Reviewer's report

Title: Novel treatment option for MUC16-positive malignancies with the targeted TRAIL-based fusion protein Meso-TR3

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Reviewer: Adnan M Nagrial

Reviewer's report:

Thank you for asking me to review this manuscript.

The authors have shown that mesothelin linked TR3 (a TRAIL-based drug platform) causes cell-death in the OVCAR3 cell-line and an OVCAR3 xenograft more effectively than either TR3 or TRAIL alone.

Interest in novel linked targeted-drugs is high with the recent approval of T-DM1 in breast cancer.

I make the following comments

Minor Essential Revisions

The cell death figures (Figures 3 and 4) are somewhat unconventional in that drug volume rather than drug concentration has been provided. It would make interpretation of the benefit of meso-TR3 easier if simple concentrations of TR3 and meso-TR3 were used.

The effect on HELA cells (Figure S3) is stated in the results section as showing a greater benefit of meso-TR3 vs TR3. Although this looks numerically true, it is not actually statistically significant and thus somewhat misleading.

Discretionary Revisions

The effect of meso-TR3 has only been shown in a single cell line and a xenograft using the same cell-line. The benefit of a MUC16 targeted drug would be more convincing if more than 1 cell line was used. The entire concept would also be more convincing if a non-ovarian cancer cell line was also used.

It is somewhat concerning that the only other MUC16 expressing cell-line used, HeLa, does not show any additional benefit of meso-TR3 over TR3 alone.

Although I have no criticism of the experimental methods and results, I am personally unconvinced of the conclusions made as the authors have only demonstrated that meso-TR3 is better than TR3 in an OVCAR3 cell-line and xenograft model. However, there are no flaws in methodology that would prevent publication.

Level of interest: An article whose findings are important to those with closely
related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests