

**Supplemental Table 1. Baseline Documentation of Target and Non-target Lesions [14]**

<b>Lesions</b>	<b>Definition</b>	<b>Baseline documentation</b>
Target lesions	Radioiodine avid areas with the largest dimension of more than or equal to 1 cm by CT scan, and in the case of metastatic lymph nodes as more than or equal to 1.5 cm in short axis when assessed by CT scan	All target lesions up to a maximum of 5 lesions total and a maximum of 2 lesions per organ were measured and the sum of the longest diameter (or in case of lymph nodes of the short axis) was recorded.
Non-target lesions	All other metastatic lesions, lesions which were subjected to additional loco-regional treatment such as additional surgery or external beam radiation therapy (EBRT) were also considered non-target lesions.	All non target lesions were recorded at baseline as present, absent, countable, uncountable or multiple.

**Supplemental Table 2. Evaluation of the Response to the Treatment with Radioiodine [14]**

<b>Response</b>	<b>Definition</b>
Complete response (CR)	1) Disappearance of all target and non-target lesions; 2) Reduction of lymph node short axis to <1 cm; 3) Undetectable serum thyroglobulin (Tg) both during suppression and after TSH stimulation.
Partial response (PR)	Decrease of 30% or more in the sum of diameters of target lesions, taking as a reference the baseline sum diameter.
Stable disease (SD)	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD or nonPD/nonCR for non target disease
Progressive disease (PD)	At least a 20% increase in the sum of diameters of target lesions taking as a reference the smallest sum on the study and an increase of at least 5 mm or appearance of one or more new lesions.

**Supplemental Table 3. WHO Classification of Side Effects after the Treatment with 131-I [16]**

<b>Leukopenia</b>	<b>WBC</b>
Grade 1	Lower normal laboratory limit
Grade 2	2000-3000/ul
Grade 3	1000-2000/ul
Grade 4	Below 1000/ul
Grade 5	death
<b>Thrombocytopenia</b>	<b>PLT</b>
Grade 1	75000-150000/ul
Grade 2	50000-75000/ul
Grade 3	25000-50000/ul
Grade 4	below 25000/ul
Grade 5	death

**Supplemental Table 4. Characteristic of the Patients with Distant Metastases Advanced Disease,  
Who Obtained Complete Response after Treatment with D-Rx and E-Rx**

<b>Patients with distant metastases</b>			
<b>Treatment</b>	<b>D-Rx</b>		<b>E-Rx</b>
<b>Response</b>	<b>CR</b>	<b>CR</b>	<b>CR</b>
	<b>Patient #1</b>	<b>Patient #2</b>	<b>Patient#1</b>
<b>Age</b>	43	30	19
<b>Sex</b>	male	female	female
<b>Histology</b>	FVPTC	PTC	PTC
<b>Clinical stage</b>	T3N1aM1	T2N1bM1	T3N1bM1
<b>Location of distant metastases</b>	Lungs	Lungs, liver	Lungs
<b>Non-target lesions (CT scan)</b>	Countable micro-nodular pulmonary	Countable micro-nodular pulmonary, liver 2 cm, subjected to thermo-ablation	Multiple micro-nodular pulmonary
<b>Target lesions sum of max diameters [cm] (CT scan)</b>	n/a	n/a	n/a
<b>non-stimulated (1) and stimulated (2) Tg [ng/ml] before the treatment with 131-I</b>	(1) n/a (2) 4.4	(1) 14.2 (2) 362	Anti-Tg (+)
<b>non-stimulated (3) and stimulated (4) Tg [ng/ml] after the treatment</b>	(3) <0.2 (4) <0.2	(3) <0.2 (4) <0.2	(3) <0.5 Ab neg (4) <0.5 Ab neg
<b>Number of 131-I doses</b>	1	1	2
<b>Total cumulative dose [mCi]</b>	312.5	200	430

Post-treatment WBS	3 focal areas of uptake within the thyroid bed, 2 focal areas in the region of supra-sternal notch, intense focal uptake at the posterior right lung base, faint area of radioiodine avid uptake in the left mid lung field which is evident also post cleaning	Multiple foci in the thyroid bed region, focal radiotracer accumulation in the base of the right lung field (might reflect liver metastasis), 2 pulmonary/breast foci of radiotracer accumulation	After 1 dose multiple foci of <sup>131</sup> I uptake in the lungs  After 2 dose two nodules with positive uptake in the right lower chest and two sites of uptake in the mediastinum, resolution of the other, previously seen nodules
Additional treatment (surgery EBRT, zoledronic acid)	No	Before the treatment with <sup>131</sup> I : 2 cm liver lesion treated with thermo-ablation, modified neck dissection for persistent disease in the cervical lymph nodes	No
Disease-free survival after the last dose [months]	24.5	25	94

**Supplemental Table 5. Characteristic of the Patients with Loco-regionally Advanced Disease, Who Obtained Complete Response after Treatment with D-Rx and E-Rx**

Patients with loco-regionally advanced disease						
	D-Rx					E-Rx
	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5	Patient #1
Response	CR	CR	CR	CR	CR	CR
Age	77	51	23	69	42	58
Sex	male	female	male	male	male	female
Histology	PTCFV	Tall cell variant	PTC	PTC	PTC	PTC
Surgical margins	Positive	Negative	Negative	Positive	Negative	Negative
Clinical stage	T4aN0M0	T4aN0M0	T4aN1bM0	T4aN1bM0	T3N1bM0	T4aN0M0
T [cm]	4	1.3	n/a	2.5	5	1.1
Non-stimulated (1) and stimulated (2) Tg before the treatment with 131-I	(1) n/a (2) 1.1	(1) 0.6 (2) 13.7	Ab +	Ab+	(1) <0.2 (2) 0.2	(1) n/a (2) 14.7
Non-stimulated (3) and stimulated (4) Tg [ng/ml] after the treatment with 131-I	(3) <0.2 (4) <0.2	(3) <0.2 (4) <0.2	(3) <0.2Ab neg (4) <0.2Ab neg	(3) <0.2Ab neg (4) <0.2Ab neg	(3) <0.2 (4) <0.2	(3) <0.2 (4) <0.2

**Supplemental Table 6.  $\Delta$ Tg after the Treatment with D-Rx vs E-Rx**

% decrease in Tg levels	Distant metastases group		Locally invasive group	
	D-Rx	E-Rx	D-Rx	E-Rx
0%-<25%	0% (n=0/21)	0% (n=0/6)	0% (n=0/6)	6.2% (n=1/16)
25% -<50%	23.8% (n=5/21)	16.7% (n=1/6)	0% (n=0/6)	0%(n=0/16)
50%-<75%	19.1% (n=4/21)	0% (n=0/6)	0% (n=0/6)	0% (n=0/16)
$\geq$ 75%	57.1% (n=12/21)	83.3% (n=5/6)	100% (n=6/6)	93.8% (n=15/16)

**Supplemental Table 7. The Medical History of the Patient, Who Developed Restrictive Pulmonary Disease after the Treatment with 131-I**

**Medical history**

A 59 year old man with PTC presenting with multiple micro-nodular pulmonary metastases treated with 2 dosimetry-based 131-I doses up to total cumulative dose of 558.2 mCi which was equal to 89.1% of MTA. The restrictive pulmonary disease with moderately reduced diffusion capacity (DLCO) was documented by pulmonary function tests (PFTs) after the first dose of 131-I. This complication occurred despite the fact that the 48h whole body 131-I retention in this patient was lower than 80 mCi, the level considered to be consistent with little risk of pulmonary fibrosis in patients with high volume pulmonary disease. Restrictive pulmonary disease in this case could have been radiation induced as well as due to the underlying pulmonary disease. The recent PFTs of this patient revealed mild restrictive lung defect (TLC 75% predicted), mild reduction in DLCO (67% predicted) and mild hypoxemia.