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### A curative approach for neuroblastoma metastatic to the CNS: Safety and efficacy of intraventricular <sup>131</sup>I-labeled monoclonal antibody 8H9 targeting the surface glycoprotein B7-H3

**Background:** Tumors metastasizing to the central nervous system (CNS) are associated with significant mortality. We tested the toxicity and dosimetry of intraventricular <sup>131</sup>I-labeled monoclonal antibody 8H9 targeting surface glycoprotein B7-H3 in patients with primary or metastatic CNS tumors.

**Methods:** Tumor B7-H3 expression was assessed by immunohistochemistry. CSF flow was determined by <sup>111</sup>Indium-DTPA cisternography. 131 patients received 2 mCi tracer of intra-Ommaya <sup>124</sup>I- or <sup>131</sup>I-8H9 for nuclear imaging followed by a therapeutic injection (10-80 mCi, dose levels 1-8 in 10 mCi increments for phase I patients; expanded cohort 50 mCi/injection) <sup>131</sup>I-8H9. Pharmacokinetics was studied by serial CSF and blood samplings over 48 hours. Dosimetry was based on pharmacokinetics and region of interest analyses on serial nuclear imaging scans. Toxicity was defined by the CTCAE v.3.0. 8H9 dosimetry and therapy injections were repeated after 1 month if no serious adverse events or progressive disease ensued. Tumor response was determined by clinical, radiographic, cytologic criteria; overall survival was noted.

**Results:** 129 patients (93 with CNS neuroblastoma) received

383 injections [median age 5.4 years (1.2-53.6 years)] Injections were well tolerated and routinely administered in the outpatient setting. Rare self-limited adverse events included grade 1 or 2 fever, headache, vomiting, biochemical elevations in AST or ALT and 1 injection with grade 3 ALT elevations (dose level 3). Although not a dose limiting toxicity, myelosuppression occurred in patients who had received craniospinal radiation and at dose levels 6 and higher (>60 mCi). Of 93 patients treated for CNS neuroblastoma, an improved overall survival was noted compared to survival reported with conventional therapies. At analysis, 48 (52%) patients with CNS neuroblastoma were alive 4.8–152 months (median 58 months) after CNS metastasis, including 56% at 36 months and 29% > 60 months. Interpatient variability for total absorbed dose to the CSF and blood was observed; mean absorbed CSF dose was 104.9 cGy/mCi by CSF sampling, and 2.6 cGy/mCi to the blood.

**Conclusions:** We conclude that intraventricular <sup>131</sup>I-8H9 was safe, permitting favorable dosimetry to the CSF, and in the Phase II expansion demonstrated activity in improving long term remission among patients with CNS neuroblastoma.

#### Biography

Kim Kramer is a pediatric oncologist who specializes in the care of children with neuroblastoma and other cancers that have spread in the central nervous system (the brain and spinal cord). She conducting translational research to better understand why this happens and to try to find more-effective treatments, particularly for relapsed disease.

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