■專題演講——婦癌

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用臨床的角度探討最近三大婦科癌症的進展

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The current review describes the recent progress of the three major gynecological cancers (GC), including endometrial cancer (EC), ovarian cancer (OC) and cervical cancer (CC) from a clinical perspective. For EC, as playing the top one GC with 3541 new cases annually in 2022 Taiwan, conventional therapy is accorded to FIGO (the International Federation of Gynaecology & Obstetrics) 2009 staging system with clinical-pathological risk factors, including surgery along or surgery and following adjuvant radiotherapy (RT) with/without chemotherapy (CT). Now current approach is switched to treating EC based on a molecular-based FIGO 2023 staging system, which newer innovative therapeutic approaches, such as immunotherapy (immune checkpoint inhibitors: ICIs, such as pembrolizumab or dostarlimab, and immunotherapy-chemotherapy: IO-CT) or many precision medicine and targeted therapy, or combination, such as IO-CT plus PARPi (Poly ADP-Ribose Polymerase inhibitors) are being continuously developed in revolutionizing EC treatment and improving patient outcomes. For OC (n=1859 annually in 2022 Taiwan), besides the standard of care (SOC) as surgical cytoreduction and CT with/without maintenance strategies, such as PARPi are increasingly necessary. For CC (n=1384 annually in 2022 Taiwan), except SOC as primary radical surgery or concurrent chemoradiation (CCRT), IO or IO-CT plays a very important role for advanced CC. Additionally, for advanced, persistent, metastatic, or resistant (APMR) GC, more and more new developed products and therapeutic approaches are being investigated to enhance treatment outcomes and prolong the overall survival. One of the famous products is antibody-drug conjugates (ADCs), and another is an individualized or adaptive RT (IRT or ART), such as three or four-dimensional conformal RT (3D- or 4D-CRT), intensity-modulated RT (IMRT), volumetric-modulated arc therapy (VMAT), stereotactic body RT (SBRT), high dose-low fraction RT and many others. Many are really a big success and make a big breakthrough in the management of these highly lethal GC and further become the SOC landscape. Current review will cover the updated information based on the clinical cases to explore the advance in managing women with three GC, initiating from diagnosis to treatment.

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子宮頸癌診斷及治療的新契機

Cervical cancer (CC) is one of the three major gynecological malignancies. However, it is not among the ten most common women cancers in Taiwan after 2023. The primary treatment modalities for CC include surgery and concurrent chemoradiation therapy (CCRT), while systemic therapy—comprising chemotherapy, targeted therapy, and immunotherapy—is typically employed for recurrent CC.

Primary therapy: Surgical Management of Early-Stage Cervical Cancer

In early-stage CC, findings from the CONCerv and SHAPE trials have established selective criteria for ultra-conservative surgical approaches. These include type A (extrafascial) hysterectomy as an alternative to traditional type B or type C radical hysterectomy. This shift aims to reduce the comorbidities associated with radical surgeries while maintaining comparable disease control rates. Following the publication of the LACC trial in 2018, minimally invasive surgery (MIS) for CC has faced significant scrutiny. The ongoing LASH trial seeks to provide new evidence to clarify the role of MIS in managing operable CC.

Primary therapy: Advances in Locally Advanced Cervical Cancer

In cases of locally advanced CC, the INTERLACE trial, published in 2024, demonstrated that administering systemic dose-dense chemotherapy with paclitaxel and carboplatin prior to CCRT improves patient outcomes. Additionally, the Keynote-A18 trial showed that incorporating the anti-PD1 agent, pembrolizumab, during CCRT improves outcomes for stage III (excluding pelvic and/or para-aortic lymph node metastases) and stage IVA cases. Based on these findings, the U.S. FDA approved pembrolizumab for this indication in January 2024. Ongoing clinical trials, such as e-VOLVE-cervical, are investigating the role of maintenance therapy with volrustomig following standard CCRT.

Recurrent therapy: Management of Recurrent Cervical Cancer

For recurrent CC, combining chemotherapy with immunotherapy has shown promising results. Several key trials have contributed to advancements in this area:

Keynote-826: Evaluated pembrolizumab in combination with chemotherapy.

BEATcc: Studied the addition of atezolizumab.

CALLA: Investigated the role of adding avelumab.

COMPASSION 16: Focused on cadonilimab.

Checkmate 358 explored the use of dual immunotherapy agents (nivolumab and ipilimumab), while the EMPOWER-Cervical 1 trial demonstrated favorable outcomes with cemiplimab. The antibody-drug conjugate tisotumab vedotin (TV) has also improved outcomes in this patient population and received FDA approval. Numerous ongoing trials continue to explore novel therapeutic options in this field.

Recurrent therapy: Challenges in Managing Field Failure After Standard CCRT

Addressing field failure following standard CCRT remains a significant challenge in recurrent CC management. Emerging radiation modalities, such as proton therapy and heavy-ion therapy, have been introduced, with small case series reported by institutions like MD Anderson Cancer Center and Johns Hopkins University hospital. Additionally, hyperthermic therapy, when combined with traditional CCRT, has shown potential role as a radiation sensitizer, enhancing the effectiveness of radiation-induced cancer cell killing.

Conclusion

Recent advancements in surgical techniques, systemic therapies, and novel treatment modalities have significantly improved the management of cervical cancer across its stages. Continued clinical trials and technological innovations will further refine these approaches, offering hope for better outcomes and reduced treatment-related morbidity.

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子宮內膜癌診斷及治療的新契機

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With the advancement of molecular biology, there are many new treatment options for endometrial cancer, such as immunotherapy, PARP inhibitors, ADCs, and more. The decision of treatment stratagy relies on FIGO stage, histologic grade, subtype, and molecular marers. A recent major breakthrough is incorporating immunotherapy with chemotherapy as a first-line treatment. The relevant trials include RUBY, NGR,-GY018, AtTEnd and KEYNOTE-B21. In addition, DUO-E and RUBY part 2 trials demonstrated that the combination of PARP inhibitor with immunotherapy in maintenance treatment may improve outcomes. The DESTINY-PanTumor02 trial on the treatment of endometrial cancer highlights the favorable outcomes of Trastuzumab deruxtecan (T-DXd).

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卵巢癌診斷及治療的新契機

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Ovarian cancer remains one of the most challenging gynecologic malignancies, with high mortality rates primarily due to late diagnosis and chemoresistance. Recent advances have opened new opportunities for improving both diagnosis and treatment outcomes.

The integration of molecular profiling has transformed our understanding of ovarian cancer heterogeneity. High-throughput sequencing has identified distinct molecular subtypes, enabling more precise treatment strategies. BRCA1/2 testing has become standard practice, leading to successful implementation of PARP inhibitors, while homologous recombination deficiency (HRD) status also guides therapeutic decisions.

Standard chemotherapy remains the backbone of ovarian cancer treatment, typically utilizing platinum-based combinations (carboplatin/paclitaxel). This first-line treatment demonstrates high initial response rates, though resistance often develops.

Targeted therapies have revolutionized treatment approaches and can be used as maintenance therapy to optimize the benefits of first-line treatment. Anti-angiogenic agents (bevacizumab) improve progression-free survival and overall survival in the patients with higher risk. PARP inhibitors (olaparib, niraparib, rucaparib) show significant benefit in BRCA-mutated and HRD-positive cases.

Novel combinations of targeted agents with chemotherapy also show promising results. Antibody-Drug Conjugates (ADCs) represent an emerging therapeutic strategy. Mirvetuximab soravtansine targets folate receptor alpha (FRα) shows promise in platinum-resistant disease and additional ADCs targeting various antigens are in development

Treatment selection increasingly relies on molecular profiling and biomarker status, enabling more personalized approaches. Ongoing clinical trials continue to explore new combinations and sequences of these therapeutic options, aiming to optimize outcomes while managing toxicities.