PRELIMINARY EVALUATION OF THE TREATMENT OF ADVANCED HEPATOCELLULAR CARCINOMA WITH SORAFENIB

Pham Nhu Hiep[1], Phan Thi Do Quyen[1], Pham Nguyen Tuong[1], Nguyen Thi Ky Giang[1], Dang Hoang An[1], Nguyen Van Phong[1]

ABSTRACT

Purpose: *To evaluate the treatment efficacy and common side effects of Sorafenib in advanced hepatocellular carcinoma patients.*

Patients and methods: *18 patients diagnosed hepatocellular carcinoma with or without first-line treatment (surgery, RFA, TOCE), were treated by Sorafenib from january-2013 to june-2014. Data processing by SPSS 20 for windows.*

Result:

Common age was >50 year old, the rate was 61.1%. The male was major, the rate was 94.4%. Most patients were in stage IIIB and IIIC with the rate of 33.3% and 38.9%, respectively. All patients wewe in Child-Pugh class A-B. Most had over 3 tumors in liver. Average diameter of tumor was 6.5cm, biggest: 13cm, smallest: 3cm. Most had Hepatitis B Virus infection. 66% patients were treated first-line with surgery or RFA, TOCE. Common side effects were hand- foot syndrome grade I-II (55.6%), without fatigue or fatigue grade I-II:83.4%. Grade I-II diarrhea was 5.6%, without anorexia (77.8%). Overall survival was 11±1.28 months (CI 95%).

Conclusion:

Hepatocellular carcinoma is one of the most common cancers. Major treatment is surgery. But with advanced stages, the tumor is unresectable, Sorafenib is a good option. Side effects are neglible. Mainly, hand foot syndrome, in addition there are fatigue, loss of appetite, diarrhea.

I. BACKGROUND

Hepatocellular carcinoma has been one of the most common cancers worldwide. As in a report of GLOBOCAN 2012, the incidence of HCC is approximately 782,000 cases per year, in which 83% are reported from developing countries. HCC is globally the 5th common cancer in men and the 9th common in women. In Vietnam, HCC is the most common cancer in men and the 3rd common in women. Annual report reveals the incidence of HCC is 21,997 new cases, prominently in men with 16,815 cases. HCC become the leading cause of cancer-related death in both sexes with increasing incidence and prevalence worldwide and nationwide. Favorable prognosis can be achieved with early stage HCC which is candidate for curative treatments as resection or local ablation with overall 5-year survival

1. Oncology Centre- Hue Central Hospital

Corresponding author: Phan Thi Do Quyen
Email: doquyen_cl@yahoo.com
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reaches 60-70%. In Vietnam, most of the cases are diagnosed, however, in advanced stage which limits treatment efficacy. In addition, systemic approaches for the management of HCC remain limited and ambiguous.

Sorafenib is a targeted therapy agent acting by inhibiting tumor-cell proliferation and tumor angiogenesis and increase the rate of apoptosis in a wide range of tumor models. FDA approved Sorafenib for the treatment of unresectable HCC since 2007. The agent has been launched in Vietnam since 2010 and at Hue Central hospital since 2011 for advanced HCC. The study was conducted with the aims to evaluate primary efficacy of Sorafenib in the treatment of advanced HCC and to determine common side effects.

II. PATIENTS AND METHODS

Patients: 18 HCC patients who were not candidate for curative treatment enrolled in this perspective cross-sectional study. All patients were administered with Sorafenib (Nexavar 200mg) 4 pills twice daily, from Jan 2013 to June 2014.

Overall survival was estimated using Kaplan-Meier chart. Patient demographic, performance status (ECOG), side effects were also documented. Data analysis by SPSS 20.

III. RESULTS

3.1. Patient characteristics before using Sorafenib:

Age and gender:

Table 1: Age

Age group	n (%)
< 30	1 (5.6)
30-50	6 (33.3)
>50	11 (61.1)
Tổng	18 (100)

Median age: 56

Men: 17 (94.4%) Women : 1 (5.6%)

Performance status

Table 2: ECOG

ECOG	n (%)
ECOG 0	8 (44)
ECOG 1	7 (38.9)
ECOG 2	3 (16.7)
Total	18 (100)

Viral hepatitis status

Table 3: Viral hepatitis status

Viral hepatitis status	n (%)
HBsAg (+)	15 (83.3)
HBsAg (-)	2 (11.1)
Anti HCV (+)	1 (5.6)
Total	18 (100)

Number of tumors:

Table 4: Number of tumors in liver

Number of tumor	n (%)
1-3	5 (27.8)
>3	13 (72.2)

Average tumor dimension 6.5cm

Child-Pugh : most child A and child B

Table 5: Child-Pugh

Child-Pugh	n (%)
Child A	13 (72.2)
Chid B	5 (27.8)

Alpha Fetoprotein (AFP) at the first diagnosic

Table 6: AFP

AFP	n (%)
<400	6 (33.3)
≥ 400	12 (66.7)

Stage

Table 7: Stage (NCCN)

Stage	n (%)
IIIA	3 (16.7)
IIIB	6 (33.3)
IIIC	7 (38.9)
IV	2 (11.1)
Total	18 (100)

Firstline treatment:

Table 8: Firstline:

Firstline 1	n (%)
Surgery	4 (22.2)
TOCE	2 (11.1)
RFA	6 (33.3)
No treatment before Sorafenib	6 (33.3)
Total	18 100)

3.2. The results of treatment

a. Overall survival after Sorafenib was estimated is 11±1.28 mos (CI 95%)

b. Overall survival rate

Table 9: Overall survival rate

Overall survival	Rate %
3 months	94.4
6 months	88.9
9 months	66.7
12 months	20

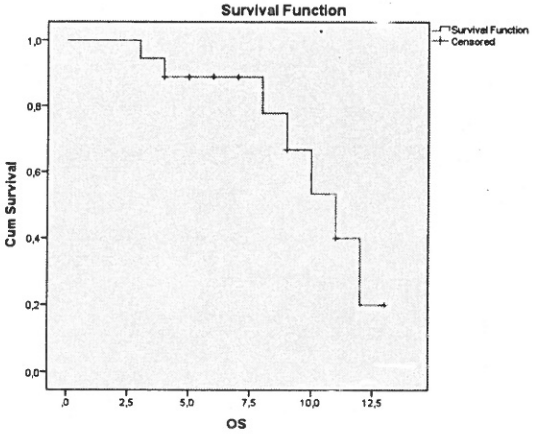

Diagram 1: Overall survival

c. Adverse effects

Table 10: Sorafinib's Adverse effects

AEs	Grade, n (%)		
	Grade 0	Grade I-II	Grade III-IV
Hand foot syndrome	6 (33.3)	10 (55.6)	2 (11.1)
Fatigue	5 (27.8)	10 (55.6)	3 (16.7)
Anorexia	14 (77.8)	2 (11.1)	2 (11.1)
Diarrhea	17 (94.4)	1 (5.6)	

IV. DISCUSSION

4.1. Patient demographic

In our series, HCC was prominent in men, over 50 years old (61.1%). This finding was similar to various reports so far. Patient's performance status at the starting point of Sorafenib was favorable with 82.9% ECOG 0-1. Most of cases were positive with HBV or HCV (88.9%), which has been proved to be strongly related to HCC by numerous studies. [2]. Multifocal HCCs were more prevalent. The rate of >3 nodules was 72.2%. Mean tumor diameter was 6.5cm. All tumors were classified stage III, IV with previous treatment such as resection, RFA or TACE, requiring no further intervention but systemic Sorafenib. All patients had preserved liver function, 72.2% Child A and 27.8% Child B. This is one of factor that improve overall survival rate in our series compared to others. AFP level is a common tumor marker use in the diagnosis of HCC. In this study, 66.7% of patients had elevated AFP level >400 UI/ml, implying that AFP level is helpful the diagnosis and monitoring of HCC [7].

4.2. Treatment results

Overall survival rate for HCC patients treated with Sorafenib in our series was 11±1.28 months (CI 95%). This result was similar to that of other reports by Llovet et al, Ghassan K.Abu-Alfa et al, Pressiani et al, as 10.7, 9.2, 9.1 months, respectively [4], [5], [6]. Other studies reported lower survival rate such as Phạm Xuân Dũng et al from Ho Chi Minh Oncology Center, [1] 6.4±0.72 months, Pinter et al, 6.5 months [1], [3]. This might be due to the fact that our patients had preserved underlying liver function.

Hand foot syndrome was the most common complaint, however, the frequency was low and with mild degree, 55.6% grade I-I, 11.1% grade III-IV and the rest reported no disturbance. Other side effects were also obtained with mild degree or unremarkable such as fatigue (16.7% grade III=IV), loss of appetite (11.1% grade III-IV), diarrhea (5.6% grade I-II) without severe diarrhea. Other reports by Llovet et al,

Ghassan K. Abu Alfa et al showed the similar finding as well [4], [5]. To the best of our knowledge, there was no report on hemorrhage. Therefore, Sorafenib seems to be safe and its side effects are controllable.

V. CONCLUSION

HCC is one of ten most common cancer in Vietnam and worldwide. In our study, we realized that patients often present at advanced stage, most at stage III-IV, which limits treatment efficacy. Sorafenib is one of best choice for liver cancer patients in advanced stage. Similar some other study, in this study showed that benefits survival of Sorafenib is significant, the side effects is negligible and manageable. In addition, the characteristic of patients (stage, ECOG, number of tumors, the size of tumor) can help prognosis in treatment time and post-treatment.

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