Nature Reviews Clinical Oncology | Published online 6 Mar 2018; doi:10.1038/nrclinonc.2018.38

SARCOMA

Local hyperthermia improves survival

Patients with localized high-risk soft-tissue sarcoma (STS) often have disease relapse after local treatment. Neoadjuvant chemotherapy (NACT) improves the survival outcomes of these patients, although emerging data suggest that additional regional hyperthermia (RHT) can further improve the efficacy of treatment. Now, the final results of the first randomized study of this therapeutic combination confirm the added benefit of RHT.

In this open-label, phase III trial (EORTC 62961-ESHO 95), 341 patients were randomly assigned 1:1 to receive doxorubicin, ifosfamide, and etoposide NACT alone or combined with RHT, which involved heating of the tumour to 42°C for 1 h concurrently with the administration of ifosfamide. All patients had localized French Fédération Nationale des Centres de Lutte Contre le Cancer grade 2 or 3 tumours ≥5 cm in diameter, deep to the fascia.

Initial results published in 2010, at a median follow-up duration of 34 months, revealed improved survival outcomes in the RHT group. Now, after a median follow-up duration of 11.3 years, the final results for the intention-to-treat population ($n = 329$) demonstrate long-term survival benefits: the hazard ratios for local progression-free, disease-free, and overall survival were 0.65 ($P = 0.002$), 0.71 ($P = 0.01$), and 0.73 ($P = 0.04$), respectively. Importantly, 5-year and 10-year overall survival were increased by 11.4% and 9.9%, respectively, with RHT–NACT versus NACT alone; the median overall survival duration was 15.4 years versus 6.2 years. Consistent improvements in survival were observed across all patient subgroups, the efficacy of NACT alone seemed consistent with that demonstated in other trials, and no differences in the effects of salvage treatment were detected between the treatment arms.

RHT affects a range of cellular targets and processes, including DNA repair, the tumour microenvironment, and anticancer immunity, which might explain the consistent prolonged benefits. Notably, these effects are not specific to STS and, therefore, the approach might be applicable to a range of cancers. Indeed, another phase III trial is currently ongoing in patients with resected pancreatic cancer.

David Killock

ORIGINAL ARTICLE Issels, R. D. *et al.* Effect of neoadjuvant chemotherapy plus regional hyperthermia on long-term outcomes among patients with localized high-risk soft tissue sarcoma: the EORTC 62961-ESHO 95 randomized clinical trial. *JAMA Oncol.* https://doi.org/10.1001/jamaoncol.2017.4996 (2018)