

# Tumor regrowth in growth hormone deficient adults with non-functioning pituitary adenomas using growth hormone replacement therapy

## a sub-analysis from the Dutch National Registry of Growth Hormone Treatment in Adults

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### Introduction

Growth hormone deficiency (GHD) frequently occurs in adult patients with (treated) clinically nonfunctioning pituitary adenomas (NFPA)<sup>1</sup>. Although growth hormone replacement therapy (GH-RT) is a widely accepted treatment in these patients, concerns remain about the safety of GH-RT because of its potentially stimulating effect on tumor (re)growth.

### Objective

To evaluate tumor progression in a large cohort of adult NFPA patients using GH-RT.

### Patients & Methods

- Nationwide surveillance study (1998-2009): The Dutch National Registry of Growth Hormone Treatment in Adults
- Retrospective collection of anonymized patient data from start of GH-RT in adulthood (baseline)
- Included in the present study: patients with a (treated) NFPA using  $\geq 30$  days of GH-RT
- Tumor progression included tumor recurrence after complete remission at baseline as well as regrowth of residual tumor
- In Cox proportional hazard analysis adjustments were made for relevant confounders (e.g. age, gender, extension of pituitary insufficiency, surgery, radiotherapy, history of tumor progression)

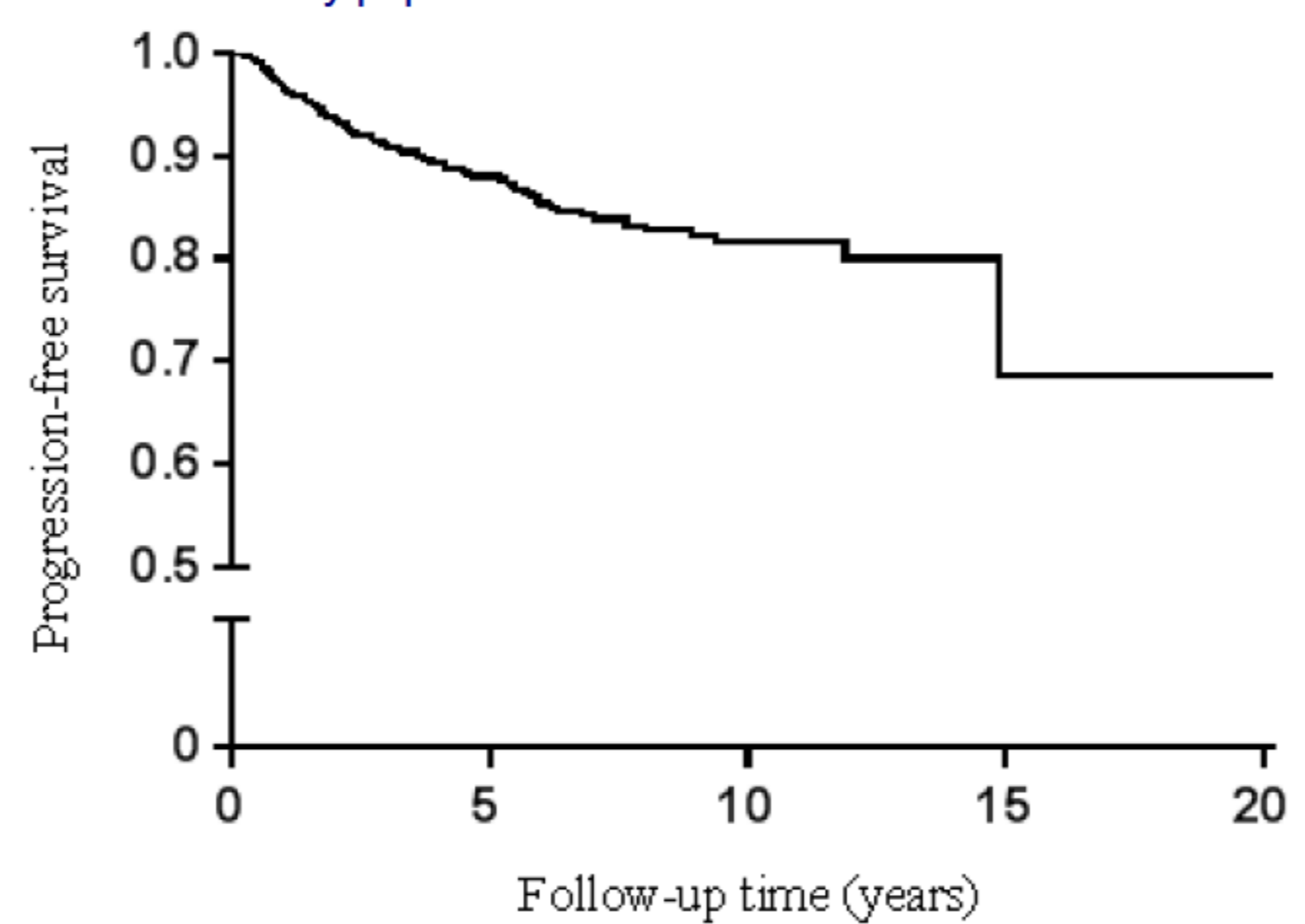
### Results

#### Total study population

Table 1. Characteristics of the total study population and of patients with and without tumor progression

|                  | All patients   | No tumor progression | Tumor progression | P value |
|------------------|----------------|----------------------|-------------------|---------|
| No. of patients  | 783            | 688 (87.5%)          | 95 (12.5%)        |         |
| Age at Baseline  | 54.8 (11.6)    | 55.1 (11.7)          | 52.8 (10.6)       | 0.07    |
| Gender, Male     | 478 (61.0%)    | 415 (60.3%)          | 63 (66.3%)        | 0.26    |
| Follow-up, years | 5.2 (0.1-20.2) | 5.1 (0.1-20.2)       | 6.0 (0.7-15.2)    | 0.10    |

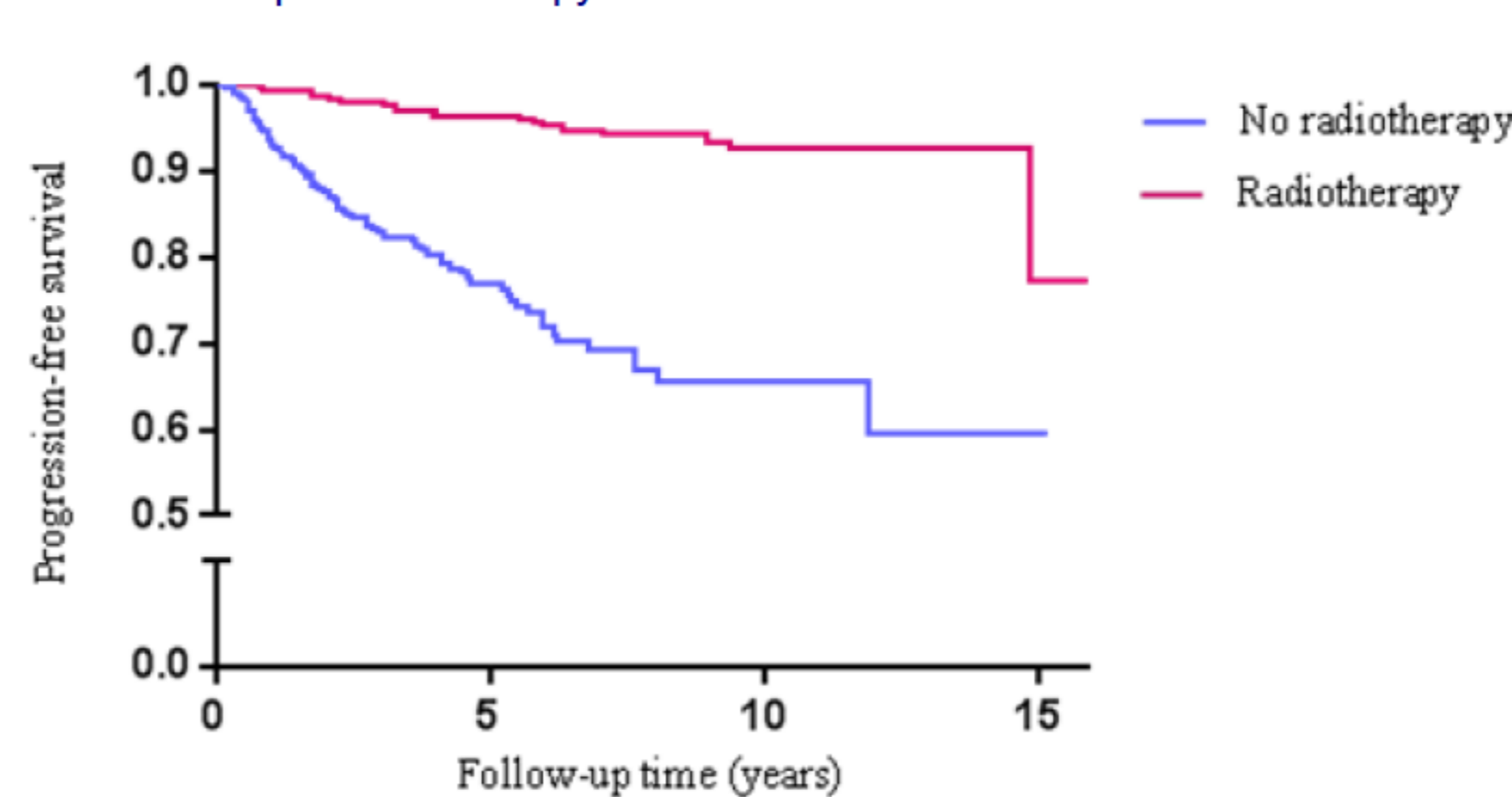
Figure 1. Kaplan-Meier curve of the progression-free survival of the total study population



#### Patients with and without radiotherapy

- Tumor progression developed in 4.8% of patients with prior radiotherapy vs. 20.1% of patients without prior radiotherapy
- Hazard ratio (HR) = 0.16, 95% confidence interval (CI) = 0.09–0.26,  $p < 0.001$

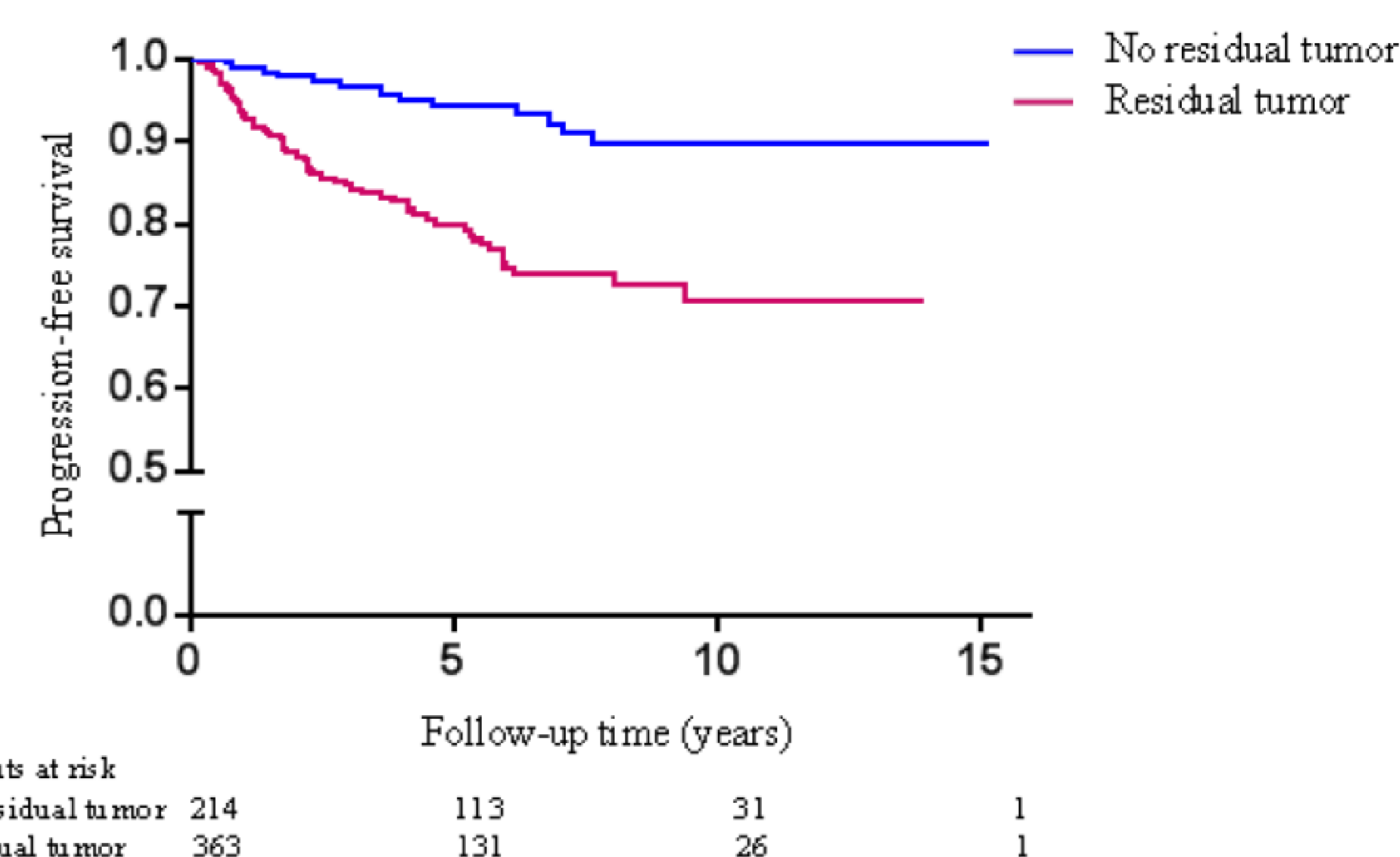
Figure 2. Kaplan-Meier curve of patients who had and had not received prior radiotherapy



#### Patients with and without residual tumor at baseline

- Tumor progression developed in 17.9% of patients with residual tumor vs. 6.1% of patients without residual tumor
- HR = 4.5, 95% CI = 2.4–8.2,  $p < 0.001$

Figure 3. Kaplan-Meier curve of patients with and without residual tumor at baseline



### Conclusions

- In this large cohort of NFPA patients using GH-RT, tumor progression developed in 12.5% of the patients
- Radiotherapy significantly decreased the risk of tumor progression, whereas residual tumor significantly increased this risk
- Findings in this study are in line with those in literature<sup>2-4</sup> and support the current view that GH-RT does not seem to increase tumor progression risk in NFPA patients
- However, as firm conclusions may only be generated by long-term randomized controlled trials, which are not likely to be performed, careful monitoring of these patients seems advisable

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2. Olson et al. Comparing progression of non-functioning pituitary adenomas in hypopituitarism patients with and without long-term GH replacement therapy. Eur J Endocrinol 2009;161:663-669.  
3. Arnold JF et al. GH replacement in patients with non-functioning pituitary adenoma (NFA) treated solely by surgery is not associated with increased risk of tumour recurrence. Clin Endocrinol (Oxf) 2009;70:435-438.  
4. Buchfelder M et al. Influence of GH substitution therapy in deficient adults on the recurrence rate of hormonally inactive pituitary adenomas: a case control study. Eur J Endocrinol 2007;157:149-156.

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