

HORMONAL RECEPTORS IN UTERINE LEIOMYOSARCOMAS: HOW FAR IS A PRIMARY TUMOR FROM MULTIPLE METASTASES?

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Background

- Nearly half of uterine leiomyosarcomas (uLMS) express estrogen (ER) or progesterone (PR) receptors. Currently, few data accessed the concordance of hormone receptor (HR) *status* in primary uLMS and metastases.
- This study compares the expression of HR in primary and metastatic uLMS, as well as within different metastases of the same patient, addressing its prognostic value.

Methods

- Retrospective cohort study (1980-2019) of all uLMS patients with recurrent/metastatic disease confirmed by histology (median follow-up 148.5 mo.). Clinical files and histological slides were reviewed.
- ER/PR immunoreexpression was assessed in primary and metastases, using a binary classification (+/-) and a semi-quantitative score by visual estimation (% positive tumor cells).
- McNemar test was used to compare binary HR expression between primary and first metastasis. Wilcoxon sign rank test was used to compare median differences in HR score. Kaplan-Meier curves and Cox regression were used for survival analysis. A p-value of 0.05 was considered significant.

Results

Twenty-eight patients (n=28) were included (≈30% of all uLMS patients treated). 23 had available histological material from the primary tumor and 13 from more than one recurrence/metastasis.

- Median age: 52 years (min 42–max 71). | Most frequent site of first relapse: lung (n=18; 64.3%).
- Median disease-free survival (DFS): **25.8 mo** (95%CI 14.3, 37.3).
- Most primary tumours were **HR-positive** (ER: n=20, **87.0%**; PR: n=16, **69.6%**).

Concordant

Concordant binary HR between primary and first metastasis in 15 patients (**65.2%**).

Discordant

Eight (n=8, **34.8%**) had discordant results
→ 7 lost HR expression, 1 changed from negative to positive.

Significant change in HR expression for **ER** (p=0.034) and **PR** (p=0.002).

HR expression score was significantly decreased in metastases compared to matched primaries (mean difference **ER**: 1-10%, p=0.028, and **PR**: 10-20%, p=0.003).

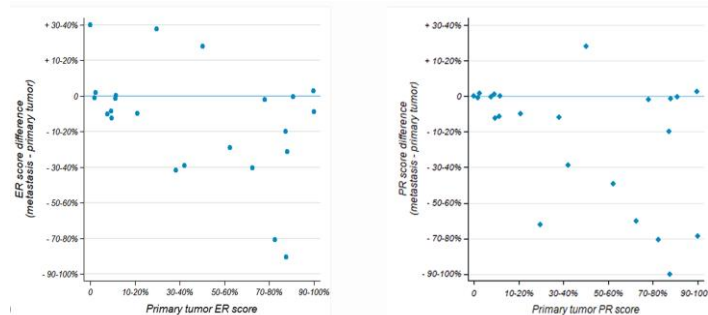


Figure 1: Scatter plots showing HR expression differences in uLMS metastasis matched to corresponding primary tumors. Most cases are below the plot horizontal line (zero difference) and thus showed decreased HR expression in metastasis.

Discordant

Three (n=3) showed discordant expression between metastases of the same patient.

Figure 2: Histological and immunohistochemistry figures of a patient's primary uLMS and corresponding metastases showing heterogeneity of HR expression.

The primary uLMS was ER 30-40% and PR 1-10%, while the colon metastasis was negative for both, and the skin metastasis was ER 60-70% and negative PR.

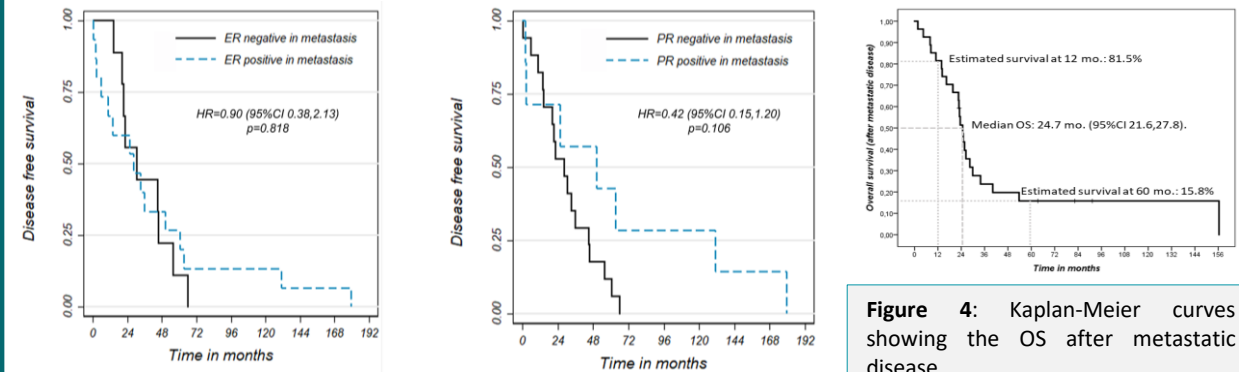
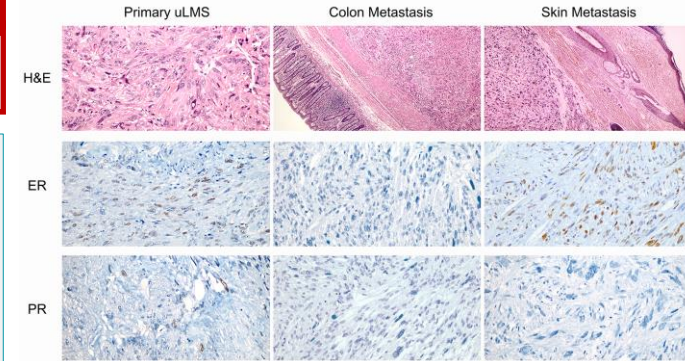


Figure 3: Kaplan-Meier curves showing a non-significant trend for improved DFS with HR expression in metastases.

Figure 4: Kaplan-Meier curves showing the OS after metastatic disease.

Overall survival (OS) did not vary with HR expression.

Conclusions

- Our study shows that HR expression discordance between primary and metastasis was present in 1/3 of uLMS. Usually, there was loss or decrease HR in metastasis.
- HR heterogeneity within same patient metastases was also observed.
- Metastasis HR expression seems to influence prognosis, warranting further confirmation in larger series and consideration in clinical trials design.