also in vivo. However, OBX1-012 like other EGFR-TKIs failed to show the efficacy for exon 20 insertion mutation or C797S point mutation.

Conclusion These results identify OBX1-012 as one of highly effective, mutant-selective EGFR-TKIs for treatment of T790M-mediated resistance.

PO-044 CISPLATIN AND RUTHENIUM(III) COMPLEXES – COMPARISON OF CELLULAR RESPONSE OF TREATED MDA-MB231 BREAST CELLS

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Introduction Since the discovery and clinical success of the platinum(II) anticancer drug, cisplatin, researchers are putting much effort to develop more efficient metal-based therapeutic compounds, with fewer side-effects and greater cytoselectivity. Ruthenium complexes arose as promising anticancer agents, due to the success of some ruthenium drug candidates in clinical trials. Here we report comparison of in vitro cytotoxic activity and mechanisms of action of cisplatin and four newly synthesised ruthenium(III) complexes with bidentate anionic Schiff base derived from 5-methylsalicylaldehyde and methylamine: complexes 1–4.

Material and methods Cytotoxicity was tested on four human cancer cell lines (K562, A549, EA.hy926, MDA-MB231) and one human non-tumour cell line (MRC-5), by MTT assay. Being the most cytotoxic of all four tested complexes, complex 1 (cisplatin) (Na[Ru(LCl)2], L=N-propyl-5-chlorosalicylidenimino) is selected for further analyses of molecular mechanisms underlying its activity toward MDA-MB231 cells.

Results and discussions The average IC50 values were in the low micromolar range 2–23 μM, depending on cell line. Investigated complexes displayed an apparent cytoselective profile, as they reduced the viability of tested tumour cell lines more efficiently than of the non-tumour MRC-5 cells. Cisplatin resistant MDA-MB231 cells showed to be ten times more sensitive to C1 (IC50=2 μM) than to cisplatin. 24 hour treatment of MDA-MB231 cells with IC50 values of C1 and cisplatin induced minor cell cycle alterations, while 48 hour treatment induced substantial accumulation of cells in Sub-G1 region, up to 22.4% (C1) and 86.4% (cisplatin), versus control 4.8%. Acridine orange/ethidium bromide dual staining confirmed the Annexin V-FITC/PI assay results of notable reduction in cell number after the treatment with C1 and cisplatin. While cisplatin-treated cells prominently die of necrosis, C1-treated cells after 24 hour treatment show apoptotic morphology, but after prolonged treatment, necrosis becomes predominant. Decrease in the intracellular levels of reactive oxygen species was comparable in the cisplatin-treated and C1-treated cells, with cisplatin displaying more conspicuous effects at higher dose. C1 entered the cells more efficiently compared to cisplatin. Intracellular C1 concentration after 4 hour treatment exceeded that of cisplatin by 7.8 times approximately.

Conclusion Present study pointed out interesting activity of this type of ruthenium(III) complex and need for further biological studies and its chemical structure optimisation.