Carcinoma hepatocelular. É importante inibir o IGF-IR: NVP-AEW541 é derivado sintético do NDGA

Possíveis tratamentos para inibir o IGF-1 e ou o IGF-1R
a- Silibinina: diminui o receptor do IGF-1 o IGF-1Rbeta e aumenta muito a proteína carregadora do IGF-1 a IGFBP-3 diminuindo assim a concentração plasmática do IGF-1
b- Ativadores da AMPK (AMP activated protein kinase):
   1- antocianinas: arroz preto (Oryza nigra), groselha preta (Black currant), uva preta, feijão preto, Sinadenium
   2- dieta com restrição de carboidratos com cetose
   3- metformina
c- Colecalciferol: aumenta IGFBP-3
d- Epigalocatequina-galato (inibe IGF-1R)
e- Resveratrol (inibe IGF-1R)
f- Genisteína: inibe IGF-1 e para outros os derivados da soja aumentam IGF-1
g- Inibidores da Angiotensina II (inibe IGF-1R)
h- Inibidores da Aldosterona (inibe IGF-1): Inspra (eplerenone), aldactone (espirolactona)
i- Amiloride: inibe o IGF-1 e o IGF-1R
j- NDGA: ácido nordihidroguaiarético, derivado da Larrea tridentata ou Larrea divaricata, “arbusto de creosoto” sendo conhecida erroneamente como “chaparral”: inibe o IGF1-R . José de Felippe Junior

Blockade of IGF-1 receptor tyrosine kinase has antineoplastic effects in hepatocellular carcinoma cells.

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Abstract
Hepatocellular carcinoma (HCC) is one of the most common cancer-related causes of death worldwide. Due to very poor 5-year-survival new therapeutic approaches are mandatory. Most HCCs express insulin-like growth factors and their receptors (IGF-R). As IGF-1R-mediated signaling promotes survival, oncogenic transformation and tumor growth and spread, it represents a potential target for innovative
treatment strategies of HCC. Here we studied the antineoplastic effects of inhibiting IGF-1R signaling in HCC cells by the novel IGF-1R tyrosine kinase inhibitor NVP-AEW541. METHODS AND RESULTS: NVP-AEW541 induced a time- and dose-dependent growth inhibition in the human hepatoblastoma and hepatocellular carcinoma cell lines SK-Hep-1, Hep-3B, Hep-G2 and Huh-7. Measurement of LDH-release showed that the antineoplastic effect of NVP-AEW541 was not due to cytotoxicity. Instead NVP-AEW541 induced apoptosis as evidenced by both caspase-3 and -8 activation as well as by apoptosis-specific morphological and mitochondrial changes. In addition, nuclear degradation was monitored by DNA-laddering. NVP-AEW541-treatment suppressed the expression of the antiapoptotic proteins Bcl-2 and survivin, while the expression of the proapoptotic protein BAX was stimulated in a dose-dependent manner. Moreover, NVP-AEW541 arrested the cell cycle at the G1/S checkpoint. When NVP-AEW541 was combined with cytotoxic chemotherapy or with a specific epidermal growth factor receptor antibody additive antiproliferative effects were observed. INTERPRETATION: Inhibition of IGF-1R tyrosine kinase (IGF-1R-TK) by NVP-AEW541 induces growth inhibition, apoptosis and cell cycle arrest in human HCC cell lines without accompanying cytotoxicity. Thus, IGF-1R-TK inhibition may be a promising novel treatment approach in HCC.

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