

Supplementary table 1. Mutation spectrum analyzed by MassARRAY tests.

Panel	Mutated Gene [Number of mutations]		
ThyroSPEC™ Panel	<i>AGK-BRAF</i>	<i>PAX8-PPARG</i>	
	<i>AKAP-BRAF</i>	<i>PIK3CA</i> [5]	
	<i>AKT1</i> [1]	<i>PTEN</i> [1]	
	<i>BRAF</i> [7]	<i>RET</i> [19]	
	<i>CRTC1-MAML2</i>	<i>RET-PTC</i> [4]	
	<i>CTNNB1</i> [11]	<i>RPS2P32-THADA</i>	
	<i>DICER1</i> [3]	<i>SND1-BRAF</i>	
	<i>EGFR</i> [1]	<i>SPOP</i> [1]	
	<i>EIF1AX</i> [4]	<i>SQSTM1-NTRK3</i>	
	<i>EML4-ALK</i>	<i>STRN-ALK</i>	
	<i>ETV6/NTRK3</i>	<i>TERT (c.1-124C>T, c.1-146C>T)</i>	
	<i>EZH1</i> [1]	<i>TFG-NTRK1</i>	
	<i>HRAS</i> [15]	<i>TMEM233-PRKAB1</i>	
	<i>IDH1</i> [1]	<i>TP53</i> [10]	
	<i>IGF2BP3-THADA</i>	<i>TPM3-NTRK1</i>	
	<i>KRAS</i> [17]	<i>TPR-NTRK1</i>	
	<i>NRAS</i> [15]	<i>TSHR</i> [2]	
	Melanoma Panel	<i>BRAF</i> [22]	<i>NRAS</i> [19]
		<i>GNA11</i> [3]	<i>PTEN</i> [5]
		<i>GNAQ</i> [3]	<i>RAC1</i> [1]
<i>HRAS</i> [3]		<i>RPS27</i> [1]	
<i>KIT</i> [51]		<i>TERT (c.1-124C>T, c.1-146C>T)</i>	
<i>KRAS</i> [5]			
Colon Panel	<i>BRAF</i> [3]	<i>NRAS</i> [30]	
	<i>EGFR</i> [2]	<i>PIK3CA</i> [4]	
	<i>KRAS</i> [46]		
BRAF Test	(V600E/V600E complex (V600Ec))	(V600K)	
	(V600D)	(V600R)	

Supplementary table 2. Analysis A: Mutation pre-screening results for 22 primary tumors of patients with RAI¹-resistant distant metastasis excluded from OCAv3² analysis.

Panel	Mutated Gene [Number of Mutations]
Melanoma Panel (n=12)	<i>BRAF</i> & <i>TERT</i> [9] <i>BRAF</i> only [1] <i>BRAF</i> & <i>TERT</i> & <i>RAS</i> [1] <i>HRAS</i> & <i>TERT</i> [1]
ThyroSPEC™ Panel (n=4)	<i>BRAF</i> only [2] <i>BRAF</i> & <i>TERT</i> [2]
Colon Panel (n=3)	<i>BRAF</i> only [3]
No Other Test (n=3)	Selected based on dsPTC ³ histology

¹ radioactive iodine

² Oncomine Comprehensive Assay v3

³ diffuse sclerosing papillary thyroid cancer

Supplementary table 3. Analysis A: Mutation pre-screening results for 20 primary tumors of patients with RAI¹-resistant distant metastasis selected for OCAv3² analysis.

Panel	Mutated Gene [Number of Mutations]
ThyroSPEC™ Panel (n=10)	<i>TPR-NTRK1</i> fusion [1] <i>RAS</i> only [1] <i>RAS & IDH1</i> [1] <i>RAS & PIK3CA</i> [1] <i>NCOA4-RET</i> fusion [1] <i>TERT</i> only [2] no mutation [3]
Melanoma Panel (n=7)	<i>RAS & TERT</i> [4] <i>TERT</i> only [2] no mutation [1]
BRAF Test (n=2)	no mutation [2]
No Other Test (n=1)	selected based on dsPTC ³ histology

¹ radioactive iodine

² Oncomine Comprehensive Assay v3

³ diffuse sclerosing papillary thyroid cancer

Supplementary table 4. Analysis B: Mutation pre-screening results for 33 ATA¹ high and intermediate recurrence risk patients and two patients with metastatic MTCs² excluded from OCAv3³ analysis.

Panel	Mutated Gene [Number of Mutations] (Histology)
ThyroSPEC™ Panel (n=22)	<i>BRAF</i> only [13] <i>BRAF</i> & <i>TERT</i> [4] <i>RET</i> only [2] <i>NCOA4-RET</i> <i>RET</i> (MTC) <i>RET</i> & <i>IDH1</i> [1] (MTC) <i>NTRK</i> only [1] <i>ETV6-NTRK3</i> No mutation [1]*
Melanoma Panel (n=10)	<i>BRAF</i> only [3] <i>BRAF</i> & <i>RPS27</i> [1] <i>BRAF</i> & <i>TERT</i> [6]
BRAF Test (n=2)	<i>BRAF</i> only [2]
Colon Panel (n=1)	<i>BRAF</i> only [1]

*Patient was previously identified as OCAv3 *BRAF* mutation-positive and was excluded from further OCAv3 analysis.

¹ American Thyroid Association

² medullary thyroid cancer

³ Oncomine Comprehensive Assay v3

Supplementary table 5. Analysis B: Mutation pre-screening results for 9 ATA¹ high and intermediate recurrence risk patients selected for OCAv3² analysis.

Panel	Mutated Gene [Number of Mutations]
ThyroSPEC™ Panel (n=6)	<i>TERT</i> only [1] No mutation [5]
Melanoma Panel (n=1)	No mutation [1]
Colon Panel (n=1)	No mutation [1]
No Other Test (n=1)	Selected based on dsPTC ³ histology

¹ American Thyroid Association

² Oncomine Comprehensive Assay v3

³ diffuse sclerosing papillary thyroid cancer