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A first-in-man phase I study of Photochemical Internalisation (PCI) of bleomycin with TPCS_{2a} in patients with solid malignancies – a dose escalation study showing promising signs of efficacy

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Purpose: This article reports on a first-in-man study of TPCS_{2a}-mediated photochemical internalisation (PCI), a new technique for enhancing and directing the effect of anti-cancer drugs by illumination. PCI was performed with bleomycin for treatment of cutaneous or subcutaneous tumours. The primary objective was to assess the safety and tolerability of TPCS_{2a} and determine the maximum tolerated dose (MTD) in PCI with bleomycin. Secondary objectives were to: (i) evaluate toxicity profile; (ii) determine TPCS_{2a} pharmacokinetics; (iii) document anti-tumour activity.

Experimental Design: The study was an open-label single centre, non-randomised Phase I dose-escalation study. Patients were administered TPCS_{2a} on day 0, followed by a fixed dose of 15,000 IU/m² bleomycin on day 4. Three hours later, the surface of the target tumour was illuminated with red laser light (fixed at 60J/cm²). The TPCS_{2a} starting dose was 0.25 mg/kg and was escalated in successive dose groups of 3 patients within a modified accelerated trial design.

Results: 22 patients were included, of which 16 had head and neck cancer. The MTD of TPCS_{2a} was determined to be 1.0 mg/kg. Dose limiting toxicities observed included skin photosensitivity (n=1) and wound infection (n=1) at 1.5 mg/kg dose level. Other common adverse events were nausea, pain and tongue oedema. Anti-tumour effects were observed through the dose range of 0.25 – 1.5 mg/kg with no obvious dose dependency; overall response rates of >80% at 28 days and >60% at the confirmation visit (at least 28 days later) were reported.

Conclusion: PCI treatment can be safely delivered to patients and a recommended phase 2 dose was established. Significant anti-tumour effects were seen at all doses tested, warranting further clinical studies with the PCI technology.

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Dental treatment of “untreatable” patients: Courage or science?

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The oral examination accompanied by X-rays and CT helps designing a treatment plan, periodontal, prosthetic and esthetic. Achieving these goals requires surgical interventions, implants, bone grafts etc. In order to perform this kind of treatments the patients are exposed to stressful situations, require the massive use of anesthetics, microbial complications, exaggerated bleeding, long periods of tissue repair and healing and eventual pains. The dentist “courage” is a necessary element for these treatments but it has to be based on a solid scientific background. Cardiac patients become treatable when using sedation protocols. Hypertensive patients become treatable with local anesthetics containing adrenalin if monitored. Anticoagulated patients will not bleed if blood tests are performed previously and antifibrinolytic medications are employed. Multiple medications used for complex patients present an enormous challenge to our profession. The present conference intends to describe the modern approach to these problems with the idea of including this continuously growing group of patients in the dental clinics for the benefit of all.

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