Supplementary Figure S1 Cell survival curves with indicated IC\textsubscript{50} concentrations of cells grown as monolayers after treatment with buparlisib, trametinib or combination with increasing drug concentrations (0.000001 μM–100 μM). (a) BRAF\textsuperscript{V600E} mutated H2 cells treated with buparlisib (left), trametinib (middle) and combination (right). (b) BRAF\textsuperscript{L577F} mutated H3 cells treated with buparlisib (left), trametinib (middle) and combination (right). (c) BRAF\textsuperscript{V600E} mutated H10 cells treated with buparlisib (left), trametinib (middle) and combination (right). The experiments were carried out in triplicate (n = 6 per drug per experiment).

Supplementary Figure S2 Protein expression of cell lysates after in vitro treatment with 10 μM buparlisib, 10 μM trametinib or combination (5 μM + 5 μM). Western blots of lysates from H2 (BRAF\textsuperscript{V600E}), H3 (BRAF\textsuperscript{L577F}) and H10 (BRAF\textsuperscript{V600E}) cells after drug treatments.
Supplementary Figure S3 In vitro colony formation of H2 cells pre-treated with buparlisib and trametinib. (a) Representative images of H2 cells pre-treated with 10 μM buparlisib, 10 μM trametinib or a combination (5 μM + 5 μM trametinib) grown as colonies. (b) The colony formation was scored and quantified as seen in the graph. The experiments were performed in triplicate. Abbreviations: *: p < 0.05, and ****: p < 0.0001.

Supplementary Figure S4 Migration of brain metastatic melanoma cells during and after pre-treatment with 10 μM buparlisib, 10 μM trametinib or combination (5 μM + 5 μM). (a) Representative micrographs of H2 (BRAFV600E), (b) H3 (BRAF L577V) and (c) H10 (BRAFV600E) cells before
(0 h) and at completion (90 h) of the scratch-wound experiment. The respective wound confluences were quantified and placed below each cell line (n = 6 per drug concentration). Scalebar = 300 μm.

Supplementary Figure S5 Cell migration towards a chemoattractant. Representative images of migrated (a) H2 (BRAFV600E), (b) H3 (BRAFL577F) and (c) H10 (BRAFV600E) cells after pre-treatments with 10 μM buparlisib, 10 μM trametinib or combination (5 μM + 5 μM). The number of cells were quantified based on three fields of view and placed below each cell line in the figure. The experiment was performed in triplicate. Abbreviations: ****: p < 0.0001.
Supplementary Figure S6 Morphology of human melanoma brain metastatic cell lines after treatment with 10 μM buparlisib, 10 μM trametinib or combination (5 μM + 5 μM). Representative images of H1 (BRAFV600E), H2 (BRAFV600E), H3 (BRAF1577F) and H10 (BRAFV600E) cells can be seen from top to bottom treated with vehicle (medium), buparlisib, trametinib or a combination left to right.