Medulloblastoma (MB) is the most common malignant pediatric brain tumour, and is categorized into four molecular subgroups: WNT, SHH, Group 3 and Group 4 of which Group 3 tumours are associated with increased chances of metastasis and poor patient outcome. Using a cell-surface marker, CD133, a subpopulation of cells with stem cell properties, termed brain tumour initiating cells (BTICs) was identified, and was further shown to drive medulloblastoma tumorigenesis in vitro and in vivo. Previous in silico analyses revealed enriched expression of many stem cell self-renewal regulatory genes in Group 3 MBs. In this work, we aim to identify and characterize the treatment-refractory BTIC population in Group 3 MBs by developing a mouse-adapted therapy treatment model that mimics the clinical treatment of MB. A mouse-adapted MB therapy model was developed using our human-mouse BTIC xenograft, in which MB cells tagged with GFP were intracranially transplanted into the frontal lobes of NOD-SCID mice. After tumour engraftment, mice assigned to receive treatment of craniospinal radiation, followed by intraperitoneal injections of chemotherapeutic drugs Vincristine, Cisplatin and Cyclophosphamide. Following enrichment of tumour cells from cultured brains, in vitro stem cell assays for self-renewal, flow characterization, and candidate gene expression profiling by NanoString were performed. Spinal cords were also harvested from mice in order to elucidate spinal dissemination of human MB cells. We found that the cells cultured from xenografts of treatment group showed an increase in self-renewal and despite evident tumour regression post-therapy, treated tumours showed an increase in expression of CD133, Sox2 and Bmi1 compared to untreated tumours. Profiling genomic changes in “treatment-responsive” tumors against those that fail therapy will generate a differential profile of the refractory BTIC, which may guide future therapeutic approaches targeting this cell, and will serve as a model for targeting such CSCs in other TIC-driven solid tumours.