AT-39. A RANDOMIZED PHASE II TRIAL OF VANDETANIB (ZD6474) IN COMBINATION WITH CARBOPLATIN VERSUS CARBOPLATIN ALONE IN ADULTS WITH RECURRENT GLIOBLASTOMA
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BACKGROUND: Vandetanib is a tyrosine kinase inhibitor of VEGFR-2, EGFR, and the RET oncogene. While vandetanib has not shown significant clinical activity, preclinical experience suggests synergistic efficacy in combination with carboplatin in glioblastoma (GBM). METHODS: This randomized non-comparative phase-II trial evaluates the efficacy and safety of vandetanib (300 mg/d NEIAED, 400 mg/d EIAED) in combination with carboplatin (AUC 6 q 4 weeks) versus carboplatin alone (AUC 6 q 4 weeks) in adults with recurrent GBM. Upon progression with single-agent carboplatin, single-agent vandetanib was offered. Contrast-enhanced-MRI before subsequent cycles were compared to baseline and response assessed using RANO criteria. Primary end-point was PFS-6. Ktrans, CBV, ADC, and HRQoL were measured before treatment and after 4 weeks and the relationship between these factors and time to progression and survival was explored. RESULTS: Thirty-two patients with recurrent GBM were accrued to each arm. Most frequent treatment related grade ≥ 3 toxicities were thrombocytopenia (n = 14), lymphopenia (n = 12), neutropenia (n = 7), seizure (n = 5), and hypertension (n = 4). There were two partial responses in the combination arm, none in the carboplatin arm. All patients had progressed at 6 months in the combination arm; one patient in the carboplatin arm was progression-free at 6 months. Median PFS and OS were 1.7 months (95% CI: 0.9 to 2.7 mo) and 5.6 months (95% CI: 4.6 to 8.6 mo) in the combination arm, and 0.9 months (95% CI: 0.89 to 0.92 mo) and 5.2 months (95% CI: 3.8 to 7.5 mo) in the carboplatin arm. Greater increase in ADC was predictive of shorter survival, and greater increase in CBV was predictive of shorter time to progression in both study arms. Changes in HRQoL were not predictive of time to progression or survival. CONCLUSIONS: The combination of vandetanib and carboplatin did not have significant activity in unselected patients with recurrent glioblastoma.