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Harnessing autophagy to potentiate the antitumor effects of the tyrosine kinase inhibitor cabozantinib in prostate cancer cells

Promotionsfach: Urologie

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Our results show that autophagy induction is an important mechanism for the acquired resistance to cabozantinib in prostate cancer cells.

We find that the Traditional Chinese Medicine derivatives IO and BIO show autophagy inhibitory properties. Similar to the known autophagy inhibitor bafilomycin A1, indirubin derivatives significantly decrease the viability in LNCaP and PC-3 cells when used in combination with cabozantinib. This *in vitro* effectiveness can be explained by the fact that cabozantinib itself functions to induce autophagy; most likely through alternative pathway to AKT signaling that may involve FOXO proteins.

Together, the present study demonstrates that targeting autophagic signaling pathways may be a promising option for the future development of therapeutic strategies for mCRPC, in particular in combination with TKIs such as cabozantinib. Our results warrant further investigations to find more selective and specific autophagy modulators with clinically acceptable toxicity profiles to improve the treatment of patients with mCRPC.