

Figure S1: Characterization of UM-SCC47 and UT-SCC60A sensitive and resistant cells. **(A)** Dose-response curve of UM-SCC47 and UT-SCC60A sensitive and resistant cell (res1 and res2) following 4-days of treatment with increasing concentration of GDC0032 (0-2 μ M) and BYL719 (0-10 μ M), respectively. **(B)** UM-SCC47 and UT-SCC60A sensitive and resistant cells treated for 24 h with DMSO, GDC0032 (500 nM) or BYL719 (2 μ M), respectively, after which cells were lysed. The indicated proteins and phosphorylated proteins were measured using western blot.

UT-SCC60A

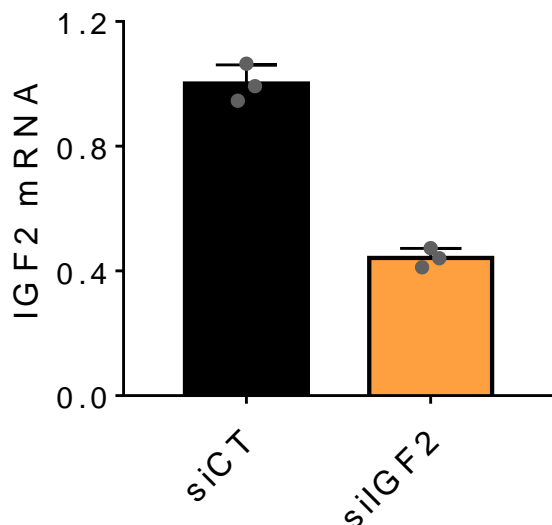


Figure S2: IGF2 silencing using siRNA. RT-PCR analysis measuring IGF2 mRNA levels in sensitive UT-SCC60A following siRNA transfection with scramble RNAi (siCT) or RNAi against IGF2 (siIGF2)

UT-SCC60A

UT-SCC60A Res2

UM-SCC47 Res2

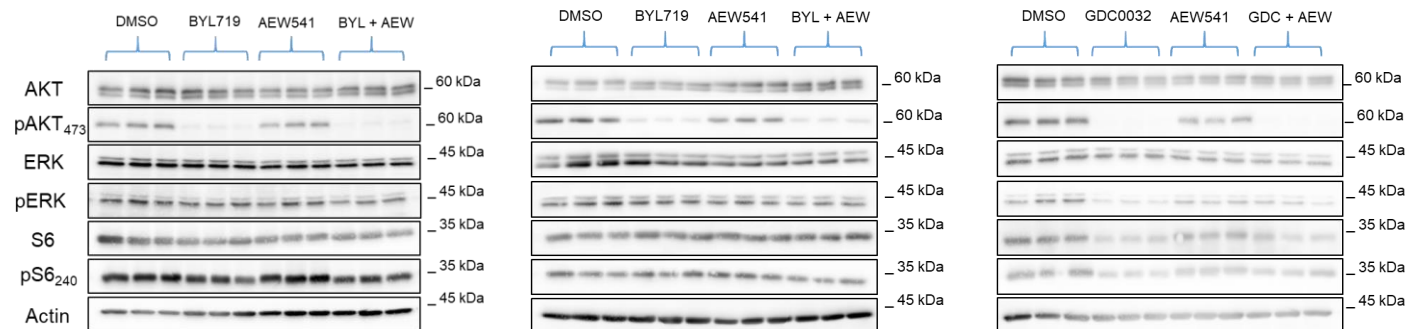


Figure S3: Characterizing of the cellular response of tumor cells to therapy combination. UT-SCC60A sensitive and resistant cells (Res2), and UM-SCC47 resistant cells (Res2) were treated for 4 h with DMSO, BYL719 (2 μ M) or GDC0032 (500 nM), AEW541 (1 μ M) and combination of both drugs, after which cells were lysed. The indicated proteins and phosphorylated proteins were probed using western blot.

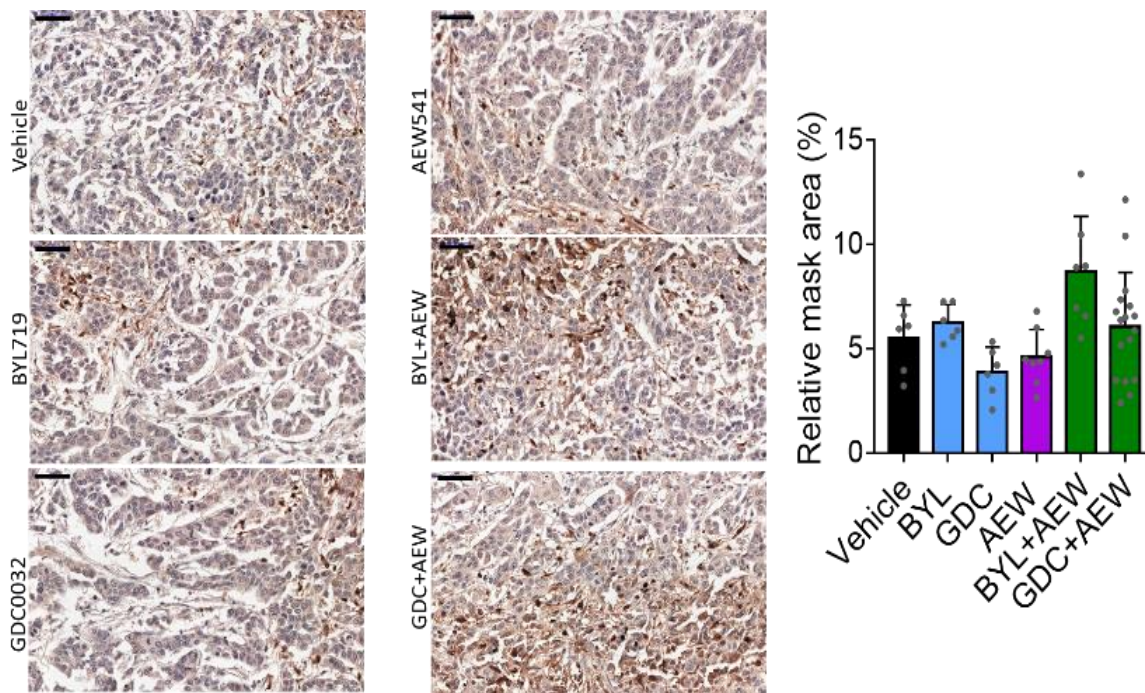
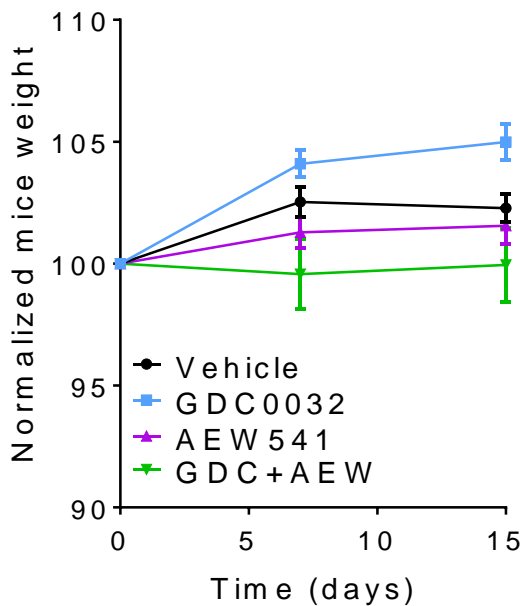


Figure S4: Cleaved Caspase3 staining. PDX^{HPV+} was cultured for 24 h in the presents of DMSO, GDC0032 (500 nM) or BYL719 (2 μ M), AEW541 (1 μ M) and combinations of drugs as indicated, after which tissue was fixed and analyzed using immunohistochemistry. Representative images of immunohistochemistry staining of Cleaved-Caspase3 are presented with quantification. Scale bar: 50 μ m.

CDX-UM-SCC47



PDX-7157

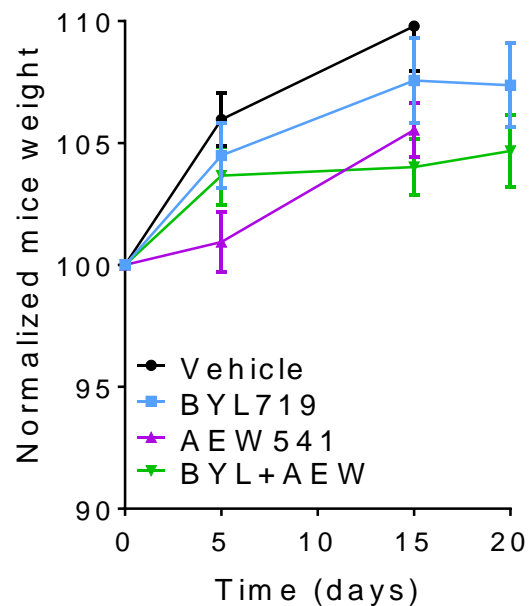


Figure S5: Toxicity of therapy in mice. The weight of NSG mice bearing CDX-UM-SCC47 and PDX-7157 treated as indicated. GDC0032 (10 mg/kg), BYL719 (25 mg/kg), AEW541 (30 mg/kg).

TCGA samples

Expression of IGF2 in HNSC based on Sample types

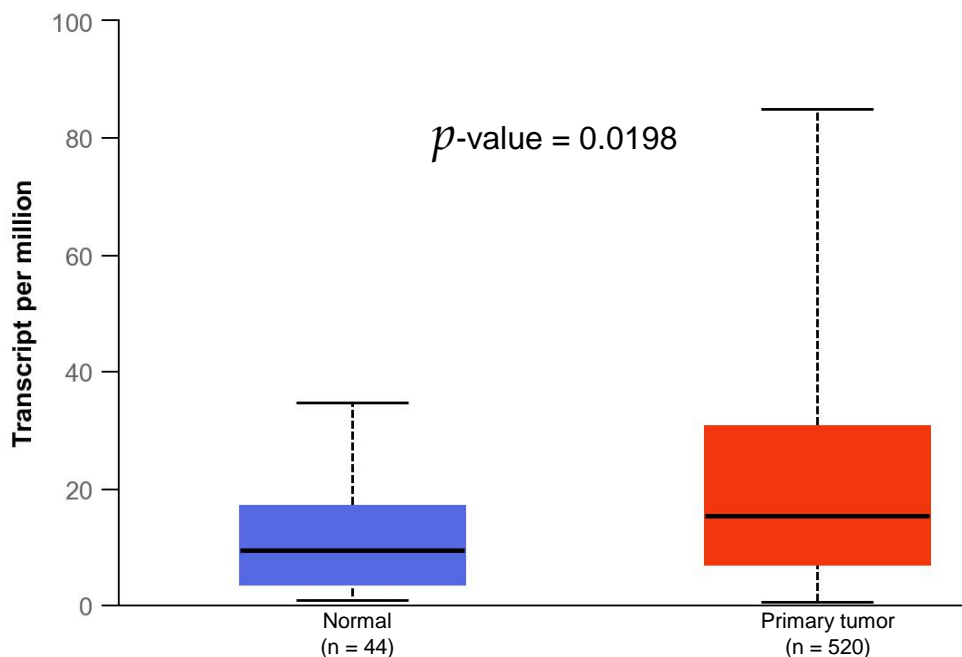


Figure S6: IGF2 expression in HNC patients. TCGA data showing IGF2 expression in HNC patients, compared to normal tissue. Data extracted from [HTTP://ulcan.path.uab.edu](http://ulcan.path.uab.edu)

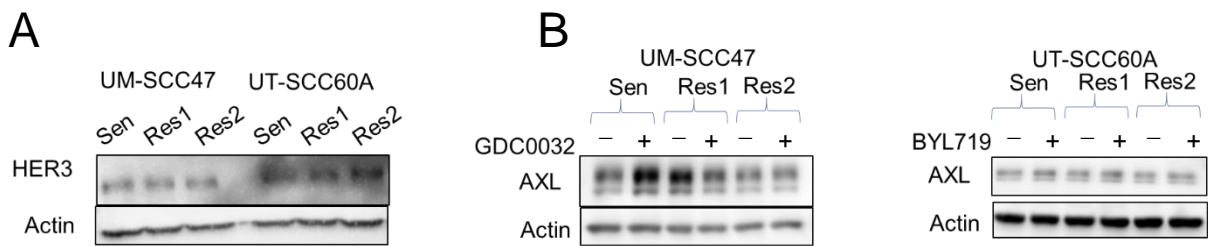


Figure S7: AXL and HER3 expression in sensitive and resistant cells. **(A)** Western blot analysis showing HER3 expression in UM-SCC47 and UT-SCC60A sensitive and resistant cells (Res1 and Res2). **(B)** UM-SCC47 and UT-SCC60A sensitive and resistant cells (Res1 and Res2) were treated with DMSO, GDC0032 (500 nM) or BYL719 (2 μ M) as indicated. The indicated proteins were measured using western blot.

Figure S8: Original Western Blot images.

Figure 5A

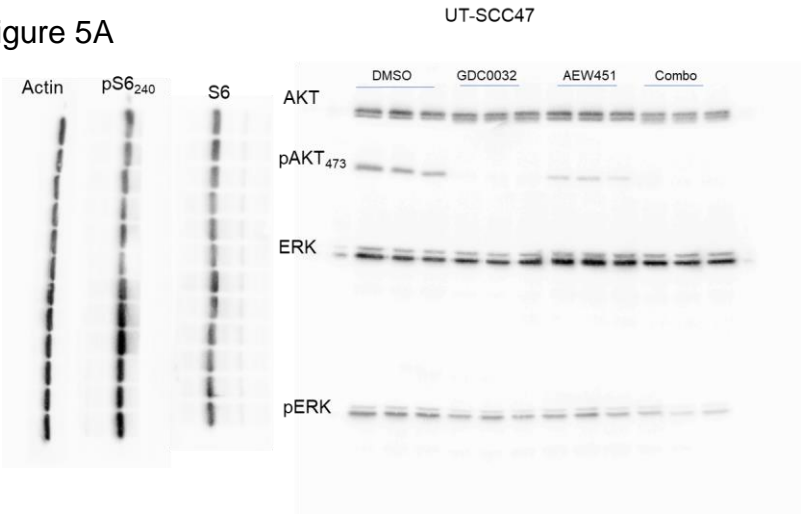


Figure S1B

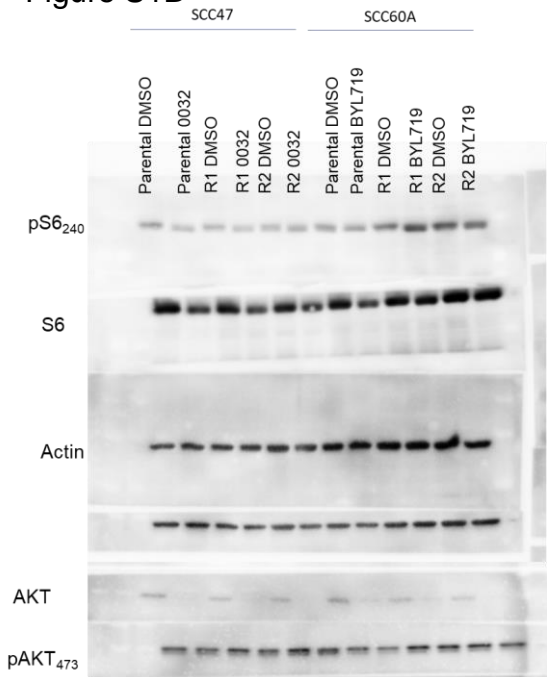


Figure S3

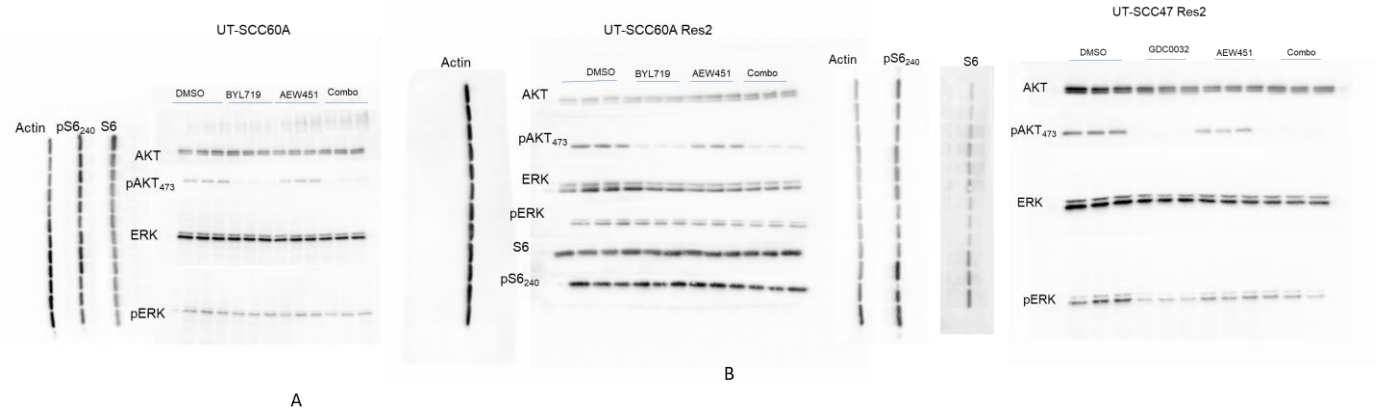


Figure S7

