Project number XX

Final Report

Efficacy of compound X on primary tumor reduction and metastasis in PC3 cell line

Client: Company X
Your contact:

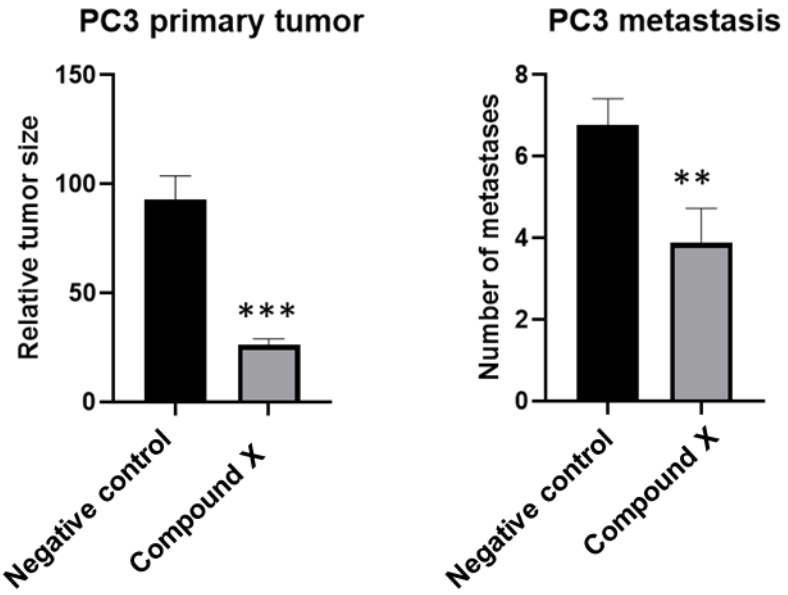
Project Manager:

Issue date:

PURPOSE

The purpose of this study is to determine the anti-cancer efficacy for Compound X (500 nM) in PC3 cell line. Anti-cancer efficacy will be determined as the change in primary tumor size (i.e tumor growth or reduction) and number of tumor cells disseminated to the distal caudal venous plexus (CVP) three days after implantation.

RESULTS



Effect of Compund X on PC3 cells showing significant reduction of primary tumor size p<0,0001 as well as reducing metastatic dissemination, p<0,0097.

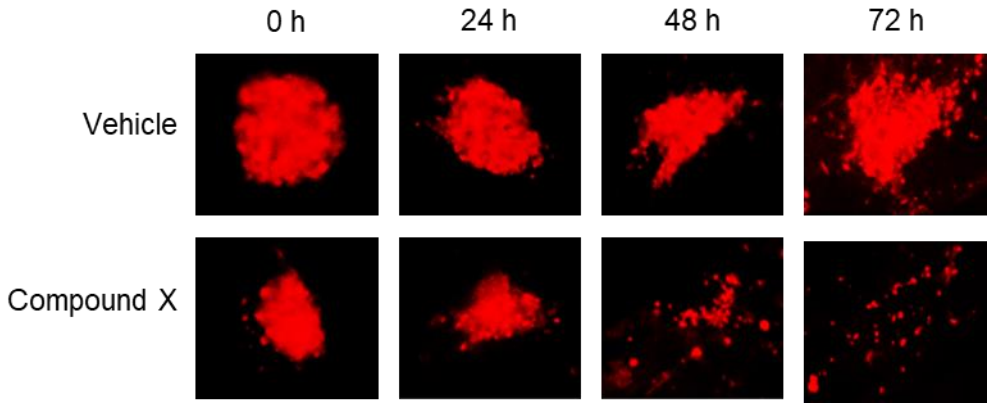


Figure 1: *Representative images of primary tumors (will be provided upon request for an additional fee).*

CONCLUSIONS

The efficacy of Compound X was good both in reducing primary tumor size as well as inhibiting metastatic dissemination of cancer cells. Significant reduction was observed for both evaluated parameters.

RECOMMENDATIONS FOR FURTHER STUDIES

This section will be much more specific once we know more about your specific compound and targets.

The effect of Compound X is well suited to be evaluated in the ZTX platform.

The ZTX model is a very suitable tool to screen both compounds and PDX models. Compound screening can select the best leads from compound libraries or different formulations to take further into mouse PDX models and find appropriate dosing.
By screening several PDX or CDX models you can get information about which patient group or sub-group that show the best response to the specific compound or to find new indications where the compound is effective. By screening several PDX models, you can also find the one most suited to test further in mouse PDX studies.

The model is also excellent for immune oncology applications. The zebrafish embryos have no adaptive immune system, and a human immune system can be added without prior immune deprivation to reconstitute the tumor microenvironment.
Combination treatment could also be applied, and many different combinations can be evaluated during the same experiment to find the optimal combination treatment.

We have more than 40 cell lines in our in-house library as well as access to over 700 fully characterized PDX models from our partners. We also have access to clinical samples collected from primary tumor and metastatic site from cancer patients (ovarian, CRC and lung) that can be used in the model for co-clinical trials.

STUDY DESIGN

Delivery and preparation of substance

The substance was delivered by Company B to BioReperia as 1 mg of powder. Powder was reconstituted in DMSO and diluted in embryo water to final concentrations.

Description of zebrafish strain

Zebrafish of the fli1a:EGFP strain were used, derived from in-house stocks.

Objective and Purpose

The objective was to determine the anti-tumor efficacy of Compound X in PC3 cell line at 500nM.

DESIGN

Group size

20 zebrafish larvae were randomly selected for each experimental group.

Statement of primary endpoints

The study was concluded three days after tumor cell implantation (five days post fertilization). The results are given as tumor growth/reduction and formation of metastasis.

Description of measures taken to minimize/ avoid bias (randomization, blinding)

Larvae were randomized to each experimental group.

Selection and Withdrawal

Unfertilized eggs or larvae that did not appear healthy or exhibited any obvious developmental defects were excluded before treatment onset. Larvae in which tumor cells had been inadvertently injected into circulation or larvae with erroneous tumor implantation in the yolk rather than the an the perivitteline space were excluded from the study. Larvae that died or were lost by other means during the study were excluded from the final analysis.

TREATMENT ADMINISTRATION

Dose

Compound X was used at 500nM.

Vehicle

DMSO 0,2% in PTU was used as vehicle/un-treated control.

Treatment period

The treatment period was three days (72 hours).

ASSESSMENT OF EFFICACY ON TUMOR GROWTH AND METASTASIS

Zebrafish larvaes were injected at 48 hpf with approximately 500 DiI stained tumor cells in 5 nL medium into the perivitelline space. The tumors were visualized immediately following implantation and larvaes transferred to individual wells in a 24-well plate in 1 ml of PTU-treated, E3 medium with or without treatment. Larvae were kept at 36^0C during the experiment and visualized again at 3 days post implantation. Images were analysed using an in-house developed software.

Statistical analysis

The statistic software used is graphpad and the analysis used for evaluating differences in primary tumor size and metastasis was made with t-test.