Poster

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

Chair: Ryuji Ikeda, Japan

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[P25-9-1] Dried plasma spot analysis for gefitinib, erlotinib, afatinib and osimertinib using high performance liquid chromatography tandem mass spectrometry

Reiko Ando Makihara[1], Makoto Maeda[2], Kota Itahashi[3], Yasushi Goto[4], Shintaro Kanda[5], Hidehito Horinouchi[6], Yutaka Fujiwara[7], Taku Tsukamoto[8], Hironobu Hashimoto[9], Tomonobu Ohtsuka[10], Yoshinori Makino[11], Noboru Yamamoto[12], Yuichiro Ohe[13], Hiroyuki Terakado[14] (1.National Cancer Center Hospital, 2.National Cancer Center Hospital, 3.National Cancer Center Hospital, 4.National Cancer Center Hospital, 5.National Cancer Center Hospital, 6.National Cancer Center Hospital, 7.National Cancer Center Hospital, 8.Shimadzu Corporation, 9.National Cancer Center Hospital, 10.National Cancer Center Hospital, 11.National Cancer Center Hospital, 12.National Cancer Center Hospital, 13.National Cancer Center Hospital, 14.National Cancer Center Hospital)

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Background

Epidermal Growth Factor Receptor (EGFR) is the target of Tyrosine Kinase Inhibitors (TKIs) in lung cancer. Gefitinib, erlotinib, afatinib and osimertinib are EGFR-TKIs currently used to treat EGFR positive non-small cell lung cancer. This study combines TKIs DPS (Dried Plasma Spot) and plasma concentrations for clinical practice using high performance liquid chromatography tandem mass spectrometry.

Methods

For each patient on gefitinib, erlotinib, afatinib and osimertinib therapy, blood sampling was performed 1-3 times and 4 mL was collected. DPS samples were prepared by applying 30 μL of spiked whole blood onto a Noviplex Card. These TKIs were extracted with diluted water and methanol. The collected extract (3 μL) was injected onto a 100 mm ×2.1 mm 3μm Mastro C18 column and eluted with acetonitrile gradient into a triple quadrupole ESI-MS/MS Shimadzu LCMS-8050. Deming regression and Bland-Altman analyses were used to determine the relation between calculated and measured plasma concentrations. The study protocol was approved by our institutional review board and informed consent was obtained from all patients.

Results

A total of 31 patients, 10 Gefitinib, 6 Erlotinib, 6 Afatinib and 9 Osimertinib aged 20-86 were entered in this study. Though DPS concentrations and plasma concentrations of gefitinib and erlotinib’s metabolite showed a strong correlation (r = 0.954, 0.939, respectively), others did not show strong correlations (erlotinib: r = 0.848, afatinib: r = 0.857, osimertinib: r = 0.638, osimertinib’s metabolite: r= 0.690). Subsequently, Bland-Altman analyses showed erlotinib: 69%, erlotinib’s metabolite: 81%, afatinib: 53%, osimertinib: 31%, osimertinib’s metabolite: 46%, of the data points were within ±20% making the results not feasible. Of these TKIs, only gefitinib data was within the predefined acceptance limits of 92%.

Conclusions

Noviplex Card due to the differentiation in extraction efficiency, causing a variation in the results, making it not viable for all TKIs to be applied for clinical use. However, for Gefitinib the results showed it could be used

for clinical applications. Although validation of DPS cards prepared by patients themselves is required, these results show that DPS sampling can be used to monitor gefitinib therapy in clinical practice.