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REVIEW ON SUNITINIB: AN OVERVIEW OF ITS POTENTIAL THERAPEUTIC USES FOR THE MANAGEMENT OF RENAL CELL CARCINOMA AND GIST

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ABSTRACT

Sunitinib is as tyrosine kinase inhibitor which is used in the treatment of certain types of cancer. Such as renal cell carcinoma (kidney cancer) and gastrointestinal stomal tumors (GISTS). Its works by blocking the action of abnormal protein. It helps to stop or slow the spread of cancel cell. Sunitinib is act as an antitumour or anti angiogenic activity because sunitinib is a protein kinase inhibitor and which work by block the action of abnormal proteins due to block the action that helps to stop or slow the spread of cancer cells and also helps to shrink.

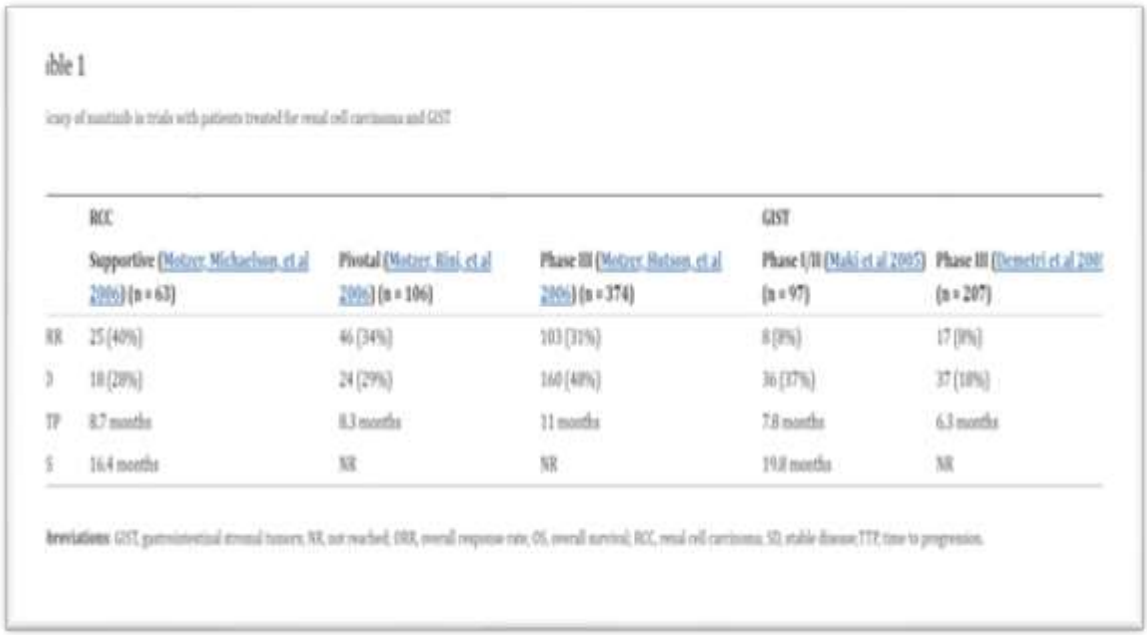
KEY WORD: *Renal Cell Carcinoma, Gastrointestinal Stomal Tumors, Angiogenic*

INTRODUCTION

Sunitinib is used in the treatment of cancer. It also called as sutent. It is administered by orally. Sunitinib is not a chemotherapy drug it is a targeted therapy. It is also available in capsule form. Before administered of sunitinib drug some blood tests are carried out like CBC test, Renal function test, Liver function test or BP. Sunitinib drug is discovered/developed by Pfizer company. Sunitinib is a class of kinase inhibitor. Sunitinib work by block the action of abnormal protein. Sunitinib helps to stop or slow the spread of cancer cells and also help to shrink tumors.

SUNITINIB FOR THE MANAGEMENT OF RENAL CELL CARCINOMA

This observation provided the basis for initiating a large phase 2 trial that included 63 patients with advanced RCC who had failed cytokine therapy. Patients were treated with sunitinib monotherapy 50 mg daily for 4 weeks followed by 2 weeks of rest (Motzer, Michaelson, et al. 2006). Fifty patients (87%) had biopsies. clear cell texture Only four patients (6%) had a response to previous cytokine therapy. The median duration of sunitinib treatment was 9 months, 25 of 63 patients (40%) achieved a partial response, and 17 patients (28%) had stable disease for more than 3 months. Twenty-four respondents had clear cell histology and one had a papillary cell type. Reactive lesions include areas of local recurrence and lymphatic metastases, liver, lungs, bones, and adrenal glands. The median duration for the adavancement was 8.7 months and the average median overall survival was 16.4 months. The most frequently reported treatment-related grade 3 adverse events were fatigue (11%), nausea (3%), and diarrhoea (3%).



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	RCC			GIST	
	Supportive (Motzer, Michaelson, et al 2006) (n = 63)	Pivotal (Motzer, Rini, et al 2006) (n = 106)	Phase III (Motzer, Hutson, et al 2006) (n = 374)	Phase I/II (Maki et al 2005) (n = 97)	Phase III (Demetri et al 200 (n = 207)
RR	25 (40%)	46 (34%)	103 (31%)	8 (8%)	17 (8%)
)	18 (28%)	24 (29%)	160 (48%)	36 (37%)	37 (18%)
TP	8.7 months	8.3 months	11 months	7.8 months	6.3 months
S	16.4 months	NR	NR	19.8 months	NR

breviations: GIST, gastrointestinal stromal tumors; NR, not reached; ORR, overall response rate; OS, overall survival; RCC, renal cell carcinoma; SD, stable disease; TTP, time to progression.

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Nonhematological					
Fatigue	11%	8%	7%	10%	7%
Diarrhea	3%	3%	5%	7%	4%
Nausea	3%	0%	3%	4%	1%
Dermatitis	2%	5%	5%	7%	5%
Stomatitis	2%	5%	1%	3%	NA
Asymptomatic lipase increase	21%	15%	4%	13%	NA
Hypertension	2%	6%	8%	17%	4%
Hematological					
Neutropenia	13%	13%	11%	NA	0%
Anemia	10%	6%	3%	NA	4%
Thrombocytopenia	0%	6%	0%	NA	5%

A phase 2 trial, conducted to confirm the antitumor activity and safety observed in the phase 1 trial (Motzer, Rini, et al 2006), included one hundred six patients with metastatic clear cell RCC. All had previous kidney surgery and had failed first-line cytokine therapy. The median treatment duration was 5 months. Thirty-six patients (34%) had a partial response (Table 1). Thirty patients (29%) had stable disease for longer than 3 months. Grade 3 adverse events at the most common treatment-related illnesses reported were fatigue (8%), high blood pressure (6%), colitis (5%), dermatitis (5%), and diarrhoea (3%) (Table 2). Level 3 is the most common. or 4 laboratory abnormalities that increased without symptoms… lipase (15%), neutropenia (16%), thrombocytopenia (6%), and anaemia (6%). Dosage was reduced from 50 mg to 37.5 mg per day in 17 patients (16%), with six of these patients receiving a dose reduction of up to 25 mg per day. Most often in the reduction are edema and fatigue.

UV ESTIMATION OF SUNITINIB

1) Chemical: Sunitinib Hammer and commercial sunitinib 50 mg capsules are supplied by Parsian Pharmaceuticals Company, Iran. Bromocresol purple (BCP), bromothymol blue (BTB), and bromophenol blue (BPB) were purchased from Merck (Darmstadt, Germany). Analytical grade chloroform from Merck (Darmstadt, Germany).
2) Instrumentations: A Shimadzu dual beam ultraviolet-visible spectrophotometer (UV-160A) was used to perform the spectrophotometric measurements. The fixed bandwidth is 2 nm and a 1 cm quartz cell is used.
3) Standard solutions: A stock standard solution (5 × 10-4 M) was prepared by dissolving 26.6 mg sunitinib malate in 100 mL distilled water. A reagent standard solution (5 × 10-4 M) was prepared by Dissolving BCP 27 mg, BTB 31.2 mg or BPB 33.5 mg in 100 ml of distilled water by dissolving an appropriate amount of NaH2PO4 in the distilled water and adjusting the pH to 1.5 -3.5 (1.5, 2.0). Prepare Phosphate buffer (0.1 M) in the pH range 2.5, 3.0, 3.5)
4) General procedure: One millilitre of sunitinib standard solution was transferred to a 100 mL separator funnel. After adding 2 mL of phosphate buffer (pH 2.0) and 3.0 mL of BCP or 3.0 mL of BTB or 2.0 mL of BPB solution, the solution was stirred. for 30 s. The resulting divalent ion complex was extracted three times with 5, 3, and 2 mL of chloroform. The organic layer was passed through anhydrous sodium sulphate and transferred to a 10 mL volumetric flask. The suction was measured. The absorbance of the solution was measured at 422 nm for BCP, 425 nm for BTB, and 427 nm for BPB in a volume of 10 mL with chloroform against the appropriate reagent blank.

RESULT AND DISCUSSION

The interaction between the reagents as electron donors (BCP, BTB and BPB) and the protonated amine of sunitinib as the electron acceptor forms a strongly colored charge transfer complex. which shows yellow color in all divalent ion complexes of sunitinib with the light-absorbing reagent in visible region The reagent blank solution showed insignificant absorption at 300-400 nm. On the other hand, strong absorption was observed after the formation of divalent ion complexes. The maximum absorption wavelengths were 422 nm, 425 nm, and 427 nm for BCP, BTB, and BPB, respectively. The ion-pair complex solutions were calibrated with blank solutions of each reagent to reduce absorption. of reagents to a minimum.

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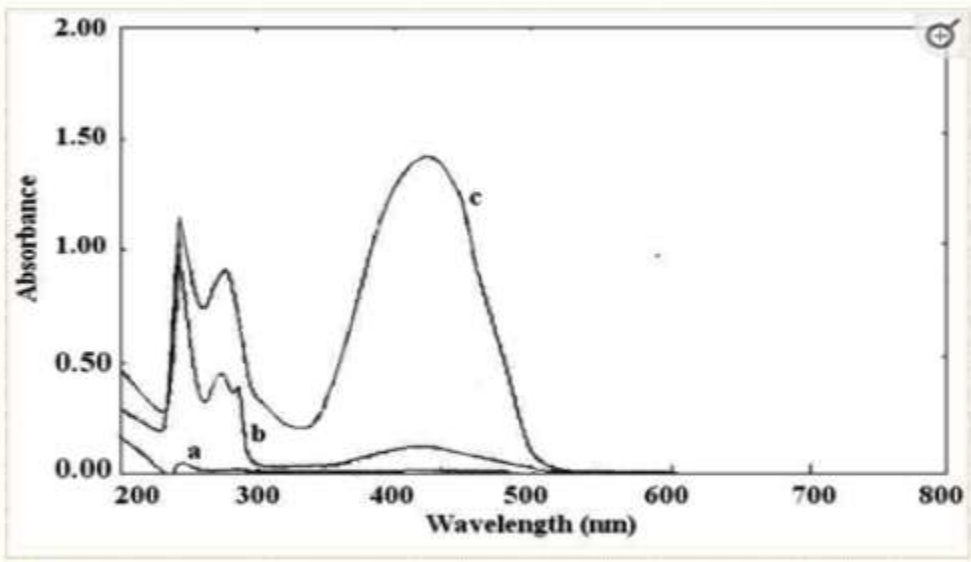

Figure 2

Absorption spectra of (a) sunitinib malate, (b) BCP, and (c) the ion-pair complex of sunitinib and BCP

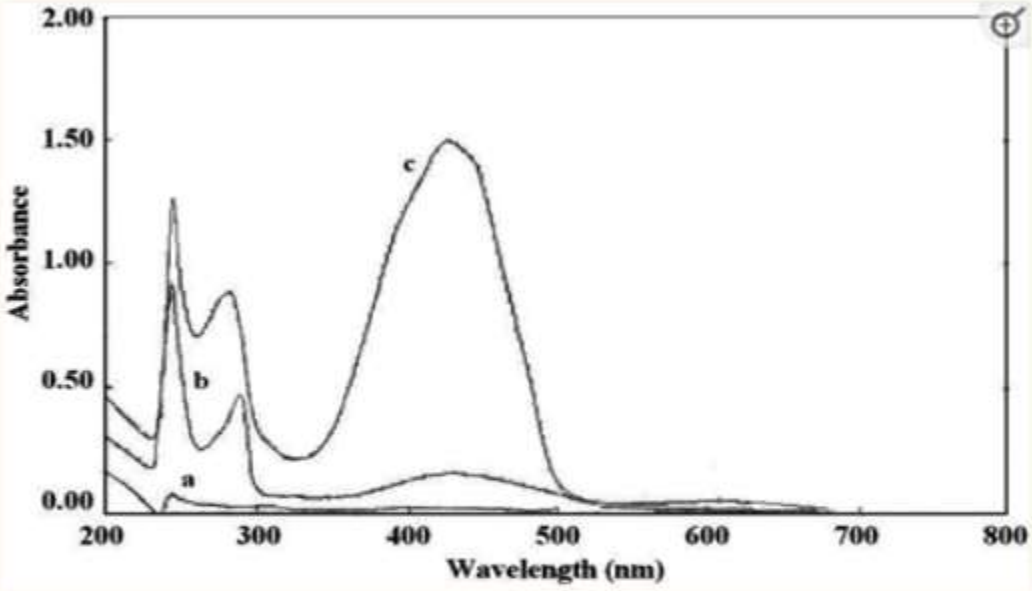

Figure 4

Absorption spectra of: (a) sunitinib malate, (b) BPB, and (c) the ion-pair complex of sunitinib and BPB

Administration and Dosing

Sunitinib is typically administered by orally in a daily regimen with doses and schedules are changed based on the specific cancer being treated and patient tolerance. Sunitinib (Sutent) drug comes in 12.5mg, 25mg, 37.5mg and 50mg capsules.

- **Advantages**
  1) Targeted therapy
  2) Effectiveness against multiple tumors.
  3) Reduced tumor growth
  4) Oral administration

- **Disadvantages**
  1) Breathing problems.

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2) Changes in vision.
3) Dark urine.
4) Feeling faint or lightheaded, falls.
5) Fever or chills, cough, sore throat.
6) High blood pressure.

- **Common side effect**
  1) Fatigue
  2) Nausea
  3) Skin rash
  4) Diarrhoea
  5) Loss of appetite
  6) Increase blood pressure

- **Serious side effect**
  1) Heart problems
  2) Liver problems
  3) Thyroid issues
  4) Hypertension

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