BCG-BIOTHERAPY FOR MELANOMA PATIENTS RESISTANT TO IL-2-IMMUNOTHERAPY

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GENERAL SURGERY

BACKGROUND: Intratumoural (i.t.) interleukin (IL)-2-immunotherapy is an effective treatment for management of cutaneous metastatic melanoma (CMM). At our centre, the overall response rate is 88%. Recently, we added Bacillus Calmette-Guérin (BCG)-biotherapy to our immunotherapy regimen for partial- and non-responders. Based on our preliminary clinical results, we hypothesise that IL-2 and BCG act synergistically to control CMM in both the human and murine host.

METHODS: *Clinical studies*: Three patients with persistent IL-2-resistant CMM deposits were treated with BCG (3-6 x 10^6 CFU/lesion) on a biweekly cycle. Responses were photodocumented. *Murine modeling studies:* Using the B16F10:C57BL/6 melanoma model, established tumours were treated with multiple doses of BCG and IL-2. Tumour growth was monitored and tumour infiltrating cells were analysed by flow cytometry. To evaluate the effect of BCG on B16F10 cells, cells were co-cultured with BCG and response measured.

RESULTS: *Clinical*: Preliminary clinical results showed that two out of three partial responders to IL-2 experienced a complete response after the addition of BCG. One demonstrated a partial response. *Murine*: Mice bearing B16F10-melanoma hind flank tumours had stable-disease responses and extensive $CD8^+$ T cell infiltration of tumours after short-term dual therapy compared to monotherapy with IL-2 or BCG.

CONCLUSION: IL-2 plus BCG appears to be a promising novel therapeutic option for therapy of CMM. To optimise the efficacy of this treatment strategy, further studies are necessary to better understand how BCG interacts with cancer and non-cancerous cells and influences anti-tumour immune responses.