Gadobenate Dimeglumine for Contrast-Enhanced MRI of the Central Nervous System in Children

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Purpose: To present results of pharmacokinetic, safety, and efficacy studies with gadobenate dimeglumine (Gd-BOPTA; MultiHance®), a weak-protein–binding gadolinium MRI contrast agent with almost twice the r1 relaxivity of conventional agents (1-2), for MRI of the CNS in children (3-5).

Materials and Methods: Pharmacokinetics (PK) of Gd-BOPTA were determined in 40 children using serial 24-hour blood and urine collections. Safety was evaluated in 177 subjects receiving Gd-BOPTA at a dose of 0.1 mmol/kg. Of these subjects, 85 participated in a comparison study in which 89 subjects received an equal dose of gadopentetate dimeglumine (Gd-DTPA; Magnevist®). Efficacy was evaluated in 70 patients receiving 0.1 mmol/kg Gd-BOPTA, including 29 children that were evaluated in comparison to 34 children who received an equal dose of Gd-DTPA.

Results: The PK data best fit a 2-compartment model, with more than 80% recovery in urine at 24 hours, with no changes in the pharmacokinetic parameters over the age range studied (Table 1). Of the 177 patients evaluated for safety, 18 (10.2%) patients experienced adverse events (AEs), most of which were mild, most commonly fever and headache. Modest increases and decreases in vital signs were recorded, but no significant changes in laboratory parameters or ECGs were observed. AE rates were similar (p=0.75) after Gd-BOPTA (11 subjects, 12.9%) and Gd-DTPA (13 subjects, 14.6%). In children with enhancing lesions, contrast enhancement with Gd-BOPTA was considered good-to-excellent in all subjects, resulting in improved definition of disease extent, lesion border delineation, and visualization of lesion internal morphology (Figure 1). In the comparison study, postdose changes in lesion visualization were significantly greater for Gd-BOPTA than Gd-DTPA, both at the lesion (p=0.011) and the patient level (p=0.008).

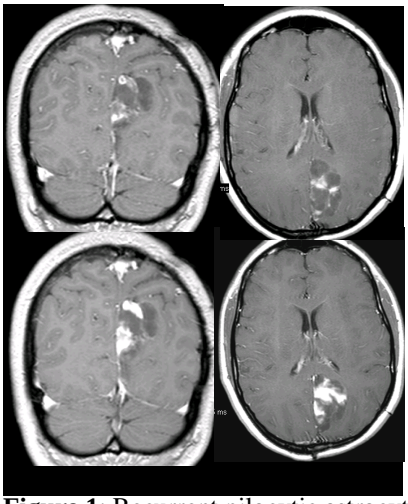

Figure 1: Recurrent pilocytic astrocytoma of the left mesial parietal lobe in a 12-year-old girl.

Table 1. PK Parameter Estimates in Children and Adults

Parameter	PK in Children Aged 2-5y (N=15)	PK in Children Aged 5-16y* (N=25)	PK in Adults (N=4)
Volume of Distribution (L/kg)	0.20 ± 0.05	0.170 ± 0.026	0.123 ± 0.028
Total Body Clearance (L/h/kg)	0.208 ± 0.030	0.199 ± 0.006	0.163 ± 0.018
Terminal Elimination Half Life (h)	1.22 ± 0.239	1.51 ± 0.27	1.21 ± 0.09
% Injected Dose Recovered in Urine	81.4% ± 11.2%	90.8% ± 5.1%	85.8% ± 5.42%

*One child was <5 years (ie, 3.2 years)

Conclusions: Gd-BOPTA is well-tolerated, with a safety and pharmacokinetic profile in children comparable to that in adults. Compared to Gd-DTPA, Gd-BOPTA was equally well tolerated and performed significantly better for visualization of CNS tumors in pediatric patients, providing excellent enhancement of enhancing brain or spine lesions. Due to its higher relaxivity, Gd-BOPTA potentially improves lesion characterization (eg, definition of tumor borders and extent of disease, visualization of vascular malformations, evaluation of the relationship between adjacent neurovascular structures and the neoplasm itself) as well as potentially augmenting detection of small or poorly-enhancing tumors.

References:

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