Conclusion

MSI/MMR testing rates among aEC patients in Europe are low and vary across countries. The majority of tested patients had non-aEC-high/pMMR tumors. Knowledge of MSI/MMR testing may be helpful for optimal utilization of targeted therapies in Europe.

Introduction/Background

Organoids are increasingly being used as complex, multi-dimensional, multi-cell structures resembling entire organs and have now been derived from a variety of tissues.

Methodology

We established endometrial organoid cultures from pipelle biopsies of 11 patients with endometrial cancer (EC) (7 endometrioid, 3 serous, 1 clear cell) and 3 patients with benign conditions. Organoids were grown in Matrigel medium and supplemented with growth factors, Fspotdin-1, Noggin, A83–01 and nicotinamide. The genomic and epigenomic features of organoids and parent tissue were compared in pairs and by histological type using targeted gene sequencing and whole-genome DNA methylation profiling.

Results

The genetic variations and mutations in seven genes (PTEN, ARID1A, PIK3CA, POLE, CTNNNB1, KRAS, TP53) were largely shared by primary tumours and EC-derived organoids and exhibited histological type-specific characteristics. Similarly, the DNA methylation fingerprint was preserved in cultured endometrial cancer organoids with only few differentially methylated positions (DMPs) compared to tumour tissue. EC epigenetic profiles were distinct to benign endometrial tissues.

Conclusion

Endometrial cancer organoids can reliably be used as replicas of primary tumour in endometrial cancer research.