**Supplemental Table 2:** Detailed description of mutations in PSEN-1.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Mutation**  **(Exon)** | **Ethnic**  **Origin** | **Frequency**  **(Family)** | **AAO**  **Range/mean**  **(Years)** | **Disease**  **Duration**  **Range/mean**  **(Years)** | **Phenotype in addition to Cognitive decline** | **Reference** |
| p.A79V (Ex4) | Netherlands,  Germany, France | 9 | 50-78/61.2 | 4-10 | - | [[1-4](#_ENREF_1)] |
| p.V82L (Ex4) | France | 1 | 53-58 | - | - | [[5](#_ENREF_5)] |
| ΔI83/M84 (Ex4) | Scotland | 1 | 34-38/36 | 6-10 | Spastic Paraparesis | [[6](#_ENREF_6), [7](#_ENREF_7)] |
| p.I83T (Ex4) | Tunisia | 1 | 56-62/59.0 | - | Psychiatric Symptoms | [[8](#_ENREF_8)] |
| p.L85P (Ex4) | Asian (Japan) | 1 | 26 | - | Visual variant,  Spastic Paraparesis | [[9](#_ENREF_9)] |
| p.V89L (Ex4) | Spain | 1 | 46-51/48.6 | 6-15 | Behavioral Disturbances | [[10](#_ENREF_10), [11](#_ENREF_11)] |
| p.C92S (Ex4) | Italy | 2 | 49-70/56.4 | 6-6/6.0 | - | [[12](#_ENREF_12)] |
| p.V94M (Ex4) | Hispanic (Colombia) | 1 | 53-53/53.0 | - | - | [[13](#_ENREF_13)] |
| p.V96F (Ex4) | Asian (Japan) | 1 | 49-60/52.5 | - | - | [[14](#_ENREF_14)] |
| p.V97L (Ex4) | Asian (China) | 1 | - | - | - | [[15](#_ENREF_15)] |
| p.T99A (Ex4) | Asian (Japan) | 1 | 43-43/43.0 | - | - | [[16](#_ENREF_16)] |
| p.F105I (Ex4) | - | 1 | 53-58 | - | - | [[17](#_ENREF_17)] |
| p.F105V (Ex4) | Spain | 1 | 52-52/52.0 | - | - | [[18](#_ENREF_18)] |
| p.F105C (Ex4) | Asian (China) | 1 | 45-45/45.0 | - | - | [[19](#_ENREF_19)] |
| p.F105L (Ex4) | Germany | 1 | 50-52/51.0 | 8-11/9.5 | - | [[2](#_ENREF_2)] |
| p.R108Q (Ex4) | Serbia | 1 | 45-45/45.0 | 15-15/15.0 | - | [[20](#_ENREF_20)] |
| p.L113Q (Ex4) | Greece | 1 | 33 | 3 | Myoclonus | [[21](#_ENREF_21)] |
| p.L113P (Ex4) | France | 1 | 38-50/42.4 | 6-11/9.3 | Frontotemporal Dementia | [[22](#_ENREF_22)] |
| Intron4; InsTAC | UK | 10 | 34-45/36.5 | 6-10/8.0 | - | [[23-27](#_ENREF_23)] |
| p.Y115H (Ex5) | France, Germany | 3 | 35-41/38.5 | - | Myoclonus | [[5](#_ENREF_5), [21](#_ENREF_21), [28](#_ENREF_28)] |
| p.Y115D (Ex5) | Caucasian | 1 | 31-31/31.0 | - | - | [[25](#_ENREF_25), [26](#_ENREF_26), [29](#_ENREF_29)] |
| p.T116N (Ex5) | Denmark, Iberia | 4 | 30-41/37.5 | 4-8/5.7 | - | [[17](#_ENREF_17), [25](#_ENREF_25), [30](#_ENREF_30), [31](#_ENREF_31)] |
| p.T116I (Ex5) | France | 3 | 38-47/45.0 | - |  | [[4](#_ENREF_4), [17](#_ENREF_17), [32](#_ENREF_32)] |
| p.P117A (Ex5) | Hispanic (Colombia) | 2 | 24-34/30.9 | 6-11/8.5 | Ataxia | [[33](#_ENREF_33), [34](#_ENREF_34)] |
| p.P117S (Ex5) | USA | 1 | 29-33/31.0 | 4-21/12.5 | - | [[35](#_ENREF_35)] |
| p.P117R (Ex5) | Poland, Spain | 2 | 33-38/36.2 | 3-5/3.7 | Myoclonus | [[18](#_ENREF_18), [36](#_ENREF_36)] |
| p.P117L (Ex5) | Poland | 2 | 24-33/31.6 | 3-5/4.0 | - | [[35](#_ENREF_35), [37](#_ENREF_37), [38](#_ENREF_38)] |
| p.E120K(Ex5) | UK, Ireland | 2 | 32-45/44.0 | - | - | [[39](#_ENREF_39), [40](#_ENREF_40)] |
| p.E120G (Ex5) | Caucasian (Spain) | 1 | 39-39/39.0 | 3-3/3.0 | - | [[18](#_ENREF_18)] |
| p.E120D (Ex5)  (g.25563A>C) | UK,  France | 3 | 41-53/43.4 | - | - | [[17](#_ENREF_17), [28](#_ENREF_28), [41](#_ENREF_41)] |
| p.E120D (Ex5)  (g.25563A>T) | Jewish-Romanian | 1 | 43-48/45.7 | 7-12/9.3 | - | [[42-44](#_ENREF_42)] |
| p.E123L (Ex5) | Asian (Japan) | 1 | 56-62/59.0 | 0-3/1.5 | - | [[45](#_ENREF_45)] |
| p.H131R (Ex5) | Asian (Japan) | 1 | 45-45/45.0 | - | - | [[16](#_ENREF_16)] |
| p.L134R (Ex5) | Turkey | 1 | 51-55/53.0 | 4-4/4.0 | - | [[46](#_ENREF_46)] |
| p.N135D (Ex5) | - | 1 | 34-38/ | - | - | [[47](#_ENREF_47)] |
| p.N135S (Ex5) | Greece | 2 | 32-36/33.4 | 3-8 | Spastic Paraparesis, Epilepsy | [[21](#_ENREF_21), [48](#_ENREF_48)] |
| p.A136G (Ex5) | Asian (China) | 1 | - | - | - | [[49](#_ENREF_49)] |
| p.M139K (Ex5) | France | 2 | 37-50/40.3 | 10-10/10.0 | - | [[4](#_ENREF_4), [50](#_ENREF_50)] |
| p.M139V (Ex5) | Caucasian, African American | 9 | 32-48/40.7 | 3-10 | Frontotemporal Dementia | [[2](#_ENREF_2), [36](#_ENREF_36), [39](#_ENREF_39), [51-58](#_ENREF_51)] |
| p.M139T (Ex5) | Spain,  France | 6 | 39-63/46.9 | 8-15 | - | [[4](#_ENREF_4), [5](#_ENREF_5), [11](#_ENREF_11), [28](#_ENREF_28), [59](#_ENREF_59), [60](#_ENREF_60)] |
| p.M139I (Ex5)  (g.25620G>A) | - | 1 | - | - | - | [[52](#_ENREF_52)] |
| p.M139I (Ex5)  (g.25620G>C) | Asian (Korea) | 1 | 35-37/36.0 | 8-10 | - | [[61](#_ENREF_61)] |
| p.I143V (Ex5) | Italy | 1 | 48-55/54.2 | 8-20/11/6 | - | [[62](#_ENREF_62)] |
| p.I143F (Ex5) | - | 1 | 53-57/55.0 | 9-13/11.0 | - | [[56](#_ENREF_56), [63](#_ENREF_63)] |
| p.I143N (Ex5) | - | 1 | 45-50 |  | - | [[17](#_ENREF_17)] |
| p.I143T (Ex5) | Belgium, Japan  Hispanic (Colombia) | 8 | 26-45/34.0 | 3-12/6.4 | - | [[13](#_ENREF_13), [17](#_ENREF_17), [25](#_ENREF_25), [29](#_ENREF_29), [64](#_ENREF_64)] |
| p.I143M (Ex5) | African (Xhosa) | 1 | 50.0 | 8.0 | - | - |
| p.M146L (Ex5) (g.25639A>C) | Italy, France, Australia | 14 | 35-47/40.1 | 4-8/6.3 | Pick Disease | [[21](#_ENREF_21), [25](#_ENREF_25), [28](#_ENREF_28), [65-69](#_ENREF_65)] |
| p.M146V (Ex5) | - | 4 | 37.7 | - | - | [[25](#_ENREF_25), [70](#_ENREF_70), [71](#_ENREF_71)] |
| p.M146L (Ex5)  g.25639A>T | Argentina | 2 | 38.9 | - | - | [[25](#_ENREF_25), [72](#_ENREF_72)] |
| p.M146I (Ex5)  g.25641G>A | Denmark, UK | 2 | 38-57/46.7 | 8-14/11.0 | - | [[26](#_ENREF_26), [40](#_ENREF_40), [71](#_ENREF_71), [73](#_ENREF_73)] |
| p.M146I (Ex5)  g.25641G>C | Sweden | 1 | 35-49/42.7 | 3-18/10.4 | - | [[74](#_ENREF_74)] |
| p.M146I (Ex5)  g.25641G>T | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.T147P (Ex5) | - | 1 | 32-32/32.0 | 8-8/8.0 | - | [[75](#_ENREF_75)] |
| p.T147I (Ex5) | France | 1 | 37-46 | - | - | [[28](#_ENREF_28)] |
| p.L150P (Ex5) | France | 1 | 54-65 | 5-10 | - | [[4](#_ENREF_4)] |
| p.L153V (Ex5) | France , UK | 4 | 34-44/35.3 | 6-13/8.6 | Myoclonus | [[17](#_ENREF_17), [22](#_ENREF_22), [26](#_ENREF_26), [76](#_ENREF_76)] |
| p.Y154N (Ex5) | Asian (Japan) | 1 | 37-45/41.0 | 24.0 | Spastic Paraparesis | [[77](#_ENREF_77)] |
| p.Y154C (Ex5) | UK | 1 | 41-41/41.0 | - | - | [[26](#_ENREF_26)] |
| InsFI (Ex5) | - | 1 | 28-28/28.0 | - | Spastic Paraparesis | [[25](#_ENREF_25), [78](#_ENREF_78)] |
| p.Y154F (Ex5) | - | 1 | 42-68/53.8 | 4-5/4.5 | - | [[79](#_ENREF_79)] |
| p.H163Y (Ex6) | Sweden | 1 | 44-65/54.2 | 5-23/11.7 | - | [[80](#_ENREF_80)] |
| p.H163P (Ex6) | - | 1 | 34-34/34.0 | - | - | [[81](#_ENREF_81)] |
| p.H163R (Ex6) | Caucasian, Japan | 15 | 37-68/45.6 | - | Myoclonus | [[18](#_ENREF_18), [82-84](#_ENREF_82)] |
| p.W165G (Ex6) | Asian (Japan) | 1 | 34-38/35.8 | 9-19/14.0 | - | [[85](#_ENREF_85)] |
| p.W165C (Ex6) | France | 1 | 37-47 | - | - | [[4](#_ENREF_4), [28](#_ENREF_28)] |
| p.L166V (Ex6) | UK | 1 | 42-42/42.0 | 8-8/8.0 | - | [[27](#_ENREF_27)] |
| p.L166del (Ex6) | - | 1 | 38-38/38.0 | 8-8/8.0 | - | [[86](#_ENREF_86)] |
| p.L166H (Ex6) | - | 1 | 30-30/30.0 | - | - | [[87](#_ENREF_87)] |
| p.L166P (Ex6) | - | 1 | 24-24/24.0 | 11-11/11.0 | - | [[88](#_ENREF_88)] |
| p.L166R (Ex6) | Spain | 1 | 32-44/38.0 | 4.0 | - | [[11](#_ENREF_11), [89](#_ENREF_89)] |
| p.I168del (Ex6) | UK, China | 2 | 38-60/47.4 | - | - | [[19](#_ENREF_19), [26](#_ENREF_26)] |
| p.I168T (Ex6) | Caucasian | 1 | 86-86/86.0 | 8-8/8.0 | - | [[27](#_ENREF_27)] |
| p.S169P (Ex6) | - | 1 | 31-35/33.3 | 7.0 | Myoclonus | [[11](#_ENREF_11), [90](#_ENREF_90)] |
| p.S169L (Ex6) | Eastern Europe | 2 | 29-31/29.5 | 6-11/8.5 | Myoclonus | [[91](#_ENREF_91), [92](#_ENREF_92)] |
| p.S169del (Ex6) | Asian (China) | 1 | 42-50/44.8 | 10-10/10.0 | - | [[93](#_ENREF_93)] |
| p.S170F (Ex6) | - | 3 | 26-29/27.9 | 7-17 | Myoclonus / Ataxia | [[94-96](#_ENREF_94)] |
| p.L171P (Ex6) | Mexico, UK | 2 | 36-40/38.0 | - | - | [[26](#_ENREF_26), [97](#_ENREF_97)] |
| p.L173W (Ex6) | France | 1 | 24-29/26.5 | - | - | [[4](#_ENREF_4), [28](#_ENREF_28)] |
| p.L173F (Ex6)  (g.38816G>C | - | 1 | 40-47/43.5 | - | - | [[98](#_ENREF_98)] |
| p.L173F (Ex6)  (g.38816G>T) | Spain or Uruguay? | 1 | 50-50/50.0 | 0.5-0.5/0.5 | - | [[60](#_ENREF_60)] |
| p.L174M (Ex6) | Hispanic (Cuba) | 2 | 50-59/54.5 | - | - | [[99](#_ENREF_99)] |
| p.L174del (Ex6) | - | 1 | 53-53/53.0 | - | - | [[100](#_ENREF_100)] |
| p.L174R (Ex6) | Germany | 1 | 46-56/48.0 | 3-11/7.0 | - | [[101](#_ENREF_101)] |
| p.F177L (Ex6) | - | 2 | 36-42 | - | - | [[17](#_ENREF_17), [25](#_ENREF_25)] |
| p.F177S (Ex6) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.S178P (Ex6) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.G183V (Ex6) | Belgium | 1 | 46-55/51.0 | 9-22/13.7 | Pick Disease; Aβ negative, tau positive pathology | [[102](#_ENREF_102)] |
| p.E184G (Ex7) | France | 2 | 43-52 | 5-14 | - | [[4](#_ENREF_4)] |
| p.E184D (Ex7) | Japan, UK | 2 | 40-44/42.0 | 7-10/8.5 | - | [[26](#_ENREF_26), [103](#_ENREF_103)] |
| p.I202F (Ex7) | Wales | 1 | 49-53/51.3 | 6-6/6.0 | - | [[104](#_ENREF_104)] |
| p.G206S (Ex7) | Asian (Korea) | 3 | 30-40/37.5 | 4-4/4.0 | - | [[17](#_ENREF_17), [25](#_ENREF_25), [105](#_ENREF_105)] |
| p.G206D (Ex7) | Serbia | 2 | 32-48/40.7 | 4-4/4.0 | - | [[17](#_ENREF_17), [20](#_ENREF_20)] |
| p.G206V (Ex7) | USA | 1 | 33-33/33.0 | 6-11/8.5 | - | [[106](#_ENREF_106)] |
| p.G206A (Ex7) | Hispanic, France | 19 | 44-69/54.2 | 7-7/7.0 | - | [[4](#_ENREF_4), [25](#_ENREF_25), [107](#_ENREF_107), [108](#_ENREF_108)] |
| p.G209R (Ex7) | Asian (Japan) | 1 | 46 – 53/ 49.6 | - | - | [[109](#_ENREF_109)] |
| p.G209E (Ex7) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.G209V(Ex7) | Germany | 1 | 30 – 48/ 41.3 | - | - | [[41](#_ENREF_41)] |
| p.S213Y (Ex7) | Caucasian | 1 | 41 – 56/ 46.3 | 11-14/13.0 | - | [[110](#_ENREF_110)] |
| p.I213L (Ex7) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.I213F (Ex7) | Poland | 1 | 33-33/33.0 | - | - | [[36](#_ENREF_36)] |
| p.I213T (Ex7) | Asian (Japan) | 1 | 42-48/45.0 | - | - | [[14](#_ENREF_14)] |
| p.H214D (Ex7) | Iberia | 1 | 55-55/55.0 | - | - | [[31](#_ENREF_31)] |
| p.H214Y (Ex7) | Iran | 2 | 37-51/51.0 | 13.0 | - | [[17](#_ENREF_17), [46](#_ENREF_46)] |
| p.G217R (Ex7) | Ireland/UK | 1 | 43-47/45.3 | 4-22/10.3 | - | [[111](#_ENREF_111)] |
| p.G217D (Ex7) | Asian (Japan) | 2 | 38-42/40.0 | 8-12/10.0 | - | [[112](#_ENREF_112)] |
| p.L219F (Ex7) | Italy | 1 | - | - | - | [[113](#_ENREF_113)] |
| p.L219P (Ex7) | - | 1 | 47-53/50.0 | 5-10/7.5 | - | [[114](#_ENREF_114)] |
| p.L219R (Ex7) | Asian (Japan) | 1 | 51-51/51.0 | - | - | [[16](#_ENREF_16)] |
| p.Q222R (Ex7) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.Q222H (Ex7) | France | 2 | 35-47/39.0 | 5-15 | - | [[4](#_ENREF_4), [115](#_ENREF_115)] |
| p.Q223R (Ex7) | Turkey | 1 | 31-38/34.3 | 4-4/4.0 | Spastic Paraparesis | [[116](#_ENREF_116)] |
| p.L226F (Ex7) | Spain | 2 | 33-36/33.8 | 6-15/12.0 | Frontotemporal Dementia | [[18](#_ENREF_18), [117](#_ENREF_117)] |
| p.L226R (Ex7) | - | 1 | - | - | - | [[118](#_ENREF_118)] |
| p.I229F (Ex7) | UK | 1 | 33-33/33.0 | - | - | [[26](#_ENREF_26)] |
| p.S230I (Ex7) | France | 1 | 50-58/54.0 | 20-20/20.0 | - | [[4](#_ENREF_4)] |
| p.S230R (Ex7) | UK | 1 | 56-56/56.0 | 10-10/10.0 | - | [[27](#_ENREF_27)] |
| p.A231T (Ex7) | France | 2 | 45-57 | - | - | [[5](#_ENREF_5), [25](#_ENREF_25), [28](#_ENREF_28)] |
| p.A231V (Ex7) | Netherlands | 1 | 55-63/58.0 | - | - | [[1](#_ENREF_1)] |
| p.M233L (Ex7) (g.44716A>T) | - | 1 | 39-39/39.0 | 6.0 | Frontotemporal Dementia only | [[25](#_ENREF_25)] |
| p.M233L (Ex7) | Spain, China, Japan | 4 | 37-60/46.5 | 2-5/3.5 | - | [[16](#_ENREF_16), [119-121](#_ENREF_119)] |
| p.M233V (Ex7) | - | 1 | 30-34/32.0 | 3-7 | - | [[122](#_ENREF_122)] |
| p.M233L (Ex7) | - | 1 | 39-39/39.0 | 6-6/6.0 | - | [[120](#_ENREF_120)] |
| p.M233T (Ex7) | France, Iberia, Korea | 6 | 34-46/34.7 | 7.0 | - | [[17](#_ENREF_17), [28](#_ENREF_28), [105](#_ENREF_105), [123](#_ENREF_123)] |
| p.M233I (Ex7)  g.44718G>A | France | 1 | 24-30/27.0 | 11-11/11.0 | - | [[4](#_ENREF_4)] |
| p.M233I (Ex7)  g.44718G>C | - | 1 | 28-28/28.0 | 8-8/8.0 | - | [[124](#_ENREF_124)] |
| p.L235P (Ex7) | France | 3 | 29-39/32.5 | 2-5/3.5 | Myoclonus | [[26](#_ENREF_26)] |
| p.L235R (Ex7) | - | 1 | 41 – 47/44.0 | - | - | [[125](#_ENREF_125)] |
| p.L235V (Ex7) | UK | 1 | 44 – 50/47.0 | - | - | [[26](#_ENREF_26)] |
| p.F237I (Ex7) | Asian (Japan) | 1 | 31-31/31.0 | - | Spastic Paraparesis | [[126](#_ENREF_126)] |
| p.F237L (Ex7) | UK | 1 | 46 – 57/51.0 | - | - | [[26](#_ENREF_26)] |
| p.I238M (Ex7) | African American | 1 | 50 – 59/54.5 | 6-6/6.0 | - | [[127](#_ENREF_127)] |
| p.K239N (Ex7) | - | 1 | 42-71/54.0 | - | Behavioural Disturbance | [[128](#_ENREF_128)] |
| p.T245P (Ex7) | Japanese-American | 1 | - | - | - | [[129](#_ENREF_129)] |
| p.A246E (Ex7) | Anglo-Saxon-Celt (Canada), Poland | 2 | 52-53/52.5 | - | - | [[130](#_ENREF_130)] |
| p.L248P (Ex7) | Asian (China) | 1 | 40-42/41.0 | - | - | [[19](#_ENREF_19)] |
| p.L248R (Ex7) | Iberia | 1 | 54-54/54.0 | 11-11/11.0 | - | [[31](#_ENREF_31)] |
| p.L250V (Ex7) | Bulgaria, Japan | 2 | 40-51/46.8 | 11.0 | Myoclonus | [[131](#_ENREF_131)] |
| p.L250S (Ex7) | UK / Ireland | 1 | 49 – 56/52.2 | 6 - 15 /11.7 | - | [[39](#_ENREF_39), [132](#_ENREF_132)] |
| p.Y256S (Ex7) | - | 1 | 25 – 30/27.5 | 2-3/2.5 | - | [[115](#_ENREF_115)] |
| p.A260V (Ex8) | Iberia, UK, France  Asian (Japan) | 4 | 27-42/37.1 | 8-19/12.0 | - | [[41](#_ENREF_41), [133](#_ENREF_133), [134](#_ENREF_134)] |
| p.V261L (Ex8) | Spain | 1 | 40-40/40.0 | 7.0 | Spastic Paraparesis | [[135](#_ENREF_135)] |
| p.V261F (Ex8) | - | 5 | 34-38/36.3 | 4-9/6.5 | Spastic Paraparesis | [[25](#_ENREF_25)] |
| p.L262V (Ex8) | Turkey, France | 2 | 51 - 65 /55.3 | 4-8 | - | [[4](#_ENREF_4), [46](#_ENREF_46)] |
| p.L262F (Ex8) | Caucasian | 1 | 47-56/50.3 | - | - | [[136](#_ENREF_136)] |
| p.C263R (Ex8) | - | 1 | 50.0 | - | - | [[137](#_ENREF_137)] |
| p.C263F (Ex8) | Belgium, UK | 2 | 58-70/64.0 | - | - | [[26](#_ENREF_26)] |
| p.P264L (Ex8) | France , UK | 11 | 47.3 | - | Atypical Dementia / Spastic Paraparesis | [[137](#_ENREF_137)] |
| p.G266S (Ex8) | Asian (Japan) | 2 | 35-44/40.8 | 8-10/9.0 | CAA; Spastic Paraparesis | [[138](#_ENREF_138)] |
| p.P267S (Ex8) | UK/ Ireland | 1 | 32 – 38/35.0 | - | - | [[39](#_ENREF_39)] |
| p.P267L (Ex8) | Poland | 1 | 56-56/56.0 | - | - | [[139](#_ENREF_139)] |
| p.R269G (Ex8) | - | 2 | 49.0 | - | Myoclonus | [[140](#_ENREF_140)] |
| p.R269H (Ex8) | USA, UK, Japan | 4 | 46-67/55.1 | 5-9/7.0 | Myoclonus | [[26](#_ENREF_26)] |
| p.L271V (Ex8) | - | 1 | 43 – 61/49.0 | - | - | [[141](#_ENREF_141)] |
| p.V272A (Ex8) | Spain, Iberia | 2 | 26-40/32.9 | 6-14/10.0 | Subcortical atrophy / Parkinsonism | [[18](#_ENREF_18), [31](#_ENREF_31)] |
| p.E273A (Ex8) | Asian (Japan) | 1 | 63-63/63.0 | - | - | [[84](#_ENREF_84)] |
| p.E273G (Ex8) | France | 1 | 50 – 63 | 9-9/9.0 | - | [[4](#_ENREF_4)] |
| p.T274R (Ex8) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.A275V (Ex8) | - | 1 | 42 – 47/44.5 | - | - | [[142](#_ENREF_142)] |
| p.R278K (Ex8) | - | 1 | 41-48/44.6 | - | Spastic Paraparesis | [[143](#_ENREF_143)] |
| p.R278T (Ex8) | - | 1 | 37.0 | - | Spastic Paraparesis | [[123](#_ENREF_123)] |
| p.R278I (Ex8) | - | 1 | 48-51/49.5 | - | Progressive Nonfluent Aphasia / Language Impairment | [[144](#_ENREF_144)] |
| p.R278S (Ex8) | - | 1 | 42.0 | - | Spastic Paraparesis | [[145](#_ENREF_145)] |
| p.E280G (Ex8) | Ireland, France, UK, Canada | 6 | 39-52/44.8 | 8-15 | Spastic Paresis | [[17](#_ENREF_17)] |
| p.E280A (Ex8) | Hispanic (Colombia)  Asian (Japan) | 12 | 36-62/47.4 | - | - | [[13](#_ENREF_13), [83](#_ENREF_83)] |
| p.L282V (Ex8) | Belgium | 1 | 41-53/44.3 | 7-9/8.0 | CAA | [[146](#_ENREF_146)] |
| p.L282F (Ex8) | Asian (Japan) | 1 | 49 – 53/51.0 | - | - | [[147](#_ENREF_147)] |
| p.L282R (Ex8) | Spain | 2 | 35 – 50/43.4 | 5-20/13.3 | - | [[18](#_ENREF_18), [119](#_ENREF_119)] |
| p.P284S (Ex8) | - | 1 | 32-45/38.3 | - | Spastic Paraparesis | [[148](#_ENREF_148)] |
| p.P284L (Ex8) | Asian (Japan) | 1 | 32-32/32.0 | 22.0 | Spastic Paresis | [[149](#_ENREF_149)] |
| p.A285V (Ex8) | Asian (Japan) | 2 | 45 – 55/50.5 | 10-10/10.0 | - | [[133](#_ENREF_133), [150](#_ENREF_150)] |
| p.L286P (Ex8) | - | 1 | 35-42/39.6 | 6-20/11.8 | CAA | [[151](#_ENREF_151)] |
| p.L286V (Ex8) | France, Germany  Asian (Japan) | 3 | 41-48/47.5 | 7-10 | - | [[4](#_ENREF_4), [65](#_ENREF_65), [152](#_ENREF_152)] |
| Δ9 ( IVS8-IVS9) (g.56305\_62162del) | - | 1 | 36-54/45.5 | 2-10/6.1 | Spastic Paraparesis | [[6](#_ENREF_6), [123](#_ENREF_123), [153](#_ENREF_153)]. |
| Δ9Finn(IVS8-IVS9) (g.56681\_61235del) | Finland | 2 | 40-57/47.1 | 2-12 | Spastic Paraparesis | [[6](#_ENREF_6), [123](#_ENREF_123), [153](#_ENREF_153)]. |
| 869-22\_869-23ins18( IVS8)(g.58282\_58283ins18) | France | 1 | 42-47 | - | Spastic Paraparesis | [[154](#_ENREF_154)] |
| Δ9 (IVS8)  g.58302A>G | France , Germany | 2 | 48-48/48.0 | - | - | [[155](#_ENREF_155), [156](#_ENREF_156)] |
| Δ9 (IVS8)  g.58303G>A | Asian (Japan) | 2 | 47.5 | 7.1 | Paraparesis | [[149](#_ENREF_149), [157](#_ENREF_157)] |
| Δ9 (IVS8)  g.58303G>T | UK / Ireland | 3 | 39 - 50 | - | - | [[157](#_ENREF_157)] |
| p.T291P (Ex9)  p.[S290C;T291\_S319del] | France | 1 | 33-33/33.0 | - | - | [[4](#_ENREF_4)] |
| p.R352C (Ex10) | Asian (China) | 1 | 56-62／59.3 | 12-22／17.0 | - | [[121](#_ENREF_121)] |
| p.R358Q (Ex10) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.S365A (Ex10) | Iberia | 1 | 55-70/62.5 | - | - | [[31](#_ENREF_31)] |
| p.R377W (Ex10) | France | 2 | 50-66/58.0 | - | Epilepsy；Frontotemporal Atrophy | [[158](#_ENREF_158)] |
| p.R377M (Ex11) | UK | 1 | 38-41/39.0 | - | - | [[26](#_ENREF_26)] |
| p.G378E (Ex11) | France, Germany  Asian (Japan) | 4 | 34-43/37.5 | - | CAA | [[21](#_ENREF_21)] |
| p.G378V (Ex11) | UK | 1 | 41-49/45.0 | - | - | [[26](#_ENREF_26)] |
| p.L381V (Ex11) | Bulgaria, Japan | 2 | 29-65/30.5 | 4-8/5.7 | Spastic Paraparesis | [[152](#_ENREF_152)] |
| p.L381F (Ex11) | - | 1 | 28-32/29.8 | 2-6/3.8 | Kufs Disease | [[159](#_ENREF_159)] |
| p.G384A (Ex11) | Belgium, Japan | 2 | 30-39/34.9 | 3-13/6.8 | - | [[29](#_ENREF_29), [83](#_ENREF_83)] |
| p.F386S (Ex11) | - | 1 | 37 - 58 | - | - | [[17](#_ENREF_17)] |
| p.F386L (Ex11) | Asian (Japan) | 1 | 40-52/46.0 | - | - | [[160](#_ENREF_160)] |
| p.S390I (Ex11) | France | 1 | 39-40 | - | - | [[28](#_ENREF_28)] |
| p.V391F (Ex11) | France | 3 | 42-55/47.5 | 3-10 | - | [[4](#_ENREF_4), [17](#_ENREF_17)] |
| p.L392V (Ex11) | Italy, France, Japan | 5 | 39-52/42.5 | - | Epilepsy | [[17](#_ENREF_17), [28](#_ENREF_28)] |
| p.L392P (Ex11) | Italy | 1 | 36-43/38.3 | - | Epilepsy | [[161](#_ENREF_161)] |
| p.G394V (Ex11) | Italy | 2 | 42-44/43.0 | 7-8/7.5 | - | [[162](#_ENREF_162)] |
| p.A396T (Ex11) | Turkey / Bulgaria) | 1 | 35-56/44.7 | 9-28/18.5 | - | [[46](#_ENREF_46)] |
| p.N405S (Ex11) | Asian (Japan) | 1 | - | - | - | [[163](#_ENREF_163)] |
| p.I408T (Ex11) | Italy | 1 | 73-73/73.0 | - | - | [[164](#_ENREF_164)] |
| p.A409T (Ex11) | Spain | 1 | 58.0 | - | - | [[119](#_ENREF_119)] |
| p.C410Y (Ex11) | France, Russian Jewish; Ashkenazi Jewish | 5 | 40-60/49.6 | 6-10/8.0 | - | [[4](#_ENREF_4), [5](#_ENREF_5), [27](#_ENREF_27), [65](#_ENREF_65)] |
| p.V412I (Ex11) | - | 1 | 31-43/37.5 | 3.0 | Frontotemporal Dementia | [[165](#_ENREF_165)] |
| p.L418F (Ex12) | France | 2 | 31-35/33.0 | 5-6/5.5 | - | [[4](#_ENREF_4), [25](#_ENREF_25)] |
| p.L420R (Ex12) | Caucasian | 1 | 38-38／38.0 | 10-10/10.0 | - | [[166](#_ENREF_166)] |
| p.L424F (Ex12)  (g.71074C>） | - | 1 | - | - | - | [[167](#_ENREF_167)] |
| p.L424F (Ex12)  (g.71074C>G） | Bulgarian | 1 | 57-60/58.5 | - | Epilepsy | － |
| p.L424H (Ex12) | - | 2 | 38-42/39.0 | - | - | [[17](#_ENREF_17), [117](#_ENREF_117)] |
| p.L424R (Ex12) | Poland | 1 | 30-30/30.0 | 8-8/8.0 | - | [[139](#_ENREF_139)] |
| p.A426P (Ex12) | Scotland-Ireland | 1 | 41-51/46.0 | - | - | [[41](#_ENREF_41)] |
| p.A431E (Ex12) | Hispanic(Mexico) | 34 | 33-48/40.5 | - | - | [[168](#_ENREF_168), [169](#_ENREF_169)] |
| p.A431V (Ex12) | Asian (Japan) | 1 | 47-47/47.0 | - | - | [[170](#_ENREF_170)] |
| p.A434T (Ex12) | Asian (China) | 1 | 35-50/43.5 | - | - | [[19](#_ENREF_19)] |
| p.A434C (Ex12) | - | 2 | 27-35/30.3 | 6-24/15.0 | - | [[25](#_ENREF_25), [171](#_ENREF_171)] |
| p.L435F (Ex12) | - | 1 | - | - | - | [[25](#_ENREF_25)] |
| p.P436S (Ex12) | UK | 1 | 44-50/47.0 | - | - | [[56](#_ENREF_56)] |
| p.P436Q (Ex12) | - | 3 | 20-42/28.3 | 12.0 | Spastic Paraparesis | [[6](#_ENREF_6)] |
| p.Ile439S (Ex12) | Spain | 1 | 55-55/55.0 | - | - | [[18](#_ENREF_18)] |
| ΔT440 (Ex12) (g.71122\_71124delACC) | Asian (Japan) | 1 | 34-35/34.5 | 13-18/15.5 | With Lewy Bodies | [[172](#_ENREF_172)] |

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