Dear Professor Mok,

We appreciate that you give us the possibility to revise our manuscript and we thank the reviewers again for their valuable comments. Based on these comments we herewith respond to all questions raised in a point-by-point manner, as follows:

Reviewer 1:

1. The authors´answer regarding the cut off is sufficient, please include this argument either in the methods section or as supplementary information.

Answer: We thank the reviewer for this comment. We include the arguments into the methods section page 3: *To define the cut-off value a ROC curve analysis was performed. The IRS cut-off value 5 reaches a sensitivity of 76.6% and a specificity of 64.2% (Youden Index. 0.408) and was chose as cut-off value (see supplement Figure S1 and Table S1).*

Additionally, we added the ROC curve and the table with sensitivity, specificity and Youden Index into a supplement section as figure S1 and table S1

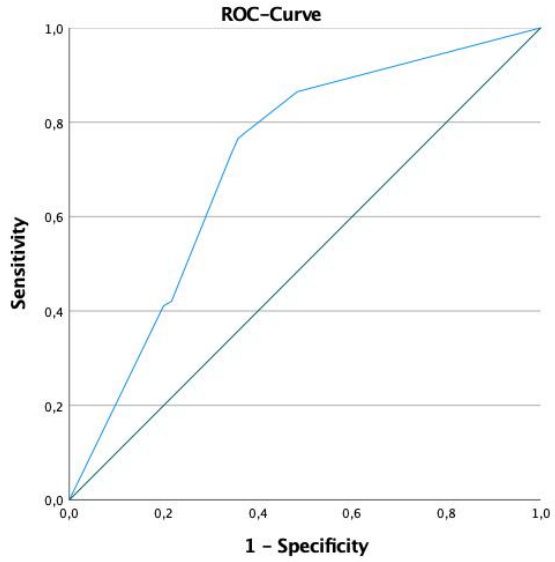

Figure S1: ROC Curve for IRS cut-off analysis (AUC 0.716 [0.656 – 0.776])

Positive if Greater than or Equal to	Sensitivity	1- Specificity	Specificity	Youden Index
-1	1	1	0	0
1	0,869	0,500	0,500	0,369
3	0,864	0,483	0,517	0,381
5	**0,766**	**0,358**	**0,642**	**0,408**
7	0,729	0,342	0,658	0,387
8,5	0,421	0,217	0,783	0,204
10,5	0,411	0,200	0,800	0,211
13	0	0	1	0

Table S1: Sensitivity, specificity and Youden Index for different IRS cut-off values.

2. The authors refer to a data "Proliferation of FLO1 EV and FLO1 MACC1 over 72 h", however I couldn´t find the figure either in the manuscript file or here in the answer.

Answer: thank you for this comment: we added the proliferation analyses by MTT into the method section page 5: *Additionally, proliferation for FLO-1/EV and FLO-1/MACC1 was analyzed over 72 h by MTT. 4x10^3 cells were plated into 96-well-plates and were allowed to accommodate for 24 h. after 48 and 72 h formazan crystals were dissolved in 150 µl of DMSO and the absorption was measured at 560 nm in the absorbance reader (Tecan infinite 200 PRO). Each cell proliferation experiment was performed in triplicates.*

We added the results of the MTT analyses into the results section page 11: *The additional analysis of the proliferation over 72 h showed no significant differences between FLO-1/EV (100% ± 4.886) and FLO-1/MACC1 (112.3% ± 12.24; p=0.113) (see supplement Figure S3).*

We added the MTT plot as figure S2 into the supplement section

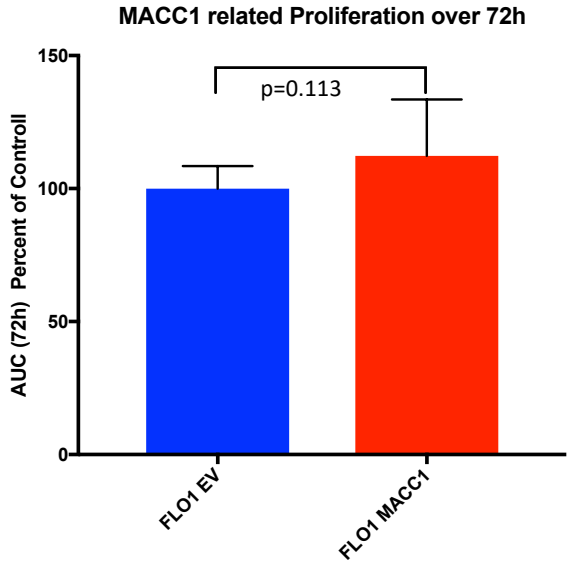

Figure S2: Proliferation of FLO1 EV and FLO1 MACC1 over 72 h. Analysis of in vitro proliferation assay.