



ICON8 ICON8B MRC Clinical Trials Unit UCL

# ICON8 trials programme

## ICON8

N=1485

Stage IC-IV EOC/PPC/FTC

Randomise 1:1:1

- Arm 1 — 6 cycles
- Arm 2 — 6 cycles
- Arm 3 — 6 cycles

| | | |
|---|---|---|
| Arm 1 | Carboplatin AUC 5 | q3w |
| | Paclitaxel 175mg/m² | q3w |
| Arm 2 | Carboplatin AUC 5 | q3w |
| | Paclitaxel 80mg/m² | q1w |
| Arm 3 | Carboplatin AUC 2 | q1w |
| | Paclitaxel 80mg/m² | q1w |

**NB.** High-risk patients remain eligible for ICON8 so that patients with contra-indications to bevacizumab and those unable to access it are still able to enter the trial

## ICON8B

N=660

High-risk* stage III -IV EOC/PPC/FTC

Randomise 1:1

- Arm B1 — 6 cycles → Maintenance bevacizumab (18 Cycles Total)
- Arm B3 — 6 cycles → Maintenance bevacizumab (18 Cycles Total)

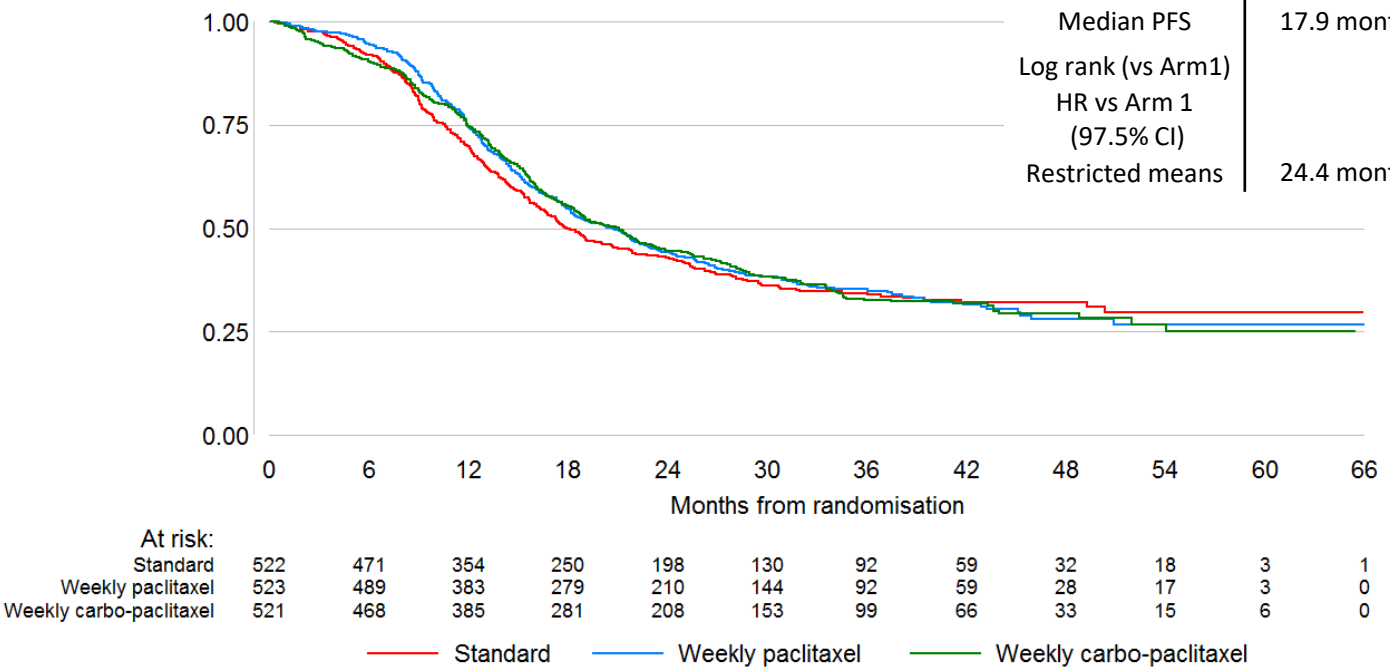
| | | |
|---|---|---|
| Arm B1 | Carboplatin AUC 5 | q3w |
| | Paclitaxel 175mg/m² | q3w |
| | Bevacizumab 7.5 mg/kg | q3w |
| Arm B3 | Carboplatin AUC 5 | q3w |
| | Paclitaxel 80mg/m² | q1w |
| | Bevacizumab 7.5 mg/kg | q3w |

***High-risk** defined as (1) FIGO (2013) stage IIIA1(ii), IIIA2 with positive retroperitoneal lymph nodes >1cm in diameter, stage IIIB or IIIC with >1cm residual disease following immediate primary surgery or planned to receive primary chemotherapy +/- delayed primary surgery and (2) FIGO (2013) stage IV

ANZGOG GICOM cancer trials ireland KGOG Korean Gynecologic Oncology Group

## ICON8 Progression Free Survival

| Total Patients | Arm 1 Standard N=522 | Arm 2 Weekly paclitaxel N=523 | Arm 3 Weekly carbo-paclitaxel N=521 |
|---|---|---|---|
| Progressions | 330 (63%) | 335 (64%) | 338 (65%) |
| Median PFS | 17.9 months | 20.6 months | 21.1 months |
| Log rank (vs Arm1) | | p=0.45 | p=0.56 |
| HR vs Arm 1 (97.5% CI) | | 0.92 (0.77, 1.09) | 0.94 (0.79, 1.12) |
| Restricted means | 24.4 months | 24.9 months | 25.3 months |




- Accrual began 6th June 2011 and ICON8 pathway closed to recruitment 28th November 2014
- Final recruitment figure = **1566**
- UK= 1397, ANZGOG= 70, GICOM= 43, KGOG= 32, ICORG= 24
- Primary PFS analysis presented at ESMO 2017. **Conclusions:** although weekly dose-dense chemotherapy can be delivered successfully as first-line EOC treatment without substantial toxicity increase, it does not significantly improve PFS compared to standard 3-weekly CT.

## ICON8B

A study of bevacizumab and weekly dose-dense paclitaxel in ovarian cancer

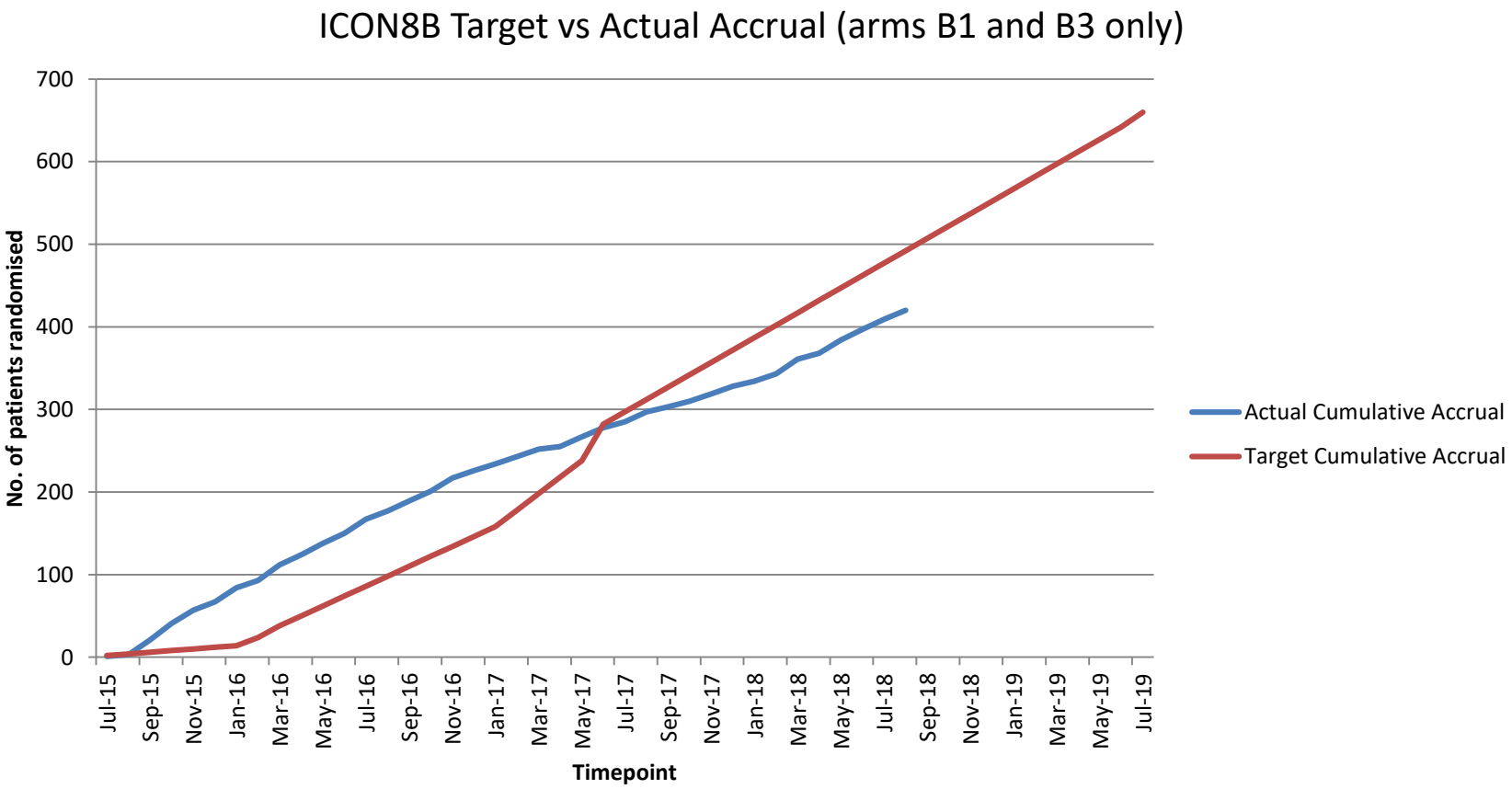
- Accrual began 21st July 2015. Planned recruitment closure: July 2019.
- Following ICON8 Primary PFS analysis in April 2017, the ICON8 TMG in consultation with IDMC and TSC immediately suspended recruitment to arm B2 in May 2017. Final approvals to continue ICON8B as a 2-arm randomised study comparing arm B1 and arm B3 were received in Aug 2017.
- **Modified recruitment target:** 660
- **Accrual total as of 31st August 2018:** 420 (omitting arm B2 patients)
- The required number of the events for the futility analysis has not yet been observed. The IDMC will review this at a later date – meeting to be arranged for early 2019.

Modified comparator arms as of May 2018:

| | | |
|---|---|---|
| Arm B1 | Carboplatin AUC 5 | q3w |
| | Paclitaxel 175mg/m$^2$ | q3w |
| | Bevacizumab 7.5mg/kg | q3w |
| Arm B3 | Carboplatin AUC 5 | q3w |
| | Paclitaxel 80mg/m$^2$ | q1w |
| | Bevacizumab 7.5mg/kg | q3w |

An international trial with 77 UK sites, 6 sites in Ireland, and 3 sites in Switzerland open to recruitment.

# ICON8B Actual vs Target Accrual (data up until 31st August 2018)




NB: On 5th May 2017 the modified ICON8B design opened to recruitment (2-arm randomisation, arms B1 vs B3). Monthly target accrual and overall accrual figures amended as per the sample size required in the modified trial design. Target accrual from July 2015-May 2017 is calculated from the original 3-arm study design target accrual / 0.66.