Author's response to reviews

Title: Effects of cytarabine on activation of human T cells - cytarabine has concentration-dependent effects that are modulated both by valproic acid and all-trans retinoic acid

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Hereby, we submit the revised manuscript entitled: "Effects of cytarabine on activation of human T cells - cytarabine has concentration-dependent effects that are modulated both by valproic acid and all-trans retinoic acid" by Elisabeth Ersvaer, Annette K. Brenner, Kristin Vetås, Håkon Reikvam, and Øystein Bruserud (MS: 9941294061496998).

Cytarabine is used in the treatment of acute myeloid leukemia (AML). Low-dose treatment of cytarabine can be combined with valproic acid and all-trans retinoic acid (ATRA). To our knowledge no study has previously investigated the possible immunotoxicity of this combination, i.e. the impact of these combined components on peripheral blood T lymphocytes. In the present study we investigated the effects of cytarabine combined with valproic acid and ATRA on in vitro activated human T cells, and we tested cytarabine at concentrations reached during in vivo treatment with high doses (i.e. 3 g/m2 single doses intravenous over few hours), conventional doses (100-200 mg/M2 intravenous infusion over 16-18 hours) and low-doses (10-20 mg subcutaneous dose). Our results indicate that cytarabine has dose-dependent effects on T cell activation, and the immunomodulatory effects of low-dose cytarabine are strengthened by ATRA and valproic acid.

In this revised version we have included: (1) Line Numbering and (2) email
addresses of all authors on Title Page

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We hope you will find our manuscript of high originality and relevant for publication in your journal.

Yours sincerely,

Elisabeth Ersvær and Øystein Bruserud