

# SHH pathway-targeted therapy in a relapsed medulloblastoma

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**Introduction:** Medulloblastoma (MB) is one of the most common paediatric brain tumour. Several molecular groups have been identified. Sonic Hedgehog (SHH) pathway activated is one of them. Relapse of the disease leads to death and there is no known effective treatment<sup>(1)</sup>.

**Case:** We present a 20-year-old male with a disseminated MB relapse of an activated SHH medulloblastoma. The NGS panel showed mutation in PTCH1 and based on phase I trials<sup>(2-3)</sup>, Sonidegib 800 mg/day was initiated. After 8 weeks of treatment, the patient experienced an almost complete response to the disease (see figures 1 and 2) and there was not relevant adverse events. Unfortunately, after 12 weeks of treatment, the patient experienced progression during treatment.

**Discussion:** PTCH1 targeted therapy such as Sonidegib (Odomzo®), which is an approved treatment for basal cell carcinoma, can produce in vivo oncogenic effect on relapsed medulloblastoma. However, responses to these drugs are transient either by mutation in the target protein or by downstream activation at the level of mTOR or other pathways<sup>(4)</sup>.

**Conclusion:** There is a desperate need to develop clinical trials for patients affected of relapsed medulloblastoma. Targeted therapy against the SHH pathway may provide an answer in a subset of patients. Administration of Sonidegib in combination with other downstream inhibitors of oncogenic activation pathways may provide a solution to early disease escape.

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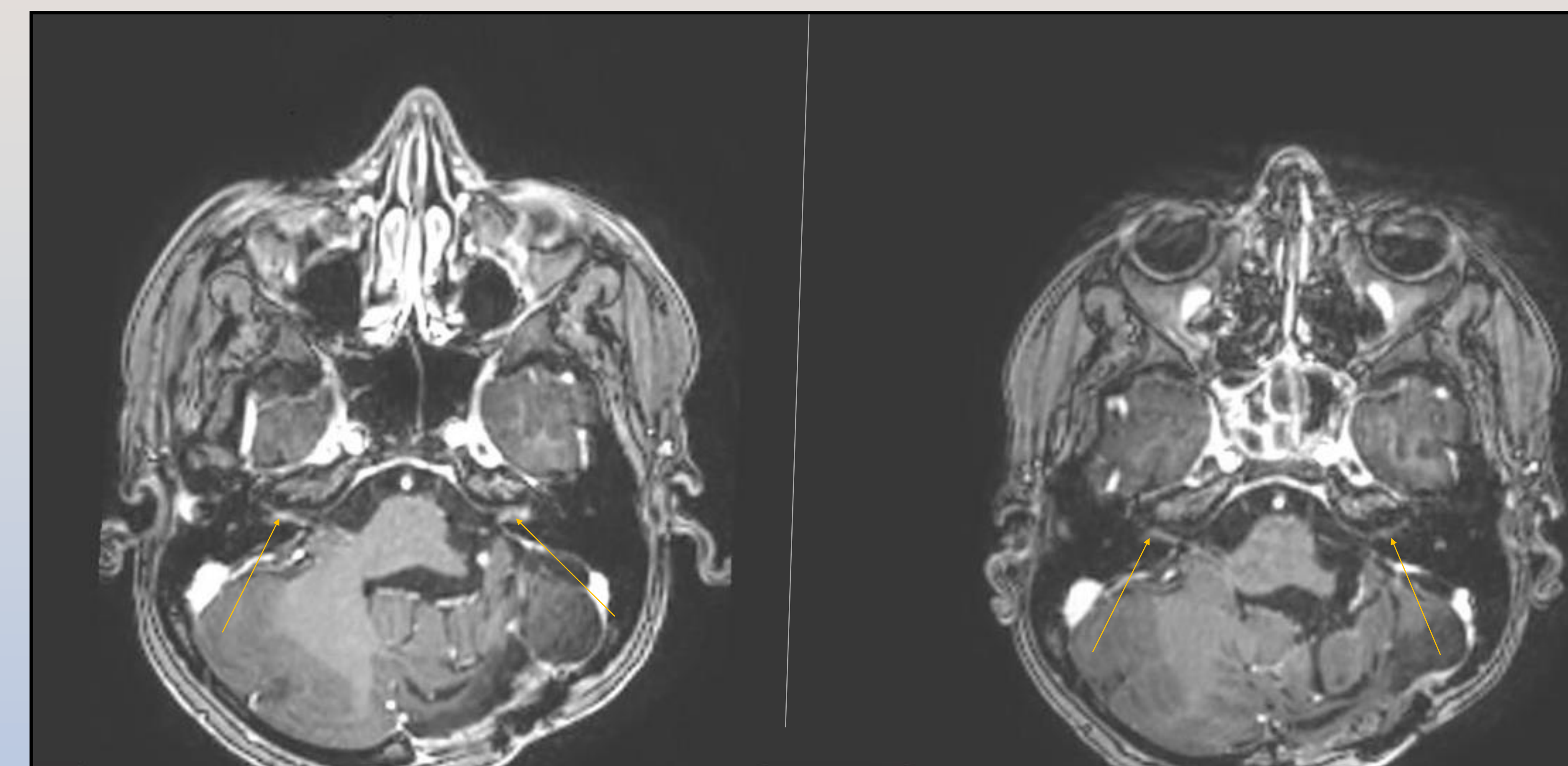
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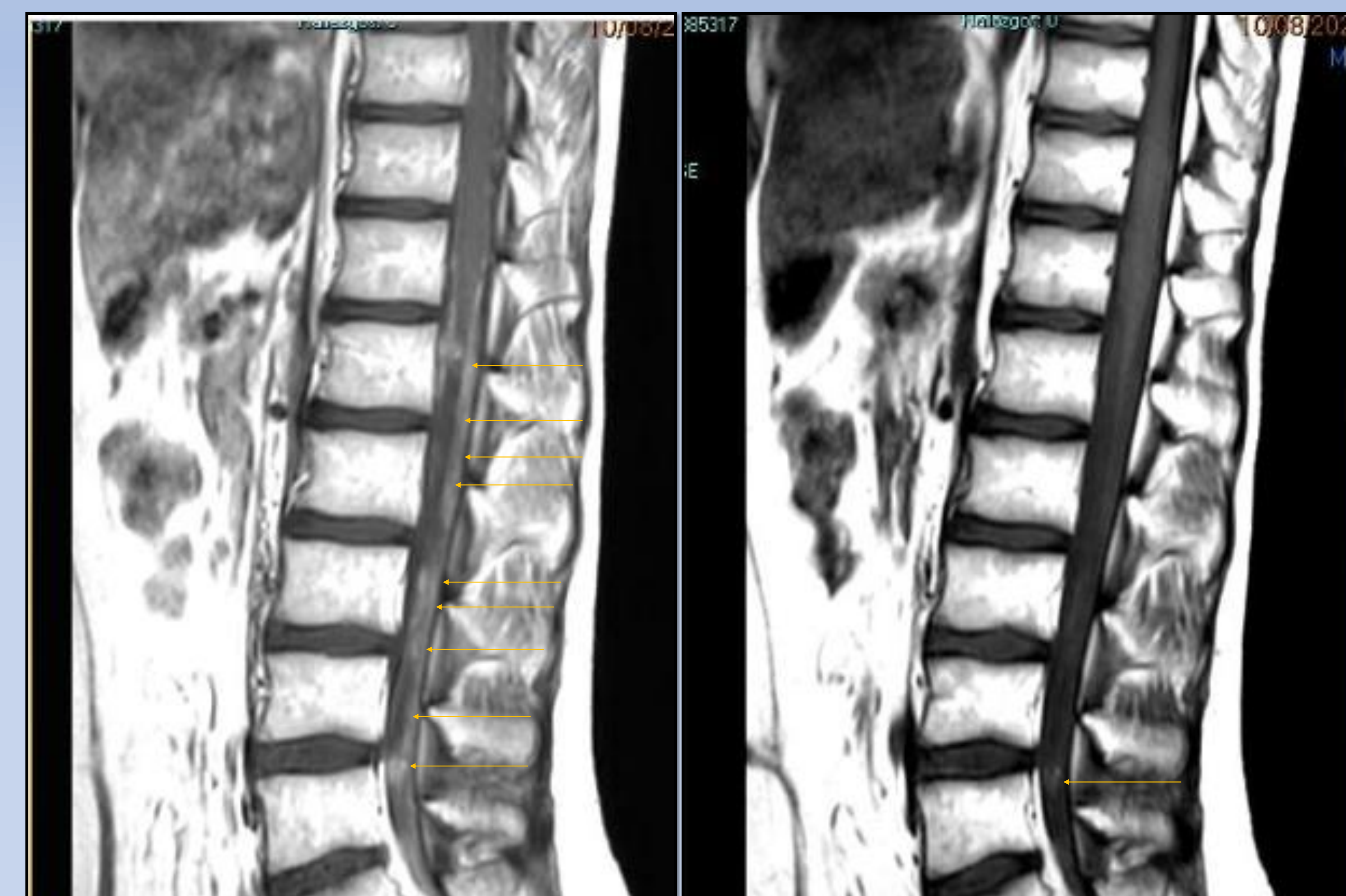
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**Figure 1:** Gadolinium enhanced cranial MRI. It can be observed clearly mitigation of contrast captation in bilateral VIII cranial nerve.



**Figure 2:** Gadolinium enhanced spinal MRI. Dramatic response of the leptomeningeal implants along the spinal cord.