

# 498: ERBB2/HER2 Status In Biliary Tract Cancer Patients In Spanish RETUD Registry

AJ Muñoz<sup>1</sup>, F Castet<sup>2</sup>, R Vera<sup>3</sup>, R Álvarez<sup>4</sup>, C Pertusa<sup>5</sup>, P Garcia-Alfonso<sup>1</sup>, R Jiménez<sup>1</sup>, R Vidal-Tocino<sup>6</sup>, I Ales<sup>7</sup>, N Luque<sup>8</sup>, J Adeva<sup>9</sup>, WG Parra<sup>9</sup>, A Carral<sup>10</sup>, RM Rodriguez-Alonso<sup>11</sup>, E Aranda<sup>11</sup>, P Cerda<sup>12</sup>, E Martínez de Castro<sup>13</sup>, A La Casta<sup>14</sup>, B Laquente<sup>15</sup>, T Macarulla<sup>2</sup>

<sup>1</sup>Medical Oncology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain; <sup>2</sup>Medical Oncology Department, Hospital Clínic, Barcelona, Spain; <sup>3</sup>Medical Oncology Department, Hospital Universitario de Navarra, Navarra, Spain; <sup>4</sup>Medical Oncology Department, Hospital Universitario HM Sanchinarro, Madrid, Spain; <sup>5</sup>Medical Oncology Department, Consorcio Hospital General Universitario de Valencia, Valencia, Spain; <sup>6</sup>Medical Oncology Department, Hospital Universitario de Salamanca, IBSAL, Salamanca, Spain; <sup>7</sup>Medical Oncology Department, Hospital Regional Universitario de Málaga, Málaga, Spain; <sup>8</sup>Medical Oncology Department, Hospital Universitario Virgen de las Nieves, Granada, Spain; <sup>9</sup>Medical Oncology Department, Hospital Universitario 12 de Octubre, Madrid, Spain; <sup>10</sup>Medical Oncology Department, Hospital Universitario de A Coruña, A Coruña, Spain; <sup>11</sup>Medical Oncology Department, Hospital Universitario Reina Sofía, Córdoba, Spain; <sup>12</sup>Medical Oncology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; <sup>13</sup>Medical Oncology Department, Hospital Universitario Marqués de Valdecilla, Santander, Spain; <sup>14</sup>Medical Oncology Department, Hospital Universitario de Donostia, San Sebastián, Spain; <sup>15</sup>Medical Oncology Department, Catalan Institut of Oncology- IDIBELL, Barcelona, Spain

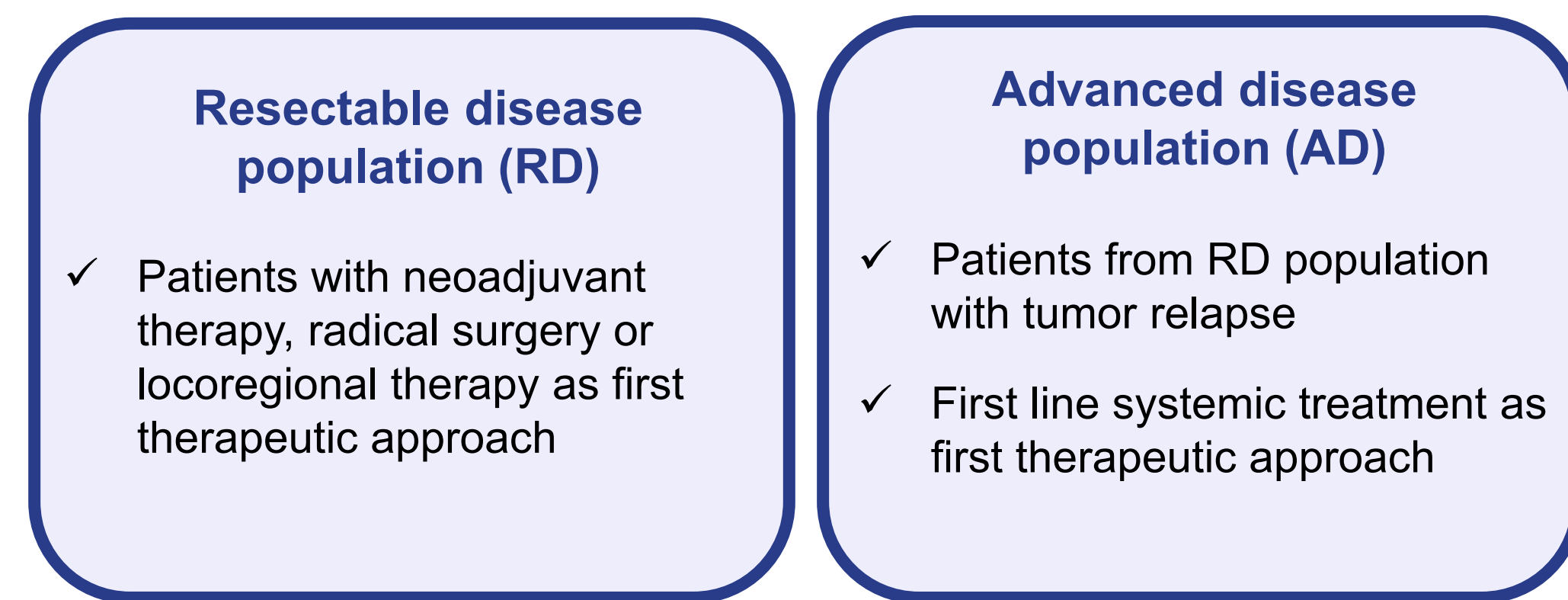
## Background

Biliary tract cancer (BTC) is a heterogeneous group of tumors, including cholangiocarcinoma (intra and extrahepatic) and gallbladder carcinoma.<sup>1</sup> ERBB2 gene amplification or HER2 receptor overexpression is a well-known oncogenic driver and represents a therapeutic target in BTC.<sup>2,3</sup> We aimed to describe the epidemiology characteristics, treatment patterns and efficacy outcomes of a cohort of BTC patients according to HER2 expression status.

## Methods

BTC diagnosis occurred between January 1st, 2017, and May 30th, 2025. Two different populations were defined for analysis (**Figure 1**). Patients initially with resectable disease (RD) and tumor relapse were analyzed in both groups.

**Figure 1.** Definition of patient populations for the analysis



ERBB2/HER2 status was assessed by next-generation sequencing (NGS), immunohistochemistry (IHC), and/or fluorescence/chromogenic in situ hybridization (FISH/CISH). HER2+ status was considered when it was overexpressed (IHC+++ and/or when it was amplified by FISH/CISH (if IHC++) or NGS.

Analysis comprised demographic and clinical data, tumor molecular profile, therapeutic procedures and efficacy outcomes. Time to next treatment (TTNT), progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method. P-value < 0.05 was considered statistically significant. All analysis were done using statistical software R version 4.5.1.

## Results

ERBB2/HER2 status was determined in 448 BTC patients from 31 centers. At diagnosis, 148 patients (33.0%) presented RD and 300 (67.0%) presented AD. 128 patients from RD population experienced tumor relapse. HER2+ was confirmed in 24 (5.4%) patients, main baseline and clinic characteristics are shown in **table 1** and **table 2**.

**Table 1.** Demographic and clinic characteristics by HER2 status

Variable	HER2 positive N = 24	HER2 negative N = 424	p-value
Median age at diagnosis (Q1, Q3)	67.50 (56.00, 72.50)	66.00 (59.00, 73.00)	0.857
Sex (female)	18 (75.00%)	186 (43.87%)	<b>0.003</b>
Median BMI (Q1, Q3)	25.65 (22.31, 29.70)	25.95 (23.37, 28.72)	0.726
Median follow-up time (Q1, Q3)	16.32 (11.35, 23.42)	16.61 (9.77, 26.61)	0.771
Advanced disease	24 (100.00%)	404 (95.28%)	0.616
Resectable disease	7 (29.17%)	141 (33.25%)	0.679
ECOG			0.191
0	3 (14.29%)	100 (30.30%)	
1	11 (52.38%)	169 (51.21%)	
2	2 (9.52%)	26 (7.88%)	
3	0 (0.00%)	3 (0.91%)	
Unknown	5 (23.81%)	32 (9.70%)	
Missing	3	94	

**Table 2.** HER2 status by tumor location

Variable	Ampulla of Vater	Extrahepatic distal	Extrahepatic hilar	Gallbladder
HER2 amplification				
HER2 positive	0 (0.00%)	2 (3.28%)	3 (7.32%)	9 (15.25%)
HER2 negative	9 (100.00%)	59 (96.72%)	38 (92.68%)	50 (84.75%)
Variable	Intra-extrahepatic	Intrahepatic	Unknown	p-value
HER2 amplification				<b>0.002</b>
HER2 positive	0 (0.00%)	9 (3.26%)	1 (100.00%)	
HER2 negative	1 (100.00%)	267 (96.74%)	0 (0.00%)	

Treatments received by RD and AD populations are shown in **table 3** and **table 4**, respectively.

**Table 3.** Treatments for resectable disease population

Variable	HER2 positive N = 7	HER2 negative N = 141	p-value
Surgery <sup>1</sup>	7 (100.00%)	130 (92.20%)	1.000
Hepatectomy	4 (57.14%)	74 (56.92%)	1.000
Lymphadenectomy	3 (42.86%)	35 (26.92%)	0.396
Duodeno-pancreatectomy	1 (14.29%)	42 (32.31%)	0.433
Cholecystectomy	2 (28.57%)	21 (16.15%)	0.334
Neoadjuvant treatment	2 (28.57%)	12 (8.51%)	0.171
Adjuvant treatment	4 (57.14%)	83 (58.87%)	1.000
ORR for neoadjuvant treatment	0 (0.00%)	4 (50.00%)	0.467
Not evaluable	0	4	

<sup>1</sup>One patient can have more than one procedure

**Table 4.** Treatments for advanced disease population

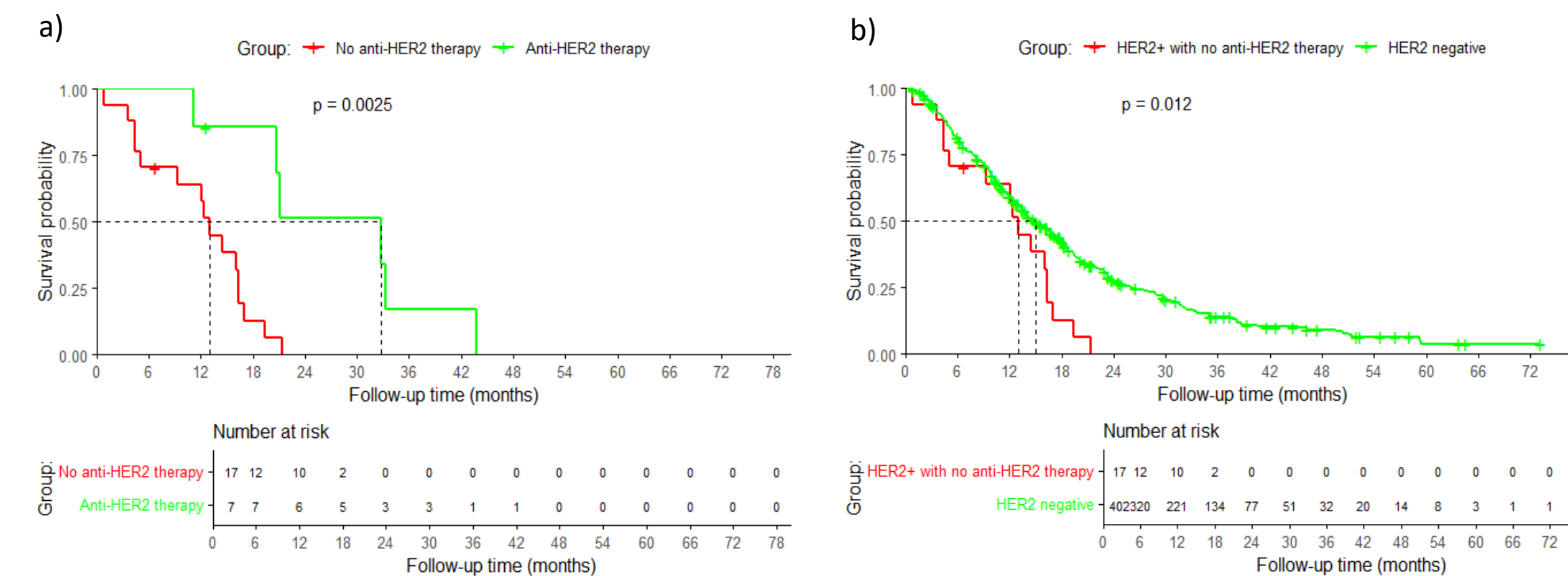
Variable	HER2 positive N = 24	HER2 negative N = 404	p-value
Surgery <sup>1</sup>	1 (4.17%)	5 (1.24%)	0.294
Hepatectomy	1 (100.00%)	4 (80.00%)	1.000
Lymphadenectomy	1 (100.00%)	1 (20.00%)	0.333
Cholecystectomy	1 (100.00%)	2 (40.00%)	1.000
First line	24 (100.00%)	399 (98.76%)	1.000
ORR for first line treatment	7 (36.84%)	95 (28.88%)	0.458
Not evaluable	5	70	
Second line	17 (70.83%)	226 (55.94%)	0.152
ORR for second line treatment	1 (7.69%)	21 (11.67%)	1.000
Not evaluable	4	46	

<sup>1</sup>One patient can have more than one procedure

A total of 7 (**29.2%**) HER2+ patients received **anti-HER2** therapy and 3 (**12.5%**) received **immunotherapy**.

Median OS (mOS) in **HER2+** AD patients treated with **anti-HER2** therapies was 32.7 months (95% CI 20.7-NA); mOS for HER2+ AD patients with other treatments was 13.1 months (95% CI 9.3-17.0) (**p=0.003**) (**Figure 2a**) versus mOS in **HER2-** AD patients of 15.0 months (95% CI 13.5-17.3) (**p=0.012**) (**Figure 2b**).

**Figure 2.** Overall survival. **a)** HER2+ patients receiving anti-HER2 therapy vs HER2+ patients without anti-HER2 therapy. **b)** HER2+ patients without anti-HER2 therapy vs HER2- patients



For HER2+ patients mPFS in first line was 6.6 months (95% CI 4.5-8.1) and 6.6 months (95% CI 5.9-7.7) for HER2- (p=0.075). HER2+ patients presented a mTTNT of 7.8 months (95% CI 6.7-NA) vs 10.0 months (95% CI 9.2-11.2) in HER2- patients (p=0.047).

This analysis provides insights into the **characterization** of real-world **HER2+ BTC** patients, with **anti-HER2** therapies showing a significant impact in **mOS**

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## Contact information

Email: andresmunmar@hotmail.com

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