Molecular, Pathological, Radiological, and Immune Profiling of Non-brainstem Pediatric High-Grade Glioma from the HERBY Phase II Randomized Trial.


1 Division of Molecular Pathology, The Institute of Cancer Research, 15 Cotswold Road, Sutton, London, Surrey SM2 5NG, UK; Division of Cancer Therapeutics, The Institute of Cancer Research, 15 Cotswold Road, Sutton, London, Surrey SM2 5NG, UK.

22 Division of Molecular Pathology, The Institute of Cancer Research, 15 Cotswold Road, Sutton, London, Surrey SM2 5NG, UK; Division of Cancer Therapeutics, The Institute of Cancer Research, 15 Cotswold Road, Sutton, London, Surrey SM2 5NG, UK. Electronic address: chris.jones@icr.ac.uk.

The HERBY trial was a phase II open-label, randomized, multicenter trial evaluating bevacizumab (BEV) in addition to temozolomide/radiotherapy in patients with newly diagnosed non-brainstem high-grade glioma (HGG) between the ages of 3 and 18 years. We carried out comprehensive molecular analysis integrated with pathology, radiology, and immune profiling. In post-hoc subgroup analysis, hypermutator tumors (mismatch repair deficiency and somatic POLE/POLD1 mutations) and those biologically resembling pleomorphic xanthoastrocytoma ([PXA]-like, driven by BRAF_V600E or NF1 mutation) had significantly more CD8+ tumor-infiltrating lymphocytes, and longer survival with the addition of BEV. Histone H3 subgroups (hemispheric G34R/V and midline K27M) had a worse outcome and were immune cold. Future clinical trials will need to take into account the diversity represented by the term "HGG" in the pediatric population.

KEYWORDS: CD8; H3F3A; MAPK; hypermutator; immune; pediatric high-grade glioma

PMID: 29763623   PMCID: PMC5956280   DOI: 10.1016/j.ccell.2018.04.004

Free PMC Article