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Melanoma brain metastases: a retrospective analysis of prognostic factors and efficacy of multimodal therapies

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Background

Cutaneous melanoma (CM) metastatic to the brain has been historically considered a dismal prognostic disease (1) although recent evidence highlighted the activity of immunotherapeutic strategies (2). The prognostic factors and the additive effect of local treatments remain not extensively elucidated (3). Herein, we performed a retrospective study to overcome these issues and explore the efficacy of multimodal strategies.

Methods

A total of 105 patients with CM metastatic to the brain were enrolled from 2017 to 2021. All patients received conventional treatments. Univariate and multivariate analyses investigated the prognostic impact of histopathological features, neurological symptoms and multimodal therapies.

Results

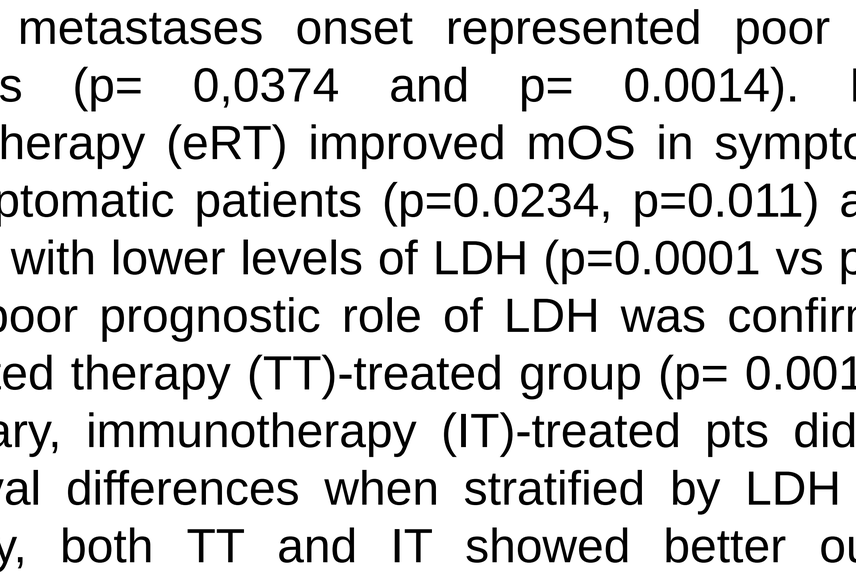
Neurological symptoms and lactate dehydrogenase (LDH) levels > 2 times the upper limit normal (ULN) at brain metastases onset represented poor prognostic factors (p= 0,0374 and p= 0.0014). Encephalic radiotherapy (eRT) improved mOS in symptomatic and asymptomatic patients (p=0.0234, p=0.011) and only in those with lower levels of LDH (p=0.0001 vs p= 0.9989). The poor prognostic role of LDH was confirmed in the targeted therapy (TT)-treated group (p= 0.0015). On the contrary, immunotherapy (IT)-treated pts did not show survival differences when stratified by LDH (p= 0.16). Finally, both TT and IT showed better outcomes if combined with eRT (p=0.001 and p=0.006).

Conclusions

Based on our analysis, LDH levels >2 times the ULN may identify a subgroup of brain metastatic CM pts with poor prognosis that did not gain any survival benefit from eRT. The poor prognostic role of LDH levels is also confirmed in pts who underwent TT. Both pts treated with IT and TT benefit from the concomitant use of eRT, showing an OS benefit suggestive of an additive effect.

Fig.1:OS by neurological symptomps
Fig.2:OS by LDH levels at encephalic progression
Fig.3:OS in patients treated with TT by LDH levels at encephalic progression.
Fig.4:OS in patients treated with IT by LDH levels at encephalic progression.

1



Neurological symptoms	mOS (95% CI)
No	9,2 (5,6 to 16,8)
Yes	5,1 (3,4 to 6,6)

Hazard ratio: 1.6 (95% CI 1.03-2.5); **p= 0,0354**

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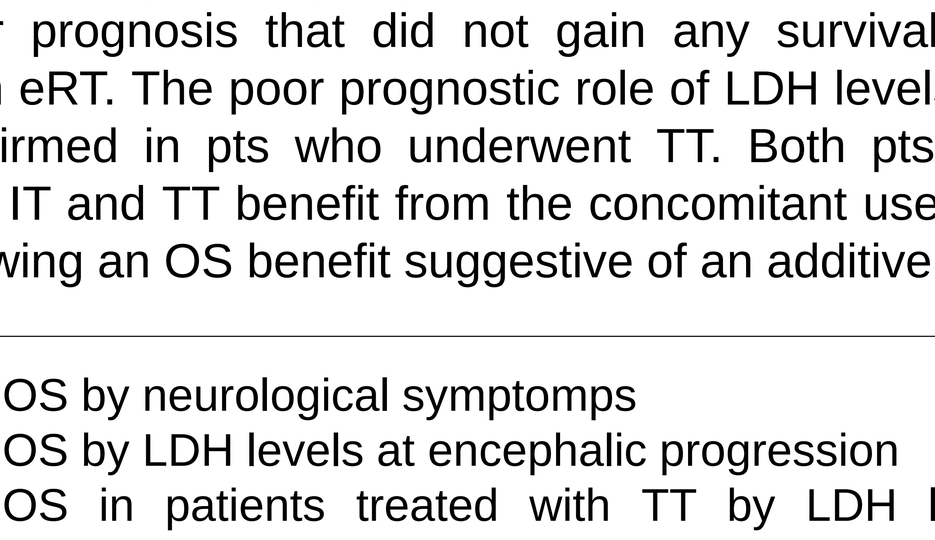

LDH levels in TT-treated patients	mOS (95% CI)
≤ 2 ULN	12,5 (4,833 to 13,667)
> 2 ULN	3,5 (4,5 to 34,37)

Log-rank test **p=0,0015**

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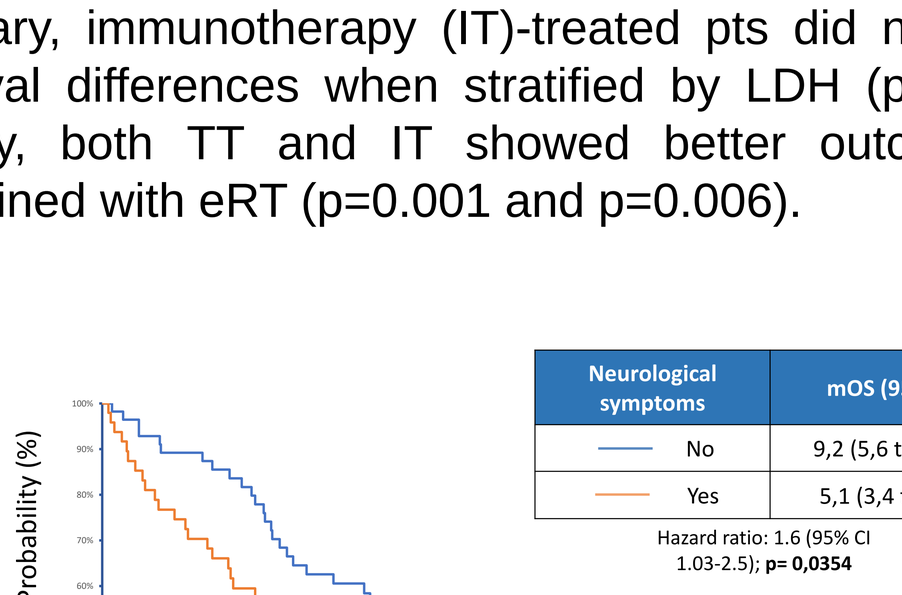

LDH levels	mOS (95% CI)
> 2 ULN	3,5 (1,600 to 5,067)
≤ 2 ULN	9,2 (5,567 to 13,033)

Multivariate-adjusted Hazard ratio: 1.92 (95% CI 0.98-3.75); **p= 0,0487**

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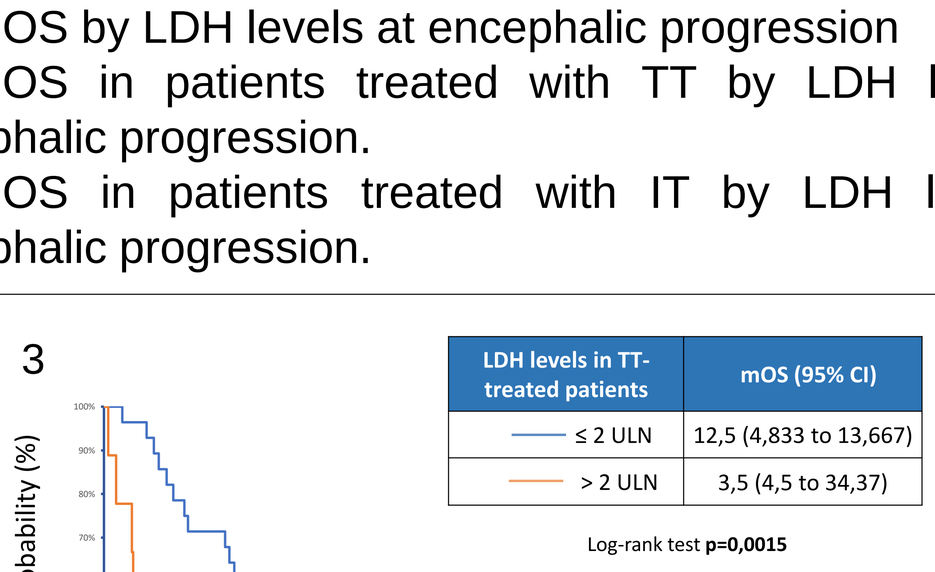

LDH levels in IT-treated patients	mOS (95% CI)
> 2 ULN	4,17 (2,87 to 6,3)
≤ 2 ULN	8,43 (4,43 to 15,27)

Multivariate-adjusted Hazard ratio: 1.92 (95% CI 0.98-3.75); **p= 0,0487**

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