Gemcitabine/Oxaliplatin/Lenvatinib (GEMOX-Len) for refractory, relapsed or unresectable fibrolamellar carcinoma

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Background

Fibrolamellar carcinoma (FLC) is a rare primary liver malignancy typically affecting young adults without underlying liver disease. Although surgical resection is the primary treatment modality, 50-80% of cases have disease recurrence post-resection. Additionally, >20% of patients have unresectable disease, with median survival for this cohort <12 months. Gemcitabine/Oxaliplatin/Lenvatinib (GEMOX-Len) is a novel systemic therapy developed by the Rush University FLC Program (Chicago, Illinois) for patients with refractory, relapsed or unresectable FLC.

Methods

Data was collected retrospectively from 15/04/2019-25/05/2024. The primary study endpoints were tumour response (measured using RECIST 1.1 criteria and volume estimates), progression-free survival (PFS) and overall survival (OS). The Kaplan-Meier method was used to construct survival curves with the log-rank test applied to compare survival distributions. Ethics was approved by UNSW Australia HREAP (2024/iRECS5847).

Results

52 patients (25F) with median age 21.4 years (IQR 18.5-25.4) received a median of 9 cycles (IQR 7.0-15.3) of GEMOX-Len (G:1000mg/m^2, O:100mg/m^2, L:8mg daily). At the commencement of neoadjuvant therapy, 5/3/44 patients had AJCC stage III/IVa/IVb disease with 50/52 deemed unresectable. At the conclusion of therapy,

0/15/26/1 patients had complete response (CR)/partial response (PR)/stable disease (SD)/progressive disease (PD) per RECIST 1.1 criteria, with a median RECIST response of -19.5% (IQR -26.8% to -7.3%) and median volume response of -39.5% (IQR -59.8% to -14.8%). Median survival from the commencement of GEMOX-Len was 31.8 months, median PFS was 21.6 months and median OS was 103 months. 28 patients were surgically candidates post-therapy: 20 subsequently underwent definitive surgery, with 10 achieving R0 resection. The only statistically significant predictor of survival were patients who underwent definitive surgery (p=0.042). Predictors of PFS include AJCC stage <4 at definitive surgery (p=0.018) and the presence of tumour necrosis post-GEMOX-Len (p=0.031). 32/48 patients (66.67%) experienced adverse effects during therapy including peripheral neuropathy (n=25), fatigue (n=6) and nausea (n=4).

Conclusion

Our cohort treated with GEMOX-Len demonstrated significantly higher OS and PFS compared to existing literature. 52% of previously unresectable patients became surgical candidates, with an R0 outcome achieve in 50% of those who underwent surgery. Further controlled, prospective studies are required.