BACKGROUND: Pediatric low-grade glioma (pLGG) is the most common central nervous system tumor of childhood. Most pLGGs are driven by BRAF alterations, but a subset harbor activating mutations or
fusions of FGFR1/2/3. Significantly less is known about the biologic activity, clinical course, and response to targeted inhibition of these FGFR-altered gliomas (FGFR pLGG). We sought to define the epidemiologic characteristics, molecular signature, prognostic markers, and clinical course of patients with FGFR pLGG. METHODS: We performed a multi-institutional, retrospective chart review of pediatric neuro-oncology patients treated at two large, academic cancer centers from 2012 – 2023 with tumor molecular profiling demonstrating any FGFR alteration. RESULTS: Sixteen eligible patients were identified; 9 (56%) were female and median age was 12 years of age (range 6 - 18 years). Reported histologies included pilocytic astrocytoma (4), rosette-forming glioneuronal tumor (3), low grade glial/glioneuronal tumor (3), low grade glioma NOS (2), intermediate grade astrocytoma (1), dysembryoblastic neuroepithelial tumor (2), and pilomyxoid astrocytoma (1). FGFR point mutations were seen in 10/16 (62.5%) patients followed by FGFR-TACC3 fusions in 4/16 (25%) patients and two patients with FGFR1 tandem duplication. Metastatic disease was noted at diagnosis in two patients and upfront gross total resection was achieved in four patients. The most common systemic therapy for the remaining patients was Vincristine and/or Carboplatin. All sixteen patients are alive at median follow up of 32 months (range 6 - 198 months). CONCLUSIONS: FGFR pLGG represent a distinct subset of tumors with unique biologic properties and clinical activity. Additional studies are needed to investigate this unique patient population to appropriately adapt our therapeutic approach and improve patient outcomes.