108P - FGFR2 Fusions and Their Impact on Efficacy of Standard Chemotherapy in Patients with Biliary Tract Cancer

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BACKGROUND

The incidence of biliary tract cancer (BTC) is increasing globally, while its survival remains dismal. The presence of *FGFR2* fusions offer a new therapeutic option with selective oral inhibitors, although the optimal treatment sequence for these patients remains unclear.

METHODS

We included patients from all three Mayo Clinic sites diagnosed with BTC who had a positive test for *FGFR2* fusion on RNA sequencing. Data from patients with *FGFR2* fusion-negative BTC were used as historical controls.

Overall survival (OS) and progression-free survival (PFS) were estimated using Kaplan-Meier techniques.

RESULTS

We identified 43 patients with BTC and an *FGFR2* fusion and 155 without *FGFR2* fusion. The most common gene fusion partner was *BICC1* in 28% (N=12) of the cases.

FGFR2 fusion was associated with age ≤65 years at diagnosis (74% vs. 44%, p=0.0011), female gender (72% vs. 45%, p=0.0021), intrahepatic BTC (95% vs. 71%, 0.0201), and advanced stage at diagnosis (60% vs. 11%, p<0.0011).

In the setting of advanced BTC, 25 patients with an *FGFR2* fusion received first-line (1L) chemotherapy, of which 14 (56%) received gemcitabine plus cisplatin.

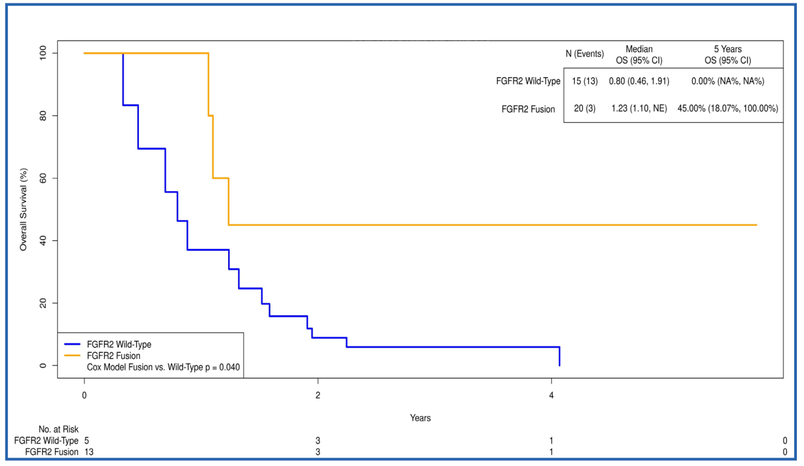
Among patients in the fusion-positive group who received second-line (2L) therapy, the median PFS was longer when treated with an FGFR inhibitor (8.2 months, 95% CI 7.2-not estimated [NE]) vs. chemotherapy (5.5 months, 95% CI 4.8-19.3) (**Table 1**).

In patients with an *FGFR2* fusion who never received an FGFR inhibitor, their median OS was significantly higher (14.8 months, 95% CI 13.2-NE) vs. patients without an *FGFR2* fusion (9.6 months, 95% CI 5.52-22.9) (p=0.04) (**Figure 1**).

TABLE 1: Progression-free survival of patients based on the status of *FGFR2* gene and the therapy regimen in the first- and second-line settings.

	FGFR2 Fusion **Negative**		*FGFR2* Fusion **Positive**	
	N	PFS, months (95% CI)	N	PFS, months (95% CI)
1L chemotherapy	37	7.6 (4.6-13.3)	21	5.4 (3.8-9)
1L FGFR inhibitor			4	7.7 (2.1-NE)
1L Overall	37	7.6 (4.6-13.3)	25	5.9 (3.8-8.5)
2L chemotherapy	20	10 (4.6-13.8)	9	5.5 (4.8-19.3)
2L FGFR inhibitor			16	8.2 (7.2-NE)
2L Overall	20	10 (4.6-13.8)	25	8.4 (7.2-13.8)

FIGURE 1: Overall survival of patients with *FGFR2* fusion-positive BTC who never received an FGFR inhibitor vs. those with *FGFR2* fusion-negative BTC



CONCLUSION

In patients with advanced BTC, the presence of a *FGFR2* fusion is associated with:

1. A significantly longer OS,
2. And a shorter PFS when treated with 1L chemotherapy vs. an FGFR inhibitor.

These findings underscore the need to evaluate the efficacy of FGFR inhibitors as 1L treatment in these patients.