

Sorafenib induces thyroid hormone alterations which affect prognosis of hepatocellular carcinoma

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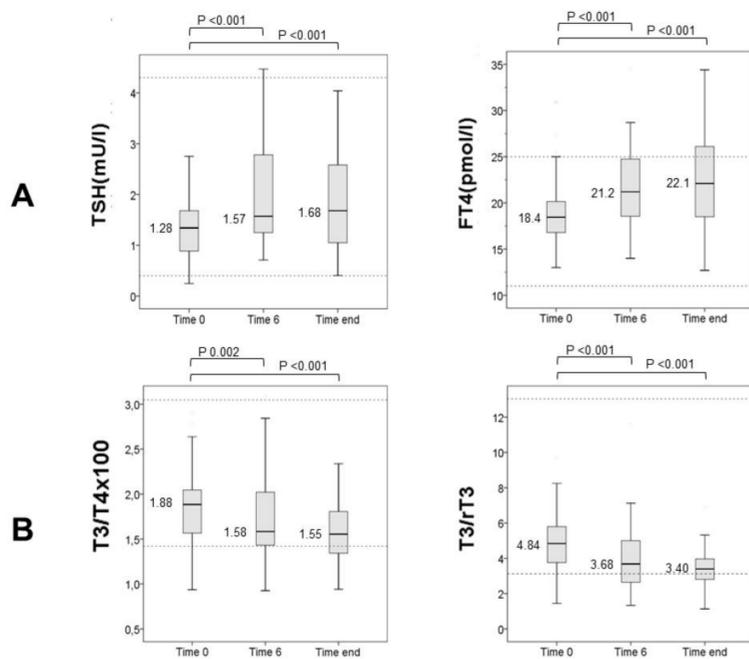
Conclusions

In this prospective study we demonstrate that sorafenib likely affects thyroid function tests via more than one mechanism.

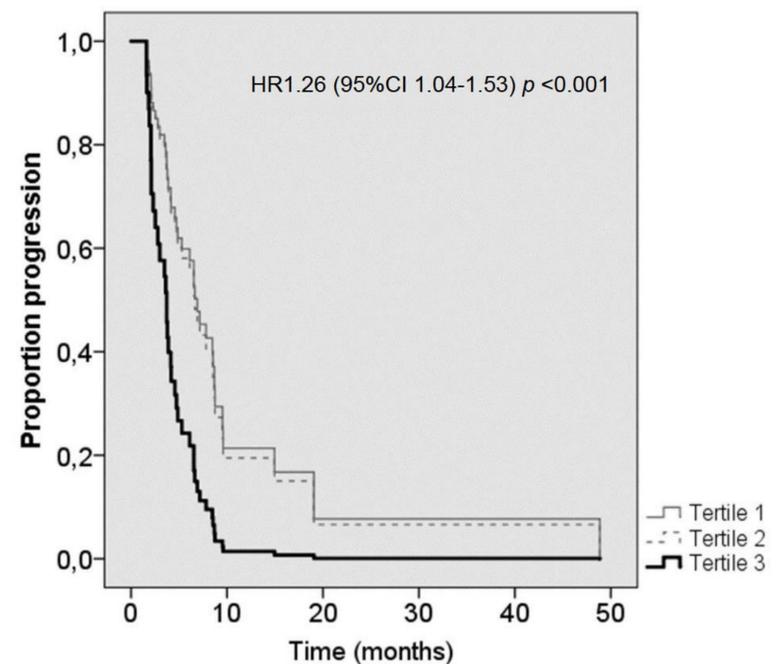
- Thyroiditis occurred in 7% of the patients.
- The combined increase in TSH and FT4 that we found in 30% of patients suggests central adaptation of the hypothalamic-pituitary-thyroid axis.
- TSH and FT4 changes are not due to Sorafenib induced alterations in the monocarboxylate transporter(MCT)8 or MCT10 transporter as measured in kidney cells.
- The marked decrease in the T3/rT3 and T3/T4 ratios during treatment with sorafenib is in line with an effect on the peripheral metabolism of thyroid hormone.
- An increase of TSH was associated with deterioration of progression free survival.

Results

Change in thyroid function tests



Progression by delta TSH tertiles



Aim

Prospective study of the effects of sorafenib on thyroid hormone levels and prognosis in patients with hepatocellular carcinoma.

Introduction

Tyrosine kinase inhibitors, especially sunitinib, are known to cause disturbances in thyroid function. For sorafenib the effects on thyroid function and thyroid hormone metabolism are less well established.

Materials and methods

We studied 56 patients with hepatocellular carcinoma who were treated with sorafenib in our tertiary referral center between 2009 and 2016.

We measured thyroid stimulating hormone (TSH) and free thyroxine (FT4) every 6 weeks and if available thyroxine (T4), triiodothyronine (T3) and reverse triiodothyronine (rT3) before treatment [time 0], after 6 weeks [time 6], and at the end of therapy with sorafenib [time end].

In addition, sorafenib induced change on thyroid hormone transport via T3 or T4 uptake by MCT8 or MCT10 transporter was tested in COS1 kidney cells.

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