

interval from first clinic consult to initiation of treatment was 85 days. The median total treatment duration was 81 days. Furthermore, only 4 women (8%) completed treatment within the recommended 56 days (8 weeks).

**Conclusion** This study showed that there was substantial delay in initiation and protraction in delivery of definitive radiation therapy in our cohort. Due to the severe imbalance of patients with ideal and protracted treatment duration, no factors were identified affecting radiation therapy delivery. Apart from supplementing the existing institutional infrastructure, other opportunities to improve the gaps in treatment planning and delivery were identified in this study.

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# **NTRK1-TPM3 FUSION POSITIVE CERVICAL SARCOMA – CASE REPORT OF A NOVEL SUBSET OF GYNAECOLOGICAL SARCOMAS, AND SUCCESSFUL TREATMENT OF RECURRENT DISEASE WITH TRK-INHIBITION THERAPY**

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**Introduction/Background** NTRK genes encode tyrosine receptor kinases (TRK), proteins promoting cellular proliferation and survival. NTRK fusions are implicated in solid tumours including gynaecological sarcomas lacking diagnostic features of any sarcoma subtype. In 2020, UK NICE approved a histology-independent TRK-inhibitor drug, larotrectinib, for treatment of such tumours in both children and adults.

**Methodology** We present the case of a 49-year old female who presented with recurrence of an NTRK1-TPM3 fusion positive cervical sarcoma nine months following primary total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO).

**Results** The patient was initially referred with a large cervical mass measuring 9 cm on imaging. Biopsy demonstrated high grade malignant tumour of spindle cell morphology. She underwent TAH and BSO. Specimen microscopy revealed a poorly differentiated sarcoma composed predominantly of spindle cells, with moderate/severe pleomorphism and brisk mitotic activity. Pan-TRK immunohistochemistry was positive, FISH revealed an NTRK1 translocation and next-generation sequencing confirmed an NTRK1-TPM3 fusion. Postoperative CT revealed no residual tumour and the patient was placed under close surveillance. Nine months later, the patient presented with vaginal bleeding. A 7 cm upper vaginal mass was seen on examination, which was diagnosed as NTRK-positive leiomyosarcoma recurrence. CT showed the presence of pulmonary metastases. Although four cycles of doxorubicin were administered, the pulmonary masses continued to progress. Larotrectinib was administered as an alternative therapy due to the tumours' NTRK positivity. The patient received 12 cycles of larotrectinib 100 mg BD over 10 months. This led to reductions in lung metastases size and no progression of the pelvic mass. Two

years postoperatively, the patient remains stable and continues to be monitored.

**Conclusion** Excellent durable response and improved survival was achieved. Testing for NTRK should be done and NTRK inhibitors considered for advanced gynaecological sarcomas. Future research will further assess the efficacy of TRK-inhibition therapy as primary, neoadjuvant and adjuvant treatment.

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# **EFFECT OF ALPHA-LIPOIC ACID SUPPLEMENTATION ON OXIDATIVE STRESS MARKERS IN PATIENTS WITH LSIL**

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**Introduction/Background** The goal of study was to examine the effects of alpha-lipoic acid (LA) supplementation on oxidative stress markers in patients with low-grade squamous intraepithelial lesion (LSIL).

**Methodology** One hundred (100) patients diagnosed with LSIL were randomized to receive 600 mg/day of LA (treatment group-T) or placebo (control-C) for three months. Ninety (90) patients finished the study (40 controls and 50 treated). Venous blood was collected for analysis of oxidative stress markers (plasma ferric reducing power (FRAP), superoxide dismutase (SOD) activity, reduced glutathione levels (GSH) and malondialdehyde levels (MDA)) at baseline and at 90th day of supplementation. All patients were instructed to fulfil validated food frequency questionnaire (FFQs) to investigate average intake of food derived antioxidants (number of fruit/vegetable portions and intake of nutrients with antioxidative potency). The normality of the distribution of obtained data was tested using the D'Agostino – Pearson test. Obtained values were presented as median ± 95% confidence range and comparison of results (before-after supplementation/control-tested) was performed using the Mann-Whitney U test for the significance level  $p < 0.05$ .

**Results** There were no significant differences between baseline FRAP, SOD, GSH and MDA levels between patients in control and treatment group. LA supplementation didn't significantly impact SOD, GSH or MDA levels but it increased TAC values, although observed changes were not statistically significant ( $p = 0.0893$ ). FFQ analysis revealed vegetable intake significantly affected baseline FRAP values—they were significantly lower in the group of patients with the lowest vegetable intake (4th quartile) in comparison to the group with the highest vegetable intake (1st quartile) ( $p = 0.0116$ ).

**Conclusion** LA supplementation in investigated regime (300 mg/day for 3 months) was not effective in improving oxidative status parameters in patients with LSIL. Analysis of FFQs revealed that nutritional patterns, rather than supplementation with antioxidant, can have significant impact on plasma antioxidant status in LSIL patients.