Young children diagnosed with medulloblastoma (MB) pose a significant challenge due to the high susceptibility of the developing brain to neurotoxic agents such as craniospinal irradiation (CSI). Different innovative strategies were developed with the aim to enhance outcomes while either delaying or avoiding CSI. We describe a case series of patients affected by infant MB treated according to the Italian Infants High Risk recommendation. Retrospective data from 42 children with MB younger than 5 years of age at diagnosis treated between 2007 and 2023 at Bambino Gesù Children’s Hospital were recorded. Demographic, clinical, surgical, radiological, molecular, and histopathological data were collected. Overall survival (OS) and event-free survival (EFS) were calculated using the Kaplan-Meier method. Seventeen patients were excluded for first-line radiotherapy. Conclusively, 25 patients (13 male, 12 female) with a median age of 2.53 months at diagnosis were eligible for the analysis. Eleven patients had metastatic disease at diagnosis. Histotype: 13/25 classic, 6/25 desmoplastic nodular (DNMB), 4/25 extensive nodularity (MBEN) and 2/25 large cell/anaplastic. DNA methylation profile: SHH subgroup: 12/25, group 3: 8/25 and group 4: 5/25. MYC amplification was detected in 3 cases. In five cases a cancer predisposition syndrome was found. The median duration of follow-up was 48 months. EFS at 12, 24 and 60 months was 80% (95% CI: 58.4-91.1), 72% (95% CI: 50.1-85.5) and 68% (95% CI: 46.1-82.5), respectively. OS at 12, 24 and 60 months was 80% (95% CI: 67.3-96), 80% (95% CI: 58.4-91.1) and 68% (95% CI: 46.1-82.5) respectively. Significant better survival was found for MBEN/DNMB histotype, with no significant difference between molecular subgroups. We reported high EFS and OS in a population of infant MB treated according Italian Infants High Risk recommendation. Our patients presented an average intelligence quotient in the normal range at a median follow-up of 4 years from diagnosis and no long-term toxicity after treatment.