
Toray Innovates Polymer-Conjugated Anticancer Agent that Selectively Accumulates and Actions Anthracycline in Tumor Tissues

– Toray Industries, Inc., the Department of Pain Control Research at the Jikei University School of Medicine, and Teikyo University announced today that joint nonclinical studies have confirmed key benefits of TXB-001. The company is researching and developing this polymer-conjugated anticancer agent. One benefit is that this agent significantly exhibits strong anticancer activity against various solid tumors. Another is that it greatly reduces several toxicities. These include cardiotoxicity (see Glossary note 1) commonly observed with existing anthracycline anticancer treatments (note 2).

These research results were presented at the annual meeting of the American Association for Cancer Research in San Diego, California, which was from April 5 through 10, 2024. Toxicology and Applied Pharmacology journal plans to present some of the research findings in issue 485, which it will publish this month.

In recent years, cancer treatment has shifted significantly toward antibody and other molecular targeted drugs (note 3). They have drawn considerable attention for their potential to offer improved benefits with fewer side effects. These therapies are not very effective with some cancer types, however, so many patients continue to rely on chemotherapeutic agents. Since chemotherapy targets cancerous and normal cells, side effects can substantially lower the quality of life (note 4). In severe cases, these downsides can make it hard to continue treatment. Anthracyclines are leading chemotherapeutic agents, commanding a global market of around \$1 billion. Common side effects of anthracyclines include hair loss and hand-foot syndrome (note 5) and their cumulative dose-limiting cardiotoxicity is another concern.

The innovative TXB-001 combines an anthracycline anticancer drug (the active ingredient) with a polymer via a functional linker. The basic design of this compound is the legacy of the late Hiroshi Maeda, a celebrated Japanese pharmacologist, chemist, and Professor Emeritus at Kumamoto University. Toray leveraged its advanced polymer complex synthesis and analysis technologies in mastering a technique to bind the active ingredient to a polymer and maintain its quality.

While it has a simple structure, as a drug delivery system (note 6) TXB-001 has a mechanism allowing drugs to selectively accumulate and act on tumor tissues. In the joint research, Teikyo University led an effort that confirmed strong anticancer effects of TXB-001 in animal models for highly malignant cancers. Among these were triple-negative breast cancer (note 7) and pancreatic cancer, which are hard to treat with molecular targeted drugs.

Researchers primarily at the Jikei University School of Medicine closely examined cardiotoxicity through echocardiography and blood tests on experimental animals. They found that TXB-001 does not adversely affect the heart, even at effective doses. This is in contrast to existing anthracycline anticancer drugs, which are known for their cardiotoxic effects. TXB-001 not only

exhibits significantly reduced cardiotoxicity but also minimizes alopecia and hand-foot syndrome, as histopathology studies in experimental animals have shown. It can lower the risk of side effects associated with conventional anthracyclines. On top of that, it has proven effective against cancer types that are challenging to treat with molecular-targeted drugs. TXB-001 stands as a promising new alternative in cancer treatment.

Toray aims to make TXB-001 available to patients as soon as possible. It accordingly seeks a business partner to undertake clinical development, and looks to commercialize it in the 2030s.

1. Cardiotoxicity refers to such side effects as heart failure, ischemic heart disease, hypertension, thromboembolism, and arrhythmia in the heart drug administration and other causes. Because anthracyclines can cause cardiotoxicity, cumulative dosages are limited.
2. Anthracyclines are standard anticancer drugs to treat a wide range of cancers, including breast, ovarian, and various hematologic tumors. They are known for side effects because they target normal and cancer cells.
3. Molecular targeted drugs are crafted to act selectively on specific molecules responsible for diseases. They efficiently attack cancers by directly targeting the proteins and genes of cancer and other cells. This approach seeks to provide therapeutic effects and minimize side effects.
4. Quality of life encompasses the physical, mental, social, and economic aspects of patient lives during treatment and recovery. Due to symptoms from their diseases or side effects from treatments, patients might find it impossible to live as they did before starting their treatment regimens.
5. Hand-foot syndrome is a condition in which skin cells in the hands and feet are damaged owing to anticancer drugs. It is characterized by abnormal numbness, pain in the hands and feet, as well as redness, swelling, and pigmentation changes.
6. Drug delivery systems