DNA plasmid melanoma cancer vaccine, SCIB1, combined with nivolumab + ipilimumab in patients with advanced unresectable melanoma: Interim efficacy and safety results from the open-label Phase 2 SCOPE trial

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Background

- Targeting of melanoma by T cells drives anti-tumor 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 requires that patients are HLA-A2, HLA-DR4, HLA-DR7, HLA-DR53 or HLA-DQ6 positive; however, iSCIB1+ has been introduced which does not require a specific haplotype SCIB1 has a dual mechanism of action. Injection of SCIB1/iSCIB1+ 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 objective response and a favorable recurrence free survival rate respectively [1]

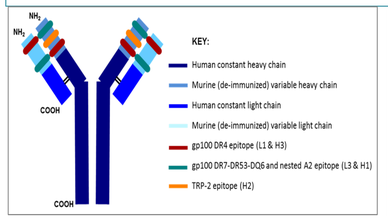

Figure 1. Engineered antibody structure

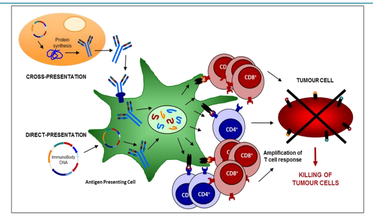

Figure 2. Mechanism of Action

Study Design

- This is a Phase 2a multicenter, multicohort, open-label study of the SCIB1 vaccine with ipilimumab plus nivolumab (cohort 1), pembrolizumab (cohort 2) or iSCIB1+ with ipilimumab plus nivolumab (cohort 3) . See figure 3.
- Eligible patients with stage IIIB/IV unresectable melanoma in whom standard of care ipilimumab plus nivolumab (cohort 1 or 3) or pembrolizumab monotherapy (cohort 2) were recruited and vaccinated with 8mg SCIB1 using a needle-free injections system (Pharmajet) at weeks 0, 7, 13,19,25 and q12 weeks until 2 years.
- RECIST 1.1 overall response rate is the primary endpoint and is designed with a Simon's two stage methodology with an early stooping rule for futility.
- Cohort 1 and 3 have been powered at 80% to detect a 20% improvement over the historical observations of 50% when the doublet checkpoints are administered in the real-world setting.
- Cohort 2 has also been powered to detect a 20% improvement over the historical observation of 35% when pembrolizumab monotherapy is administered as the standard of care in this setting.
- Cohort 1 and 3 require 9/15 responders for non-futility and an overall 27/43 patients to respond.
- Presented here are the Stage 1 results of Cohort 1 (SCIB1 plus ipilimumab and nivolumab)

Study Schema

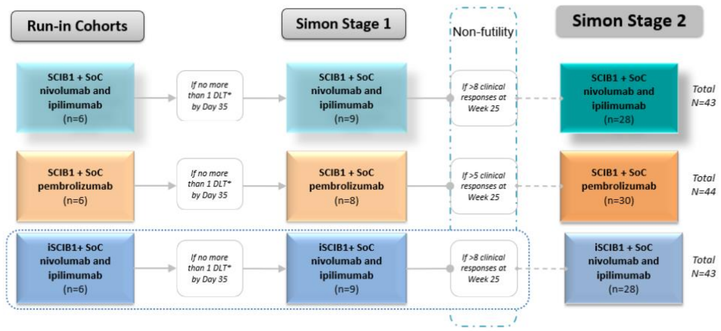

Figure 3. Schema of SCOPE study Design

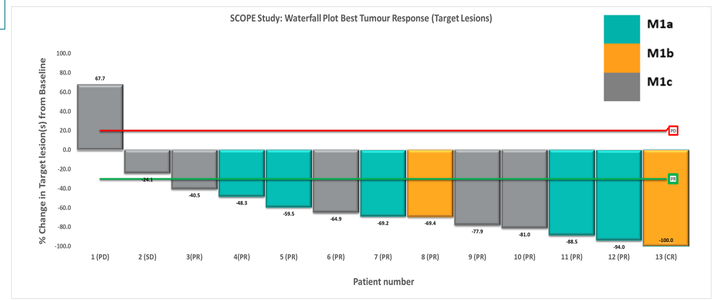

Figure 4. Waterfall Plot of Simon Stage 1, Best Response in Cohort 1 (SCIB1 + ipi-nivo)

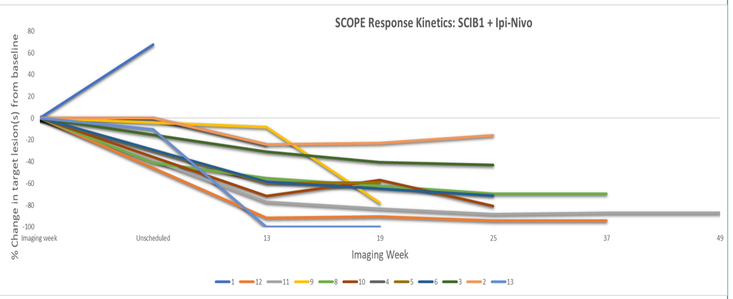

Figure 5 Spider Plot of Simon Stage 1 showing kinetics of responses in cohort 1 (SCIB1 + ipi-nivo)

Demographics

Evaluable Patients Only	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
Dabrafenib and Trametinib	1	0
No	9	2

Table 1 Demographics and Baseline Disease Characteristics

Results

As of April 2024:

- 27 pts in whom the combinations of ipilimumab with nivolumab was planned (cohort 1), were vaccinated with 8mg SCIB1 i.m. using a needle free injections system (Pharmajet).
- 13 patients in cohort 1, had reached at least the second imaging timepoint at 19 weeks post-vaccination.
- 11/13 patients had a RECIST 1.1 objective response an **85% ORR,** see figure 4.
- All patients imaged beyond week 13 showed a **sustained shrinkage** of their target lesions, see figure 5.
- SCIB1 was well tolerated when given in combination with ipilimumab and nivolumab; 116 adverse events were reported and only 16 were related to SCIB1. Of these, only one was Grade 3 vitiligo the other events were mild to moderate in severity. There were no SAEs related to SCIB1.
- Other adverse reactions were as expected for the CPIs

Discussion

This poster focusses on Cohort 1 as it had reached an important milestone in the completion of the first stage of Simon in a 2-stage design. 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%. Due to the target of 9 responses being achieved earlier than expected, non-futility was declared, and this cohort advanced to the second stage of Simon. Of the two patients that did not achieve a RECIST 1.1 response, 1 patient had progressive disease within 7 weeks of entering the study and the other patient had a decrease of 24.1% of their target lesions at 13 weeks (a RECIST 1.1 SD). This patient is currently ongoing with their study treatment . In stage 2, an additional 16 responders are required in a maximum of 30 additional patients. Based on the current data, the probability of success is expected to be ~90%. Cohorts 1, 2 and 3 are ongoing.

Table 1 demonstrates the profile of patients that have been entered and the key prognostic factors are shown. All patients had metastatic (stage IV) unresectable melanoma. The predominant site of metastases is the lung (n=6), but patients also entered the study with metastases in the liver, distant nodes or musculoskeletal. Two patients had metastases in both the liver and the lung.

All eleven patients in whom a response was detected, showed a sustained reduction in the sum of target lesions. This durability of response was also seen in seven patients reaching week 25 and three reaching week 37 imaging timepoints. In the three patients that had reached week 37 the shrinkage was between -65 and -94%. Patients will be observed for the total study period of 2 years.

Conclusions

- SCIB1 is well tolerated, and the ORR efficacy data of 85% in the first stage of cohort 1 is highly encouraging.
- This level of effectiveness in the immunotherapy combination setting has excellent 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.

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References

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.

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