**Figure Legends**

**Figure S1. Experimental scheme.** Mice were given 4NQO (50ppm) in the drinking water for 8 weeks, after which mice were changed to regular water and followed up for 8 weeks or 16 weeks.

**Figure S2. Immunohistochemical analyses of the E20/p53 mouse.** Expression of p16, p53, E-cadherin, and phospho-S6 were analyzed in lesions of various tumor stages from the E20/p53 mice. Representative stains of these proteins in normal, atypical/dysplastic, and SCC-grade lesions from the E20/p53 mice are shown.

**Figure S3**. **Representative YFP (+) metastatic cells isolated from the lymph node of an E20p53(YFP) double mutant mouse**. ***A***. YFP filter. ***B***. Bright field filter. ***C***. Merge.

**Figure S4**. **Combination index calculation using COMPUSYN indicates a synergy between BYL719 and cisplatin *in vitro* in an E20/p53 SCC cell line, S24-658.**