Background

- Fibrolamellar cancer (FC): rare cancer, M=F, median age 23 years
- Multidisciplinary treatment including surgery, liver-directed therapy, radiation, and medication therapy
- Systemic therapy options – no consensus/established regimens
  - 5-Fluorouracil (FU) + IFN-α2b
  - Gemcitabine + cisplatin/oxaliplatin +/- lenvatinib
  - Immunotherapy combination (e.g., nivolumab + ipilimumab)
  - Others: sorafenib, PIAF, FOLFOX, atezolizumab/bevacizumab, neratinib, ENMD2076
- Fibrolamellar cancer has several immune suppressive mechanisms.
- 5-Fibrolamellar (FU) + IFN-α2: Fibrolamellar cancer and other types of cancer - 5-FU + IFN-α2b is immune modulatory.
- IFN-α2 increases 5-FU efficacy and decreases/modulate immunosuppressive mechanisms that cancer uses to evade immune system attack.
- Treatment with 5-FU + IFN-α2 leads to an increase in CTLA-4, ICOS, PD-1, TIM-3 in tumor, Teffs, and Tregs, modulates the tumor environment.

Methods

- A clinical of 5-FU + IFN-α2b with addition of nivolumab for the Treatment of Unresectable Fibrolamellar Cancer (NCT04380545)
- First 2 cycles (5-FU + IFN-α2b only), addition of nivolumab from C3. Biopsy at pre-treatment and on-treatment before adding nivolumab.
- Endpoints: primary (safety), secondary (ORR, PFS, OS), exploratory (immune profiling of tumor tissues)

Results

- 6 Screened, 3 patients enrolled-2 patients received the trial medications, and unresectable cancer converted to a resectable disease, underwent surgery, received adjuvant therapy.
- 1 patient achieved stable disease, but there was a complication of tumor bleeding, and the patient was taken off the study.

Gene expression analysis indicating an increase in immune cell subsets after treatment with 5FU+IFN

IHC analyses correlates with gene expression studies indicating an increase in CD8+ T cell infiltration after treatment with 5FU+IFN

#531; Combination of 5-fluorouracil (FU), interferon (IFN)-alpha2, and nivolumab in unresectable fibrolamellar liver cancer

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