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Antiangiogenic therapy for squamous cell carcinoma using combinatorial agents

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Background: Squamous cell carcinoma (SCC) is an invasive neoplasm affecting epithelial tissues including mucocutaneous surfaces. Conventional therapies involve surgery or destructive modalities. Because angiogenesis is a critical event in tumor progression, antiangiogenic therapy may be a molecular strategy for SCC. We developed protocol OLCAT-005 (imiquimod, tretinoin, calcipotriene, diclofenac, hydrocortisone valerate) as a topical treatment for cutaneous SCC. Each drug targets specific antiangiogenic mechanisms, including upregulating interferons, IL-12, RAR-alpha, endothelial survival, COX-2 mediated VEGF production, and basement membrane integrity. **Methods:** OLCAT-005 was used to treat in situ and invasive squamous cell carcinoma (SCC) in 20 patients unable to undergo or refusing conventional treatment modalities. Punch biopsies confirmed the SCC diagnosis. OLCAT-005 was initiated 2x/week (M, F) and increased to at least 3x/week (M, W, F). Dose schedule per lesion was optimized by the Individualized Maximally Tolerated Dose (IMTD) algorithm. Monthly clinical assessment was performed. At 18 weeks, sites were re-biopsied and evaluated for tumor presence, and immunostained for CD31 and SMA. Quality of life (QoL), cosmesis, and SCC recurrence were evaluated at follow-up visits. **Results:** A total of 61 SCC lesions (35 invasive, 26 in situ) received OLCAT-005 from 1998–2004. Complete response with pathological clearance occurred after 12 treatment weeks in 33/35 (94%) of invasive SCC and 23/26 (88%) of SCC in situ. In the SCC in situ partial responders (3/26), all residual tumors cleared with 6 more weeks of treatment. No recurrence was observed in follow-up to 5 years. OLCAT-005 was well tolerated and erythema was the most frequent tissue reaction. In treated lesions, vascular density was inhibited and microvessels appeared normalized. QoL and cosmesis were excellent. **Conclusions:** OLCAT-005 is well tolerated and highly effective in regressing cutaneous SCC in situ and invasive SCC in patients unable to undergo or refusing conventional treatment modalities. An antiangiogenic mechanism is evident. This approach merits evaluation in other forms of SCC.

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