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Adjustment of DOSE of ifosfamide (If.) in children after the first treatment session.

Sub-category:
Pediatric Solid Tumors

Category:
Pediatric Oncology

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2008 ASCO Annual Meeting

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Abstract Disclosures

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Abstract:

Background: Ifosfamide (If) is one of the current reference agents for the treatment of sarcoma in children. Treatment comprises several courses (4 or 5) of If. administered as a continuous infusion. 60 patients,18 over 4 treatment sessions, aged from 6 to 21 years and suffering from bone and soft tissue sarcoma were followed during their treatment session (5 days, 3g/m²/d). This prodrug, capable of autoinduction, is metabolized to produce the dechloroethylated metabolites 2DIf and 3DIf, responsible of the neurotoxicity, or with hydroxylation to produce 4 OH If the alkylating compound. The goal of this study was to determine if neurotoxicity and alkylating potential can be estimated after the first treatment session. **Methods:** Blood samples were withdrawn each day of the infusion (T 0,24,48,72,96 and 120h). Determination of each compound (If, 2DIf and 3DIf. and 4OHIf.) were performed using GC/NPSD method. PK analysis was performed on the basis of Area under Curve (AUC) for Ifos. and metabolites using Excel Spreadsheet. **Results:** We calculated the metabolite index (MI) : ratio of the cumulated AUC metabolite / AUC If, for each day. The global pharmacokinetic profiles for the different treatment sessions showed a similar shape. Ifos blood levels raised to a maximum at the end of day1, then they regularly decreased. The percentage of induction was equal to 48.9% ±21.2%. The MI.of 2DIf. and 3D If showed a continuous increase mainly important during the 3 first days and then reach a relative steady state. The final values were respectively 18.5%± 8.7% and 22.9%± 5.3%. The MI of 4OHIf confirmed the previous increase of its amount. The final value for this compound was 2.3%±0.8%. For a given patient, no significant differences were demonstrated for the variation of MI during the infusion whatever treatment session (1 to 4) was considered. Consequently, at the end of the first infusion, calculation of the MI inform us on the comportment of the patient toward the drug. **Conclusions:** The difference between the MI average reported above and the patient MI is applied to reduce or increase the next course. Potential risk of neurotoxicity is minimized by a reduced dose. Low MI of the 4OHIf metabolite is followed by an increased dose. This method in now applied routinely and no major toxicity have been noted.

Associated Presentation(s):

1. Adjustment of DOSE of ifosfamide (If.) in children after the first treatment session.
Meeting: 2008 ASCO Annual Meeting
Presenter: Bernard Gourmel
Session: Pediatric Cancer (General Poster Session)

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