growth factor receptor inhibitor (EGFRI), that is, it is known as a PRIDE syndrome (a common skin response of the EGFRIs is called the PRIDE syndrome, wherein P" refers to papulopustule and paronychia, "R" refers to regulation and change of hair growth, "I" refers to itching, "D" refers to dryness, and "E" refers to EGFRIs). In the phase III clinical study of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs), the incidence of skin rash/acne-like skin rash was 15.5%-89.1%. About 1 to 2 weeks after the start of treatment, itching/painful maculopapules and purulent herpes were developed in areas rich in sebaceous glands, such as the face, chest and back, of the patients, one third of the patients had obvious related itching and scorching hot, and 38% of the patients had secondary skin infections, all of which led to the decline of the patients' quality of life.

For the management of EGFR-TKIs related skin rash at home and abroad, there is not enough therapeutic research evidence to support it, and most of the evidences are based on preventive medication research. At home and abroad, antibiotics and hormones are suggested to be used as symptomatic treatment in therapy, but the actual clinical efficacy is not clear, and meanwhile adoption of a systemic treatment solution may affect the anti-tumor autoimmune response level of the patient to reduce the efficacy of EGFR-TKIs. Furthermore, for patients with moderate to severe skin rash, they often choose to reduce dosage, take medicine intermittently or stop taking medicine because of intolerance, which limits these patients from getting benefits from the targeted therapy.

SUMMARY

The present inventor has found through research that EGFR-TKIs related skin rash belongs to the category of "drug toxicity rash", "damp toxin sore" and "wind toxin swelling" in the category of traditional Chinese medicine. Based on the knowledge and clinical experience of predecessors, modern physicians have concluded that the basic pathogenesis of skin rash caused by EGFR-TKIs is that yin deficiency and blood dryness are in the body, and toxic and pathogenic factors are concentrated outside, so it is advisable to nourish yin and moisten dryness in the treatment to help the root vacuity, and then to relieve its tip repletion

case 1 of Example 5 (a is before treatment; and b is after treatment).

FIG. 6 is a comparison of EGFR-TKIS related skin rash before and after treatment in case 2 of Example 5 (a is before treatment; and b is after treatment).

FIG. 7 is a comparison of EGFR-TKIS related skin rash before and after treatment in case 3 of Example 5 (a is before treatment; and b is after treatment).

DETAILED DESCRIPTION OF EMBODIMENTS

In order to show the technical solution, objective and advantages of the present disclosure more concisely and clearly, the present disclosure will be further described in detail below with reference to specific examples and accompanying drawings of the present disclosure.

Example 1: This example provided a traditional Chinese medicine composition for treating EGFR-TKIs related skin rash.

15 g of *Lonicera japonica*, 15 g of *Taraxacum mongolicum*, 9 g of *Sophora flavescens*, 15 g of *Kochiae fructus*, 10 g of *dictamni cortex*, 12 g of the *moutan cortex*, 12 g of *Phellodendri Chinensis Cortex,* and 6 g of *Menthae Haplocalycis Herba* (added lately). The whole prescription was 94 g, which was decocted in water and concentrated to 50 ml, containing 1.88 g crude drug per ml.

Example 2: This example provided a traditional Chinese medicine composition for treating EGFR-TKIs related skin rash.

5 parts of *Lonicera japonica*, 5 parts of *Taraxacum mongolicum*, 3 parts of *Sophora flavescens*, 5 parts of *Kochiae fructus*, 3 parts of *dictamni cortex*, 5 parts of *moutan cortex,* 5 parts of *Phellodendri Chinensis Cortex,* and 2 parts of *Menthae Haplocalycis Herba*.

Example 3: This example provided a traditional Chinese medicine composition for treating EGFR-TKIs related skin rash.

15 parts of *Lonicera japonica*, 10 parts of *Taraxacum mongolicum*, 8 parts of *Sophora flavescens*, 10 parts of *Kochiae fructus*, 12 parts of *dictamni cortex*, 6 parts of *moutan cortex,* 8 parts of *Phellodendri Chinensis Cortex,* and 10 parts of *Menthae Haplocalycis Herba*.

Example 4: This example provided a traditional Chinese medicine composition for

when the expected count < 5 was no more than 20% and the minimum expected count ≥ 1; continuity correction was used when the expected count < 5 was more than 20% and the minimum expected count was ≥ 1; and a fisher or likelihood ratio method was used when the minimum expected count < 1 or n < 40. Measurement data were expressed by mean ± standard error (mean ± SD), and all measurement data used a homogeneity test for variance. On the contrary, a Mann-Whitney U test or t' test was used for inter-group comparison, and a Wilcoxon signed-rank test or Wilcoxon signed rank test was used for intra-group comparison.

The outcome indicators of the research included the score change of the WoMo scale, such as a baseline (T0), after the first week of intervention (T1) and after the second week of intervention (T2), which belonged to replicate measurement data. A Generalized Estimation equation (GEE) is used for calculation of the replicate measurements.

$p < 0.05$ was considered to be statistically difference. All confidence intervals were bilateral 95% confidence intervals. The differences between the two groups were compared, and all statistical hypotheses were 2-side tests. Empowerstats (www.empowerstats.com; X&Y solutions Inc., Boston, MA) and R (http://www.R-project.org) would be used for analysis.

4. Treatment results

(1) The traditional Chinese medicine composition of the present disclosure could decrease the score of the WoMo scale

The generalized estimating equation (GEE) was used for comparing the score changes of the WoMo scale before and after two weeks of treatment on the patients. As could be seen from FIG. 1 and Table 2, in the analysis, a baseline time was taken as the baseline of dependent variables, and for comparison at different time points, the partial regression coefficients of the week 1 (Time 1) and the week 2 (Time 2) were -2.4809 and -3.5863, respectively, which were both statistically significant (both with p values < 0.0001). It showed that over time, the part C score of the WoMo scale has a significant decreasing trend, suggesting that the treatment was effective.

Table 2. Estimation of fixed effect parameters of linear mixed effect model (part C of WoMo

found during the treatment.

Example 9: Clinical experiment of the traditional Chinese medicine composition of the present disclosure in treatment of EGFR-TKIs related paronychia

1. Case 1

In case 1, the patient was Wu XX, a 49 years old female. In June, 2019, she was diagnosed as stage IV of lung adenocarcinoma. and had exon 19 mutation as detected by Gene detection. She took 40 mg QD of Afatinib, and paronychia occurred in her 2 months later, and gradually worsened with formation of granulation-like tissue (FIG. 3a). From August 3rd, 2019, she was soaked and washed with a topical skin rash-eliminating prescription (i.e., the traditional Chinese medicine composition of the present disclosure) twice a day, and after 1 week, the granulation tissue subsided, leaving only nail fold edema (FIG. 3b). The CTCEA grade was reduced from grade 2 to grade 1.

2. Case 2

In case 2, the patient was Guan XX, a 59 years old male. In August, 2019, he was diagnosed as stage IV of lung adenocarcinoma. and had exon 19 mutation as detected by Gene detection. He took 40 mg QD of Afatinib, and paronychia occurred in him 1 months later, and gradually worsened with nail fold edema accompanied with pain appeared on the lateral edges of both thumbs (FIG. 4a). From August 25th, 2019, he was soaked and washed with a topical skin rash-eliminating prescription (i.e., the traditional Chinese medicine composition of the present disclosure) twice a day, and after 1 week, the nail fold edema subsided without pain and discomfort, and he was basically recovered (FIG. 4b). The CTCAE score was reduced from grade 2 to recovery.

Example 10: Clinical experiment of the traditional skin rash composition of the present disclosure in treatment of EGFR-TKIs related skin rash

1. Case 1

The patient was Huang XX, a 57-year-old male, who was diagnosed as left upper lobe adenocarcinoma with systemic multiple bone metastases after operation. From December, 2017 to October, 2018, he was treated by oral administration of Iressa, after more than 10 months, the tumor was progressed, and a severe skin rash was occurred after more than 4

months of administration. In November, 2018, Huaxia gene detection: Exon-21 (L858R mutation) and TP53 pathogenic variation were detected. In November, 2018, he had the first visit to our outpatient department, and was changed to oral administration of Tagrisso. In March, 2019, when the patient visited, the skin rash of him was progressively worsened. At that time, the skin rash on the face was mainly located on the left and right cheeks, was mainly papules and erythema, and had a dark red color. The total score of WoMo was 50, and the C part score of WoMo was 9 (FIG. 5a). After two weeks of intervention by administration of this protocol, the skin rash on the face was improved, and the facial papules and erythema obviously subsided. The total score of WoMo was 30, and the C part score of WoMo was 5 (FIG. 5b).

2. Case 2

The patient was Shen XX, a 60 years old male. He was diagnosed as adenocarcinoma of the lower lobe of the left lung complicated with multiple M (IVa stage) in both lungs, bilateral supraclavicular bone, mediastinum and right hilum. From November 14th, 2018, he was given 7 courses of a platinum-pemetrexed (PP) regimen of chemotherapy + Avastin and immunotherapy. From May 9, 2019, he was given Alfatinib (30 mg) + Anlotinib (8mg), and the skin rash was occurred on the 16th day. The skin rash on the face of the patient was mainly located in the nose, cheeks of both sides and lower jaw, and was especially obvious in the nose. Meanwhile, erythema, papules and abscesses were also existed (FIG. 6a). The total score of WoMo was 60, and the C part score of WoMo was 13. After two weeks of external application of the skin rash-eliminating and itching-stopping prescription, the total score of WoMo was 30 and the C part score of WoMo was 7. The abscess of the nose was basically disappeared, leaving only a few papules and erythema (FIG. 6b).

3. Case 3

The patient was Chen XX, a 57 years old male. On August 20th, 2018, the CT examination of the patient showed a left upper lung occupying lesion. Pathological examination: Lung adenocarcinoma. EGFR detection: Exon 19 mutation. He was subsequently treated with the traditional Chinese medicine. On May 22, 2019, the CT showed that the upper left lung adenocarcinoma was larger than before, with liver metastasis.

Then he took Alfatinib. On September 10th, 2019, the reexamination of CT showed that the upper left lung adenocarcinoma was reduced by 50%. Then he was subjected to left lung and liver metastases ablation, and the first small lesions of liver metastases appeared. Therefore, he was treated with "1 g of pemetrexed disodium + 0.5 g of Bevacizumab" in the same period on October 15th, 2019 and November 14th, 2019. During the treatment, the patient developed severe skin rash, accompanied by cysts, abscesses, papules and erythema at the same time. The total score of WoMo was 80, and the C part score of WoMo was 10 (FIG. 7a). From October 27th, 2019, he began to be treated with the skin rash-eliminating and itching-stopping prescription. On the fourth day, the condition began to show obvious improvement, abscess began to heal, papules and cysts subsided, and the area of erythema was decreased. The total score of WoMo was 50, and the C part score of WoMo was 5 (FIG. 7b), so that the treatment effect was remarkable.

The examples described above are merely illustrative of several embodiments of the present disclosure, the description of them is more specific and detailed, but cannot be construed as limiting the scope of the present disclosure accordingly. It should be noted that, several variations and modifications can be made by those of ordinary skills in the art, under the premise of not departing from the concept of the present disclosure, and these variations and modifications all fall within the claimed scope of the present disclosure. Therefore, the scope of protection of the present disclosure shall be determined by the appended claims.