

Increased Neoadjuvant Chemotherapy to Surgery Time Interval is Associated with Decreased Tumor Percent Necrosis in Osteosarcoma

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INTRODUCTION: Delays in completion of chemotherapy and surgery in osteosarcoma have been shown to be associated with decreased event-free survival (EFS). The effect of a longer time interval between the end of neoadjuvant chemotherapy and surgical resection on oncologic outcome has not been studied. The purpose of this study was to evaluate the association of the time interval between the completion of neoadjuvant chemotherapy and surgical resection and tumor percent necrosis, EFS, and postoperative infection rate.

METHODS: We queried our institution's orthopaedic oncology registry, which includes all patients treated for a musculoskeletal bone or soft tissue tumor at our single tertiary academic hospital since 1987. We identified all patients who received neoadjuvant chemotherapy, had surgical resection at our institution with a confirmed final pathologic diagnosis of osteosarcoma, and had tumor percent necrosis documented. For the 190 patients included in this study, we retrospectively collected patient, tumor, treatment and oncologic outcome data (Table 1). We analyzed the association between the time interval between end of neoadjuvant chemotherapy and surgical resection and tumor percent necrosis, postoperative infection rate, and five-year EFS (defined as the time from surgical resection to local recurrence, metastatic recurrence, death, or last date of oncologic follow-up within five years).

RESULTS: The mean time interval between end of neoadjuvant chemotherapy and surgical resection was 25 days (SD 18 days, range 1-171 days). The mean duration of neoadjuvant chemotherapy was 69 days (SD 41 days, range 1-248 days). End of neoadjuvant chemotherapy to surgical resection time interval greater than 3 weeks was associated with significantly decreased tumor percent necrosis (n = 82, mean 58%, SD 34%, range 0%-100%) compared to time interval less than or equal to 3 weeks (n = 108, mean 73%, SD 28%, range 0%-100%) (p = 0.001) (Figure 1). End of neoadjuvant chemotherapy to surgical resection time interval greater than 3 weeks was not significantly associated with five-year EFS (p = 0.192) (Figure 2) or development of a post-operative infection (p = 0.524) compared to time interval less than or equal to 3 weeks. The total duration of neoadjuvant chemotherapy was not significantly associated with tumor percent necrosis (p = 0.093), EFS (p = 0.356), or post-operative infection (p = 0.486).

DISCUSSION AND CONCLUSION: A time interval greater than 3 weeks between the end of neoadjuvant chemotherapy and surgical resection of osteosarcoma was associated with decreased tumor percent necrosis compared to a time interval less than or equal to 3 weeks. A time interval greater than 3 weeks was not associated with EFS or post-operative infection. The total duration of neoadjuvant chemotherapy was not associated with tumor percent necrosis, EFS, or post-operative infection. These data suggest longer wait times between chemotherapy and surgery may impact response to chemotherapy

Table 1. Patient, tumor and treatment data		
	n	%
Total	190	100%
Age (mean, SD)	23.2	16.0
Sex		
Female	81	42.6%
Male	109	57.4%
Race		
White	148	77.9%
Black	20	10.5%
Hispanic	14	7.4%
Asian	2	1.1%
Other/Multiple/Unknown	6	3.2%
Neoadjuvant Chemotherapy Regimen		
Methotrexate, adriamycin, cisplatin	134	70.5%
Adriamycin, cisplatin	41	21.6%
Other	15	7.9%
Tumor Location		
Femur	95	50.0%
Tibia	32	16.8%
Fibula	6	3.2%
Humerus	22	11.6%
Radius	1	0.5%
Ulna	1	0.5%
Pelvis	19	10.0%
Spine/Vertebrae	2	1.1%
Sacrum	2	1.1%
Rib cage	2	1.1%
Other	8	4.2%
Tumor Subtype		
Chondroblastic	29	15.3%
Fibroblastic	13	6.8%
Giant Cell	1	0.5%
Osteoblastic	107	56.3%
Periosteal	5	2.6%
Small Cell	3	1.6%
Telangiectatic	7	3.7%
Other	14	7.4%
Unknown	11	5.8%

Figure 1. Tumor Percent Necrosis and Time Interval between End of Chemotherapy and Surgery

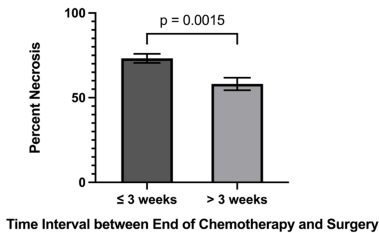


Figure 2. Five-Year Event Free Survival and Time Interval between End of Chemotherapy and Surgery

