

consensus guideline using MR images. The goal of the current project is to expand on the previous atlas by including CT-based contours without and with PET±MRI registrations, to add common and complex scenarios, and to ask about simulation and treatment planning techniques.

Methods 28 experts contoured 3 cases, first on a non-contrast CT simulation scan, then with registered diagnostic images. The cases included (1) FIGO IIIC1 with a bulky tumor and a vaginal metastasis, (2) FIGO IIB with calcified uterine fibromas, and (3) FIGO IIIC2 with large lymph nodes. The contours were analyzed for consistency using an expectation-maximization algorithm for simultaneous truth and performance level estimation (STAPLE) with kappa statistics as a measure of agreement.

Results Analysis of the contours showed considerable agreement between experts in each of the cases with kappa statistics of 0.67–0.72. For each case, use of diagnostic PET±MRI was associated with an increase in volume. The largest increase was in the CTV primary for Case 2 (20% increase in average volume, 64% increase in STAPLE estimate volume), which may be due to variance in registration priorities. For the third case, 92.9% of participants increased their CTVs based on the addition of the PET scan.

Conclusion/Implications Here we show the value as well as the challenges of using co-registered diagnostic imaging. The main areas of variance remain determining the superior extent of CTV coverage, coverage of the mesorectum, simulation and planning protocols.

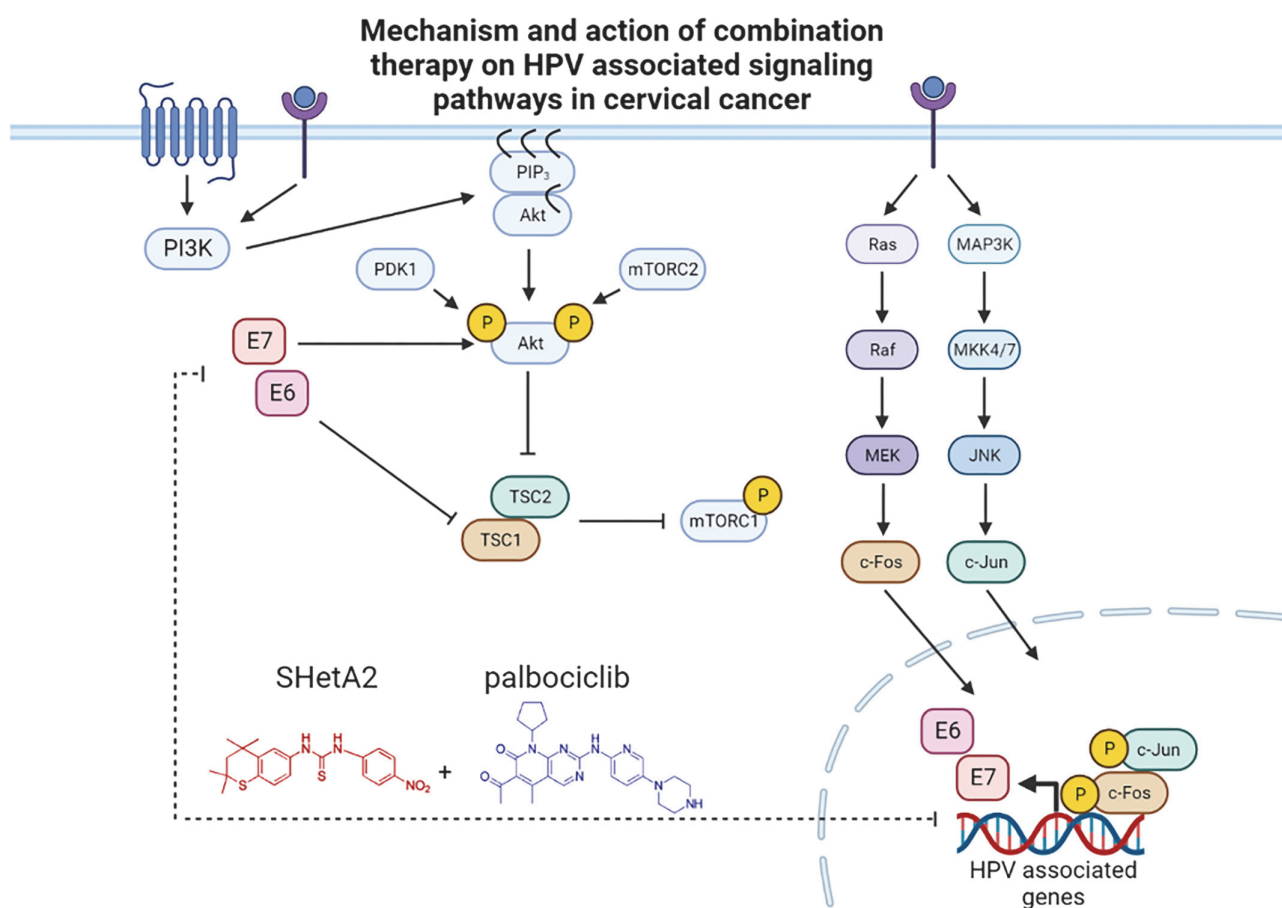
EP060/#474

POTENTIAL ANTI-HUMAN PAPILLOMAVIRUS THERAPEUTICS: MECHANISM AND ACTION OF COMBINATION THERAPY IN CERVICAL CANCER CELLS

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Introduction Cervical cancer is the most common malignancy among women caused due to persistent high-risk human papillomavirus (HR-HPV) infection. The carcinogenesis of HPV is attributed to its early viral onco-proteins E6/E7, which increase cellular proliferation and survival mechanisms by interacting with cellular survival pathways including AKT/mTOR kinases, and activator protein-1 (AP-1; Jun/Fos) and E2F transcription factors. Cervical cancer cells become addicted to E6/E7 expression and undergo apoptosis when E6/E7 are disrupted. Previously, we demonstrated functional synergism between the HSP70-inhibitor SHetA2 and the CDK4/6-inhibitor palbociclib in cervical cancer. However, this synergism's mechanism was not explored with respect to targeting HPV E6/E7 onco-proteins. Hence, the objective of this study was to evaluate the impact of SHetA2 and palbociclib alone,



Abstract EP060/#474 Figure 1

and in combination, on HPV E6/E7 and associated survival pathways.

Methods Individual or combination treatments of SHetA2 and palbociclib in HR-HPV positive cervical cancer cell lines were evaluated for specific mRNA and protein modulation by western blotting, quantitative polymerase chain reaction (qPCR) and immunofluorescence.

Results We demonstrated for the first time that combination treatment of SHetA2 and palbociclib causes significant down-regulation of E6/E7 viral proteins and up-regulation of c-Jun and c-Fos host proteins (figure 1). The effects of the combination treatment were greater than either single treatment. Consistent with the down-regulation of E6/E7, SHetA2 impacted AKT/mTOR phosphorylation.

Conclusion/Implications This study identifies potential anti-HPV preventative and therapeutic strategies using combination therapy of SHetA2 and palbociclib. Future research will study SHetA2 and/or palbociclib mechanisms in pre-clinical models and conduct clinical trials of HR-HPV-driven pre-cancerous lesions.

EP064/#761

A POTENTIAL THERAPEUTIC METHOD FOR UTERINE CERVICAL CANCER BY ARSENIC TRIOXIDE VIA INDUCING CARBONYL REDUCTASE 1 EXPRESSION

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Introduction Carbonyl Reductase1 (CBR1) has been reported to be involved in cancer progression. Recently, we reported that CBR1 overexpression repressed malignant behavior of uterine cervical cancer (CC) via epithelial mesenchymal transition. Arsenic trioxide (ATO) is known as an effective chemotherapeutic agent for acute promyelocytic leukemia with a low toxicity. ATO is reported to upregulate CBR1 expression by activating the transcription factor activator protein-1. In this study, we investigated the effect of ATO on the malignant behavior of CC via CBR1 expression.

Methods We investigated the effect of ATO on malignant behavior in CC cell lines (SiHa and SKGII) in vitro by Cell proliferation Assay, Wound healing Assay, and Invasion Assay, and using the mouse models transplanted with CC cells subcutaneously.

Results ATO increased CBR1 expression dose-dependently in the cultured cells. ATO significantly inhibited the activities of cell proliferation, invasion, and migration. 1.0×10^6 cells of SiHa or SKGII were subcutaneously injected into the back of immunodeficient mice (Bulb-C), and 5.0 mg/kg ATO were given intravenously every two days after the tumor development on the host mice. Seven weeks after injection of ATO, the tumor growth was significantly inhibited in SiHa and SKGII ($P < 0.05$). The CBR1 expression level in the tumor treated with ATO was significantly higher than that of control.

Conclusion/Implications ATO inhibited the cancer growth and malignant behavior with increased CBR1 expression in CC cells. This result suggests that ATO can be the novel agent targeting CBR1 in CC treatment.

EP066/#602

LESS THAN WHOLE UTERUS IRRADIATION FOR LOCALLY ADVANCED CERVICAL CANCER MAINTAINS LOCOREGIONAL CONTROL AND DECREASES RADIATION DOSE TO BOWEL

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Introduction Current consensus guidelines for definitive cervical cancer intensity modulated radiation therapy (IMRT) recommend inclusion of the entire uterus within the clinical target volume, however this is controversial. We aimed to evaluate outcomes of patients with cervical cancer who were treated with less than whole uterus irradiation.

Methods We identified 112 patients with FIGO Stage IB-IVA cervical cancer treated definitively with concurrent chemoradiation, including IMRT and brachytherapy, from 2010 to 2022 at a single institution where the practice was to include the gross cervix tumor plus additional margin. Local, regional, and distant recurrences were analyzed using competing risk methods, and a Wilcoxon rank sum test was performed to assess differences in bowel dose based on the proportion of the uterus included in the planning target volume (PTV).

Results With a median follow up time of 30.1 months, the 2-year cumulative incidence of local recurrence was 5%. Compared with patients who had $\geq 90\%$ of the uterus included in the PTV ($n=35$), patients who had $< 90\%$ ($n=77$) of the uterus included in the PTV had significantly lower bowel D200cc ($p < 0.01$). The cumulative incidence of locoregional failure was not significantly different between the two groups. Only one patient experienced an isolated local failure and their PTV included $\geq 90\%$ of the uterus.

Conclusion/Implications Including less than the whole uterus for definitive cervix cancer IMRT does not compromise locoregional control. Less than whole uterus irradiation should be considered for cervix cancer patients to decrease bowel dose and treatment-related toxicity.

EP067/#487

EFFICACY OF INTERSTITIAL BRACHYTHERAPY FOR THE PATIENT WITH LOCALLY ADVANCED CERVICAL CANCER

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Introduction Locally advanced cervical cancers with bulky and asymmetrical tumors treated with intracavitary brachytherapy are more likely to relapse in a few years due to insufficient dose prescription to the entire tumor, resulting in poor prognosis. The purpose of this study is to evaluate the efficacy and safety of 3-dimensional (3D) image-guided multi-catheter interstitial brachytherapy, which could increase flexibility in dose distribution for patients with bulky (≥ 4 cm) and high-risk, stage IIB-IVA advanced cervical cancer.

Methods Twenty one patients who underwent concurrent chemoradiotherapy with multi-catheter interstitial brachytherapy