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JOURNAL OF CLINICAL ONCOLOGY

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Clinical presentation, pathological features, and natural course of metastatic uveal melanoma (MUM) as an orphan and commonly fatal disease

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Abstract

e20005

Background: Uveal melanoma (UM) is a rare disease characterized by an unpredictable course and variable outcome ranging from cure by local treatment to the occurrence of untreatable metastasis. The current project analyzed patients with the metastatic phenotype. **Methods:** We performed data collection in 76 pts with MUM treated in Leuven between 1957–2008. Statistical analysis involved nonparametric tests, Kaplan Meyer and log rank test. **Results:** The med. age at diagnosis of UM was 58 yrs (range 30–94). Common initial treatments were surgery (71%), brachytherapy (20%) and external beam RT (7%). MUM was more common in women (F:M ratio 48:28) and independent from the side of the primary tumor (left vs. right eye). Synchronous metastasis was found in 9% of cases, all others had metachronous disease after a med. interval of 40 mos (range, 7–420). Statistical analysis failed to identify predisposing factors for MUM with the exception of a significant negative correlation between age at diagnosis of UM and time until metastatic disease (Spearman $\rho = -0.4$, $p < 0.001$). Metastasis in >1 organ, usually liver plus another site, was seen in 47% of

cases. The most frequent sites were liver (96%), lung (23%), subcutaneous (13%), bone (11%) and brain (3%). The med. OS from diagnosis of UM was 46 mos (range, 2–182), and 4,5 mos after diagnosis of metastasis (range, 1–128). 65% of MUM pts qualified for further treatment, including systemic therapy (60%), radiotherapy (7%) and surgery (7%). Systemic therapy (45 pts) included mainly chemo- (50%), chemo- plus hormones (12%), immuno- (3%) or hormonal therapy (3%). The most common drugs given were DTIC (43%), cisplatin (27%), tamoxifen (10%) or phase I agents (8%). Patient benefit (PR+SD) was seen in 16/45 pts (36%), including 2 PR. **Conclusions:** In this orphan disease with female predominance metastasis occurs late, is mainly found but not confined to the liver, and is associated with high morbidity, as >1/3 of pts do not qualify for further therapy. Advances in MUM can only be achieved by networking of sites interested in this tumor with systematic collection of data and tissue to improve our understanding of the molecular biology of the disease.

No significant financial relationships to disclose.

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