Scancell Holdings Plc

SCIB1 data update in resected melanoma patients

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Scancell provides positive update on SCIB1 data in resected melanoma patients

Median survival time of 34 and 31 months for Stage III and IV patients

Scancell Holdings plc (‘Scancell’ or the ‘Company’), the developer of novel immunotherapies for the treatment of cancer, is pleased to announce further encouraging results from its on-going Phase 1/2 clinical trial of SCIB1, its DNA ImmunoBody® being developed for the treatment of patients with melanoma. Updated data on patients with resected Stage III or Stage IV melanoma was presented in a poster at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago on Monday 1 June 2015.

The poster entitled: “A clinical trial of SCIB1, a DNA vaccine that targets dendritic cells in vivo, in fully resected melanoma patients: a vaccine to prevent recurrence” by PM Patel et al, demonstrates that the latest clinical data on patients with fully resected tumours is highly promising, and suggests that SCIB1 may uniquely offer protection from recurrence of melanoma with little associated toxicities.

Highlights

- All 16 patients with resected disease (two in Part 1 and 14 in Part 2) are still alive.

- Survival times are very encouraging: median survival time for Stage III patients (n=9) and Stage IV patients (n=7) is 34 and 31 months, respectively.

- Only five patients (31%) have had a recurrence of the disease; all other patients have been disease-free for between 27 and 46 months since study entry* (median follow-up of 34 months).

- The median for disease-free survival and overall survival (when 50% of patients have progressed or died, respectively) have therefore not yet been reached.
· All 16 patients showed melanoma-specific immune responses.

· All patients who continued treatment showed strong T cell memory responses following three monthly boosts with SCIB1.

· SCIB1 was safe and well-tolerated, with no grade 4/5 toxicities observed other than those related to disease progression and one case of pneumonia.

Following the conclusion of the conference the poster will available for download from Scancell's website at: www.scancell.co.uk

Prof Lindy Durrant, Joint CEO of Scancell and Professor of Cancer Immunotherapy at Nottingham University, commented: "We are excited to report this latest clinical data on melanoma patients with fully resected tumours. The on-going positive results from this Phase 1/2 trial gives us confidence that our SCIB1 ImmunoBody® has the potential to become the first non-toxic effective adjuvant treatment for resected melanoma. All 16 participants in this part of the study remain alive, suggesting that SCIB1 may offer protection from tumour recurrence in these patients. Data to date demonstrates that SCIB1 is safe and well-tolerated, and the very encouraging survival times suggest a strategy of using SCIB1 in such resected melanoma patients to extend their lives."

Prof Poulam Patel, Chief Investigator for the trial and Professor of Clinical Oncology at the University of Nottingham, added: "The cancer immunotherapy field is rapidly advancing and although checkpoint inhibitors are continuing to deliver positive results in late stage melanoma, there is an unmet need for non-toxic adjuvant therapy in patients with earlier stage disease. All resected patients in this Phase 1/2 trial with SCIB1 have shown melanoma-specific immune responses and survival times that are extremely promising. These results suggest that SCIB1 could help to prevent recurrence of melanoma and so improve overall outcomes in these patients."

The Phase 1/2 clinical trial is an open label, non-randomised study to determine the safety and tolerability of SCIB1 administered intramuscularly using an electroporation device (TriGrid Delivery System, manufactured by Ichor Medical Systems, USA). While the primary objective of the study is to access safety and tolerability, the study is also assessing immune response and anti-tumour activity, and the ability of SCIB1 to delay or prevent disease recurrence in patients with resected disease.

Poster overview

The poster summarises current data from a subset of patients in the trial with resected tumours. 16 patients with fully resected Stage III (n=9) or Stage IV (n=7) melanoma were immunised with 4mg of SCIB1 by intramuscular electroporation at 3-weekly intervals, then subsequently at three and six months. Patients tolerating treatment were allowed to continue treatment for up to five further years. Immune responses were assayed by proliferation and Elispot assays.

· **SCIB1 was safe and well-tolerated**
  More than 190 doses administered and no CTC grade 4/5 toxicities were reported except those that were disease-related and one case of pneumonia (grade 4). Most common adverse events were injection site reactions (pain, tenderness, bruising, erythema and swelling).

· **Highly encouraging clinical responses**
  Impressive clinical responses continue to be seen in these patients. Only five out of 16 patients (31%) have had a recurrence of disease at one, four, 14, 17 and 18 months, and none have died. All other patients have been disease-free for between 27 and 46 months since study entry. Median survival time for Stage III patients (n=9) and Stage IV patients (n=7) is 34 and 31 months, respectively.

· **Immune responses generated in all patients**
  Significant immune responses have also been produced by these patients. All 16 patients showed a SCIB1-epitope specific proliferation response...
vivo and γIFN Elispot responses \textit{in vitro} after T cell expansion. 12 patients responded to all four epitopes, two patients to three epitopes, one patient to two epitopes and one patient to one epitope. All patients who continued treatment showed strong T cell memory responses following three monthly boosts with SCIB1.

*This compares very favourably with reported data from a peptide vaccine trial in which 48% of Stage III/IV patients had disease progression and 21% had died after three years (Slingluff \textit{et al.}, 2011 J Clin Oncol 29:2924-2932). In addition, a study of untreated Stage IV patients showed that 84% had disease progression and 64% had died after three years (Sosman \textit{et al}, 2011 Cancer 117(20), 4740-4746).

\textbf{For Further Information:}

Dr Richard Goodfellow, Joint CEO  
Professor Lindy Durrant, Joint CEO  
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\textbf{SCIB1 mechanism of action}

SCIB1 is a DNA ImmunoBody® immunotherapy encoding a human IgG1 antibody, with three epitopes from gp100 and one from TRP-2 engineered into its CDR regions. This immuno-stimulatory antibody targets dendritic cells \textit{in vivo} via the high affinity Fc receptor, CD64, and stimulates high avidity T cells. Extensive research studies suggest SCIB1 ImmunoBody® has a dual mechanism of action that combines cross-presentation with direct-presentation. This results in amplification of the immune response to induce high frequency, high avidity T cells which translates into a potent anti-tumour response.

\textbf{Overview of the Phase 1/2 trial design}

Part 1 of this single arm, open label, Phase 1/2 clinical trial, conducted in five UK centres, was a dose-escalation designed to determine the dose for Part 2. Eleven patients, ten with Stage IV and one with Stage III malignant melanoma were given up to five doses of 0.4mg, 2mg or 4mg of SCIB1, delivered by Ichor Medical Systems' TriGrid™ electroporation delivery device, over a period of six months. One patient in the 0.4mg dose group and one in the 4mg dose group who received only a single dose of SCIB1 were withdrawn from the study due to progressive disease shortly after study entry and were replaced to ensure that at least three patients in each dose cohort could be fully evaluated for immune response. During the course of the study, regulatory approval was granted to increase the SCIB1 dose from 2mg to 4mg in patients in the 2mg cohort, if the treatment was well tolerated. Two patients in this group received two 4mg doses of SCIB1 and one patient received a single 4mg dose. Regulatory approval was subsequently obtained for treating a cohort of patients with 8mg of drug in Part 1; five patients were enrolled. One patient received three 8 mg doses and one patient received four 8 mg doses of SCIB1. One patient received two doses of 4mg followed by three doses of 8mg and the other two patients both received five 8 mg doses of SCIB1.

In Part 2 of the study, 14 patients with resected Stage III/IV melanoma (nine with Stage III and five with Stage IV) entered the study. One patient was only able to tolerate three doses of 2mg and withdrew from the study. Of the remaining patients, 12 received a full 4mg dose of SCIB1 on five occasions over a period of 6 months and one received four doses of 4mg and one dose of 2mg. In the absence of any serious toxicity in the Part 1 8mg cohort, approval was also obtained to further expand Part 2 to dose up to 13 additional patients with 8mg. Recruitment and dosing of these patients is currently on-going.
During the course of the study, regulatory approval was also granted to continue treating eligible patients for a period of up to five years after they completed the main part of the study. During this period patients can receive further doses of SCIB1 every three to six months. Six patients in Part 2 (five receiving 4mg and one receiving 8mg doses) are currently receiving extended SCIB1 treatment.

About Scancell
Scancell is developing novel immunotherapies for the treatment of cancer based on its ImmunoBody® and Moditope® technology platforms.

Scancell's first ImmunoBody®, SCIB1 is being developed for the treatment of melanoma and is being evaluated in a Phase 1/2 clinical trial. Data from the trial demonstrate that SCIB1, when used as monotherapy, has a marked effect on tumour load, produces a melanoma-specific immune response and highly encouraging survival trend without serious side effects. In patients with resected disease there is increasing evidence to suggest that SCIB1 may delay or prevent disease recurrence.

Scancell's ImmunoBody® vaccines target dendritic cells and stimulate both parts of the cellular immune system: the helper cell system where inflammation is stimulated at the tumour site and the cytotoxic T-lymphocyte or CTL response where immune system cells are primed to recognise and kill specific cells.

Pre-clinical data on a combination of SCIB1 or SCIB2 and checkpoint inhibition (blockade of the PD-1 or CTLA-4 immune checkpoint pathways) have shown enhanced tumour destruction and significantly longer survival times than when either treatment was used alone.

Scancell has also identified and patented a series of modified epitopes that stimulate the production of killer CD4+ T cells that destroy tumours without toxicity. The Directors believe that the Moditope® platform could play a major role in the development of safe and effective cancer immunotherapies in the future.

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