Supplementary Materials: Results and Clinical Interpretation of Germline RET Analysis in A Series of Patients with Medullary Thyroid Carcinoma: The Challenge of the Variants of Uncertain Significance.

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| Patient number | Family ID | Family phenotype | Affected/Healthy | Type of analysis | RET variant |
|----------------|-----------|------------------|------------------|-----------------|-------------|
| 1              | 10-O-02   | MTC              | A                | C               | NO          |
| 2              | 28-O-03   | MTC              | A                | C               | NO          |
| 3              | 91-O-03   | MTC              | A                | C               | YES         |
| 4              | 91-O-03   | MTC              | A                | T               | YES         |
| 5              | 31-O-04   | MTC              | A                | C               | NO          |
| 6              | 144-O-04  | MTC              | A                | C               | YES         |
| 7              | 59-M-04   | MTC              | A                | C               | NO          |
| 8              | 91-O-03   | MTC              | A                | T               | YES         |
| 9              | 91-O-03   | MTC              | A                | T               | YES         |
| 10             | 91-O-03   | MTC              | H                | T               | YES         |
| 11             | 91-O-03   | MTC              | H                | T               | NO          |
| 12             | 91-O-03   | MTC              | H                | T               | NO          |
| 13             | 27-O-05   | MTC              | A                | C               | NO          |
| 14             | 91-O-03   | MTC              | H                | T               | YES         |
| 15             | 91-O-03   | MTC              | A                | T               | YES         |
| 16             | 91-O-03   | MTC              | H                | T               | NO          |
| 17             | 42-O-07   | MTC              | A                | C               | NO          |
| 18             | 9-O-08    | MTC              | H                | T               | YES         |
| 19             | LAB-01    | UK               | UK               | C               | NO          |
| 20             | LAB-02    | UK               | UK               | C               | NO          |
| 21             | LAB-03    | IG               | UK               | C               | NO          |
| 22             | 9-O-08    | MTC              | H                | T               | NO          |
| 23             | 9-O-08    | MTC              | H                | T               | YES         |
| 24             | 91-O-03   | MTC              | H                | T               | NO          |
| 25             | 19-O-09   | MTC              | A                | C               | NO          |
| 26             | LAB-04    | UK               | A                | C               | NO          |
| 27             | 21-O-09   | MTC              | A                | C               | NO          |
| 28             | 31-O-09   | MTC              | A                | C               | NO          |
| 29             | 54-O-09   | MTC              | A                | C               | YES         |
| 30             | 54-O-09   | MTC              | A                | T               | YES         |
| 31             | 42-O-10   | MTC              | A                | C               | NO          |
| No. | O-D | Tumor | Mutation | Age | Gender | Diagn. |
|-----|-----|-------|----------|-----|--------|--------|
| 32  | 91-O-13 | MTC | H | T | NO |
| 33  | 13-O-10 | MTC | A | C | NO |
| 34  | 44-O-10 | MTC | A | C | NO |
| 35  | 53-O-10 | MTC | A | C | NO |
| 36  | 63-O-10 | MTC | A | C | NO |
| 37  | 54-O-09 | MTC | H | T | YES |
| 38  | 54-O-09 | MTC | H | T | YES |
| 39  | 12-O-11 | MTC | A | C | NO |
| 40  | 13-O-11 | MEN2A | A | C | YES |
| 41  | 29-O-11 | MTC | A | C | NO |
| 42  | 33-O-11 | MTC | A | C | NO |
| 43  | 53-O-11 | MTC | A | C | NO |
| 44  | 67-O-11 | MTC | A | C | NO |
| 45  | 68-O-11 | MTC | A | C | YES |
| 46  | 92-O-11 | MTC | A | C | NO |
| 47  | 74-O-11 | CCH | A | C | NO |
| 48  | 87-O-11 | MTC | A | C | NO |
| 49  | 13-O-12 | MTC | A | C | NO |
| 50  | 54-O-11 | MTC | A | C | NO |
| 51  | 35-O-12 | CCH | A | C | NO |
| 52  | 190-O-13 | PHPT | A | C | NO |
| 53  | 190-O-13 | PHPT | A | C | NO |
| 54  | 58-O-12 | MTC | A | C | NO |
| 55  | 65-O-12 | MTC | A | C | NO |
| 56  | 100-O-12 | MTC | A | C | NO |
| 57  | LAB-05 | PHPT | UK | C | NO |
| 58  | 228-O-18 | MTC | A | C | YES |
| 59  | LAB-06 | PGL/PCC | A | C | NO |
| 60  | 58-O-13 | MTC | A | C | NO |
| 61  | 53-O-13 | PHPT | A | C | NO |
| 62  | 72-O-13 | MTC | H | T | YES |
| 63  | 136-O-13 | PHPT | A | C | YES |
| 64  | 81-O-13 | MTC | A | C | NO |
| 65  | 89-O-13 | MTC | A | C | NO |
| 66  | 54-O-09 | MTC | H | T | YES |
| 67  | 103-O-13 | MTC | A | C | NO |
| 68  | LAB-07 | PHPT | UK | C | NO |
| 69  | 121-O-13 | MTC | A | C | NO |
| 70  | 228-O-18 | MTC | A | T | YES |
| 71  | 228-O-18 | MTC | A | T | YES |
| 72  | 228-O-18 | MTC | H | T | YES |
| 73  | 228-O-18 | MTC | A | T | YES |
| 74  | 228-O-18 | MTC | H | T | NO |
|    |    |    |    |    |
|----|----|----|----|----|
| 75 | 10-O-14 | MTC | A | C | NO |
| 76 | 81-O-14 | MTC | A | C | NO |
| 77 | 228-O-18 | MTC | H | T | YES |
| 78 | 228-O-18 | MTC | H | T | NO |
| 79 | 228-O-18 | MTC | H | T | NO |
| 80 | 144-O-14 | MTC | A | C | NO |
| 81 | 168-O-14 | MTC | A | C | YES |
| 82 | 175-O-14 | MTC | A | C | NO |
| 83 | LAB-08 | PTC | UK | C | NO |
| 84 | 204-O-14 | MTC | A | C | NO |
| 85 | 168-O-14 | MTC | H | T | YES |
| 86 | 120-O-14 | PGL/PCC | A | C | NO |
| 87 | LAB-09 | UK | UK | C | NO |
| 88 | LAB-10 | UK | UK | C | NO |
| 89 | 269-O-14 | MTC | A | C | NO |
| 90 | LAB-11 | CCH | UK | C | NO |
| 91 | 168-O-14 | MTC | H | T | YES |
| 92 | 168-O-14 | MTC | H | T | YES |
| 93 | 168-O-14 | MTC | H | T | NO |
| 94 | LAB-12 | UK | UK | T | YES |
| 95 | LAB-13 | PHPT | UK | C | NO |
| 96 | 31-O-15 | PGL/PCC | A | C | NO |
| 97 | 39-O-15 | MTC | A | C | NO |
| 98 | 45-O-15 | PGL/PCC | A | C | NO |
| 99 | 53-O-15 | PGL/PCC | A | C | NO |
| 100 | 89-O-15 | MTC | A | C | YES |
| 101 | 89-O-15 | MTC | H | T | NO |
| 102 | 89-O-15 | MTC | H | T | YES |
| 103 | 89-O-15 | MTC | H | T | YES |
| 104 | 89-O-15 | MTC | H | T | YES |
| 105 | 169-O-15 | MEN2B | A | C | YES |
| 106 | 169-O-15 | MEN2B | H | T | NO |
| 107 | 169-O-15 | MEN2B | H | T | NO |
| 108 | 169-O-15 | MEN2B | H | T | NO |
| 109 | 169-O-15 | MEN2B | H | T | NO |
| 110 | 169-O-15 | MEN2B | H | T | NO |
| 111 | 32-O-15 | MTC | A | C | NO |
| 112 | 70-O-15 | PGL/PCC | A | C | NO |
| 113 | 219-O-15 | PGL/PCC | A | C | NO |
| 114 | 316-O-15 | PGL/PCC | A | C | NO |
| 115 | 13-O-16 | MTC | A | C | NO |
| 116 | 121-O-16 | PGL/PCC | A | C | NO |
| 117 | LAB-14 | UK | UK | C | NO |
| No. | Lab Code | Region | Tumor Type | Gene | Mutation | Result |
|-----|----------|--------|------------|------|----------|--------|
| 118 | LAB-15   | UK     | UK         | C    | NO       |        |
| 119 | LAB-16   | UK     | UK         | C    | YES      |        |
| 120 | LAB-17   | UK     | UK         | C    | NO       |        |
| 121 | 204-O-16 | PGL/PCC| A          | C    | NO       |        |
| 122 | 275-O-16 | MTC    | A          | C    | NO       |        |
| 123 | 371-O-16 | CCH    | A          | C    | NO       |        |
| 124 | 166-O-17 | MTC    | A          | C    | NO       |        |
| 125 | 191-O-17 | MTC    | H          | T    | YES      |        |
| 126 | 288-O-17 | PGL/PCC| A          | C    | NO       |        |
| 127 | 359-O-17 | PGL/PCC| A          | C    | NO       |        |
| 128 | 1-MAG-CRC| PGL/PCC| A          | C    | NO       |        |
| 129 | LAB-18   | UK     | UK         | C    | NO       |        |
| 130 | 43-O-18  | MTC    | A          | C    | NO       |        |
| 131 | 55-O-18  | MTC    | A          | C    | YES      |        |
| 132 | 55-O-18  | MTC    | H          | T    | NO       |        |
| 133 | LAB-19   | UK     | UK         | C    | NO       |        |
| 134 | LAB-20   | MEN2B  | A          | C    | YES      |        |
| 135 | LAB-20   | MEN2B  | H          | T    | NO       |        |
| 136 | LAB-20   | MEN2B  | H          | T    | NO       |        |
| 137 | 55-O-18  | MTC    | H          | T    | NO       |        |
| 138 | 55-O-18  | MTC    | H          | T    | NO       |        |
| 139 | LAB-21   | UK     | UK         | C    | YES      |        |
| 140 | LAB-21   | UK     | UK         | T    | NO       |        |
| 141 | LAB-21   | UK     | UK         | T    | NO       |        |
| 142 | 142-O-18 | MEN2A  | A          | T    | YES      |        |
| 143 | 142-O-18 | MEN2A  | H          | T    | NO       |        |
| 144 | 142-O-18 | MEN2A  | H          | T    | NO       |        |
| 145 | LAB-22   | UK     | UK         | C    | NO       |        |
| 146 | 228-O-18 | MTC    | A          | T    | YES      |        |
| 147 | 228-O-18 | MTC    | H          | T    | YES      |        |
| 148 | 228-O-18 | MTC    | H          | T    | NO       |        |
| 149 | 228-O-18 | MTC    | H          | T    | NO       |        |
| 150 | 228-O-18 | MTC    | A          | T    | YES      |        |
| 151 | LAB-23   | UK     | UK         | C    | NO       |        |
| 152 | LAB-24   | UK     | UK         | C    | NO       |        |
| 153 | LAB-25   | UK     | UK         | C    | NO       |        |
| 154 | LAB-26   | UK     | UK         | C    | NO       |        |
| 155 | LAB-27   | UK     | UK         | T    | NO       |        |
| 156 | LAB-28   | UK     | UK         | C    | NO       |        |
| 157 | 228-O-18 | MTC    | H          | T    | NO       |        |
| 158 | 520-M-18 | MTC    | A          | C    | NO       |        |
| 159 | 324-O-19 | MTC    | A          | C    | NO       |        |
| 160 | 330-O-19 | PGL/PCC| A          | C    | NO       |        |
|   |   |   |   |   |
|---|---|---|---|---|
| 161 | 83-OB-19 | PHPT | A | C | NO |
| 162 | 115-O-20 | MTC | H | T | YES |
| 163 | 91-O-03 | MTC | H | T | YES |

Abbreviations: MTC = Medullary Thyroid Carcinoma; UK = Unknown; IG = Intestinal Ganglioneuromatosis; MEN2A = Multiple Endocrine Neoplasia type 2 A; CCH = C Cell Hyperplasia; PGL/PCC = Paraganglioma/Pheochromocytoma; PHPT = Primary Hyperparathyroidism; MEN2B = Multiple Endocrine Neoplasia type 2 B; C = Complete analysis; T = Targeted analysis