



Micrometastases and Isolated tumor cells: Relevant and Robust Or Rubbish? The MIRROR study

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On behalf of the Dutch Breast Cancer Trialists' Group (BOOG)

Funded by The Netherlands organization for health research and development (ZonMw)



- **Impacto pronóstico de**

 - Cel aisladas (pNo(i+), ≤ 0.2 mm)

 - micrometástasis (pN1mic, $>0.2-2$ mm)

- Resultados conflictivos en estudios previos

antecedentes

- Holanda: no hay consenso en tratamiento sistémico adyuvante(TSA) ante presencia de cel aisladas o micrometástasis en tu de características favorables
- Práctica habitual: 50 % TSA
- **Oportunidad :**
Evaluar el pronóstico del depósito de cel neoplásicas pqñas en diferente cohorte con y sin TSA



Design: cohort study

patients with favorable
primary tumor characteristics
(no indication for AST)

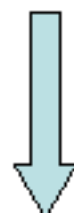
sentinel lymph node procedure

pN0, pN0(i+) or pN1mi



pN0

no adjuvant
systemic therapy



pN0(i+) or pN1mi

no adjuvant
systemic therapy



pN0(i+) or pN1mi

adjuvant
systemic therapy



objetivos

- **¿Cuál es el impacto pronóstico pNo(i+) y pN1mic BLNC ?**
- ¿Cuál es el impacto de la TSA en pacientes con pNo(i+) y pN1mic?

Pacientes y método

- Pacientes seleccionadas del registro de cancer holandés
Ca mama invasor diagnosticado entre 1997 y 2005
BLNC
Estado nodal final pNo, pNo(i+), pN1mic
Tumor de características favorables (guía holandesa 2002)
tu \leq 1cm independiente de grado nuclear
tu 1-3 cm y grado I-II
- **Revisión patológica central**
- 1º endpoint : sobrevida libre enf a 5 años (DFS)



Accrual

n = 3205
selected from Netherlands
Cancer Registry



no pathology review n = 212

n = 2993
for pathology
review

macrometastases n = 179
unfavorable tumour
characteristics n = 71
other reasons n = 115

n = 2628
inclusion after
pathology review

pN0
no adjuvant
systemic therapy
n = 838

pN0(i+) or pN1mi
no adjuvant
systemic therapy
n = 832

pN0(i+) or pN1mi
adjuvant
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n = 958



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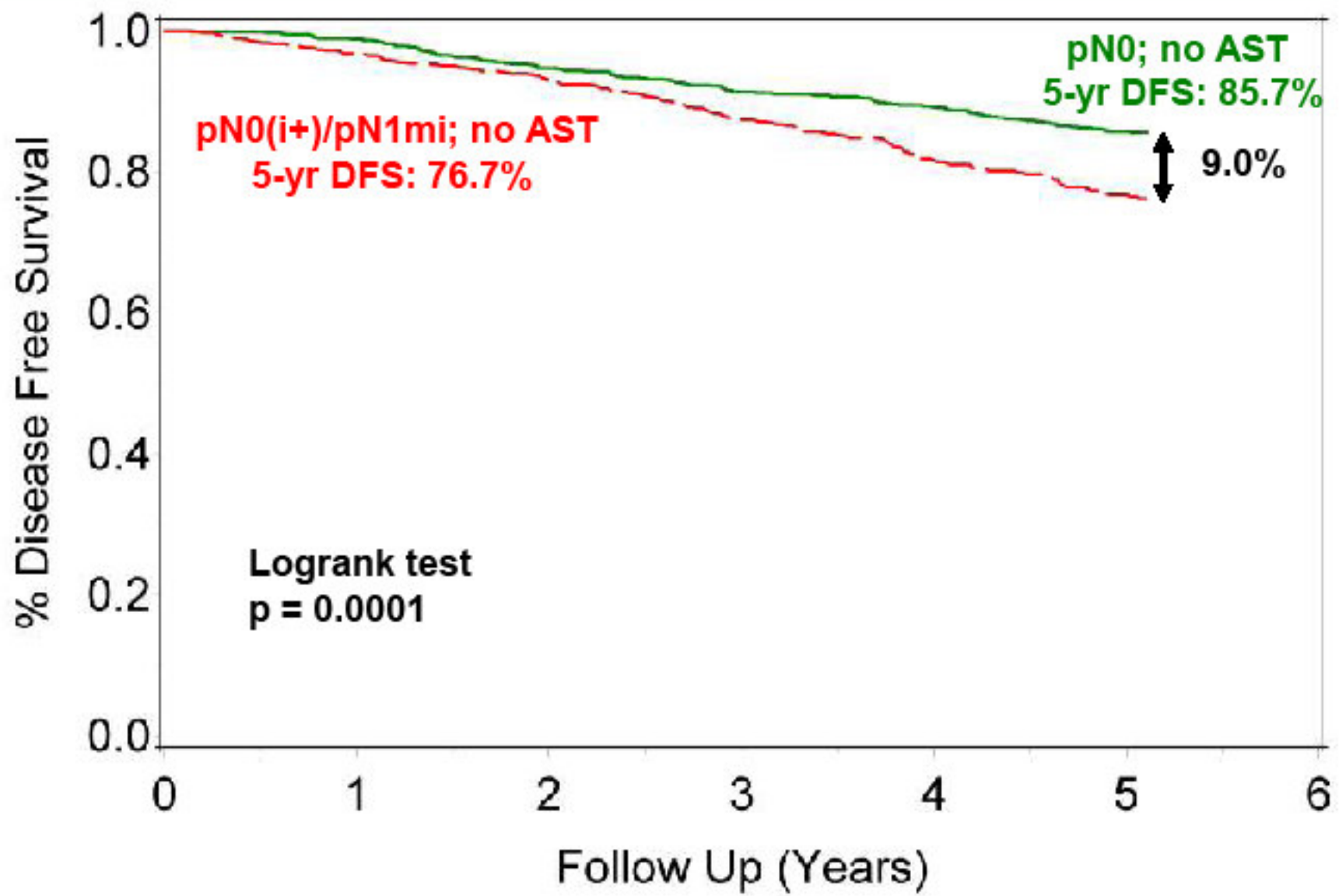
Baseline characteristics: pN0 versus pN0(i+)/pN1mi

		pN0 No AST n = 838	pN0(i+) or pN1mi No AST n = 832	p-value
Age (mean)		60 yr	58 yr	<0.0001
Tumor size	≤ 1 cm	41%	28%	
	1.1 – 2.0 cm	52%	61%	0.0001
	2.1 - 3.0 cm	7%	12%	
Tumor grade	I	37%	36%	
	II	55%	58%	0.30
	III	6%	4%	
ER/PgR status	ER + and/or PgR +	89%	90%	
	ER - and PgR -	6%	8%	0.09
Axillary lymph node dissection and/or axillary irradiation	No	86%	39%	
	Yes	14%	61%	<0.0001





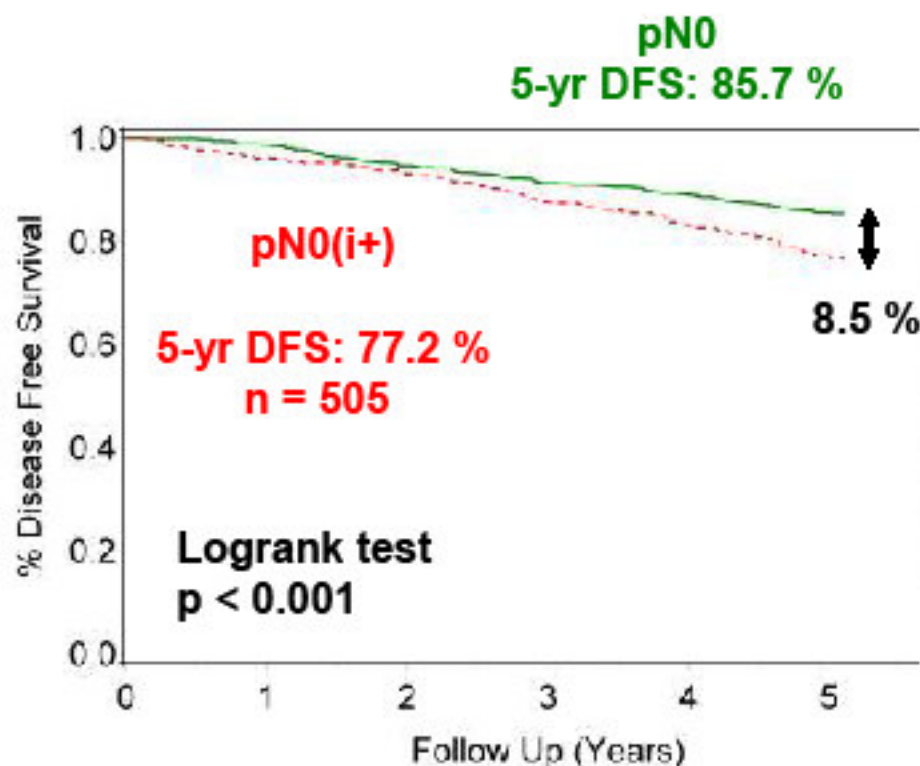
Results: disease free survival pN0 vs. pN0(i+)/pN1mi



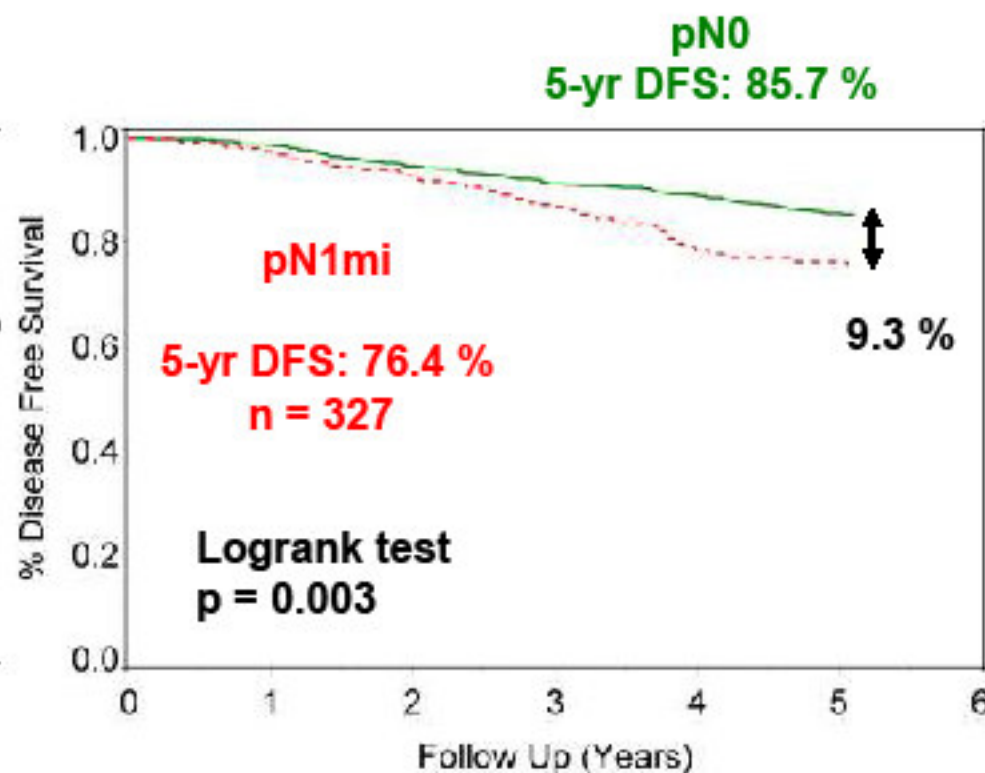


Results: disease free survival

pN0 vs pN0(i+)
pN0 vs pN1mi



pN0 vs pN0(i+)



pN0 vs pN1mi

No adjuvant systemic therapy





MV analysis: disease recurrence pN0(i+) / pN1mi

Variable	HR	95 % CI	p-value
pN0	1.00		
pN0(i+) / pN1mi	1.49	1.18 – 1.89	0.001
pN0(i+)	1.50	1.15 – 1.95	0.003
pN1mi	1.52	1.11 – 2.09	0.009

Corrected for age¹, tumor size², differentiation grade, ER/PgR status

¹modeled as continuous variable ²modeled as log size (continuous)



Conclusiones

- **Pacientes con pNo(i+) o pN1mic presentaron peor DFS comparados con pacientes pNo**
- **El resultado de pNo(i+) fue similar al de pN1mic y peor que el de pNo**
- **Nota: ninguno de estos pacientes recibió TSA
→ impacto pronóstico puro**

objetivo

- ¿Cuál es el impacto pronóstico de BLNC con pNo(i+) y pN1mic?
- **¿Cuál es el impacto de la TSA en pacientes con pNo(i+) y pN1mic?**



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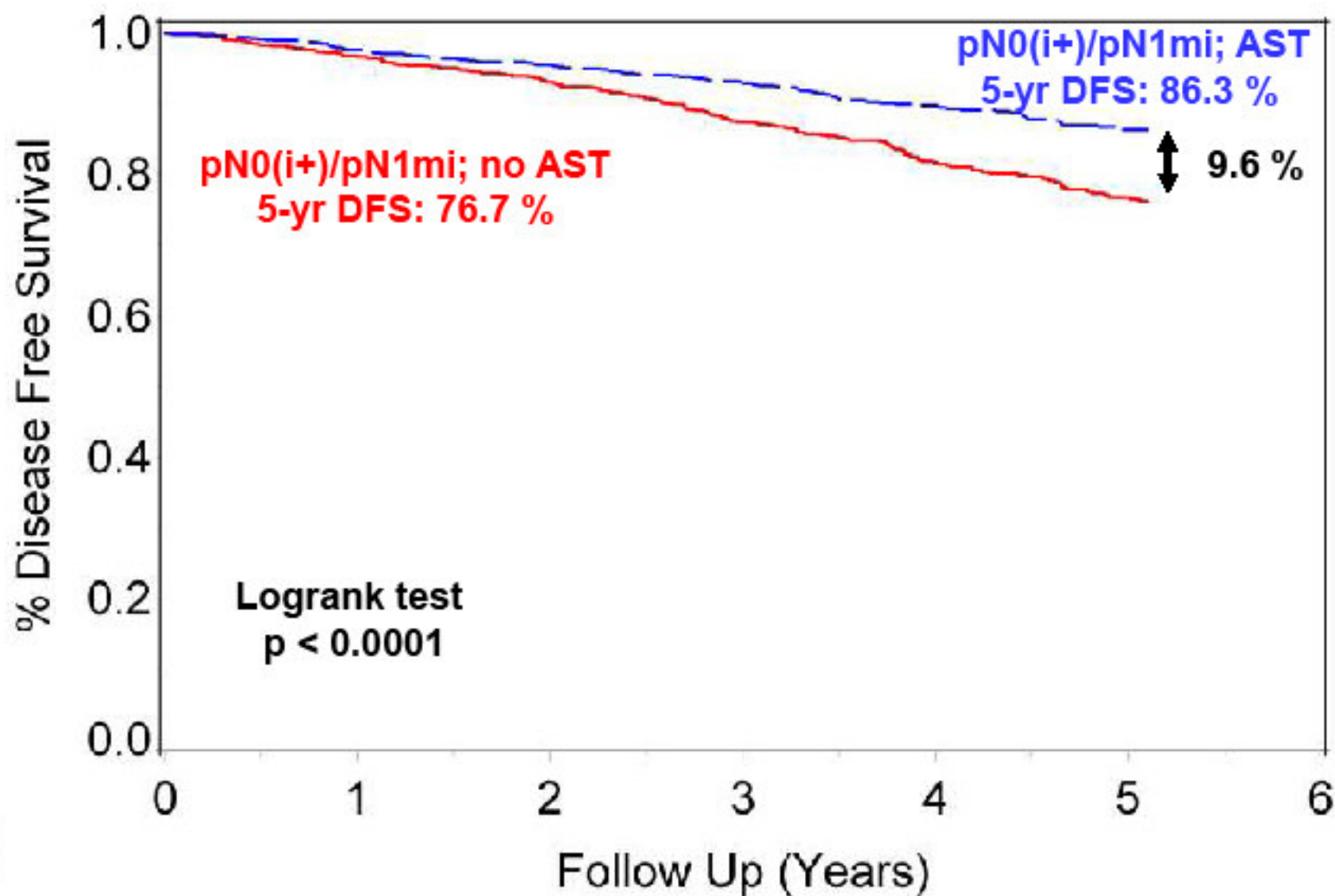
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Results: disease free survival

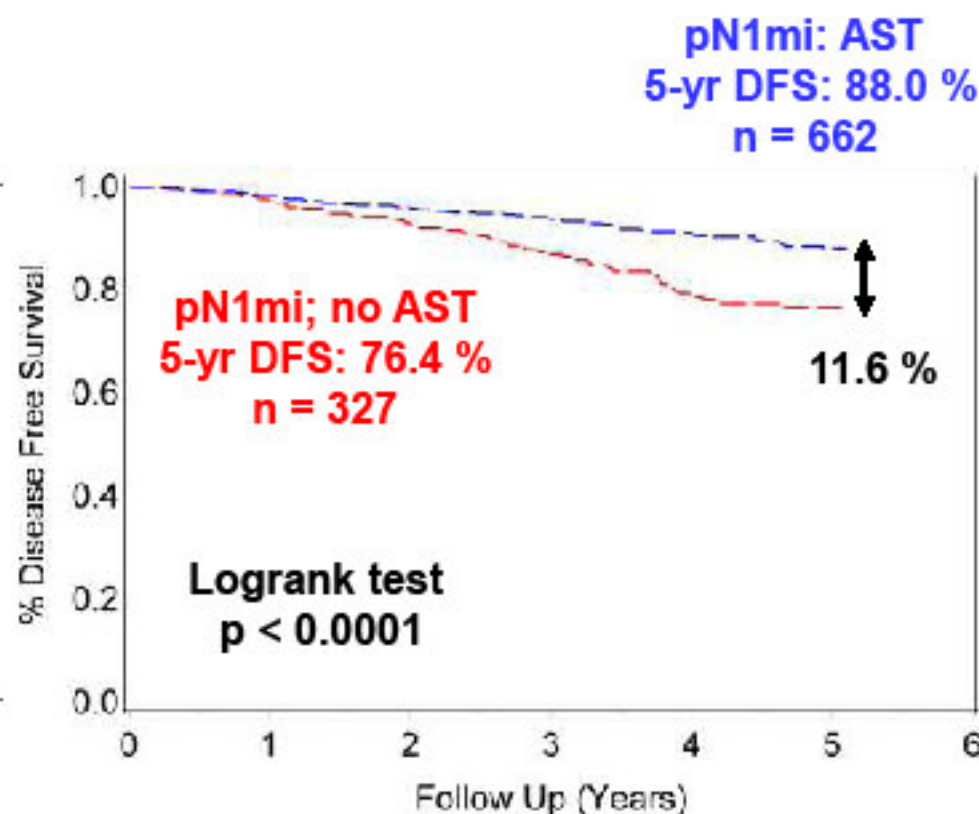
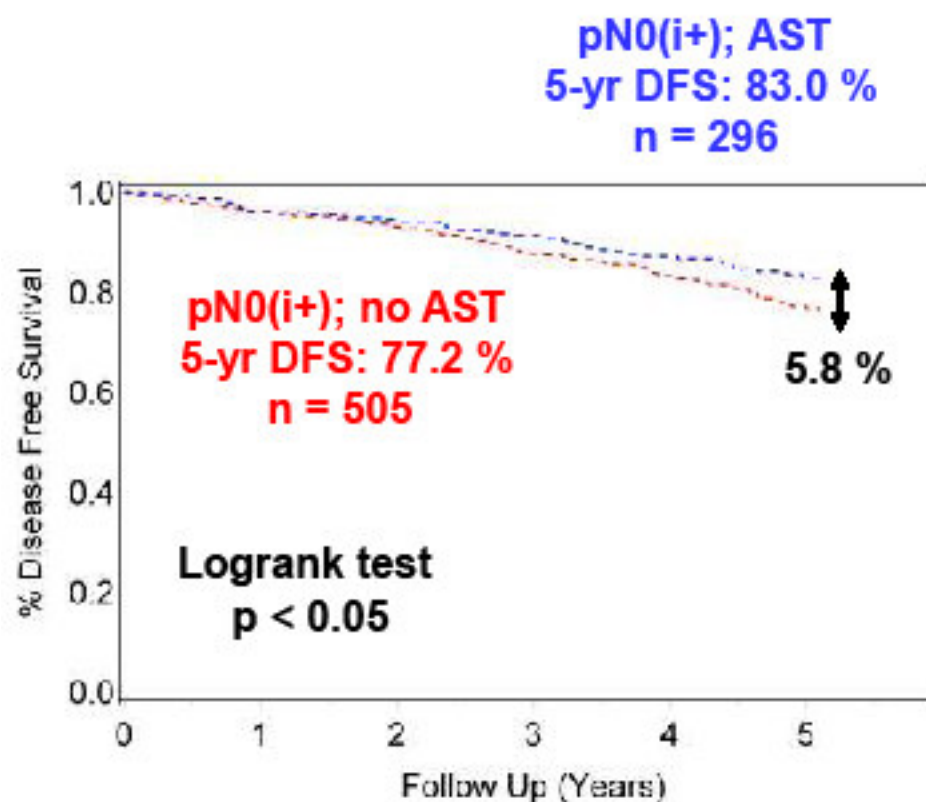
AST vs no AST





Results: disease free survival

pN0(i+) +/- AST
pN1mi +/- AST



pN0(i+) +/- AST

pN1mi +/- AST





MV analysis: disease recurrence pN0(i+)/pN1mi + AST

Variable	HR	95 % CI	p-value
pN0(i+)/pN1mi no AST	1.00		
pN0(i+)/pN1mi + AST	0.57	0.44 – 0.74	<0.0001
pN0(i+) no AST	1.00		
pN0(i+) + AST	0.67	0.46 – 0.96	0.03
pN1mi no AST	1.00		
pN1mi + AST	0.50	0.35 – 0.72	0.0002

Corrected for age¹, tumor size², differentiation grade, axillary treatment

¹modeled as continuous variable ²modeled as log size (continuous)



Conclusión: impacto de TSA en pNo(i+) y pN1mic

- **Pacientes con pNo(i+) y pN1mic que recibieron TSA tuvieron una significativa mayor DFS al compararla con pacientes que no recibieron TSA**

Conclusión final

- **Es el 1º estudio en pN0(i+) y pN1mic en la era del LNC con nº considerable de pacientes y análisis separado para TSA**
- **En el grupo que no recibe TSA, pNo(i+) y pN1mic , ambos constituyen factor pronóstico para DFS**
- **El impacto pronóstico de pNo(i+) fue tan importante como el impacto de pN1mic**
- **Nuestros datos muestran que AMBOS grupos se beneficiarían de TSA**