Implementation of Endometrial Cancer TCGA Classification Using ProMisE: Experience at a Tertiary Care Center

Lynelle P Smith MD\(^1\), Devon Pino\(^4\), Kurtis Davies PhD\(^1\), Amber Berning MD\(^1\), Miriam D Post MD\(^1\), Bradley R Corr MD\(^2\), Saketh Guntupalli MD\(^2\), Christine Fisher MD MPH\(^3\), Mario J Perez MD MPH\(^5\), Dara L Aisner MD PhD\(^1\), Rebecca J Wolsky MD\(^1\)

Departments of Pathology\(^1\), Obstetrics & Gynecology\(^2\), Radiation Oncology\(^1\), School of Medicine\(^4\), Psychiatry\(^4\), University of Colorado Anschutz Medical Campus, Aurora, CO

Background

In 2013, The Cancer Genome Atlas (TCGA) identified 4 prognostic groups of endometrial carcinomas (EMCA). The ProMisE algorithm employs IHC where possible, rendering the TCGA classification more accessible, which has been endorsed by the WHO. Other recent consensus guidelines also encourage molecular testing in EMCA (NCCN, European Society of Gynaecological Oncology), thus guiding the clinical application of EMCA classification into the 4 prognostic groups:

- **POLE** mutated
- Mismatch repair deficient (MMRd)
- p53 wild-type/No specific molecular profile (NSMP)
- p53 abnormal

Here we describe the de novo implementation of EMCA testing at one tertiary care center and the related results utilizing the Exploration, Preparation, Implementation, Sustainment (EPIS) framework (Figure 1).

Results

The Sustainment phase includes tracking the distribution of molecular subtypes and histotypes (Table 1). There were 9 dual classifier cases:

- 2 POLE-p53
- 7 MMRd-p53

Notably, 13 cases (11%) harbored TP53 mutations but were p53 IHC wild-type (wt); all were endometrioid:

- **7 (54%)**: dual classifiers (6 MMRd-p53, 1 POLE-p53)
- **6 (46%)**: single classifier, grade 1 endometrioid

Conclusions

The highly anticipated results from the ongoing PORTEC 4a trial of molecular profile-based adjuvant therapy will inform standardized, specific, practical recommendations for EMCA testing and reporting. This study describes the implementation process at one tertiary care center using the EPIS framework and the results through July 2021, including a subset of low-stage, low-grade endometrioid carcinomas that are TP53 mut, yet p53 wt, an unexpected result.

### References

