|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| RET domains | Residues | Miss-sense (N=29) | Nonsense-Frame-shift (N=12) | Silent (N=14) |
|  |  |  | S-HSCR (N=18) | L/TCAa (N=6) | NA (N=5) | S-HSCR (N=4) | L/TCAb (N=4) | NA (N=4) | S-HSCR (N=8) | L/TCA (N=2) | NA (N=4) |
| Extracellular N= 36 | Cadherin N= 32 | 28-516 | 12 | 4 | 2 | 3 | 2 | 2 | 3 | 2 | 2 |
| Cystein N= 4 | 517-635 | 1 |  |  |  | 1 | 2 |  |  |  |
| Transmembrane N= 3 | 636-657 |  |  |  |  | 1 |  | 2 |  |  |
| Intracellular N= 16 |  | 658-723 | 1 |  | 1 |  |  |  | 1 |  |  |
| Tyrosine kinase N= 8 | 724-1016 | 2 | 1 | 2 |  |  |  | 2 |  | 1 |
|  | 1016-1114 | 2 | 1 |  | 1 |  |  |  |  | 1 |

a:includes G731del in frame deletion; b:includes K549\_G550del (*de* *novo* 10 bp deletion that affects both exon and intron 8); the only variant identified in the 5’UT is not included. R114H, T278A, V292M and T295T were found in more than one patient and in more than one phenotype.