ID: A18-15331 APR-246 & Azacitidine for the Treatment of TP53 Mutant Myelodysplastic Syndromes (MDS) NCT03745716

Results Preview

Hide All

Participant Flow

Recruitment Details	
Pre-assignment Details	

Arm/Group Title	Experimental Arm: APR-246 + Azacitidine	Control Arm: Azacitidine	Total (Not public)
Arm/Group Description	APR-246 4.5mg/day (D1-4 of 28 day cycle) Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)	Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)	
Period Title: **Overall Study**			
Started	78	76	154
Completed	75	74	149
Not Completed	3	2	5

Baseline Characteristics

NOTE : A Study Specific Baseline Measure for an Outcome Measure has not been entered.

Arm/Group Title	Experimental Arm: APR-246 + Azacitidine	Control Arm: Azacitidine	Total
Arm/Group Description	APR-246 4.5mg/day (D1-4 of 28 day cycle) Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)	Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)	
Overall Number of Baseline Participants	78	76	154
Baseline Analysis Population Description	ITT		

Age, Categorical Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	78 participants		76 participants		154 participants	
	<=18 years	0	0%	0	0%	0	0%
	Between 18 and 65 years	22	28.21%	22	28.95%	44	28.57%
	>=65 years	56	71.79%	54	71.05%	110	71.43%
Age, Continuous Median (Full Range) Unit of measure: years	Number Analyzed	78 participants		76 participants		154 participants	
		69 (34 to 90)		69.5 (29 to 86)		69 (29 to 90)	
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	78 participants		76 participants		154 participants	
	Female	36	46.15%	29	38.16%	65	42.21%
	Male	42	53.85%	47	61.84%	89	57.79%
Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	78 participants		76 participants		154 participants	
	American Indian or Alaska Native	0	0%	0	0%	0	0%
	Asian	1	1.28%	2	2.63%	3	1.95%
	Native Hawaiian or Other Pacific Islander	0	0%	0	0%	0	0%
	Black or African	1	1.28%	4	5.26%	5	3.25%

	American			
	White	61 78.21%	58 76.32%	119 77.27%
	More than one race	0 0%	0 0%	0 0%
	Unknown or Not Reported	15 19.23%	12 15.79%	27 17.53%
Region of Enrollment Measure Type: Number Unit of measure: participants	Number Analyzed	78 participants	76 participants	154 participants
United States		65	67	132
France		13	9	22

Outcome Measures

1. Primary Outcome

Title:	Complete Response Rate (CR)
▼ Description:	To compare the complete response rate, defined as the proportion of patients who achieve complete remission (CR) with APR 246 + azacitidine treatment vs. azacitidine only.
Time Frame:	Data Cut-off 07 APR 2021

▼ Outcome Measure Data ✓

▼ Analysis Population Description
ITT

Arm/Group Title	Experimental Arm: APR-246 + Azacitidine	Control Arm: Azacitidine
▼ Arm/Group Description:	APR-246 4.5mg/day (D1-4 of 28 day cycle) Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)	Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)
Overall Number of Participants Analyzed	78	76
Measure Type: Count of Participants Unit of Measure: participants	27 34.62%	17 22.37%

Adverse Events

Time Frame	Data Cut-off 07 APR 2021	
Adverse Event Reporting Description	Treatment-Emergent Adverse Events (TEAEs) were defined as adverse events that occurred after the first dose of study medication up to 30 days after last dose. National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 is used to grade severity of TEAEs. Severity Grade: 1=Mild, 2=Moderate, 3=Severe, 4=Life-Threatening, 5= Fatal. SAE and AE data reported for Safety Evaluable population. (Experimental Arm n=76; Control Arm n=61).	
Source Vocabulary Name for Table Default	MedDRA (22.1)	
Collection Approach for Table Default	Systematic Assessment	
Arm/Group Title	Experimental Arm: APR-246 + Azacitidine	Control Arm: Azacitidine
▼ Arm/Group Description	APR-246 4.5mg/day (D1-4 of 28 day cycle) Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)	Azacitidine 75mg/m2 (D4-D10 of 28 day cycle)

All-Cause Mortality

	Experimental Arm: APR-246 + Azacitidine	**Control Arm: Azacitidine**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	46/78 (58.97%)	36/76 (47.37%)

▼ **Serious Adverse Events**

	Experimental Arm: APR-246 + Azacitidine	**Control Arm: Azacitidine**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	53/76 (69.74%)	38/61 (62.3%)
Blood and lymphatic system disorders		
Anemia † A	0/76 (0%)	2/61 (3.28%)
Febrile bone marrow aplasia † A	1/76 (1.32%)	0/61 (0%)
Febrile neutropenia † A	25/76 (32.89%)	14/61 (22.95%)
Thrombocytopenia † A	0/76 (0%)	2/61 (3.28%)
Cardiac disorders		
Atrial fibrillation † A	0/76 (0%)	1/61 (1.64%)
Atrial flutter † A	1/76 (1.32%)	1/61 (1.64%)
Cardiac failure † A	0/76 (0%)	1/61 (1.64%)

Cardiac failure acute †A	1/76 (1.32%)	0/61 (0%)
Myocardial infarction †A	1/76 (1.32%)	0/61 (0%)
Myocarditis †A	1/76 (1.32%)	0/61 (0%)
Pericarditis †A	2/76 (2.63%)	0/61 (0%)
Sinus tachycardia †A	1/76 (1.32%)	0/61 (0%)
Eye disorders		
Vitreous hemorrhage †A	1/76 (1.32%)	0/61 (0%)
Gastrointestinal disorders		
Abdominal pain †A	1/76 (1.32%)	1/61 (1.64%)
Anal fistula †A	1/76 (1.32%)	0/61 (0%)
Ascites †A	1/76 (1.32%)	0/61 (0%)
Colitis †A	1/76 (1.32%)	0/61 (0%)
Dysphagia †A	1/76 (1.32%)	0/61 (0%)
Fecaloma †A	1/76 (1.32%)	0/61 (0%)
Gastrointestinal hemorrhage †A	0/76 (0%)	1/61 (1.64%)
Melaena †A	0/76 (0%)	1/61 (1.64%)
Neutropenic colitis †A	1/76 (1.32%)	0/61 (0%)
Proctalgia †A	1/76 (1.32%)	0/61 (0%)
Small intestinal obstruction †A	0/76 (0%)	1/61 (1.64%)
Upper gastrointestinal hemorrhage †A	0/76 (0%)	1/61 (1.64%)
General disorders		
Asthenia †A	2/76 (2.63%)	0/61 (0%)
General physical health deterioration †A	1/76 (1.32%)	0/61 (0%)
Hypothermia †A	1/76 (1.32%)	0/61 (0%)
Injection site erythema †A	1/76 (1.32%)	0/61 (0%)
Mucosal inflammation †A	0/76 (0%)	1/61 (1.64%)
Pyrexia †A	6/76 (7.89%)	4/61 (6.56%)
Hepatobiliary disorders		
Cholecystitis acute †A	1/76 (1.32%)	0/61 (0%)
Hyperbilirubinemia †A	1/76 (1.32%)	0/61 (0%)
Immune system disorders		
Hemophagocytic lymphohistiocytosis †A	1/76 (1.32%)	0/61 (0%)
Infections and infestations		
Abdominal infection †A	1/76 (1.32%)	0/61 (0%)
Acute sinusitis †A	0/76 (0%)	1/61 (1.64%)
Anal abscess †A	1/76 (1.32%)	0/61 (0%)
Anorectal infection †A	1/76 (1.32%)	0/61 (0%)
Bacterial sepsis †A	1/76 (1.32%)	0/61 (0%)
Bronchopulmonary	0/76 (0%)	1/61 (1.64%)

aspergillosis †A		
Cellulitis †A	2/76 (2.63%)	1/61 (1.64%)
Coronavirus infection †A	2/76 (2.63%)	1/61 (1.64%)
Corynebacterium bacteremia †A	1/76 (1.32%)	0/61 (0%)
Diverticulitis †A	0/76 (0%)	1/61 (1.64%)
Enterobacter infection †A	0/76 (0%)	1/61 (1.64%)
Escherichia bacteremia †A	0/76 (0%)	1/61 (1.64%)
Herpes zoster †A	1/76 (1.32%)	0/61 (0%)
Influenza †A	0/76 (0%)	1/61 (1.64%)
Perirectal abscess †A	1/76 (1.32%)	0/61 (0%)
Pneumonia †A	8/76 (10.53%)	8/61 (13.11%)
Pneumonia fungal †A	1/76 (1.32%)	0/61 (0%)
Pseudomonal bacteremia †A	1/76 (1.32%)	0/61 (0%)
Pseudomonas infection †A	1/76 (1.32%)	0/61 (0%)
Rhinovirus infection †A	1/76 (1.32%)	0/61 (0%)
Sepsis †A	5/76 (6.58%)	4/61 (6.56%)
Septic shock †A	3/76 (3.95%)	1/61 (1.64%)
Sialadenitis †A	1/76 (1.32%)	0/61 (0%)
Sinusitis †A	0/76 (0%)	1/61 (1.64%)
Skin infection †A	1/76 (1.32%)	1/61 (1.64%)
Staphylococcal bacteremia †A	0/76 (0%)	1/61 (1.64%)
Staphylococcal infection †A	0/76 (0%)	1/61 (1.64%)
Thrombophlebitis septic †A	1/76 (1.32%)	0/61 (0%)
Tooth infection †A	1/76 (1.32%)	0/61 (0%)
Urinary tract infection †A	2/76 (2.63%)	0/61 (0%)
Injury, poisoning and procedural complications		
Fall †A	1/76 (1.32%)	2/61 (3.28%)
Subdural hematoma †A	1/76 (1.32%)	0/61 (0%)
Vascular access complication †A	1/76 (1.32%)	0/61 (0%)
Investigations		
Alanine aminotransferase increased †A	1/76 (1.32%)	0/61 (0%)
Electrocardiogram QT prolonged †A	1/76 (1.32%)	0/61 (0%)
Electrocardiogram T wave inversion †A	1/76 (1.32%)	0/61 (0%)
Platelet count decreased	1/76 (1.32%)	1/61 (1.64%)

† A		
Troponin increased † A	1/76 (1.32%)	0/61 (0%)
White blood cell count increased † A	0/76 (0%)	1/61 (1.64%)
Metabolism and nutrition disorders		
Dehydration † A	0/76 (0%)	1/61 (1.64%)
Hypercalcemia † A	1/76 (1.32%)	0/61 (0%)
Hyponatremia † A	0/76 (0%)	1/61 (1.64%)
Musculoskeletal and connective tissue disorders		
Back pain † A	0/76 (0%)	1/61 (1.64%)
Flank pain † A	1/76 (1.32%)	0/61 (0%)
Muscular weakness † A	5/76 (6.58%)	2/61 (3.28%)
Osteoarthritis † A	1/76 (1.32%)	0/61 (0%)
Pain in extremity † A	1/76 (1.32%)	0/61 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adenocarcinoma † A	1/76 (1.32%)	0/61 (0%)
Erythroleukemia † A	1/76 (1.32%)	0/61 (0%)
Myelodysplastic syndrome † A	0/76 (0%)	1/61 (1.64%)
Squamous cell carcinoma † A	1/76 (1.32%)	0/61 (0%)
Nervous system disorders		
Aphasia † A	1/76 (1.32%)	0/61 (0%)
Ataxia † A	1/76 (1.32%)	0/61 (0%)
Cerebellar syndrome † A	1/76 (1.32%)	0/61 (0%)
Cerebral infarction † A	1/76 (1.32%)	1/61 (1.64%)
Dizziness † A	1/76 (1.32%)	0/61 (0%)
Encephalopathy † A	2/76 (2.63%)	0/61 (0%)
Headache † A	1/76 (1.32%)	1/61 (1.64%)
Hemorrhage intracranial † A	1/76 (1.32%)	1/61 (1.64%)
Metabolic encephalopathy † A	1/76 (1.32%)	0/61 (0%)
Sciatica † A	1/76 (1.32%)	0/61 (0%)
Transient ischemic attack † A	0/76 (0%)	1/61 (1.64%)
Psychiatric disorders		
Confusional state † A	3/76 (3.95%)	3/61 (4.92%)
Delirium † A	1/76 (1.32%)	0/61 (0%)
Mental status changes † A	1/76 (1.32%)	0/61 (0%)
Renal and urinary disorders		
Acute kidney injury † A	0/76 (0%)	2/61 (3.28%)

Respiratory, thoracic and mediastinal disorders		
Acute respiratory distress syndrome † A	2/76 (2.63%)	0/61 (0%)
Apnea † A	0/76 (0%)	1/61 (1.64%)
Dyspnea † A	2/76 (2.63%)	0/61 (0%)
Hemothorax † A	1/76 (1.32%)	0/61 (0%)
Hypoxia † A	2/76 (2.63%)	0/61 (0%)
Oropharyngeal pain † A	0/76 (0%)	1/61 (1.64%)
Pneumonitis † A	1/76 (1.32%)	1/61 (1.64%)
Pulmonary oedema † A	0/76 (0%)	1/61 (1.64%)
Respiratory distress † A	0/76 (0%)	1/61 (1.64%)
Respiratory failure † A	4/76 (5.26%)	1/61 (1.64%)
Skin and subcutaneous tissue disorders		
Acute febrile neutrophilic dermatosis † A	1/76 (1.32%)	2/61 (3.28%)
Rash maculo-papular † A	0/76 (0%)	1/61 (1.64%)
Vascular disorders		
Hypertension † A	1/76 (1.32%)	0/61 (0%)
Hypotension † A	1/76 (1.32%)	1/61 (1.64%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (22.1)

▼ Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

	Experimental Arm: APR-246 + Azacitidine	**Control Arm: Azacitidine**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	76/76 (100%)	61/61 (100%)
Blood and lymphatic system disorders		
Anemia † A	33/76 (43.42%)	27/61 (44.26%)
Febrile neutropenia † A	31/76 (40.79%)	16/61 (26.23%)
Neutropenia † A	16/76 (21.05%)	17/61 (27.87%)
Thrombocytopenia † A	18/76 (23.68%)	13/61 (21.31%)
Gastrointestinal disorders		
Abdominal pain † A	7/76 (9.21%)	9/61 (14.75%)
Constipation † A	48/76 (63.16%)	32/61 (52.46%)
Diarrhea † A	23/76 (30.26%)	17/61 (27.87%)
Nausea † A	51/76 (67.11%)	21/61 (34.43%)
Stomatitis † A	12/76 (15.79%)	5/61 (8.2%)

Vomiting †A	40/76 (52.63%)	8/61 (13.11%)
General disorders		
Chills †A	12/76 (15.79%)	10/61 (16.39%)
Fatigue †A	30/76 (39.47%)	20/61 (32.79%)
Injection site reaction †A	16/76 (21.05%)	17/61 (27.87%)
Oedema peripheral †A	18/76 (23.68%)	14/61 (22.95%)
Pyrexia †A	21/76 (27.63%)	17/61 (27.87%)
Infections and infestations		
Pneumonia †A	10/76 (13.16%)	9/61 (14.75%)
Injury, poisoning and procedural complications		
Contusion †A	4/76 (5.26%)	10/61 (16.39%)
Fall †A	9/76 (11.84%)	5/61 (8.2%)
Investigations		
Lymphocyte count decreased †A	14/76 (18.42%)	6/61 (9.84%)
Neutrophil count decreased †A	34/76 (44.74%)	23/61 (37.7%)
Platelet count decreased †A	25/76 (32.89%)	26/61 (42.62%)
White blood cell count decreased †A	31/76 (40.79%)	29/61 (47.54%)
Metabolism and nutrition disorders		
Decreased appetite †A	17/76 (22.37%)	11/61 (18.03%)
Hypoalbuminaemia †A	15/76 (19.74%)	5/61 (8.2%)
Hypokalemia †A	18/76 (23.68%)	12/61 (19.67%)
Hyponatremia †A	12/76 (15.79%)	8/61 (13.11%)
Hypophosphatemia †A	14/76 (18.42%)	5/61 (8.2%)
Musculoskeletal and connective tissue disorders		
Arthralgia †A	7/76 (9.21%)	9/61 (14.75%)
Back pain †A	10/76 (13.16%)	5/61 (8.2%)
Muscular weakness †A	11/76 (14.47%)	5/61 (8.2%)
Nervous system disorders		
Dizziness †A	24/76 (31.58%)	12/61 (19.67%)
Headache †A	24/76 (31.58%)	13/61 (21.31%)
Paresthesia †A	14/76 (18.42%)	5/61 (8.2%)
Tremor †A	14/76 (18.42%)	1/61 (1.64%)
Psychiatric disorders		
Anxiety †A	11/76 (14.47%)	9/61 (14.75%)
Confusional state †A	11/76 (14.47%)	14/61 (22.95%)
Insomnia †A	10/76 (13.16%)	9/61 (14.75%)
Respiratory, thoracic and mediastinal disorders		

Cough † A	16/76 (21.05%)	10/61 (16.39%)
Dyspnea † A	14/76 (18.42%)	13/61 (21.31%)
Skin and subcutaneous tissue disorders		
Pruritus † A	12/76 (15.79%)	5/61 (8.2%)
Rash † A	12/76 (15.79%)	8/61 (13.11%)
Vascular disorders		
Hypertension † A	11/76 (14.47%)	4/61 (6.56%)
Hypotension † A	7/76 (9.21%)	11/61 (18.03%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (22.1)

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact

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