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Title: Photodynamic therapy using methylene blue in lung cancer animal models

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Body: Introduction: Photodynamic therapy (PDT) is used to treat early proximal bronchial cancer during a flexible bronchoscopy. The technique relies on the excitation of a photosensitizer by an appropriate wavelength, which is delivered into the bronchus in close contact with the tumor. Objective: To assess methylene blue (MB) as a PDT agent for the treatment of lung cancer in preclinical models. Methods: MB induced PDT was performed on cancerous lesions obtained both in the cheek pouch model, and on NCI-H460 tumoral xenografts in nude mice. Bilateral tumors were induced in each animal. PDT was carried out on right-sided tumors after intratumoral injection of methylene blue 1% (w/v) and illumination at 630 nm at 200 J/cm (Diomed PDT 630). The left tumor was used as control (illumination alone or methylene blue alone). The tumoral volume was assessed before and 15 days after PDT. Results: Nine carcinomas were treated in the cheek pouch model. MB-PDT produced a mean volume decrease of 85.8% (from 44.8% to 100%) (initial mean volume = 210 mm³ vs. final mean volume = 97 mm³). Histology analysis showed 4/9 complete responses. 14 xenografts were treated in mice, including 7 treated with MB-PDT, producing a 52% mean tumor volume regression (1568mm³ vs. 544mm³) compared to 7 controls in which tumor volume increased (p=0.007, Mann-Whitney test). Conclusion: Topical methylene blue appears unexpensive and efficient as PDT agent for lung cancer treatment. Further studies are needed to assess the safety and efficacy of MB-associated PDT for the treatment of cancerous bronchial lesions in humans. Financial support: French Ligue nationale against Cancer (Seine maritime and Eure Committees) and ADIR, Rouen France.