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# Abstract B79: Evaluation of active hexose correlated compound (AHCC) for the prevention or delay of tumor growth in human cervical cancer xenograft model

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## Abstract

**Purpose**: Active hexose correlated compound (AHCC) is a mixture of polysaccharides, amino acids, lipids and minerals extracted from the culture of the basidiomycete mushroom Lentinula edodes (shiitake) that has been proposed to have many health benefits including both immunomodulatory and anti-tumor effects. In clinical studies AHCC has demonstrated numerous immunomodulating and potential restorative effects on natural killer (NK) cells, macrophages and cytokines. The objectives of this study were to evaluate if daily treatment with AHCC would eradicate human papillomavirus (HPV) 16/18 expression and prevent or delay cervical tumor growth using human xenograft mouse model.

**Methods**: Selected cervical cancer cells, SiHa (HPV 16/18 positive), and C-33A (HPV negative) were treated in vitro with a single dose AHCC 0.42 mg/mL and incubated for 72 hours. In the second study AHCC dose was repeated once every 24 hours for total of seven days. This was followed by a three arm in vivo study in two xenograft cervical cancer mouse models, SiHa (HPV 16/18 positive), and C-33A (HPV negative), in which each cell line had ten mice for the treatment arm, vehicle control arm and no treatment arm. Mice in the treatment arm received 50 mg/kg AHCC in 0.25 mL of sterile water every day for seven days before the injection of the tumor cells and until the completion of the study. Tumors were measured three times per week. After 90 days of treatment, there was a 30 day observation period to evaluate the potential for recurrence of the HPV infection and the impact on tumor growth. At the end of the study, tumors were extracted and RT-PCR was completed on DNA samples from extracted protein to evaluate the HPV expression.

**Results**: In vitro treatment with a single dose of AHCC for 72 hour incubation suppressed HPV expression in the first 24 hours but then HPV expression recovered by 48 hours. However, with continuous in vitro exposure, sustained HPV suppression was observed. In the in vivo animal studies, expression of HPV was eradicated with once daily AHCC dosing for 90 days and no detection of HPV expression was sustained after 30 days off treatment. In addition, AHCC daily treatment was associated with a 15.9% decrease in SiHa (HPV 16/18 positive) tumor growth compared to the untreated control ($P < 0.05$). AHCC did impact the growth rate of the C-33A (HPV negative) tumors.

**Conclusion**: In conclusion, these data suggest daily dosing of AHCC will eradicate HPV 16/18 infections and may have a role in the prevention of HPV-related cervical cancer. Furthermore, there is a potential for the addition of AHCC to primary treatment regimens for cervical cancer, which may potentially improve response rates and prevent recurrence. A confirmatory pilot study in HPV positive women is underway.

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