Statement of End of the Study

Name of Company: Adaptimmune LLC

Study No: ADP-0055-002 (EudraCT# 2020-005802-24)

Product: ADP-A2M4CD8

Title: A Phase 2 Open-Label Clinical Trial of ADP-A2M4CD8 in Subjects with Advanced Esophageal or Esophagogastric Junction Cancers

Phase: 2

Study Period: 05-Oct-2021 to 09-Jun-2023

Centers: 3

Number of Subjects: 3

Statement on discontinuation of the study: This phase 2 study was undertaken to further evaluate the efficacy, safety, and tolerability of ADP-A2M4CD8 specifically in subjects with advanced esophageal or gastroesophageal junction (GEJ) cancers. This study was closed early due to difficulty recruiting subjects and lack of efficacy.

Results

Subject Enrollment/Disposition

	Esophageal (N=2) n (%)	Esophagogastric Junction (N=1) n (%)	Overall (N=3) n (%)
Subjects enrolled (ITT population)[a]	2 (100)	1 (100)	3 (100)
Subjects underwent leukapheresis	2 (100)	1 (100)	3 (100)
Subjects lymphodepleted	2 (100)	1 (100)	3 (100)
mITT Population[b]	2 (100)	1 (100)	3 (100)
Subjects Discontinued from Interventional Phase	2 (100)	1 (100)	3 (100)
Primary Reason for Discontinuation from Interventional Phase			
Death[c]	1 (50)	0	1 (33.3)
Disease Progression[c]	1 (50)	1 (100)	2 (66.7)
Subjects Entered LTFU	1 (50)	1 (100)	2 (66.7)
Subjects Completed Study	0	0	0
Subjects Discontinued from Study	2 (100)	1 (100)	3 (100)
Primary Reason for Discontinuation from Study			
Death[c]	2 (100)	1 (100)	3 (100)

[a] The ITT population includes all subjects who were enrolled in the trial.
[b] The mITT population includes all enrolled subjects who received at least one T-cell infusion.
[c] Percentages are calculated using the number of subjects discontinued as the denominator.

Demographic Characteristics (mITT Population)

Parameter	Category/ Statistic	Esophageal (N=2)	Esophagogastric Junction (N=1)	Overall (N=3)
Age at Time of Consent (years)	n	2	1	3
	Mean	68.0	72.0	69.3
	Standard deviation	1.41	-,-	2.52
	Median	68.0	72.0	69.0
	Min, Max	67, 69	72, 72	67, 72
Gender	Male, n (%)	2 (100)	1 (100)	3 (100)
Ethnicity	Not Hispanic or Latino, n (%)	2 (100)	1 (100)	3 (100)
Race	White, n (%)	2 (100)	1 (100)	3 (100)

Baseline Characteristics (Modified Intent-to-Treat Population)

Parameter	Category/ Statistic	Esophageal (N=2)	Esophagogastric Junction (N=1)	Overall (N=3)
Histological Grade	G2 – Moderately differentiated (Intermediate grade), n (%)	2 (100)	1 (100)	3 (100)
Stage of Cancer	Stage IV, n (%)	2 (100)	1 (100)	3 (100)
Time from Initial Diagnosis to Enrolment (months)[a]	n	2	1	3
	Mean	12.2	17.5	14.0
	Standard deviation	3.55	-,-	3.93
	Median	12.2	17.5	14.8
	Min, Max	10, 15	17, 17	10, 17
Time from Initial Diagnosis to T-Cell Infusion (months)[b]	n	2	1	3
	Mean	14.3	19.1	15.9
	Standard deviation	3.62	-,-	3.77
	Median	14.3	19.1	16.8
	Min, Max	12, 17	19, 19	12, 19

Parameter	Category/ Statistic	Esophageal (N=2)	Esophagogastric Junction (N=1)	Overall (N=3)
Histological Grade	G2 – Moderately differentiated (Intermediate grade), n (%)	2 (100)	1 (100)	3 (100)
Stage of Cancer	Stage IV, n (%)	2 (100)	1 (100)	3 (100)
Time from Initial Diagnosis to Enrolment (months)[a]	n	2	1	3
	Mean	12.2	17.5	14.0
	Standard deviation	3.55	-,-	3.93
	Median	12.2	17.5	14.8
	Min, Max	10, 15	17, 17	10, 17
Time from Initial Diagnosis to T-Cell Infusion (months)[b]	n	2	1	3
	Mean	14.3	19.1	15.9
	Standard deviation	3.62	-,-	3.77
	Median	14.3	19.1	16.8
	Min, Max	12, 17	19, 19	12, 19
Prior Lines of Systemic Therapy (continuous)	n	2	1	3
	Mean (standard deviation)	1.5	2.0	1.7
	Standard deviation	0.71	-	0.58
	Median	1.5	2.0	2.0
	Min, Max	1, 2	2, 2	1, 2
Prior Lines of Systemic Therapy (categorical)	1, n (%)	1 (50)	0	1 (33.3)
	2, n (%)	1 (50)	1 (100)	2 (66.7)
Bridging Therapy (categorical)	Yes, n (%)	1 (50)	1 (100)	2 (66.7)
	No, n (%)	1 (50)	0	1 (33.3)
ECOG Score	1, n (%)	2 (100)	1 (100)	3 (100)

Parameter	Category/ Statistic	Esophageal (N=2)	Esophagogastric Junction (N=1)	Overall (N=3)
P Score at Screening	n	2	1	3
	Mean	72.5	100	81.7
	Standard deviation	24.75	-,-	23.63
	Median	72.5	100	90.0
	Min, Max	55, 90	100, 100	55, 100
H Score at Screening	n	2	1	3
	Mean	197.5	300	231.7
	Standard deviation	74.25	-,-	79.11
	Median	197.5	300	250.0
	Min, Max	145, 250	300, 300	145, 300

[a] Time from initial diagnosis to enrollment in months is calculated as: (Enrollment Date - Date of Initial Diagnosis + 1) * (12/365.25).
[b] Time from Initial Diagnosis to T-cell Infusion in months is calculated as: (Date of T-cell Infusion - Date of Initial Diagnosis + 1) * (12/365.25).

Primary Endpoint: ORR per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 by independent radiological assessment committee (IRAC).

No subject images were assessed by the Independent Reviewer due to lack of efficacy observed on Investigator Review. Thus no results are reported.

Secondary Endpoints

Endpoint: Adverse events, including serious adverse events (mITT Population)

	Esophageal (N=2) n (%)	**Esophagogastric Junction (N=1) n (%)**	**Overall (N=3) n (%)**
Subjects with Any Adverse Events	2 (100)	1 (100)	3 (100)
Subjects with Any TEAE	2 (100)	1 (100)	3 (100)
Subjects with Any Related TEAEs[a]	2 (100)	1 (100)	3 (100)
Related to Cyclophosphamide	2 (100)	1 (100)	3 (100)
Related to Fludarabine	2 (100)	1 (100)	3 (100)
Related to T-Cell Infusion	2 (100)	1 (100)	3 (100)
Subjects with Any TEAEs ≥ Grade 3	2 (100)	1 (100)	3 (100)
Subjects with Any ≥ Grade 3 Related TEAEs[a]	1 (50)	1 (100)	2 (66.7)
Related to Cyclophosphamide	1 (50)	1 (100)	2 (66.7)
Related to Fludarabine	1 (50)	1 (100)	2 (66.7)
Related to T-Cell Infusion	0	0	0
Subjects with Any TESAEs	1 (50)	1 (100)	2 (66.7)
Subjects with Any Treatment-Related TESAEs[a]	0	1 (100)	1 (33.3)
Related to Cyclophosphamide	0	0	0
Related to Fludarabine	0	0	0
Related to T-Cell Infusion	0	1 (100)	1 (33.3)
Subjects with Any TEAEs with Fatal Outcome	0	0	0

[a] Related TEAEs/TESAEs: definitely, probably, or possibly related AEs or if the relationship is missing. CTCAE v5.0.

Preferred Term	**Number (%) of Subjects with TEAE (n=3)**				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Any Grade**
Subjects with any TEAEs	3 (100)	3 (100)	3 (100)	2 (66.7)	3 (100)
Vomiting	3 (100)	0	0	0	3 (100)
Cytokine release syndrome	1 (33.3)	1 (33.3)	0	0	2 (66.7)
Dyspnoea	1 (33.3)	0	1 (33.3)	0	2 (66.7)
Lymphocyte count decreased	0	0	0	2 (66.7)	2 (66.7)

Preferred Term	Number (%) of Subjects with TEAE (n=3)				
	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade
Nausea	1 (33.3)	1 (33.3)	0	0	2 (66.7)
Neutrophil count decreased	0	0	0	2 (66.7)	2 (66.7)
Pyrexia	2 (66.7)	0	0	0	2 (66.7)
White blood cell count decreased	0	0	1 (33.3)	1 (33.3)	2 (66.7)
Abdominal pain	1 (33.3)	0	0	0	1 (33.3)
Anaemia	0	0	1 (33.3)	0	1 (33.3)
Anxiety	1 (33.3)	0	0	0	1 (33.3)
Aspartate aminotransferase increased	1 (33.3)	0	0	0	1 (33.3)
Asthenia	0	1 (33.3)	0	0	1 (33.3)
Back pain	1 (33.3)	0	0	0	1 (33.3)
Bronchial hyperreactivity	1 (33.3)	0	0	0	1 (33.3)
Constipation	0	1 (33.3)	0	0	1 (33.3)
Cough	0	1 (33.3)	0	0	1 (33.3)
Cytomegalovirus infection reactivation	0	1 (33.3)	0	0	1 (33.3)
Decreased appetite	1 (33.3)	0	0	0	1 (33.3)
Diarrhoea	1 (33.3)	0	0	0	1 (33.3)
Dysphagia	1 (33.3)	0	0	0	1 (33.3)
Epistaxis	1 (33.3)	0	0	0	1 (33.3)
Fatigue	0	1 (33.3)	0	0	1 (33.3)
Haematemesis	1 (33.3)	0	0	0	1 (33.3)
Insomnia	1 (33.3)	0	0	0	1 (33.3)
Migraine with aura	1 (33.3)	0	0	0	1 (33.3)
Oesophageal haemorrhage	0	0	1 (33.3)	0	1 (33.3)
Platelet count decreased	0	0	1 (33.3)	0	1 (33.3)
Rash maculo-papular	1 (33.3)	0	0	0	1 (33.3)
Respiratory failure	0	0	1 (33.3)	0	1 (33.3)
Rhinorrhoea	1 (33.3)	0	0	0	1 (33.3)
Sciatica	0	1 (33.3)	0	0	1 (33.3)

Preferred Term	Number (%) of Subjects with TEAE (n=3)				
	Grade 1	Grade 1	Grade 1	Grade 1	Grade 1
Tumour pain	1 (33.3)	0	0	0	1 (33.3)

AEs were coded using MedDRA version 25.0.
Subjects were counted once for each preferred term under the most severe grade. AEs with missing severity were included under 'Any Grade' only.

Secondary Endpoint: Incidence, severity, and duration of the AEs of special interest

Cytokine release syndrome:

Maximum Grade	Onset Day	Duration (Days)	SAE	Relationship to Treatment	Anti-IL-6/ IL-6 Receptor
1	2	2	No	T-cell infusion	None
2	4	14	No	T-cell infusion	Tocilizumab
1	2	8	Yes	T-cell infusion	Tocilizumab

No subjects experienced AESIs of prolonged cytopenia or immune effector cell-associated neurotoxicity syndrome.

Secondary Endpoint: Replication competent lentivirus

All tested samples were negative for RCL.

Secondary Endpoint: T-cell clonality and insertional oncogenesis

Not assessed. No subject reached 1-year post-infusion.

Secondary Endpoints (efficacy): Time to response per RECIST v1.1 by IRAC, and by investigator radiological assessment; duration of response per RECIST v1.1 by the IRAC, and by investigator radiological assessment; best overall response per RECIST v1.1 by the IRAC, and by investigator radiological assessment; progression free survival per RECIST v1.1 by the IRAC, and by investigator radiological assessment; overall survival; overall response rate per RECIST v1.1 by investigator radiological assessment.

Due to the lack of response based on Investigator assessment in all 3 subjects, no radiological assessments were performed by IRAC. All 3 subjects had a BOR of stable disease based on Investigator assessment using RECIST v1.1.

Parameter	Category/ Statistic	Esophageal (N=2)	Esophagogastric Junction (N=1)
Progression Free Survival (Weeks)	Median	14.43 (8.14 to 20.71)	8.43 (8.43 to 8.43)
Overall Survival (Weeks)	Median	19.64 (18.57 to 20.71)	29.71 (29.71 to 29.71)

Secondary Endpoint (persistence): Peak expansion (i.e., maximum persistence) and time to peak expansion by responder status and overall

Subject Number	Peak Persistence Value (Copies/µg DNA)	Time to Peak Persistence (Study Day post-infusion)
70059	41432.7	8
70060	135581.5	17
70090	77660	15