index (CI) using Chou-Talalay method. Clinical information was extracted for correlation.
Results 62.5% (5/8) of serous EC PDX tumors had GIS≥42 while only 19.2% (5/26) of non-serous ones did. Synergy (CI<1.0) between rucaparib and SN38 was demonstrated in 85.7% (6/7) of serous EC PDX ex vivo 3D cell culture experiments, but only 62.5% (10/16) of non-serous ones. 66.7% (6/9) of serous EC primary patient 3D cell culture experiments also showed synergy.
Conclusion/Implications Most serous EC PDX tumors had high GIS, consistent with HRD, compared to a minority of non-serous histologies. Combination therapy demonstrated synergy in almost all serous and most non-serous EC PDX models. Additional studies including more tumors and in vivo correlation are needed to assess the predictive value of GIS on synergy between rucaparib and SN38.

PR046/#280 THE GENOMIC LANDSCAPE OF DISTANT METASTATIC ENDOMETRIAL CANCER

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Introduction While the genomic landscape of untreated primary endometrial carcinoma (EC) is well characterized, the molecular underpinnings of distant metastatic EC are poorly understood. We sought to define genomic alterations associated with distant metastatic EC.
Methods We obtained sequencing data from distant metastatic ECs from a total of 1888 ECs subjected to a clinical tumor-normal sequencing panel between 8/2013 and 6/2020; these metastatic ECs were compared against 711 primary ECs using appropriate statistical analyses.
Results One hundred thirty-seven ECs met the study inclusion criteria, with distant metastases in the lung (n=66, 48%), liver (n=21, 15%), soft tissue (n=15, 11%), distant lymph nodes (n=15, 11%), gastrointestinal tract (n=10, 7%), central nervous system (n=5, 4%), bone (n=4, 3%), and renal system (n=1, 1%). The majority of distant metastases were of copy number (CN)-high (42%) or CN-low (39%) molecular subtype; 18% were microsatellite instability (MSI)-high and 1% were of POLE molecular subtype. Distant EC metastases were significantly more chromosomally unstable compared with primary ECs (p<0.0001) and were enriched in AKT1, CTNNB1, ANKRD11, and ZFHX3 mutations. Clinically actionable alterations, particularly tumor mutational burden (TMB) ≥10 mut/Mb and MSI-high status, were significantly less common in metastatic compared with primary ECs (4% vs 29%; p=0.017). Epigenetic, PI3K, and TP53 pathways were the most commonly altered pathways among all anatomic sites.
Conclusion/Implications Compared with primary tumors, distant metastatic ECs exhibited increased chromosomal instability but decreased hypermutator phenotypes. Exploitation of genetic differences to understand the pathogenesis of metastatic EC is necessary to develop biomarkers for targeted therapy.

AS05. Fertility/Pregnancy

PR047/#570 UTERINE TRANSPOSITION IN THE TREATMENT OF INVASIVE CERVICAL CANCER FOR PRESERVE FERTILITY

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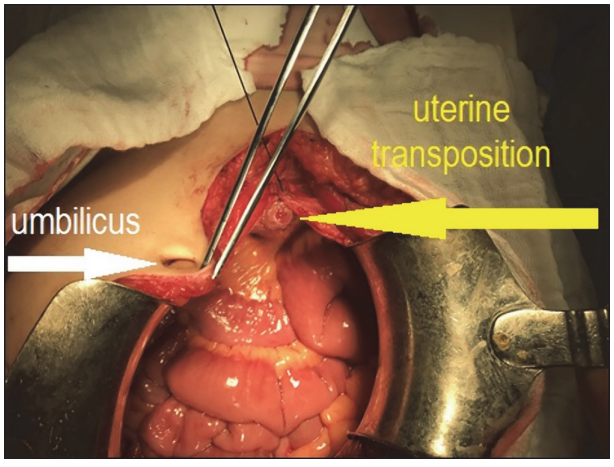
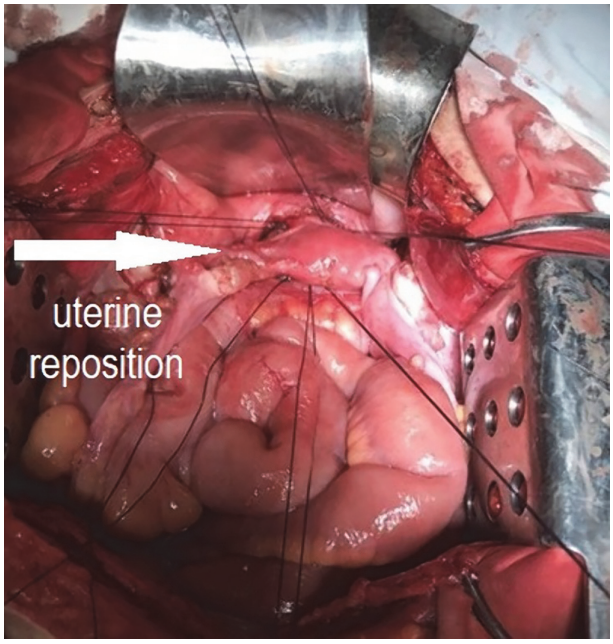
Introduction Indications for a radical trachelectomy can be significantly expanded if an adjuvant concurrent chemoradiotherapy can be provided. These conditions can be achieved by the uterine transposition which must be done during the period of radiotherapy. When the radiation treatment is completed, the uterus can be repositioned back to the pelvic.
Methods Our research has included 11 patients with stage Ib1-IIb cervical cancer. Median of their age is 29 year old. At the first step of treatment, 2–3 courses of chemotherapy were carried out. At the second step radical trachelectomy (Piver type III) with uterine and ovarian transposition were done (photo 1). The oncological stages of operation corresponded to a routine radical trachelectomy. Paraumbilically uterine transposition created conditions for performing the radiotherapy. The third step included a concurrent chemoradiotherapy. On the next step of treatment uterine reposition with uterovaginal anastomosis was conducted (photo 2). Today all the patients has no sign of recurrence and may start to realize the pregnancy.
Results The median observation is 23,4 months so far. All our patient's menses have been recovered. No one has any signs of recurrence. Three of them are preparing to the in vitro fertilization.
Conclusion/Implications The uterine transposition enhanced limits of treatment for patients with stage Ib1-IIb cervical cancer and makes feasible to provide a radiotherapy according to



Abstract PR047/#570 Figure 1



Abstract PR047/#570 Figure 2

the prescribed standards and, haven't negative effect for ovarian function and menses. It is very important to continue and carrying out research which make possible to preserve fertility for patients with cancer.

AS07. Global health/economic challenges

PR048/#466

COST-EFFECTIVENESS ANALYSIS OF SINGLE-DOSE OR 2-DOSE OF BIVALENT, QUADRIVALENT, OR NONAVALENT HPV VACCINE IN A LOW/MIDDLE INCOME COUNTRY SETTING

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Introduction To evaluate the health impact and economic benefits of one dose or two doses of 2-valent (2vHPV), 4-valent (4vHPV), or 9-valent (9vHPV) HPV vaccine compared to no vaccination along with primary HPV testing in a low/middle income country setting, specifically in Thailand.

Methods A Markov model was used to simulate HPV infection and cervical cancer in a cohort of 100,000 12-year-old HPV-naive girls. The study compared nine strategies: one dose and two doses of 2vHPV (Cervarix®), 2vHPV (Cecolin®), 4vHPV (Gardasil®), 9vHPV vaccine (Gardasil9®), and no vaccination. Main outcome measure was quality-adjusted life year (QALY) of each strategy. Incremental cost-effectiveness ratios (ICER) were estimated over a lifetime horizon, univariate and probabilistic sensitivity analyses were conducted for uncertain variables in different scenarios.

Results In the base case scenario, all vaccination programs resulted in 41,298–71,057 QALYs gained with a cost saving of 14,914,186–19,821,655 USD compared to no vaccination. Based on the incremental analysis, two doses of 9vHPV vaccine was the most cost-effective strategy with an ICER of 406 USD/QALY. Sensitivity analysis showed that the probability of being cost-effective for two doses of 9vHPV vaccine was 80%, and uncertainty around the costs of vaccination and vaccine efficacy caused the largest variation in the cost-effectiveness findings.

Conclusion/Implications Two doses of 9vHPV vaccine along with a primary HPV test for screening program represent the most cost-effective option for school-based HPV vaccination of 12-year-old girls in Thailand, with a lower willingness to pay of one time the per-capita GDP. This finding provides important evidence to policymakers for cervical cancer prevention.

AS08. Gynecologic pathology/cytology and disease pathogenesis

PR049/#741

IMPROVED RISK PREDICTION IN HPV-ASSOCIATED ENDOCERVICAL ADENOCARCINOMA THROUGH ASSESSMENT OF BINARY SILVA PATTERN-BASED CLASSIFICATION: INTERNATIONAL MULTICENTER RETROSPECTIVE STUDY OF THE INTERNATIONAL SOCIETY OF GYNECOLOGICAL PATHOLOGISTS

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Introduction Endocervical adenocarcinomas (EACs) are neoplasms associated with diverse pathogenesis, morphology, and clinical behavior. The Silva pattern-based classification categorizes HPV-associated EACs based on the morphology of the invasion and predicts lymph node metastasis and recurrence. Traditionally the Silva classification was a three-tier system (pattern A, B, and C). A two-tier/binary system has recently been proposed whereby tumors are classified into low risk (pattern A/pattern B without lymphovascular invasion (LVSI)) and high risk (pattern B with LVSI/pattern C). Our aim was to develop a prognostic model for surgically treated FIGO stage IA2-IB3 EACs that incorporates patient age, LVSI, FIGO stage and three- and two-tier Silva systems.

Methods The International Society of Gynecological Pathologists (ISGyP) established a multicenter consortium to pool de-identified individual patient data for patients with HPV-associated EACs. All participating pathologists completed mandatory online training.

Results Our cohort comprised 792 HPV-associated EACs (table 1). On multivariate analysis a binary Silva system was