2019 Health Technology Reassessment Report

Safety and Effectiveness Assessment of F-18 Fluorothymidine Positron Emission Tomography

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Summary (English)

▫ Assessment background

F-18 FLT positron emission tomography (PET) is a nuclear medicine imaging diagnosis method for non-invasively assessing cell proliferation based on images and it is used to assess the treatment effect and differential diagnosis of tumor. This health technology was recognized as a new health technology in South Korea in 2012. Subsequently, it was registered as a non-coverage item (do-225) by the decree of the Ministry of Health and Welfare in 2015 and is still used today. The present study aimed to perform health technology reassessment to confirm the safety and effectiveness of this health technology at the present time effectiveness after the initial health technology assessment.

▫ Subcommittee operation

The subcommittee for this health technology was jointly operated with C-11 acetate PET health technology. The subcommittee consisted of a total of seven members. The members were preferentially invited among those who participated in the previous new health technology assessments for both health technologies, and if it was difficult for them to participate, members were randomly selected from a pool of professional assessment committee members for various fields within the new health assessment project headquarters. A total of three subcommittee sessions were held.

▫ Assessment objectives and methods

A systematic review was performed to reassess the clinical safety and effectiveness of F-18 FLT PET used on patients with lung cancer. For the

assessment, the technology was defined in accordance with the notification (do-225) stipulated by the Health Insurance Review and Assessment Service and search strategy used in the previous new health technology assessment was followed.

For systematic review, five Korean and three foreign databases were searched based on the key question. Two reviewers independently screened and selected the articles according to the selection and exclusion criteria. Risk of bias assessment was performed independently by two reviewers using QUADAS-2 until an agreement was reached. Data were extracted independently by two reviewers using pre-determined format. If there was a disagreement between the reviewers, such cases were discussed with a third party to reach an agreement. Meta-analysis was performed when quantitative analysis was possible and qualitative review was applied when otherwise.

▫ Assessment results

A total of 21 articles related to F-18 FLT PET or PET/CT were identified through the systematic review and these articles were used for the safety and effectiveness assessment.

One article reported that there was no incidence of adverse events associated with F-18 FLT PET/CT. Accordingly, it was determined that there are no safety concerns.

The effectiveness of this test was assessed by the diagnostic accuracy for metastasis, accuracy of disease staging, cell proliferation (correlation with comparator test), treatment response, and impact on health outcomes.

With respect to diagnostic accuracy for metastasis and accuracy of disease

staging, three articles compared F-18 FLT PET and F-18 FDG PET and all three articles reported that F-18 FLT PET showed higher accuracies. However, the study by Yamamoto et al. (2008) reported that there was no statistical significance.

With respect to cell proliferation assessment, there was a total of seven articles that compared the correlation between the index test and comparator tests (Ki-67 in six articles and cyclin D1 in one article). The results showed that F-18 FLT PET (or PET/CT) has a moderately significant correlation with comparator tests in the cell proliferation assessment (r=0.555, 95% CI 0.048, 0647).

Treatment response was assessed by progression-free survival (PFS), overall survival (OS), and standardized uptake value (SUV).

A total of seven articles reported on PFS. Five out of six studies that compared PFS between F-18 FLT PET (or PET/CT) response and non-response groups after chemotherapy reported that there were significant differences between the two groups. In particular, early outcomes (first week) were found to be significant predictors of PFS. However, one study (Bhoil et al., 2014) reported no significant difference, presenting conflicting results on prediction of PFS. One study (Everitt et al., 2017) that compared PFS between F-18 FLT PET (or PET/CT) response and non-response groups after chemoradiotherapy reported that the non-response group showed better PFS, but the difference was not statistically significant.

A total of eight articles reported on OS. All five studies that compared OS between F-18 FLT PET (or PET/CT) response and non-response groups after chemotherapy reported no significant differences between the two groups, and thus, predicting OS with F-18 FLT PET (or PET/CT) was found to be difficult. Two studies that compared OS between F-18 FLT PET (or PET/CT) response and non-response groups after chemoradiotherapy also reported no significant differences between the two groups. One study (Scheffler et al., 2013) compared

OS between F-18 FLT PET (or PET/CT) response and non-response groups before treatment and reported that F-18 FLT PET and F-18 FDG PET non-response group had statistically significantly better OS than the response group.

Eight studies reported on SUV of F-18 FLT PET (or PET/CT). Three studies that reported on SUV of F-18 FLT PET/CT at before and after treatment reported that SUV of F-18 FLT PET/CT decreased after the treatment.

There were no studies that reported any impact on treatment outcomes, such as changes in patient care by performing this test.

▫ Conclusions

The F-18 FLT PET subcommittee proposed the following based on the currently available assessment results. While F-18 FLT PET was found to have no safety concerns, its effectiveness was confirmed only in some results. Evidence currently available has confirmed clear clinical effectiveness for diagnostic accuracy (metastasis and disease staging) and cell proliferation assessment, whereas, evidence of its effectiveness for prognosis/prediction through treatment response assessment has not been found. However, the subcommittee determined that such results did not demonstrate much inferior effectiveness than F-18 FDG PET, which is universally used today, and that the effectiveness of treatment response assessment was at a similar level. Accordingly, it was determined that F-18 FLT PET is a safe and effective test method for determining treatment effect and predicting prognosis after chemotherapy or radiotherapy in patients in lung cancer.

The Health Technology Reassessment Committee reviewed and determined that the findings of the subcommittee on F-18 FLT PET are valid (October 11, 2019).