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gastrointestinal tumours, non-colorectal

703P

HER2/HER3 pathway in biliary tract cancers: A systematic review and meta-analysis. A novel therapeutic druggable target?

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Background: HER2 overexpression and/or amplification has been reported as predictive factor to HER2 targeted therapy in breast and gastric cancer, whereas HER3 is emerging as a potential resistance factor. The aim of this study was to perform a systematic review and meta-analysis of the HER2 and HER3 up-regulation in biliary tract cancers (BTCs).

Methods: An electronic search of MEDLINE, ASCO, ESMO and AACR was performed to identify studies reporting HER2 and/or HER3 membrane protein expression by immunohistochemistry (IHC) and/or gene amplification by in situ hybridisation (ISH) in BTCs.

Results: Out of 440 studies screened, 40 met the inclusion criteria. Globally, HER2 expression rate was 26.5% (95% CI, 18.9% - 34.1%). Studies were classified as “high-quality” (HQ; 27 studies) [IHC overexpression defined as presence of moderate/strong staining] and “low-quality” (11 studies) [“any” expression was considered positive]. When HQ studies were analysed, extra-hepatic BTCs (EH-BTCs) showed a higher HER2 overexpression rate compared to intrahepatic cholangiocarcinoma (IHCC) [19.9% (95% CI, 12.8 - 27.1%) vs. 4.8% (95% CI, 0 - 14.5%); p-value 0.0049]. HER2 amplification rate was higher in those patients selected by HER2 overexpression [57.6% (95% CI, 16.2 - 99%)] compared to “unselected” patients [17.9% (95% CI, 0.1 - 35.4%); p-value 0.0072]. HER3 overexpression (4/4 HQ studies) and amplification rates were 27.9% (95% CI, 9.7 - 46.1%) and 26.5% (one study), respectively.

Conclusions: Up to 20% of EH-BTCs might be HER2 overexpressed, ~60% of HER2 overexpressed BTCs can be considered amplified while HER3 is overexpressed or amplified in ~25% of BTCs. These findings may be considered in future trial development.

Table: 703P

HER2 status	No. studies	Up-regulation rate mean (95% CI, %)	P-Value
Overall expression by IHC	38	26.5% (18.9 - 34.1%)	
Region of provenience			
Asia	17	28.4% (14.5 - 42.3%)	
West	16	19.7% (10.1 - 29.2%)	0.4936
IHC assessment			
Low quality	11	41.7% (22.9 - 60.5%)	
High quality	27	20.3% (13.2 - 27.5%)	0.0336
Site of Primary regardless IHC scoring			
IHCC	12	21.1% (2.3 - 39.7%)	
EHBTC	32	22.5% (15.5 - 29.5%)	0.2557
EHCC	11	17.4% (3.4 - 31.4%)	0.4752
GBC	14	24.2% (14.1 - 34.3%)	0.2339
AC	7	27.2% (7.2 - 47.2%)	0.4652
Site of Primary by HQ/IHC			
IHCC	8	4.8% (0 - 14.5%)	
EHBTC	28	19.9% (12.8 - 27.1%)	0.0049
EHCC	11	17.4% (3.4 - 31.4%)	0.0134
GBC	12	19.1% (11.2 - 26.8%)	0.0123
AC	5	27.9% (0 - 60.7%)	0.0642
Overall amplification by ISH	16	30.1% (11.7 - 48.5%)	
Site of Primary			
IHCC	6	17.6% (0 - 60.1%)	
EHBTC	14	22.5% (7.9 - 37.2%)	0.0468
Amplification by selection population			
No	12	17.9% (0.1 - 35.4%)	
Yes	5	57.6% (16.2 - 99%)	0.0072

Legal entity responsible for the study: Istituto Europeo di Oncologia, Milano (IT)

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