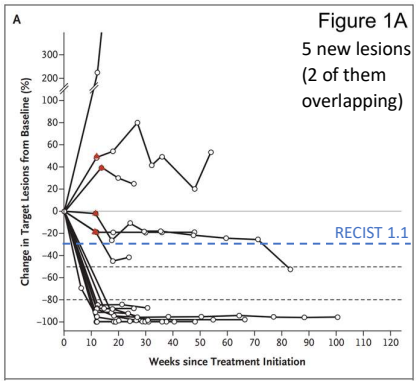
Version 2 – Sci102 scioneotwo@gmail.com

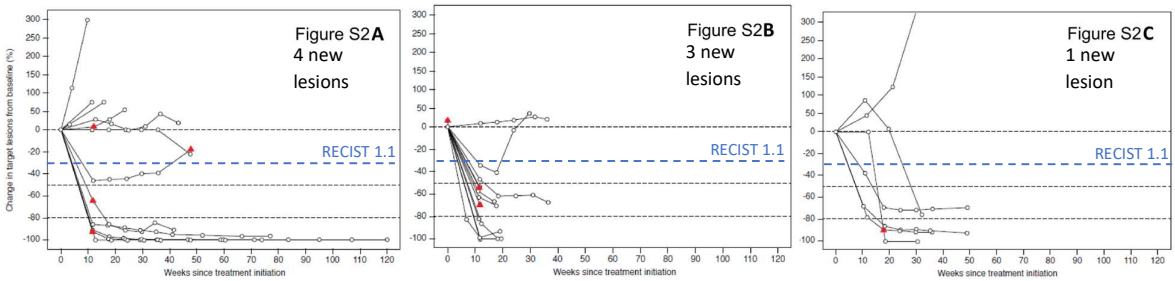
Scancell ltd recently reported updates from their Scope clinical trial with SCIB1 in combination with checkpoint inhibitors and an update on their "next-gen" version, iSCIB1+. This note is intended for people already familiar with Scancell's Immunobody platform and recent company developments.

Note on SCIB1

Original study testing concurrent CPI combinations in patients with uresectable metastatic melanoma have demonstrated ORR of around 50%. However, in that study there was frequent presence (25%) of new lesions, even if the target lesions demonstrated size reduction. This, according to RECIST 1.1 (or the modified WHO criteria that the original study followed), automatically categorises patients as with progressive disease (PD), regardless of the changes in the target lesions.

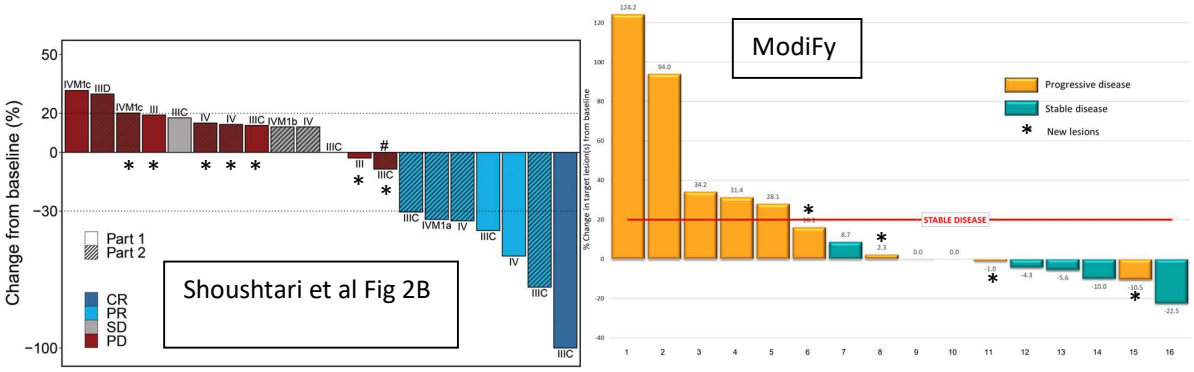
In more detail, in Wolchok et al Figure 1A and Figure S2 A,B and C (concurrent CPI treatments) 13/53 (ca 25%) of patients presented new lesions after start of treatment (red triangles on the graphs). In contrast, according to the recent AGM presentation (slide 11), no new lesions were reported in the responders (patients with new lesions would have been categorised as with PD per RECIST 1.1). According to RECIST 1.1, size reduction of target lesions ≥30% in the absence of new lesions is categorised as partial response (PR), while according to the WHO modified criteria, PR is defined as ≥50% reduction of target lesions in the absence of new lesions. If we restate concurrent CPI treatment data in Wolchok et al to RECIST 1.1 while ignoring new lesions, the ORR observed at 20 weeks ranged from 43% (Figure S2 A , lowest nivolumab dose, not typical in clinical practice) to 67% (Figure S2 B, 3mg/kg nivolumab + 1mg/kg ipilimumab, a combination that has been recommended as optimal; see Lebbe et al). In the originally FDA approved combination (1 mg/kg nivolumab + 3 mg/kg ipilimumab, Figure 1A), ORR at 20 weeks was 59%, when restated to RECIST 1.1 and ignoring new lesions.





Also note that in the latest update on the ModiFY trial (AGM presentation slide 16), 4/16 (25%) of ovarian cancer patients treated with Modi-1 as monotherapy presented new lesions during treatment (indicated with dots on the waterfall plot at AGM slide 16). In addition, in Shoushtari et al in PD-1 resistant melanoma, ORR

w/ CPI + vaccine as expected was lower at ca35% and with numerically increased prevalence of new lesions than in Wolchock et and ModiFY (7/20, 35% vs 25%).



	n	% ORR (PFS/DCR)	New lesions	% ORR ignoring new lesions (PFS/DCR)
1 mg/kg nivo + 3 mg/kg ipi	17	53 (53)	5	59 (64)
0.3 mg/kg nivo + 3 mg/kg ipi	14	28 (50)	4	43 (71)
3 mg/kg nivo + 1 mg/kg ipi	15	53 (60)	3	67(73)
3 mg/kg nivo + 3 mg/kg ipi	6	50 (67)	1	67 (83)
Overall Wolchock et al	**53**	**46 (56)**	**13**	**58 (71)**
Excl. 0.3 mg/kg nivo cohort	**39**	**52.5 (58)**	**9**	**63 (71)**
Overall Shushtari et al	**20**	**35 (55)**	**7**	**35 (70)**
SCOPE	**13**	**85 (92)**	**0**	**85 (92)**

ORR in Wolchok et al and Shoushtari et al vs SCOPE (adapted from Wolchock et al Table 3). For Wolchok et all ORR/PFS was calculated at 20 weeks. All responses were restated to RECIST 1.1. Averages in "overall Wolchock" are weighted according to n. PFS/DCR = CR + PR + SD per RECIST. PFS/DCR: Progression Free Survival/Disease Control Rate.

Overall, it appears that the absence of new lesions in SCOPE data may explain much of the enhanced ORR observed. This thought is in the light of previous data with SCIB1 where patients that were given the vaccine, following full resection of tumours, showed great long term PFS and OS. This, if sustained in current and verified in additional patients, adds confidence to the fully resected melanoma data.

Nevertheless, note that in current SCOPE data, the number of patients is small. Consequently, if we compare the prevalence of new lesions in the 13 patients in SCOPE (0/13, assuming the single patient with PD also did not present new lesions) to the prevalence of new lesions in the 53 patients in Wolchok et al (13/53, 25%), the difference is not statistically significant at $p < 0.01$ by chi-square or, the more appropriate due to sample size, Fisher's exact test ($p = 0.046$ and 0.056, respectively). Even If we pool Wolchock and Shoushtari (caution: a different population) data together, p-values are 0.02 and 0.03 for Chi-square and Fisher's, respectively. We would need data on about 18-20 patients to reach significance at $p < 0.01$, assuming the current trend continues.

During the AGM, the CEO indicated that, to date, 21 patients are under treatment in SCOPE study. If the current trend of ORR in absence of new lesions continues, before the end of Q1 2024 the prevalence of new lesions in SCOPE study will be statistically significant vs historical controls. **Far**

more importantly, by mid Q2 2024 there could be early (6 months) but unprecedented PFS data for about 18 - 20 patients and close to 1 year PFS data for 5 patients (in September presentation, 5 responders had already been in the trial for 20 weeks). At that point we could be looking at >90% 6mo PFS and in Q4 at extraordinary 1 year PFS/OS on 20+ patients. If SCIB is not partnered by then, this will be an inflection point.

Comments regarding the adaptive phase 2/3 trial planned for H2 2024 are in the next note below.

Wolchok et al 2013 https://www.nejm.org/doi/full/10.1056/nejmoa1302369

Lebbe et al 2019 https://ascopubs.org/doi/full/10.1200/JCO.18.01998

Lebbe et al 2021 https://ascopubs.org/doi/10.1200/JCO.2021.39.15_suppl.9516

SITC poster https://www.scancell.co.uk/Data/Sites/1/media/publications/posters/2023/sitc_scope-study-poster_october-23_final.pdf

AGM presentation https://www.scancell.co.uk/Data/Sites/1/media/docspres/agm-presentation-november-2023.pdf

Shoushtari et al https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9811163/

Note on iSCIB1+

iSCIB1+ is the next generation of SCIB1. It includes additional epitopes which, in contrast to SCIB1, are not HLA-A2 restricted, as well as the AvidiMab Fc modification, thereby increasing the TAM for the vaccine and, presumably, potency. Company expects to get approval and initiate iSCIB1+ cohort within current SCOPE study in Q1 2024.

The CEO during AGM 2023 emphasised that they don't think there is any chance iSCIB1+ wouldn't work the same since it is 95% similar to SCIB1. This is debatable. Largest part of SCIB vaccines is structural (antibody backbone), the active part of the vaccines lies in the variable regions where the epitopes are engineered in. Therefore, iSCIB1+ is substantially more different than 5% in terms of active regions, this comes with additional safety risks. Indeed, the MHRA did ask for additional safety studies, possibly in additional humanised mice expressing HLA corresponding to the new epitopes and/or with additional safety readouts. Scancell has published mouse data on SCIB1 and iSCIB1+ in their WO2022043400A1 patent. In particular, in Figure 35 (page 181) SCIB1+/iSCIB1+ shows a similar response in ELIspot assays in C57BI/6 (non-humanised), HHDII (HLA-A2, CD8+), HHDII/DP4 (HLA-A2/DP4, CD8+/CD4+) and DR4 (CD4+) mice, while SCIB1 and iSCIB1+ showed similar responses to TRP2 180-188 in DR4 and non-humanised mice and to GP100 44-59 epitope in DR4 mice. In Figure 36 (page 182, described in Example 13 on page 79) the potential benefit of the avidimab modification, as well as efficacy of SCIB1 vs iSCIB1+ are demonstrated in non humanised C57BI/6 mice. In more detail, somewhat increased efficacy is shown for iSCIB1 vs SCIB1 (A, top panel), substantially increased efficacy is shown for iSCIB1+ vs SCIB1+ (A, bottom panel). Accordingly, in the Kaplan survival curve (Figure 36C) there are only minor differences between SCIB1 and iSCIB1, while there is a clear benefit in iSCIB1+ vs SCIB1+, with iSCIB1+ impressively standing out from the rest. Taken all together, it is hard to explain (other than the broadly recognised limitations of these models) why avidimab modification has so much more pronounced

effect in SCIB1+ in particular, while it should also be noted that these detailed tumour growth/survival experiments happened in non-humanised mice.

Though aforementioned mouse data are generally supportive, fundamentally, we cannot conclude that the new epitopes in iSCIB1+ would **definitely** translate into similar efficacy in **humans** with the corresponding HLA as with SCIB1 in HLA-A2 patients. Sub-par efficacy and/or safety issues of additional epitopes in non-HLA-A2 patients could raise questions about the SCIB platform as a whole and at a time (Q2 2024 when preliminary data with iSCIB1+ are expected) when the company could be looking at transformational results with original SCIB1. Perhaps, the company should sharply focus on SCIB1 and on securing a favourable partnership before moving forward with clinical development of iSCIB1+ or at least not allow recruitment for iSCIB1+ (assuming the MHRA does not ask for a phase 1, despite additional animal safety studies) to delay progression of SCIB1. In practice, this means delaying initiation of iSCIB1+ trial towards the end of Q1 2024, which may happen anyway since the MHRA hasn't approved it yet. This should not influence the monetisation Scancell can achieve from the SCIB platform in unresectable melanoma as they could easily negotiate milestones tied to efficacy/safety of SCIB1 and iSCIB1+ and according to their respective TAMs, eventually halting SCIB1 development altogether if all goes as planned.

Timelines as I see them:

Q1 2024: ORR data on 20+ patients with SCIB1, if trend continues this will be the first study were no patients under treatment developed new lesions, resulting in excellent ORR sustained over a meaningful period of time (expected median around 4-5 months). In addition, SCIB1 cohort is fully recruited. iSCIB1+ starts recruiting towards the end of Q1.

Q2 2024: 6 month PFS data for 18-20 patients, 12 month PFS/OS data for 5 patients and additional 3 month ORR data for about 10 patients (SCIB1), at this point it is likely that SCIB platform for melanoma will be partnered assuming current trend continues. Preparation to initiate phase 2/3 blinded, controlled, adaptive registrational trial is announced.

Q3 2024: By mid Q3, we should have solid ORR data on iSCIB1+ (assuming they recruit at least 10 patients per month from end of Q1 2024).

If we partnered the platform by Q2:
If iSCIB1+ early data actually the same as SCIB1, SCIB1 is put on hold and phase 2/3 initiates with iSCIB1+. If discrepancies are observed, SCIB1 moves forward with phase 2/3 and iSCIB1+ is reevaluated for any potential HLA selectivity or safety issues and/or goes back to the drawing board.

If we haven't secured the partnership:
Phase 2/3 is postponed. SCIB1/iSCIB1+ stops recruiting in current SCOPE and we wait for longer term PFS data and early OS data in Q4 for SCIB1 and early PFS/robust ORR for iSCIB1+ also in Q4.

Q4 2024: If data on SCIB1 or iSCIB1+ is as expected it is extremely likely we will secure a sponsor to initiate phase 2/3 in 2025. If the data for any reason is not as stellar as expected, we will have to wait for more robust PFS/OS data (2/4 years) from current trial. Another capital raise will be necessary.

Important

This document is meant to be a basis for discussion. **This is not investment advice.** Also note that mistakes happen, I am not responsible if you made an investment decision based on this document and lost money, even if I made mistakes on the facts and/or the assumptions in this document. This is the internet, I could be an experienced scientist or a Nigerian Prince for all you know. I am invested in Scancell which means I may be biased. You may not distribute the document in parts or without my contact details at the end of this document. You may not present this work as if it was your own.

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Version 2 incorporates data published in Scancell patent WO2022043400A1