A Phase 1b/2 Study of Aldoxorubicin + Ifosfamide/Mesna in Untreated Sarcoma Patients

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Abstract

**Objectives:**
- To determine the preliminary safety of aldoxorubicin in combination with ifosfamide/mesna in subjects with metastatic, locally advanced, or unresectable soft tissue sarcomas.
- To evaluate the overall response rate, PFS, and PFS at 4 and 6 months.

**Background:**
- Patients with metastatic, locally advanced, or unresectable soft tissue sarcomas have a survival of approximately 15 months after treatment with single agent doxorubicin. Adjuvant or neoadjuvant chemotherapy (including doxorubicin) allowed if no tumor recurrence.

**Aldoxorubicin**
- Aldoxorubicin is a prodrug of the anticancer agent doxorubicin which is derivatized at its C-13 keto-position with a thiol-binding spacer molecule (6-maleimidocaproic acid hydrazide).
- Aldoxorubicin is quantitatively and selectively bound to the cysteine-34 position of endogenous albumin within a few minutes. The reaction follows second-order kinetics.
- Toxicological studies in mice, rats, and dogs demonstrated a 3- to 5-fold increase in the MTD, moderate and reversible myelosuppression, no liver toxicity and immunotoxicity, and no new toxicity compared to doxorubicin.

**Study Design**
- Aldoxorubicin administered at either 170 or 250 mg/m² (125 and 185 mg/m² doxorubicin equivalents) intravenously on Day 1 every 4–6 days plus 1 g/m² ifosfamide by continuous infusion every 4–6 days for up to 10–14 days as port-a-cath or PICC line.

**Key Eligibility Criteria**
- Age between 15 and 80 years, male or female.
- High grade pleomorphic sarcoma
- Dedifferentiated liposarcoma
- Monophasic synovial sarcoma
- Osteosarcoma
- Ewing sarcoma.

**Conclusions**
- No clinically significant cardiotoxicity has been observed.
- No patients had clinically significant decrease in LVEF or QGS prolongation.
- No patients had clinical congestive heart failure.

**Serious Adverse Events**
- SAEs included febrile neutropenia (1) and sepsis (1).
- No treatment-related deaths occurred.

**References**