

Variation of the Induction Effect of Ifosfamide in 7 Children During a 5 Day Continuous Infusion Over 4 Treatment Sessions.

Sub-category:

Developmental Therapeutics - Clinical Pharmacology and Immunotherapy

Category:

Developmental Therapeutics

Meeting:

2000 ASCO Annual Meeting

Abstract No:

843

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Proc Am Soc Clin Oncol 19: 2000 (abstr 843)

Author(s):

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Abstract:

7 patients (6 - 21 yr.) suffering from bone and soft tissue sarcoma, were followed over 4 months, during their 5-day treatment (tt) session by ifosfamide (If.) 3g/m²/day. We estimate the variations of If., and its metabolites 2 d-If., 3 d-If. and mainly 4 OH-If. using a GC/NPD technic². Pharmacokinetic analysis was performed to estimate daily AUC for each compound during each tt session. The percentage of induction (PI) for If. was defined as Conc.₂₄ / Cone.₁₂₀ & daily metabolite index (MI) as AUC metabolite/AUC If. The 4 tt session profiles of If. showed a similar shape: levels raised to a C_{max} reached at the end of day 1, & then regularly decreased to reach a steady state, on day 5. The PI were respectively: 33.6%±20.2, 41.9%±18.4, 48.0%±33.4 and 48.9%±31.2. No statistical significant difference (t test) was shown between sessions 1 to 4 either for the blood levels niether for the PI. The daily MI for inactive metabolites showed a continuous increase during the infusion duration over each tt sessions. For 2d-If., the last day MI were 18.5%±18.7, 18.0%±10.2, 17.3%±9.9 and 16.8%± 9.8 and for 3d-If. 22.9%±5.0, 21.8%±5.8, 21.0%±7.9 and 19.8%±6.3 (not significantly different: t test). The active metabolite 4OH If. blood levels remained low during the entire infusion. The MI increase of 4OH-If. during the infusion was observed for any of the studied tt sessions. 4OH-If. last day MI were respectively 2.3%±0.8, 2.0%±0.6, 2.1%±0.5 and 1.8%±0.5 for the different sessions, (not significantly different, whatever tt session considered). Such regimen confirmed a relevant induction phenomenon in children during the 4 sessions. Each MI increase during the duration of the infusion, was mainly due to a decrease of the If. rather than a relevant increase of the metabolites blood levels. For 4OH-If., a more significant blood level increase was noted. Therefore, the global induction process remains especially favorable for the 4OH-If. pathways. These data did not permit to demonstrate a statistical significant difference for the different sessions. (Supported by a "Ligue nationale Paris" grant N°98/RS-PH/86). ²Gourmel & al. J. Chromatogr B. 1999; 732 (1) :3-15.

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