

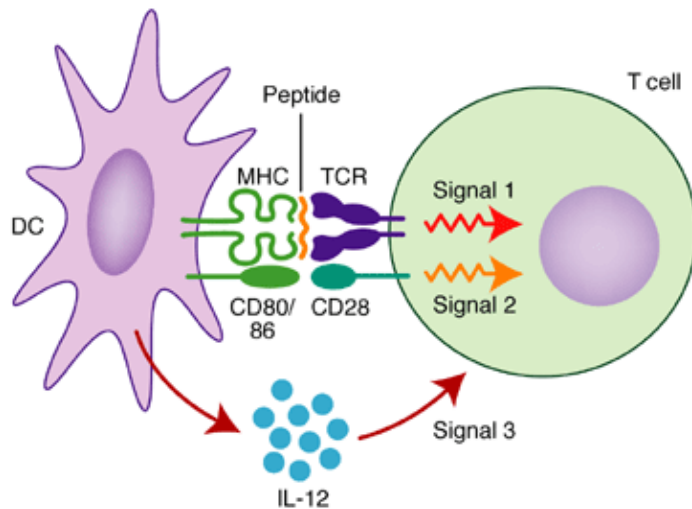
Long-term Follow-up of Patients with Acute Myelogenous Leukemia Receiving an Autologous Telomerase-based Dendritic Cell Vaccine

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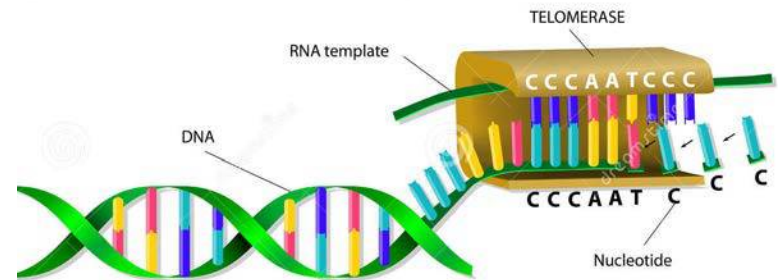
ASCO
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AST-VAC1: Autologous Dendritic Cells Pulsed with hTERT mRNA

Dendritic Cells: Potent Antigen Presenting Cells



Telomerase: “Universal” Tumor Antigen



AST-VAC1 is an immunotherapeutic product that comprises mature DC transfected with mRNA encoding hTERT and the lysosomal targeting signal, LAMP (4,5) - enhances immunostimulatory capacity

Objective: Stimulate Anti-Tumor Immune Responses in Patients with AML

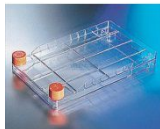
AST-VAC1 Production

Product Release Based on:

- Demonstration of positive hTERT transfection
- Mature Dendritic Cells by immunophenotype
- Product Sterility
- 1×10^7 viable cells/dose post-thaw



Mature Dendritic Cells



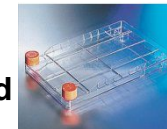
Cryopreserved Autologous DC Vaccine



Leukapheresis Harvest

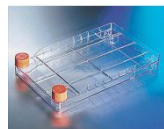


Monocyte Enriched PBMCs



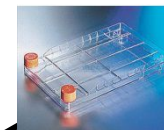
Differentiation

DC Maturation

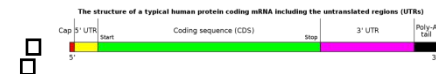


Immature Dendritic Cells

Immature Dendritic Cells



LAMP hTERT mRNA

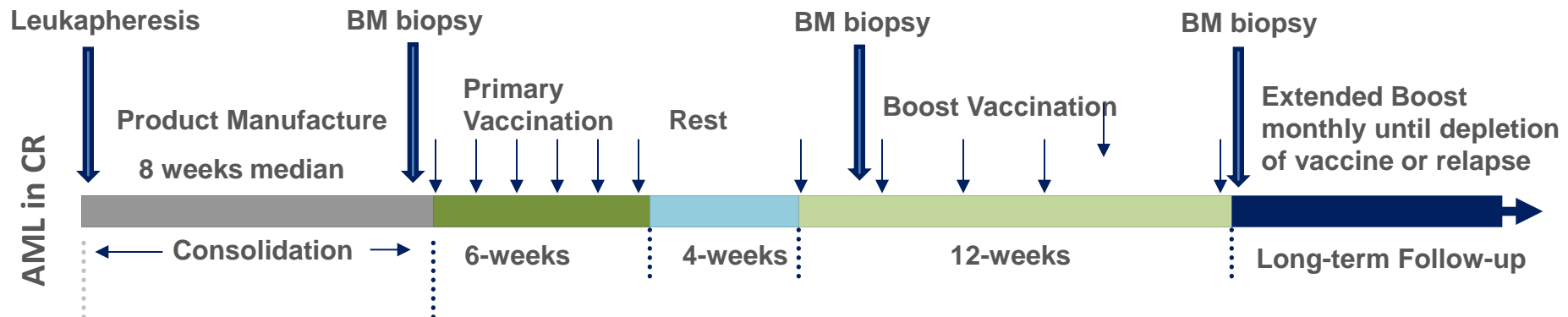


AML Clinical Trial Design and Study Schema: Patient Enrollment 2007-2010

- Multicenter, open-label study.
- Primary Objectives:
 - **Feasibility of manufacture**
 - **Safety and tolerability of vaccine**
- Secondary objectives:
 - **hTERT immunologic response**
 - **Relapse-free survival**

Eligibility Criteria

- 18 years or older
- AML with intermediate or high risk cytogenetics in CR1 within 6 months from induction chemotherapy and may or may not have received consolidation including autologous stem cell transplantation
- AML in CR2 with a CR1 of > 6 months duration
- Exclusion: AML with t(15;17), t(8;-21), inv(16), or t(16:16)], leptomeningeal disease, candidates for allogeneic stem cell transplant within 6 months of screening, documented allergy to penicillin or beta-lactam antibiotics, active or ongoing autoimmune disorder, active second malignancy or history of another malignancy within the last 2 years



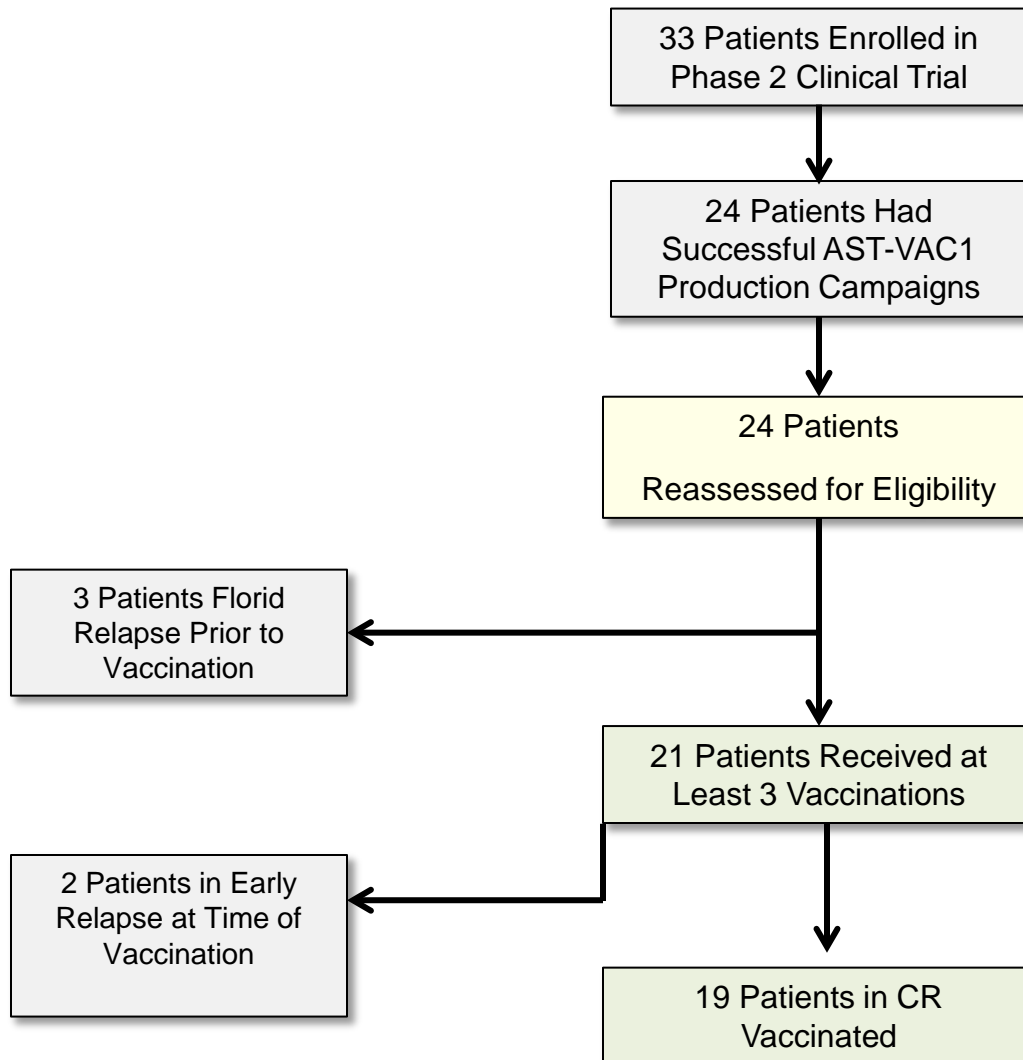
Patient Demographics and Disease Status

Median Follow-up 52 (13-59) mos.

	Total Patients: N=33
Age (years)	
Median	61.2
Mean (SD)	58.3 (11.79)
Min, Max	30.5, 75.4
Sex	
Male	17 (51.5%)
Female	16 (48.5%)
Race	
American Indian or Alaska Native	0
Asian	0
Black or African American	5 (15.2%)
Native Hawaiian or Other Pacific Islander	0
White	28 (84.8%)
Duration from AML Diagnosis to Leukapheresis (months)	
Median	7.1
Mean (SD)	8.9 (7.23)
Min, Max	2.5, 39.3
In First CR at Screening?	
Yes	29 (87.9%)
No	4 (12.1%)

AST-VAC1: Manufacturing Review and Disposition to Patients

AST-VAC1 Successfully Produced for 73% of Patients



- Median Time to Product Release 8 weeks
- Production of AST-VAC1 success in 24 or 33 (73%) AML patients
 - 2 Required a Second Manufacturing Campaign
 - Most common production failures.
 - Low leukapheresis cell numbers
 - Poor DC maturation
 - No telomerase expression
- 5 of 23 (22%) patients relapsed before vaccination of product.

- Mean # Doses Delivered 17.2 (9.7)
- # Patients Receiving All 12 Intended Doses: 13 (14th pt withdrew consent before last dose)

AST-VAC1 in AML: Excellent Safety Profile

**All “Possibly Related”
Adverse Events Occurred
within One Year Post-
Vaccination:
Majority within 100 days**

**21 Total Patients
Received AST-VAC1**

- 16 CR1
- 3 CR2
- 2 Early Relapse

Database Through 2010

Safety and Tolerability

During Leukapheresis:

- No Grade 3-4 Adverse Events

During Vaccination Period:

- Serious Adverse Events Grade 3-4 (2)
 - Possibly Related: Idiopathic thrombocytopenic purpura (1 day 73)
 - Unrelated: Appendicitis with perforation/obstruction, hypokalemia (1)
- Grade 3-4 Adverse Events: 4 patients
 - Unrelated: (4)
 - Cytopenias associated with impending relapse (2)
 - Hypertension (1)
- Grade 1-2 Adverse Events: 14 patients
 - Headache (5)
 - Fatigue (3)
 - Rash (3)
 - Sinus Congestion (3)
 - URI (3)
 - Diarrhea (2)
 - Erythema (2)
 - Hemorrhoids (2)

AST-VAC1 in AML: DTH and hTERT Specific T Cell Responses

hTERT specific T cell responses

19 Total Patients in CR
At Time of AST-VAC1
Administration

- 16 CR1
- 3 CR2

11 of the 19 AML
patients in CR
developed cell immune
responses to telomerase

γ -IFN Elispot used with 90 hTERT
overlapping peptides spanning the
entire hTERT protein*

* In one case , hTERT mRNA transfected
autologous dendritic cells were used to detect
hTERT specific T cell responses.

DTH responses

11 of the 19 AML
patients in CR
developed DTH
responses

Patients self-recorded the presence
and size of induration at the vaccination
site. A patient was considered a DTH
responder if induration of at least 5 mm
(0.2 inches) in diameter at the injection
site was recorded 24 to 72 hours after
the third or subsequent vaccinations.

AST-VAC1 in AML: Kinetics of Development of Detectable hTERT Specific T Cell Responses

hTERT Specific T Cells Responses Were First Detected in the Primary Vaccination, Rest, or Boost Phases

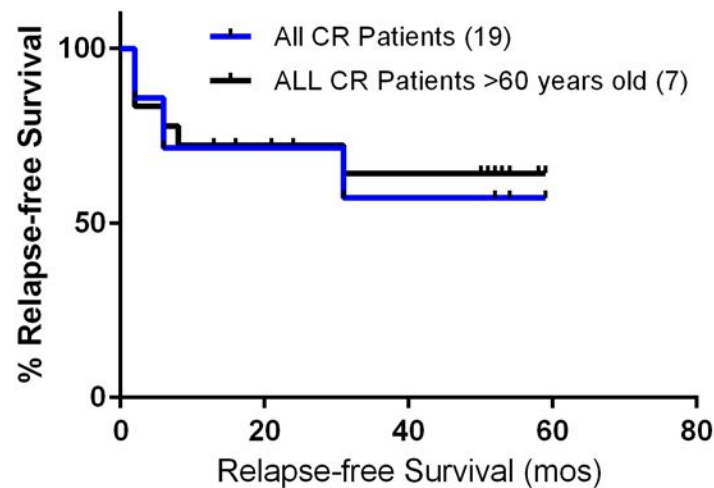
ID	Age	Status at Start of Vaccination	Detection of Positive hTERT Specific T cell Responses Timepoints Post Vaccination			
			Any Timepoint	Primary Vaccinations	Rest	Boost Vaccinations
1641	33	CR1	+	+	-	+
2141	37	CR1	+	-	-	+
2411	41	CR1	-	-	-	-
1541*#	43	CR1	+	-	+	-
2021	48	CR1	-	-	-	-
1911*	50	CR1	-	-	-	-
3432	52	CR2	+	+	-	-
2741	54	CR1	-	-	-	-
3051	54	CR1	+	+	-	+
1711	54	CR2	-	-	-	-
0221*	55	CR1	-	-	-	-
2221	57	CR1	-	-	-	-
3531	61	CR1	+	-	-	+
0321	61	CR1	-	-	-	-
3951*	63	CR1	+	-	+	+
2531	65	CR1	+	+	+	+
2831	66	CR1	+	+	-	+
0421	72	CR2	+	+	-	-
1012*	75	CR1	+	+	-	-

*: terminated during vaccination stage #DC based ELISpot Used.

Long-term Relapse Status: Greater Than 50% Of Patients Relapse-free (median 52 +/- 17 months)

Favorable Outcome Compared to Historical Data Especially in Patients Over 60 years old where 5 year relapse-free survival <10%

	Long-term Follow-up (2013-2014)		
	% Patients Relapse-free***	Median (Range) Follow-up (mos)	Relapse-free Patients with hTERT specific T cell responses
All Patients in CR	11/19* (58%)	52 (13-59)	7/11 (64%)
Patients in CR2	3/3** (100%)	50 (24-59)	2/3 (67%)
Patients >60 years old	4 [#] /7 (57%)	54 (52-59)	4/4 (100%)



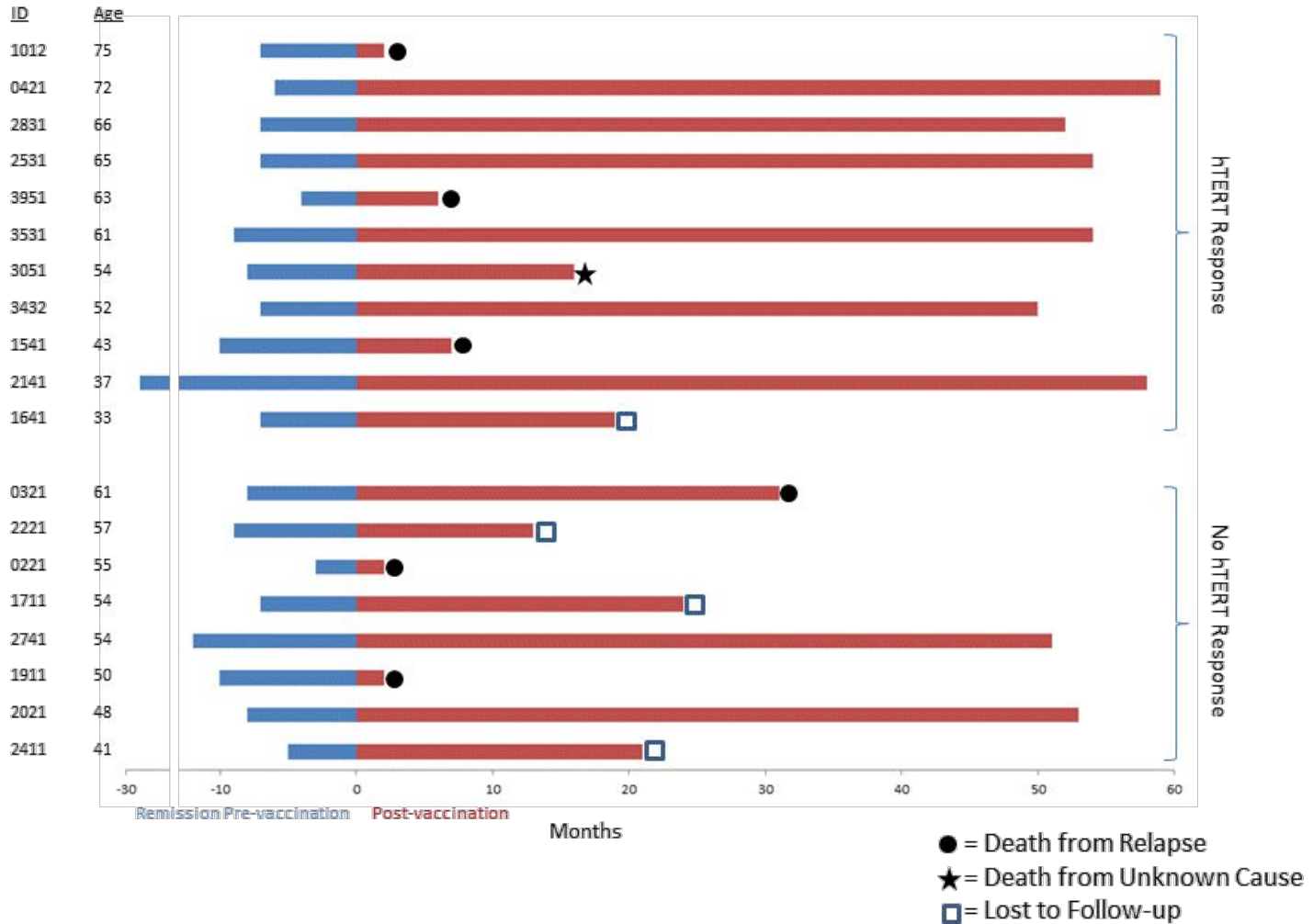
*five patients lost to long-term follow-up or date of relapse unavailable

**One patient lost to long-term follow-up at 24 months

[#] One patient Received nilotinib during vaccination period for a secondary Philadelphia chromosome positive abnormality observed in first relapse which was not observed in the vaccination period

Relapse Free-Survival and hTERT-Immune Response

No Significant Association of Detectable hTERT Immune Responses and Relapse-Free Survival



Summary

- AST-VAC1 Produced for 73% of Patients Enrolled in Trial
- Mean 17.2 Doses AST-VAC1 Delivered per Patient
- 11/19 developed hTERT Specific T cell Responses
- 58% Relapse-free median 52 mos follow-up.
- 4/7 patients >60 years old relapse-free median 54 mos follow-up
- Favorable Survival Compared to Historical Analyses
- Outcome Requires Confirmation in Additional Clinical Trials

Acknowledgements

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“The Patients and their Families”