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ICON8: Overall survival results in a GCIG phase III randomised controlled trial of weekly dose-dense chemotherapy in first line epithelial ovarian, fallopian tube or primary peritoneal carcinoma treatment

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Background

ICON8 investigated the safety and efficacy of weekly dose dense chemotherapy (q1w) in patients with epithelial ovarian cancer (EOC) compared to standard three weekly chemotherapy (q3w). ICON8 had co-primary outcomes of progression free (PFS) and overall survival (OS). Mature OS and updated PFS results are reported here.

Methods

Eligible women with FIGO stage IcG3-IV EOC were randomised 1:1:1 to arm 1 standard chemotherapy (q3w carboplatin AUC5/6 + q3w paclitaxel 175mg/m^2); arm 2 weekly paclitaxel (q3w carboplatin AUC5/6 + q1w paclitaxel 80mg/m^2); arm 3 weekly carboplatin-paclitaxel (q1w carboplatin AUC2 + q1w paclitaxel 80mg/m^2). Patients received immediate primary surgery (IPS) prior to entering ICON8 or neo-adjuvant chemotherapy with planned delayed primary surgery (DPS) during chemotherapy. Analyses are performed on an intention to treat basis, comparing arms 2v1 and 3v1.

Results

From Jun 2011 - Nov 2014, 1566 patients were randomised, 522, 523, 521 in arms 1, 2, 3 respectively. Baseline characteristics were well-balanced – median age 62 years; serous histology 72%; stage Ic-II 19%, IIIa-IIIb 10%, IIIc-IV 72%. 48% patients had IPS, 50% planned DPS and 2% inoperable. At 1st Oct 2019, 923 deaths had been reported, arm 1 319 (61%); arm 2 300 (57%); arm 3 304 (58%). No significant improvement in OS was observed in either comparison: arm 2v1 log rank p=0.14, hazard ratio (HR) = 0.88 (97.5% confidence interval (CI) 0.74, 1.06); arm 3v1 log rank p=0.27, HR = 0.91 (97.5% CI 0.76, 1.09). Median OS was 47.4, 54.1 and 53.4 months in arms 1, 2, 3 respectively. No heterogeneity in treatment effect was noted on subgroup analysis by surgical approach (IPS vs DPS). Updated PFS was also analysed. As in the primary analysis, no significant difference in PFS was observed with either weekly treatment (log-rank arm 2v1 p=0.37, arm 3v1 p=0.48; restricted mean PFS time 25, 25.5, 25.9 months in arms 1, 2, 3 respectively).

Conclusions

The final analysis for ICON8 confirms that, although weekly dose-dense chemotherapy is a safe alternative to q3w chemotherapy and can be delivered successfully in first-line EOC treatment, it does not significantly improve PFS or OS.

Clinical trial identification

NCT01654146; ISRCTN Registry number 10356387.

Legal entity responsible for the study

MRC Clinical Trials Unit at University College London.

Funding

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Disclosure

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