



Past, Present, and Future in the Treatment of Advanced Perihilar Cholangiocarcinoma: Future Perspective of Precision Cancer Medicine by Patient-Derived Orthotopic Xenograft (PDOX)

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Editorial

Perihilar cholangiocarcinoma is a relatively rare cancer that has a poor prognosis. Treatment options include chemotherapy and radiation therapy, but surgery is the only way to cure this condition. Radical surgery entails major hepatectomy and caudate lobectomy with biliary reconstruction. In some cases, vascular resection and reconstruction, and/or pancreaticoduodenectomy are added [1]. Following the establishment of preoperative portal vein embolization, postoperative short-term outcomes improved, but mortality rates are still high, even at high-volume centers. Even with radical resection, the 5-year survival rate is 20% to 40% [2,3], and the prognosis for unresectable cases is 10 months [3]. Although patient selection criteria are controversial, liver transplantation with preoperative chemoradiotherapy has good results and is the treatment of choice in some countries [2]. Chemotherapy consisted of only 5-FU for unresectable biliary tract cancer in the 1990s, but gemcitabine has been the mainstay for the past 20 years. Gemcitabine, cisplatin, and S-1 are now the key drugs. There are cases of conversion surgery in which chemotherapy is quite effective. Chemotherapy combining gemcitabine, cisplatin, and nab-paclitaxel has shown good results as a new treatment [4]. Although there is still insufficient evidence to support postoperative adjuvant chemotherapy, it is suggested that capecitabine may be effective [5]. Furthermore, a phase 3 clinical trial of adjuvant S-1 is ongoing. The evidence of neoadjuvant chemotherapy is still insufficient. Both Stereotactic Body Radiation Therapy (SBRT) combined with chemotherapy and Intensity-Modulated Radiation Therapy (IMRT) combined with chemotherapy for unresectable perihilar cholangiocarcinoma showed slightly extended survival [6,7]. New treatments are being developed. Clinical studies are being conducted using molecular-targeted drugs such as Fibroblast Growth Factor Receptor (FGFR) inhibitors, which were developed when driver abnormalities such as FGFR2 were found in bile duct cancer [8]. Clinical studies are also being conducted on PD-1 inhibitor as immunotherapy [9]. Photo immunotherapy developed by Kobayashi et al. is a breakthrough in the field of anti-cancer therapy [10]. Although it has not been used for the treatment of bile duct cancer, it is a potential game changer. With the progress of transplant oncology, liver transplantation may become the standard treatment in combination with various preoperative and postoperative treatments [2]. Finally, the era of precision cancer medicine is about to come. As one of them, the use of molecular-targeted drugs by genomic diagnosis using a gene panel is widely known in various types of cancer. In the aforementioned clinical studies using FGFR inhibitors for bile duct cancer, only patients with genetic abnormalities were included [8]. Another perspective is precision cancer medicine using Patient-Derived Xenograft (PDX) and Patient-Derived Orthotopic Xenograft (PDOX) mouse models in which tumors of individual patients are transplanted into immunodeficient mice [11]. In particular, the PDOX mouse model shows metastases. This is interesting as the model shows clinicopathological features similar to the clinical tumor behavior of individual patients [11]. For some cancers, clinical research on precision cancer medicine using the PDOX mouse model has started [12]. Although the PDOX mouse model for bile duct cancer has not yet been developed, we are currently developing it for precision cancer medicine. As mentioned at the beginning, treatment outcomes for advanced perihilar cholangiocarcinoma are still poor. However, there is steady progress in medical care, and the future of treatment for advanced hilar cholangiocarcinoma is somewhat bright.

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