Second-line sunitinib for Chinese patients with advanced gastrointestinal stromal tumor: 37.5 mg schedule outperformed 50 mg schedule in adherence and prognosis

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Background: Sunitinib is widely accepted as a second-line treatment for advanced gastrointestinal stromal tumor (GIST). This study aimed to evaluate patients’ adherence to sunitinib treatment and optimize the dosing schedule for Chinese patients.

Methods: The present study analyzed medical data of patients with advanced GIST treated in Shanghai Ruijin Hospital and Shaoxin Shangyu People's Hospital. Adherence to sunitinib was evaluated through questionnaires. Treatment outcomes were evaluated during follow-up.

Results: Medical data of 107 patients were included in the analysis. The overall progression free survival (PFS) was 41 weeks (95% CI: 39.0–43.0 weeks), and overall survival (OS) was 70 weeks (95% CI: 68.1–71.9 weeks). Sixty-five patients completed the questionnaire evaluation of sunitinib adherence. Patients with good adherence had longer PFS than patients with poor adherence (P=0.032). Patients following the 37.5 mg continuous daily dosage (CDD) schedule had significantly longer PFS and OS than those following the 50 mg “4-week on 2-week off” schedule (50 mg 4/2 schedule), (P=0.044, and 0.016 respectively). Meanwhile, 64.1% of patients following the 50 mg 4/2 schedule suffered severe treatment toxicity Grade 2–3, and this percentage was significantly higher than that of patients following the 37.5 mg CDD schedule (P=0.010). The 50 mg 4/2 schedule and severe treatment toxicity were independent risk factors related to poor adherence (P=0.039, and 0.006 respectively).

Conclusions: Sunitinib 37.5 mg CDD schedule was related to improved adherence and prognosis compared with 50 mg 4/2 schedule. Sunitinib 37.5 mg CDD schedule might be a more suitable dosage schedule in Chinese patients with advanced GIST after imatinib failure.

Keywords: Gastrointestinal stromal tumors (GIST); adherence; prognosis; sunitinib

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**Introduction**

Gastrointestinal stromal tumors (GISTs) represent the most common mesenchymal tumors of the gastrointestinal tract (1). Sunitinib, a second-generation tyrosine kinase inhibitor (TKI) was widely recognized as standard second-line therapy for GISTs after imatinib failure (2-4). The classical dosing schedule is 50 mg “4 weeks on/2 weeks off” regime (50 mg 4/2 schedule), and an alternative 37.5 mg continuous daily dosage schedule (37.5 mg CDD schedule) was also proposed. Studies comparing the two dosing schedules are few, thereby indicating the similar efficacy and probably better tolerability of 37.5 mg CDD schedule (5,6). Long-term sunitinib therapy with adequate and continuous dosing is important for good clinical outcomes. However, patients self-administering oral drugs were susceptible to poor adherence compared with those undergoing traditional parenteral chemotherapy (7,8). In this study, we performed a dual-center retrospective research to compare the two dosage schedules in terms of treatment outcomes and self-dosage adherence among GIST patients who received sunitinib as second-line therapy after imatinib failure. We analyzed potential parameters on patients’ medication adherence and further discussed the influence of dosage schedule on patients’ medication adherence and prognosis.

We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/tcr-21-613).

**Methods**

**Patients and treatment outcomes**

We reviewed medical data from Database of Department of Gastroenterology of Shanghai Ruijin Hospital and Shaoxin Shangyu People’s Hospital. We focused on patients with advanced or metastatic GIST after imatinib failure who started sunitinib treatment from January 2008 through January 2020. The 50 mg 4/2 schedule and 37.5 mg CDD schedule were both recommended in guidelines (1). Thus, we provided patients with both choices. The 37.5 mg CDD schedule was chosen especially by those who have concerns regarding the adverse events (AEs) related to sunitinib treatment. During sunitinib treatment, concomitant medications with known impact on sunitinib serum level were routinely avoided. Medical data were collected including patients’ general information, Eastern Cooperative Oncology Group (ECOG) score, primary tumor location, surgery history, metastatic sites, mutation status, imatinib treatment history, concomitant medications, medication adherence, and treatment outcomes were determined. Data processing and analysis were performed after obtaining the ethics committee’s approval. Patients with incomplete baseline data were excluded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics committee of Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (No. 2018-086). Informed consent was collected from all the patients.

During the routine follow-ups, patients underwent follow-ups every 4–6 weeks and radiological assessment every 3 months. Therapeutic effects were evaluated according to RECIST criteria (9). Progression-free survival (PFS) was calculated from the date of the start of sunitinib to the date of the most recent follow-up (if not progress) or disease progression. Overall survival (OS) was calculated from the date of the start of sunitinib treatment to the date of the most recent follow-up (if not dead) or death due to the disease. The AEs of sunitinib were evaluated by experienced doctors according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (CTCAE3.0) (10).

**Assessment of medication adherence**

Adherence to sunitinib treatment was assessed by the 8-item Morisky medication adherence scale (MMAS), which has been translated to Chinese and is widely used for patients with chronic medications (11-13). The 8-item MMAS is composed of seven items that can be answered with “yes” or “no” alternatives and one item rated on a 5-point Likert scale. The summary score ranged from 0 to 8 and was divided into two levels, scores <8 were defined as poor adherence, whereas an 8 point score was considered good adherence.

**Statistical analysis**

The Statistical Package for the Social Sciences ver. 23.0 (SPSS 23.0; SPSS, Chicago, IL) was used for statistical analysis. Measurable data were expressed in terms of average values or median values with 95% confidence interval (95% CI), and categorical variables were represented by case numbers and the composition ratio. T-test and chi-square
test were used to analyze the significance of differences among proportions. The Kaplan–Meier survival analysis and Log-rank rank test were used to perform single-factor survival analysis and to draw survival curves. The Logistic analysis and the Cox proportional hazards regression model were applied for multiple-factor analysis. P value less than 0.05 was considered statistically significant.

**Results**

**Baseline characters**

By the end of the 31 June 2020, which was the date of the last patient follow-up, the medical records of 113 patients were retrieved and 107 were included in further analysis. The median follow-up time was 70 weeks (range, 19–112 weeks). Baseline characters were listed in Table 1. The overall

| Characteristics | Patients number |
|-----------------|----------------|
| n=107, n (%)    |                |
| Age, year, average (95% CI) | 55.6 (54.2-57.1) |
| Gender, Female | 35 (32.7) |
| BMI            |                 |
| <18.5          | 24 (22.4) |
| 18.5–23        | 77 (72.0) |
| >23            | 6 (5.61) |
| ECOG score     |                 |
| 0              | 42 (39.3) |
| 1              | 65 (60.7) |
| Primary tumor site |              |
| Esophagus      | 6 (5.6) |
| Stomach        | 49 (45.8) |
| Intestine      | 38 (35.5) |
| Colon          | 9 (8.4) |
| Omentum/mesentery | 5 (4.7) |
| Surgery history |                |
| Gastrectomy    | 42 (39.3) |
| Enterectomy    | 41 (38.3) |
| Mutation status of primary tumor |          |
| Exon 9         | 21 (19.6) |
| Exon 11        | 69 (64.5) |
| Exon 13        | 4 (3.7) |
| Exon 17        | 2 (1.9) |
| PDGFRA exon 12 | 3 (2.8) |
| PDGFRA exon 18 | 3 (2.6) |
| Wild type      | 5 (4.7) |
| Metastatic site |                |
| Liver          | 59 (55.1) |
| Abdominal cavity | 21 (19.6) |
| Pelvic cavity  | 15 (14.0) |
| Lung + liver   | 1 (0.9) |
| Abdominal cavity + liver | 11 (10.3) |

Table 1 (continued)

| Characteristics | Patients number |
|-----------------|----------------|
| n=107, n (%)    |                |
| Best response to first-line imatinib |          |
| Complete remission | 2 (1.9) |
| Partial remission  | 65 (60.7) |
| Stable disease    | 25 (23.4) |
| Progressive disease | 14 (13.1) |
| Intolerance       | 1 (0.9) |
| Maximum daily dose of imatinib |          |
| 400 mg           | 32 (29.9) |
| 600 mg           | 57 (53.3) |
| 800 mg           | 18 (16.8) |
| Imatinib duration, months, (IQR) | 24 (19, 26) |
| Sunitinib dose schedule |          |
| 50 mg 4/2 schedule | 39 (36.4) |
| 37.5 mg CDD schedule | 68 (63.6) |
| Concomitant medications |          |
| Anti-diabetics   | 6 (5.6) |
| Anti-hypertension | 12 (11.2) |
| Anti-coagulation | 11 (10.3) |

Table 1 Baseline characteristics of 107 patients

Table 1 (continued)
median PFS was 41 weeks (95% CI: 39.0–43.0), and OS was 70 weeks (95% CI, 68.1–71.9 weeks) (Figure 1A,B). Fifteen patients had stable disease, and 47 patients were alive according to the last follow-up. Thirty-nine (36.4%) patients followed the 50 mg 4/2 schedule, whereas 68 patients (63.6%) followed the 37.5 mg CDD schedule. Most patients experienced AEs during treatment, 78 (72.9%) patients had Grade 1–2 AEs, whereas 18 (16.8%) patients had Grade 3 AEs. Thirteen patients switched from 50 mg 4/2 schedule to 37.5 mg CDD schedule due to AE intolerance by the end of the follow-up period. During sunitinib treatment, none of the patients achieved complete remission; 51 (47.7%) achieved partial remission as the best response to sunitinib treatment; 44 (41.1%) achieved stable disease; 10 (9.3%) experienced disease progression; and two (1.9%) showed intolerance to sunitinib medication. During follow-up, 65 patients completed the MMAS questionnaires. Forty-one (63.1%) patients maintained good adherence to sunitinib treatment, whereas 24 (36.9%) had poor adherence. Among the above-mentioned 65 patients, the baseline characters of patients following different sunitinib schedules are listed and compared in Table 2. No statistically significant inter-group differences were found between the two groups.

**Prognostic analysis and multi-variate analysis**

According to Kaplan–Meier analysis, patients with exon 9 mutation in the primary tumor had significantly longer PFS and OS compared with patients with other mutation status (P=0.043, 0.048 respectively). Patients following 37.5 mg CDD schedule had significantly longer PFS and OS compared with patients following 50 mg 4/2 schedule (P=0.023, 0.006 respectively). Patients with good adherence to sunitinib treatment had significantly longer PFS and OS compared with patients with poor adherence (P=0.008, 0.010 respectively; Figures 2-4, Tables 3,4). To determine independent prognostic risk factors, all factors with P values under 0.20 were included in the Cox regression analysis. Sunitinib dosage schedule was an independent risk factor for patients’ PFS and OS (P=0.044, 0.016 respectively). The 37.5 mg CDD schedule was related to longer PFS and OS compared with 50 mg 4/2 schedule. Poor adherence to sunitinib treatment was an independent risk factor for shorter PFS (P=0.032).

**Impact of different parameters on patients’ adherence**

The present study further analyzed the potential factors that might have influenced patients’ adherence, as shown in Table 5. According to the chi-square test results, patients following the sunitinib 37.5 mg CDD schedule had better adherence than those following the 50 mg 4/2 schedule (P=0.035). Patients suffering from Grade 0–1 treatment toxicity had better adherence than those suffering from Grade 2–3 treatment toxicity (P=0.003). We included all factors with P values under 0.20 into the Logistic analysis. Consequently, sunitinib 37.5 mg CDD schedule and lower grade treatment toxicity were determined as two independent factors that contributed to good sunitinib adherence (P=0.039, 0.006 respectively).

**Figure 1** Kaplan–Meier survival curves for all the patients. PFS of all the patients (A), and OS for all the patients (B).
| Characteristics       | 50 mg 4/2 n (%) | 37.5 mg CDD n (%) | χ²    | P  |
|-----------------------|-----------------|-------------------|-------|----|
| Gender                |                 |                   |       |    |
| Female                | 11 (50.0)       | 16 (37.2)         | 0.98  | 0.322 |
| Male                  | 11 (50.0)       | 27 (62.8)         |       |     |
| Age                   |                 |                   | 0.227 | 0.634 |
| <60 y                 | 13 (59.1)       | 28 (65.1)         |       |     |
| ≥60 y                 | 9 (40.9)        | 15 (34.9)         |       |     |
| BMI                   |                 |                   | 0.982 | 0.612 |
| <18.5                 | 5 (22.7)        | 14 (32.6)         |       |     |
| 18.5–23               | 16 (72.7)       | 26 (60.5)         |       |     |
| >23                   | 1 (4.55)        | 3 (6.98)          |       |     |
| ECOG score            |                 |                   | 1.759 | 0.185 |
| 0                     | 6 (27.3)        | 19 (44.2)         |       |     |
| 1                     | 16 (72.7)       | 24 (55.8)         |       |     |
| Primary tumor site    |                 |                   | 0.198 | 0.656 |
| Gastric               | 11 (50.0)       | 24 (55.8)         |       |     |
| Non-gastric           | 11 (50.0)       | 19 (44.2)         |       |     |
| Gastrectomy           |                 |                   | 0.87  | 0.351 |
| Yes                   | 4 (18.2)        | 14 (32.6)         |       |     |
| No                    | 18 (81.8)       | 29 (67.4)         |       |     |
| Mutation status of primary tumor |                 |                   | 1.41  | 0.511 |
| Exon 9                | 3 (13.6)        | 11 (25.6)         |       |     |
| Exon 11               | 16 (72.7)       | 28 (65.1)         |       |     |
| Others                | 3 (13.6)        | 4 (9.3)           |       |     |

**AEs related to sunitinib and dose interruption**

Regarding toxicity, the proportion of patients following 50 mg 4/2 schedule who suffered from AEs over grade 2 was 64.1%, which was significantly higher than that of patients following 37.5 mg CDD schedule (38.2%; P=0.010). Sunitinib-related AEs were recorded and demonstrated in Table 6. Fatigue, anorexia, hand-foot syndrome reaction, stomato-mucositis, anemia, leucopenia, neutropenia, and thrombopenia were the most current AEs with occurrence rates of over 40%. Dosage suspensions were systematically organized when AEs over Grade 3 occurred, which led to the remarkable alleviation of AEs. Thirteen patients switched from 50 mg 4/2 schedule to 37.5 mg CDD schedule, including seven patients who were suffering from refractory Grade 3 AEs and six patients who were intolerant of certain Grade 2 AEs. Most AEs were mitigated in 12 patients after the shift in dosage.

**Discussion**

Prognostic and life quality of patients with GIST were obviously improved due to the application of oral TKI. In general, 50 mg 4/2 dosing schedule was the first choice according to current guidelines, whereas 37.5 mg CDD schedule was considered an alternative dosage strategy (1,14). In an open label phase II study, patients with advanced GIST received sunitinib in the 37.5 mg CDD schedule and reached a median PFS at 34 weeks (95% CI:
24–49 weeks) and a median OS at 107 weeks (95% CI: 72–not calculable weeks) (15). However, studies concerning alternative sunitinib dosing schedules for GIST patients are few, and controversies still exist in treatment outcomes (16). On the other hand, uncertainty was higher in patients’ adherence to oral therapy compared with traditional intravenous treatment. The interruption of oral anti-tumor therapy could lead to various problems (17). An increasing number of researchers are focusing on oral medication adherence, which was closely related to treatment outcomes according to existing clinical studies (18–20). To the best of our knowledge, the present study was the first to comprehensively evaluate the impact of dosing strategy and medical adherence on treatment outcomes for patients with advanced GIST after imatinib failure in a Chinese population.

In this study, patients with good adherence to sunitinib treatment had significantly longer PFS than patients with poor adherence. The former tended to have longer OS than the latter despite a P value of over 0.05 in the multi-factor
Figure 4 Kaplan–Meier survival curves for patients with different adherence levels. PFS of patients with different adherence levels (A), and OS of patients with different adherence levels (B).

Table 3 Prognostic analysis of PFS for patients following sunitinib treatment

| Factors                              | PFS (week) | Cox analysis |
|--------------------------------------|------------|--------------|
|                                      | Medium (95% CI) | $\chi^2$ | P     | HR (95% CI) | P     |
| Gender                               |            |              |        |              |        |
| Male                                 | 40 (35.7, 44.3) | <0.001 | 0.987 |
| Female                               | 42 (38.9, 45.1) |        |       |
| Age                                  | 1.305 | 0.253 |
| <60 y                                | 43 (39.2, 46.8) |        |       |
| ≥60 y                                | 40 (35.3, 44.7) |        |       |
| ECOG score                           | 0.125 | 0.724 |
| 0                                    | 43 (33.8, 52.2) |        |       |
| ≥1                                   | 41 (39.0, 43.0) |        |       |
| Primary tumor site                   | 1.077 | 0.299 |
| Gastric                              | 42 (39.8, 44.2) |        |       |
| Non-gastric                          | 40 (36.1, 43.9) |        |       |
| Mutation status of primary tumor site| 6.287 | 0.043 |
| Exon 9                               | 45 (41.3, 48.7) | 1.447 (0.924, 2.266) | 0.106 |
| Exon 11                              | 40 (37.0, 43.0) |        |       |
| Others                               | 39 (33.9, 44.1) |        |       |
| Sunitinib dosing schedule            | 5.141 | 0.023 |
| 50 mg 4/2                            | 36 (28.9, 43.1) | 0.555 (0.313, 0.984) | 0.044 |
| 37.5 mg CDD                          | 42 (39.5, 44.5) |        |       |
| Adherence                            | 7.092 | 0.008 |
| Poor adherence                       | 37 (33.4, 40.6) | 0.530 (0.297, 0.947) | 0.032 |
| Good adherence                       | 42 (39.4, 44.6) |        |       |
### Table 4 Prognostic analysis of OS for patients following sunitinib treatment

| Factors                          | OS (week) | Cox analysis |
|----------------------------------|-----------|--------------|
|                                  | medium (95% CI) | $\chi^2$ | P | HR (95% CI) | P |
| Gender                           |           | 1.995 | 0.295|
| Male                             | 70 (64.6, 75.4) | | |
| Female                           | 73 (70.4, 75.6) | | |
| Age                              |           | 1.122 | 0.29 |
| <60 y                            | 76 (67.2, 84.8) | | |
| ≥60 y                            | 71 (62.9, 79.1) | | |
| ECOG score                       |           | 0.615 | 0.433 |
| 0                                | 73 (64.3, 81.7) | | |
| ≥1                               | 70 (66.6, 73.4) | | |
| Primary tumor site               |           | 0.012 | 0.913 |
| Gastric                          | 72 (68.6, 75.4) | | |
| Non-gastric                      | 70 (63.7, 76.3) | | |
| Mutation status of primary tumor site |          | 6.074 | 0.048 | 1.729 (0.935, 3.199) | 0.081 |
| Exon 9                           | 90 (64.3, 115.6) | | |
| Exon 11                          | 70 (68.0, 72.0) | | |
| Others                           | 75 (66.4, 83.6) | | |
| Sunitinib dosing schedule        |           | 7.506 | 0.006 | 0.427 (0.213, 0.855) | 0.016 |
| 50 mg 4/2                        | 70 (66.5, 73.5) | | |
| 37.5 mg CDD                      | 76 (71.2, 80.8) | | |
| Adherence                        |           | 6.708 | 0.01 | 0.502 (0.244, 1.036) | 0.062 |
| Poor adherence                   | 69 (66.0, 72.0) | | |
| Good adherence                   | 75 (68.7, 81.3) | | |

analysis. We speculated that good adherence probably indicated a better prognosis for GIST patients receiving second-line sunitinib, which was in accordance with existing reports in anti-tumor treatment (21-23). Existing studies focusing on the management of different chronic diseases revealed that female gender, old age, and rural residence might be related to worse medication adherence (24-26). However, in the present study, patients with the above-mentioned characters demonstrated similar adherence to treatment compared with others. Possibly, different studies focused on different populations, and the present study focused on patients with progressive malignant disease, who generally had stronger motivation and better adherence to anti-tumor treatment.

Patients in the current study who experienced more severe side-effects of sunitinib had worse adherence to treatment, which was consistent with the findings of studies on other oral anti-tumor drugs. Unnikrishnan et al. found that patients with chronic myeloid leukemia had better adherence to imatinib when they experienced mild toxicity (27). Chrisoulidou et al. discovered that patients with recurrent thyroid cancer had better adherence to oral regorafenib if they experienced mild side-effects (28). In the present study, patients who followed the 37.5 mg CDD schedule had significantly less severe side-effects and better medication adherence than those who followed the 50 mg 4/2 schedule. In addition, we witnessed a significant decrease of severity of sunitinib-related AEs in patients...
Table 5 Potential factors influencing patients adherence to sunitinib treatment

| Factors                  | Adherence  | Logistic regression |
|--------------------------|------------|---------------------|
|                          | Good, n (%) | Poor, n (%) | χ²  | P | ExpB (95% CI) | P |
| Gender                   |            |           | 1.055 | 0.304 |
| Male                     | 22 (53.7)  | 16 (66.7) |       |     |              |   |
| Female                   | 19 (46.3)  | 8 (33.3)   |       |     |              |   |
| Age                      |            |           | 2.322 | 0.128 |
| <60 y                    | 23 (56.1)  | 18 (75.0)  |       |     |              |   |
| ≥60 y                    | 18 (43.9)  | 6 (25.0)   |       |     |              |   |
| Marital status           |            |           | 0.595 | 0.441 |
| Living alone             | 14 (34.1)  | 6 (25.0)   |       |     |              |   |
| Living with couple       | 27 (65.9)  | 18 (75.0)  |       |     |              |   |
| Income level             |            |           | 1.297 | 0.255 |
| Low                      | 13 (31.7)  | 11 (45.8)  |       |     |              |   |
| Middle-high              | 28 (68.3)  | 13 (54.2)  |       |     |              |   |
| Residence                |            |           | 0.744 | 0.388 |
| Rural                    | 16 (39.0)  | 12 (50.0)  |       |     |              |   |
| Urban                    | 25 (61.0)  | 12 (50.0)  |       |     |              |   |
| Education                |            |           | 0.874 | 0.35  |
| Low                      | 14 (34.1)  | 11 (45.8)  |       |     |              |   |
| Middle-high              | 27 (65.9)  | 13 (54.2)  |       |     |              |   |
| ECOG score               |            |           | 0.015 | 0.903 |
| 0                        | 16 (39.0)  | 9 (37.5)   |       |     |              |   |
| ≥1                       | 25 (61.0)  | 15 (62.5)  |       |     |              |   |
| Sunitinib schedule       |            |           | 4.434 | 0.035 |
| 50 mg 4/2                | 10 (24.4)  | 12 (50.0)  |       |     |              |   |
| 37.5 mg CDD              | 31 (75.6)  | 12 (50.0)  |       |     |              |   |
| Concomitant oral medication |            |           | 0.289 | 0.591 |
| No                       | 16 (39.0)  | 11 (45.8)  |       |     |              |   |
| Yes                      | 25 (61.0)  | 13 (54.2)  |       |     |              |   |
| Treatment toxicity       |            |           | 8.635 | 0.003 |
| Grade 0–1                | 29 (70.7)  | 8 (33.3)   |       |     |              |   |
| Grade 2–3                | 12 (29.3)  | 16 (66.7)  |       |     |              |   |

who switched from 50 mg 4/2 schedule to 37.5 mg CDD schedule, which was in accordance to existing studies (15,29). In the present study, patients following the 37.5 mg CDD schedule tended to have better prognosis than those following the 50 mg 4/2 schedule. One possible explanation was that 37.5 mg CDD schedule leads to less severe toxicity, which in turn improves patients’ adherence and may result in less dosage interruption and better control of tumor...
Table 6 Adverse events related to sunitinib (n=107)

| Adverse events                      | Grade 1/2 |       | Grade 3 |       | Total |       |
|-------------------------------------|-----------|-------|---------|-------|-------|-------|
|                                     | n         | %     | n       | %     | n     | %     |
| General status                      |           |       |         |       |       |       |
| Fatigue                             | 53        | 49.5  | 6       | 5.6   | 59    | 55.1  |
| Fever                               | 9         | 8.4   | 0       | 0     | 9     | 8.4   |
| Peripheral edema                    | 9         | 8.4   | 0       | 0     | 9     | 8.4   |
| Anorexia                            | 45        | 42.1  | 0       | 0     | 45    | 42.1  |
| Skin and mucosal reaction           |           |       |         |       |       |       |
| HFSR                                | 58        | 54.2  | 4       | 3.7   | 62    | 57.9  |
| Hair color change                   | 40        | 37.4  | 0       | 0     | 40    | 37.4  |
| Skin color change                   | 35        | 32.7  | 0       | 0     | 35    | 32.7  |
| Alopecia                            | 23        | 21.5  | 0       | 0     | 23    | 21.5  |
| Stomato-mucositis                   | 43        | 40.2  | 3       | 2.8   | 46    | 43.0  |
| Cardiovascular system               |           |       |         |       |       |       |
| Hypertension                        | 34        | 31.8  | 3       | 2.8   | 37    | 34.6  |
| Digestive system                    |           |       |         |       |       |       |
| Nausea/Vomiting                     | 30        | 28.0  | 2       | 1.9   | 32    | 29.9  |
| Diarrhea                            | 28        | 26.2  | 0       | 0     | 28    | 26.2  |
| GI bleeding                         | 15        | 14.0  | 0       | 0     | 15    | 14.0  |
| Nervous system                      |           |       |         |       |       |       |
| Tinnitus                            | 9         | 8.4   | 0       | 0     | 9     | 8.4   |
| Paralgesia                          | 38        | 35.5  | 0       | 0     | 38    | 35.5  |
| Blurred vision                      | 7         | 6.5   | 0       | 0     | 7     | 6.5   |
| Laboratory indicators               |           |       |         |       |       |       |
| Hematologic system                  |           |       |         |       |       |       |
| Anemia                              | 55        | 51.4  | 5       | 4.7   | 60    | 56.1  |
| Leucopenia                          | 47        | 43.9  | 3       | 2.8   | 50    | 46.7  |
| Neutropenia                         | 41        | 38.3  | 2       | 1.9   | 43    | 40.2  |
| Thrombopenia                        | 51        | 47.7  | 0       | 0     | 51    | 47.7  |
| Non-hematologic system              |           |       |         |       |       |       |
| Elevated ALT/AST                    | 38        | 35.5  | 3       | 2.8   | 41    | 38.3  |
| Elevated bilirubin                  | 23        | 21.5  | 0       | 0     | 23    | 21.5  |
| Hypothyroidism                      | 6         | 5.6   | 0       | 0     | 6     | 5.6   |
| Proteinuria                         | 34        | 31.8  | 6       | 5.6   | 40    | 37.4  |
progression.

The present study featured several advantages. First, studies on adherence of sunitinib medication are scarce. Hence, the present study made up for gaps in this field. Second, the timespan of follow-up was relatively large. Thus, most of the patients had reached endpoints, making the survival analysis results more convincing. However, the current study had some limitations. First, the sample scale was relatively small due to the rarity of the disease. Second, MMAS was obtained from the patients’ self-report. Thus, selection and recall bias existed. Third, other data reflecting patients’ adherence, such as serum drug concentration, were absent. A prospective large-scale multi-center research with random design is required to further confirm our findings.

In conclusion, sunitinib 37.5 mg CDD schedule was related to better medication adherence and less severe sunitinib-related AEs compared with the classical 50 mg 4/2 schedule. This improvement in adherence possibly leads to better prognosis. The management of certain AEs needs to be emphasized to avoid poor adherence to sunitinib treatment. For Chinese patients with advanced GIST after imatinib failure, sunitinib 37.5 mg CDD schedule was probably more suitable than the classical 50 mg 4/2 schedule.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/tcr-21-613

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/tcr-21-613). The authors have no conflicts of interest to declare.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics committee of Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine (No. 2018-086). Informed consent was taken from all the patients.

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