Aim: Glandular metastasis (GM) as defined by pancreas, breast, parotid, thyroid and contralateral adrenal metastasis are rare in clear cell renal cell carcinoma. We have performed a multicenter comparison of metastatic clear cell RCC (mRCC) with GM and non-GM to determine if GM impacts on overall survival (OS).

Methods: Data were collected from mRCC pts with GM or non-GM at metastatic presentation. GM: pts with at least one GM with or without other sites. Non-GM: pts without GM at metastatic presentation. Pts were treated in 5 French, 1 Belgian and 3 UK centers between January 2004 and October 2013. Association between OS and site of metastasis was assessed using the log-rank test for univariate analysis and the chi-square test for multivariable Cox regression.

Results: 188 GM and 453 non-GM mRCC pts were analyzed. The majority were male (70.2%), median age was 59y, with no difference between the GM and non-GM groups. Interval from diagnosis to metastasis was 25.7 months (mo) (0.03-272.8) for GM and 4.8 mo (0.03-334) for non-GM (p < 0.001). 39% GM pts were MSKCC favorable risk compared with 23% non-GM pts (p <0.0001) and 6.7% GM pts were MSKCC poor risk vs 16.7% non-GM. Fuhrman grade was I/II in 48.7% GM pts and 33.6% in the non-GM (p = 0.005). Median follow-up was 82.4 mo (68.9-89.5). Median OS was 64.8 mo (52.7-86) for GM and 39.8 mo (34.8-46.1) for non-GM (HR = 1.66 [95% CI = 1.32-2.1], p < 0.001). Age (<60y vs >60y), delay between renal tumor and metastatic diagnosis, MSKCC risk group and GM or non-GM group were significant parameters in univariate OS analysis (p < 0.001). In a multivariate analysis adjusted according to MSKCC risk group, GM status was a strong prognostic factor (HR = 0.76 [95% CI = 0.59-0.98], p < 0.035).

Conclusions: This large retrospective study shows that the presence of at least one GM at metastatic presentation of clear cell mRCC was associated with a significantly longer OS compared to non-GM pts. The presence of GM vs non-GM disease was an independent prognostic factor for OS. Further translational studies will be performed on matched primary tumor and metastasis samples to assess molecular differences between GM and non-GM.

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