Importance of Early Initiation of Treatment to Avoid Upstaging in Locally Advanced Cervical Cancer

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Introduction
Locally advanced cervical cancer (LACC) is a public health problem. Objectives: Determine importance of initiation of treatment of LACC in limited-resource settings. Evaluate the concordance between CT and PET/CT for FIGO 2018 staging.

Methods
Retrospective analysis of 175 patients with LACC was performed in a national reference center. FIGO 2018 staging was established by clinical evaluation and CT scan. PET/CT was requested when CT was highly suspicious of more advanced disease or when initiation of treatment was delayed. Descriptive and inferential statistics, Cohen kappa index and ROC curve were performed.

Results
Population analyzed was Mexican with median age at diagnosis 47 years. Most common FIGO stage by clinic evaluation was IIIB (43%), by CT was IIIC1 (46%), and IIIC1 (43%) by PET/CT. Concordance of CT with PET/CT within 25 days of initial study was substantial (k=0.719, p = 0.0001) and after 25 days with moderate agreement (k = 0.468, p = 0.0001). Time to upstage was 25 days by ROC (AUC 0.763, p = 0.0001). FIGO IV was 9.2% with CT against 20.6% with PET/CT.

Conclusion/Implications
Image studies make FIGO 2018 in cervical cancer more accurate. PET/CT in not accessible and is expensive for the general population in limited resource settings. According to our results, we can rely on the initial staging with CT within 25 days from diagnosis to initiation of treatment, after this period, upstage must be considered and a more accurate image study such as PET/CT might be recommended to reconsider the therapeutic plan and prognosis.

Pathologic Response to Hypofractionated Chemoradiation in Locally Advanced Cervical Cancer

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Introduction
Standard treatment for locally advanced cervical cancer (LACC) is chemoradiotherapy, in limited resource settings hypofractionated treatment might be an option. Objectives: Determine pathologic response to hypofractionated external concurrent chemoradiation followed by surgery in comparison to standard treatment in LACC.

Methods
Fifty-nine patients with LACC, as part of a clinical trial, were evaluated after being allocated to standard treatment (45gy in 25 fractions) (29 patients) or Hypofraction treatment (37.5Gy in 15 fractions) (30 patients) followed by a type C1 radical hysterectomy and pelvic node dissection. Pathologic response to treatment was evaluated. Descriptive and inferential statistics, chi-square and multivariable analysis with logistic regression were performed.

Results
In the standard external chemoradiotherapy group, complete pathology response was 22% (13 patients), partial response 5.1% (3 patients), microscopic disease 22% (13 patients). The hypofraction group, complete pathology response was 20.3% (12 patients), partial response 3.4% (2 patients), microscopic disease 27.1% (16 patients) (p= 0.834). Compared by histology, squamous cell carcinoma had complete response in 38% (19 patients), partial response 2% (1 patient), while adenocarcinoma with complete pathology response in 4% (2 patients), partial response 2% (1 patient) (p=0.296), independently to treatment arm. In the multivariable analysis, treatment was not an independent factor for pathologic response OR 0.954 (p=0.938).

Conclusion/Implications
Hypofractionation seems to be as effective, in relation to pathologic response, as standard...
treatment and could be implemented where economic limitations are important or patients have to travel long distances. More prospective studies are needed.

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**MULTI-OMICS CHARACTERIZATION OF CELLULAR STATE DIVERSITY AND BIDIRECTIONAL TUMOR-STROMA/IMMUNE INTERACTIONS IN CERVICAL SQUAMOUS CELL CARCINOMA**

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**Introduction**

Cervical cancer ranks as the fourth leading cause of cancer-related deaths among women, with low response rates to immune-checkpoint blockade (ICB).

**Methods**

Here we conducted a multidimensional analysis encompassing single-cell RNA-seq (scRNA-seq), spatial transcriptomics, and spatial proteomics, combined with genetic and pharmacological perturbations to systematically develop a high-resolution and spatially-resolved map of intra-tumoral expression heterogeneity in cervical squamous cell carcinoma (CSCC).

**Results**

Three context-specific tumor states (Epithelial-cytokeratin (Epi-Krt), epithelial-immune (Epi-imm) and epithelial senescence (Epi-Sen)) that recapitulate squamous differentiation substantially alter the tumor immune microenvironment (TIME). Bidirectional interactions between Epi-Krt malignant epithelial cells and MMP11 CAF form an immune exclusionary microenvironment through TGFβ pathway signaling mediated by FABP5. Epi-Imm malignant epithelial cells and NK/T cells interact bidirectionally through interferon signaling. Notably, preliminary analysis of the NACI clinical trial (NCT04516616) demonstrated neoadjuvant chemotherapy (NACT) induce a state transition to Epi-Imm with the extent of this transition being associated with pathological complete remission (pCR) to subsequent ICB treatment.

**Conclusion/Implications**

These findings provide a comprehensive and nuanced understanding of cellular state diversity and have significant implications for developing novel therapeutic strategies in CSCC and potentially other squamous cancers.

**CD112 PROMOTES THE PROGRESSION OF CERVICAL CANCER THROUGH SLC7A11/GPX-4 PATHWAYS**

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**Introduction**

Expression of the immunoglobulin superfamily member CD112 was increased in multiple malignancies. Importantly, its expression was observed in both PD-L1negative and positive tumors. However, the role of CD112 in tumorigenesis and tumor development in cervical cancer has not been elucidated.

**Methods**

The expression of CD112 in cervical cancer tissues was detected using immunohistochemistry (IHC) and gene expression profiling. CCK-8, edu tests, wound healing and migration assays were used to assess the biological effects of CD112 overexpression and knockdown. Furthermore, proteomic analysis revealed the potential mechanism of CD112 in cervical cancer.

**Results**

CD112 is expressed at high levels in cervical cancer tissues and is negatively correlated with the level of infiltrating CD8+ T cells. In addition, in vitro and in vivo, reducing the expression of CD112 inhibited cell proliferation and migration. Antibody array-based profiling of protein analysis revealed that CD112 knockdown can inhibited the SLC7A11/GPX-4 pathway and activated ferroptosis; the opposite effects were observed upon CD155 has overexpression. We further confirmed the mechanism between CD112 and SLC7A11/GPX-4 pathway through rescue experiments, CD112 overexpression reversed the ferroptosis effects and inhibition of the SLC7A11/GPX-4 pathway induced by GPX-4 inhibitor (ol3).

**Conclusion/Implications**

Our research demonstrated that CD112 can activates the SLC7A11/GPX-4 pathway and inhibit ferroptosis. Thus, CD112 is a potential screening and therapeutic biomarker for cervical cancer.

**DOES HIGHER NODAL DOSE IMPACT NODAL SIMULTANEOUS INTEGRATED BOOST FOR CERVICAL CANCER**

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**Introduction**

The dose prescription for nodes is heterogenous and choice of optimal dose is unclear. This study was designed to report nodal response in patients receiving simultaneous integrated boost (sIB) for stage IIIc cervical cancer.

**Methods**

Patients who received chemoradiation and nodal dose escalation through sIB followed by brachytherapy were included. As per RECIST 1.1, baseline lymph node was categorized as pathological if short axis diameter (SAD) was ≥10 mm and measurable if SAD ≥15 mm or as a non-target if SAD ≥10 mm but <15 mm. On follow-up, if SAD was <10 mm, the node was considered non-pathologic. Nodal Control and Disease-Free Survival (DFS) was determined. Log-rank test was used for evaluation of impact of nodal RECIST baseline nodal category, nodal volume and dose on nodal control and disease-free survival (DFS).

**Results**

Sixty-six patients with 153 nodes were included. Patient characteristics and treatment details are depicted in table 1. Median SIB dose was 55Gy (45-56.5Gy). Number of nodes receiving dose <50Gy were 7 (4.6%), 51-55Gy: 36 (23.5%) and >55Gy:110 (71.9%). At response assessment 92.2% nodes (n=141) had complete response, 6.5% (n=10) had partial response and 1.3% (n=2) had progressive disease. The median follow up was 33 months (9–66 months). Patients receiving >55Gy had better 5-year nodal control (84.6% vs 58.7%, p=0.02, figure 1). Reduced 5-yr DFS (76% vs 44%, p=0.15) was also observed based on RECIST definition though it was not statistically significant.