

Editorial

# Management of Endometrial Cancer: Molecular Identikit and Tailored Therapeutic Approach

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Gynecologic oncology management has undergone numerous changes over the past few years. A greater understanding of tumor biology and genetic patterns has changed the therapeutic approach, especially with ovarian and endometrial cancers.

Efforts have focused on improving safety, efficiency, and cost of care in gynecologic oncology.

Endometrial cancer (EC) is the most common gynecological malignancy in developed countries. Considerable progress has recently been made in the management of patients affected by EC, mostly regarding molecular biology and minimally invasive treatment.

90% of patients with EC have abnormal vaginal bleeding as the first main symptom, most frequently during the postmenopausal period, making an early diagnosis possible. Endometrial sampling and imaging based on pelvic Magnetic Resonance Imaging (MRI) are mandatory to provide an accurate diagnosis [1–3].

Pathologic analysis to determine the tumor type and grade, is the standard for tumor risk stratification. Due to a new diagnostic classification centered on molecular and immunohistochemical indicators, the risk classification is much more accurate. On the basis of the outcomes of the Cancer Genome Atlas, and the ProMisE (Proactive Molecular Risk Classifier for EC), tumors are divided into four subgroups according to the presence of polymerase-epsilon (POLE) exonuclease domain mutations (EDMs), and protein 53 (p53) immunohistochemistry and mismatch repair (MMR) proteins, creating four different subgroups: POLEmut, p53 wild type (low copy number–CNL-or non-specific molecular profile-NSMP) p53 null/missense mutations (high copy number) and mismatch repair deficient (MMRd) [4–8]. This molecular classification optimizes EC clinical management, defining different risk classes. If this molecular classification is not available, it is necessary to consider traditional pathologic classification. The prognostic risk group defines the adjuvant treatment; European Society of Medical Oncology (ESMO), European Society of Gynaecological Oncology (ESGO), European Society for

Radiotherapy and Oncology (ESTRO) and European Society of Pathology (ESP) guidelines recommend specific management depending on the risk category: low, intermediate, high- intermediate, high, and advanced disease [9]. Each category has a precise management profile for patients with EC, predicting the outcome and making the management of EC very focused, based on protocols by the principal international gynecological oncological societies for the treatment of EC patients.

No adjuvant treatment is recommended for low-risk patients. The low-risk category includes stage I and II POLE ultramutated and stage IA MMRd/NSMP endometrioid carcinoma, without lymph vascular space invasion (LVSI) [10].

Adjuvant brachytherapy decreases vaginal recurrence in patients with intermediate risk. This category includes patients with stage IB MMRd/NSMP endometrioid carcinomas and low grade, LVSI negative, stage IA MMRd/NSMP endometrioid carcinomas and high grade, no LVSI or focal invasion and stage IA p53abn, and/or non-endometrioid carcinomas [11].

Adjuvant radiotherapy is recommended in the intermediate-high-risk group. This risk group comprises stage IA or IB low-grade endometrioid carcinomas with positive LVSI or stage IB high-grade endometrioid carcinomas unrelated to LVSI, and stage II endometrioid carcinomas [9].

Stage III–IVA MMR-d or NSMP endometrioid carcinomas and stage I–IVA p53abn all-histology or stage IB–IVA non-endometrioid carcinomas are included in the high-risk group. Because of the high risk of recurrence for patients in this group, post-operative combined chemo-radiotherapy is recommended. Patients who underwent combined therapy (chemo-radiotherapy) showed better overall survival than patients who underwent chemotherapy alone, according to PORTEC-3 trial results [1,12,13].

The molecular biology state creates an EC patient identikit that guides individualized therapeutic approach and follow-up, avoiding overtreatment and improving the



clinical outcomes of these patients. NCCN National Comprehensive Cancer Network (NCCN) guidelines identified more risk factors for EC patients: age >60 years, LVSI status, and tumor size, making the identikit even more precise. Studies have also focused on the effect of comorbidities and/or drugs on EC prognosis [14].

Molecular classification can be considered the future standard approach for gynecological cancer management, particularly for endometrial and ovarian cancer, and has avoided unnecessary treatments in patients with good molecular profiles.

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OD and DC designed the research study. AG contributed to the analysis of the data and supervision. AG and ARB wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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### Conflict of Interest

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