A Phase II study of single agent Buparlisib in recurrent/refractory primary (PCNSL) and secondary CNS lymphoma (SCNSL)

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PCNSL is an aggressive primary brain tumor. Outcome and treatment options are poor for recurrent/refractory (r/r) patients with response rates between 30–60% and progression free survival (PFS) of 2–6 months. PIIK inhibition has shown promising response in some B-cell malignancies. This phase II trial investigates Buparlisib in patients with r/r PCNSL and SCNSL. Eligible patients had r/r PCNSL, age ≥18, KPS ≥50, normal end-organ function, unrestricted number of prior therapies. Systemic disease needed to be absent in SCNSL patients. Patients received Buparlisib 100mg daily. The trial was closed prematurely due to limited clinical response. Four patients were enrolled: age 55, 60, 68, 79 with KPS of 90, 100, 90, 60, respectively. Three patients developed neurologic symptoms at a median of 37 days after trial drug initiation all due to (CNS) progression. Median progression free survival was 39 days. Median overall survival was 196 days. Buparlisib concentrations were assessed 2h after treatment on day 15 in plasma and CSF. Mean plasma concentration was 110 ng/ml (range: 56–290), mean CSF concentration 13 ng/ml (3–30). CSF concentrations in the trial population (median: 3400 ng/ml; range: 202–499) was below the IC50 observed to induce cell death in lymphoma cells in vitro>5000mM. CD79B mutations were found in 3/4 patients. Patients with CNS lymphoma tolerate drug with acceptable toxicities. Treatment did not result in clinical response possibly due to CNS concentration below a meaningful IC50. Additionally, Buparlisib might not have single agent activity.