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# PERIPHERAL NEUROPATHIES IN CHILDREN TREATED BY HIGH DOSE IFOSFAMIDE (18 TO 21 G/M²).

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**Purpose** : This study was designed to assess the toxicity of high-dose ifosfamide (HDI) administered by continuous infusion at a dose of 18 to 21 g/m² per cycle over 5 to 7 days (3 g/m²/day), every 4 weeks, in children and teenagers with bone and soft tissue sarcomas without autologous stem cell rescue .

**Patients and Methods** : Between 02 1993 and 08 1996, 20 patients (p.) were entered onto the study. All p. were pretreated with a multidrug regimen, 9 p. had evolutive disease, 11 p. were treated after surgical resection without visible disease. Evolutive p. were treated until progression or major toxicity, and p. in complete remission until the end of the protocol.

**Results** : 56 cycles of HDI were administered. Neutropenia was dose-limiting with 100 % of p. experiencing grade 3 or 4 toxicity and 40 admissions for febrile neutropenia. Thrombocytopenia grade II-IV was observed in 37/56 courses. Central neurotoxicity was detectable in 7 p.. Peripheral neuropathy was observed in 6 p.. Two acute renal failure were observed but Fanconi's syndrome was noted in 15 courses.

Objective responses were observed in 6/9 p. with advanced evaluable sarcomas.

**Conclusion** : HDI chemotherapy 18 g/m² to 21 g/m² is feasible in children and teenagers. Nevertheless **a significant percentage of central and peripheral neurotoxicity is a limiting factor**. Indeed, we observed 33 % of peripheral neuropathies that were dose limiting in 4 p.. These peripheral neuropathies were not yet described with this importance and could be the major limiting factor of the use of IFX at this dose.