

for the cohort as a whole, and stratified by stage of diagnoses in table 1 and 2 respectively. Decreased overall survival was associated with lymphovascular invasion and p16 negativity, however when stratified by stage, LVI significantly impacted survival in stage I to III patients only. Increased survival was associated with surgical resection, radical radiotherapy (RT), brachytherapy, concurrent cisplatin and 5 weeks of chemotherapy (vs. <5 weeks). When stratified by stage, surgical resection only improved survival in stage I patients, with no significant difference in any other stage. The use of radical RT, brachytherapy, and concurrent chemotherapy did not show survival differences in stage I disease, but did in stage II to IV. As a whole, peri-RT chemotherapy was not associated with survival benefit in adeno/adenosquamous carcinoma. 180 women recurred (23.1%) with mostly distant metastases (42.8%). There was lower incidence of recurrence after primary surgical resection in those with tumor size <2cm vs. tumors >2cm (4.1% vs 24.7%, $p=0.0004$). Though only 37.7% of recurrence/metastases was treated with first-line carboplatin/paclitaxel/bevacizumab, it was associated with better overall survival compared to other regimens (median OS 40.1 vs. 24.8 months, $p=0.03$).

Conclusion* A significant number of women had recurrence (23.1%), and LVI and p16 negativity is associated with poor survival. Surgical resection in stage I is associated with improved survival but not in stage II to IV. Use of radical chemoradiation treatment is associated with survival differences in stage II to IV disease, but not stage I. First line carboplatin/paclitaxel/bevacizumab for recurrence shows improves survival but only a small proportion of women received it.

143 DRUG REPURPOSING AS A SOURCE OF INNOVATIVE THERAPIES IN CERVICAL CANCER

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Introduction/Background* Cervical cancer is the fourth cancer in terms of incidence and mortality in women worldwide. Relative to other cancers, there has been limited progress in the discovery of effective new therapies. Drug repurposing is an alternative development pathway that utilise the properties of drugs approved for other diseases and builds on available safety and pharmacological data to develop the drug as a potential (cervical) cancer drug.

We screened the literature to identify drug repurposing opportunities in cervical cancer to inform future research and trials.

Methodology A literature-based approach was undertaken to identify whether the drugs included in ReDO_DB (database of 317 non-cancer drugs on the market with at least one article reporting a possible effect on any cancer type) or CDcervix_DB (database containing 217 drugs approved for one or more malignancies by a regulatory agency, but excluding drugs currently used in cervical cancer). PubMed was queried for each drug and all abstracts were assessed for relevance and

Abstract 143 Table 1 Five examples of repurposing candidates for cervical cancer

Drug <i>Main approved indications</i>	Proposed mechanism of action in cervical cancer	Potential role <i>single agent/ radiosensitizer/ immunomodulation</i>	Proposed setting(s)	Cervical cancer trials
Nelfinavir <i>HIV</i>	PI3K-Akt inhibition and induction of endoplasmic reticulum stress	radiosensitizer	with CRT	ongoing
Hydralazine & valproate <i>Hypertension & epilepsy, respectively</i>	HDAC and DNA methyltransferase inhibition	radiosensitizer immunomodulation	with CRT, adjuvant, recurrent/ metastatic	yes
Sonidegib <i>Basal cell carcinoma</i>	smoothened inhibition and radiosensitizer	radiosensitizer	with CRT, adjuvant	no
Plerixafor <i>Mobilisation of haematopoietic stem cells</i>	prevention of CRT-induced CXCL12/CXCR4 signalling	radiosensitizer Immunomodulation	with CRT	no
Cetuximab <i>Squamous cell head and neck cancer</i>	EGFR inhibition and radiosensitizer	radiosensitizer	with CRT, recurrent/ metastatic	yes

type of evidence (*in vitro*, *in vivo*, clinical trial, *etc.*). Subsequently, a clinical trial database (clinicaltrials.gov and WHO-ICTRP) search was performed to generate a list of registered trials in cervical cancer with drugs from our databases.

Result(s)* We queried 534 drugs from our drug databases. Of these, 169 drugs had at least one relevant abstract or registered trial in cervical cancer. Ninety-three drugs had at least human data available with 52 drugs evaluated in registered trials. Forty-two drugs had at most *in vitro* data.

All 169 drugs were assessed for strength of scientific rationale, feasibility for integration in cervical cancer standard of care, evidence of radiosensitisation and an assessment of the availability of the drug for clinical trials. Out of these 169 drugs, we present 5 examples, *i.e.* nelfinavir, plerixafor, valproate with hydralazine, sonidegib and cetuximab (table 1) of potential candidates out of 39 that have been prioritised for further investigation.

Conclusion* This study has identified potential candidates that are worth evaluating in cervical cancer. Although many drugs warrant additional preclinical and clinical investigation, we are exploring the possibility of conducting international collaborative multi-arm trials with one or several of these drugs.

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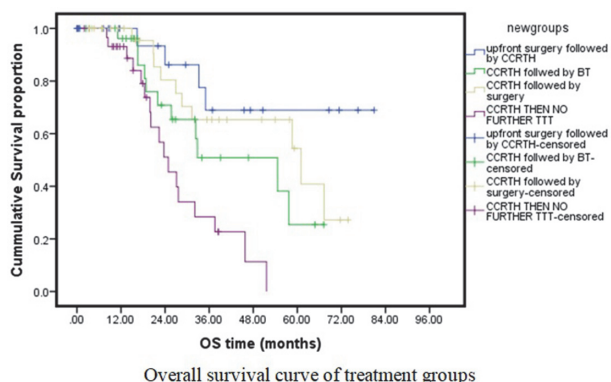
OUTCOMES OF MANAGEMENT OF LOCALLY ADVANCED CERVICAL CANCER, NATIONAL CANCER INSTITUTE EXPERIENCE, CAIRO UNIVERSITY

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Introduction/Background* Cervical cancer is the 4th most common cancer affecting females with 85% of cases occurring in developing countries. There is limited data available in the literature about locally advanced cervical cancer management outcomes from Egypt. This is the first and the largest study to describe locally advanced cervical cancer treatment outcomes from Cairo University National Cancer Institute (NCI), the largest tertiary center for cancer in Egypt.

Methodology A retrospective study was conducted including 160 patients with pathologically proven cervical cancer, locally advanced disease (FIGO stage IIB till IVA) who presented to gynecology group, Radiation Oncology Department, NCI from 2013 to 2017. Data were collected retrospectively from patients' medical records. Demographic, clinicopathological,



Abstract 148 Figure 1 Overall survival curve of treatment groups

treatment, and survival outcome data were retrieved. Survival analysis was estimated using the Kaplan-Meier method and compared using the log-rank test.

Result(s)* Data analysis showed a great disparity in management plans. Local control (LC) was achieved in 65.1% of the patients, and 31% had metastatic disease progression. Non-compliance to treatment was seen in 18.8% of the patients. Three years overall survival (OS) and five years OS were 45.6% and 35% respectively. Non-compliant patients had significantly lower 3 years OS (28.4%, $P < 0.001$). The most common modality of treatment was concurrent chemoradiation therapy (CCRTH) followed by radical surgery. There was no significant difference in OS, LC, and time to the distant metastasis between the different treatment modalities.

Conclusion* Locally advanced cervical cancer management represents a challenging burden in developing countries like Egypt. Patient compliance was found to be the most important factor affecting survival in our population. Proper assessment of the factors causing low compliance should be properly evaluated. Strict follow-up and improving patient compliance are essential to achieve a favorable outcome.

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PHASE 3 RECURRENT/METASTATIC CERVICAL CARCINOMA TRIAL: SUBGROUP EFFICACY ANALYSIS OF CEMIPIMAB VERSUS INDIVIDUAL INVESTIGATOR'S CHOICE CHEMOTHERAPY

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Introduction/Background* There is no standard of care regimen in the second-line setting for women with recurrent/metastatic (R/M) cervical carcinoma. Cemiplimab was recently shown to significantly improve overall survival (OS) compared with investigator's choice (IC) chemotherapy in patients with R/M cervical cancer after first-line platinum-based chemotherapy (NCT03257267; ESMO-VP-2021). We present a pre-planned exploratory subgroup analysis comparing cemiplimab to individual IC chemotherapy options.

Methodology EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9 is an open-label, randomised (1:1), multi-centre, Phase 3 clinical trial of anti-programmed cell death (PD)-1 cemiplimab vs IC single agent chemotherapy in R/M cervical cancer that has progressed after first-line platinum-based treatment. The selection of single-agent chemotherapy by the investigator (gemcitabine, pemetrexed, vinorelbine, topotecan or irinotecan) was not protocol-defined, but the regimen had to be