SITE-SPECIFIC IMMUNOMODULATORS (SSIs): A NOVEL IMMUNOTHERAPY FOR CANCER

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Introduction

The immune system has an intrinsic capacity to recognize and eliminate cells that have undergone malignant transformation, although this activity is mitigated by tumour-induced immune suppression. Induction of acute-type inflammation can reverse tumour-induced immune suppression, leading to immune-mediated tumour regression. To mimic acute infection-type immune responses, Qu Biologics developed Site-Specific Immunomodulators (SSIs), a platform of immunotherapies derived from specific species of killed bacteria known to commonly cause infection in a particular organ or tissue. Repeated subcutaneous injection of SSI induces monocyte/macrophage expansion and recruitment to targeted organs (**Figure 1**) and may provide an effective method for the induction of site-specific acute-type inflammation. In preclinical cancer models, SSIs stimulate the immune system and reverse dysfunction in the tumor microenvironment, enabling effective anti-cancer immune responses (see Kalyan *et al*., Poster 50). Therefore, Qu evaluated the anti-cancer efficacy of SSIs in compassionate use protocols.

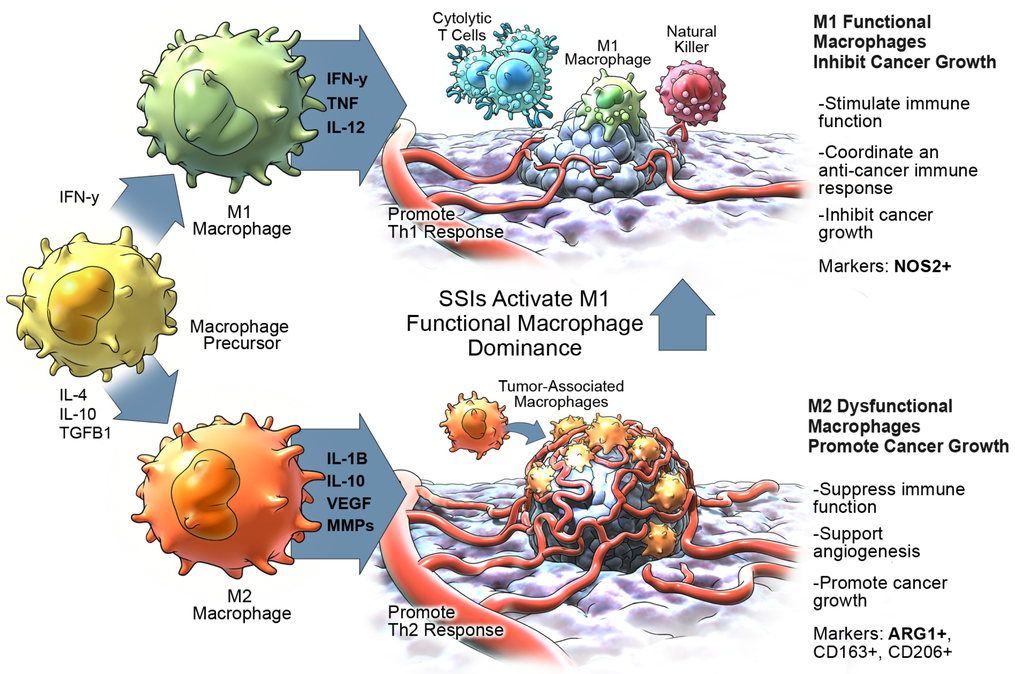

Figure 1. Model of SSI-mediated anti-tumour immune responses. Macrophage dysfunction is a major impediment to effective anti-tumour immunity. SSIs are designed to recruit immune competent macrophages to tumour-infiltrated organs, thereby reversing cancer-induced immune suppression.

Results

Retrospective Analysis of Killed Bacterial Preparations in Patients with Lung Cancer

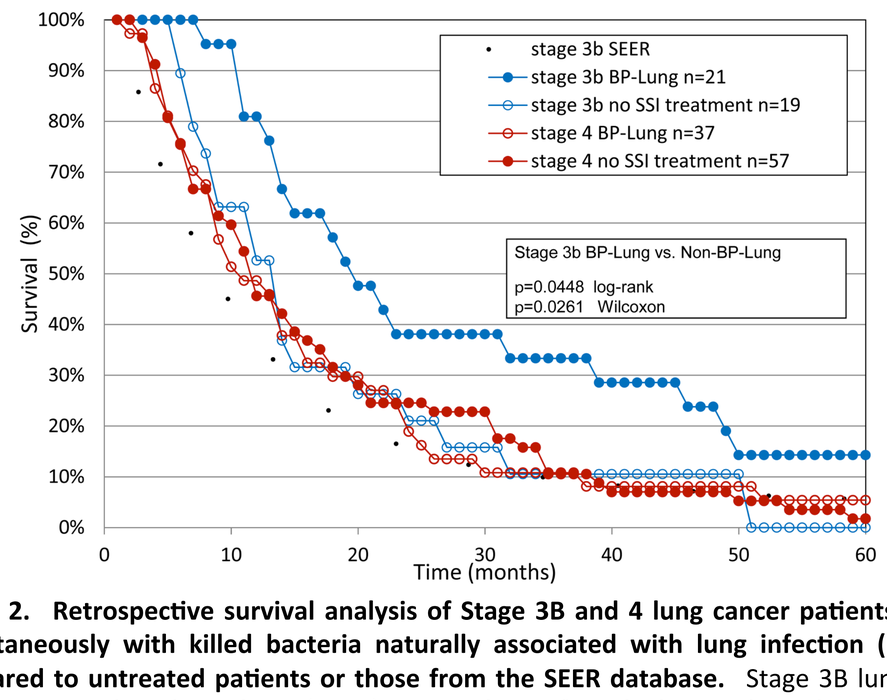

Figure 2. Retrospective survival analysis of Stage 3B and 4 lung cancer patients treated subcutaneously with killed bacteria naturally associated with lung infection (BP-lung), compared to untreated patients or those from the SEER database. Stage 3B lung cancer patients treated with BP-lung (n=21) survived significantly linger than those stage 3B patients not treated (n-19; p = 0.0448 by log rank test). Although this retrospective analysis was not a placebo-controlled trial, these results suggest that treatment may provide a significant survival advantage.

Retrospective Analysis of Metastatic Breast Cancer Patients Treated with SSI Therapy

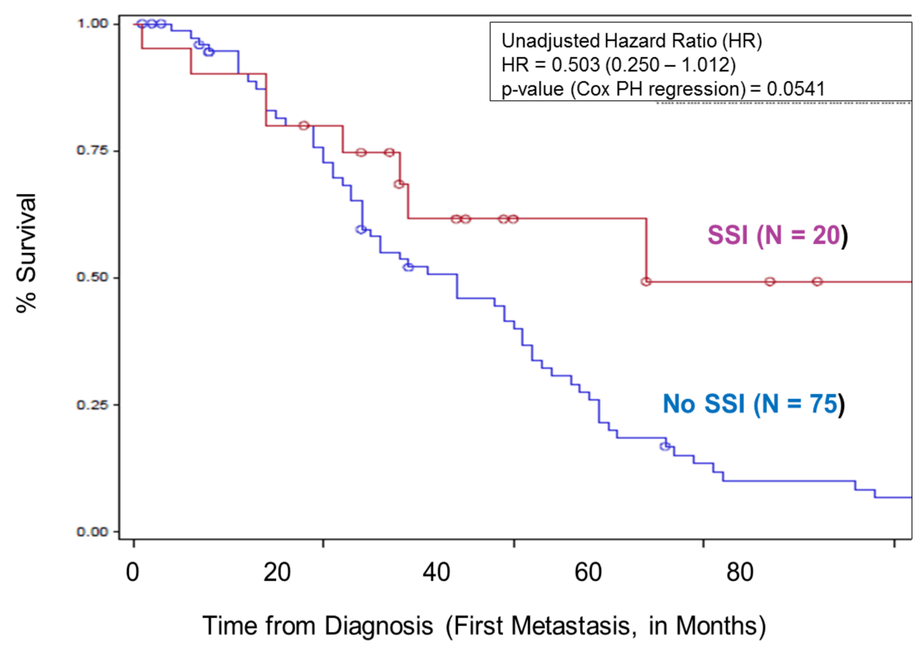

Figure 3. SSI treatment is associated with a significant increase in survival of metastatic breast cancer patients. Independent 3rd-party analysis of the survival of metastatic breast cancer patients treated with SSI therapy (IWI, Austria). Horizontal lines represent the number of patients living; vertical lines represent a patient or patients dying; circles represent patients still alive at the time of analysis (censored). As patients were diagnosed and started SSI therapy at different times, many patients are still alive but have not achieved the longest survival time. Eleven patients (55%) in the SSI treatment group were still alive 82 months after diagnosis, vs. only 8 patients (11%) in the no SSI control group.

Case-matched Retrospective Analysis of Late-Stage Cancer Patients Treated with SSI Therapy

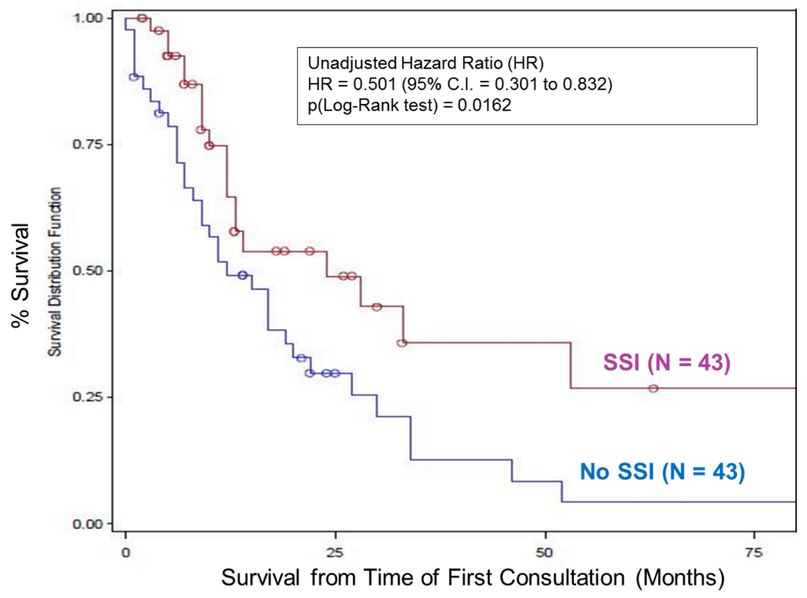

Figure 4. SSI treatment is associated with increased survival in late stage cancer. Independent 3rd-party retrospective case-matched analysis of the survival of late stage cancer patients treated with SSI therapy (IWI, Austria). Horizontal lines represent the number of patients living; vertical lines represent a patient or patients dying; circles represent patients still alive at the time of analysis (censored). As patients were diagnosed and started SSI therapy at different times, many patients are still alive but have not achieved the longest survival time.

Conclusions

- **Patients treated with SSIs had longer median survival than those not treated with SSIs.**
- **While this experience comprises uncontrolled, unblinded observations, the data suggest that SSI may induce productive anti-tumour immunity.**
- **Qu's QBKPN SSI product, designed to induce a lung site-specific response, is currently being studied in a Phase 2a clinical trial in patients with non-small cell lung cancer, in collaboration with the BC Cancer Agency (Trial NCT02256852).**