

*Clinical Trial Summary*

Phase II Trial of Buserelin in Hepatocellular Carcinoma

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ANDROGEN RECEPTORS are present in hepatocellular carcinoma (HCC) where they are also functional [1]. Clinical benefit has been reported in patients with HCC treated with cyproterone acetate [2]. The present trial was undertaken to investigate the effects of androgen deprivation using the gonadotropin-releasing hormone antagonist buserelin in patients with advanced, measurable, histologically confirmed advanced HCC.

The patient data are shown in Table 1. Fourteen male patients with a median age of 57 years were entered on study. Eastern Cooperative Oncology Group (ECOG) performance status was 0-1 in four patients, 2 in nine patients and 4 in one patient. The median age was 57 years. Five hundred micrograms of buserelin was given subcutaneously 8 hourly for the first 21 days followed by 400 µg intranasally three times per day.

All patients were evaluable for response and toxicity. One patient showed no change in disease status for 7 weeks, the other 13 patients had progressive disease (95% confidence limit 0-23%). No patient had a decrease in serum alpha-fetoprotein levels. The median time on study was 4 weeks. Twelve of the patients have died. The median survival time is 14 weeks (range 2-92). One patient has survived longer than 90 weeks. The patient with a PS of 4, due to spinal metastases, lived 13 weeks.

Toxicity was mild, loss of libido in two patients and hot flushes in two patients. A significant reduction in the serum testosterone, luteinizing hor-

mone (LH) and follicle stimulating hormone (FSH) occurred in all patients. The testosterone levels fell to less than 2.5 µmol/l in all patients within 3 weeks (median value 1.7 µmol/l). On treatment the median LH fell to 16.7 IU/l and FSH to 4.5 IU/l. *Post mortem* examination was carried out on eight of

Table 1. Characteristics of patients with HCC treated with buserelin

	No. of patients
Patients on study	14
No. of patients evaluated	14
Median age (range 38-78 years)	57
Sex—male	14
Race	
Black	12
White	2
Extent of disease	
Confined to liver	9
Lung metastases	3
Bone metastases	2
ECOG performance status	
0-1	4
2	9
3	0
4	1
Disease symptoms	
Abdominal pain	11
Loss of appetite	10
Jaundice	5
Bone pain	1
Median pretreatment testosterone (µmol/l)	10.4
FSH (IU)	13.7
LH (IU)	30.5
Previous treatment	
None	12
Menogaryl	2

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the patients. All had extensive disease with livers weighing between 4 and 6 kg.

No objective response was seen in this study and the median survival time is similar to that described in previous studies where patient discriminants have been shown to be of greater prognostic significance than treatment [3]. A possible reason for lack of

response could be the relatively low androgen levels in many of the patients at the start of treatment. Although the testosterone levels were significantly reduced no clinical benefit was derived and further trials of buserelin in HCC do not appear warranted.

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#### REFERENCES

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