MOLECULAR CHARACTERIZATION OF ENDOMETRIAL CANCER

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Objectives

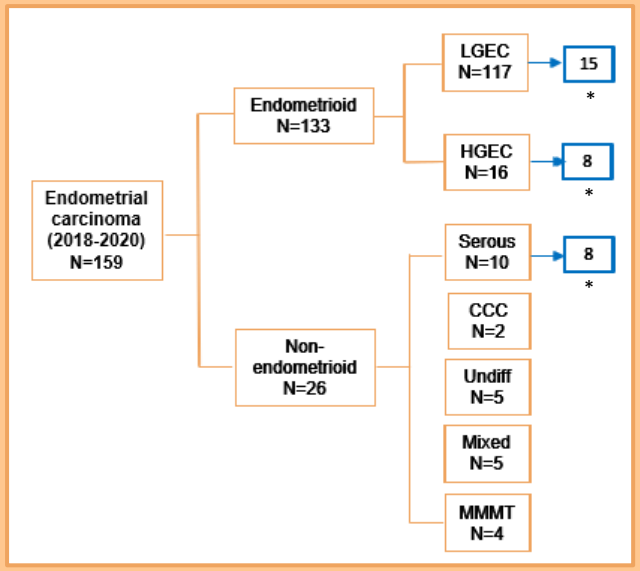
In light of the ESGO/ESTRO/ESP 2020 guidelines, the study aims to evaluate the clinical applicability of NGS analysis to define an appropriate risk class for a better diagnostic and prognostic definition of endometrial carcinoma.

Methods

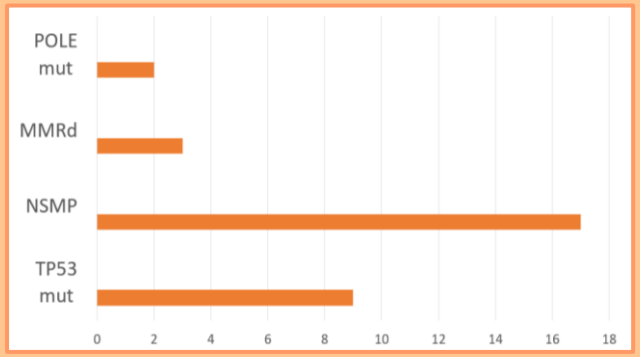
Cases of serous endometrial carcinoma (SEC), high (HGEC) and low (LGEC) grade endometrioid carcinoma (period 2018-2020) diagnosed with the morphological and immunohistochemical protocol were considered. After a standardized pre-analytical phase, the tumour DNA was semi-automatically extracted and analyzed by NGS with Oncomine On Demand Tumor Specific custom panel on 14 genes (BRIP, CTNNB1, KRAS, MLH1, MLH3, MSH2, MSH6, PALB2, PMS2, POLE, PTEN, TP53, RAD51C e RAD51D).

Results

31 cases were considered (n=8 HGEC, n=8 SEC, n=15 LGEC) and NGS analysis gave good analytical results. Cases were classified according to immunohistochemical assays and molecular results into: POLEmut (n = 2), MMRd (n = 3), NSMP (n = 17), TP53mut (n = 9); among the HGECs: 2 POLE, 4 NSMP, 2 TP53mut.



* cases selected for molecular testing



Study population in the four molecular classes

POLE Pathogenic Variant	VAF
c.890C>T p.(Ser297Phe)	26%
c.1231G>C p.(Val411Leu)	13%
MMR Pathogenic Variant	**VAF**
MSH2 c.1077A>T p.(Arg359Ser)	81%
MSH6 c.1483C>T p.(Arg495*)	6%
MSH6 c.3132C>G p.(Tyr1044*)	15%
TP53 Pathogenic Variant	**VAF**
c.357del p.(Lys120Serfs*3)	47%
c.524G>A p.(Arg175His)	50%
c.659A>G p.(Tyr220Cys)	75%
c.722C>T p.(Ser241Phe)	68%
c.734G>T p.(Gly245Val)	76%
c.817C>T p.(Arg273Cys)	24%
c.839G>A p.(Arg280Lys)	93%
c.878A>G p.(His193Arg)	81%
c.880G>T p.(Glu294*)	94%

Pathogenetic variants found by NGS

Conclusions

The study showed that the protocols of the pre-analytical and analytical phases used are robust and can lead to molecular results that fall within the standards required for use in clinical practice for a more precise diagnostic-therapeutic management of patients. The implementation of the molecular classification is particularly relevant for better prognostic stratification of HGECs.

References

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Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Vol. 31, International Journal of Gynecological Cancer. 2021.