BACKGROUND

• Soft tissue sarcomas are rare malignancies of mesenchymal origin comprising about 1% of all adult cancers.
• Metformin use has been associated with prolonged cumulative survival in patients with various visceral carcinomas (non-small cell lung, pancreas, colon, head and neck).
• Preclinical studies demonstrate that metformin impairs tumor cellular metabolism, alters matrix turnover and suppresses oncogenic signaling pathways, including receptor tyrosine kinase, PI3K/Akt, and mTOR pathways.

The objective of this study was to investigate the association between metformin use and overall survival in soft tissue sarcoma patients.

METHODS

• The Surveillance Epidemiology and End Results (SEER) - Medicare database was used to identify patients who were diagnosed with a soft tissue sarcoma from 2007-2016.
• ICD-9 primary site codes and HCPCS codes identified cancer treatment, comorbidities and procedures within the Medicare claims files.
• Concomitant medication use was identified with the National Drug Codes using the Medicare Part D event files.
• Survival was assessed comparing metformin users to non-users using a Log Rank Test for Equality of Survivor functions.
• Covariate analysis was performed for patient-related (age, gender), tumor specific (grade) and treatment-related (radiation modality, surgery and the timing of radiation with surgery) factors.

RESULTS

• The SEER database identified 13843 patients eligible for interpretation.
• Of these, 12,138 patients were not taking metformin, while 1705 were taking it at the time of diagnosis and throughout the disease course.
• Patient follow up duration for the patients without metformin was 51.6 ±41.4 months and for those taking metformin was 56.3 ±42.2 months.
• Log Rank Test for the Equality of Survival was significantly different between the groups with patients taking metformin experiencing prolonged survival (p < 0.001).
• 50% mortality was seen in the metformin group at 90.5 months, compared to 61.9 months in the group without metformin.
• The 5-year survival: with metformin 57% versus 50% in the patients without metformin.
• The overall hazard ratio for patients on metformin was 0.83 (P< 0.001).
• The patient groups (taking metformin versus without metformin) did not differ significantly with respect to tumor grade, age at diagnosis, surgery, radiation modality, and timing of radiation relative to surgery.

DISCUSSION

• Only gender differed significantly between the study groups with more males taking metformin compared to females (12.95% vs 11.5%).
• Adjusted for these covariates, the hazard ratio for patients on metformin was 0.84 (p<0.01).
• Interestingly, the hazard ratios for patients receiving preoperative radiation only and those receiving postoperative radiation only were identical, 0.28, (p<0.001).

REFERENCES