

Tuesday, April 23, 2002

Dear Sirs,

#### Clinical Appraisal of BEC5

You have requested us to detail our clinical experience with BEC5 in the treatment of malignant lesions of the skin. We understand that this may be shown to potential purchasers of or its interest in the BEC5 project.

#### Background

The Dermatology Department at the Royal London Hospital has acted as an approved and designated center in two clinical trials to determine the safety and efficacy of BEC5 cream in the treatment of cancerous lesions of the skin. In the first of these, a pivotal double blind randomized study, Royal London recruited, treated and monitored 21 of the 94 patients. In the second trial, comprising 41 patients, Royal London was the sole designated centre. This trial was an open study, conducted primarily to assess the safety of the product. Herewith we summarize our observations on the use, safety, efficacy, cosmetic result and resource effectiveness of the product.

#### Use

The trials were formally restricted to patients diagnosed by physician as having superficial basal cell carcinoma. Hence patients with morpheic lesions were excluded. However, subsequently conducted punch biopsy results demonstrated that several trial patients did in fact have invasive basal cell carcinoma. Even so, our findings in respect of these patients were that successful treatment of the invasive form of basal cell carcinoma paralleled the general success rate of BEC5, i.e. around 78%.

In our view these results, in the least, justify a more extensive clinical trial of BEC5 against such cancers. We note in this respect that treatment of the morpheic form of the affliction is presently confined to surgical removal. We are not aware of any emerging therapy, for example, photodynamic therapy that has the potential to extend to treatment of other than superficial skin cancers.

#### Safety

Our clinical experience has shown that BEC5 is safe. In the two trials frequent (twice daily) and prolonged (8 weeks) application of a cream incorporating BEC5 under occlusive dressing resulted only in local skin irritation and erythema. Very few patients under our supervision withdrew from treatment on this account. Hence we consider treatment with BEC5 to be a safe therapy.

Furthermore, patient blood and urine was analyzed using very sensitive methods to determine the presence of the BEC5 during and after a standard treatment regime (twice daily for 8 weeks). Such analysis produced no evidence of the active pharmaceutical ingredients to BEC5 or their breakdown products. Hence it was

### Efficacy

Royal London has a large dedicated skin cancer clinic as it is a Skin Cancer Center for the North East Thames Network. This fact, coupled with the results of the first trial, was instrumental in Royal London's conduct of the second open study. Success rates in this open trial paralleled the multi-center efficacy rate of 78%. Success was defined as zero presence of basal cell carcinoma after histological examination of samples extracted from the lesion site by punch biopsy.

We consider that this rate of treatment success more than justifies the physician considering BEC5 as an alternative to currently predominant treatments such as surgical excision or cryotherapy.

### Cosmetic Evaluation

BEC5 results in ulceration of the lesion site during treatment. However, we have observed that post treatment the wound is quickly replenished with normal tissue and that residual scarring is minimal. Whether such scarring proves more or less extensive than that consequent upon surgical excision is dependent upon a number of factors including lesion size, location and so on. However, it can be said that the cosmetic results offered by treatment with BEC5 are comparable to that resulting from surgical excision.

### Resource Effectiveness

Basal cell carcinoma is a slow growing, locally invasive malignant skin tumor which mainly affects Caucasians. Dermatologists, plastic surgeons and radiotherapists jointly manage the affliction. Such management usually involves surgery. The risks of surgical intervention are well known.

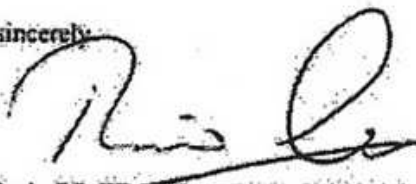
Moreover, excision of basal cell carcinoma from the facial area often involves reconstructive surgery, which can be both time consuming and costly. Hence an alternative, safe and efficacious method of treatment of basal cell carcinoma that does not require physician or hospital attendance must be encouraged.

In our view and experience BEC5 is a topical preparation, which is safe and effective, ideal therapy for outpatient treatment. Hence BEC5 is a much needed alternative to surgery for basal cell carcinoma. This is the commonest cancer in Caucasians worldwide and the prevalence continues to increase with an increasing ageing population.

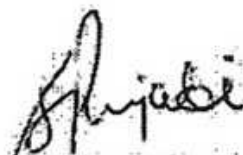
It is a cost effective treatment for both primary and secondary skin cancer care.

We trust that the forgoing is adequate for your purposes.

Yours sincerely



Rino Cerio BScFRCP(Lond) FRCP(Edin)  
FRCPath Consultant Dermatologist and  
Senior Lecturer in Dermatopathology



Dr Sangeta Punjabi MBBS, DVD DipNB  
(Dermatology) Research Registrar, Royal  
London Hospital

**Above is a scanned copy of the clinical trial report.**

**Below is a transcript of the clinical trial report.**

**CLINICAL APPRAISAL ON RESULTS FROM PHASE III Clinical Trials and OPEN STUDIES FROM ROYAL LONDON HOSPITAL**

**Dr Sangeeta Punjabi**

*MBBS DVD DipNB (Dermatology)*

*Research Registrar, Royal London Hospital*

**Rino Cerio**

*BScFgRCP (Lond) FRCP (Edin)*

*Consultant Dermatologist and Senior Lecturer in Dermatopathology*

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Furthermore, patient blood and urine was analyzed using very sensitive methods to determine the presence of the BEC5 during and after a standard treatment regime (twice daily for 8 weeks). Such analysis product no evidence of the active pharmaceutical ingredients to BEC5 or their breakdown products. Hence, it was concluded that there is no systemic absorption of BEC5. This is extremely important from the clinical perspective and may be contrasted with other topical preparations. For example, 5 fluouracil shows systemic absorption and can prove to toxic when used with large lesions.

### **Efficacy**

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Moreover, excision of basal cell carcinoma from the facial area often involves reconstructive, of which can be both time consuming and costly. Hence an alternative, safe and efficacious method of treatment of basal cell carcinoma that does not require physician or hospital attendance must be encouraged.

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