LONG-TERM EXPERIENCE WITH RADIOFREQUENCY-INDUCED HYPERTHERMIA COMBINED WITH INTRAVESICAL CHEMOTHERAPY FOR NON-MUSCLE INVASIVE BLADDER CANCER.

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BACKGROUND: The recurrence rate of non-muscle invasive bladder cancer (NMIBC) is high, despite intravesical treatments. Importantly, patients are frequently unfit or unwilling to undergo a recommended radical cystectomy when standard intravesical treatments fail, due to the substantial risk of morbidity and mortality. For these patients, radiofrequency-induced hyperthermia combined with intravesical chemotherapy (RF-CHT) has shown promising results. We aim to determine treatment outcomes and assess the effect of (ablative) dose.

METHODS: 299 intensively pretreated patients treated with RF-CHT were included in safety analysis. Of these, 274 patients who fulfilled induction treatments were included in efficacy analysis. Six-month complete response (CR) and durable response were reported for (concomitant) carcinoma in situ (CIS) patients and recurrence-free survival (RFS) for papillary patients.

RESULTS: For CIS, six-month CR-rate was 56.0%; and durable response rates were 79.7%, 66.5%, and 40.3% at one-, two- and five-year, respectively. RFS rates for papillary patients were 77.9%, 57.5%, and 37.2%, respectively. Patients treated with ablative dose are less likely to develop recurrence (adjusted Hazard Ratio 0.54, p = 0.01), compared to adjuvant dose.

CONCLUSIONS: RF-CHT is effective in NMIBC patients in whom standard intravesical treatments have failed and should be considered in patients who are unwilling or unfit to undergo radical cystectomy. Patients with CIS or residual papillary tumor at baseline benefit from ablative dose.

Univariable analysis of overall survival, relative survival, and cancer specific survival.

Survival $(n = 274)$	5-Year, % (95% CI)	10-Year, % (95% CI)
os ⁷	72.3 (66.4–87.2)	51.0 (43.4–58.6)
RS 8	80.6 (74.0–87.1)	65.1 (55.2–75.1)
CSS ⁷	86.6 (81.7–91.5)	77.6 (70.3–84.9)

Risk stratification (EAU)

Intermediate: 28.1%

High: 71.9%

Previous BCG treatment

BCG unresponsive 85.4%

Refractory: 65.0% Intolerant: 7.7%

Baseline histology:

CIS with or without concomitant papillary tumor: 46.7%

Efficacy following Synergo:

During the mean follow-up period of 55.5 months, 80 patients (29.2%) received a radical cystectomy with or without neoadjuvant chemotherapy. The bladder preservation rate for this follow-up period was thus 70.8%. In 76.0% of patients, a radical cystectomy could be prevented for two years from last TURB, and in 61.1% a radical cystectomy could be prevented for five years. OS rate of patients who received a radical cystectomy was 71.0% at five years and 42.6% at ten years.

⁷ Overall survival (OS) and cancer specific survival (CSS) estimates with 95% confidence interval (CI) were obtained with Kaplan-Meier method. ⁸ Relative survival (RS) is determined as the overall survival in this cohort divided by the expected survival in a similar Dutch population.



