Gut Microbiome Profile and Clinical Correlations in Advanced EGFR-WT and EGFR-Mutant Non-Small Cell Lung Cancer

Woraseth Saifon, Insee Sensorn, Narumol Trachu, Songporn Oranratnachai, Angkana Charoenyingwattana, Chakkaphan Runcharoen, Nanamon Monnamo, Warawut Sukasem, Pimpin Inchareon, Phichai Chansriwong, Touch Ativitavas, Ravat Panvichian, Wasun Chantratita and Thanyanan Reungwetwattana

Background: Gut microbiome affecting clinical responses to cancer therapy has been demonstrated. However, considering about targeted therapy and chemotherapy, the relevance remains unknown. This study aims to explore relationship between gut microbiome and clinical outcomes in Thai advanced NSCLC patients (pts) according to EGFR status.

Methods: Thirteen EGFR-WT advanced NSCLC pts treated with chemotherapy and 15 EGFR-mutant pts treated with EGFR-TKIs were enrolled in this study. Fecal samples were collected at baseline and at first disease evaluation. 16s rRNA gene sequencing by NGS was applied to assess our microbiota profile. Gut microbiome and clinical correlations were explored.

Results: The clinical characteristics were balance between 2 cohorts, except high albumin level was significantly higher in EGFR-mutant group. Albumin was the only significant clinical factor affecting the treatment response in multivariate analysis (ORR=15.6, P = 0.03). Proteobacteria was higher in EGFR-WT group while Bacteriodota and Firmicutes were higher in EGFR-mutant group. EGFR-mutant pts significantly harbored higher alpha diversity of gut microbiome at baseline compared to EGFR-WT pts (Shannon index 3.82 VS 3.25, P = 0.022). Proteobacteria was decreased, but Bacteroidota and Firmicutes were increased after treatment in both cohorts but it was prominent in EGFR-WT cohort. There was no significant correlation between microbiome profile and treatment response in our study. However, beta diversity of microbiota was significantly different in pts with different severity of adverse events (AEs). Enrichment of Clostridia and Bacteriodia were associated with higher AEs in EGFR-WT cohort.

Conclusions: EGFR+ve NSCLC pts had significantly higher gut microbiome composition and alpha diversity from those whom had EGFR-WT. Proteobacteria was dominate in lung cancer pts and may associated with lung cancer carcinogenesis. Chemotherapy altered the gut microbiota whereas EGFR-TKIs less altered between pre and post treatment. There was no association between microbiota and treatment response. Microbiota probably use as biomarker for lung cancer in the future. The larger cohort should be conducted.