Reviewer’s report

Title: Phase I study of OM-174, a lipid A analogue, with assessment of immunological response, in patients with refractory solid tumors.

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Reviewer: Inge Marie Svane

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Manuscript by Isambert et al.
Phase I study of OM-174, a lipid A analogue, with assessment of immunological response, in patients with refractory solid tumors.

The manuscript presents clinical and biological data from a phase I trial testing OM-174 a synthetic lipd A analogue with TLR-2 and -4 activity. In total 17 patients were included on 6 different dose levels over a period of approx. 2½ year.

Major comments.

Trial design including in-and exclusion criteria as well as aims of the study are adequately described. The trial was approved by legal authorities and a trial ID is given, however, a trial identification number from registration in a public trial registry such as www.clinicaltrial.gov is missing.

The authors have declared that they have no competing interests (page 22) however, further disclosure to clarify the commercial relationship is needed; is OM-174 patented by any of the authors or the manufacturing company? OM Pharma is stated as the drug supplier; according to the website OM Pharma Pharmaceuticals does not exist and have been integrated in Vifor Pharma in 2009, if true, this information should be included. The author Jacques Bauer is affiliated with OM-Pharma this should be stated under competing interests.

Table 3 summarize non-haematological adverse events as written on page 14, and no grade 3 or 4 events are reported. However, it seems reasonable to include the grade severe bronchospasm described on page 15 in order to make the table complete.

According to the authors 7 patients experienced fever and were treated with antipyretics (page 14). Why was antipyretics used if the patients only experienced grad 1 or 2 fever? Did the authors consider a possible link between fever and treatment activity? Fever has previously been shown to correlate with objective response and survival after cancer immune therapy with Interleukin-2 (abstract 8569, ASCO 2010), this should be commented on in the discussion.

NK activity is the only cellular immune activity assessed (page 17); a possible increase in NK number and activity is reported in some patients. These data
should be shown.

Three patients are reported to achieve SD during treatment. To make it possible for the reader to appreciate these data more information is needed; e.g. was time from baseline to first evaluation? On page 11 it is only written that tumor measurements were performed at baseline and at the end of the treatment; the 3 patients were treated bi-weekly with 5, 10, and 15 doses respectively were they evaluated at the same time point? And in this regard, how should SD of 1 and 2 months for patient 9 and 17 be interpreted? Please add to discussion.

More information on disease state is needed; include ‘disease burden’ or ‘number of metastatic sites’ in table 2 and 5.

Figure 1a,b,c; Insert explanation of symbols and number of patients included in the analyses.

Minor comments.

The last sentence on page 21 (We have shown....) is hard to follow and should be revised.

The last sentence on page 17; ‘not trend’ should be ‘no trend’

Figure legend 1B and 1C; 'The most important peak...' another wording is suggested

**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