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A bioequivalence study of a novel liquid and ready-to-use temozolomide oral suspension and temozolomide capsules in patients with primary tumors central nervous system malignancies.

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Background: Oral temozolomide capsule is approved for the treatment of glioma and malignant glioblastoma in adults and in Europe in children over 3-years. As recommended by international pediatric medical associations, temozolomide is also used for the treatment of high-risk relapsed or refractory neuroblastoma, a solid tumor affecting young children. Nevertheless, capsules are not adapted to the pediatric population leading caregivers to handle temozolomide capsules, which bears major risks (i.e. dose inaccuracy, temozolomide instability and exposure to cytotoxic drug). To overcome this situation, a temozolomide oral suspension (Kimozo) was developed. The aim of this phase I study was to demonstrate bioequivalence between the temozolomide oral suspension and the temozolomide capsules (Temodal) and to assess the general and local safety in adult patients. **Methods:** A randomized, open-label, two-way crossover, single-dose bioequivalence study was performed in 8 centers. Adult patients with primary malignancies and treated with temozolomide 200 mg/m^2 as monotherapy received a single oral administration of the oral suspension (test) or capsule (reference) on days 1 and 2 of a 5-day cycle, depending on the randomization, and under fasting conditions. Fourteen blood samples were collected over 10-hr in each period for pharmacokinetic purpose. General and buccal safety was assessed along the study. The assessment of bioequivalence was based upon 90% confidence intervals (CI) for the ratio of the population geometric means (test/reference) for maximum plasma concentration (C_{max}) and area under the curve (AUC_{0-t}). **Results:** Among the thirty-six patients enrolled in the study, thirty were assessable for pharmacokinetic primary endpoint. The point estimate and the 90% CI of the ratios of C_{max} and AUC_{0-t} were 107.62 (98.07-118.09) and 97.18 (95.05-99.35), respectively. The results obtained satisfy the bioequivalence criteria of the Bioequivalence Guidelines (90% CI between 80.00% and 125.00%). Neither serious adverse events nor adverse events of special interest (i.e. mucositis) were reported. **Conclusions:** The oral suspension of temozolomide (Kimozo) and capsule of temozolomide (Temodal) are bioequivalent under fasting conditions in patients with CNS primary malignancies, supporting that they are therapeutic equivalent. Clinical trial information: NCT04467346. Research Sponsor: ORPHELIA Pharma.