SCOPE Phase 2 clinical trial program evaluating off-the-shelf DNA plasmid vaccines, SCIB1 and iSCIB1+ administered in combination with checkpoint inhibitors in advanced unresectable melanoma.

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ABSTRACT

SCIB1 and iSCIB1+ are DNA plasmid off-the shelf melanoma vaccines encoding two clusters of CD8 epitopes, TRP-2 and gp100. When administered by needle-free injection these are taken up by Antigen Presenting Cells which directly present epitopes on MHC class I or II molecules to T cells to amplify the anti-tumour immune response, further boosted by dendritic cell cross presentation. Monotherapy SCIB1 induced dose dependent T cell responses in 88% of advanced melanoma patients with minimal side effects (Patel et al, 2018).
In patients with unresectable melanoma, immunotherapy with anti-PD-1 and anti-CTLA-4 checkpoint inhibitors reports an overall response rate (ORR) of 50%, with substantial adverse events (Lebbe et al, 2019). The addition of SCIB1 / iSCIB1+ could overcome the inadequate tumour recognition that causes immunotherapy to fail.

Trial Design

The SCOPE phase 2 open label single arm clinical program evaluates within defined cohorts the safety and efficacy of SCIB1 and iSCIB1+ in over 140 patients with unresectable melanoma receiving standard of care check point inhibition at 16 UK clinical trial sites. The objective is to determine efficacy as measured by Progression Free Survival, Overall Response Rate as measured by RECIST 1.1 and Disease Control Rate as determined by imaging at weeks 13, 19, 25 and then 12 weekly. T cell responses are assessed with a cultured ELISpot assay and adverse events recorded.
Cohort 1 has immunised 43 patients with the target HLA haplotype, namely, A2 positive and one of DR4, DR7, DR53 or DQ6, receiving ipilimumab and nivolumab with 10 doses of SCIB1 administered intra-muscularly via a needle free injector over a 24-month period. Whilst in Cohort 2, 10 such patients, received pembrolizumab.
iSCIB1+ designed to broaden eligible HLA haplotypes to include MHC-class 1 HLA A2, A3, A31, Bw4, B44 & B35 as well as increase avidity is evaluated in Cohort 3, within two sub-groups without and with the target HLA haplotype.
Intra-dermal administration has enhanced T cell responses in pre-clinical studies. Accelerated dosing with three priming immunisations would prevent disruption of the dosing regimen by checkpoint inhibitor induced adverse events. This is being evaluated in Cohort 4.
Evaluation of these cohorts will determine the optimal product, patient characteristics and dosing regimen for the follow-on randomised clinical trial

STUDY POPULATION

Advanced melanoma in combination with standard of care Check Point Blockade

Inclusion Criteria (Summary)
- Histologically confirmed, unresectable Stage III or Stage IV Melanoma
- Not received prior systemic treatment for advanced disease.
- ECOG Performance Status 0 or 1.
- At least one measurable lesion per RECIST 1.1
- Human leukocyte antigen HLA status known

Exclusion Criteria (Summary)
- Acral, Ocular & Mucosal Melanoma
- CNS Metastases
- Exposure to CPI as adjuvant treatment in previous 6 months

Phase 2 open label parallel multi cohort translational program at 16 UK clinical trial sites enrolling over 140 patients over 3 years.
Objective: select product, target population, dosing & endpoints for phase 3 trial

Cohort 1 (n=43)
SCIB1 and SoC nivolumab & ipilimumab
Target HLA A2

Cohort 2 (n=10)
SCIB1 and SoC pembrolizumab
Target HLA A2

Cohort 3 (n=50)
40 Target HLA, 10 Non-Target
iSCIB1+ and SoC nivolumab & ipilimumab

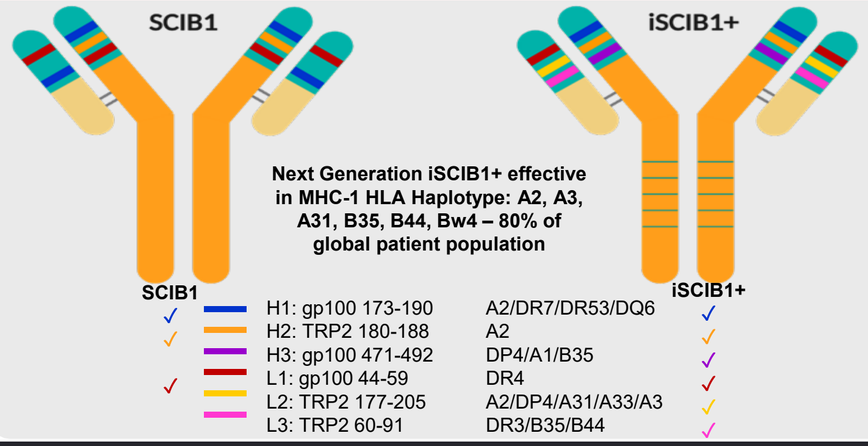
Cohort 4 (n=31)
24 Target HLA, 7 Non-Target
iSCIB1+ accelerated priming and
SoC nivolumab & ipilimumab

Seek to improve outcomes with SOC Checkpoint Blockade (Efficacy, Durability, Safety)

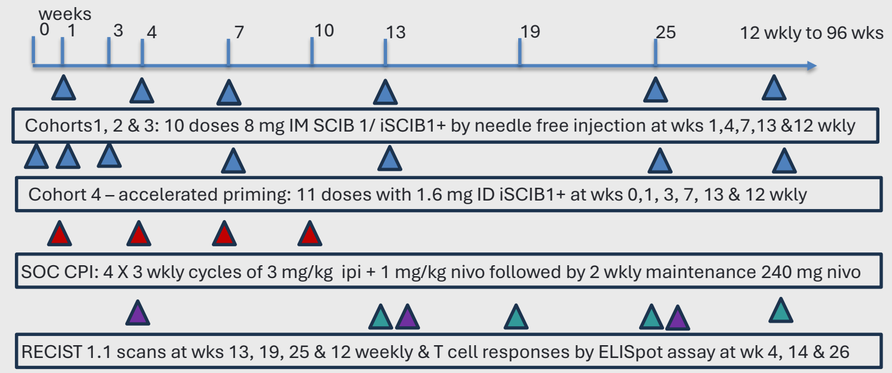
Nivolumab & ipilimumab:
- PFS: 46% at 12 months
- ORR: 50% (checkmate 067), ORR: 48% (RWE)
- Grade 3 Adverse Events in 53% of patients

Pembrolizumab:
ORR: 41% (Keynote-001)
PFS: 35% at 12 months
Grade 3 Adverse Events in 14% of patients

VACCINE DESIGN

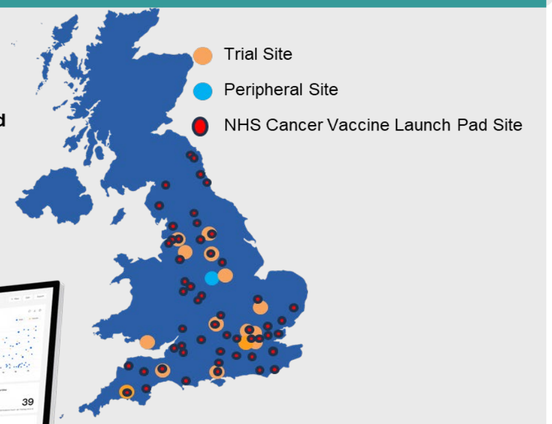


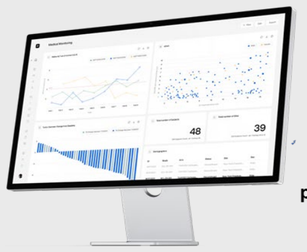
STUDY DESIGN



STUDY PARTNERS

Partnership with NHS Cancer Vaccine Launch Pad to enable NHS patient enrolment across England and Wales





Adoption of Rivia, a unified data and analytics platform to integrate fragmented trial data in real time allowing for actionable insights.

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REFERENCES
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2. Evaluation of Two Dosing Regimens for Nivolumab in Combination With Ipilimumab in Patients With Advanced Melanoma: Results From the Phase IIIb/IV CheckMate 511 Trial. Lebber et al, J Clin Oncol. 2019 Apr 10;37(11):867-875. doi: 10.1200/JCO.18.01998