765P Prediction of overall survival with 2nd-line (L2OS) chemotherapy (CT) in patients with advanced biliary tract cancer (aBTC): AGEO CT2BIL cohort update and international multicenter external validations

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Background: Benefit of CT beyond standard 1st-line (L1) gemcitabine plus cisplatin (GEMCIS) or oxaliplatin (GEMOX) in aBTC is unclear. Our aim was to identify and validate prognostic factors for L2OS in aBTC to guide patient selection for 2nd line (L2) CT.

Methods: All consecutive patients with aBTC receiving L2 CT after GEMCIS/GEMOX L1 between 2003-2016 in 28 French centers were included. The association of clinico-biological data with L2OS was investigated in univariate and multivariate Cox analyses. A simple score was derived from the multivariate model. The model and score were validated in 3 external cohorts with similar inclusion criteria (Italy, France, UK).

Results: The development cohort included 405 patients treated with L1 GEMOX (91%) or GEMCIS. 55% were men; median age was 64 years. 27% had prior surgical resection; 95% had metastatic disease. Performance status (PS) was 0/1/2 in 18%/52%/30%. Of the 251 patients with available CA19.9 at the beginning of L2, 35% had a CA19.9 $\geq$ 400 IU/L. Among 22 clinical parameters, 8 were associated with L2OS in univariate analysis. In multivariate analysis, 4 were independent prognostic factors: PS, reason for L1 stopping, prior surgery, peritoneal carcinomatosis (PC) (Table). Type of L2 CT regimen was not associated with L2OS. The clinical model had a C-index of 0.659, a good calibration and was validated in the 3 external cohorts (Table). Analysis of patients with complete data for the 4 clinical factors and CA19.9 (multiple imputations for missing data) showed that CA19.9 was independently associated with L2OS. A score was derived from this model.

Table: 765P Multivariate Cox Model for L2OS (HR, P-value)

	AGEO (N = 405)		ITALY (N = 288)		France (N = 70)		UK (N = 24)	
Prior surgery								
Yes No	1 1.3	0.031	1 1.4	0.013	1 1.8	0.16	1 4.8	0.045
Reason for L1 stopping								
Toxicity/ Other	1 1.5	<0.001	1 1.8	<0.001	1 3.0	0.0063	1 31.9	<0.001
Progression								
PS								
0 1 2	1 1.5 3.0	<0.001	1 1.2 2.1	0.001	1 2.0 6.7	<0.001	1 7.4 20.4	0.011
PC								
No Yes	1 1.3	0.018	1 1.4	0.019	1 1.0	1.0	1 15.3	0.001

Conclusions: We validated L2OS prognostic factors previously reported and identified PC as a new pejorative one in 800+ patients. Our model and score will be useful for guiding therapeutic decisions and stratifying randomization in future clinical trials.

Legal entity responsible for the study: AGEO (Association des GastroEntérologues Oncologues) academic group.

Funding: Has not received any funding.

Disclosure: C. Neuzillet: Research funding (outside the study): Celgene; Clinical trial PI: AstraZeneca. A. Casadei Gardini: Consulting, Advisory role: Eisai; Speakers' bureau: Bayer. B.J.-C. Rousseau: Advisory board: Bayer. M. Scartozzi: Consulting Advisory role, Speakers' bureau: Bayer, Amgen, Merck, Sanofi; Research funding : Bayer, Msd,

Bms, Sanofi. A. Lievre: Consulting, Advisory role: Merck, Amgen, Bayer, Ipsen, Shire; Speakers' bureau: Merck, Roche, Amgen, Bayer, Ipsen, Novartis, BMS. All other authors have declared no conflicts of interest.