

Complementary radioiodine (RAI) treatment reduces the risk of relapse in low advanced differentiated thyroid carcinoma (DTC)

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Introduction

Complementary RAI treatment after total thyroidectomy constitutes the main strategy in postoperative management of DTC patients. European and American guidelines in accordance recommend RAI ablation in high risk patients (T3,T4 and/or N1) but its routine administration, in low risk subjects remains controversial due to the lack of unequivocal evidences of RAI effectiveness in radically operated subjects.

So far, there is still no prospective study demonstrated the efficacy of complementary RAI treatment. However, numerous retrospective analyses are available but their results

are divergent, especially with reference to the low risk DTC.

Thus, the aim of the study was a retrospective evaluation of long-term outcomes of combined DTC treatment to assess the impact of adjuvant RAI therapy in the low risk group.

The primary hypothesis was: "if adjuvant RAI treatment was unnecessary, a delay in RAI administration would have no impact on long-term outcomes".

Material

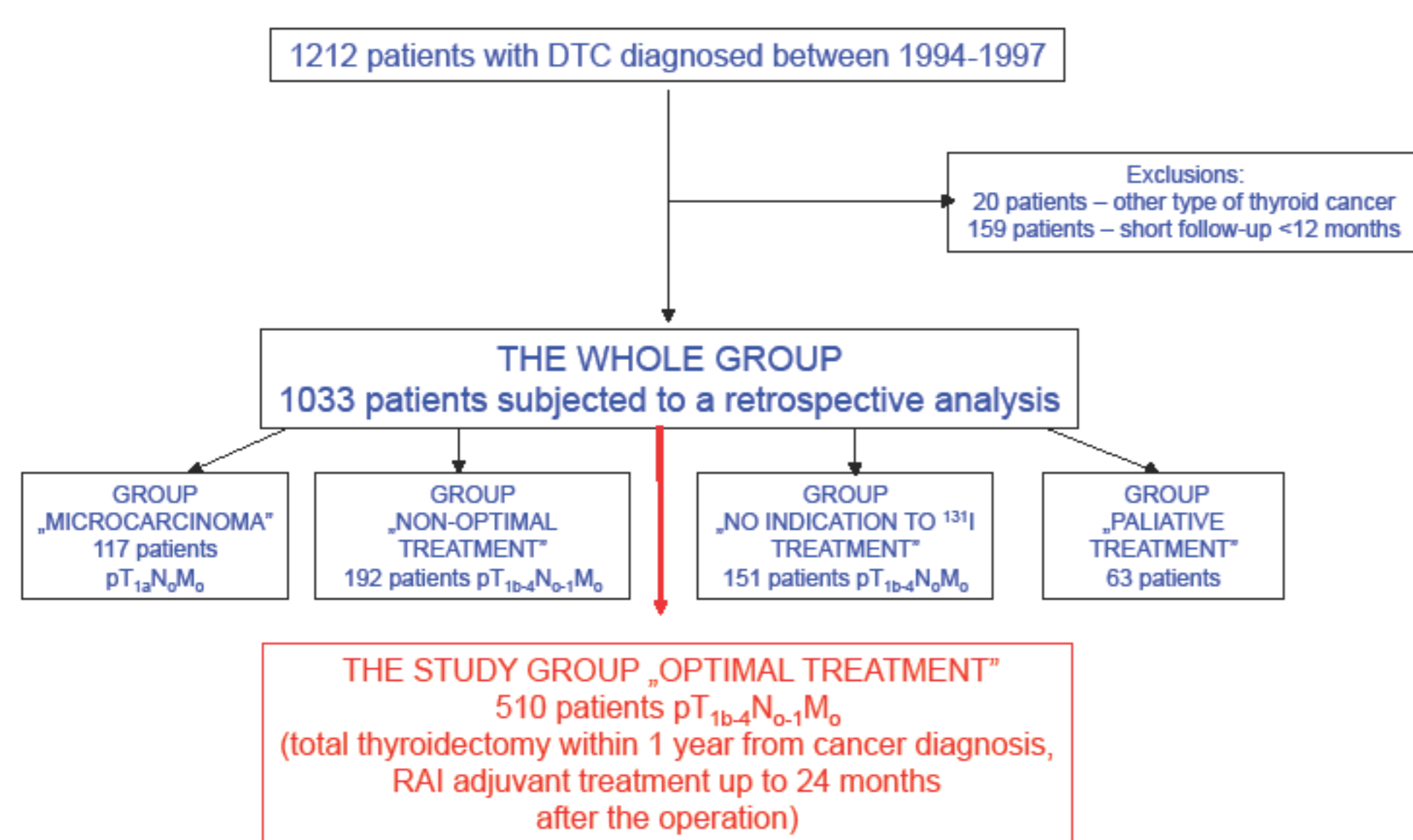


Fig. 1. Selection of the study group from the population of 1212 DTC patients

Medical records of 1212 DTC patients, admitted for the first time in Cancer Center in Gliwice between 1 Jan 94 and 31 Dec 97, were retrospectively analyzed. 20 patients diagnosed with non-DTC and 159 patients, with either further treatment carried out in other center (N=125) or with follow-up shorter than one year (N=34), were excluded. The remaining group of 1033 patients was subjected to the further analysis. Next, 510 DTC patients, staged pT1b-T4N0-N1M0, were selected from the whole group. They constituted "the study group" (Fig. 1). There were 409 women and 101 men, mean age at cancer diagnosis 42.2 years.

All subjects were treated with total thyroidectomy followed by complementary RAI therapy. Total thyroidectomy was carried out within one year after DTC diagnosis and ¹³¹I treatment within 24 months after surgery. In 71% (362) papillary thyroid carcinoma was diagnosed, whereas in 29% (148) – follicular thyroid cancer. Based on TNM classification (revised 1997), 11.6% patients were classified as T1, 35.1% – T2, 8.4% – T3, 9.4% – T4, and 35.5% as Tx. Lymph node metastases (N1) were present in 24.7% cases. Median follow-up was 12.1 years (range 1.5-15.2).

The overall recurrence rate in the study group was 12.55%

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Results

The risk factors influencing recurrence free survival (FFP – freedom from progression) were selected on the basis of a multivariate Cox regression analysis. Stimulated serum Tg level above 30 ng/ml, evaluated before RAI treatment, was the most potent, an independent risk factor as it increased the risk of DTC recurrence nearly six-fold. Lymph node involvement (N1) was associated with a nearly 4-fold increase in the risk of cancer relapse. Among other independent poor prognostic factors were tumor size (T feature), age at DTC diagnosis and thyroid remnant uptake (T₂₄) before RAI treatment (Fig. 2)

Due to the small number of deaths overall survival was not analyzed.

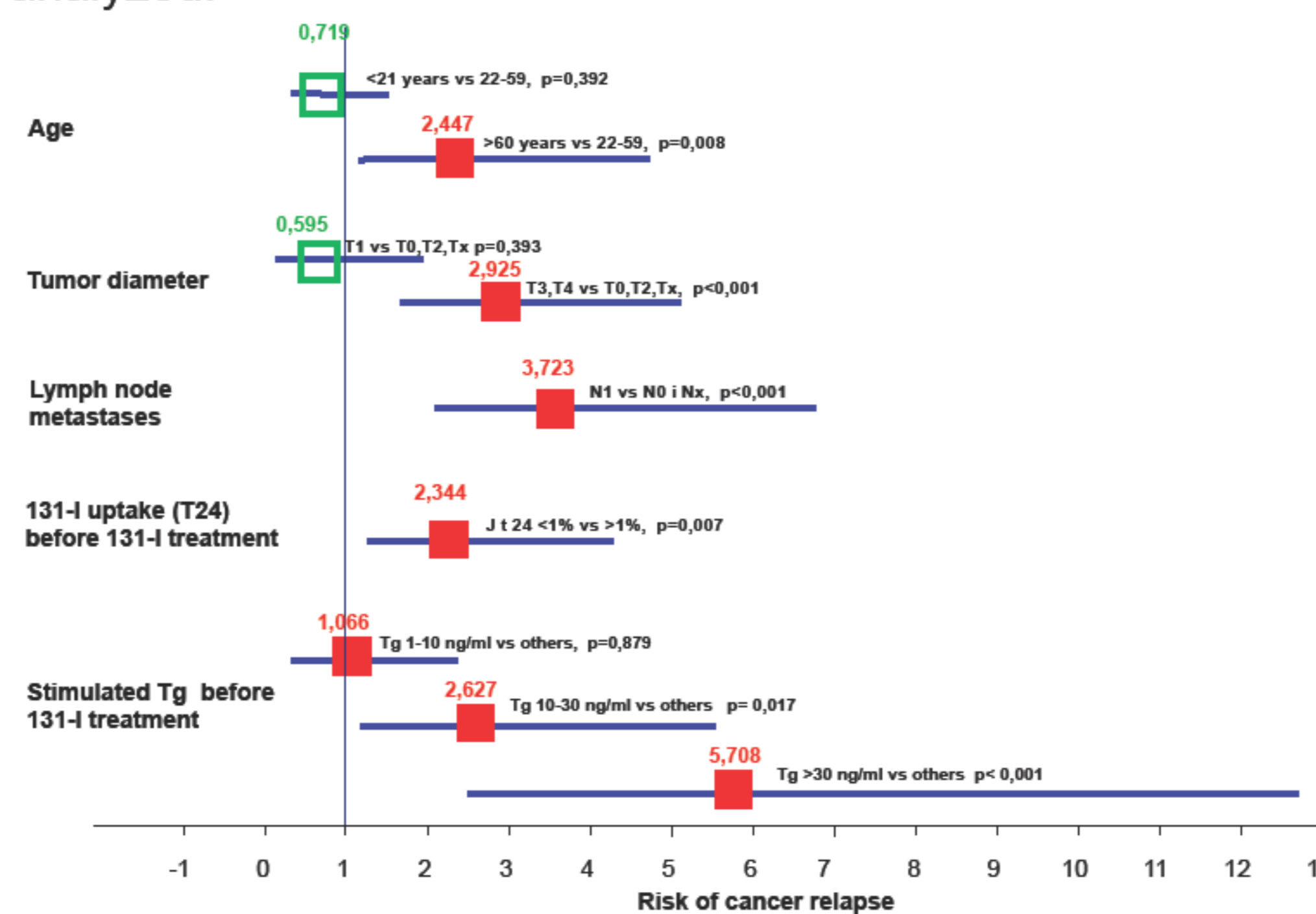


Fig. 2 Serum stimulated Tg > 30 ng/ml was the most important, independent risk factor in a multivariate Cox regression analysis

Next, to properly evaluate the efficacy of RAI adjuvant treatment, the study group was divided into three classes depending on the initial stage of the disease (T;N) and postoperative stimulated Tg level: class I „LOW RISK” – patients T1-T3, N0Nx, Tg <10 ng/ml (n=272); class II „INTERMEDIATE RISK” – patients T1-T3 + Tg between 10-30 ng/ml and T1-T3N1 + Tg <10 ng/ml, and T4N0N1 + Tg <10 ng/ml (n=148); class III „HIGH RISK” – patients T4 or N1 + Tg 10-30 ng/ml and patients with stimulated Tg >30 ng/ml (n=90) (Fig.3). Only after such stratification the efficacy of adjuvant RAI therapy was evaluated. A subgroup of patients treated with RAI ablation up to 9 months since cancer diagnosis was compared to subgroups treated later: within 9-24 and > 24 months

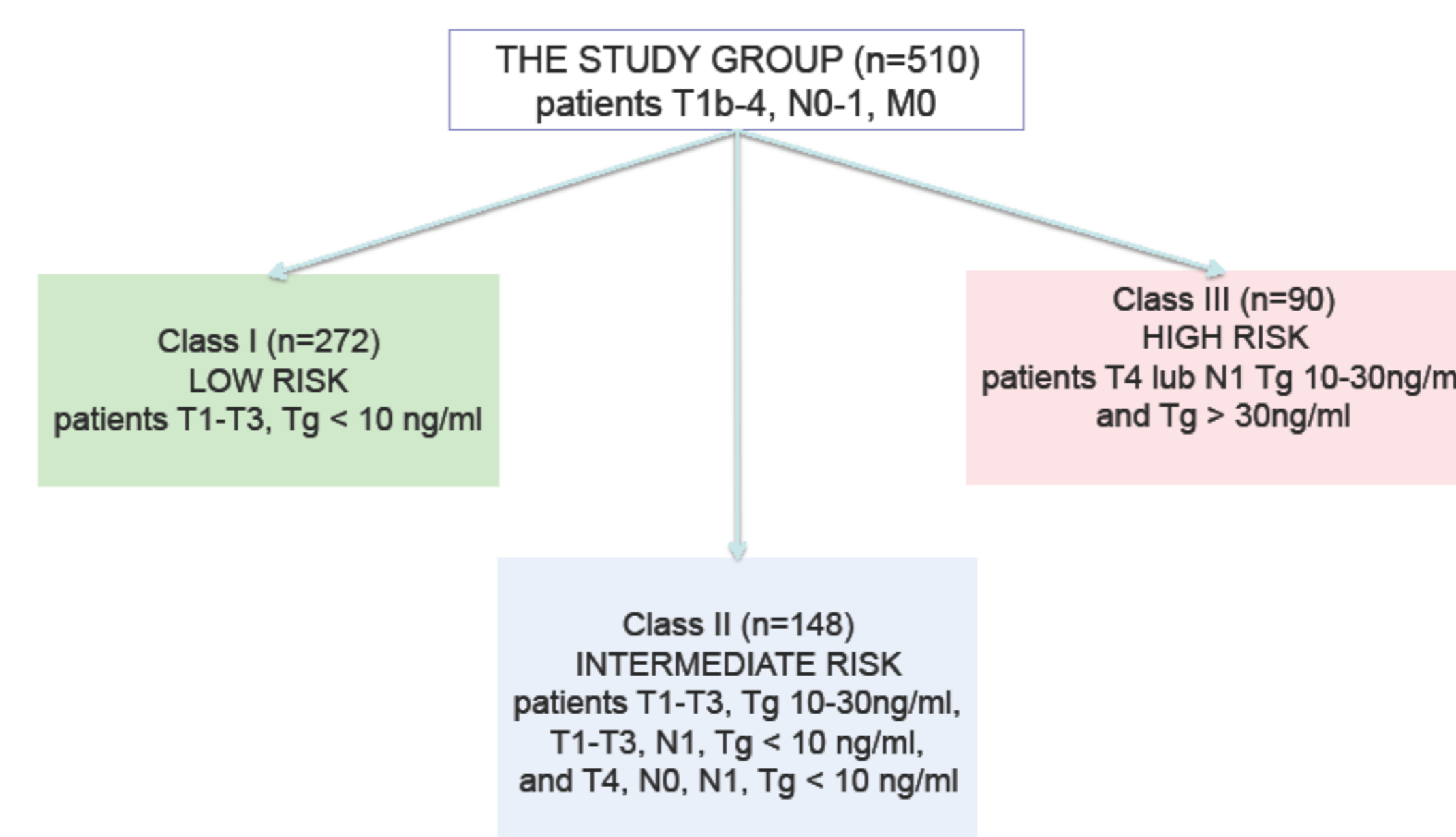


Fig. 3. The division of the study group into three risk classes stratified on the basis of a multivariate Cox regression analysis

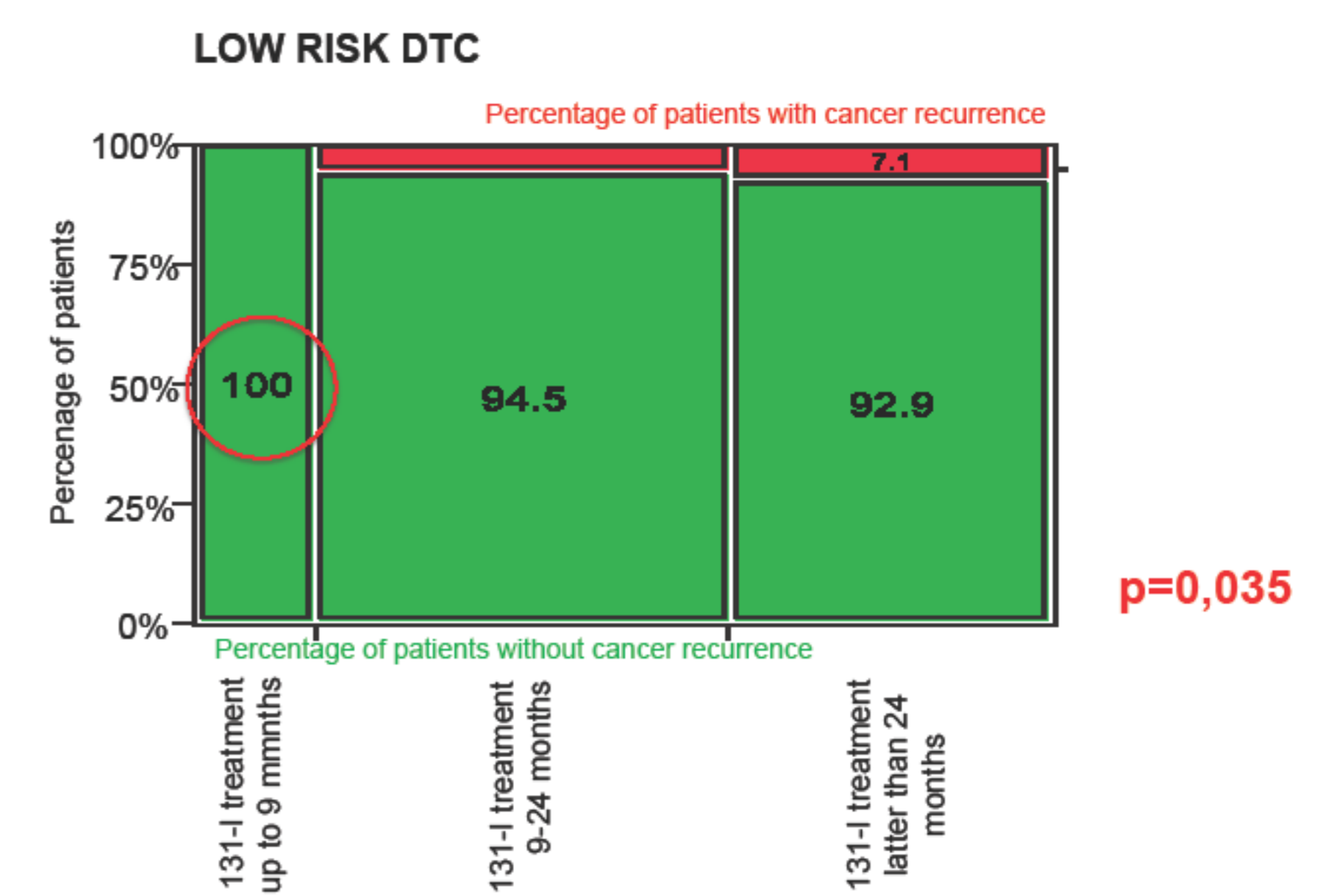


Fig.4 Within a low risk class, in a subgroup treated with RAI at the optimum time up to 9 months from disease diagnosis, no cancer recurrences was observed.

In the low risk class, patients treated with RAI ablation within 9 months from DTC diagnosis, showed no recurrences, whereas, among those, treated in the other time periods: 9-24 months and > 24 months from DTC diagnosis, the risk of relapse was 5.5% and 7.1%, respectively. These differences were statistically significant (Fig.4). However, no significant differences with reference to the time of RAI administration were noticed in both intermediate and high risk groups (Fig. 5).

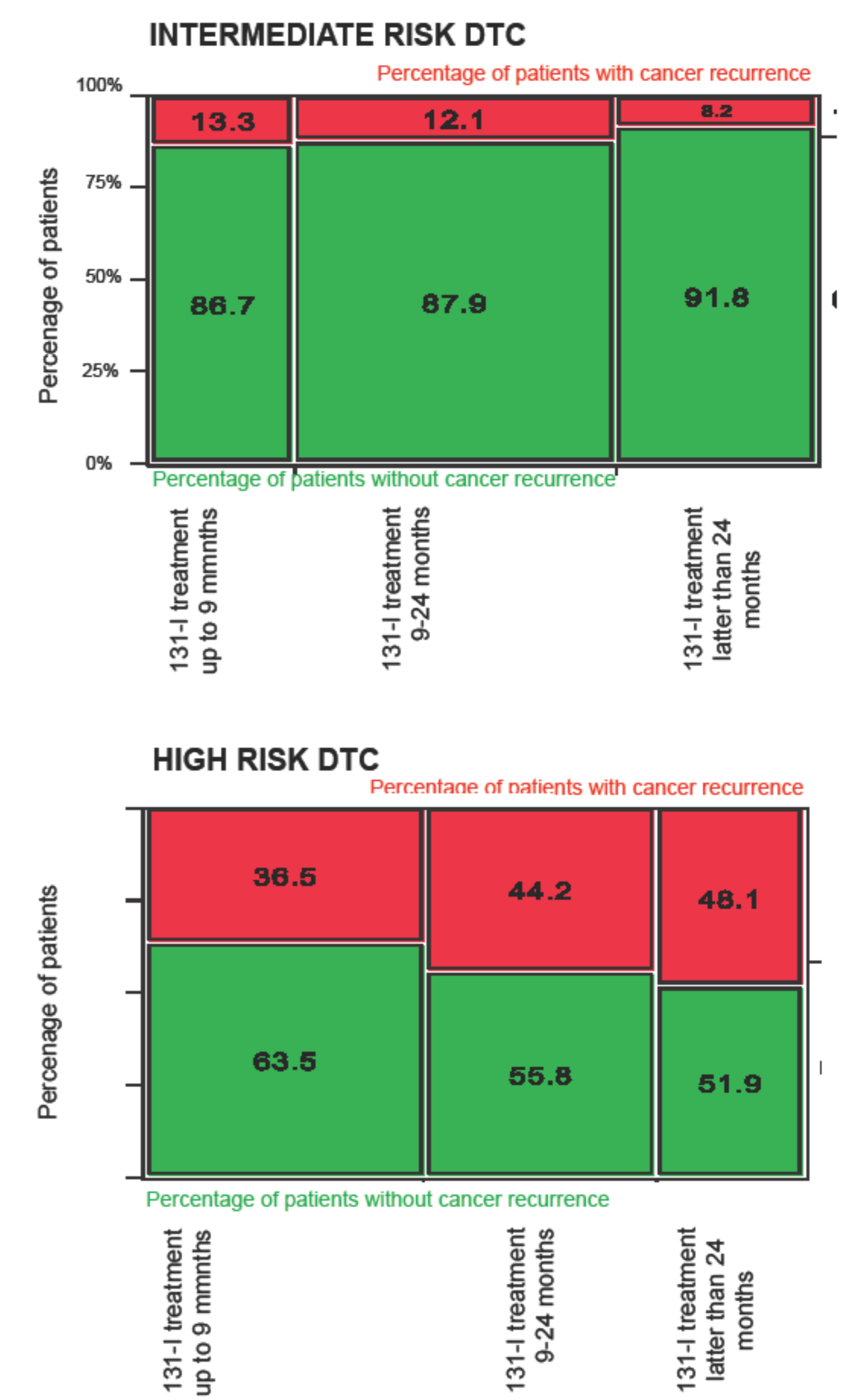


Fig.5. Intermediate (above) and high risk (below) classes showed no significant difference in the risk of cancer relapse depending on the time of RAI administration.

Conclusions

Complementary RAI therapy, administered within a short time period after the operation significantly reduces the risk of cancer recurrence in the low advanced differentiated thyroid carcinoma. We believe that the exclusion of low risk patients from RAI therapy, suggested by the ATA and European guidelines, is not justified.

Disclosure: None of the authors have any potential conflict of interest to this work

