Patients with advanced pediatric sarcomas have a poor prognosis and novel combination therapies are needed to improve the response rates. Hematological and organ related toxicities have been observed when administering topotecan in combination with, e.g., high dose thiotepa. This study evaluates the toxicity of escalating doses of topotecan alone or in combination with thiotepa or treosulfan. We compared the toxicity including death of complication (DOC) of topotecan alone or in combination with thiotepa or treosulfan in advanced pediatric sarcomas (n = 12). Ten of 12 patients (0.83) suffered from advanced tumors of the Ewing family (i.e., bone or marrow metastases or relapse<24 month after diagnosis, including one neuroepithelial tumor of the kidney) and two from alveolar rhabdomyosarcoma stage IV (0.17). Median age was 15 years (range 5-28). Ratio of female to male was 1:1. Two patients received topotecan alone (1.25 mg/m(2) q 5d and 1.5 mg/m(2) q 5d), three patients received four courses of topotecan (2 mg/m(2) q d 1-5) in combination with thiotepa (100 mg/m(2) q d 1-5), and seven patients received topotecan (2 mg/m(2) q d 1-5) in combination with treosulfan (10g/m(2) q d 3-5). Overall toxicity was not different between all three groups; mean scores were 1.6, 1.8, and 1.7 according to WHO grading (Scale 0-4). Organ related toxicity ranged between 0 and 4 and was not different.
as well. DOC was 0/2, 1/3, and 0/7 patients respectively. Escalating therapy with topotecan in combination with treosulfan has acceptable toxicity and warrants further investigation in advanced pediatric sarcomas.