

## **Hypoxia induced gene-profile in sarcoma patients: A new prognostic marker**

*Ninna Aggerholm-Pedersen<sup>1</sup>, Jan Alsner<sup>1</sup>, Brita Singer Sørensen<sup>1</sup>, Steen Barentzen<sup>2</sup>, Marianne Nordmark<sup>3</sup> and Akmal Safwat<sup>3</sup>*

<sup>1</sup>Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus. <sup>2</sup>Department of Pathology, Aarhus University Hospital, Aarhus. <sup>3</sup>Department of Oncology, Aarhus University Hospital, Aarhus

**Background and purpose:** The prognosis of soft tissue sarcoma (STS) patients has not changed in decades and new treatment modalities are needed. It is known that tumor-hypoxia is important in tumor progression and resistance to treatment for several cancers. However, little attention has been paid to the role of hypoxia in sarcomas. We investigated the prognostic value of a hypoxia induced gene-profile in sarcoma patients.

**Patients and methods:** A validated hypoxia-induced gene-profile of head and neck cancer was explored by RT-qPCR in diagnostic biopsies or resected specimens from 74 patients diagnosed with localized high grade STS in the period 1990-2008. The patients were allocated to 2 groups: a more hypoxic and a less hypoxic group, according to the median rank of the gene-profile. The primary endpoint was disease specific mortality estimated using Kaplan-Meier and the proportional hazard model. Adjustments were made for comorbidity and stage.

**Results:** The 5-year disease specific mortality was 25% (95%CI: 13-43) for patients with less hypoxic tumours compared to 44% (29-62) for patients with more hypoxic tumours. The adjusted Hazard ratio (HR) was 2.3 (1.01-5.1). Radiation treated patients allocated to the group of more hypoxic tumours (n=18) had a significantly higher disease specific mortality compared to radiation treated patients allocated to the less hypoxic group (n=19). HR: 4.2 (1.3-15).

**Interpretation:** This hypoxia-induced gene-profile may have prognostic value in STS patients and it may facilitate improvements in the choice of treatment modality for patients with hypoxic tumors.