Abstracts

HG-85. INTER-OBSERVER AGREEMENT IN NEUROPATHOLOGICAL HGG DIAGNOSIS : EXPERIENCE OF THE PRE-RANDOMISATION CENTRAL REVIEW IN THE HERBY TRIAL

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In previous large paediatric multicentre trials for High-Grade Glioma

(HGG), high proportions of diagnostic disagreement across neuropathologists were reported. The HERBY trial is a Phase-II open-label, randomised, multicentre trial evaluating bevacizumab in paediatric patients with newly diagnosed supratentorial HGG. METHODS: Confirmation of HGG diagnosis by reference pathology was mandatory before randomisation, followed by a review by five independent expert neuropathologists. Inter-observer agreement was assessed using Cohen's Kappa coefficients. RESULTS: Slides from 169/187 patients screened for eligibility were centrally reviewed, within 3 days in 69% of cases. HGG diagnosis was centrally confirmed in 149 cases (88%), whereas diagnosis was low-grade glioma in 5% (n = 8), anaplastic ganglioglioma/PXA (n = 8), miscellaneous diagnoses (n = 4). 124 patients entered the randomised trial. Three cases were not confirmed by the pathology panel (reclassified in grade II oligodendroglioma or anaplastic ganglioglioma). The Kappa coefficient between local and reference pathologist was moderate for the subtype and substantial for the WHO grade (Kappa = 0.45 and 0.68, respectively). Agreement varied according to the initial diagnosis with the confirmation of subtype and grade for 23% cases of oligodendroglioma or mixed oligo-astrocytoma, 76% of WHO grade III astrocytoma and 95% of glioblastoma. The review panel registered some degree of discordance for subtype or grade in 52% cases, with dispersed conclusions from the experts (> 3 out of 5) in 10% cases. However, Kappa coefficient reached 85% for the grading between the reference pathologist and the consensus. These data highlight the interest and feasibility of a pre-randomised real-time central neuropathological review in multicentre trials.