Mutations in the exonuclease domain of the DNA polymerase epsilon (POLE) gene define one such subtype, which causes an ultra-mutated tumour phenotype. These tumours may have an improved progression-free survival and may be receptive to specific therapies. However, the clinical phenotype of these tumours is unknown.

Elevated CD8+ cell infiltration was found to be associated with the presence of a mutation in the gene encoding for DNA polymerase epsilon, POLE (51.6 cells/hpf in wild-type tumors vs 95.9 cells/hpf in mutant tumors; p = 0.0199). In a retrospective cohort of 173 patients, the presence of any mutation in POLE was found to be associated with a 46% reduction in hazard of progression (HR 0.54, 95% CI 0.311-0.952; p = 0.033). The most frequent mutation was a near-C-terminal nonsense mutation.

A potential association was found between mutant POLE and both an increase in CD8+ cell infiltration and progression-free survival. The predominant mutation was found outside of the known exonuclease hot spot; however, it was still associated with a slight increase in mutational burden, CD8+ cell infiltration, and progression-free survival. Alterations in gene expression, resulting from alterations in POLE, may yield an increased presentation of neoantigens, and, thus, greater CD8+ cell-mediated apoptosis of neoplastic cells. These findings have suggested the utility of checkpoint inhibitors in the treatment of POLE-mutant meningiomas [1].

1)
Rutland JW, Dullea JT, Gill CM, Chaluts D, Ranti D, Ellis E, Arrighi-Allisan A, Kinoshita Y, McBride RB, Bederson J, Donovan M, Sebra R, Fowkes M, Umphlett M, Shrivastava RK. Association of mutations in DNA polymerase epsilon with increased CD8+ cell infiltration and prolonged progression-free survival in patients with meningiomas. Neurosurg Focus. 2022 Feb;52(2):E7. doi: 10.3171/2021.11.FOCUS21592. PMID: 35104796.