Final Statistical Analysis Plan for:

NCT03009058

Study IMM-101-011

A Novel Phase I/IIa Open-label Study of IMM-101 in Combination with Selected Standard of Care (SOC) Regimens in Patients with Metastatic Cancer or Unresectable Cancer at Study Entry

Statistical Analysis Plan

Immodulon Therapeutics Limited

Protocol: IMM-101-011

Treatment: IMM-101

A Novel Phase I/IIa Open-label Study of IMM-101 in Combination with Selected Standard of Care Regimens in Patients with Metastatic Cancer or Unresectable Cancer at Study Entry

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Contents

2 Abbreviations

AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
eCRF	Electronic Case Report Form
CSR	Clinical Study Report
Immodulon	Immodulon Therapeutics Limited
irRC	Immune-related response criteria
011 study	IMM-101-011 study
MedDRA	Medical Dictionary for Regulatory Activities
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAF	Safety Analysis Set (All randomised patients from the Main Study who receive at least one dose of study drug)
SQN	Syne qua non Ltd
SOC	Standard of Care
WHO	World Health Organisation

3 Introduction

This document presents the statistical analysis plan (SAP) for Immodulon Therapeutics Limited (Immodulon), Protocol No. IMM-101-011: A Novel Phase I/IIa Open-label Study of IMM-101 in Combination with Selected Standard of Care Regimens in Patients with Metastatic Cancer or Unresectable Cancer at Study Entry.

3.1 Protocol Status and Termination by Immodulon

On 31st July 2017, Immodulon took the decision to enroll no further patients into this Phase I/IIa open-label study and to close the study early.

On 31st July 2017, 2 patients were on study and 1 patient was a screen failure. Both enrolled patients were consented into Cohort 6 (IMM-101 + Anti-PDI (Pembrolizumab, Nivolumab) in metastatic melanoma). For these 2 treated patients the last study visit completed was Visit 5 – Week 10. The End of Study / Withdrawal Visit was completed in place of Visit 6 – Week 12 for both patients.

It was planned to evaluate up to 20 patients in each SOC (standard of care)/tumour type, with a total of approximately 300 patients enrolled overall (across 7 tumour types), with assessment of both safety and efficacy by each SOC/tumour type. Further details of the sample size evaluations are given in the study protocol. A minimum of 10 patients per cohort were required for an evaluation of futility with respect to the primary activity endpoint of response to treatment (based on immune-related response criteria [irRC]). Given that only two patients were enrolled into the study, the objectives of the study described in the study protocol cannot be met.

The planned statistical analysis described in the study Protocol will not now be performed due to the early closure of the study. However all clinical study data will be presented in data listings, as described in this statistical analysis plan (SAP) and in the separate document containing detailed Planned Listings Shells. Both documents will be approved before database lock. The listings will be produced in accordance with the approved Listings Shells, by Syne qua non Ltd (SQN) (SQN Study No: ICS16001).

This analysis plan is based on the final protocol version 4 (released 25 October 2016) and the final 011 study electronic case report form (eCRF), version 4, dated 3 March 2017. Given the early termination of the study, this SAP is therefore abbreviated. Relevant sections of the study Protocol are referred to and for ease of reference, the full study activity schedule is reproduced from the study Protocol.

4 Study Objectives

Full details of the study objectives, endpoints and evaluation methodology are given in the study Protocol.

5 Study Design

Full details of the study design are provided in the study Protocol.

5.1 Study Schedule

For the 2 patients enrolled into the study, the last study visit completed was Visit 5 – Week 10. The End of Study / Withdrawal Visit was completed in place of Visit 6 – Week 12 for both patients.

The study schedule of assessments is presented in Sections 5.1.1 and 5.1.2. Note that a number of inconsistencies within the study Protocol version 4.0 were noted by Immodulon (file note IMM/011/FN/0008), approved 16 Mar 2017, as follows:-

- The screening phase was between Day -28 to Day -1 (not Day -7 as indicated in the Protocol version 4.0 study schedule of assessments)
- The response to treatment was to be assessed at Weeks 6 and 10 and End of Study/Withdrawal Visit (this was omitted from the assessment schedule in error)
- Footnote 42 (Screening and Treatment phases) and 21 (Long-term maintenance phase): Full text was amended to 'Solicited and visible injection site reactions will be recorded and patients will be asked to assess any impact on their daily activities and whether the reactions are getting better, worse or staying the same. (The question asked was omitted from the assessment schedule in error).

5.1.1 Flowchart of Assessments: Screening and Treatment Phases

	Screening Phase	**Treatment Phase**									
	Week -4/-1	**Week 0**	**Week 2**	**Week 4**	**Week 8**	**Week 10**	**Week 12**	**Week 16**	**Week 20**	**Week 24**	**Week 28**
Day	**Day -28 to -7**	**Day 0 Visit 1**	**Day 14 Visit 2**	**Day 28 Visit 3**	**Day 56 Visit 4**	**Day 70 Visit 5**	**Day 84 Visit 6**	**Day 112 Visit 7**	**Day 140 Visit 8**	**Day 168 Visit 9**	**Day 196 Visit 10**
Visit window (days)	-	-	**±3 days[1]**					**±14 days[1]**			
Informed consent[2]	✓										
Inclusion/exclusion criteria	✓	✓[3]									
Demography & baseline data[4]	✓										
Complete medical history[5]	✓										
Physical examination[6]	✓										✓
Safety blood and serum samples[7,8]	✓[9,10,11]	✓[11]	✓[11,12]	✓[11,12]	✓[11,12]	✓[11,12]	✓[11,12]	✓[11]	✓[11]	✓[11]	✓[11,12]
HLA serotyping[13]	✓										
Immunomarkers[14]	✓[9]						✓[12]			✓[12]	
Serum pregnancy test[15]	✓										
Vital signs[16]	✓	✓[17]									✓
Weight	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12-lead ECG[18]	✓										
ECOG/WHO performance status[19]	✓[20]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tumour biopsy - slides[21,22]	✓[23]										✓[24,25]
Tumour biopsy – core samples [22,26]	✓[27,28]				✓[25,29]						✓[25,29]
Microsatellite phenotyping[30]	✓										
CT/MRI scan	✓[31]						✓[32]				✓[32]
Measure diameter of erythema and skin biopsy[26,27,33,34]			✓[35,36]		✓[35,36]						✓[35,36]

	Screening Phase	**Treatment Phase**									
	Week -4/-1	**Week 0**	**Week 2**	**Week 4**	**Week 8**	**Week 10**	**Week 12**	**Week 16**	**Week 20**	**Week 24**	**Week 28**
Day	**Day -28 to -7**	**Day 0 Visit 1**	**Day 14 Visit 2**	**Day 28 Visit 3**	**Day 56 Visit 4**	**Day 70 Visit 5**	**Day 84 Visit 6**	**Day 112 Visit 7**	**Day 140 Visit 8**	**Day 168 Visit 9**	**Day 196 Visit 10**
Visit window (days)	**-**	**-**	**±3 days[1]**					**±14 days[1]**			
Prior/concomitant therapy[37]	✓[38]	✓[38]	✓	✓	✓	✓	✓	✓	✓	✓	✓
Adverse event reporting[39]	✓[40]	✓[41]	✓	✓	✓	✓	✓	✓	✓	✓	✓
Assess injection site reactions[12]			✓[42]	✓[42]	✓[42]	✓[42]	✓[42]	✓[42]	✓[42]	✓[42]	✓[42]
Record time interval since last dose of IMM-101[1,12]			✓	✓	✓	✓	✓	✓	✓	✓	✓
Check time interval since last dose of IMM-101 is ≥11 days (14 days ±3 days)[1,12]			✓	✓	✓	✓	✓				
IMM-101 administration		✓[41]	✓[43]	✓	✓	✓[43]	✓	✓	✓	✓	✓

Footnotes:
ALP: alkaline phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; β-hCG: β-human chorionic gonadotropin; BCG: Bacillus Calmette–Guérin; CA19.9: carbohydrate antigen 19.9; CEA: carcinoembryonic antigen; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; CRP: C-reactive protein; CT: computerised tomography; ECG: Electrocardiogram; ECOG: Eastern Cooperative Oncology Group; eCRF: electronic case report form; eGFR: estimated glomerular filtration rate; FACS: fluorescence-activated cell sorting; FBC: full blood count; GEM: gemcitabine; GGT: gamma-glutamyl transferase; Hb: haemoglobin; HLA: human leukocyte antigen; INR: international normalised ratio; LDH: lactate dehydrogenase; LFT: liver function test; MCH: mean cell haemoglobin; MCV: mean cell volume; miRNA: micro ribonucleic acid; MPV: Mean platelet volume; MRI: magnetic resonance imaging; Pt: prothrombin time; PTT: partial thromboplastin time; RBC: red blood cell; WBC: white blood cell; WHO: World Health Organisation.

1. During the Treatment Phase of the study (Doses 1 to 3 and Doses 4 to 6), at the discretion of the Investigator, the dose interval may be modified provided the minimum period between doses is at least 11 days (14±3 days). However, in the event that this minimum dosing interval cannot be maintained, at the discretion of the Investigator, a half dose of IMM-101 (0.5 mg/0.05 mL intradermal injection) should be given and at no point in the study should any doses of IMM-101 be administered at less than a 7-day interval. Where this reduced dosing interval is being used the 4-week interval between Dose 3 and Dose 4 and between Dose 6 and Dose 7 should still be maintained. In the event of an injection site reaction of ≥Grade 3 (severe) as measured by the NCI CTCAE v4.0, at the discretion of the Investigator, patients may be administered a half dose of IMM-101 (i.e., a single 0.05 mL intradermal injection of IMM-101).
2. Before beginning any study procedure, the patient will read and sign an informed consent form. The patient will be given a copy of the signed informed consent form.

3. Inclusion/exclusion criteria will be re-checked before commencing any study treatment including confirmation of anticipated life expectancy ≥3 months and a review of blood and serum samples. Final determination of patient eligibility will be made upon receipt of all clinical laboratory results and assessment of all inclusion and exclusion criteria.
4. Gender, date of birth, ethnicity and height.
5. Full medical history including disease history and treatment, any concurrent illnesses and history of previous injections (e.g. smallpox, yellow fever, BCG).
6. A full physical examination will be performed, including assessment of injections received prior to Screening and pre-existing injection site reactions (i.e. BCG or prior cancer treatment reactions). Any additional physical examinations to those scheduled for this study will be performed as per the Investigator's routine procedures.
7. Blood and serum samples (6 mL blood) CRP, FBC (Hb, Haematocrit, RBC count, WBC count, WBC differential count, platelet count, MPV, MCV, MCH), LFTs (ALT, ALP, AST, bilirubin [total, direct], albumin, total protein, GGT, Pt/PTT, INR, LDH), calcium, urea and electrolytes (kidney function: sodium, potassium, creatinine, urea, eGFR [using CKD-EPI creatinine calculation]), CEA, CA19.9.
8. Any additional blood tests to those scheduled will be performed as per the Investigator's routine procedures.
9. Screening blood tests should be taken within 7 days prior to the start of the study.
10. Review of blood test results: Screening blood test results must be available at least 24 hours prior to IMM-101 administration.
11. Patients in the anti-PD1 and anti-CTLA-4 cohorts only, prior to every course of checkpoint inhibitor as per the label: thyroid function test; ACTH; blood glucose test; lipase.
12. Prior to administration of IMM-101.
13. 4 mL whole blood (Only needs to be taken if the result is not already available for the patient).
14. Immunological markers:
    6 mL whole blood: miRNA panel, circulating metabolites.
    6 mL whole blood will be collected from a subset of patients for FACS analysis: immune cell quantification.
    6 mL whole blood will be collected from a subset of patients to be analysed in the TruCulture system: cytokines, chemokines, immune mediators; functional immune cell assays, tumour markers.
15. A Screening serum pregnancy test (β-hCG) will be performed on all eligible female patients of child bearing potential within 72 hours prior to the start of the study. A negative serum pregnancy test result must be obtained prior to a female patient of child bearing potential receiving study medication. Serum pregnancy tests should be repeated as warranted during the study.
16. Resting blood pressure, pulse, and body temperature will be recorded as vital signs. Additional measures of vital signs to those scheduled for this study will be performed as per the Investigator's routine procedures.
17. Patients should be followed by vital sign monitoring for at least 2 hours after administration of IMM-101, under medical supervision with resuscitation facilities available as a precautionary measure.
18. 12-lead ECG measures will be recorded at Screening. Additional 12-lead ECG measures to those scheduled for this study will be performed as per the Investigator's routine procedures.
19. Two observers will be required to assess performance status. If there is any discrepancy between the two scores, the highest (worst) assessment will be used
20. To be eligible for inclusion in the study, patients must have an ECOG/WHO performance status of ≤2 at Day 0.
21. Not for patients with metastatic pancreatic cancer who will receive GEM monotherapy, and patients with metastatic melanoma who will receive a PD1 checkpoint inhibitor
22. Any trauma and clinical sequelae related to the mechanics of the tumour biopsy should be reported as related to the study procedure
23. Document results and record the date of the last tumour biopsy on the patient's eCRF.

-For patients receiving first line treatment, if no biopsy has been performed in the 3 months prior to Screening, a biopsy should be performed during the Screening period, or at Day 0, when eligibility has been confirmed and before first dose of IMM-101 is administered and 10 anonymised, unstained slides prepared from the diagnostic specimen (any additional biopsies to those scheduled for this study will be performed as per the Investigator's routine procedures).
-For patients receiving second, third and fourth line treatment, if no biopsy has been performed in the 2 years prior to Screening a biopsy should be performed during the Screening period, or at Day 0, when eligibility has been confirmed and before first dose of IMM-101 is administered and 10 anonymised, unstained slides prepared (any additional biopsies to those scheduled for this study will be performed as per the Investigator's routine procedures).

24. This tumour biopsy is optional and undertaken only if the patient provides consent for it.
25. The Investigator will schedule the biopsy at this visit. The biopsy will be performed within 2 weeks after this visit
26. Only in patients with metastatic pancreatic cancer who will receive GEM monotherapy, and patients with metastatic melanoma who will receive a PD1 checkpoint inhibitor
27. The Investigator will select the lesion to be biopsied, on the basis of a lesion that will be the most feasible to access and which provides the lowest risk to the patient. Three core biopsy samples will be taken from the target lesion and prepared as follows: 1 core snap frozen, 1 core paraffin embedded, 1 core cryoblock.
28. These patients will undergo a tumour biopsy during the Screening period, or at Day 0, when eligibility has been confirmed and before first dose of IMM-101 is administered.
29. The Investigator will biopsy the same lesion that was biopsied at Screening
30. For patients with colorectal cancer only (if not already available for the patient)
31. Document results and record date of last CT/MRI scan on the patient's eCRF. If no scan has been performed in the 30 days prior to Screening a scan should be performed.
32. Scans performed to assess progression or response must match the baseline scan (i.e. if CT scan at baseline then CT scan for all other scans). Additional CT/MRI scans to those scheduled for this study will be performed as per the Investigator's routine procedures.
33. Prior to administration of IMM-101
34. Length and width
35. From the arm into which the previous dose was administered
36. Skin punch biopsy reactions assessed at the following visit. Any trauma and clinical sequelae related to the mechanics of the skin biopsy should be reported as related to the study procedure and not reported as an injection site reaction.
37. All prescription and over-the-counter medications, including herbals, homeopathic remedies etc., will be recorded.
38. Record any prior/concomitant therapy/medications taken up to 4 weeks before initiation of Screening and any prior/concomitant depot corticosteroids taken up to 6 weeks before initiation of Screening
39. All AEs will be followed until resolution, death, or 30 days after the Withdrawal/EOS visit (whichever comes first)
40. Pre-existing conditions will be recorded.
41. Patients will be observed for 2 hours post dose, prior to leaving the study site.
42. Solicited and visible injection site reactions will be recorded.
43. Patients receiving the reduced intensity IMM-101 dosing regimen will not receive IMM-101 at this visit.

5.1.3 Flowchart of Assessments: Long-term Maintenance Treatment Phase

	Long-term Maintenance Treatment Phase											**End of Study/ With-drawal Visit[4]**
Nominal Time Point	**Week 32**	**Week 36**	**Week 40**	**Week 44**	**Week 48**	**Week 52[1]**	**Week 56**	**Week 60**	**Week 64**	**Week 68**	**Week nn[2,3]**	
Visit/Dose	**Visit 11**	**Visit 12**	**Visit 13**	**Visit 14**	**Visit 15**	**Visit 16**	**Visit 17**	**Visit 18**	**Visit 19**	**Visit 20**	**Visit nn**	
Visit window (days)	**±14 days[5]**											
Physical examination[6]												✓
Safety blood and serum samples[7,8,9]	✓[10]	✓[10,11]	✓[10]	✓[10]	✓[10,11]	✓[10]	✓[10]	✓[10,11]	✓[10]	✓[10]	✓[10,11]	✓[12]
Immunomarkers[8,13]		✓[11]			✓[11]			✓[11]			✓[11]	✓
Vital signs[14]												✓[14]
Weight	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12-lead ECG[15]												✓
ECOG/WHO performance status[16]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CT/MRI scan[17]												✓[18]
Prior/concomitant therapy[19]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Adverse event reporting[20]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Assess injection site reactions[8,21]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Record time interval since last dose of IMM-101[5,8]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
IMM-101 administration	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	

Footnotes:
ALP: alkaline phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; CA19.9: carbohydrate antigen 19.9; CEA: carcinoembryonic antigen; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; CRP: C-reactive protein; CT: computerised tomography; ECG: Electrocardiogram; ECOG: Eastern Cooperative Oncology Group; eGFR: estimated glomerular filtration rate; EOS: End of Study; FACS: fluorescence-activated cell sorting; FBC: full blood count; GGT: gamma-glutamyl transferase; Hb: haemoglobin; INR: international normalised ratio; LDH: lactate dehydrogenase; LFT: liver function test; MCH: mean cell haemoglobin; MCV: mean cell volume; miRNA: micro ribonucleic acid; MPV: Mean platelet volume; MRI: magnetic resonance imaging; Pt: prothrombin time; PTT: partial thromboplastin time; RBC: red blood cell; WBC: white blood cell; WHO: World Health Organisation.

1. A reduction in dose and/or an increase in the dosing interval may be required after one year
2. Should the study extend beyond 68 weeks, the same pattern of assessments will continue for subsequent visits as described in this Schedule of Assessments.
3. A reduction in dose and/or an increase in the dosing interval may be required after one year.
4. Patients withdrawing from the study at any time should attend this EOS visit within 28±7 days after the final dose of IMM-101.
5. During the Maintenance Phase of the study, in the event of an injection site reaction ≥Grade 3 (severe) as measured by the NCI CTCAE v4.0[1], or at the discretion of the Investigator, patients may be administered a half dose of IMM-101 (0.5 mg/0.05 mL) or the dosing interval may be increased or both. If the dosing interval is increased, the patient should attend the study site for safety assessments at least every 14 weeks.
6. A full physical examination will be performed. Any additional physical examinations to those scheduled for this study will be performed as per the Investigator's routine procedures.
7. Any additional blood tests to those scheduled will be performed as per the Investigator's routine procedures.
8. Prior to administration of IMM-101.
9. Blood and serum samples (6 mL blood) CRP, FBC (Hb, haematocrit, RBC count, WBC count, WBC differential count, platelet count, MPV, MCV, MCH), LFTs (ALT, ALP, AST, bilirubin [total, direct], albumin, total protein, GGT, Pt/PTT, INR, LDH), calcium, urea and electrolytes (kidney function: sodium, potassium, creatinine, urea, eGFR [using CKD-EPI creatinine calculation]), CEA and CA19.9.
10. Patients in the anti-PD1 and anti-CTLA-4 cohorts only, prior to every course of checkpoint inhibitor as per the label: thyroid function test; ACTH; blood glucose test; lipase.
11. Every 14 weeks or as close to this time frame as possible.
12. Patients in the anti-PD1 and anti-CTLA-4 cohorts only: thyroid function test; ACTH; blood glucose test; lipase.
13. Immunological markers:
    6 mL whole blood: miRNA panel, circulating metabolites.
    6 mL whole blood will be collected from a subset of patients for FACS analysis: immune cell quantification.
    6 mL whole blood will be collected from a subset of patients to be analysed in the TruCulture system: cytokines, chemokines, immune mediators; functional immune cell assays, tumour markers.
14. Resting blood pressure, pulse, and body temperature will be recorded as vital signs at the EOS visit. Additional measures of vital signs to those scheduled for this study will be performed as per the Investigator's routine procedures.
15. Additional 12-lead ECG measures to those scheduled for this study will be performed as per the Investigator's routine procedures.
16. Two observers will be required to assess performance status. If there is any discrepancy between the two scores, the highest (worst) assessment will be used
17. Scans performed to assess progression or response must match the baseline scan (i.e. if CT scan at baseline then CT scan for all other scans). Additional CT/MRI scans to those scheduled for this study will be performed as per the Investigator's routine procedures.
18. Only required if no scan has been performed in the 6 weeks prior to the EOS visit.
19. All prescription and over-the-counter medications, including herbals, homeopathic remedies etc. will be recorded.
20. All AEs will be followed until resolution, death, or 30 days after the Withdrawal/EOS visit (whichever comes first)
21. Solicited and visible injection site reactions will be recorded.

5.2 Study Data Sets

The definitions of the data sets for the IMM-101-011 study are given below.

5.2.1 All Enrolled Patients

Enrolled patients are patients who enter the study at Visit 1 Day 0, following completion of screening assessments and confirmation of eligibility to enter the study. All listings are based on this set of patients. Hence data for the patient who failed screening will not be listed.

5.2.2 Safety Analysis Set (SAF)

The safety analysis set (SAF) includes all patients who took at least one administration of study treatment (IMM-101).

5.3 Withdrawn Patients

Details of withdrawal procedures are described in the study Protocol.

On 31st July 2017, Immodulon took the decision to enroll no further patients into this Phase I/IIa open-label study and to close the study early. Hence, the 2 enrolled patients who were on study at this date both completed their withdrawal visit in place of Visit 6 – Week 12. Their last study visit completed was Visit 5 – Week 10 for both patients.

5.4 Randomisation

Not applicable.

5.5 Blinding

Not applicable.

5.6 Sample Size

The study was terminated by the sponsor and the two enrolled patients were withdrawn. The last study visit completed was Visit 5 – Week 10. The End of Study / Withdrawal Visit was completed in place of Visit 6 – Week 12 for both patients.

5.7 Changes in Conduct or Planned Analyses from the Protocol

Due to the early termination of the study with only 2 enrolled patients, both of whom were withdrawn early, the objectives of the study could not be met. Hence the planned analyses described in the study Protocol will not be carried out. However, the data collected in the eCRF will be listed.

6 Statistical Methodology

6.1 Planned Presentations of Data: Listings

The presentation of listings and conventions for the listings are contained in a separate document. Both this SAP and the listings shells document will be approved before database lock.

This section therefore provides a tabular summary of the planned listings including listing number, title, medical coding dictionary data (and version), additional derived data and details of derivation.

All patient data will be presented in separate data listings by data type.

6.1.1 Standard Calculations

Study day will be calculated as visit number date (or date of assessment/date of finding/AE/medication etc.) - date of Day 0 (first study drug administration dosing date) and will appear on all relevant dates throughout the listings. Day numbers prior to first study drug administration dosing date (for example screening assessments) will therefore be represented by a negative number of days.

The baseline value (for change from baseline calculations) will be defined as the last assessment prior to the first administration of study drug. The baseline value will be the Screening value if there is no Visit 1 day 0 value.

Listing number	Listing title	Medical dictionary coding items	Derived data	Derivation
16.2.1.1	Patient Completions and Withdrawals		Time on study (months)	(Date of study withdrawal – date of Day 0 +1 day)/30.4375
16.2.2.1	Protocol Deviations			
16.2.2.2	Eligibility			
16.2.2.3	Informed Consent			
16.2.3.1	Analysis Sets		SAF	All patients who took at least one administration of study treatment (IMM-101).
16.2.4.1	Demography		Age (years)	Age is calculated in years from the date of informed consent, as the number of full months between date of birth and informed consent divided by 12 and rounded to the lowest integer.
			Body Mass Index (kg/m^2)	Weight (kg)/height (m)^2).

16.2.4.2	Medical History (Other Than Cancer History)	Medical history will be coded using the Medical Dictionary For Regulatory Activities (MedDRA) version 20		
16.2.4.3	Cancer Diagnosis	Cancer diagnoses will be coded using MedDRA version 20	Time since diagnosis (months)	(Day 0 (i.e. first study medication administration date) - date of diagnosis + 1)/30.4375
16.2.4.4	HLA Serotyping at Screening			
16.2.4.5	Serum Pregnancy Test			
16.2.4.6	Microsatellite Phenotyping at Screening			
16.2.4.7	Prior and Concomitant Medications (Excluding Cancer Medications)	Medications will be coded using WHO Drug Dictionary, version September 2017		
16.2.4.8	Standard of Care Therapy	Medications will be coded using WHO Drug Dictionary, September 2017		

16.2.4.9	New Cancer Medications (Post-standard of Care)	Medications will be coded using WHO Drug Dictionary, version September 2017		
16.2.4.10	Radiotherapy			
16.2.4.11	Cancer-related Surgery			
16.2.5.1	Study Drug Administration		Duration of exposure (days)	Date of last study treatment administration – date of first study treatment administration + 1
16.2.6.1	Tumour Biopsy - Core Samples			
16.2.6.2	Target Lesions			
16.2.6.3	Non-target Lesions			
16.2.6.4	Target Lesion Response to Treatment			
16.2.6.5	Overall Response to Treatment			
16.2.7.1	Adverse Events	Adverse events will be coded using MedDRA version 20	Treatment emergent	An adverse event that started after administration of study drug
			Time to onset	Time from date of first administration of study

			(d:hh:mm)	drug to onset of adverse event. Note: For missing or partial dates and times, not calculated and is reported as unknown (UK).
16.2.8.1.1	All Haematology Values		Change from baseline	Value at assessment time point – baseline value
			H, L	Above normal range, below normal range
16.2.8.1.2	Patients with Clinically Significant Haematology Values		H, L	Above normal range, below normal range
16.2.8.2.1	All Biochemistry Values		Change from baseline	Value at assessment time point – baseline value
			H, L	Above normal range, below normal range
16.2.8.2.2	Patients with Clinically Significant Biochemistry Values		H, L	Above normal range, below normal range
16.2.9.1	Immunology Sampling			
16.2.9.2	Injection Site Reactions			
16.2.9.3	Vital Signs		Change from baseline	Value at assessment time point – baseline value
16.2.9.4	Weight		Change from	Value at assessment time

			baseline	point – baseline value
16.2.9.5	ECG Results		Change from baseline	Value at assessment time point – baseline value
16.2.9.6	Physical Examination			
16.2.9.7	ECOG/WHO Performance Status		Highest (worst) Maximum ECOG/WHO performance status	Maximum score of the first and second evaluators' assessments
16.2.9.8	Diameter of Erythema and Skin Biopsy			

6.2 Adjustment for Covariates

Not applicable.

6.2.1 Centre Effects

Not applicable.

6.3 Protocol Violations

Protocol deviations are recorded in the eCRF and presented in a data listing.

6.4 Missing Values – Missing Visits

There is no intention to implement any procedure for replacing missing data, other than as specified in this SAP.

6.5 Deviations from Statistical Analysis Plan

All deviations from this approved SAP will be described and justified in the final CSR. No pre-database lock data review meeting will be held, however the data will be reviewed by Immodulon prior to database lock.