

ICON8 trials programme

N=1485

ICON8

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

N=660

ICON8B

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

Randomise 1:1

Arm B1
6 cycles

Arm B3
6 cycles

Maintenance bevacizumab
(18 Cycles Total)

Maintenance bevacizumab
(18 Cycles Total)

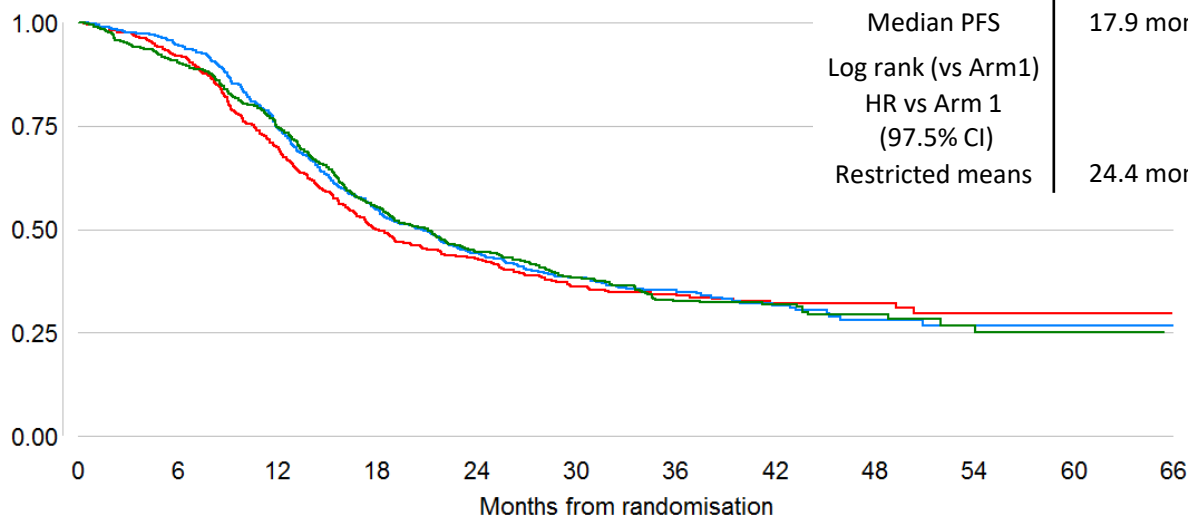
Arm B1 Carboplatin AUC 5 q3w
Paclitaxel 175mg/m² q3w
Bevacizumab 7.5 mg/kg q3w

Arm B3 Carboplatin AUC 5 q3w
Paclitaxel 80mg/m² q1w
Bevacizumab 7.5 mg/kg q3w

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

***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

ICON8 Progression Free Survival



	Arm 1 Standard N=522	Arm 2 Weekly paclitaxel N=523	Arm 3 Weekly carbo- paclitaxel N=521
Total Patients			
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

At risk:	0	6	12	18	24	30	36	42	48	54	60	66
Standard	522	471	354	250	198	130	92	59	32	18	3	1
Weekly paclitaxel	523	489	383	279	210	144	92	59	28	17	3	0
Weekly carbo-paclitaxel	521	468	385	281	208	153	99	66	33	15	6	0

— Standard — Weekly paclitaxel — Weekly carbo-paclitaxel

- 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 3rd Oct 2017: 303** (omitting arm B2 patients)
- Interim analysis planned Summer 2018 to confirm it is favourable for the trial to continue.

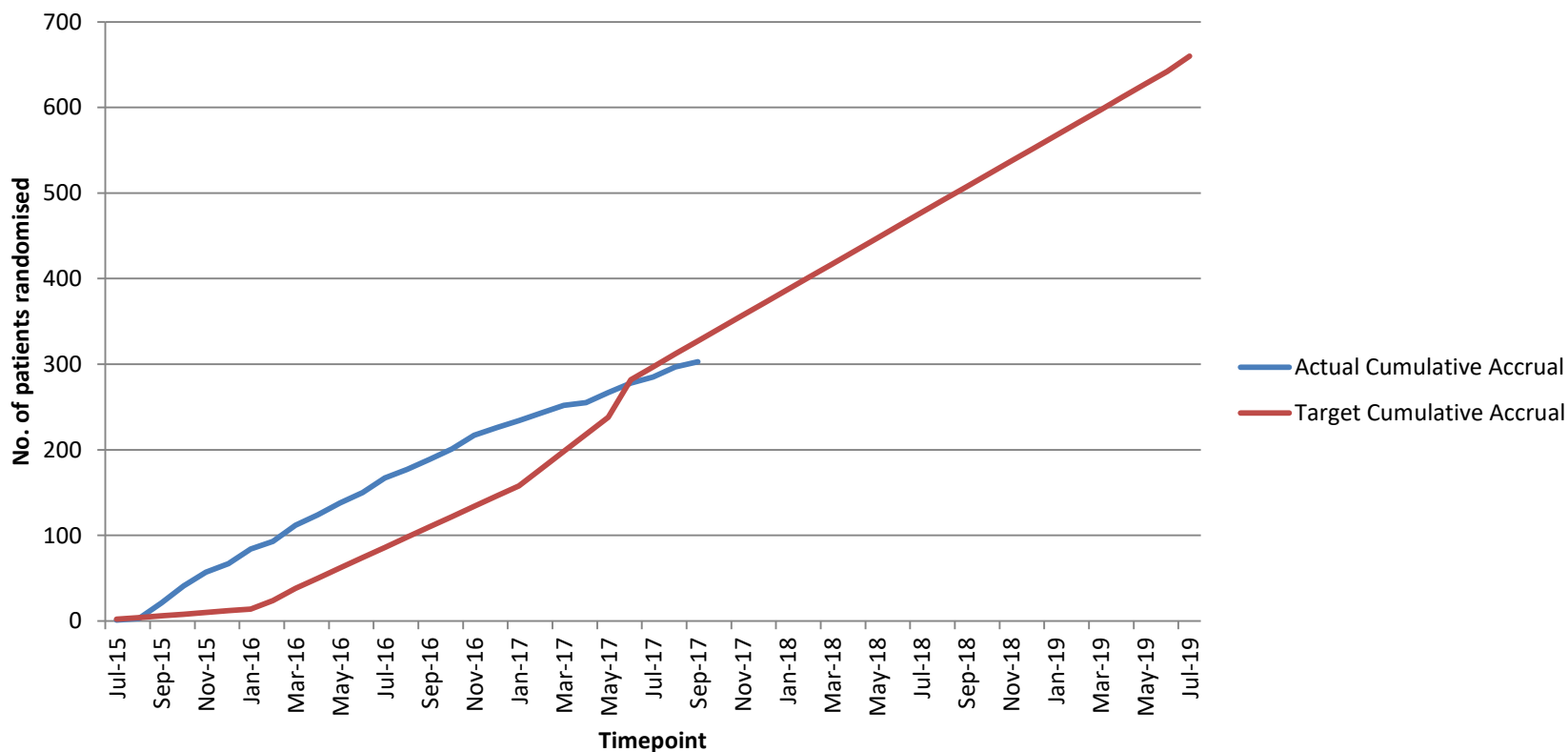
Modified comparator arms as of May 2017:

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

77 UK sites and 6 sites in Ireland open to recruitment. Will be an international trial with participation interest from Switzerland and Mexico

ICON8B Actual vs Target Accrual (data up until 3rd Oct 2017)

ICON8B Target vs Actual Accrual (arms B1 and B3 only)



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.