

**Student:** Ovida Ortiz Saikam

**Project:** Assess dose intensity of methotrexate and other chemotherapy agents in AYA patients treated for osteosarcoma in New Zealand 2000-2009

**Supervisors:** Dr Kate Gardner, Dr Ruth Spearing, Mr Gordon Beadel and Dr Tristan Pettit

**Sponsor:** The Ruth Spearing Cancer Research Trust

### **Introduction:**

Osteosarcoma is a type of bone cancer that originates from the bone. It is the most common primary solid bone tumour in adolescent and young adult (AYA) population. Osteosarcoma patients usually present with pain and soft tissue swelling at the affected region. Osteosarcoma patients' treatment usually comprises of both chemotherapy and surgery.

The current recommendation involves implementation of chemotherapy regimen, both pre-operative and post-operatively to achieve optimum response rate and to prevent recurrence rate. Chemotherapy works by stopping or slowing the growth of cancer cells. Currently, doxorubicin, cisplatin, methotrexate, ifosfamide and etoposide are the five types of chemotherapy drugs most commonly used in New Zealand to treat osteosarcoma. The efficacy of these five chemotherapy drugs were well established in previously published literatures. A recent study in New Zealand reported that the country's survival outcome of AYA osteosarcoma patients was lower when compared to other developed countries (Ballantine, 2015). It has been postulated that inadequate chemotherapy dosages and treatment delays might contribute to the cause of New Zealand's poor survival outcome.

### **Aim:**

This research aims to assess the impact of dose intensities of chemotherapy agents on survival outcome for AYA patients treated for osteosarcoma in New Zealand from 2000 to 2009. Dose intensity refers to the amount of drug or drug dosages given to a patient in a week during the treatment course. This research aims to assess whether giving higher dosages of chemotherapy without significant delays will lead to a better survival outcome or not.

### **Method:**

This research looked at the patients between the ages of 15-29 years old, who were diagnosed with osteosarcoma between 2000 and 2009. Patients with metastases (advanced stage) were excluded from the analysis.

This research was done through collaboration with a research team in Auckland led by Dr George Laking. The Auckland team was responsible for doing the analysis on patients treated in Auckland hospital, whereas the Christchurch team led by Dr Kate Gardner was responsible for doing the analysis on patients treated in Christchurch hospital. Data collection was done by referring to Concerto/Health South Connect database. This is an electronic system that is used by health professionals to store patients' information in New Zealand. Patients' files were also retrieved from the Clinical Records Departments.

Important records such as prescriptions, administration charts, surgery reports, assessment letters by specialists and oncology letters were printed off and copied.

All the required data was then extracted from the hard copies and inputted onto a spreadsheet for further investigation. The available data contain important information in regards of patients' survival status, surgery dates and chemotherapy treatment details. We performed an audit that contained the calculated dose intensities for all patients. The dose intensity calculation was done based on The National Cancer Institute (NCI) method (Longo et al., 1991). We also calculated the percentage dose intensity for each chemotherapy agent received by patients in this study. The percentage dose intensity is an indication whether patients have received an optimum dose without significant delays. Survival outcome was then analysed based on the percentage dose intensity for each chemotherapy drug.

### **Results:**

Initially, there were 41 patients identified in this study. Of the 41 patients, 22 patients were not included as their chemotherapy records were not accessible. This left a total of 19 patients in the final analysis. The mean age of patients treated for osteosarcoma was 19 years old and they were most commonly male (68% male and 32% female). There were more non-Maori (84%) than Maori (16%) patients diagnosed with osteosarcoma. Femur was the most common site identified in osteosarcoma patients (37%). All patients received more than 3 cycles (100%) of chemotherapy during their treatment course. Doxorubicin (100%) and cisplatin (100%) were the two most commonly prescribed chemotherapy drugs.

The results of the analysis showed that there were positive relationships between higher dose intensities of doxorubicin, cisplatin, methotrexate and ifosfamide and survival outcome. However, these results were not statistically significant. For etoposide, higher dose intensity was not correlated with better survival outcome; however this result was not statistically significant as well. Patients on average received 90% of their proposed total chemotherapy dose for the course. However, this study found no relationship between the average of dose intensity of all drugs and survival ( $p=0.6784$ ).

### **Conclusion:**

The results of the analysis showed a positive relationship between higher dose intensities of doxorubicin, cisplatin, methotrexate and ifosfamide and survival outcome. This was a not statistically significant. It could be postulated that the lack of statistical significance may be due to the very small numbers in the study population (19 patients). There was no positive correlation with etoposide and survival. Future research with a larger study population and extended time frame for osteosarcoma diagnosis is needed before establishing a definite conclusion in regards of the relationship between dose intensity and survival outcome for AYA osteosarcoma patients in New Zealand.