

ICON7

Bevacizumab in Ovarian Cancer

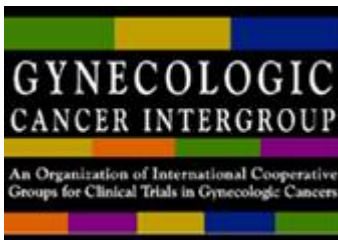
MRC

Clinical
Trials
Unit

ICON7: A phase III Gynaecologic Cancer InterGroup (GCIg) trial of adding bevacizumab to standard chemotherapy in women with newly diagnosed epithelial ovarian, primary peritoneal, or fallopian tube cancer

Interim analysis on overall survival

**Gunnar Kristensen, Tim Perren, Wendi Qian, Jacobus Pfisterer, Jonathan Ledermann, Françoise Joly, Mark Carey, Philip Beale, Andreas Cervantes, Amit Oza
on behalf of the GCIg ICON7 collaborators
(MRC/NCRI, AGO-OVAR, GINECO, NSGO, ANZGOG, GEICO, NCIC-CTG)**



MRC | Medical Research Council



American Society of Clinical Oncology
Making a world of difference in cancer care

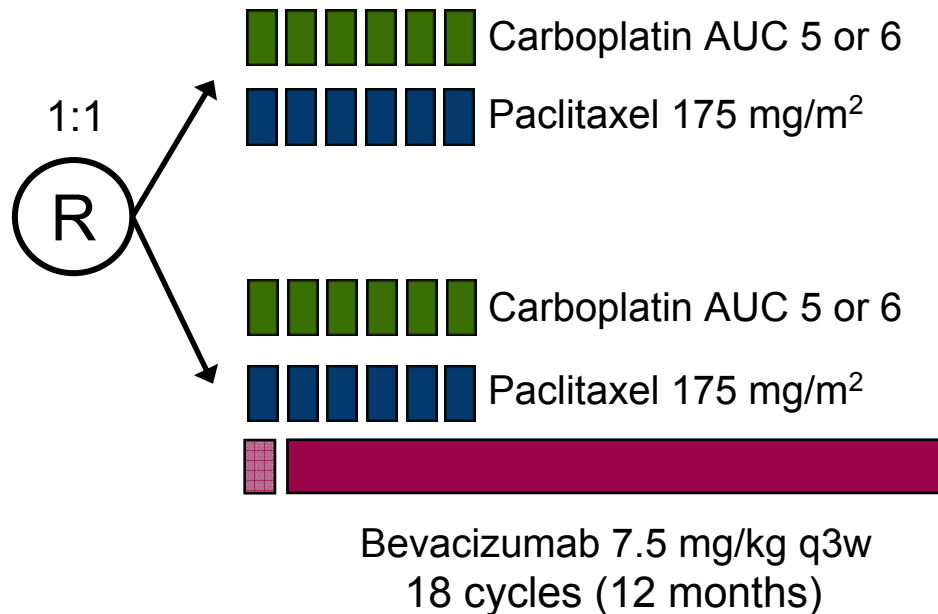
-
- **The women who participated in the trial and their families**
 - **Participating GCIG groups**
AGO, ANZGOG, GEICO, GINECO, MRC/NCRI, NSGO, NCIC CTG
 - **The 263 clinical sites and their staff**
 - **Trial Management Group**
T Perren, A Oza, AM Swart, W Qian, M Parmar, L Farrelly, C Kwakye, N Thompson, C Irl, G Jayson, D Stark, M Sculpher, J Pfisterer, G Elser, A Kruger, P Beale, J Martyn, K Gillies, A Cervantes, F Nepote, E Pujade-Lauraine, F Marmion, B Votan, M Carey, M Bacon, R Meyer, G Kristensen, G Anderson
 - **MRC Clinical Trials Unit Coordination**
C Kwakye, L Farrelly, AM Swart, W Qian, E Hainsworth, C Griffin
 - **Trial Physicians**
F al-Terkait, S Sim, F Collinson

Background for updated OS analysis

- Results presented at ESMO 2010: Bevacizumab combined with standard carboplatin–paclitaxel followed by continued single-agent bevacizumab
 - Demonstrated a benefit in progression-free survival (PFS)
 - Suggested a trend for overall survival (OS) improvement but results were immature (only 34% of the events required for final OS analysis)
- Regulatory authorities requested an interim OS analysis with at least 365 (51%) of 715 required events, to support filing
 - Approved by the trial management group and independent data monitoring and steering committees

Academic-led, industry-supported trial to investigate use of bevacizumab and to support licensing

- High-risk FIGO stage I–IIA or FIGO stage IIB–IV
 - Surgically debulked histologically confirmed OC
- n=1528*



Stratification variables:

- **Stage & extent of debulking** (I–III debulked ≤ 1cm vs I–III debulked >1 cm vs IV and inoperable stage III)
- **Timing of intended treatment start** (≤4 vs >4 weeks after surgery)
- **GCIG group**

*Dec 2006 to Feb 2009

OC = epithelial ovarian, primary peritoneal, or fallopian tube cancer

Overview of analyses

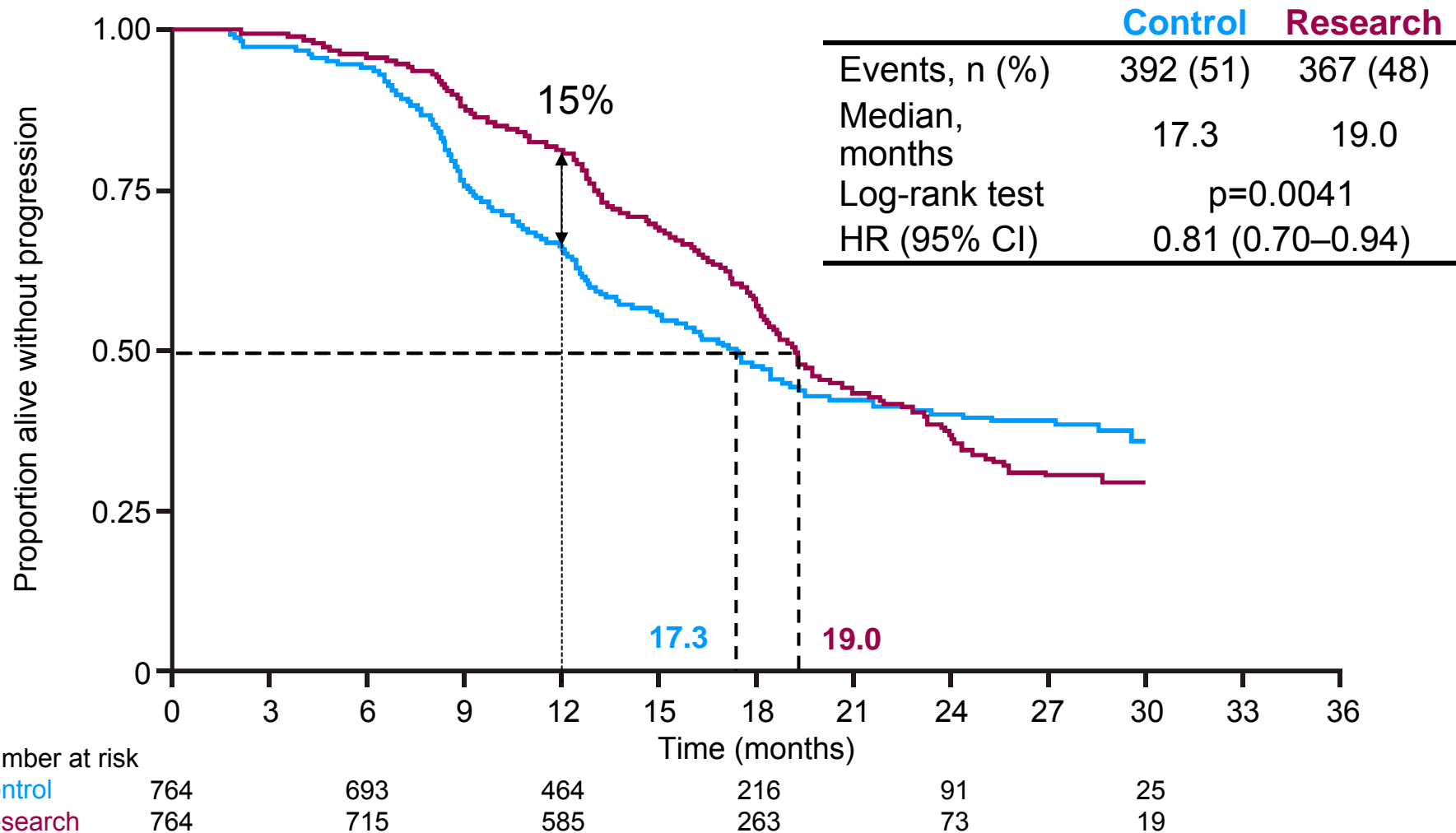
ICON7 was powered for both PFS and OS, designed to detect:

- PFS HR = 0.78 (684 events; 90% power)
- OS HR = 0.81 (715 events; 80% power)

	Median follow-up, months	PFS events, n	OS events, n (% of required events)
Mature PFS analysis (cut-off Feb 28, 2010; ESMO 2010)	19	759	241 (34%)
Updated interim OS analysis requested by regulatory authorities (cut-off Nov 30, 2010; ASCO 2011)	28	934	378 (53%)
Final OS analysis			715 (due in 2013)

Baseline characteristics

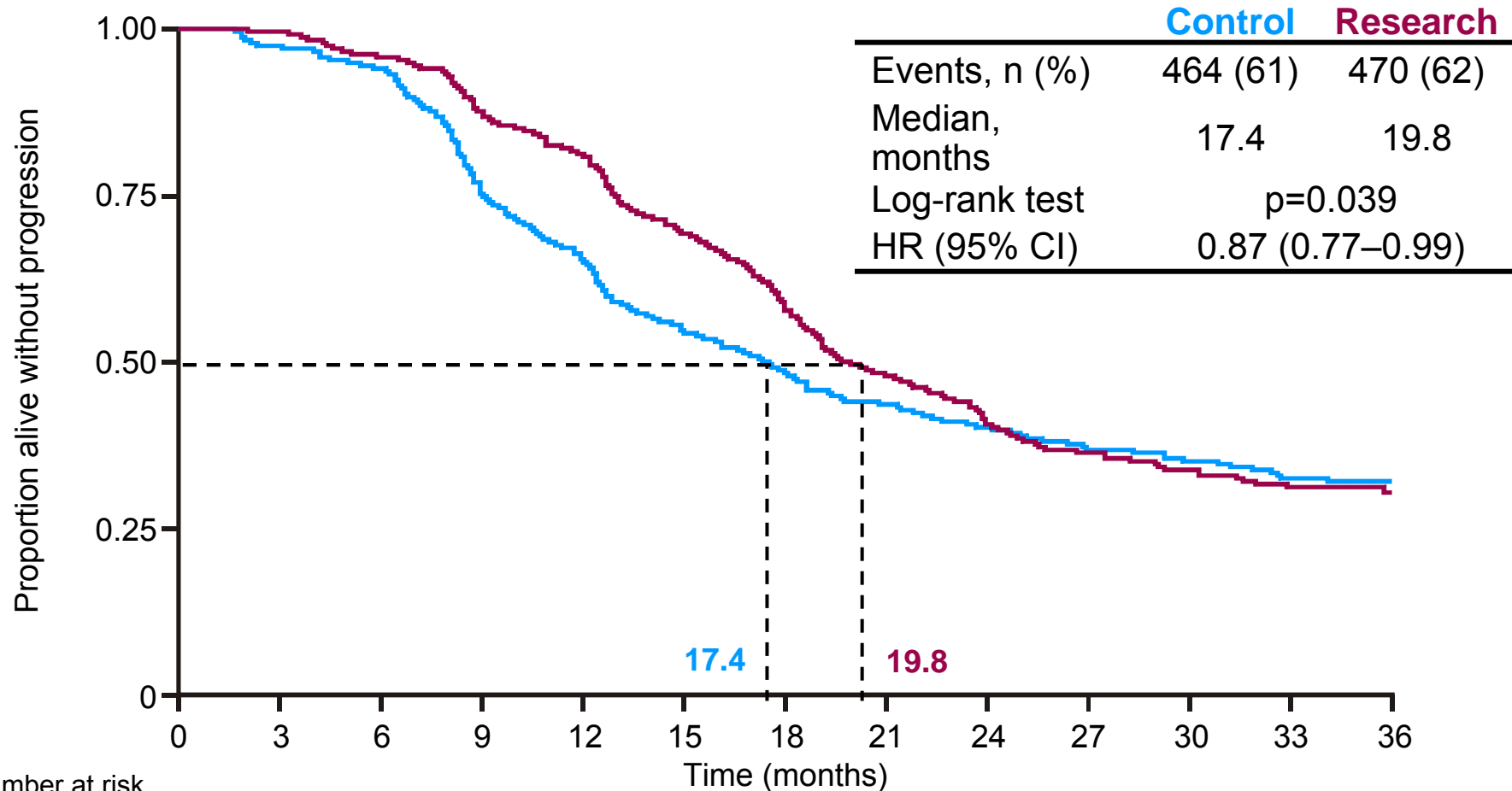
Characteristic		Control (n=764)	Research (n=764)
Median age, years (range)		57 (18–81)	57 (24–82)
Origin of cancer, %	Ovary (epithelial)	87	88
Histology, %	Serous	69	69
	Clear cell	8	9
FIGO stage, %	I/IIA	10	9
	IIB–IIIB	21	20
	IIIC/IV	69	71
Debulking surgery/ residuum, %	≤1 cm	72	73
	>1 cm	25	25
	No surgery	2	2
Risk group, %	FIGO III >1 cm/FIGO IV debulking	31	30
	All the rest	69	70



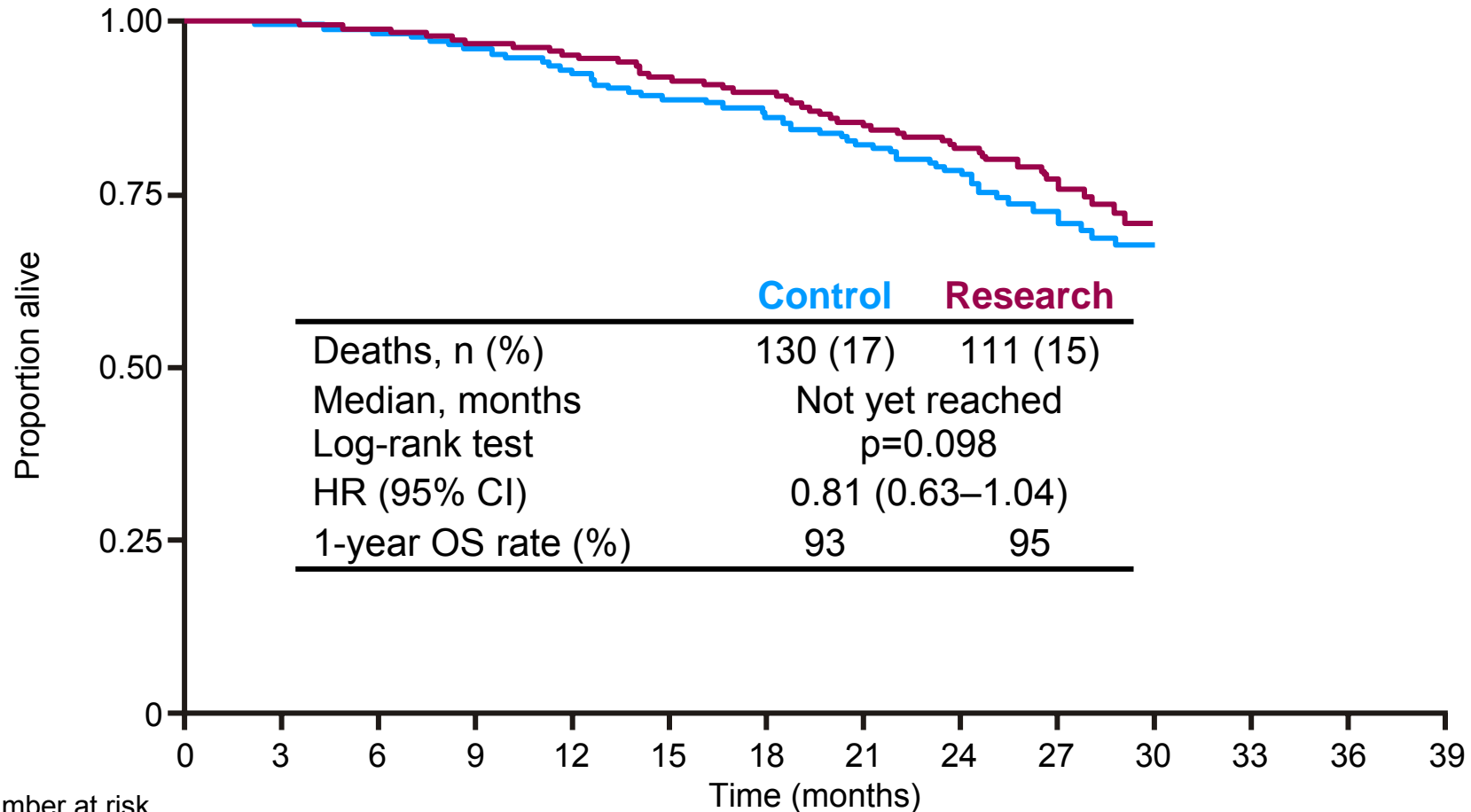
ICON7

Bevacizumab in Ovarian Cancer

Updated PFS

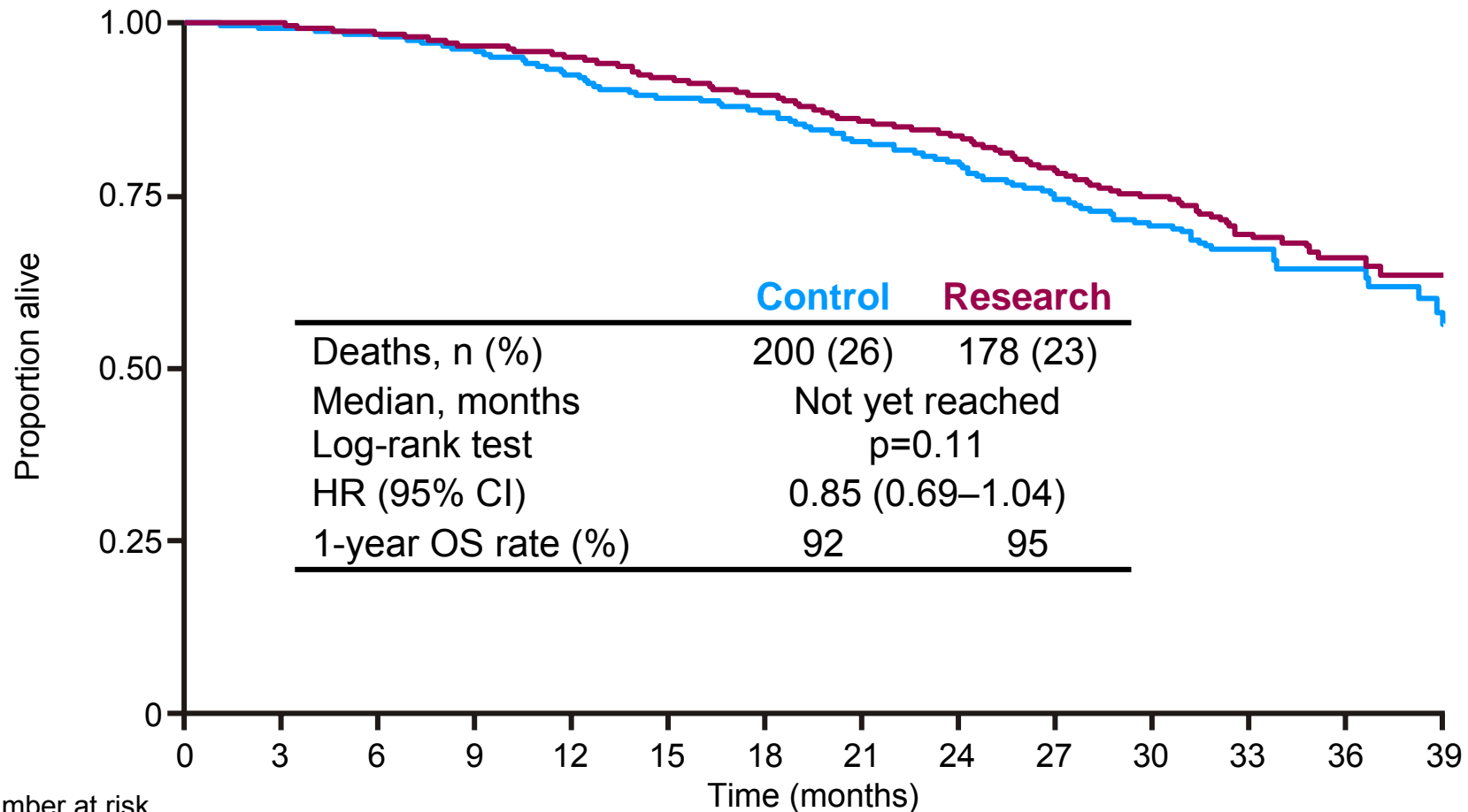


Number at risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Control	764	693	614	514	424	350	284	221	164	114	74	44	39
Research	764	716	664	599	514	430	350	284	229	164	107	64	27



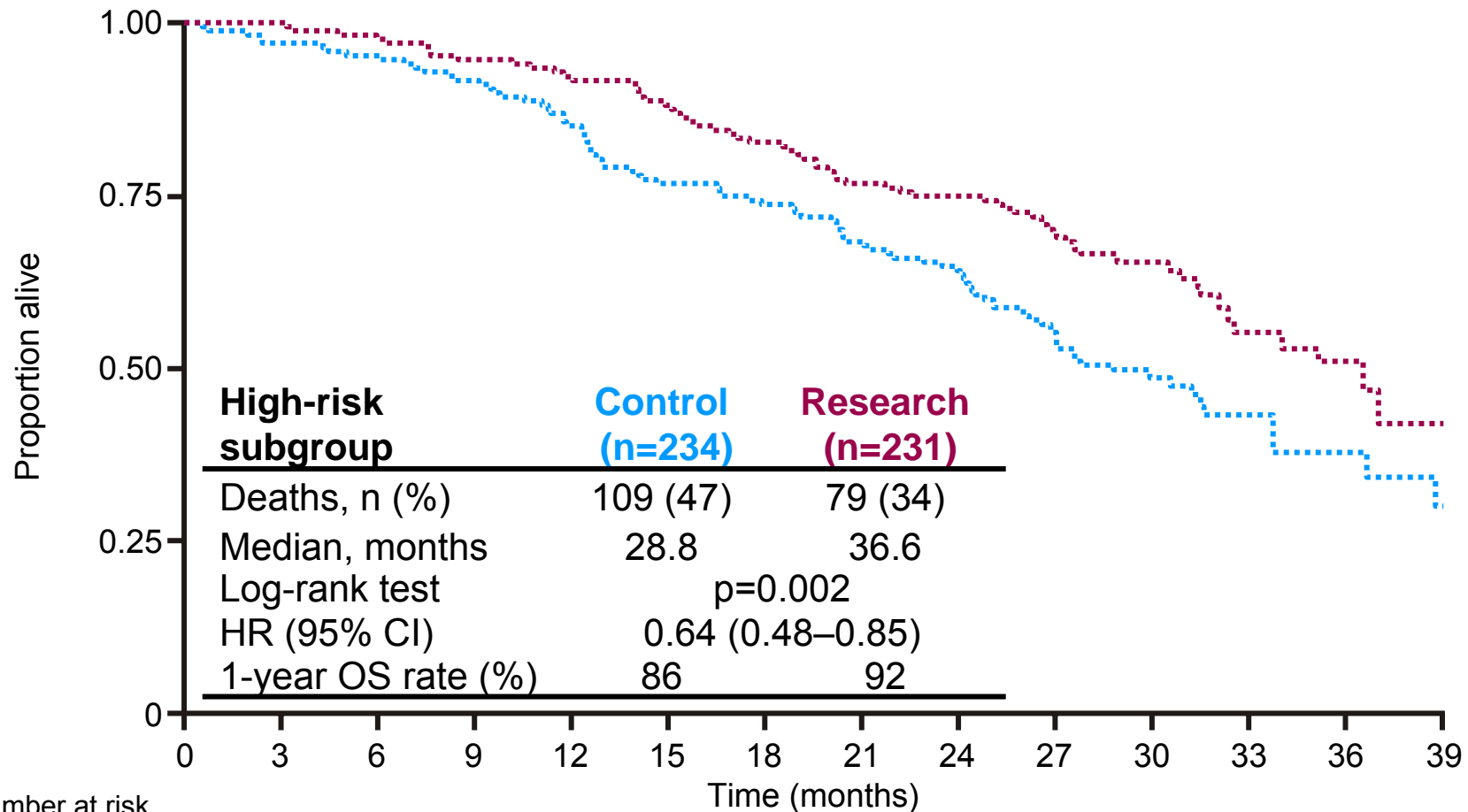
	0	3	6	9	12	15	18	21	24	27	30
Number at risk											
Control	764	741	724	701	652	486	368	252	159	83	33
Research	764	753	737	716	678	525	404	259	162	89	40

Interim OS analysis (regulatory request)

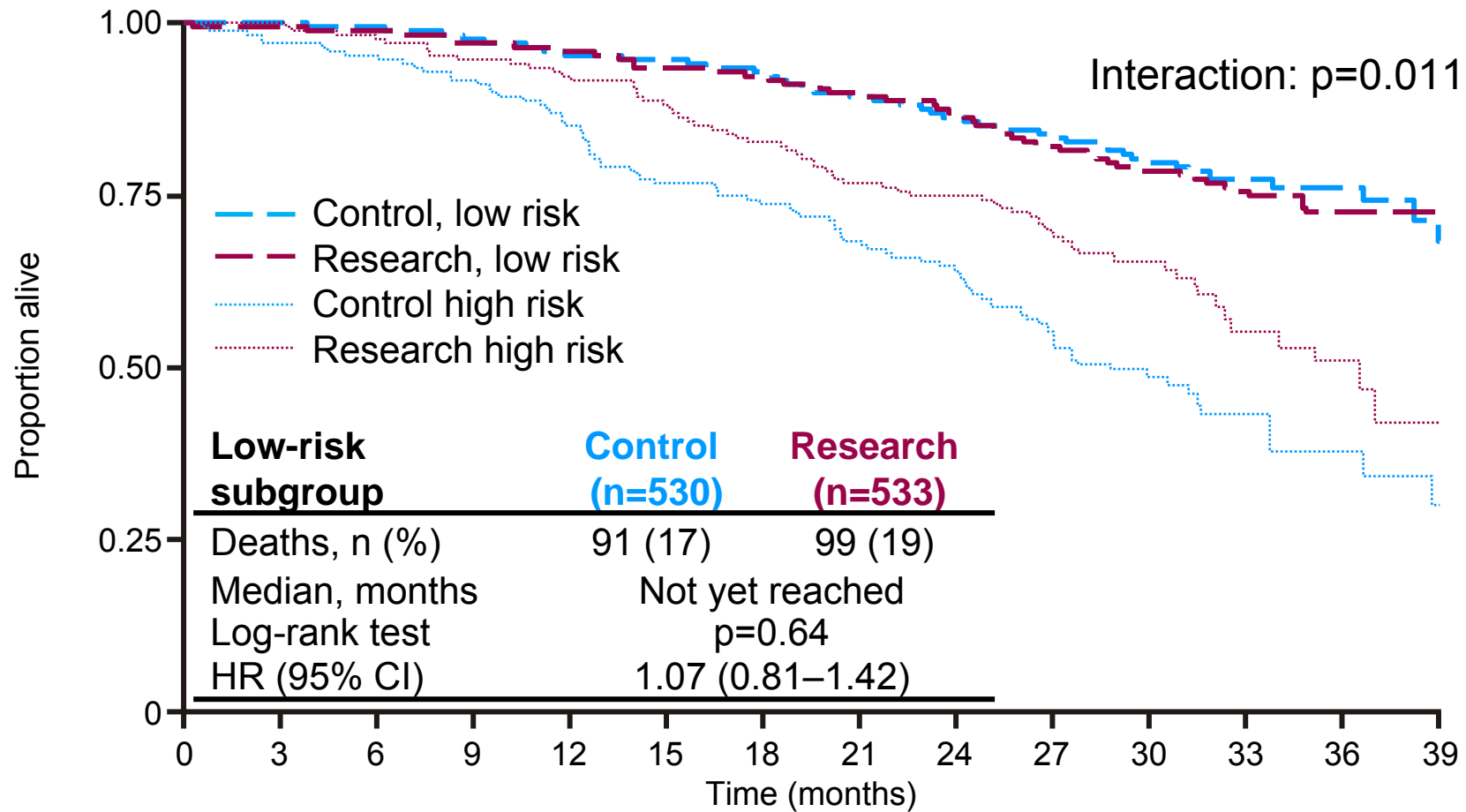


	0	3	6	9	12	15	18	21	24	27	30	33	36	39
Number at risk														
Control	764	741	724	703	672	646	623	542	421	304	212	132	71	26
Research	764	753	737	717	702	680	657	592	459	329	228	129	69	19

OS: High-risk subgroup



Number at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39
Control	234	219	194	166	107	46	15							
Research	231	222	208	186	134	65	18							



-
- Bevacizumab combined with chemotherapy and continued alone (7.5 mg/kg for 12 months) vs chemotherapy demonstrates
 - Continued improvement in PFS with no crossing of curves
 - Trend for improved OS continues in the total population
 - Treatment effect is greater in patients at high risk of recurrence, which may be of clinical relevance
 - These are interim OS results requested by regulatory authorities; final OS results are due in 2013