# Gemcitabine-Oxaliplatin-Lenvatinib (GEMOX-LEN) For Unresectable Fibrolamellar Carcinoma: Promising Results in First 16 Patients


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## BACKGROUND:

Fibrolamellar carcinoma (FLC), an extremely rare primary liver cancer of children and young adults with no underlying liver disease, that often presents at an advanced stage with minor and non-specific symptoms. There are no proven systemic therapies for the treatment of FLC, and surgery remains the only potentially curative option. There is a need for effective systemic treatments. We describe 12 patients, most of whom had multiple prior surgeries and systemic therapies, who were judged unresectable. We chose gemcitabine-oxaliplatin (GEMOX) as a backbone based on case reports of GEMOX efficacy in FLC, combined with the oral antiangiogenic/multi-kinase inhibitor lenvatanib (LEN), based on hepatocellular carcinoma (HCC) data and similarity to the GEMOX- sorafenib approach in the current COG trial AHEP1531, but with expected less toxicity and more efficacy then sorafenib, as previously reported for HCC.

## METHODS:

Data from all patients receiving GEMOX-LEN between April 15, 2019 and April 22, 2021 were reviewed. All were assessed for toxicity. Those having received at least 3 cycles with follow up imaging obtained at least two months after initiation were assessed for: objective response based on RECIST 1.1, progression free survival, and overall survival.

## RESULTS:

During the study period, 19 patients were treated with GEMOX-Len. Sixteen patients met our inclusion criteria, with median/mean age 16.5 / 22.5 (7-45, 7M/9F), with a median of 10 cycles (3-24) and 9 months (2-11). Three patients were excluded – one died 5 week after one cycle of GEMOX-Len, 2 patients have not had first follow up imaging.

All 19 patients had metastatic disease when starting GEMOX-Len and 17 of 19 were unresectable. Fourteen of 19 patients had relapsed previously (mean 3.0, 0-8), 12 patients had previous systemic chemotherapy treatments (mean 2.8, 1-5). Mean progression-free survival (PFS) was 6.4 months (2-14). Six patients previously had GEMOX (*with no LEN*) and all but one of these had progressed. Five patients had received Nivolumab concurrently.

By RECIST 1.1 criteria, one patient achieved clinical remission, 8 had a partial response, and 8 had stable disease (figure 1). The overall objective response (clinical remission + partial response) was 53%, and tumor control rate (clinical remission + partial response + stable disease) was 100% (figure 2a, 2b). Only two people were surgical candidates before therapy, with 5 additional patients becoming surgical candidates and were able to have aggressive resections. Four patients discontinued therapy due to toxicity, and no other patients had dose reduction due to side effects There (figure 3). were no deaths during therapy. One person died from disease progression 4 months after stopping GEMOX-Len, for an overall survival is 94%.


*Figure 1*

**Examples of Tumor Reduction on GEMOX-Len**

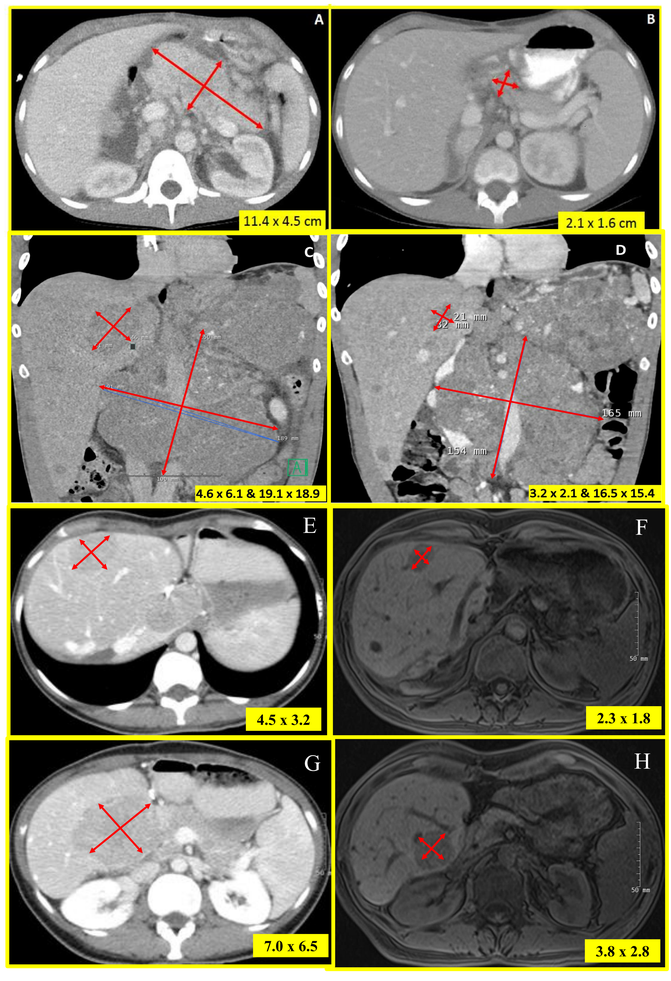


*Figure 3*

| Toxicities | | |
|---|---|---|
| Toxicity | Grade 1-4 | Grade 3-4 |
| Allergy | 2 (12.5%) | 2 (12.5%) |
| Nausea | 1 (6.3%) | 0 |
| Neuropathy | 6 (37.5%) | 1 (6.3%) |
| Neutropenia | 1 (6.3%) | 1 (6.3%) |
| Transaminitis | 2 (12.5%) | 0 |
| TTP-like | 1 (6.3%) | 1 (6.3%) |
| Thrombocytopenia | 1 (6.3%) | 1 (6.3%) |

## CONCLUSION:

This is preliminary, uncontrolled data. However, we believe gemcitabine-oxaliplatin-lenvatanib to be a promising option in FLC who are not surgical candidates, with 3 patients now in clinical remission. Overall this regimen has been well-tolerated with manageable side effects and can be administered safely in the outpatient setting. Research on GEMOX-Len is ongoing, and prospective trials will be opened soon. GEMOX-Len may offer a choice to highly pre-treated, high risk Fibrolamellar carcinoma patients with few or no options.

*Figure 2a*

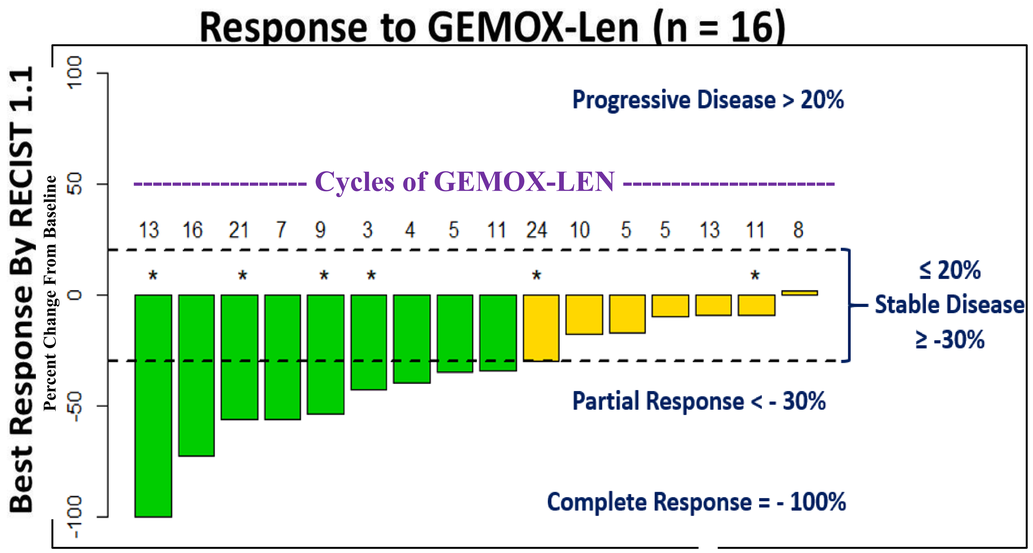


*Figure 2b*