DIFFERENCES IN ACTIVITY BETWEEN EMD 72000® AND ERBITUX® IN A431 CELLS MAY RELY ON MAPK CASCADE INHIBITION

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Summary: The present study was undertaken to examine the effects of the monoclonal antibodies against Epidermal Growth Factor receptor (EGFr) EMD 72000® (EMD) or Erbitux® (C225) alone, or in combination with cisplatin (CDDP) and RxT in the vulval squamous carcinoma cell line A431. No significant difference in citotoxicity [MTT and clonogenic assays (CA)] was observed when EMD was combined with RxT, CDDP, or both. In contrast, C225 plus RxT or CDDP led to a stronger inhibition (n=3, $P<0.05$) of A431 cell proliferation than each treatment alone. We performed Western Blotting analysis to detect phosphorylated EGFr residues (Tyr 845, 992, 1045 and 1068) in cells that were treated with EMD or C225 (100 ug/mL). No difference in the phosphorylation of these residues was found for any of the treatments and no changes were observed in the amount of total or phosphorylated HER2, SRC and AKT proteins. In contrast, ERK 1/2 protein phosphorylation was strongly inhibited by Erbitux® but, surprisingly, not by EMD 72000®. These data suggest that there is no additive effect when EMD is combined with RxT, CDDP, or both and we observed an additive effect of C225 treatment plus CDDP or CDDP/RxT in decreasing A431 cell viability and survival. This difference may be explained by a marked inhibition of the MAPK cascade by C225, which is not observed with EMD treatment.