



Morphological and functional alterations of thyroid gland during treatment with tyrosine kinase inhibitors in advanced renal cell carcinoma



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Introduction

Sunitinib (SUN) is a novel oral multitarget tyrosine-kinase inhibitor (TKI) that has demonstrated its efficacy in the treatment of metastatic renal cell carcinoma (mRCC). The thyroid dysfunction is one of the most common side effects of SUN. The mechanisms inducing thyroid dysfunction are still poorly understood.

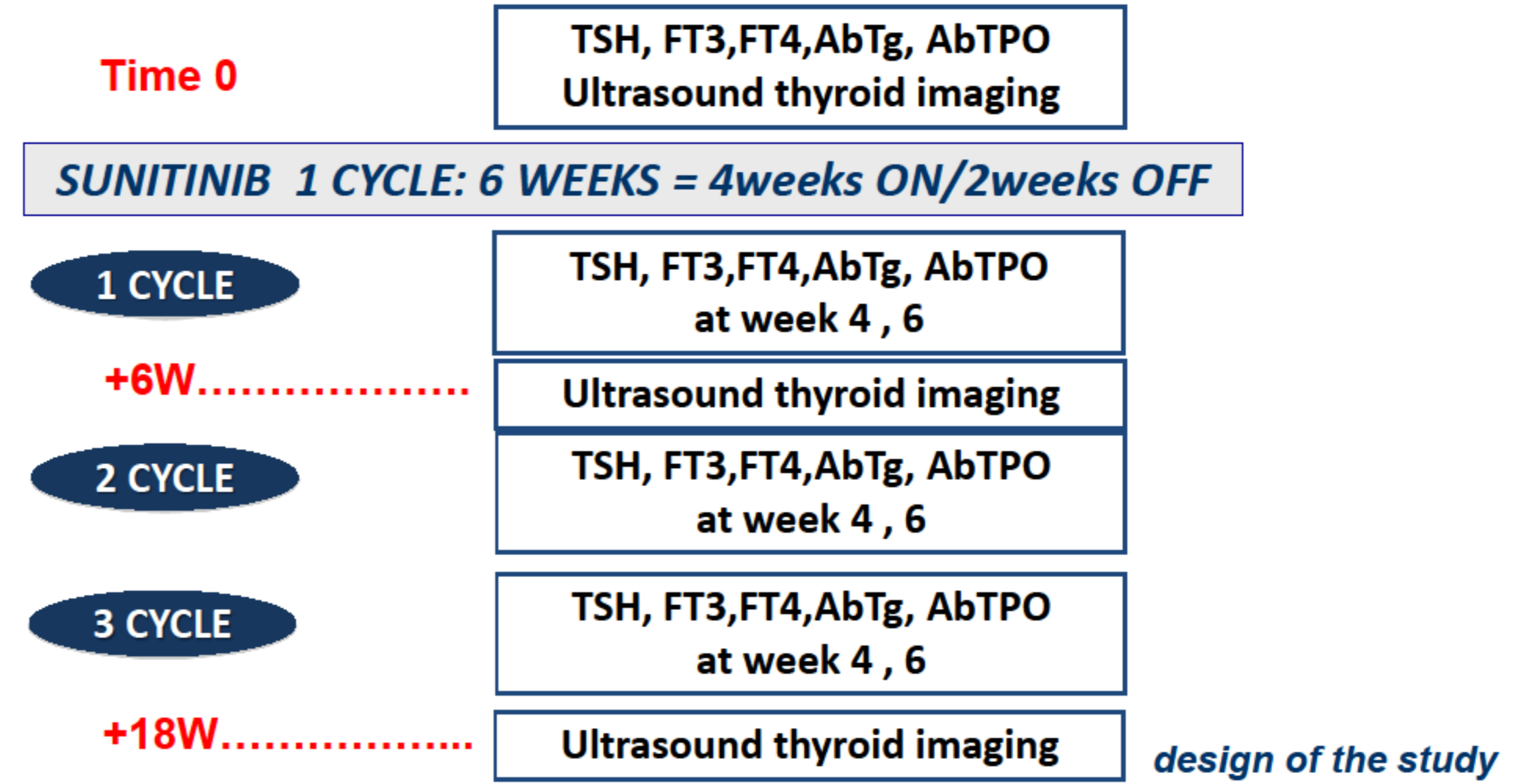
Objectives

Identify the incidence, severity, ultrasonographic changes and pattern of response of thyroid function tests during treatment with SUN.

Methods

This ongoing prospective observational study to date has completed the evaluation of 25 mRCC patients: 10 women (59±18 yrs) and 15 men (65.5±7 yrs). 5/25 patients received LT4 replacement therapy and 11/25 had thyroid nodules at enrollment.

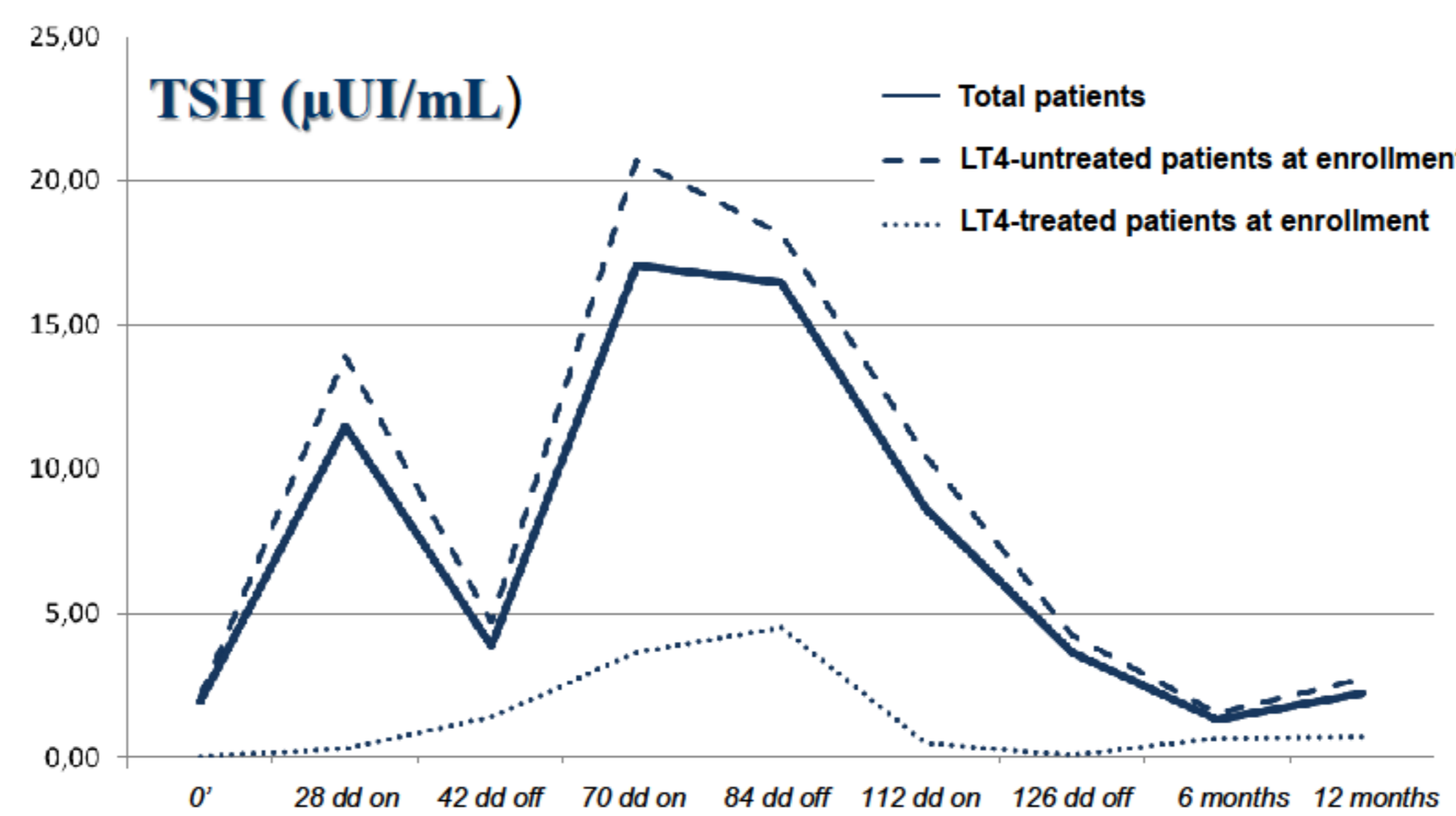
SUN was administered at daily dose of 50 mg (schedule 4/2). Thyroid function tests were assessed at baseline and at week-4 and -6 of each cycle, ultrasound at baseline and after the first and the third SUN cycle (See design of the study)



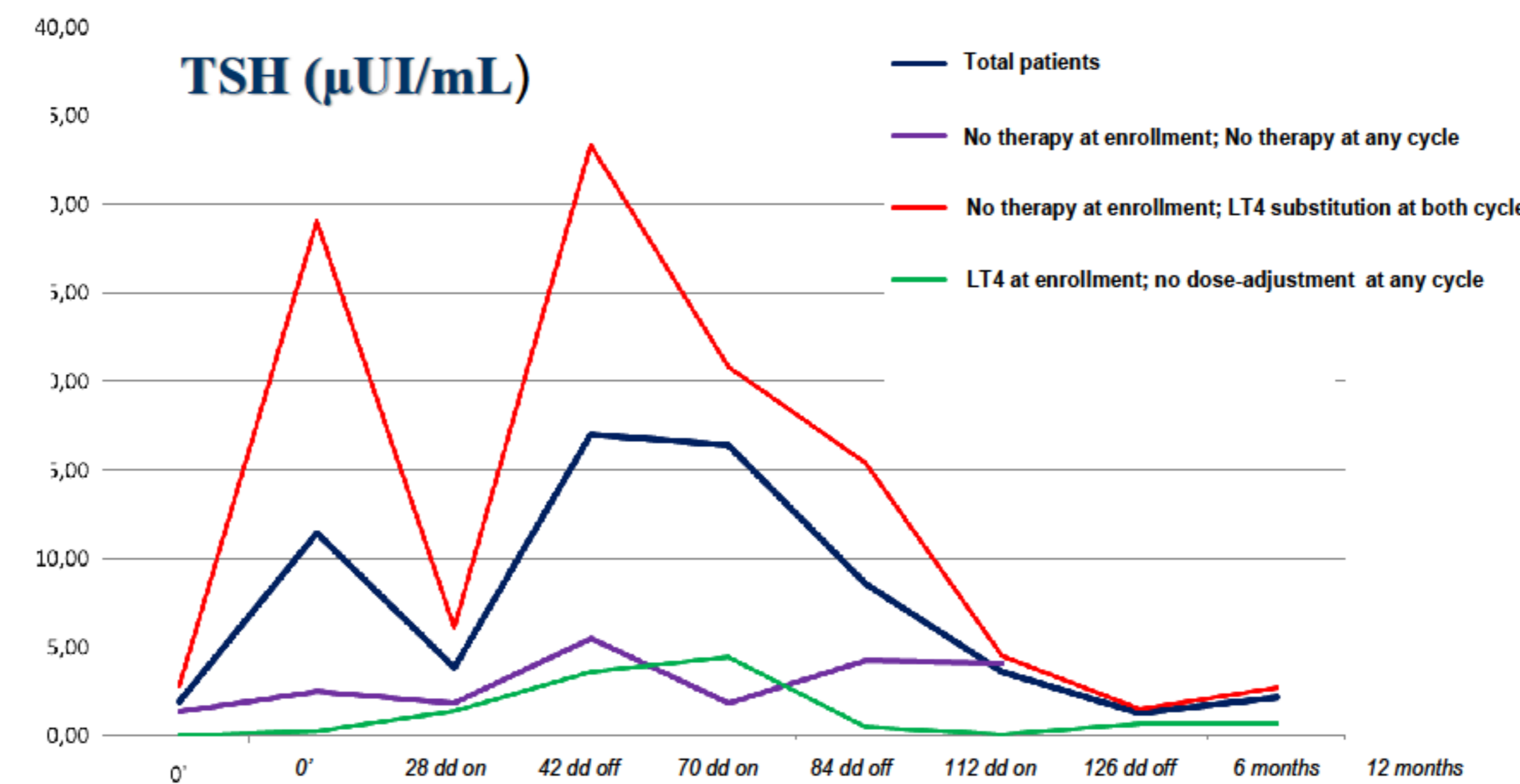
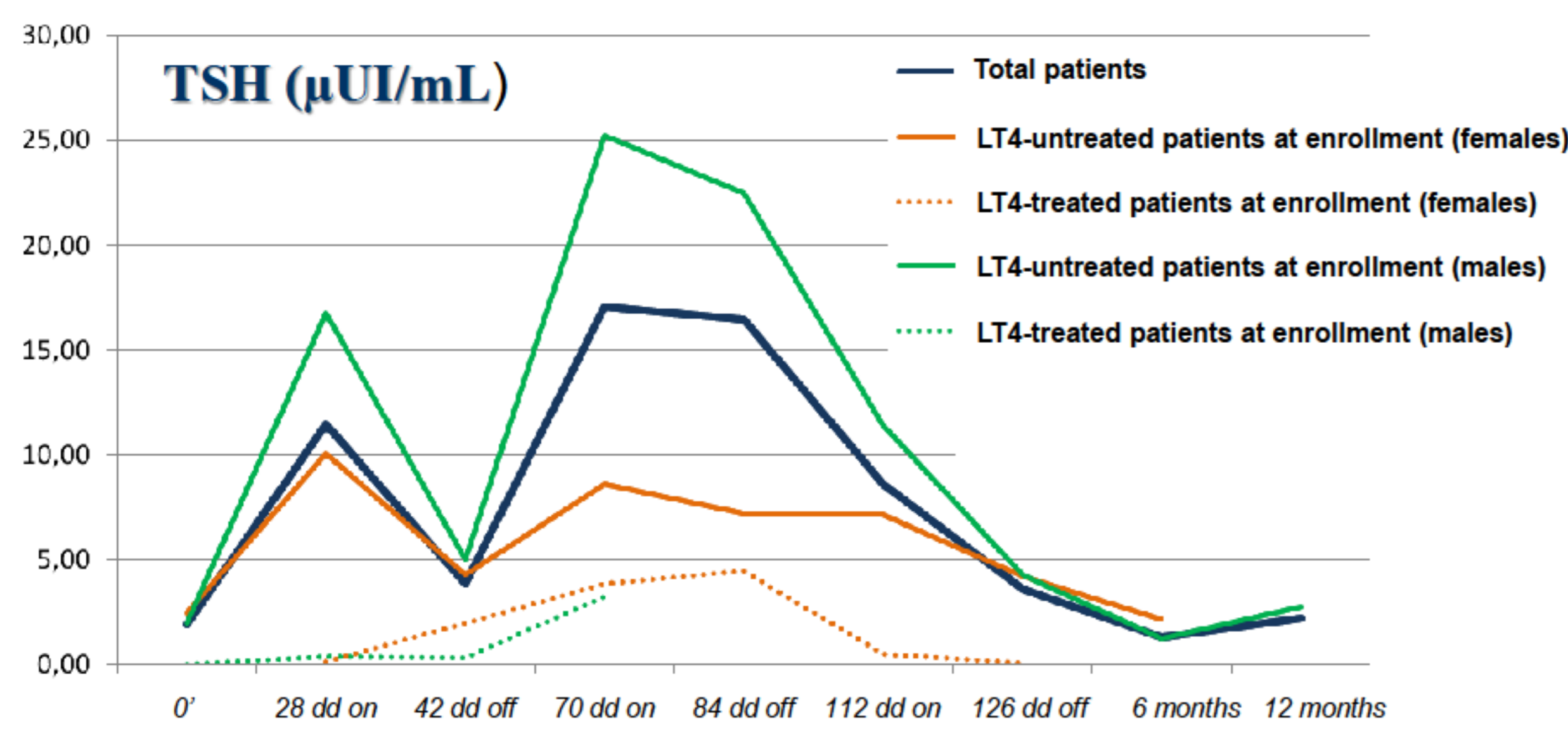
Results

Mean-TSH of each cycle

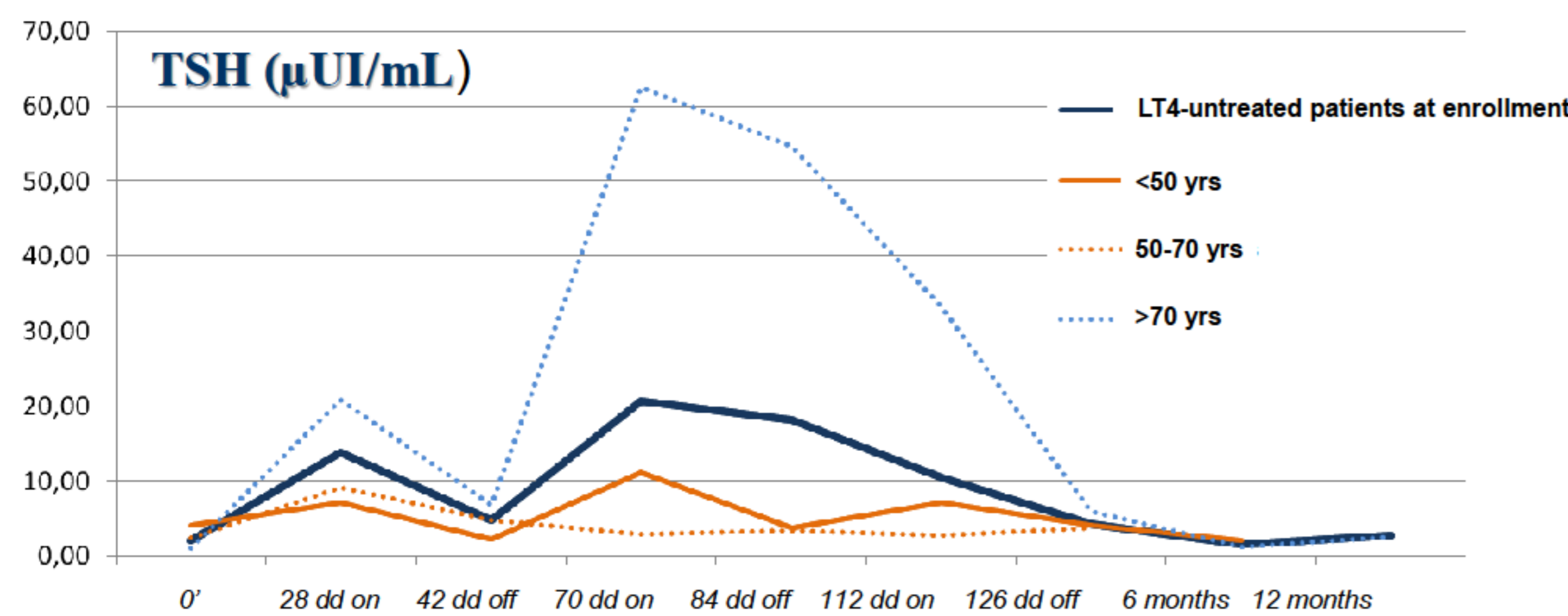
	Total population					Females			Males				
	Pt	media	Std. Dev.	Min	Max	<50 yrs	50-70 yrs	>70 yrs	50-70 yrs	>70 yrs	Pt		
0'	13	1,96	1,73	0,02	6,64	4,08	2	0,86	2	2,01	6	1,17	3
28 dd on	17	11,49	26,55	0,03	108,47	7,21	2	19,27	2	2,49	3	2,49	7
42 dd off	12	3,88	3,82	0,01	10,20	2,32	2	4,76	2	3,51	2	3,03	5
70 dd on	14	17,05	43,56	0,00	167,40	11,13	2	3,90	1	3,69	2	3,03	7
84 dd off	8	16,44	31,17	0,05	92,35	3,82	1	7,55	2	0	1	1,14	3
112 dd on	11	8,63	17,11	0,08	58,54	7,15	2	0,08	1	0,87	1	2,67	5
126 dd off	7	3,65	2,93	0,07	7,90	4,24	2	0,07	1	0	0	3,73	3
6 months	4	1,33	0,70	0,67	2,17	2,17	1	0	0	0	0	0,67	1
12 months	4	2,22	1,71	0,68	4,20	0	0	0,68	1	0	0	3,09	1



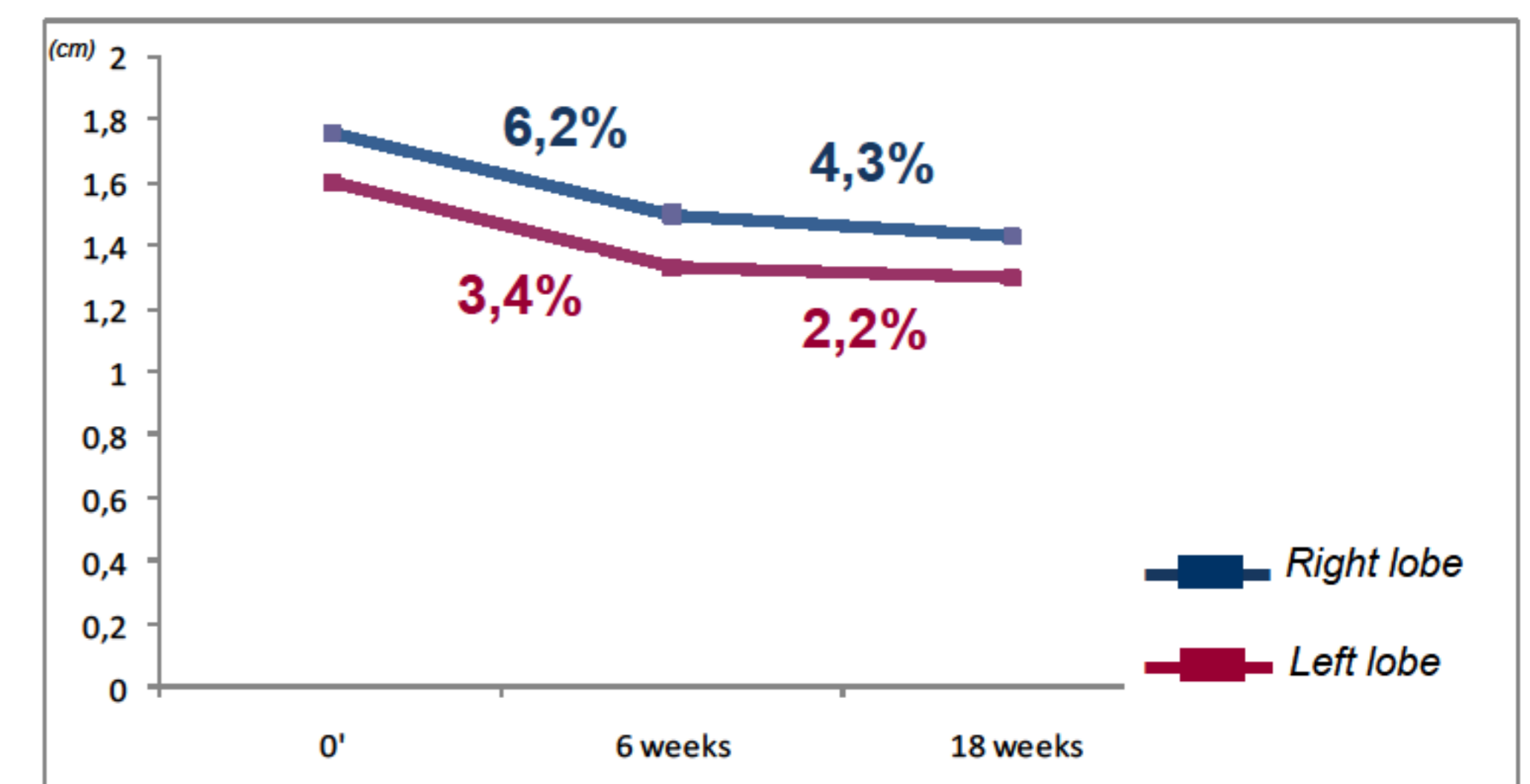
We observed an increase in TSH values, most frequently after the second cycle of SUN (mean-TSH 17.05±43.56 µUI/mL) and in older men (mean-TSH 91.95±106.4 µUI/mL). TSH rose above normal range (0.35-4.94 µUI/mL) only in patients which were not on LT4 replacement at enrolment.



Half of untreated patients had an increase of TSH which required L-T4 substitution after the first cycle; all of them required a further dosage increase after the second cycle. Patients already on L-T4 at the enrollment required no dose-adjustment at any cycle. No significant changes occurred in thyroid immunity.



In all patients, a main volumetric reduction of thyroid lobes occurred at week-6. Ultrasound at week-18, detected the appearance of a hypochoic solid nodule in one patient and a volumetric increase of pre-existing nodules in two other patients.



Conclusions

SUN is associated with thyroid functional and morphological changes occurring rapidly, within few weeks, in most but not all patients. Distinct individual patterns of response to TKI are identified allowing a better prognosis and management. The development of thyroid nodules and the mechanisms by which SUN impairment thyroid function deserve further investigations.

References

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