Poster

[P26-8] P26-8: Oncologic drugs (4): Pharmacokinetics, TDM practice

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[P26-8-6] Development of new monitoring system of antibody drug in human plasma by liquid chromatography-mass spectrometry using CDR-peptide selective proteolysis nSMOL

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Background

The efficacy of therapeutic drugs has some individual difference, so treatment by drug levels in plasma is an alternative options for effective chemotherapy. To date, some drugs like cardiotonics, immunosuppressant, and antiepileptics have been performed the treatment by drug monitoring. However for antibody drugs, we have not carried out by adequate monitoring technology. Indicators for drug efficacy is also important for the development of innovative drugs such as immune checkpoint inhibitors and combination therapy.
Liquid chromatography-mass spectrometry (LCMS) are the most optimal approach for the structure identification and quantitation with direct, sequential and comprehensive manner. For high-MW biopharmaceuticals, reproducible LCMS bioanalysis cannot obtain by common proteomics. Therefore new bioanalysis will be desired independent of a variety of antibodies. One of this solution is an accurate plasma level of antibody drugs. For reproducible antibody assay by the LCMS, it should be consider the highly composite and overall optimized approaches. Therefore, we have focused on the structure similarity and sequence specificity of antibodies.

Methods

As the antibody specificity is defined by the somatic mutation on Fv, antibody analysis is possible using the selective quantitation of complementarity-determining regions (CDRs). Immunoglobulin (IgG) was immobilized in pore (100 nm) via Fc. Proteolysis was performed by immobilized trypsin on the surface of nanoparticles (200 nm). Owing to diameter difference, trypsin proteolysis occurs at the accessible surface, and Fab is selectively proteolysed. This chemistry, named nSMOL, can be minimizing the sample complexity and protease contamination, while keep the antibody specificity.
For this assay validation in plasma, we have purchased Trastuzumab, Bevacizumab, Cetuximab, Rituximab, Nivolumab, and Brentuximab vedotin, and performed the full analytical validation.

Results

We have reported the nSMOL validation for several antibodies mentioned above in accordance with the regulated guideline for low-MW drug compounds. Furthermore, multiplex quantitation of Rituximab, Brentuximab vedotin, and Cetuximab has succeeded using the same validated criteria.

Conclusions

Using our approach, almost antibodies have been fulfilled the guideline criteria. And we have another activity into the expanded application, comparative original/biosimilar verification, and drug monitoring. Antibody monitoring based on nSMOL may be expected to aid the acceleration of new therapy strategy and discovery.