Reviewer's report

Title: Oleanane triterpenoid CDDO-Me induces apoptosis in multidrug resistant osteosarcoma cells through inhibition of Stat3 pathway

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Reviewer: Konstantin Leskov

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The article by Keinosuke Ryu et al., titled “Oleanane triterpenoid CDDO-Me induces apoptosis in multidrug resistant osteosarcoma cells through inhibition of Stat3 pathway” is the first to date to explore the effect of CDDO-Me on osteosarcoma cell lines. The paper essentially re-iterates the results found in ovarian, breast and lung cancer treated with CDDO-Me. The changes in Stat3 phosphorylation after treatment with CDDO-Me had been previously reported in other types of cancer. The authors of this paper are the first to report such changes in osteosarcoma.

The methods presented are adequate to demonstrate the alterations of Stat3 status in osteosarcoma.

The paper in general is a bit light on data. Only the MTT assay was used to estimate compound toxicity. Colony forming assay would be a good compliment to MTT to assess reproductive cell death in addition to metabolic cell death and apoptosis.

No animal data was presented. The sensitivity of osteosarcoma xenografts to CDDO-Me would strengthen author’s point of usefulness of this compound in clinic.

The measurement of IC50 of CDDO-Me was mentioned in methods, but I did not find the actual values of IC50 for MDR and non-MDR osteosarcoma cells anywhere else in the paper. Since no IC50 was shown, the reason for using specific doses of the compound is unclear. In particular, using 1 uM of CDDO-Me in the nuclear translocation experiment is unclear. 1 uM seems a bit high to be clinically relevant. I wonder if 0.1-0.2 uM would have the same effect.

The writing in general is acceptable; the conclusions drawn are adequate for the experimental results.

Level of interest: An article of limited interest

Quality of written English: Acceptable

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