Objectives The relevance of hormonal biomarkers in endometrial cancer (EC) has been well-established. A revised cut-off for estrogen receptor/progesterone receptor (ER/PR) expression into three subgroups was shown to improve prognostication, however, this has not been related to the four molecular subgroups. Therefore, we aimed to investigate the prognostic relevance of this three-tiered ER/PR model within the molecular subgroups in EC.

Methods A retrospective multicenter study within the European Network for Individualized Treatment (ENITEC) network was performed. ER/PR expression was classified into: high-risk (0–10%), intermediate-risk (20–80%) and low-risk (90–100%). The molecular subgroups were conducted based on Next Generation Sequencing, allocating patients into polymerase epsilon (POLE)-mutant, microsatellite instable (MSI), TP53-mutated, lymphovascular space invasion and FIGO stage remained independent prognostic factors for reduced disease-specific survival (DSS) compared to ER/PR 20–80% or 90–100%. Interestingly within TP53-mutated, patients with ER/PR 90–100% expression showed an excellent DSS (100%) compared to ER/PR 20–80% and 0–10% (figure 1). In multivariable analyses ER/PR 0–10%, TP53-mutated, lymphovascular space invasion and FIGO stage remained independent prognostic factors for reduced DSS (respectively, HR 2.59 (95%-CI 1.32–5.03) P=0.005, HR 2.71 (95%-CI 1.35–5.43) P=0.005, HR 2.27 (95%-CI 1.15–4.45) P=0.018, HR 4.42 (95%-CI 2.16–9.01) P<0.001).

Conclusions ER/PR expression remains prognostic relevant in all molecular subgroups, strengthened by the three-tiered cut-off. We therefore recommend routine evaluation of ER/PR expression in clinical practice.