**Supplementary table 1.** Table resuming clinical features of the studied cohort of MAS patients. Legend: diag.age, molecular diagnosis age; FD, bone fibrous dysplasia; PP, precocious puberty; SP, cafè-au-lait pigmented skin lesions; add. clin. features, additional clinical features; F, female; M, male; WT, wild-type; MUT, mutated.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **PT ID** | **SEX** | **DIAG.AGE** | **FD** | **PP** | **OC** | **TL** | **SP** | **HT** | **GH** | **nHC** | **Add. Clin. features** | **c.604C>T genotype** | **c.605G>A genotype** |
| **1** | F | 43 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **2** | F | 8 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **3** | M | 13 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **4** | F | 22 | X |  |  |  |  |  |  |  |  | WT | WT |
| **5** | F | 18 | X |  |  |  |  |  |  |  | Hodgkin's lymphoma | WT | **MUT** |
| **6** | F | 11 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **7** | F | 53 | X |  |  |  |  |  |  |  |  | WT | WT |
| **8** | F | 34 | X |  |  |  |  |  |  |  |  | WT | WT |
| **9** | F | 11 | X |  |  |  | X |  |  |  |  | WT | WT |
| **10** | M | 5 | X |  |  |  | X | X |  |  |  | WT | WT |
| **11** | F | 4 | X |  |  |  |  |  |  |  |  | WT | WT |
| **12** | M | 22 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **13** | F | 1 |  | X |  |  | X |  |  |  |  | WT | WT |
| **14** | F | 22 |  |  | X |  | X |  |  |  | osseous cyst | WT | WT |
| **15** | F | 12 |  | X |  |  | X |  |  |  | short stature - bilateral genu valgum -bilateral clinodactyly | WT | WT |
| **16** | F | 2 |  | X |  |  | X |  |  |  |  | WT | WT |
| **17** | M | 10 |  | X |  |  |  |  |  |  | psychomotor delay - bilateral testicular calcifications | WT | WT |
| **18** | M | 6 |  | X |  |  | X |  |  |  | gynecomastia | WT | WT |
| **19** | M | 2 | X |  |  |  | X |  |  |  |  | WT | **MUT** |
| **20** | F | 6 |  |  |  |  | X |  |  |  | adrenal tumor - clitoral hypertrophy | WT | WT |
| **21** | F | 12 |  | X |  |  | X |  |  |  |  | WT | WT |
| **22** | F | 3 |  |  |  |  | X | X | X |  | hyperchromic nevus | WT | **MUT** |
| **23** | F | 3 |  | X | X |  |  |  |  |  |  | WT | WT |
| **24** | F | 12 | X |  |  |  | X |  |  |  |  | WT | WT |
| **25** | M | 7 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **26** | F | 11 | X |  |  |  |  |  |  |  |  | WT | WT |
| **27** | F | 2 |  | X |  |  |  |  |  |  | muscular hypotonia, absent language | WT | WT |
| **28** | F | 9 |  | X |  |  | X |  |  |  |  | WT | **MUT** |
| **29** | F | 6 |  | X |  |  | X |  |  |  | advanced bone age | WT | WT |
| **30** | F | 1 |  | X |  |  |  |  |  |  |  | WT | WT |
| **31** | F | 2 | X |  |  |  | X |  |  |  |  | WT | WT |
| **32** | M | 14 |  |  |  |  | X |  |  |  | overweight - mild sindactyly | WT | WT |
| **33** | F | 2 |  | X |  |  | X |  |  |  |  | WT | WT |
| **34** | M | 46 | X |  |  |  |  |  |  |  |  | WT | WT |
| **35** | F | 2 |  | X | X |  |  |  |  |  |  | WT | WT |
| **36** | M | 2 | X |  |  |  |  |  |  |  |  | WT | WT |
| **37** | M | 56 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **38** | F | 3 |  | X | X |  | X |  |  |  |  | WT | WT |
| **39** | M | 12 |  |  |  |  | X |  |  |  |  | WT | **MUT** |
| **40** | F | 5 |  | X |  |  | X |  |  |  | hypovitaminosis D | WT | WT |
| **41** | F | 48 |  |  |  |  | X |  |  |  |  | **MUT** | WT |
| **42** | M | 15 | X |  |  |  |  |  |  |  |  | WT | WT |
| **43** | F | 11 | X | X |  |  | X |  |  |  |  | WT | **MUT** |
| **44** | F | 6 |  | X | X |  | X |  |  |  |  | **MUT** | WT |
| **45** | M | 17 | X |  |  |  |  |  |  |  |  | WT | WT |
| **46** | F | 6 |  | X | X |  |  |  |  |  |  | WT | **MUT** |
| **47** | F | 1 | X | X | X |  | X |  |  |  | hypophosphoremia | WT | **MUT** |
| **48** | F | 6 | X | X | X |  |  |  |  |  |  | WT | **MUT** |
| **49** | F | 5 | X | X | X |  | X |  |  |  |  | WT | **MUT** |
| **50** | F |  |  | X | X |  |  |  |  |  |  | WT | **MUT** |
| **51** | M | 9 | X |  |  |  | X |  |  |  |  | WT | **MUT** |
| **52** | M | 1 |  |  |  |  | X |  |  |  | intrahepatic cholestasis - posterior embriotoxon | WT | **MUT** |
| **53** | F | 2 | X |  |  |  |  |  |  |  |  | WT | **MUT** |
| **54** | F | 46 | X |  |  |  |  |  |  |  |  | WT | WT |

**Supplementary table 2.** Table resuming the cluster of MAS mutated patients. BO, bone. BL, blood. LJ, left jaw. M, maxilla. RJ, right jaw, S, symphysis. CB, cutaneous biopsy. FB, fibroblast. OCL, ovarian cyst liquid. OC, ovarian cyst. OT, ovarian tissue. nd, not determined because methods failed due to the reduced amount or the poor quality of material available for testing. WT, wild-type.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **c.604C>T** | **c.605G>A** |
| **PT ID** | **TISSUE** | **SANGER** | **AS-PCR** | **dPCR** | **dPCR cpm** | **dPCR RMA** | **COLD-MAMA PCR** | **COLD-MAMA RMA** | **SANGER** | **AS-PCR** | **dPCR** | **dPCR cpm** | **dPCR RMA** | **COLD-MAMA PCR** | **COLD-MAMA RMA** |
| **1** | **BO** | WT | WT | WT | 0.181 |   |   |   | WT | WT | **MUT** | **0.892** | **>6** |   |   |
| **2** | **BO** | WT | WT | WT | 0.000 |   |   |   | **MUT** | **MUT** | **MUT** | **8.712** | **>50** |   |   |
| **3** | **BO** | WT | WT | WT | 0.095 |   |   |   | **MUT** | **MUT** | **MUT** | **17.626** | **100** |   |   |
| **5** | **BO** | WT | nd | WT | 0.000 |   | nd |   | WT | nd | **MUT** | **6.594** | **50** | nd |   |
| **6** | **BO** | WT | WT | WT | 0.000 |   | WT |   | WT | **MUT** | **MUT** | **3.604** | **25** | **MUT** | **3** |
| **12** | **BO** | WT | nd | WT | 0.260 |   | nd |   | WT | nd | **MUT** | **3.196** | **25** | nd |   |
| **19** | **BL** | WT | WT | WT | 0.117 |   | WT |   | WT | WT | **MUT** | **0.815** | **>6** | WT |   |
| **22** | **BL** | WT | WT | WT | 0.000 |   |   |   | WT | WT | **MUT** | **0.644** | **6** |   |   |
| **25** | **BL** | WT | WT | WT | 0.000 |   | nd |   | WT | WT | **MUT** | **2.252** | **>12.5** | nd |   |
| **28** | **BL** | WT | WT | WT | 0.000 |   | nd |   | WT | **MUT** | **MUT** | **2.170** | **>12.5** | nd |   |
| **51** | **BL** | WT | nd | WT | 0.000 |   | nd |   | WT | nd | **MUT** | **1.216** | **12.5** | nd |   |
| **53** | **BL** | WT | nd | WT | 0.258 |   | nd |   | WT | nd | **MUT** | **1.043** | **<12.5** | nd |   |
| **37** | **BL** | WT | WT | WT | 0.166 |   | WT |   | WT | WT | **MUT** | **0.622** | **>6** | **MUT** | **6** |
| **BO-LJ** | WT | WT | WT | 0.195 |   | WT |   | **MUT** | **MUT** | **MUT** | **32.654** | **100** | **MUT** | **>40** |
| **BO-M** | WT | nd | WT | 0.000 |   |   |   | **MUT** | nd | **MUT** | **22.108** | **100** | nd |   |
| **BO-RJ** | WT | WT | WT | 0.169 |   | WT |   | WT | **MUT** | **MUT** | **2.121** | **<25** | **MUT** | **3** |
| **BO-S** | WT | nd | WT | 0.188 |   |   |   | **MUT** | nd | **MUT** | **22.904** | **100** | nd |   |
| **39** | **BL** | WT | WT | WT | 0.319 |   |   |   | WT | WT | **MUT** | **0.509** | **6** |   |   |
| **CB** | WT | WT | WT | 0.000 |   |   |   | WT | WT | **MUT** | **1.251** | **<12.5** |   |   |
| **52** | **BL** | WT | WT | WT | 0.112 |   | nd |   | WT | **MUT** | **MUT** | **0.598** | **6** | nd |   |
| **CB** | WT | WT | WT | 0.000 |   | nd |   | WT | **MUT** | **MUT** | **6.208** | **50** | nd |   |
| **41** | **BL** | WT | WT | **MUT** | **2.249** | **<12.5** | **MUT** | **<2.5** | WT | WT | WT | 0.254 |   | WT |   |
| **43** | **BL** | WT | WT | WT | 0.188 |   |   |   | WT | WT | **MUT** | **0.873** | **>6** |   |   |
| **FB** | WT | WT | WT | 0.000 |   |   |   | WT | WT | **MUT** | **1.633** | **>12.5** |   |   |
| **44** | **BL** | WT | WT | **MUT** | **0.777** | **<3** | WT |   | WT | WT | WT | 0.293 |   | WT |   |
| **OCL** | WT | WT | **MUT** | **4.995** | **<25** | **MUT** | **<2.5** | WT | WT | WT | 0.256 |   | WT |   |
| **OT** | WT | WT | **MUT** | **1.485** | **>6** | WT |   | WT | WT | WT | 0.184 |   | WT |   |
| **46** | **OC** | WT | WT | WT | 0.083 |   | WT |   | **MUT** | **MUT** | **MUT** | **2.969** | **<25** | **MUT** | **10** |
| **OT** | WT | WT | WT | 0.182 |   | WT |   | WT | WT | **MUT** | **0.520** | **6** | **MUT** | **<0.5** |
| **47** | **OC** | WT | WT | WT | 0.102 |   | WT |   | WT | WT | **MUT** | **1.135** | **<12.5** | WT |   |
| **OT** | WT | WT | WT | 0.084 |   | WT |   | WT | WT | **MUT** | **1.164** | **<12.5** | **MUT** | **3** |
| **48** | **BL** | WT | WT | WT | 0.334 |   | WT |   | WT | **MUT** | **MUT** | **5.347** | **<50** | **MUT** | **16** |
| **OC** | WT | WT | WT | 0.000 |   | WT |   | WT | **MUT** | **MUT** | **10.169** | **>50** | **MUT** | **>40** |
| **49** | **BL** | WT | WT | WT | 0.101 |   | WT |   | WT | WT | **MUT** | **0.465** | **3** | WT |   |
| **OC** | WT | WT | WT | 0.192 |   | WT |   | WT | WT | **MUT** | **1.578** | **>12.5** | **MUT** | **26** |
| **50** | **OC** | WT | WT | WT | 0.412 |   | WT |   | WT | **MUT** | **MUT** | **3.312** | **25** | **MUT** | **<0.5** |
| **OCL** | WT | WT | WT | 0.205 |   | WT |   | WT | **MUT** | **MUT** | **7.275** | **>50** | **MUT** | **2.5** |