Combined Therapy of two RTKs: Erbitux und BGJ398 Treatment in HNSCC cell lines

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Head and Neck Squamous Cell Carcinoma (HNSCC)
- express several Receptor Tyrosine Kinases (RTKs):
  - Epithelial Growth Factor Receptor (EGFR)
  - Fibroblast Growth Factor Receptors (FGFRs)

We hypothesized that the tumor cells can switch between the different RTKs to maintain survival and proliferation and overcome the therapy.

Research was performed in-vitro in the Detroit-562, CAL-27 and PJ-15 cell lines. Immunohistochemically detection of RTKs, a functional sphere assay and a drug treatment study was performed.

The histochemical staining of the cell lines showed:
- High levels of EGFR and Keratinocyte Growth Factor Receptor (KGF).
- Low expression of FGFR1 and sporadic FGFR3 expression.

The performance of the RTKs was tested in an sphere assay to prove anoikis resistance and proliferation stimulation. All cell lines reveal:
- Increased sphere induction by ligands of EGFR or FGFRs compared to the unstimulated control.

RTKs could replace each other to promote survival and proliferation of floating tumor cells.

To improve the therapy in HNSCC, this study determined the effectiveness of a combined treatment targeting multiple RTKs. The cell lines were treated with BGJ398 (Novartis) that inhibits FGFRs and/or the EGFR targeting antibody Erbitux = EBX (Merck).
- Singular drug administration significantly inhibited proliferation and survival in all cell lines.
- In two cell lines the combination of both drugs enhanced the effect compared to the single drug treatment.

FGFR1 (1), FGFR3 (2), EGFR but also KGF seemed to be important therapy targets. RTKs treatment results are comparable with findings of Marshall and colleagues (3).

This study demonstrated that the combination of BGJ-398 and Erbitux is a promising treatment regime for HNSCCs.


Expression of RTKs Head and Neck Squamous Cell Carcinoma Cell lines:

In-vitro Treatment with BGJ and EBX

<table>
<thead>
<tr>
<th>Cell Line</th>
<th>Control</th>
<th>BGJ</th>
<th>EBX</th>
<th>BGJ+EBX</th>
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<td>Detroit-562</td>
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100x, Hematoxylin Counterstaining

<table>
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<tr>
<th>EGFR</th>
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<th>KGFR</th>
<th>FGFR3</th>
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