A DNA plasmid melanoma cancer vaccine, SCIB1, combined with nivolumab + ipilimumab in patients with advanced unresectable melanoma

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Background

- Targeting of melanoma by T cells drives anti-tumour responses
- SCIB1 (a DNA vaccine) incorporating T cell epitopes from TRP-2 and gp100 into an antibody framework allows Fc targeting of activated dendritic cells (see Figure 1)
- SCIB1 has a dual mechanism of action. Injection of SCIB1 results in:
  - the uptake of the plasmid and expression of the engineered antibody by antigen-presenting cells. The antigen is processed, and epitopes presented on either MHC class or II molecules, which react with the T cell receptor of CD8 or CD4 cells (see Figure 2). This is known as direct presentation,
  - and secretion of an engineered human IgG1 antibody molecule containing the CD8 and CD4 epitopes. This fusion protein targets the CD64 FcγR present on dendritic cells via the heavy chain Fc region, resulting in uptake and cross-presentation of the epitopes to CD8 and CD4 T cells.
- A previous clinical trial of SCIB1 monotherapy in patients with unresectable and resectable melanoma demonstrated a 60% DCR and an 88% five-year survival respectively[1].

Figure 1.Engineered antibody structure

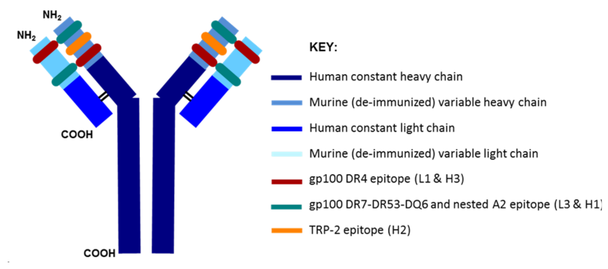
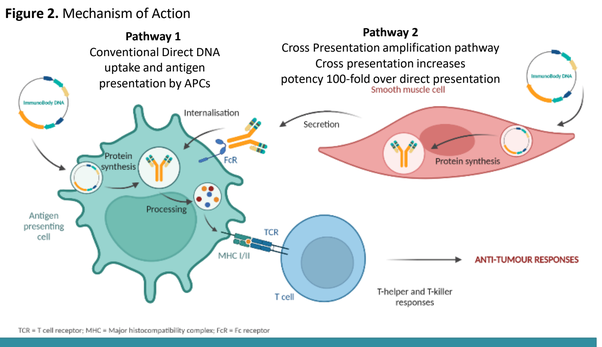


Figure 2. Mechanism of Action



Study Design

- A Phase 2, Multicentre, Open-Label, Umbrella Study of SCIB1 (Cohorts 1 and 2) and iSCIB1+ (Cohort 3) in Patients with Advanced Unresectable Melanoma Receiving Either Nivolumab with Ipilimumab or SCIB1 with Pembrolizumab (The SCOPE Study, See Figure 3). The patient demographics and baseline disease characteristics are shown in Figure 4.
- Eligible patients with stage IIIB/IV unresectable melanoma in whom standard of care checkpoint inhibitor therapy was planned, were recruited and vaccinated with 8 mg SCIB1 or iSCIB1+ using a needle-free injections system (Pharmajet). For Cohort 1 and 2 patients must be HLA-A2 positive and positive for at least one HLA-DR4, HLA-DR7, HLA-DR53 or HLA-DQ6. Cohort 3 has no HLA restriction requirements and patients are enrolled if all eligibility criteria has been met.
- RECIST 1.1 overall response rate is the primary endpoint, and the study is designed with a Simon's two stage methodology with an early stooping rule for futility.
- Historical observations of 50% response rate when the doublet checkpoints are administered in the real-world setting.

Study Schema and Dermographics

Figure 3. Study Schema

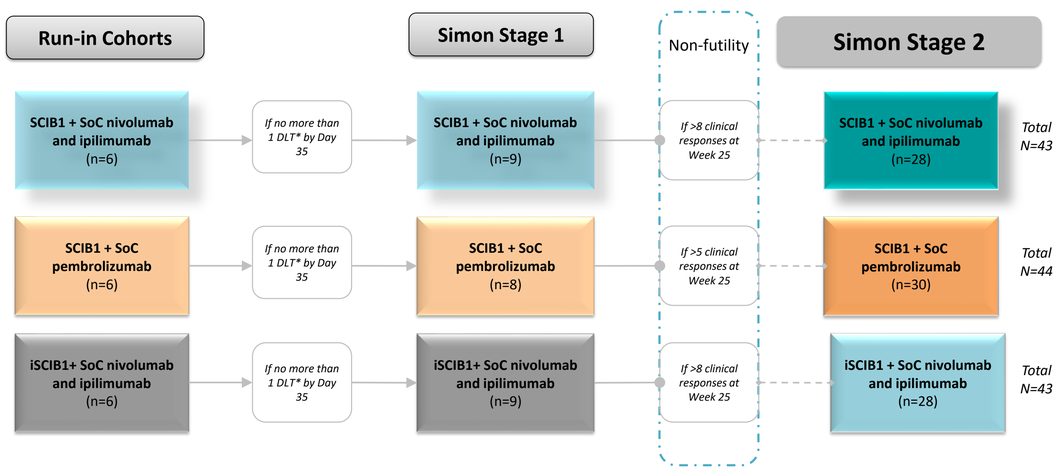


Figure 4. Demographics and Baseline Disease Characteristics

Evaluable Patients Only		
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	Number of patients (n)	
	Cohort 1:SCIB1+ipi-nivo (n=13)	**Cohort 2: SCIB1+pembro (n=3)**
Gender		
Male	10	1
Female	3	2
Age		
<65	9	0
≥65- <75	2	0
≥75	2	3
Stage of disease at study entry		
IV	13	3
M1a	5	1
M1b	2	1
M1c	6	1
Braf		
Mutation	5	2
Wildtype	8	1
Lactate Dehydrogenase		
>Upper limit of normal	6	1
≤ULN	7	2
Total Tumour Burden		
≥20 mm – ≤40mm	4	2
≥41 mm -≤80mm	3	0
≥81mm-≤150mm	5	0
150mm+	1	1
Prior treatment in the adjuvant setting		
Yes	4	1
Pembrolizumab	2	1
Nivolumab	1	0
No	8	2

Objective Response Rate Waterfall Plot

Figure 5. SCOPE Study Waterfall Plot: Best Tumour Response (Target lesions)

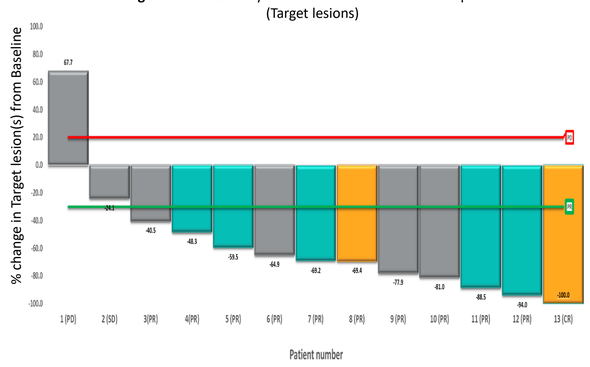
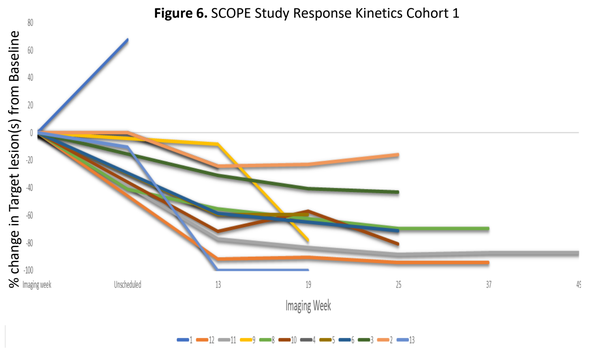
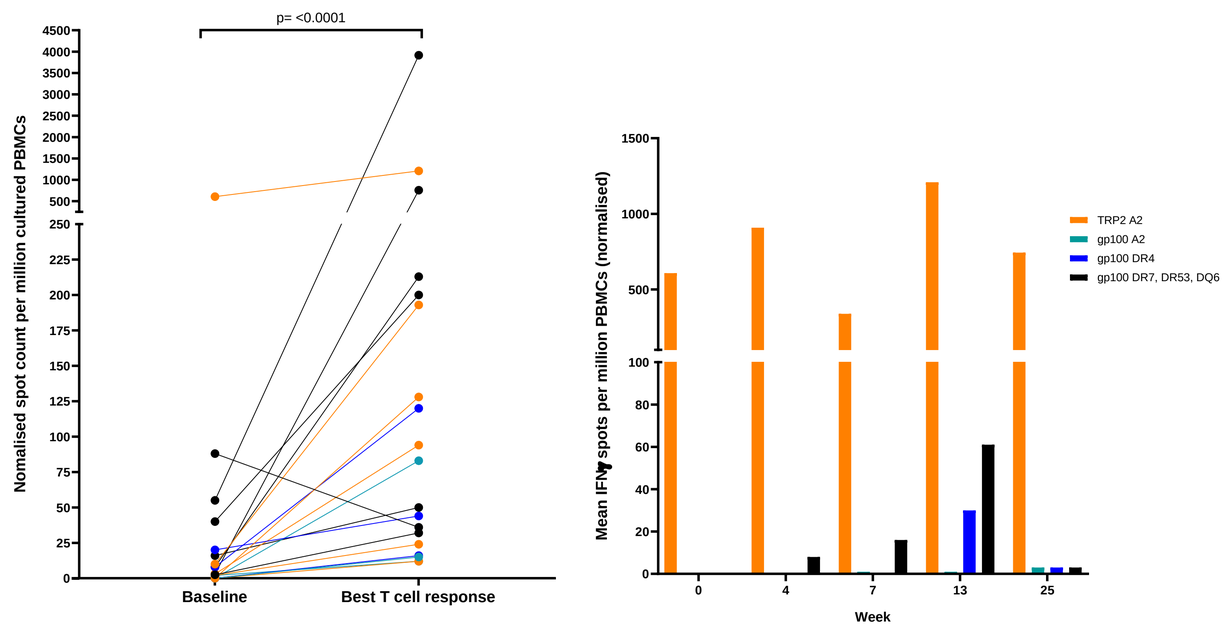


Figure 6. SCOPE Study Response Kinetics Cohort 1



T Cell Responses

Figure 7. SCOPE Study T cell responses



- SCIB1 received at weeks 0, 4, 7, 13, 25 then every 12 weeks, unless patient receives steroids for the treatment of CPI related toxicity.
- 9/13 (64%) patients have detectable T cell responses by IFNγ ELISpot assay.
- Blood samples taken 3 weeks post immunisation, recent results from ModiFY trial increased T cell response rate from 55% to 83% by taking blood earlier at 1 week post immunisation.

Results

As of November 2023:

- 19 pts received the combination of SCIB1 with ipilimumab with nivolumab (Cohort 1), were vaccinated with 8 mg SCIB1 i.m. using a needle free injections system (Pharmajet).
- 13 patients in Cohort 1, had reached at least the first imaging timepoint at 13 weeks post- vaccination.
- Patients were vaccinated with SCIB1 8 mg i.m. at weeks 0, 7, 13, 19, 25 and q12 weeks until 2 years.
- 11/13 patients had a RECIST 1.1 objective response an 85% ORR, see Figure 4.
- 10 confirmed partial responses at 19+ weeks with 1 confirmed complete response.
- All patients imaged beyond week 13 showed a sustained shrinkage of their target lesions, see Figure 5.
- T cell responses detected in 64% patients, work ongoing to test isolated specific TCRs and improving response rate by taking blood samples 1 week post vaccination.

Discussion

When SCIB1 was included to the standard of care regimen of ipilimumab with nivolumab, the overall size of metastatic melanoma lesions had reduced significantly in 11/13 patients, yielding a RECIST 1.1 overall response rate of 85%.

SCIB1 is well tolerated when given in combination with ipilimumab and nivolumab, and the ORR efficacy data of 85% so far in Cohort 1 is highly encouraging. This level of effectiveness in the combination setting has trailblazing potential for the ImmunoBody® platform in further improving the survival rates in patients with unresectable melanoma. This study is ongoing, and a phase 2/3 registration study is currently under planning.

References

1. Patel PM, Ottensmeier CH, Mulatero C, et al. Targeting gp100 and TRP-2 with a DNA vaccine: Incorporating T cell epitopes with a human IgG1 antibody induces potent T cell responses that are associated with favourable clinical outcome in a phase I/II trial. Oncoimmunology. 2018;7(6):e1433516.