This is the first demonstration that AG-120 treatment may induce an increase in cholangiolar histology upon AG-120 treatment (Figure 6). This association was subsequently reproduced in a larger set of ~500 adult liver-specific genes (Figure 7).

Patients with increased cholangiolar histology show increased expression of liver-specific genes

- Cluster analysis identified the liver-specific genes Csf3r, Cxcl12, Aoc1, Dlk1, Ttr, and C2 in the set of ~500 adult liver-specific genes with an increased cholangiolar histology upon AG-120 treatment (Figure 8).

CONCLUSIONS

- This is the first demonstration that the AG-120 treatment may induce morphologic and molecular changes in a subset of mIDH1 CCs.
- Increased cholangiolar histology was associated with increased progression-free survival; however, this result should be interpreted with caution due to the small sample size and single-arm setting.
- Tumors with increased cholangiolar histology showed upregulation of genes associated with mature liver cell differentiation.
- The increased expression of immune response-related genes in some tumors suggested a potential rationale for AG-120 in combination with immunotherapies.
- Given the limited sample size of this dataset, additional studies are warranted to explore the biological and clinical significance of these observations.
- AG-120 is under further evaluation in an ongoing, global, phase 3, randomized, placebo-controlled trial in previously treated mIDH1 CC (ClinicalTrials.gov NCT03286687).