

**Clinical trial results:****A Phase 1b/2, Open-label, Multicenter, Dose-escalation and Expansion Trial of Intratumoral SD-101 in Combination With Pembrolizumab in Patients With Metastatic Melanoma or Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma****Summary**

EudraCT number	2016-004461-47
Trial protocol	DE
Global end of trial date	24 April 2020

Results information

Result version number	v1 (current)
This version publication date	02 February 2022
First version publication date	02 February 2022
Summary attachment (see zip file)	SYNERGY-001_Final_Am 1_08Feb2021 - Synopsis (SYNERGY-001_CSR_-_Final_Am 1_08Feb2021 - Synopsis.pdf)

Trial information**Trial identification**

Sponsor protocol code	DV3-MEL-01[SYNERGY-001]
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02521870
WHO universal trial number (UTN)	-
Other trial identifiers	US IND number: 125878

Notes:

Sponsors

Sponsor organisation name	Dynavax Technologies Corporation
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2020
Global end of trial reached?	Yes
Global end of trial date	24 April 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase 1 (Dose Escalation: Metastatic Melanoma) is closed.

- To assess the safety and tolerability of escalating intratumoral doses of SD-101 in combination with intravenous pembrolizumab in patients with metastatic melanoma
 - To evaluate the expression of IFN-inducible genes in whole blood 24 hours after intratumoral injection of SD-101 given with pembrolizumab in patients with metastatic melanoma as a pharmacodynamic marker of SD-101 activity
 - To determine an RP2D of SD-101 in combination with pembrolizumab to be evaluated in Phase 2
- Phase 2 (Dose Expansion: Metastatic Melanoma or Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma):
- To assess the tumor response both locally and systemically including:
 - Treatment response of the injected lesion(s) (local response)
 - Treatment response of the non-injected lesion(s) (systemic response)
 - Treatment response of all lesions
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Protection of trial subjects:

This study was conducted in accordance with the protocol, good clinical practice (GCP) as defined in International Council on Harmonisation (ICH) guidelines, and applicable local regulatory requirements. In Phase 1, assessments of injection-site reactions were collected for a minimum of 90 minutes through the first 4 weekly injections and for 30 minutes following the remaining injections of SD-101 at the clinical site.

In Phase 2, injection-site reactions that persisted for more than 7 days were recorded as AEs. All other AEs and laboratory safety measurements were graded per NCI CTCAE Version 4.03. All AEs, whether gradable by CTCAE or not, were also to be evaluated for seriousness. AEs were collected through 28 days after the last dose of SD-101. During combination treatment, patients would undergo targeted physical examinations and laboratory assessments, which included a complete blood count (CBC) with differential, platelet assessment, coagulation testing, thyroid function tests, and serum chemistry (including creatinine, liver function tests, and lactate dehydrogenase [LDH]). During monotherapy, safety was evaluated through the careful monitoring of the results of all clinical and laboratory assessments.

Injection site reactions were expected to spontaneously subside and adverse reactions could be treated with oral medications. The combination of SD-101 and pembrolizumab was well tolerated in the 4 patient populations evaluated here. The typical adverse reaction to SD-101 is an injection-site reaction or flu-like illness starting the evening of an injection that may include pyrexia, headache, myalgia, malaise, or chills and is treatable with over-the-counter medication. Adding SD-101, an innate immune stimulant, to pembrolizumab, an immune checkpoint blocker, did not lead to an increased rate of irAEs over pembrolizumab monotherapy.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No
Notes:	

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 33
Country: Number of subjects enrolled	New Zealand: 10
Country: Number of subjects enrolled	United States: 186
Country: Number of subjects enrolled	Germany: 12
Worldwide total number of subjects	241
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	116
From 65 to 84 years	116
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

Number of Subjects Planned was 24 subjects in Phase 1 Dose Escalation and 260 subjects in Phase 2 Dose Expansion. In final, 241 subjects were enrolled: 22 subjects in Phase 1 Dose Escalation (1 mg n = 6; 2 mg n = 5; 4 mg n = 5; 8 mg n = 6); 219 subjects in Phase 2 Dose Expansion.

Pre-assignment

Screening details:

Routine laboratory tests (serum chemistry, hematology) for screening should be performed within 28 days prior to enrollment or can be obtained from a standard of care visit within 28 days of first dose of pembrolizumab. Laboratories obtained within 7 days of Day 1 visit, with the exception of a CBC with ANC, do not need to be repeated on Day 1.

Period 1

Period 1 title	Dose expansion study phase 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This is an open-label trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg

Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 1 (SD-101 2 mg) and participants in Phase 2 Dose Expansion Cohort 1 and Cohort 5.

Dose Expansion Cohort 5: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Arm type	Experimental
Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion.

Dose Expansion Cohort 5: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Arm title	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg
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Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 3 (SD-101 8 mg) and participants in Phase 2 Dose Expansion Cohort 1.

Dose Expansion Cohort 1: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion if 1 lesion is selected or 2.0 mg per lesion if 2 to 4 lesions are selected for injection

Arm type	Experimental
Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion.

Dose Expansion Cohort 1: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Arm title	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg
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Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 1 (SD-101 2 mg) and participants in Phase 2 Dose Expansion Cohort 2 and Cohort 8.

Dose Expansion Cohort 8: Participants with melanoma who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions

Arm type	Experimental
Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion.
Dose Expansion Cohort 8: Participants with melanoma who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.
Dose: 2.0 mg per lesion in 1 to 4 lesions.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Arm title	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
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Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 3 (SD-101 8 mg) and participants in Phase 2 Dose Expansion Cohort 2.

Dose Expansion Cohort 2: Participants with melanoma who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.
Dose: 8.0 mg in a single lesion.

Arm type	Experimental
Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion.
Dose Expansion Cohort 2: Participants with melanoma who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.
Dose: 8.0 mg in a single lesion.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Arm title	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg
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Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.
The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 3 and Cohort 6.

Dose Expansion Cohort 6: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-

101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions

Arm type	Experimental
Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion.

Dose Expansion Cohort 6: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Arm title	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg
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Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 3.

Dose Expansion Cohort 3: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Arm type	Experimental
Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion.

Dose Expansion Cohort 3: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Arm title	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg
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Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 4 and Cohort 7.

Dose Expansion Cohort 7: Participants with HNSCC who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Arm type	Experimental
Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion.

Dose Expansion Cohort 7: Participants with HNSCC who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Arm title	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
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Arm description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 4.

Dose Expansion Cohort 4: Participants with HNSCC who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Arm type	Experimental
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Investigational medicinal product name	SD-101
Investigational medicinal product code	SD-101
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intratumoral use

Dosage and administration details:

SD-101 drug product was administered by intratumoral injection into a single target lesion. Dose Expansion Cohort 4: Participants with HNSCC who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression. Dose: 8.0 mg in a single lesion.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg was administered intravenously every 3 weeks (Q3W) for two years for up to 35 treatments (35 doses) or until disease progression.

Number of subjects in period 1^[1]	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg
Started	45	41	31
Completed	5	3	0
Not completed	40	38	31
Consent withdrawn by subject	3	4	-
Adverse Event	9	8	-
Non-Compliance with Study Drug	1	1	-
Death	1	1	2
Other	14	6	7
Lost to follow-up	1	-	-
Progressive disease	11	18	22

Number of subjects in period 1^[1]	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg
Started	30	28	23
Completed	0	0	0
Not completed	30	28	23
Consent withdrawn by subject	1	1	1
Adverse Event	2	-	-
Non-Compliance with Study Drug	-	-	-
Death	1	5	3
Other	3	5	2
Lost to follow-up	-	-	-

Progressive disease	23	17	17
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Number of subjects in period 1 ^[1]	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
Started	23	9
Completed	0	0
Not completed	23	9
Consent withdrawn by subject	2	-
Adverse Event	1	-
Non-Compliance with Study Drug	-	-
Death	2	1
Other	1	1
Lost to follow-up	-	-
Progressive disease	17	7

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: This study was conducted in 2 Phases. Phase 1 enrolled 22 patients for the Dose Escalation to determine an RP2D of SD-101 in combination with pembrolizumab to be evaluated in Phase 2 Dose Expansion. The dose cohorts for SD-101 were 1 mg, 2 mg, 4 mg, and 8 mg. Two RP2Ds were selected (2 mg and 8 mg). Patients who received 1 mg (n=6) or 4 mg (n=5) of SD-101 in the Dose Escalation Phase are not included in phase 2 of the study (n=241 (enrolled for phase 2) - 11 = 230 patients for the analysis set).

Baseline characteristics

Reporting groups

Reporting group title	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 1 (SD-101 2 mg) and participants in Phase 2 Dose Expansion Cohort 1 and Cohort 5.

Dose Expansion Cohort 5: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Reporting group title	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 3 (SD-101 8 mg) and participants in Phase 2 Dose Expansion Cohort 1.

Dose Expansion Cohort 1: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion if 1 lesion is selected or 2.0 mg per lesion if 2 to 4 lesions are selected for injection

Reporting group title	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 1 (SD-101 2 mg) and participants in Phase 2 Dose Expansion Cohort 2 and Cohort 8.

Dose Expansion Cohort 8: Participants with melanoma who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions

Reporting group title	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 3 (SD-101 8 mg) and participants in Phase 2 Dose Expansion Cohort 2.

Dose Expansion Cohort 2: Participants with melanoma who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion.

Reporting group title	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 3 and Cohort 6.

Dose Expansion Cohort 6: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions

Reporting group title	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 3.

Dose Expansion Cohort 3: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Reporting group title	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 4 and Cohort 7.

Dose Expansion Cohort 7: Participants with HNSCC who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Reporting group title	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 4.

Dose Expansion Cohort 4: Participants with HNSCC who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Reporting group values	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg
Number of subjects	45	41	31
Age categorical Units: Subjects			
≤ 18 years	0	0	0
Between 18 and 65 years	16	18	13
≥ 65 years	29	23	18
Age continuous			
Age were summarized with descriptive statistics such as mean, standard deviation, median, minimum, and maximum. Age was calculated between a subject's birth date and the date of his/her consent.			
Units: years			

arithmetic mean	66.2	65.3	65.6
standard deviation	± 13.34	± 12.44	± 12.99

Gender categorical			
Units: Subjects			
Female	13	14	10
Male	32	27	21

Race

Count and percentage are reported for categorical variables such as sex, race, and ethnicity.

Units: Subjects			
White	44	41	30
Black or African American	1	0	0
Asian	0	0	1
Other	0	0	0

Ethnicity

Count and percentage are reported for categorical variables such as sex, race, and ethnicity.

Units: Subjects			
Hispanic or Latino	0	2	1
Not Hispanic or Latino	43	37	28
Unknown or Not Reported	2	2	2

Reporting group values	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg
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Number of subjects	30	28	23
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Age categorical			
Units: Subjects			
≤ 18 years	0	0	0
Between 18 and 65 years	17	16	10
≥ 65 years	13	12	13

Age continuous

Age were summarized with descriptive statistics such as mean, standard deviation, median, minimum, and maximum.
Age was calculated between a subject's birth date and the date of his/her consent.

Units: years			
arithmetic mean	62.4	62.6	67.2
standard deviation	± 15.25	± 10.66	± 9.59

Gender categorical			
Units: Subjects			
Female	7	9	2
Male	23	19	21

Race

Count and percentage are reported for categorical variables such as sex, race, and ethnicity.

Units: Subjects			
White	25	24	20
Black or African American	0	0	2
Asian	1	2	1
Other	4	2	0

Ethnicity

Count and percentage are reported for categorical variables such as sex, race, and ethnicity.

Units: Subjects			
Hispanic or Latino	4	0	0
Not Hispanic or Latino	26	28	22
Unknown or Not Reported	0	0	1

Reporting group values	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg	Total
Number of subjects	23	9	230
Age categorical			
Units: Subjects			
≤ 18 years	0	0	0
Between 18 and 65 years	15	4	109
≥ 65 years	8	5	121

Age continuous

Age were summarized with descriptive statistics such as mean, standard deviation, median, minimum, and maximum.
Age was calculated between a subject's birth date and the date of his/her consent.

Units: years			
arithmetic mean	61.0	65.2	
standard deviation	± 12.94	± 12.35	-

Gender categorical			
Units: Subjects			
Female	8	1	64
Male	15	8	166

Race

Count and percentage are reported for categorical variables such as sex, race, and ethnicity.

Units: Subjects			
White	19	9	212
Black or African American	2	0	5
Asian	2	0	7
Other	0	0	6

Ethnicity

Count and percentage are reported for categorical variables such as sex, race, and ethnicity.

Units: Subjects			
Hispanic or Latino	2	1	10
Not Hispanic or Latino	20	8	212
Unknown or Not Reported	1	0	8

End points

End points reporting groups

Reporting group title	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 1 (SD-101 2 mg) and participants in Phase 2 Dose Expansion Cohort 1 and Cohort 5.

Dose Expansion Cohort 5: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Reporting group title	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 3 (SD-101 8 mg) and participants in Phase 2 Dose Expansion Cohort 1.

Dose Expansion Cohort 1: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion if 1 lesion is selected or 2.0 mg per lesion if 2 to 4 lesions are selected for injection

Reporting group title	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 1 (SD-101 2 mg) and participants in Phase 2 Dose Expansion Cohort 2 and Cohort 8.

Dose Expansion Cohort 8: Participants with melanoma who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions

Reporting group title	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101. The participants in this analysis group include participants in Phase 1 Dose Escalation Cohort 3 (SD-101 8 mg) and participants in Phase 2 Dose Expansion Cohort 2.

Dose Expansion Cohort 2: Participants with melanoma who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion.

Reporting group title	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 3 and Cohort 6.

Dose Expansion Cohort 6: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions

Reporting group title	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 3.

Dose Expansion Cohort 3: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Reporting group title	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 4 and Cohort 7.

Dose Expansion Cohort 7: Participants with HNSCC who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 2.0 mg per lesion in 1 to 4 lesions.

Reporting group title	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
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Reporting group description:

Phase 1 Dose Escalation cohorts and Phase 2 Dose Expansion cohorts were rearranged as analysis groups for analyses to assess study objectives, based on tumor indications, anti-PD-1/L1 experience, and dose of SD-101.

The participants in this analysis group include participants in Phase 2 Dose Expansion Cohort 4.

Dose Expansion Cohort 4: Participants with HNSCC who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Primary: Phase 1 Dose Escalation and Phase 2 Dose Expansion - Overall Response Rate (ORR) by Analysis Group

End point title	Phase 1 Dose Escalation and Phase 2 Dose Expansion - Overall Response Rate (ORR) by Analysis Group ^[1]
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End point description:

Overall response rate (ORR) by analysis group based on investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 was evaluated from Baseline (Day 1) through Day 743 or End of Study (EOS).

The intent-to-treat (ITT) population comprises of all participants who were enrolled in the study.

The objective response rate is defined by the total of CR plus PR of the each relevant subject analysis set.

As of Protocol Amendment 9, efficacy and exploratory endpoints were no longer collected. The collection of safety endpoints was simplified.

End point type	Primary
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End point timeframe:

Day 1 through Day 743

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis: all analysis were descriptive.

End point values	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	41	31	30
Units: Count of Participants				
Complete Response	9	4	0	1
Partial Response	25	16	7	3
Stable Disease	2	8	8	8
Progressive Disease	5	8	12	11
Not Evaluable	4	5	4	7

End point values	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	23	23	9
Units: Count of Participants				
Complete Response	2	0	0	1
Partial Response	4	6	2	0
Stable Disease	7	5	3	2
Progressive Disease	10	9	10	4
Not Evaluable	5	3	8	2

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate

End point title	Objective Response Rate ^[2]
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End point description:

The objective response rate is defined by the total of CR and PR.

As of Protocol Amendment 9, efficacy and exploratory endpoints were no longer collected. The collection of safety endpoints was simplified.

End point type	Primary
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End point timeframe:

Day 1 Through Day 743

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis: all analysis were descriptive.

End point values	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	41	31	30
Units: Counts of participants	34	20	7	4

End point values	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	23	23	9
Units: Counts of participants	6	6	2	1

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 Dose Escalation and Phase 2 Dose Expansion - Time to Objective Response by Analysis Group

End point title	Phase 1 Dose Escalation and Phase 2 Dose Expansion - Time to Objective Response by Analysis Group
End point description:	
Time to objective response by analysis group based on investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 was evaluated from Baseline (Day 1) through Day 743 or End of Study (EOS). The intent-to-treat (ITT) population comprises of all participants who were enrolled in the study. This subset of participants analyzed comprises of participants with objective response. As of Protocol Amendment 9, efficacy and exploratory endpoints were no longer collected. The collection of safety endpoints was simplified.	
End point type	Secondary
End point timeframe:	
Day 1 through Day 743	

End point values	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	20	7	4
Units: month				
arithmetic mean (standard deviation)	3.2 (± 1.6)	4.1 (± 2.96)	5.1 (± 3.06)	4.3 (± 2.98)

End point values	HNSCC Anti-	HNSCC Anti-	HNSCC Anti-	HNSCC Anti-
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	PD-1/L1 Naïve SD-101 2 mg	PD-1/L1 Naïve SD-101 8 mg	PD-1/L1 Experienced SD-101 2 mg	PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	2	1
Units: month				
arithmetic mean (standard deviation)	2.3 (± 0.92)	2.4 (± 0.87)	2.7 (± 1.09)	2.1 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 Dose Escalation and Phase 2 Dose Expansion - Duration of Response by Analysis Group

End point title	Phase 1 Dose Escalation and Phase 2 Dose Expansion - Duration of Response by Analysis Group
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End point description:

Duration of response by analysis group based on investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 was evaluated from Baseline (Day 1) through Day 743 or End of Study (EOS).

The intent-to-treat (ITT) population comprises of all participants who were enrolled in the study. This subset of participants analyzed comprises of participants with objective response.

As of Protocol Amendment 9, efficacy and exploratory endpoints were no longer collected. The collection of safety endpoints was simplified.

End point type	Secondary
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End point timeframe:

Day 1 through Day 743

End point values	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	20	7	4
Units: month				
arithmetic mean (standard deviation)	11.1 (± 6.42)	11.7 (± 5.96)	4.6 (± 6.57)	7.6 (± 7.28)

End point values	HNSCC Anti- PD-1/L1 Naïve SD-101 2 mg	HNSCC Anti- PD-1/L1 Naïve SD-101 8 mg	HNSCC Anti- PD-1/L1 Experienced SD-101 2 mg	HNSCC Anti- PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	2	1
Units: month				
arithmetic mean (standard deviation)	5.9 (± 4.93)	6.3 (± 3.96)	2.1 (± 0.07)	8.1 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 Dose Escalation and Phase 2 Dose Expansion - Disease Control Rate (DCR) by Analysis Group

End point title	Phase 1 Dose Escalation and Phase 2 Dose Expansion - Disease Control Rate (DCR) by Analysis Group
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End point description:

Disease Control Rate (DCR) by analysis group based on investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 was evaluated from Baseline (Day 1) through Day 743 or End of Study (EOS).

The intent-to-treat (ITT) population comprises of all participants who were enrolled in the study.

As of Protocol Amendment 9, efficacy and exploratory endpoints were no longer collected. The collection of safety endpoints was simplified.

End point type	Secondary
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End point timeframe:

Day 1 through Day 743

End point values	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	41	31	30
Units: Participants	36	28	15	12

End point values	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	23	23	9
Units: Participants	13	11	5	3

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 Dose Escalation and Phase 2 Dose Expansion - Progression-Free Survival Rate by Analysis Group

End point title	Phase 1 Dose Escalation and Phase 2 Dose Expansion - Progression-Free Survival Rate by Analysis Group
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End point description:

Progression-Free Survival (PFS) rate by analysis group based on investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 was evaluated from Baseline (Day 1) through Day 743 or End of Study (EOS).

The intent-to-treat (ITT) population comprises of all participants who were enrolled in the study.

As of Protocol Amendment 9, efficacy and exploratory endpoints were no longer collected. The collection

of safety endpoints was simplified.

End point type	Secondary
End point timeframe:	
Day 1 through Day 743	

End point values	Melanoma Anti-PD-1/L1 Naïve SD-101 2 mg	Melanoma Anti-PD-1/L1 Naïve SD-101 8 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 2 mg	Melanoma Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	41	31	30
Units: Month rate				
arithmetic mean (confidence interval 95%)				
3-month rate	85.7 (70.9 to 93.3)	71.9 (54 to 83.8)	46.7 (28.4 to 63)	48 (27.8 to 65.6)
6-month rate	78.4 (62.6 to 88.1)	63.3 (45.2 to 76.8)	33 (17.2 to 49.8)	24 (9.8 to 41.7)
9-month rate	70.8 (54.3 to 82.3)	60.4 (42.4 to 74.4)	21.4 (8.6 to 37.9)	14.4 (3.9 to 31.4)
12-month rate	70.8 (54.3 to 82.3)	53.7 (35.7 to 68.7)	21.4 (8.6 to 37.9)	9.6 (1.7 to 25.7)
15-month rate	65.1 (48.2 to 77.8)	49.9 (31.9 to 65.5)	0 (0 to 0)	9.6 (1.7 to 25.7)
18-month rate	61.5 (44 to 75)	40.3 (22.3 to 57.7)	0 (0 to 0)	9.6 (1.7 to 25.7)
21-month rate	61.5 (44 to 75)	40.3 (22.3 to 57.7)	0 (0 to 0)	0 (0 to 0)

End point values	HNSCC Anti-PD-1/L1 Naïve SD-101 2 mg	HNSCC Anti-PD-1/L1 Naïve SD-101 8 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 2 mg	HNSCC Anti-PD-1/L1 Experienced SD-101 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	23	23	9
Units: Month rate				
arithmetic mean (confidence interval 95%)				
3-month rate	46.4 (26.6 to 64.1)	43.5 (23.3 to 62.1)	31.6 (12.9 to 52.2)	37.5 (8.7 to 67.4)
6-month rate	26.5 (10.5 to 45.7)	17.4 (5.4 to 35)	0 (0 to 0)	25 (3.7 to 55.8)
9-month rate	21.2 (7.1 to 40.3)	17.4 (5.4 to 35)	0 (0 to 0)	12.5 (0.7 to 42.3)
12-month rate	15.9 (4.2 to 34.4)	8.7 (1.5 to 24.2)	0 (0 to 0)	0 (0 to 0)
15-month rate	15.9 (4.2 to 34.4)	4.3 (0.3 to 18.2)	0 (0 to 0)	0 (0 to 0)
18-month rate	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
21-month rate	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through Day 743

For Dose Escalation purposes, a DLT would be defined as any selected AEs as per protocol occurring from the time of the first injection (Day 1) through Study Day 29.

Adverse event reporting additional description:

The safety population included all enrolled patients who received at least 1 dose of SD-101.

The measures of safety in the trial were routine clinical and laboratory procedures. AEs, SAEs, and abnormal laboratory values were summarized by the proportion of subjects who experienced them.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	SD-101 8 mg in Anti-PD-1/L1-Naïve Melanoma
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Reporting group description:

Dose Expansion Cohort 1: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion if 1 lesion is selected or 2.0 mg per lesion if 2 to 4 lesions are selected for injection

Objective: determine the safety and efficacy of SD-101(2) and pembrolizumab in anti-PD-1/L1 therapy naïve patients with recurrent or metastatic melanoma.

Reporting group title	SD-101 8 mg in Anti-PD-1/L1-Experienced Melanoma
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Reporting group description:

Dose Expansion Cohort 2: Participants with melanoma who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion.

Determine the safety and efficacy of SD-101(2) and pembrolizumab in anti-PD-1/L1 therapy progressing patients with recurrent or metastatic melanoma.

Reporting group title	SD-101 8 mg in Anti-PD-1/L1-Naïve HNSCC
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Reporting group description:

Dose Expansion Cohort 3: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 8 mg intratumorally starting on Day 22 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Objective: determine the safety and efficacy of SD-101(2) and pembrolizumab in anti-PD-1/L1 therapy naïve patients with recurrent head and neck squamous cell carcinoma.

Reporting group title	SD-101 8 mg in Anti-PD-1/L1-Experienced HNSCC
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Reporting group description:

Dose Expansion Cohort 4: Participants with HNSCC who are anti-PD-1/L1-experienced were administered SD-101 8 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 7 doses, then 9 weeks off, then dose Q1W for 4 weeks followed by dose Q3W for 7 doses (up to 22 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.

Dose: 8.0 mg in a single lesion

Objective: determine the safety and efficacy of SD-101(2) and pembrolizumab in anti-PD-1/L1 therapy progressing patients with recurrent head and neck squamous cell carcinoma.

Reporting group title	SD-101 2 mg in Anti-PD-1/L1-Naïve Melanoma
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Reporting group description:

Dose Expansion Cohort 5: Participants with melanoma who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.
Dose: 2.0 mg per lesion in 1 to 4 lesions.

Objective: determine the safety and efficacy of SD-101(3) and pembrolizumab in anti-PD-1/L1 therapy naïve patients with recurrent or metastatic melanoma.

Reporting group title	SD-101 2 mg in Anti-PD-1/L1-Naïve HNSCC
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Reporting group description:

Dose Expansion Cohort 6: Participants with HNSCC who are anti-PD-1/L1-naïve were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.
Dose: 2.0 mg per lesion in 1 to 4 lesions

Objective: determine the safety and efficacy of SD-101(3) and pembrolizumab in anti-PD-1/L1 therapy naïve patients with recurrent head and neck squamous cell carcinoma.

Reporting group title	SD-101 2 mg in Anti-PD-1/L1 Refractory or Resistant HNSCC
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Reporting group description:

Dose Expansion Cohort 7: Participants with HNSCC who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.
Dose: 2.0 mg per lesion in 1 to 4 lesions.

Objective: determine the safety and efficacy of SD-101(3) and pembrolizumab in anti-PD-1/L1 therapy refractory or resistant patients with recurrent head and neck squamous cell carcinoma.

Reporting group title	SD-101 2 mg in Anti-PD-1/L1 Refractory or Resistant Melanoma
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Reporting group description:

Dose Expansion Cohort 8: Participants with melanoma who are anti-PD-1/L1 refractory or resistant were administered SD-101 2 mg intratumorally starting on Day 1 dose Q1W for 4 weeks followed by dose Q3W for 16 doses (up to 20 total doses). Participants were also administered Pembrolizumab 200 mg intravenously Q3W starting on Day 1 for up to 35 treatments or until disease progression.
Dose: 2.0 mg per lesion in 1 to 4 lesions

Objective: determine the safety and efficacy of SD-101(3) and pembrolizumab in anti-PD-1/L1 therapy refractory or resistant patients with recurrent or metastatic melanoma.

Serious adverse events	SD-101 8 mg in Anti-PD-1/L1-Naïve Melanoma	SD-101 8 mg in Anti-PD-1/L1-Experienced Melanoma	SD-101 8 mg in Anti-PD-1/L1-Naïve HNSCC
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 39 (43.59%)	9 / 30 (30.00%)	5 / 23 (21.74%)
number of deaths (all causes)	3	7	13
number of deaths resulting from adverse events	1	0	0
Vascular disorders			
Hypotension			

subjects affected / exposed	2 / 39 (5.13%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial rupture			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 39 (2.56%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 39 (0.00%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal			

disorders			
Pneumonitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion Related Reaction			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Autoimmune Myocarditis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina Pectoris			

subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 39 (0.00%)	1 / 30 (3.33%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Eosinophilia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile Neutropenia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Autoimmune retinopathy			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 39 (0.00%)	2 / 30 (6.67%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune Hepatitis			

subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 39 (0.00%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular Weakness			
subjects affected / exposed	1 / 39 (2.56%)	1 / 30 (3.33%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	1 / 39 (2.56%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 39 (2.56%)	3 / 30 (10.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 39 (0.00%)	0 / 30 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 39 (7.69%)	1 / 30 (3.33%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	1 / 3	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SD-101 8 mg in Anti-PD-1/L1-Experienced HNSCC	SD-101 2 mg in Anti-PD-1/L1-Naïve Melanoma	SD-101 2 mg in Anti-PD-1/L1-Naïve HNSCC
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	15 / 44 (34.09%)	8 / 27 (29.63%)
number of deaths (all causes)	3	2	6
number of deaths resulting from adverse events	1	1	3
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial rupture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration site conditions			
Influenza like illness			

subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	1 / 9 (11.11%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion Related Reaction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Autoimmune Myocarditis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina Pectoris			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			

subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile Neutropenia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Autoimmune retinopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune Hepatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypophysitis			

subjects affected / exposed	0 / 9 (0.00%)	1 / 44 (2.27%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular Weakness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 9 (11.11%)	2 / 44 (4.55%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	2 / 27 (7.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 44 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SD-101 2 mg in Anti-PD-1/L1 Refractory or Resistant HNSCC	SD-101 2 mg in Anti-PD-1/L1 Refractory or Resistant Melanoma	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 23 (43.48%)	6 / 31 (19.35%)	
number of deaths (all causes)	7	5	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial rupture			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised oedema			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	0 / 23 (0.00%)	2 / 31 (6.45%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate Aminotransferase Increased			

subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion Related Reaction			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Autoimmune Myocarditis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Pectoris			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myasthenia gravis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Neutropenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Autoimmune retinopathy			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune Hepatitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular Weakness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			

subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	SD-101 8 mg in Anti-PD-1/L1-Naïve Melanoma	SD-101 8 mg in Anti-PD-1/L1-Experienced Melanoma	SD-101 8 mg in Anti-PD-1/L1-Naïve HNSCC
Total subjects affected by non-serious adverse events subjects affected / exposed	39 / 39 (100.00%)	30 / 30 (100.00%)	23 / 23 (100.00%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	13 / 39 (33.33%) 13	2 / 30 (6.67%) 2	2 / 23 (8.70%) 2
Nervous system disorders Headache subjects affected / exposed occurrences (all)	25 / 39 (64.10%) 25	14 / 30 (46.67%) 14	10 / 23 (43.48%) 10
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Malaise subjects affected / exposed occurrences (all) Injection site erythema subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Influenza Like Illness subjects affected / exposed occurrences (all) Injection Site Pain subjects affected / exposed occurrences (all) Injection Site Swelling	31 / 39 (79.49%) 31 20 / 39 (51.28%) 20 20 / 39 (51.28%) 20 9 / 39 (23.08%) 9 15 / 39 (38.46%) 15 7 / 39 (17.95%) 7 6 / 39 (15.38%) 6	22 / 30 (73.33%) 22 16 / 30 (53.33%) 16 11 / 30 (36.67%) 11 13 / 30 (43.33%) 13 7 / 30 (23.33%) 7 4 / 30 (13.33%) 4 8 / 30 (26.67%) 8	17 / 23 (73.91%) 17 10 / 23 (43.48%) 10 0 / 23 (0.00%) 0 4 / 23 (17.39%) 4 6 / 23 (26.09%) 6 2 / 23 (8.70%) 2 0 / 23 (0.00%) 0

subjects affected / exposed occurrences (all)	5 / 39 (12.82%) 5	0 / 30 (0.00%) 0	3 / 23 (13.04%) 3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed occurrences (all)	10 / 39 (25.64%) 10	4 / 30 (13.33%) 4	5 / 23 (21.74%) 5
Neutropenia			
subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 30 (0.00%) 0	0 / 23 (0.00%) 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed occurrences (all)	11 / 39 (28.21%) 11	7 / 30 (23.33%) 7	7 / 23 (30.43%) 7
Nausea			
subjects affected / exposed occurrences (all)	15 / 39 (38.46%) 15	10 / 30 (33.33%) 10	8 / 23 (34.78%) 8
Vomiting			
subjects affected / exposed occurrences (all)	6 / 39 (15.38%) 6	6 / 30 (20.00%) 6	3 / 23 (13.04%) 3
Constipation			
subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	6 / 30 (20.00%) 6	4 / 23 (17.39%) 4
Dysphagia			
subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 30 (0.00%) 0	6 / 23 (26.09%) 6
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed occurrences (all)	9 / 39 (23.08%) 9	4 / 30 (13.33%) 4	0 / 23 (0.00%) 0
Cough			
subjects affected / exposed occurrences (all)	4 / 39 (10.26%) 4	6 / 30 (20.00%) 6	2 / 23 (8.70%) 2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed occurrences (all)	6 / 39 (15.38%) 6	7 / 30 (23.33%) 7	4 / 23 (17.39%) 4

Rash subjects affected / exposed occurrences (all)	7 / 39 (17.95%) 7	1 / 30 (3.33%) 1	1 / 23 (4.35%) 1
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 30 (0.00%) 0	3 / 23 (13.04%) 3
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	1 / 30 (3.33%) 1	2 / 23 (8.70%) 2
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	17 / 39 (43.59%) 17	16 / 30 (53.33%) 16	9 / 23 (39.13%) 9
Arthralgia subjects affected / exposed occurrences (all)	8 / 39 (20.51%) 8	4 / 30 (13.33%) 4	0 / 23 (0.00%) 0
Neck Pain subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 30 (0.00%) 0	0 / 23 (0.00%) 0
Infections and infestations Cellulitis subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	0 / 30 (0.00%) 0	0 / 23 (0.00%) 0
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	11 / 39 (28.21%) 11	9 / 30 (30.00%) 9	3 / 23 (13.04%) 3
Blood Creatinine Increased subjects affected / exposed occurrences (all)	8 / 39 (20.51%) 8	0 / 30 (0.00%) 0	2 / 23 (8.70%) 2

Non-serious adverse events	SD-101 8 mg in Anti-PD-1/L1- Experienced HNSCC	SD-101 2 mg in Anti-PD-1/L1-Naïve Melanoma	SD-101 2 mg in Anti-PD-1/L1-Naïve HNSCC
Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 9 (100.00%)	44 / 44 (100.00%)	25 / 27 (92.59%)

Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	4 / 44 (9.09%) 4	1 / 27 (3.70%) 1
Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 9 (44.44%) 4	23 / 44 (52.27%) 23	3 / 27 (11.11%) 3
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	5 / 9 (55.56%) 5	33 / 44 (75.00%) 33	15 / 27 (55.56%) 15
Chills subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	19 / 44 (43.18%) 19	3 / 27 (11.11%) 3
Malaise subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	14 / 44 (31.82%) 14	0 / 27 (0.00%) 0
Injection site erythema subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	17 / 44 (38.64%) 17	1 / 27 (3.70%) 1
Pyrexia subjects affected / exposed occurrences (all)	4 / 9 (44.44%) 4	10 / 44 (22.73%) 10	6 / 27 (22.22%) 6
Influenza Like Illness subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	13 / 44 (29.55%) 13	2 / 27 (7.41%) 2
Injection Site Pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	11 / 44 (25.00%) 11	0 / 27 (0.00%) 0
Injection Site Swelling subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	9 / 44 (20.45%) 9	2 / 27 (7.41%) 2
Blood and lymphatic system disorders Anaemia			

subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	7 / 44 (15.91%) 7	4 / 27 (14.81%) 4
Neutropenia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 44 (2.27%) 1	0 / 27 (0.00%) 0
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	21 / 44 (47.73%) 21	2 / 27 (7.41%) 2
Nausea subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	13 / 44 (29.55%) 13	8 / 27 (29.63%) 8
Vomiting subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	6 / 44 (13.64%) 3	5 / 27 (18.52%) 5
Constipation subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	8 / 44 (18.18%) 8	4 / 27 (14.81%) 4
Dysphagia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 44 (2.27%) 1	5 / 27 (18.52%) 5
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	5 / 44 (11.36%) 5	0 / 27 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	8 / 44 (18.18%) 8	3 / 27 (11.11%) 3
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	14 / 44 (31.82%) 14	2 / 27 (7.41%) 2
Rash subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	11 / 44 (25.00%) 11	2 / 27 (7.41%) 2
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	0 / 44 (0.00%) 0	1 / 27 (3.70%) 1
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	11 / 44 (25.00%) 11	2 / 27 (7.41%) 2
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	18 / 44 (40.91%) 18	1 / 27 (3.70%) 1
Arthralgia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	16 / 44 (36.36%) 16	0 / 27 (0.00%) 0
Neck Pain subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2	1 / 44 (2.27%) 1	0 / 27 (0.00%) 0
Infections and infestations Cellulitis subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	5 / 44 (11.36%) 5	0 / 27 (0.00%) 0
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	11 / 44 (25.00%) 11	3 / 27 (11.11%) 3
Blood Creatinine Increased subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	7 / 44 (15.91%) 7	1 / 27 (3.70%) 1

Non-serious adverse events	SD-101 2 mg in Anti-PD-1/L1 Refractory or Resistant HNSCC	SD-101 2 mg in Anti-PD-1/L1 Refractory or Resistant Melanoma	
Total subjects affected by non-serious adverse events subjects affected / exposed	22 / 23 (95.65%)	31 / 31 (100.00%)	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	

Nervous system disorders			
Headache			
subjects affected / exposed	2 / 23 (8.70%)	9 / 31 (29.03%)	
occurrences (all)	2	9	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 23 (30.43%)	13 / 31 (41.94%)	
occurrences (all)	7	13	
Chills			
subjects affected / exposed	2 / 23 (8.70%)	6 / 31 (19.35%)	
occurrences (all)	2	6	
Malaise			
subjects affected / exposed	2 / 23 (8.70%)	4 / 31 (12.90%)	
occurrences (all)	2	4	
Injection site erythema			
subjects affected / exposed	1 / 23 (4.35%)	4 / 31 (12.90%)	
occurrences (all)	1	4	
Pyrexia			
subjects affected / exposed	6 / 23 (26.09%)	7 / 31 (22.58%)	
occurrences (all)	6	7	
Influenza Like Illness			
subjects affected / exposed	0 / 23 (0.00%)	10 / 31 (32.26%)	
occurrences (all)	0	10	
Injection Site Pain			
subjects affected / exposed	2 / 23 (8.70%)	4 / 31 (12.90%)	
occurrences (all)	2	4	
Injection Site Swelling			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 23 (13.04%)	4 / 31 (12.90%)	
occurrences (all)	3	4	
Neutropenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences (all)	0	0	

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	6 / 31 (19.35%)	
occurrences (all)	0	6	
Nausea			
subjects affected / exposed	0 / 23 (0.00%)	9 / 31 (29.03%)	
occurrences (all)	0	9	
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)	6 / 31 (19.35%)	
occurrences (all)	0	6	
Constipation			
subjects affected / exposed	0 / 23 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	2	
Dysphagia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 23 (8.70%)	6 / 31 (19.35%)	
occurrences (all)	2	6	
Cough			
subjects affected / exposed	1 / 23 (4.35%)	3 / 31 (9.68%)	
occurrences (all)	1	3	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 23 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Rash			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			

Hypothyroidism subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	
Musculoskeletal and connective tissue disorders			
Myalgia subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	2 / 31 (6.45%) 2	
Arthralgia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	3 / 31 (9.68%) 3	
Neck Pain subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	0 / 31 (0.00%) 0	
Infections and infestations			
Cellulitis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 31 (0.00%) 0	
Metabolism and nutrition disorders			
Decreased Appetite subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	3 / 31 (9.68%) 3	
Blood Creatinine Increased subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	0 / 31 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2015	Amendment 1
18 December 2015	Amendment 2
30 March 2016	Amendment 3
23 September 2016	Amendment 4
02 June 2017	Amendment 5
02 April 2018	Amendment 6
22 June 2018	Amendment 7
08 February 2019	Amendment 8
20 November 2019	<p>Amendment 9: the original protocol was amended 9 times.</p> <p>For Protocol Amendment 9 and based on available data from the trial (including efficacy, safety, and pharmacodynamics biomarkers), Cohorts 5 and 6 were CLOSED. Additionally, Cohort 8 (melanoma anti-PD- 1/L1–refractory or resistant) was expanded to approximately 50 patients.</p> <p>Note: As of Protocol Amendment 9, enrollment was closed for all cohorts. Enrolled patients continued to receive their assigned trial treatments as per the protocol. As of Protocol Amendment 9, efficacy and exploratory endpoints were no longer collected. The collection of safety endpoints was simplified.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 April 2020	A strategic restructuring including the planned conclusion of clinical oncology development programs and no further sponsoring of the development of SD-101.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The sponsor terminated the trial early due to strategic restructuring, including the planned conclusion of clinical oncology development programs and no further sponsoring of the development of SD-101.

Notes: