112P Clinical, genomic and transcriptomic characteristics of young-onset biliary tract cancers

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Introduction

- Cholangiocarcinoma (CCA) is a rare malignancy affecting epithelial cells of the biliary tract
- The incidence of young onset (YO) gastro-intestinal cancers, commonly defined as a diagnostic before 50 years, is rising and the reasons are poorly understood
- Rising incidence of YO-CCAs is particularly preoccupying
- Management of YO-CCAs is a challenge and identifying their clinical and molecular characteristics could help to improve their outcomes

Objective

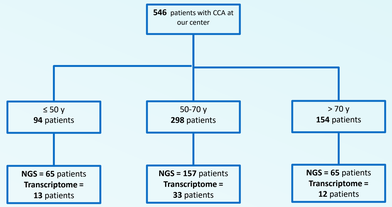
- The aim of our study is to describe the clinical, genomic and transcriptomic charateristics of YO-CCAs

Materials and Methods

- Patients with biliary tract cancer followed in our institution from 2015 and 2022 were included
- The different molecular panels included:
  - In-house panel of 75 oncogenes and tumor suppressor genes
  - FoundationMedicine ® panel including 324 oncogenes, tumor suppressor genes or gene rearrangement as well as microsatellite stability status and tumor mutational burden.
- Growth modulator index (GMI), defined as the ratio of time to progression (TTP) under the MMT (TTPn, e.g. oriented treatment line) to TTP under the treatment received prior to MMT (TTPn−1). A GMI ≥1.3 is considered as relevant clinical benefit, meaning TTPn is at least superior by 30% as compared to TTPn-1
- Survival curves are based on Kaplan-Meier non-parametrical estimation.
- Univariate analysis was performed with Log-rank test.
- Multivariate analysis was performed with a proportional hazard Cox model

Results

Flowchart



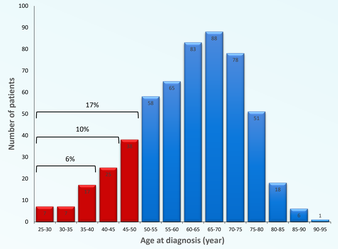


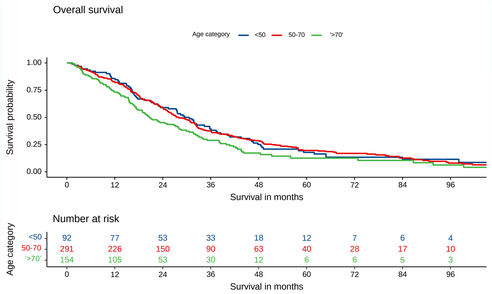
Table 1 : Clinical characteristics

Clinical characteristics	≤ 50 y N=94	50 – 70 y N=298	> 70 y N=154
Sex, No. (%)			
Female	55 (58.5)	150 (51.0)	73 (47.4)
Male	39 (41.5)	144 (48.0)	81 (52.6)
ECOG, No. (%)			
0 – 1	85 (98.9)	259 (93.5)	124 (84.9)
> 1	1 (1.1)	18 (6.5)	22 (15.1)
Anatomic localization, No. (%)			
Extrahepatic	15 (16.7)	46 (15.8)	36 (23.8)
Intrahepatic	52 (57.8)	159 (54.6)	68 (45.1)
Vesicular	10 (11.2)	40 (13.7)	20 (13.2)
Peri-hiliary	13 (14.4)	46 (15.8)	27 (17.9)
Co-morbidities, No. (%)			
Cirrhosis	4 (4.3)	25 (8.6)	13 (8.5)
HBV	1 (1.1)	1 (0.3)	1 (0.7)
HCV	0 (0)	4 (1.4)	2 (1.3)
Tobacco active smoking	12 (18.7)	51 (25.2)	9 (8.5)
Diabetes	1 (1.1)	30 (10.6)	32 (20.8)
Obesity	3 (3.2)	19 (6.4)	13 (8.4)
Constitutional deleterious variant, No.			
Lynch syndrome	0	1	0
BRCA1	0	0	1
BRCA2	1	0	0
Metastatic at diagnosis, No. (%)	56 (70.9)	156 (68.1)	70 (58.3)
Non metastatic at diagnosis, No. (%)			
Localized	13 (34.2)	40 (28.2)	33 (39.3)
Locally advance	9 (23.7)	26 (18.3)	14 (16.7)
Missing information	16 (42.1)	76 (53.5)	37 (44.0)
CA19.9 at diagnosis, Med. (IQR)	635 (73; 7351)	120 (16; 900)	250 (25; 2009)
Surgery, No. (%)	51 (56.0)	166 (57.2)	89 (58.5)
Metastasis localization, No. (%)			
Hepatic	44 (48.9)	140 (48.3)	57 (37.2)
Extra hepatic	40 (43.0)	109 (37.6)	47 (30.9)

Table 1 : Genomic characteristics

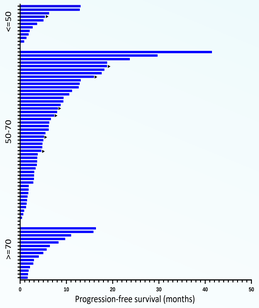
Genomic characteristics		≤50y n=94		50-70y n=298		>70 n=154	
		n	%	n	%	n	%
Molecular profile available	No	30	32%	116	39%	88	57%
	Yes	64	68%	182	61%	66	43%
Actionable alteration	No	41	64%	100	55%	41	62%
	Yes	23	36%	82	45%	25	38%
Main actionable alterations	No alteration	10	16%	31	17%	9	14%
	Mutation IDH1/2	8	13%	30	16%	10	15%
	Fusion FGFR 2	7	11%	18	10%	3	5%
	Mutation FGFR2	9	14%	14	8%	2	3%
	Amplification HER2	3	5%	10	6%	5	8%%
	Mutation BRAF V600E	0	0%	9	5%	1	2%
	Mutation EGFR	2	3%	5	3%	1	2%
	Fusion NTRK	6	9%	5	3%	6	9%
	Mutation PI3KCA	6	9%	15	8%	4	6%
	Mutation KRAS G12C	1	2%	2	1%	0	0%
	Mutation BRCA1	3	5%	7	4%	4	6%
	Mutation BRCA2	6	9%	14	9%	2	3%
	Mutation MET	2	3%	3	2%	2	3%
	Fusion ALK	3	5%	3	2%	3	5%
	Mutation ATM	9	14%	17	9%	5	8%
Other relevant alterations	KRAS	16	25%	29	16%	12	18%
	TP53	25	39%	59	32%	31	47%
	CDKN2A/B	8	13%	49	27%	14	21%
	ARID1A	8	13%	21	12%	2	3%
	SMAD4	5	8%	11	6%	4	6%
	PTEN	3	5%	9	5%	2	3%
MMR status (n=199)	dMMR/MSI	0	0%	8	7%	3	7%
	pMMR/MSS	47	100%	101	93%	40	93%
Targeted therapies administration	No	49	77%	129	71%	54	82%
	Yes	15	23%	50	27%	12	18%

Overall survival

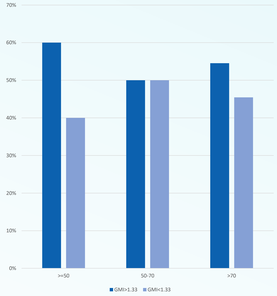


Targetable alterations and molecularly-matched treatments

Progression free survival (PFS) under molecularly-matched treatment

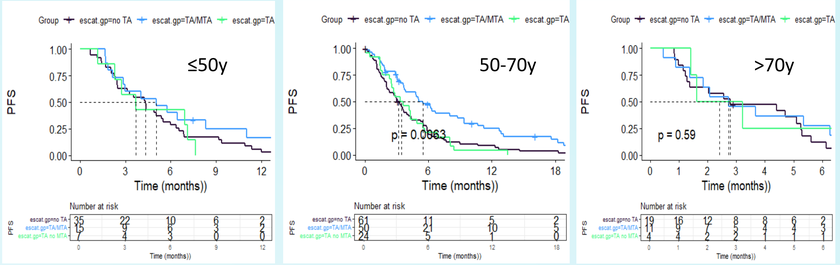


Growth modulator index (PFSn/PFSn-1

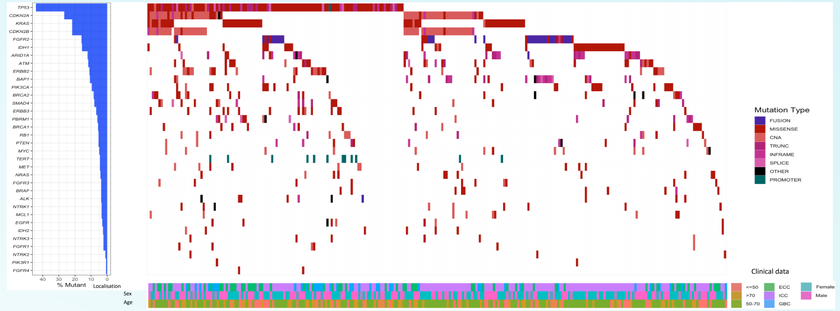


Results

PFS with targetable alteration and molecularly-match treatment (TA/MTA), TA without MTA (TA) and no TA



Main molecular alterations



Conclusion

- YO-CCAs tend to have a more aggressive disease at diagnosis
- Although molecular profiles were made more often in YO-CCAs, we did not find any significant differences in terms of targetable alterations
- Non YO-CCAs harbored more alterations in CDKN2A/B
- Molecular matched treatment tend to have a better activity in YO-CCAs
- YO-CCAs had a better overall survival than >70y and not significantly higher than 50-70y