Reviewer's report

Title: Characterization and drug sensitivity profiling of primary malignant mesothelioma cells from pleural effusions

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Reviewer: Elisa Paolicchi

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Characterization and drug sensitivity profiling of primary malignant mesothelioma cells from pleural effusions
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Major Compulsory Revisions

1- The manuscript of Szulkin A et al. provides an interesting profiling of primary malignant mesothelioma cells. The article gives an overview of several anticancer agents and their efficiency in different primary malignant mesothelioma with particular emphasis on the RRM1 and ERCC1 expression. The article focuses primarily on malignant mesothelioma cells from pleural effusions and correlates drug sensitivity and % of malignant cells with the overall survival of patients. While the article touches upon many important areas, one is left feeling that certain areas could be presented in more depth. For example since authors correlates in vitro results with overall survival, they should report detailed information about each patients, including a table (Female/male, Age, chemotherapy, other therapies, surgery, medical history, Asbestos exposure, SV40 infection, toxicities etc..) to allow a deeper understanding of the whole study.

2- Authors state that there is a great variability in chemo-sensitivity of primary cell samples, this part should be explained more in the discussion. One of the more frequent characteristics in mesothelioma is the variability between patients. How you could explain more this variability? Do you have information about the stage and the grade of the disease at the time of each pleural effusion? Authors should be aware of this, and also of the time when the chemotherapy started, to be able to explain better this variability. For example it is necessary to know if the pleural effusions were withdrawn before or after the administration of chemotherapy to avoid the possibility that cells have created resistance to drugs before the experiments ex vivo.

3- Could authors include some information (and a table) about the four benign samples? Do Authors have results of Mesothelin and Hyaluronan expression? Are the benign samples from healthy volunteers? Do they have pleural disease (Pleural plaques etc…)? How the authors could explain in the discussion the
resistance to some anticancer agents in benign samples?
4- Could authors try to explain in the discussion why ERCC1 staining was not correlated to the proportion of effective drugs or the survival time of patients?

Minor Essential Revisions
5- At line 70 and 80 before the reference, authors write “reviewed in”, probably it is enough only the reference without “reviewed in”.
6- At line 95, authors could cite more recent articles together with the reference 26.
7- Why pemetrexed was only tested on 50% of the samples?

Discretionary Revisions
Recent studies identify cancer stem cells as the seed of chemoresistance in several tumors including malignant mesothelioma. Authors could extend the study to the identification of mesothelioma cancer stem cells markers (CD44+/CD24+/CD26+) to correlate the percentage of cancer stem cells with the sensitivity to drugs and to the overall survival. These data could be useful to explain mechanisms that actually are not clarified.

Level of interest: An article of importance in its field

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