Author's response to reviews

Title: The pan-HDAC inhibitor panobinostat acts as a sensitizer for erlotinib activity in EGFR-mutated and -wildtype non-small cell lung cancer cells

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Author's response to reviews: see over
Cover letter

Dear Dr. Solera,

we wish to submit enclosed manuscript entitled "The pan-HDAC inhibitor panobinostat acts as a sensitizer for erlotinib in EGFR-mutated and -wildtype cell lung cancer cells" by Greve et al. for consideration for publication in BMC Cancer.

The aim of the study is the development of a "priming" model to sensitize TKI-insensitive NSCLC cells to the anti-tumoral effects of erlotinib, by additional treatment with the pan-HDAC inhibitor panobinostat. The strategy chosen for comprehensive dose-finding experiments was explicitly to determine low, clinically non-toxic concentrations of the HDAC inhibitor, and thus not aiming at chemotherapy-like cytotoxicity but rather at gene reactivation. This is based on our long-term goal of developing well-tolerated cancer treatments also feasible in elderly, non-fit cancer patients with comorbidities and a reduced performance status, who would not tolerate aggressive polychemotherapy.

The significant and novel findings of the study are i. a significantly additive effect of both drugs upon cell growth inhibition and cell differentiation, strongly supporting the rationale to combine these drugs in NSCLC, and ii. the novel result of activating effects of erlotinib alone on histone acetylation and methylation of these cell lines, which were synergistically enhanced when the HDAC inhibitor was added. We believe that these findings warrant further studies of this combination of a “de-repressive” epigenetically active agent like histone deacetylase inhibitors with a TKI.

We confirm that all authors have read the paper (not submitted elsewhere) and agree with its contents. As potential reviewers we would like to suggest the following experts in the field:

Sincerely yours

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Update of the changes made within the new version (12/12/2014):

• Line numbering was included in the main manuscript.
• Ethics statement was added: Since we only used commercially available cell line since our study, no approval of an appropriate ethics committee was need.