.
- Watanabe, N., Miyagawa, I., Higasibori, Y., Nakahara, T., Sumi, F., Ishida, G., Abe, B., Inoue, A. and Hanamoto, N.: Phase II study of intravesical chemoprophylaxis of epirubicin after transurethral resection of bladder tumors. Tottori University Oncology Group. Cancer Chemother. Pharmacol., suppl., 35: S57, 1994.
- van der Meijden, A. P., Kurth, K. H., Oosterlinck, W. and Debruyne, F. M.: Intravesical therapy with adriamycin and 4-epirubicin for superficial bladder cancer: the experience of the EORTC GU Group. Cancer Chemother. Pharmacol., suppl., **30**: S95, 1992.
- Abel, P. D., Hall, R. R. and Williams, G.: Should pT1 transitional cell cancers of the bladder still be classified as superficial? Brit. J. Urol., 62: 235, 1988.
- Carbin, B.-E., Ekman, P., Gustafson, H., Christensen, N. J., Silfverswärd, C. and Sandstedt, B.: Grading of human urothelial carcinoma based on nuclear atypia and mitotic frequency. II. Prognostic importance. J. Urol., 145: 972, 1991.
- Garnick, M. B., Schade, D., Israel, M., Maxwell, B. and Richie, J. P.: Intravesical doxorubicin for prophylaxis in the management of recurrent superficial bladder cancer. J. Urol., 131: 43, 1984.
- Matsumura, Y., Tsushima, T., Ozaki, Y., Yoshimoto, J., Akagi, T., Obama, T., Nasu, Y. and Ohmori, H.: Intravesical chemotherapy with 4'-epi-Adriamycin in patients with superficial bladder tumors. Cancer Chemother. Pharmacol., 16: 176, 1986.
- 22. Shinohara, N., Nonomura, K., Tanaka, M., Nagamori, S., Takakura, F., Seki, T., Koyanagi, T., Togashi, M. and Maru, A.: Prophylactic chemotherapy with anthracyclines (adriamycin, epirubicin and pirarubicin) for primary superficial bladder cancer. Hokkaido University Bladder Cancer Collaborative Group. Cancer Chemother. Pharmacol., suppl., **35**: S41, 1994.
- Burk, K., Kurth, K. H. and Newling, D.: Epirubicin in treatment and recurrence prophylaxis of patients with superficial bladder cancer. Progr. Clin. Biol. Res., 303: 423, 1989.
- Crawford, E. D., McKenzie, D., Mansson, W., Totonchy, M., Grossman, H. B., Davis, M., Lamm, D. L. and Duchek, M.: Adverse reactions to the intravesical administration of doxorubicin hydrochloride. Report of 6 cases. J. Urol., 136: 668, 1986.
- 25. Kurth, K. H., Schröder, F. H., Tunn, U., Ay, R., Pavone-Macaluso, M., Debruyne, F., de Pauw, M., Dalesio, O., ten Kate, F. and Members of the European Organization for Research on Treatment of Cancer, Genitourinary Tract Cancer Cooperative

Group: Adjuvant chemotherapy of superficial transitional cell bladder carcinoma: preliminary results of a European Organization for Research on Treatment of Cancer randomized trial comparing doxorubicin hydrochloride, ethoglucid and transurethral resection alone. J. Urol., **132**: 258, 1984.

- Kurth, K. H., v. d. Vijgh, W. J. F., ten Kate, F., Bogdanowicz, J. F., Carpentier, P. J. and van Reyswoud, I.: Phase 1/2 study of intravesical epirubicin in patients with carcinoma in situ of the bladder. J. Urol., 146: 1508, 1991.
- Jacobi, G. H. and Kurth, K. H.: Studies on the intravesical action of topically administered G³H-doxorubicin hydrochloride in men: plasma uptake and tumor penetration. J. Urol., **124:** 34, 1980.
- Edsmyr, F., Berlin, T., Boman, J., Duchek, M., Esposti, P. L., Gustafsson, H., Wijkström, H., and Collste, L. G.: Intravesical therapy with adriamycin in patients with superficial bladder tumors. Eur. Urol., 6: 132, 1980.

EDITORIAL COMMENT

In this study the 2 cytostatics, epirubicin and doxorubicin of the anthracycline family, were given intravesically after complete resection of stage Ta/T1 bladder carcinoma to prolong time to first recurrence and decrease the recurrence rate per 100 patient months (recurrence rate per year would have been more understandable) compared to transurethral resection alone. It is concluded that epirubicin has better efficacy than doxorubicin. This finding is surprising and I do not believe that the results justify the conclusion. In earlier studies in which cystostatics with proved therapeutic activity given intravesically were prospectively compared, none was superior (reference 25 in article).¹⁻⁴ For adjuvant chemotherapy doses of 50 and 80 mg. epirubicin, and 50 mg. doxorubicin were used. Although the pooled epirubicin results for time to first recurrence were superior to those of 50 mg. doxorubicin, 50 mg. epirubicin were not significantly better than 50 mg. doxorubicin (p = 0.159). Whereas for the end point of time to first recurrence no significant difference among the 3 chemotherapy arms was found, 80 mg. epirubicin significantly decreased the recurrence rate per 100 patient months compared to 50 mg. epirubicin. Thus, the superior results of the pooled epirubicin group are at least mainly due to the higher dose of epirubicin used in 1 arm. The 95% confidence interval for time to first recurrence is great in all treatment arms (15.0 to 37.4, 9.5 to 28.9, 24.6 to 50.1 and 52.3 to 77.3 in arms 1 to 4, respectively), although adjuvant treated patients undoubtedly do better than those treated with resection alone. The same observation holds true for recurrence rate per 100 patient months. No significant difference was found among the 4 treatment arms for progression to T2 disease or greater in this population of patients with an intermediate to high risk for progression. This finding confirms a recent combined analysis of patients treated by the European Organization for Research and Treatment of Cancer, Genitourinary Tract Cancer Cooperation Group and the Medical Research Council of the United Kingdom, showing no advantage of adjuvant chemotherapy over resection alone for preventing progression to T2 disease or greater.⁵ It seems that neither adjuvant chemotherapy nor immunotherapy, compared to chemotherapy, can prevent progression to muscle invasive disease.^{6.7} As even with the higher dose of epirubicin, significantly fewer cases and a significantly lower occurrence of local and systemic side effects were observed than after doxorubicin. Epirubicin may have advantages over doxorubicin. Although the finding of contracted bladder after adjuvant chemotherapy has been previously reported, 2.1% of patients (4 of 192) seems high and one wonders whether it can be explained by the high percent (38.5% or 74 of 192) of bladder tumors associated with bilharziasis.

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 Bouffioux, Ch., Denis, L., Oosterlinck, W., Viggiano, G., Vergison, B., Keuppens, F., de Pauw, M., Sylvester, R., Cheuvart, B. and members of the European Organization for Research and Cancer Genitourinary Group: Adjuvant chemotherapy of recurrent superficial transitional cell carcinoma: results of a European Organization for Research on Treatment of Cancer randomized trial comparing intravesical instillation of thiotepa, doxorubicin and cisplatin. J. Urol., **148**: 297, 1992.

- Huland, H., Klöppel, G., Fedderson, I., Otto, U., Brachmann, W., Hubmann, H., Kaufmann, J., Knipper, W., Lantzius-Beninga, F. and Huland, E.: Comparison of different schedules of cystostatic intravesical instillations in patients with superficial bladder carcinoma: final evaluation of a prospective multicenter study with 419 patients. J. Urol., part 2, 144: 68, 1990.
- Bouffioux, Ch., Kurth, K. H., Bono, A., Oosterlinck, W., Boeken Kruger, C., de Pauw, M., Sylvester, R. and Members of European Organization for Research and Treatment of Cancer Genitourinary Group: Intravesical adjuvant chemotherapy for superficial transitional cell bladder carcinoma: results of 2 European Organization for Research and Cancer randomized trials with mitomycin C and doxorubicin comparing early versus delayed and short-term versus long-term treatment. J. Urol., 153: 934, 1995.
- 4. Zincke, H., Benson, R. C., Jr., Hilton, J. F. and Taylor, W. F.: Intravesical thiotepa and mitomycin C treatment immediately after transurethral resection and later for superficial (stages Ta and Tis) bladder cancer: a prospective, randomized, stratified study with crossover design. J. Urol., **134**: 1110, 1985.
- 5. Pawinski, A., Sylvester, R., Kurth, K. H., Bouffioux, Ch., Van der Meijden, A., Parmar, M. K. B. and Bijnens, L. for members of European Organization for Research and Cancer Genitourinary Tract Cancer Cooperative Group and Medical Research Council Working Party on Superficial Bladder Cancer: A combined analysis of European Organization for Research and Treatment of Cancer, and Medical Research Council randomized clinical trials for the prophylactic treatment of stage TaT1 bladder cancer. J. Urol., **156**; 1934, 1996.
- Lamm, D. L., Blumenstein, B. A., Crawford, E. D., Crissman, J. D., Lowe, B. A., Smith, J. A., Jr., Sarosdy, M. F., Schellhammer, P. F., Sagalowsky A. I., Messing, E. M., Loehrer, P. and Grossman, H. B.: Randomized intergroup comparison of bacillus Calmette-Guerin immunotherapy and mitomycin C chemotherapy prophylaxis in superficial transitional cell carcinoma of the bladder. Urol. Oncol., 1: 119, 1995.
- Lundholm, C., Norlén, B. J., Ekman, P., Jahnson, S., Lagerkvist, M., Lindeborg, T., Olsson, J. O., Tveter, K., Wijkström, H., Westberg, R. and Malmström, P.-U.: A randomized prospective study comparing long-term intravesical instillations of mitomycin C and bacillus Calmette-Guerin in patients with superficial bladder carcinoma. J. Urol., **156**: 372, 1996.