Abstract Title

The Correlative Study between Efficacy of Pemetrexed Combined Platinum Chemotherapy and Polymorphism of TYMS、GSTP1 Gene in Advanced Non-Small Cell Lung Cancer

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Background

Pemetrexed Combined Platinum Chemotherapy was gradually increased in advanced NSCLC treatment, but there were large differences in efficacy between individuals. Polymorphism of TYMS、GSTP1 Gene may play important roles in it . In order to confirm this, we investigated the correlation between Polymorphism of TS 、 GSPT1 gene and the chemotherapy efficacy (pemetrexed combined platinum) in the patients with advanced NSCLC. It provides the reference for further study on individualized therapy and chemotherapy sensitivity of Pemetrexed Combined Platinum Chemotherapy to advanced NSCLC .

Hypothesis

TYMS gene(5`UTR-2R/3R) of peripheral blood leukocytes might reflect the content of thymidylate synthase in tumor cells of patients with advanced NSCLC ,and this appearance may lead to the efficacy and PFS of patients with TYMS(2R/3R) were higher than those with TYMS(3R/3R) in pemetrexed combined platinum chemotherapy in advanced NSCLC treatment. GSPT1(I105V) may have the same characteristic.

Methods: 30 cases of advanced non-small cell lung cancer have been selected to finish the study during the period from 1st January, 2013 to 1st January, 2015. Before the first Pemetrexed Combined Platinum Chemotherapy, 2 millimeters vein blood had been extracted from those 30 cases to analyze genomic DNA. The patients gene were grouped by using Real-time PCR technology to test the polymorphism of TYMS, GSTP1. Follow-up study was applied to investigate the relationship between the Polymorphism of TYMS/GSTP1 and the sensitivity of Pemetrexed Combined Platinum chemotherapy.

Results:

1.In the study of 30 cases, 3 genotypes of GSTP1exited in the 105th animo acid sites of GSTP1 gene. GSTP1 genotype frequencies were A/A(60%), A/G(36.3%) and G/G(3.3%). According to 28bp tandem repeat exited in 5`UTR, TYMS gene was divided into 3 types: 2R/2R(3.3%), 2R/3R(43.4%),

3R/3R(53.3%).

2.Among 14 immunocytochemical cases, the positive frequencies of TYMS protein were 64.3%(9/14), the negative frequencies were 35.7(5/14). 2R/2R&2R/3R were low express group, 3R/3R was high express group. TYMS genotype (2R/3R, 3R/3R) and TYMS protein expression existed negative correlation（γ= 0.757 , P=0.036）

3. In the single factor analysis, efficiency of patients with G allele in GSTP1(I105V) were significantly higher than those with A/A genotype (58.3% vs. 16.7%, P<0.05). The median PFS was significantly longer than A/A (5.7 months vs. 4.0 months, P=0.047). Age, differentiation, stage, short-term remission were not statistically different with PFS.

4. In the single factor analysis, there was no statistical difference between TYMS gene and recent efficiency(P>0.05), but different from patients' PFS. The median PFS of patients with 3R/3R genotype and of patients with 2R/3R genotype were significantly different (4.3 months vs. 7.8 months, P=0.036).

5. With Cox proportional hazard model analyzing, Sex and genotypes are closely related with PFS(P<0.05). Risk of disease progress of female is 2.12 times as large as male(P<0.05). Risk of disease progress of patients with TYMS(3R/3R) genotype is 1.763 times as large as the patient with TYMS(2R/3R) genotype (P<0.05). Risk of disease progress of patients with genotype of AA in GSTP1 (I105V) site is 1.537 times as large as patient with G allele (P<0.05).

Conclusion:

1. In PP/PC therapy of patients with advanced NSCLC, the efficacy of patients with TYMS(2R/3R) and G allele in GSTP1(I105V) and PFS were higher than those with A/A. PFS of patients with 5 UTR in TYMS (2R/3R) was longer than those with 3R/3R.

2. The testing results of polymorphism of TYMS 2R/3R and GSTP1(I105V) could be the one of the reference index to predict Pemetrexed Combined Platinum Chemotherapy to patients with advanced NSCLC.

3.TYMS gene(5`UTR-2R/3R) of peripheral blood leukocytes of patients with advanced NSCLC might reflect the content of thymidylate synthase in tumor cells of patients with advanced NSCLC.