BACKGROUND: The distinction of MB into four methylation-dependent subgroups was recognized by the WHO in 2021. However, these subgroups have not previously been defined by international experimental consensus and their clinico-molecular features and behavior have not formally been investigated in large cohorts. We aimed to robustly identify SHH subgroups through analysis of MB, with DNA-methylation profiling. METHODS: A cohort of 683 MB patients classified using the Heidelberg classifier v12.3, was assembled for analysis from multiple international studies. To define subgroups, we applied consensus sampling-based clustering approaches to tumor methylomes, including assessment of confidence in class-definition and inter-technique concordance. The clinico-molecular features of consensus subgroups were investigated. RESULTS: Lowest complexity analysis supported the division of MB into the 4 WHO-subtypes. SHH-1 and SHH-2 were associated with lower age and infrequent mutations of PTCH1/SUFU; SHH-2 was distinguished from SHH-1 by enriched MBEN histology, absence of chromosome 2 gain, less frequent metastasis and more favorable overall-survival. SHH-4 presented in older children and adults (3-57; median 24 years), and was primarily defined by mutations in TP53 (27%; 85/312). SHH-3 was defined by MYCN amplification and upfront craniospinal irradiation revealed that survival of SHH-3 was worse than metastatic relapses compared to non-SHH-MB (p=0.01). CONCLUSIONS: The SHH-3C subtype is associated with a coalescence of high-risk features (LCA histology, TP53mut, MYCNamp/GLI2amp) alongside 3p, 10q, and 17p loss, and had dismal survival. The remaining SHH-3B subgroups were characterized by 9q loss, frequent focal amplifications of TERT and PPM1D, and equivalent better survival. CONCLUSIONS: This study affirms the distinction of MB into 4 major subgroups. For infant disease, SHH-2 is a favorable-risk marker. For childhood-MB, the SHH-3C subtype provides a molecular definition of high-risk that subsumes other previously-defined high-risk disease markers (LCA, MYCNamp, TP53mut) into a unified high-risk disease group. The other SHH-3 subtypes behave similarly and are favorable-risk. These subtypes have potential to enhance molecularly-guided risk-stratification in routine diagnostics, to improve patient outcomes and quality-of-life.