#### Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study

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Terms and Conditions

## Cohort

- 2733 women breast cancer diagnosed <40</li>
- 338 (12%) BRCA mutations
- Of 558 TNT:
  - 123 were B1(22%)
  - 13 (2%) were B2
  - 76% were BRCA neg
- 20% overall were TNT
- No mention of FH
   Only 14% had service BRCA testing



### Survival

- Median follow up 8.2 y
- Contralateral tumours in 151 (6%)
  - 18% B1
  - 12% B2
  - 4% B-neg
- There was NO difference in overall survival between B+ and B-, even when B1 and B2 compared separately
- At 2, 5 and 10y



#### Comments

- Some differences in short-term survival with B1/2, and TNT, but none overall
- Bilateral risk-reducing mastectomy is not a necessary part of treating a unilateral breast cancer but unilateral mastectomy might enable breast radiotherapy to be omitted.
- In the POSH cohort, immediate bilateral mastectomy was not associated with improved survival, although the reported use of risk-reducing surgery was low; (32 BSO 107 RRM)
- One theory that could explain the slight survival advantage for BRCA mutation carriers **not** undergoing immediate bilateral mastectomy is that a major surgical intervention might compromise host immunity at a time when this is particularly important for eradicating micrometastases.

- risk-reducing surgery, particularly for BRCA1 gene carriers is an appropriate management; in our analysis, the rising hazard for death in BRCA carriers over time women was negated by removing from the analysis all patients who developed a second new primary breast or ovarian cancer during the follow-up period.
- With modern MRI-based breast screening, we conclude that patients who choose to delay additional surgery for 1 or 2 years until they are psychologically and physically recovered from their cancer treatment can be reassured that this choice is unlikely to lead to any substantial survival disadvantage.

# Triple neg breast cancers

A	100	· · · · · · · · · · · · · · · · · · ·				BRCA — BRCA	negative positive
(%	80 -			<u> </u>			•
ırvival (	60 -						
all su	40 -					1. C	
Over	20						
	20 -						
	0	7	1		10	12 Γ	15
	0	2.5	5	/·5	10	12.2	15
Number at risk				inte to event (ye	ears)		
(number censore	ed) ivo 422 (52)	261 (52)	267 (8)	165 (4)	62(2)	4 (1)	0(0)
BRCA positi	ive 136 (10)	120 (14)	94(7)	63 (1)	26 (1)	2 (0)	1(0)
<ul> <li>Unadjusted Adjusted</li> </ul>				Number of events (number of patients)*		HR (95% CI)	p value
BRCA negative (R	Ref)			120 (422)		1.00 (Ref)	
UVA BRCA positiv	e (at 2 years)	⊢●		33 (136)		0.59 (0.35-0.99)	0.044
UVA BRCA positiv	e (at 5 years)	H		33 (136)		1.09 (0.67-1.75)	0.75
UVA BRCA positiv	e (at 10 years)	H		33 (136)		1.96 (0.76–5.05)	0.17
MVA BRCA positiv	ve (at 2 years)			33 (136)		0.59 (0.35-0.99)	0.047
MVA BRCA positiv	ve (at 5 years)	H		33 (136)		1.13 (0.70–1.84)	0.62
MVA BRCA positiv	ve (at 10 years)	H		33 (136)		2.12 (0.82-5.49)	0.12
Age at diagnosis				153 (558)		1.03 (0.98–1.08)	0.25
BMI <25 (Ref)				63 (274)		1.00 (Ref)	
≤25-30			⊢●⊣	54 (149)		1.51 (1.04–2.21)	0.032
≥30		H		33 (123)		1.09 (0.71–1.67)	0.71
Maximum invasiv	ve tumour size (cn	n)		143 (523)		1.11 (1.04–1.18)	0.0012
N0 stage (Ref)				58 (341)		1.00 (Ref)	
N1 stage			HeH	94 (211)		2.72 (1.91–3.86)	<0.0001
White ethnicity (	(Ref)			140 (500)		1.00 (Ref)	
Black ethnicity				10 (26)		2.17 (1.12–4.21)	0.021
Asian ethnicity	H	•		1 (19)		0.19 (0.03–1.36)	0.098
Other ethnicity	F	•		1 (5)		0.66 (0.09-4.74)	0.68
No use of taxane	s (Ref)			98 (384)		1.00 (Ref)	
Use of taxanes		н	•	55 (161)		1.18 (0.84–1.68)	0.34
	0.02		)				
Reduced risk Increased risk							