UK real world evidence of using durvalumab plus gemcitabine and cisplatin for biliary tract cancers in an early access scheme

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Background:

Following the survival benefit reported by the TOPAZ-1 phase III trial, durvalumab (anti-PD-L1) in combination with gemcitabine-cisplatin has been established as the new standard of care for patients with locally advanced or metastatic biliary tract cancers. This study used data from UK centres participating in an early access scheme via AstraZeneca before national approval, to evaluate the safety and efficacy of this approach as a first line treatment in the real world setting.

Method:

The population included patients with locally advanced or metastatic adenocarcinoma of the biliary tract, treated with combination durvalumab and gemcitabine-cisplatin. The data was drawn from seven centres in the UK. The primary endpoint was progression-free survival (PFS). Secondary endpoints were overall survival (OS), overall response rate (ORR), disease control rate (DCR) and safety data, including chemotherapy and immunotherapy adverse events (AE). Survival analysis was performed using R software.

Results:

94 patients, whose treatment began from April 2022 to December 2023, were enrolled, with 57 male patients and 37 female patients. The median follow-up time was 7.7 months (95% CI: 5.73 – 12.9 months). The median PFS was 7.1 months (95% CI: 5.6 - 10.3 months), similar to TOPAZ-1's median PFS of 7.2 months (95% CI, 6.7 – 7.4 months). Median OS was 10.9 months (95% CI: 10.7 - 10.9 months), with UK patients performing slightly worse compared to the TOPAZ-1 finding of 12.8 months (95% CI 11.1 – 14.0 months). OS was found to be site dependent, with intrahepatic and extrahepatic disease having an OS of 10.7 and 20.5 months respectively.

The ORR was 27.7% (TOPAZ-1: 26.7%), and DCR was 60.9%, with extrahepatic disease being associated with increased ORR and presence of stenting or drainage associated with decreased ORR. In terms of safety, 43 patients (45.7%) experienced any-grade adverse events (AE), with 7 patients experiencing grade 3-4 AEs (7.4%). AE rates were lower than found in TOPAZ-1. Nineteen patients (20.1%) experienced immunotherapy-related AEs, with 2.1% of patients having grade 3-4 immunotherapy related AEs.

Patient Demographics

Table 1. Patient Characteristics

Variable	Patient Group: Intrahepatic, N = 51[1]	Extrahepatic, N = 30[1]	Gallbladder, N = 13[1]
Age	65 (59, 71)	67 (59, 72)	60 (55, 63)
Sex			
Female	18 (35%)	10 (33%)	9 (69%)
Male	33 (65%)	20 (67%)	4 (31%)
Drainage or Stent			
No	41 (80%)	10 (33%)	11 (85%)
Yes	10 (20%)	20 (67%)	2 (15%)
BMI			
Normal	17 (33%)	13 (43%)	4 (31%)
Obese	14 (27%)	4 (13%)	3 (23%)
Overweight	20 (39%)	13 (43%)	5 (38%)
Underweight	0 (0%)	0 (0%)	1 (7.7%)
ALT at diagnosis			
Elevated	13 (25%)	9 (30%)	4 (31%)
Normal range	38 (75%)	21 (70%)	9 (69%)
NLR			
NLV <3	19 (37%)	16 (53%)	10 (77%)
NLV > 3	32 (63%)	14 (47%)	3 (23%)
Previous surgery			
Yes	6 (12%)	9 (30%)	4 (31%)
No	45 (88%)	21 (70%)	9 (69%)
Platelets at diagnosis			
> 100	49 (96%)	28 (93%)	13 (100%)
≤ 100	2 (3.9%)	2 (6.7%)	0 (0%)
Durvalumab given on first cycle			
Yes	10 (20%)	19 (63%)	11 (85%)
No	41 (80%)	11 (37%)	2 (15%)
ECOG PS at diagnosis			
>0	19 (37%)	18 (60%)	4 (31%)
0	32 (63%)	11 (37%)	9 (69%)
Not reported	0 (0%)	1 (3.3%)	0 (0%)

[1]Median (IQR); n (%)

Figure 1: Kaplan-Meier curve for OS/PFS

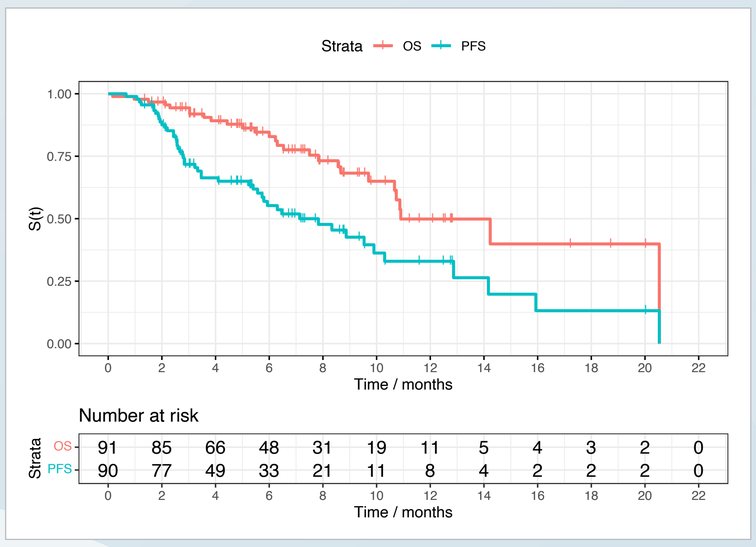


Figure 2: Kaplan-Meier curve for OS stratified by site of malignancy

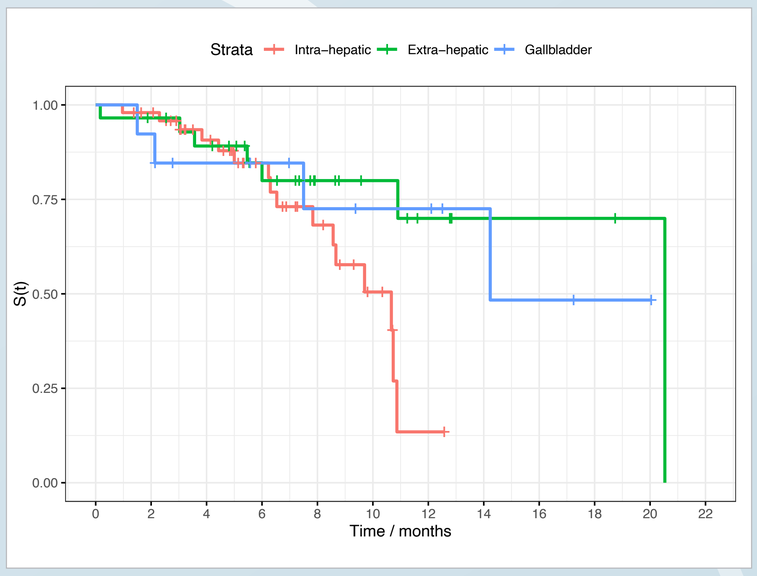
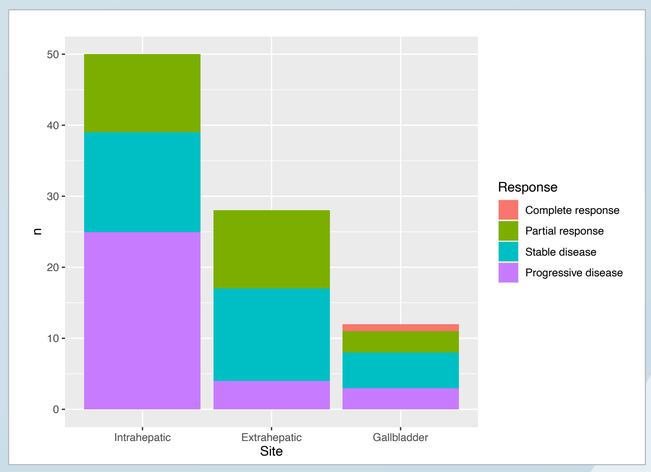


Figure 3: Initial response stratified by site of malignancy following initiation of therapy



Conclusion:

Our data demonstrates that the real world data from the UK is consistent with that reported in the phase 3 TOPAZ-1 trial. Further follow-up is needed, particularly in the case of extrahepatic disease and gallbladder disease given the high OS relative to the median follow-up time. The decreased rates of immunotherapy and chemotherapy related AEs relative to the TOPAZ – 1 trial may reflect this.