

Abstracts

AT-23. A PHASE II STUDY OF LAPATINIB AND DOSE-DENSE TEMOZOLOMIDE (TMZ) FOR ADULTS WITH RECURRENT EPENDYMOMA: A CERN CLINICAL TRIAL

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BACKGROUND: Ependymoma is an uncommon adult primary CNS tumor. Initial treatment includes extensive resection often followed by but there is no standard treatment for recurrent disease. Molecular studies show most tumors have ErbB2 overexpression and unmethylated MGMT promoter status. We developed a clinical trial combining lapatinib(targets ErbB1, ErbB2) with dose-dense temozolomide. **METHODS:** Eligibility criteria included adults(≥ 18), KPS ≥ 70 , with centrally confirmed ependymoma

(grades I, II, or III). Treatment plan: TMZ(125mg-150mg/m²/d, 7on/7off) plus lapatinib(1250 mg po/qd) continuous dosing. Cycle = 4wks; imaging and patient reported outcomes measures(PRO:MDASI-BT/MDASI-Spine) every 2 cycles, maximum 24 cycles. The primary endpoint was median progression free survival(PFS); secondary objectives: 6-month PFS, 12-month PFS, response rate, overall survival, and change in symptom burden. A Bayesian design sequentially monitored treatment efficacy based on posterior probabilities. **RESULTS:** Fifty patients enrolled. Median age 47(20-81), women = 28(56%), median KPS = 90. Tumor grade: anaplastic (III) = 18; ependymoma (II) = 24; myxopapillary(I) = 8. Tumor location: supratentorial (ST) = 14; infratentorial(IT) = 5; spinal cord(SC) = 25; multifocal (MF) = 6. Median PFS: overall = 36 wks. By grade: I = 96 wks; II = 45 wks; III = 25.3 wks. By location: ST = 24 wks; IT = 21 wks; SC = 96 wks. PFS rates(6-month,12-month): Grade I(88%,75%), Grade II(63%,46%), Grade III(50%,28%); ST(43%,29%), IT(40%,20%), SC(80%,64%), MF(50%,17%). Best response: CR = 1(Gr III), PR = 4(Gr II = 2, III = 1), SD = 33, PD = 12. Treatment was well tolerated with only modest myelotoxicity and rash. No cardiotoxicity. All patients completed the MDASI-BT/ SP(reported separately). Preliminary gene expression analysis(23 tumors) correlated response with higher ErbB2 mRNA expression($p = .03$). **CONCLUSION:** Daily lapatinib with dose-dense TMZ was well tolerated and demonstrated activity in the spectrum of ependymoma defined by location and tumor grade. Ongoing molecular profiling will determine whether there is a potential predictive marker for response, given the preliminary correlation of response with ErbB2 expression. This is the first prospective clinical trial in adult ependymoma and demonstrates feasibility of accrual, tumor and PRO collection and efficacy with a possible predictive marker requiring validation in a subsequent clinical trial.