FOLFIRINOX as a first-line chemotherapy for patients with advanced biliary tract cancer

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ABSTRACT

Background: FOLFIRINOX is a first-line regimen in the treatment of pancreatic cancer. Historically, BTC and pancreatic cancers were treated similarly with gemcitabine alone or combined with a platinum compound. A growing body of evidence supports the role of fluoropyrimidines in the treatment of BTC. **Methods:** We retrospectively analyzed data of all our pts with locally advanced (LA) or metastatic (M) BTC who received FOLFIRINOX as a first-line therapy from 12/2013 to 11/2017 at Paul Brousse university hospital. The main endpoints were OS, TTP, ORR, DC, secondary resection and toxicity. **Results:** There were 42 pts, 17 male (40%) and 25 female (60%), aged 36 to 84 years (median: 67). Pts had PS of 0 (55%) and 1 (45%). They had intrahepatic cholangiocarcinoma (iCCA) (21 pts, 50%), gallbladder carcinoma (8 pts, 19%), perihilar CCA (7 pts, 17%), distal CCA (4 pts, 10%) and ampulloma (2 pts, 5%). No biopsy could be obtained in 2 pts. BTC was LA or M in 9 (21%) and 33 pts (79%) respectively. Biliary stent was placed in 14 pts (33%). A median of 10 courses was given with median treatment duration of 6 months (mo). At the cutoff on 01/01/2018, regimen was ongoing in 7 pts (18%). Median dose intensity was 74, 34 and 1150 mg/m2/w for irinotecan, oxaliplatin and 5FU respectively. The most common nonhematological toxicity was sensory neuropathy: grade 1/2 in 15 pts (36%), no grade 3/4. We observed 15 PR (36%), 16 SD (38%), and 10 PD (24%); 1 pt has not been evaluated yet for efficacy. Fifteen pts (36%) were alive, 24 pts (57%) died, 3 pts (7%) were lost to follow-up. Four out of 5 pts who underwent resection were alive without disease. At a median follow-up time of 12 mo (1 to 26), median TTP was 9 mo [95%CL, 5 – 12] and median OS was 15 mo [14 – 16]. Median TTP was better for LA (not reached) as compared to M (8 mo), p=0.05; OS was statistically similar. Median TTP was worse in pts with iCCA as compared to other primaries (7 mo [4 – 10] vs 14 mo [9 – 19], p=0.005); OS was not significantly different. ORR and DC were associated with both better TTP and OS. ORR: TTP (median, 16 vs 5 mo, p<0.001), OS (median, 19 vs 11 mo, p=0.010); DC: TTP (median, 10 vs 2 mo, p<0.001), OS (median, 18 vs 7 mo, p=0.002). **Conclusions:** First-line FOLFIRINOX offers promising results in patients with LA and M-BTC. It deserves prospective evaluation to further improve outcomes for advanced BTC.

OBJECTIVES

The objective of the study was to evaluate retrospectively the outcome of routine administration of FOLFIRINOX as a first-line chemotherapy in patients with advanced biliary tract cancer.

METHODS AND RESULTS (updated on July 27th, 2018)

Table 1: Patient characteristics

Characteristics	Number of pts (N=42)
Sex	
Male	17 (40.5%)
Female	25 (59.5%)
Age (years)	
Median (range)	*67 (36 – 84)*
≤ 65	18 (42.9%)
> 65	24 (57.1%)
WHO PS	
0	23 (54.8%)
1	19 (45.2%)
Primary tumor location	
Intrahepatic CCA	21 (50.0%)
Other locations:	21 (50.0%)
- Gallbladder	*8 (19.0%)*
- Perihilar CCA	*7 (16.7%)*
- Distal CCA	*4 (9.5%)*
- Ampulloma	2 (4.8%)
Disease extension	
Locally advanced (LA)	10 (23.8%)
Metastatic (M)	32 (76.2%)
Site of metastases	
None (LA)	10 (23.8%)
M in liver only	11 (26.2%)
M in liver + other sites	15 (35.7%)
M in other sites only	6 (14.3%)
Biliary stent placed	14 (33.3%)

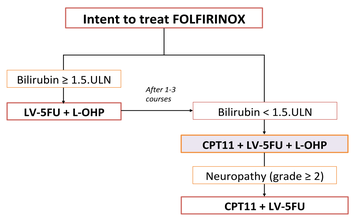

Figure 1: Therapeutic plan

Table 2: Efficacy according to disease extension

Efficacy parameters	Locally advanced (n=10)	Metastatic (n=32)	All (N=42)	p
Complete response	0	0	0	
Partial response	3 (30.0%)	9 (28.1%)	12 (28.6%)	
Stable disease	5 (50.0%)	14 (43.8%)	19 (45.2%)	ns
Progressive disease	2 (20.0%)	8 (25.0%)	10 (23.8%)	
Not assessed	1 (3.1%)	0	1 (2.4%)	
Objective response	3 (30.0%)	9 (28.1%)	12 (28.6%)	ns
Disease control	8 (80.0%)	23 (71.9%)	31 (73.8%)	ns
TTP. months Median [95% CL]	4.7 [1.1 – 8.3]	9.5 [7.1 – 11.9]	8.0 [5.8 – 10.1]	ns
OS. months Median [95% CL]	9.1 [0.0 – 19.2]	15.1 [13.0 – 16.9]	15.1 [14.3 – 16.0]	ns

Table 3: Cox Model analysis, predictive factors of TTP

Prognostic factors	Hazard ratio (HR)	p-value
Male sex	0.55 [0.23 - 1.32]	0.181
Age ≤ 65years	1.89 [0.68 - 5.26]	0.224
Intrahepatic cholangiocarcinoma	**4.84 [1.46 - 16.04]**	**0.010**
Jaundice	0.17 [0.02 - 1.47]	0.107
Biliary stent placed	5.62 [0.87 - 36.50]	0.070
Locally advanced disease	3.96 [0.90 - 17.46]	0.069
WHO PS=0	0.91 [0.32 - 2.58]	0.866
Secondary R0R1 resection	**0.03 [0.00 - 0.55]**	**0.019**
Objective response	0.56 [0.14 - 2.26]	0.412
Disease control	**0.01 [0.00 - 0.13]**	**0.000**

Table 4: Cox Model analysis, predictive factors of OS

Prognostic factors	Hazard ratio [95% CL]	p-value
Male sex	0.98 [0.33 - 2.88]	0.971
Age ≤ 65years	2.35 [0.75 - 7.42]	0.145
Intrahepatic cholangiocarcinoma	1.40 [0.46 - 4.27]	0.554
Jaundice	3.28 [0.39 - 27.54]	0.275
Biliary stent placed	0.76 [0.13 - 4.48]	0.763
Locally advanced disease	1.64 [0.41 - 6.56]	0.488
WHO PS=0	1.77 [0.63 - 4.96]	0.281
Secondary R0R1 resection	**0.08 [0.01 - 1.33]**	**0.079**
Objective response	1.93 [0.43 - 8.78]	0.393
Disease control	**0.16 [0.04 - 0.65]**	**0.010**

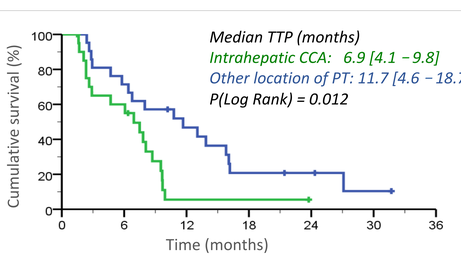

Figure 3: TTP according to primary tumour location

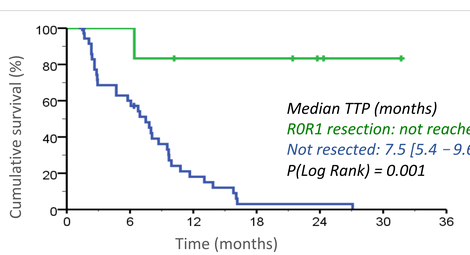

Figure 4: TTP according to R0R1 resection

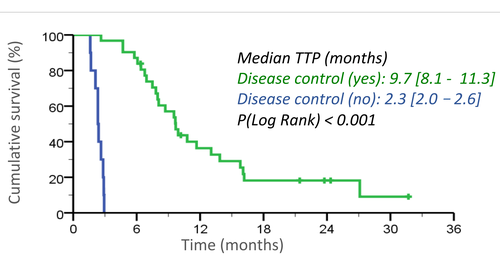

Figure 5: TTP according to disease control

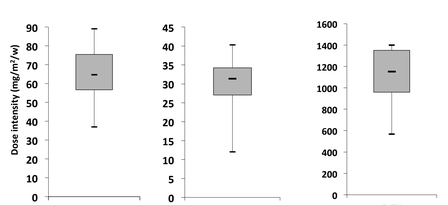

Figure 2: Dose intensity of Irinotecan, Oxaliplatin and 5-FU

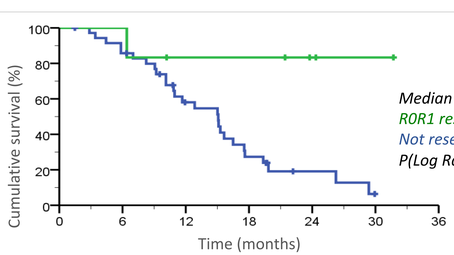

Figure 6: OS according to R0R1 resection

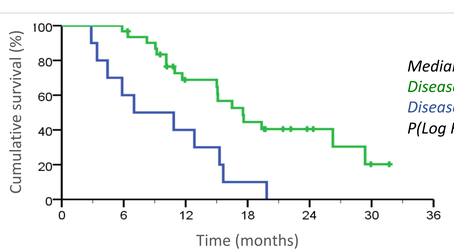

Figure 7: OS according to disease control

CONCLUSION

FOLFIRINOX regimen with dose reductions according to patient profile and tolerance seems to offer promising results in patients with advanced biliary tract cancer. It deserves prospective evaluation to further improve outcomes for advanced biliary tract cancer.

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