

## HAEMATOLOGICAL CANCER

**Resiquimod—a topical CTCL therapy**

Early stage cutaneous T-cell lymphoma (CTCL) is a form of skin-limited non-Hodgkin lymphoma. No curative therapies exist for this lifelong disease, except stem-cell transplantation, which is reserved for patients with aggressive and progressive disease. However, resiquimod, a Toll-like receptor 7/8 (TLR7/8) agonist, has now shown curative potential in a phase I trial.

“The highest response rates previously reported for topical therapy for early stage CTCL have been in the 50% range,” explains Alain Rook, who led the trial. “Considering that the participants in our study had progressed on up to 11 previous treatments (mean of six), the observation that 11 of 12 (92%) experienced >50% clinical improvement, with two durable complete responses (CRs) lasting beyond 2 years, is unprecedented.” Five of the 12 patients had the difficult-to-control folliculotropic CTCL variant, four of whom had marked improvements in skin involvement, including one CR. “Considering that only four or five lesions

( $\leq 100$  cm<sup>2</sup> of skin) could be treated, these results are exceptional,” Rook opines.

The malignant T-cell clones were found to be eradicated from treated lesions, sometimes completely, and replaced by benign proinflammatory T cells. “Unlike imiquimod, which can only stimulate TLR7-bearing plasmacytoid dendritic cells (DCs), resiquimod stimulates all classes of DCs in skin, and can thus enhance antigen presentation and immune responses,” adds Rachael Clark, who led the immunological experiments. Of note, ~50% of the patients had activation of circulating DCs and natural killer cells, indicating a systemic immune response, and untreated lesions typically regressed. “To our knowledge, this is the first demonstration of regression of untreated skin lesions using a topical medication,” states Clark.

“In view of the unprecedented response rates, along with the ability to possibly eradicate the malignant clone, we are hopeful that a pharmaceutical partner will help develop a larger phase II trial,”



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Rook concludes. The authors note that resiquimod and IFN $\gamma$  synergistically enhance cellular immunity, warranting a combination therapy trial in patients with CTCL, and possibly other tumours.

*David Killock*

**Original article** Rook, A. H. et al. Topical resiquimod can induce disease regression, eradicate malignant T cells and enhance T cell effector functions in cutaneous T cell lymphoma. *Blood* doi:10.1182/blood-2015-02-630335