Treatment of metastatic colorectal cancer with aimpila, a glycoside/alpha-fetoprotein complex

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1 Background

Alpha-fetoprotein (AFP) is a normal serum protein synthesized by the liver and certain tissues during embryonic development. High levels are found in serum when embryonic cells outgrow the normal hepatic cells and develop into fetal liver and extrahepatic liver-like structures. AFP is also elevated in patients with a variety of tumors, such as hepatocellular carcinoma, lung cancer, ovarian cancer, and others. In clinical trials with aimpila in liver metastatic colorectal cancer, 35% of AFP receptor positive tumor cells were observed.

We investigated the single agent activity of aimpila in patients (pts) with liver metastatic colorectal cancer (mCRC), given that the majority of CRC cells are AFP receptor positive (Figure 3), and treatment options remain limited for patients with metastatic disease.

Aimpila is a non-covalent complex of porcine alpha-fetoprotein (PAFP) and a glycosidic apoptosis inducer (AI). The complex binds to AFP naturally collects polyunsaturated fatty acids (PUFA) from mothers albumin, then effectively and precisely transports the PUFA into embryo cells through the AFP receptor.

AFP receptor positive cancer cells and the AI is delivered intracellularly through AFP receptor-mediated endocytosis (Figure 1). The AI opens mitochondrial permeability transition pores, resulting in apoptosis. Through this mechanism, p53-dependent or other multiple drug resistance (MDR) related mutations can be overcome (Figure 2).

2 Methods

Highly informative Age ≥ 18 yrs, mCRC, any prior treatments, having documented progression metastatic liver disease. Treatment consisted of oral capsules at a fixed sub-maximal dose (0.3 mg of aimpila in an oral capsule, twice a day for 8 weeks).

3 Results

Of the 12 late-stage mCRC pts, 9 were evaluable for response by RECIST:

- 1 achieved partial response (PR) (Figure 5);
- 1 achieved stabilization (SD) (Figure 6);
- 3 experienced disease progression.

Of the 3 non-evaluable pts:

- 1 pt (radiological CR) going from 816 ng/ml to 268 ng/ml;
- 1 showed stable disease >2 months, but with both lesions <10 mm in diameter; and
- 1 experienced clinical deterioration without a CT scan.

Median survival has not yet been reached, with a median follow-up of 4 months.

4 Discussion

Aimpila naturally collects polyunsaturated fatty acids (PUFA) from mothers' albumin, then effectively and precisely transports the PUFA into embryonic cells through the AFP receptor.

By substituting a glycoside for the PUFA, we can kill cancer cells that re-express the AFP receptor. Aimpila works in this natural way, using AFP naturally collects polyunsaturated fatty acids (PUFA) from mothers' albumin, then effectively and precisely transports the PUFA into extrahepatic liver-like structures. High levels of AFP are found in patients with a variety of tumors, such as hepatocellular carcinoma, lung cancer, ovarian cancer, and others. In clinical trials with aimpila in liver metastatic colorectal cancer, 35% of AFP receptor positive tumor cells were observed.

5 Conclusion

Single agent aimpila was well-tolerated and produced major objective responses in patients with liver mCRC. Further studies are warranted.

6 References