analysis evaluated the prevalence of MMRd, MSI-high, and LS in ovarian cancer, as well as the tests performance characteristics.

**Methods** We systematically searched the MEDLINE, Cochrane Central Register of Controlled Trials, and Embase databases from inception until February 2022. We included studies assessing MMRd using immunohistochemistry (IHC), MSI, and/or germline LS by next-generation sequencing (NGS).

**Results** A total of 45 studies were included. The incidence for MMRd was 9% (95% CI 6–14%), MSI-high 12% (12–15%), and LS 5% (2–14%) in all epithelial ovarian cancer respectively. Hypermethylation was identified in 77% (95% CI 63–87%) of those with MLH1 deficiency. MMR IHC for LS diagnosis had 92% sensitivity, 77% specificity, 58% positive predictive value, and 98% negative predictive value, whereas MSI performance characteristics were 97%, 91%, 25% and 77% respectively. Synchronous ovarian and endometrial cancers had highest rates of MMRd (26%) and MSI-H (34%). Serous histology had lowest prevalence of 1% for MMRd and 7% for MSI. The highest prevalence of germline pathogenic variants in MMR genes (LS) were found in those with synchronous endometrial-ovarian cancer (53%) as well as clear cell ovarian cancer (25%) with the lowest prevalence in serous ovarian (1%) cancer.

**Conclusions** MMR deficiency, MSI, and LS are frequent in ovarian cancer, in particular in non-serous histological subtypes.

**EP015/#546 IN VITRO AND IN VIVO EFFICACY OF TRASTUZUMAB DERUXTECAN (T-DXd) IN EPITHELIAL OVARIAN CANCER WITH HER2/NEU OVEREXPRESSSION**

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**Objectives** Epithelial ovarian cancer (EOC) has high recurrence rates, and treatment options are limited. T-DXd is a novel anti-HER2 antibody linked to the topoisomerase 1 inhibitor. This study aimed to determine the in vitro and in vivo efficacy of T-DXd in EOC.

**Methods** HER2 expression was analyzed with flow cytometry in primary high grade serous (KRCH31 and OVA3) and clear cell (OVA10 and OVA12) EOC cell lines. Cell lines were treated with T-DXd or Control antibody drug conjugate (CTL ADC). The IC_{50}, apoptosis, bystander antitumor assays were performed. KRCH31 cells were injected into the SCID mice and animals were treated with PBS, CTL ADC or T-DXd.

**Results** KRCH31 and OVA10 EOC cell lines expressed HER2 by flow cytometry, OVA3 and OVA12 had negligible expression. T-DXd mean IC_{50} were 0.014 μg/ml and 0.017 μg/ml for KRCH31 and OVA10 cell lines, but no effect was observed in the OVA3 or OVA12 cell lines. Apoptotic cells increased to 65% and 60% in the KRCH31 and OVA10 cell lines after T-DXd. T-DXd did not show cytotoxicity on AR4-K-GFP cells; however, substantial cytotoxicity was observed due to bystander antitumor activity when cocultured with KRCH31 and OVA10 cell lines (live ARK4-GFP cells 55% and 50%). Day 8 mean tumor volumes were 0.86, 0.81 and 0.43 cm³ in PBS, CTL ADC and T-DXd treated mice, respectively (p=<0.001). Median overall survival was 15, 16.5 days and not reached in PBS, CTL ADC, T-DXd treated mice, respectively (p=0.0002).

**Conclusions** T-DXd showed in vitro and in vivo preclinical efficacy in HER2 overexpressing EOC. Further clinical trials are warranted.