|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Patient** | **Position on Chromosome 15** | **Ref** | **Alt** | **Impact** | **ExAC03**  **Frequency** | **MetaSVM** |
| MET111-1P,2P | 67073775 | C | T | R465C | 9.38 x 10-6 | D |
| MET115-1P | 67073851 | T | C | I490T | Novel | D |
| MET127-1P | 66996263 | C | T | Q223\* | Novel | Stop |
| MET148-1P | 67073350 | C | T | P323L | Novel | D |
| MET153-1P | 67073550 | G | T | G390C | Novel | D |
| MET154-1P,2P | 67073601 | G | T | E407\* | 9.00 x 10-6 | Stop |
| MET179-1P | 66995977 | TC | del | S130fs\*146 | Novel | Frameshift |
| SAGMET100-1P | 67073437 | A | AAT | A353fs\*187 | Novel | Frameshift |
| SAGMET101-1P | 66995828 | 19bp | del | Q78fs\*41 | Novel | Frameshift |
| SAGMET107-1P | 67004047 | G | A | E287K | 3.30 x 10-5 | D |
| SAGMET104-1P,2P | 67073416 | G | del | R345fs\*194 | Novel | Frameshift |
| SAG158-1P | 67073502 | G | T | E374\* | Novel | Stop |
| SAG210-1P | 67008800 | A | G | T306A | Novel | D |
| SAG220-1P | 67004027 | T | TT | R281fs\*13 | Novel | Frameshift |
| SAG-PROBAND3 | 66995873 | A | T | M93L | Novel | T |

**Figure 2- Source Data 1.** **Variants identified in *SMAD6*.** Highlighted variants indicate *de novo* mutations; “D” and “T” respectively denote damaging and tolerated missense variants called by MetaSVM.