Poster

[P25-9] P25-9: Oncologic drugs (1)

Chair: Ryuji Ikeda, Japan

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[P25-9-7] Quantification of total Dinutuximab in neuroblastoma patients with LC-MS/MS

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Background

Neuroblastoma is one of the most commonly found solid tumors in children. Dinutuximab targets the sialic acid-containing glycosphingolipid GD2 expressed on almost all Neuroblastoma tumor cells and induces cell lysis. However, the expression of GD2 is not limited to tumor cells only, but is also present on central nerve tissue and peripheral nerve cells leading to increased toxicity. The most common adverse reactions are pain and discomfort, which may lead to discontinuation of the treatment. Furthermore, there is little to no information available about the pharmacokinetic of dinutuximab and it is still unclear at which dosage strength and rate the optimum effect lies. We therefore developed an easy method in order to track serum dinutuximab levels in patients in time. Melon gel purification was investigated due to its inherent simplicity to facilitate fast and easy sample preparation compared to the generic IgG pull down methods.

Methods

Melon gel 96 well plates were loaded with 75L Tris, 15L serum sample, 15L internal standard rituximab. Thereafter, the plate was centrifuged and the purified antibodies were captured in a lobind well plate. Samples and standard extracts were treated with RapiGest and were reduced with 5mM dithiothreitol followed by an overnight digestion with trypsin. The liberated peptides were separated and the signature peptide was analyzed on a LC-MS/MS.

Results

A signature peptide in the heavy chain was identified and was found to provide a high signal to noise ratio enabling a LLOQ of 0.5g/mL. The working range was 0.5 –32g/ml with an R^2=0.998. Quality control samples LLOQ, QC Low, QC Med and QC High were within acceptance criteria of 15% RSD and where in concordance with EMA guidelines.

Conclusions

A fast and easy method was set up to determine the concentration dinutuximab in serum. The use of 96 well plates enables high throughput and the limited amount of steps required for sample purification ensures a robust and foolproof method. The cost of consumables and ease of use make it an ideal substitute for the widely used generic sample purification methods based on protein A, G or anti FC antibodies.