CNS tumours

THE HERBY STUDY: A PHASE 2 OPEN-LABEL, RANDOMIZED, MULTICENTER STUDY OF BEVACIZUMAB-BASED THERAPY IN PEDIATRIC PATIENTS WITH NEWLY DIAGNOSED HIGH-GRADE GLIOMA


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Background: Despite recent therapeutic advances, outcomes in pediatric high-grade glioma (HGG) remain poor. A phase 1 study (Glade-Bender et al., J Clin Oncol. 2008) indicated that bevacizumab (BEV) is well tolerated in children with refractory solid tumors and yielded pharmacokinetic data that support further studies of BEV in childhood cancer.

Trial design: A total of 120 eligible patients aged 3 to 18 years with newly diagnosed, localized supratentorial or infratentorial cerebellar or peduncular, histologically confirmed World Health Organization grade 3 or 4 HGG (central independent histologic confirmation) will be randomized to 6 weeks of concomitant temozolomide (TMZ) and local radiotherapy, followed by a 4-week TMZ treatment break and 48 weeks of adjuvant TMZ ± BEV every other week. Children aged 6 months to 3 years with recurrent disease are eligible in a young patient cohort; at relapse, these patients will receive TMZ + BEV without radiotherapy. All patients/parents must provide written informed consent per the local institutional review boards. The primary end point is event-free survival, defined as the time to earliest occurrence of tumor progression/recurrence (by central independent assessment per Response Assessment in Neuro-Oncology criteria), secondary malignancy, or death. Secondary end points include overall survival, response rate, safety, feasibility, and tolerability. The usefulness of multimodal MRI will be explored with respect to the diagnosis of pseudoprogression and prognostication of tumor evolution. All randomized patients will be followed for ≥3 years. A futility analysis will be performed after the first 60 randomized patients have been followed for 1 year. The primary analysis will be performed after all patients have been followed for 1 year, and an updated analysis will be performed 3 years after the last patient has been randomized. HERBY is being conducted at 87 clinical sites in 15 countries. The first patient was randomized in October 2011. Among 118 patients screened to date, 79 have been randomized, and 1 has been enrolled in the young patient cohort. Completion of the study is expected in 2016. Some content has been presented at ASCO 2012 (abs TPS9596), SNO 2013 (abs PC-007), and ISPN 2013 (abs P109).

Disclosure: D. Hargrave: Advisory board: Roche; P. Varlet: Advisory board: Roche Other substantive relationships: Roche; J. Grill: Advisory board: Genentech; T. Jaapar: Corporate sponsored research: Roche; C. Jones: Advisory board: Genentech Paediatric Oncology Advisory Board Corporate sponsored research: Roche/Genentech - HERBY trial M. Massimino: Advisory board: Roche; P. Morgan: Advisory board: Trial Steering Group for F Hoffmann-La Roche sponsored HERBY study (BO25041) Corporate sponsored research: Roche; M. Zheng: Corporate sponsored research: Roche; C. Berger: Corporate sponsored research: Roche; G. Zahlmann: Corporate sponsored research: Roche; E. Bouffet: Advisory board: Boehringer Ingelheim. All other authors have declared no conflicts of interest.