学位論文審査結果の要旨

所　属	三重大学大学院医学系研究科 乙　生命医科学専攻　臨床医学系講座 運動器外科学・腫瘍集学治療学分野	氏　名	矢田　祐基（やだ　ゆうき）
審　査　委　員	主　査　俵　功 副　査　岩本　卓也 副　査　渡邉　昌俊		

（学位論文審査結果の要旨）

Screening for Synergistic Reagents With Pazopanib Against Osteosarcoma Using a Compound Library

【主論文審査結果の要旨】

著者らは論文において下記の内容を述べている。

Background/aim: Osteosarcoma (OS) is the most common malignant bone tumor. As the same agents have been in use since the mid-1970s, new therapeutic approaches are needed to improve prognosis. Pazopanib (PZP) has already demonstrated marked antitumor activity clinically and can be effective in patients with metastasis OS. We investigated the combination treatment of candidate agents with PZP and examined effects on tumor growth using an in vivo model.

Marerials and methods: A library of 324 compounds was used. MG63 OS cells were treated with PZP and each compound. Cell viability was measured. The antiproliferative effects of compound combination on four OS cell lines was tested. Cell signaling was evaluated by western blot analysis. In vivo antitumor testing was performed using 143B-bering mice.

Result: The screening process identified crizotinib (CRZ) as the most effective drug for combination with PZP. The combination of PZP and CRZ demonstrated effects compared to control or single therapy. Cell signal investigation showed that dual therapy down-regulated c-MYC, p-AKT, p-STAT3, p-cyclin D1 and surviving and up-regulated cleaved caspase-3 and

cleaved PARP compared to control or single therapy. In vivo analys is showed dual therapy achieved synergic effects for tumor growth compared to control or single-treatment groups. No significant difference in the change in body weight was observed among groups.
Conclusion: Combined use of PZP and CRZ offers synergic anti-tumor effect against OS, inducing apoptosis in vitro and in vivo by down- regulating AKT and STAT3. Our data suggest that these agents can be used for patients clinically.

PZP と CRZ の併用が骨肉腫に対する高い腫瘍増殖抑制効果を持つ可能性を示した論文であり、学術上極めて有益であり、学位論文として価値のあるものと認めた。

ANTICANCER RESERCH 2024;44(3):1071-1078
Published: March 2024
doi: 10.21873/anticanres.16902

YUKI YADA,KUNIHIRO ASANUMA,TAKUYA KAKIMOTO,KAZUMA OKUNO, TAKAYUKI OKAMOTO, TAKAHIRO IINO, TOMOKI NAKAMURA and AKIHIRO SUDO