Clinical phase I/II trial to investigate preoperative dose-escalated intensity-modulated radiation therapy (IMRT) and intraoperative radiation therapy (IORT) in patients with retroperitoneal soft tissue sarcoma: interim analysis.

To report an unplanned interim analysis of a prospective, one-armed, single center phase I/II trial (NCT01566123). Between 2007 and 2013, 27 patients (pts) with primary/recurrent retroperitoneal sarcomas (size > 5 cm, M0, at least marginally resectable) were enrolled. The protocol attempted neoadjuvant IMRT using an integrated boost with doses of 45-50 Gy to PTV and 50-56 Gy to GTV in 25 fractions, followed by surgery and IOERT (10-12 Gy). Primary endpoint was 5-year-LC, secondary endpoints included PFS, OS, resectability, and acute/late toxicity. The majority of patients showed high grade lesions (FNCLCC G1: 18%, G2: 52%, G3: 30%), predominantly liposarcomas (70%). Median tumor size was 15 cm (6-31). Median follow-up was 33 months (5-75). Neoadjuvant IMRT was performed as planned (median dose 50 Gy, 26-55) in all except 2 pts (93%). Gross total resection was feasible in all except one patient. Final margin status was R0 in 6 (22%) and R1 in 20 pts (74%). Contiguous-organ resection was needed in all grossly resected patients. IOERT was
performed in 23 pts (85%) with a median dose of 12 Gy (10-20 Gy). We observed 7 local recurrences, transferring into estimated 3- and 5-year-LC rates of 72%. Two were located outside the EBRT area and two were observed after more than 5 years. Locally recurrent situation had a significantly negative impact on local control. Distant failure was found in 8 pts, resulting in 3- and 5-year-DC rates of 63%. Patients with leiomyosarcoma had a significantly increased risk of distant failure. Estimated 3- and 5-year-rates were 40% for PFS and 74% for OS. Severe acute toxicity (grade 3) was present in 4 pts (15%). Severe postoperative complications were found in 9 pts (33%), of whom 2 finally died after multiple re-interventions. Severe late toxicity (grade 3) was scored in 6% of surviving patients after 1 year and none after 2 years. Combination of neoadjuvant IMRT, surgery and IOERT is feasible with acceptable toxicity and yields good results in terms of LC and OS in patients with high-risk retroperitoneal sarcomas. Long term follow-up seems mandatory given the observation of late recurrences. Accrual of patients will be continued with extended follow-up. NCT01566123.