(n=26) received a single dose of local therapy with 85% TCA while the second group (n=27) was treated on two separate occasions with a two-week interval. Two participants (one in each group) were lost to follow-up. At the two-month follow-up after, a colposcopy-guided biopsy was performed for all patients and the pathological specimens were studied by a single experienced pathologist to determine the post-intervention grading of CIN

Results Two groups were comparable in terms of age and base-line lesion grading, as CIN 1 lesions comprised the majority of cases (54%), followed by CIN 2(37%). While our sample was a poor representative of CIN3 lesions (7%), no significant difference was noticed between the single and twice TCA treated groups with a response rate of 52% and 54% respectively (either complete remission to normal histology or regression to any low-grade lesion). Either separate analysis (with respect to the base-line grading within each treatment group) or combined analysis (regardless of CIN sub-group) could not generate any statistical significance. The second dose of TCA did not increase the frequency of reported adverse events

Conclusion The second dose of topical 85% TCA does not seem to increase the CIN response rate more so than its single dose. However, further controlled clinical trials with larger samples are warranted to verify current findings. The use of TCA was not limited by any major side effect, therefore, the potential to achieve an increased efficacy with more frequent TCA applications is appealing

2022-RA-260-ESGO UM-6 INDUCES AUTOPHAGY AND APOPTOSIS VIA THE HIPPO-YAP SIGNALING PATHWAY IN CERVICAL CANCER

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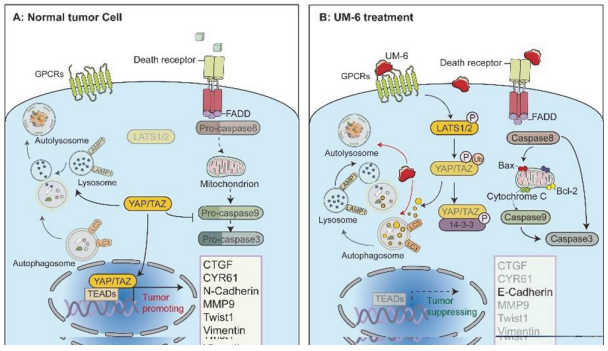
Introduction/Background The clinical application of Melittin is limited by its non-specific cytotoxicity and hemolytic activity. Here, we synthesized a novel antineoplastic peptide UM-6 based on melittin and explored the mechanism related to its anti-proliferation and metastasis on cervical cancer.

Methodology The function of UM-6 on proliferation, invasion, and migration was assessed by MTT assay, colony formation assay, transwell assay, and 3D invasion assay. To identify the anti-tumor molecular mechanism of UM-6,we used flow cytometry, immunoprecipitation, real-time quantitative PCR, dual-luciferase reporter assay, Western Blot, immunofluorescence, and immunohistochemistry. Finally, mouse xenograft models were constructed to further investigate the role of UM-6 in inhibiting cervical cancer proliferation and metastasis in vivo.

Results Firstly, UM-6 inhibits the proliferation of cervical cancer cells and less cytotoxic to normal epithelial cells in vitro; Secondly, UM-6 inhibits the invasion and migration of cervical cancer cells in vitro; Thirdly, UM-6 induces apoptosis and autophagosome accumulation in cervical cancer cells; Concretely, UM-6 promotes autophagic flux by promoting autophagosome degradation, and blocking autophagy reverses UM-6-induced cell death. Thus, we discovered that UM-6 inhibited cervical cancer cell viability while also inducing apoptosis (type I cell death) and autophagy-dependent cell death (type II cell death). UM-6 triggers the Hippo signaling pathway and promotes cytoplasmic retention and phosphorylation-dependent degradation of YAP; inhibits YAP-TEAD binding and reduces transcriptional activity, thereby suppressing the expression of downstream target genes. Injection of UM-6 in mice can significantly inhibit the growth of xenograft tumors without significant toxicity, and greatly reduce the number, volume, and burden of abdominal tumors in the metastasis model driven by cervical cancer cell lines.



Abstract 2022-RA-260-ESGO Figure 1

Conclusion UM-6 has the potential to serve as a new anticancer drug candidate. As a regulator of apoptosis and autophagy, UM-6 also regulates the Hippo/YAP pathway, providing a new avenue for efficient anti-cervical cancer therapy.

2022-RA-262-ESGO PREDICTORS OF ONCOLOGIC OUTCOME IN RECURRENT CERVICAL CANCER PATIENTS RECEIVING PHASE 1 CANCER THERAPY

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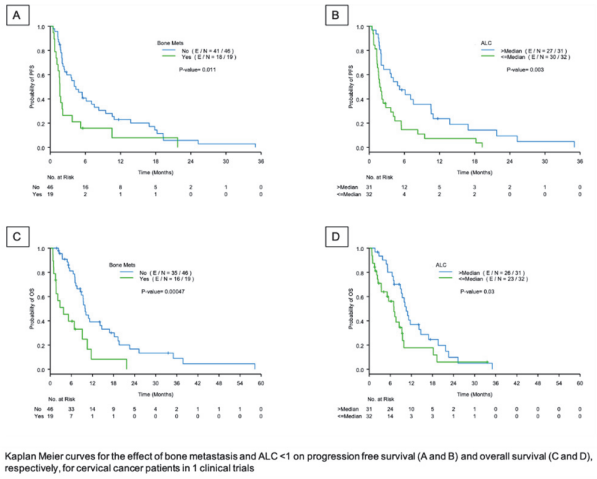
10.1136/ijgc-2022-ESGO.16

Introduction/Background Few treatment options exist in recurrent cervical cancer, which makes phase 1 clinical trials a compelling option. In order to identify candidates for referral, we analyzed factors predictive of response and survival in cervical cancer patients referred to phase 1 trials.

Methodology Cervical cancer patients who received at least 1 cycle of a phase 1 agent between 2014–2022 were retrospectively reviewed. Clinical and pathologic data were abstracted, Log-rank test was used to test the difference in progression-free survival (PFS) and overall survival (OS). Multivariable regression analysis was performed for predictors of response and survival.

Results 65 patients met eligibility. At trial entry, patient characteristics included the following median (range) values: age 41 years (20,74), 3 prior therapies (1,7), and 5-month progression-free interval before trial (1,32). 67.7% had squamous carcinoma, 27.7% adenocarcinoma, 4.5% other. The rate of distant metastasis was 84.6%. The most common alterations included *PIK3CA* (46.5%), PDL1+ (46.2%), EPH (30.0%),

and CREBBP (23.1%). 23.1% received a prior check point inhibitor. The phase 1 trials were immunotherapy (58.5%) and targeted therapy (41.5%). In all, objective response rate was 10.8%, median PFS 3.6 months, and OS 9.3 months. On multivariable analysis of significant covariates, factors at study entry that were associated with worse survival were the presence of bone metastasis (PFS 1.6 vs 4.4 months, HR 2.8; OS 3.8 vs 10.0 months, HR 3.9; both p<0.001), and absolute lymphocyte count (ALC) <1k/µl (PFS 1.8 vs 5.2 months, HR 2.9; OS 7.0 vs 10.6 months, HR 3.2; both p<0.0009). Other factors associated only with negative OS were Hb<11g/dl, absolute neutrophil count>4.7k/µl, and current or former smoking status. The rate of grade 3+ treatment-related adverse events was 16.9%.



Kaplan Meier curves for the effect of bone metastasis and ALC <1 on progression free survival (A and B) and overall survival (C and D), respectively, for cervical cancer patients in 1 clinical trials

Abstract 2022-RA-262-ESGO Figure 1

Conclusion The presence of bone metastasis and ALC below normal range at phase 1 study entry portend poor survival in recurrent cervical cancer patients.

2022-RA-265-ESGO A CLINICAL STUDY ON THE APPLICATION OF 3D PRINTING TEMPLATE IN BRACHYTHERAPY OF PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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10.1136/ijgc-2022-ESGO.17

Introduction/Background To explore the clinical application of 3D-printing minimally invasive-guided template in brachytherapy of patients with locally advanced cervical cancer.**Methodology** From May 2016 to December 2018, 59 patients with locally advanced cervical cancer with clear pathological diagnosis and initial treatment. All patients were treated with radical radiotherapy, intensity-modulated radiotherapy was carried out with a radiation dose of 45 Gy in 25 fractions. The included patients were randomly divided into 2 groups. In the template group, 29 patients assisted by 3D-printing templates to place intrauterine tubes and implant for insertion of needles. In the free implantation group, 30 patients were assisted with free-hand implanted intrauterine tubes and implant needles. All patients underwent CT to adjust the position and depth of the insertion needle, and the final CT image was transmitted to the Oncentra brachytherapy planning system, to outline the target area and organs at risk, make treatment plans, and perform treatment.

Results A total of 283 times of combination of intra-luminal and interstitial insertion radiotherapy were undertaken, including 141 times in template group and 142 times in free insertion radiotherapy. Importantly, D_{90} of HR-CTV and IR-CTV in the template group were significantly higher than those in the free implantation group (P<0.05). D_{2cm3} of bladder, rectum and sigmoid colon was significantly reduced (P<0.05). The incidence of radiation cystitis and radiation proctitis was 14.3%and 17.9%lower in the template group than in the free implantation group.Therefore, the incidence of grade 1, 2 and 3 acute radiation proctitis in the template group was noticeably lower than that in the free transplantation group (P<0.05).

Conclusion For large-block or eccentric cervical cancer, application of the 3D-printing template in brachytherapy of patients with locally advanced cervical cancer can reflect its dose-based advantages, associating with a remarkable reduction of patients' adverse reactions and a satisfactory therapeutic effect.

2022-RA-368-ESGO POTENTIAL ROLE OF PARA-AORTIC LYMPH NODES DISSECTION IN EARLY-STAGE CERVICAL CANCER

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10.1136/ijgc-2022-ESGO.18

Introduction/Background Standard treatment for early-stage cervical cancer patients is radical hysterectomy (RH) with pelvic lymphadenectomy. Even in the absence of pelvic lymph nodes involvement, para-aortic lymph nodes (PAN) may include the first draining nodal metastasis, setting survival rates at 20–45%. Primary aim of our review was to investigate whether PAN sampling has an impact on metastases detection and/or disease recurrence in early-stage cervical cancer.

Methodology We systematically explored 4 search engines to establish eligible studies: PubMed, EMBASE, Scopus, and Cochrane Library. We adopted the following string of idioms: *'Uterine Cervical Neoplasms'[Mesh]) AND 'Lymph Node Excision'[Mesh] early-stage AND para-aortic*. We focused on patients with IB1-to-IIA1 stages of cervical cancer who underwent PAN sampling.

Results According to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), full-text studies assessed for eligibility were 9 (Table 1). Matsuo et al. demonstrate that early-stage cervical cancer is associated with PAN positivity in 1.2% of patients ($p < 0.001$) and with recurrence of disease in 2.7% of patients ($p < 0.001$) in 62.2 months on average. In Li et al. prospective trial, neither patient with stage I developed PAN positivity nor para-aortic recurrence, with an overall recurrence-free survival rate of 100% during a median follow-up (FU) of 38 months. On the contrary, Barquet-Muñoz et al. identified more elevated rates of PAN positivity (35%) and disease recurrence (35%) in a median FU time of 32.2 months. Those data positively correlate with stage of disease ($p < 0.001$). Ouldamer et al. do