

Therapeutic and Prophylactic AdE1- LMPpoly-Based Adoptive T cell Immunotherapy for Epstein–Barr Virus- Associated Nasopharyngeal Carcinoma

Corey Smith, AACR Meeting, New Orleans, 2016



Disclosure Information

AACR Meeting 2016

Corey Smith

I have the following financial relationships to disclose:

QIMR Berghofer and Atara Biotherapeutics have entered a licensing agreement for the EBV-polyepitope T cell therapy program

Consultant for: Atara Biotherapeutics



Nasopharyngeal Carcinoma

- Nasopharyngeal Carcinoma (NPC) is Endemic in South-east Asia
- Undifferentiated NPC is associated with Epstein Barr Virus (EBV) infection
- 80,000 new cases annually
- **Stage I Five Year Survival: 80%**
- **Stage III Five Year Survival: 62%**
- **Stage IV Five Year Survival: 38%**



Epstein Barr Virus Associated Cancers

Immunocompetent

Burkitt Lymphoma

Gastric Carcinoma

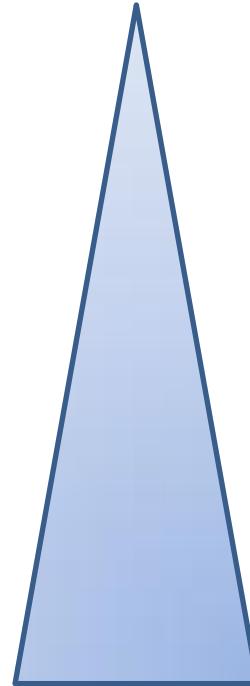
NK/T cell Lymphoma

Nasopharyngeal Carcinoma

Hodgkin Lymphoma

Immunocompromised

Post-transplant
lymphoproliferative disorders



EBNA1

EBNA1; LMP2

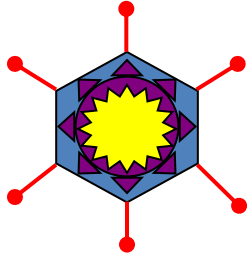
EBNA1;LMP1-2

EBNA1; LMP1-2 EBNA2-6 (+/-)

EBNA1-6; LMP1-2

Latent Antigen Expression

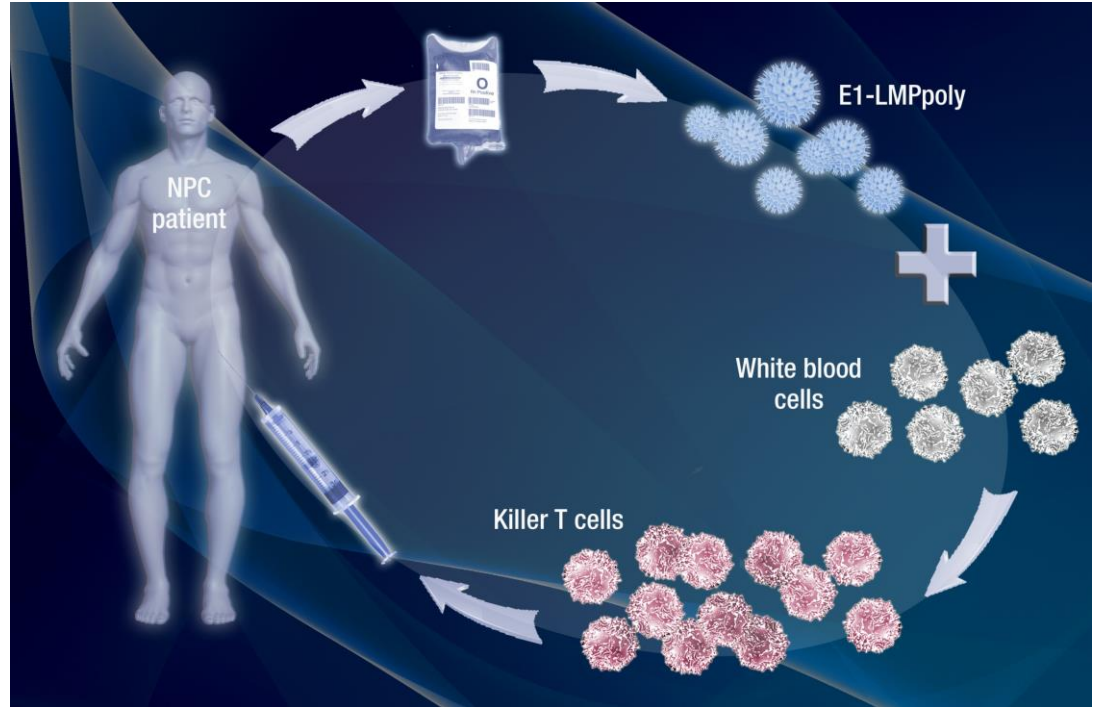
Multiepitope technology: E1-LMPpoly



Adenochimera™



Polyepitope of LMP 1 & 2 HLA class I
CD8+ T cells peptide epitopes
conjugated to a truncated EBNA1
gene and incorporated into
adenoviral vector
(E1-LMPpoly)



Enrolment

NPC Patients assessed for eligibility (n=52)

Withdrawn
(n=6)

Allocation

Allocated to intervention (n=46)

- Received allocated intervention (n=30)
- Did not receive allocated intervention (process failed, n=11; withdrawn, n=5;)

Follow-Up

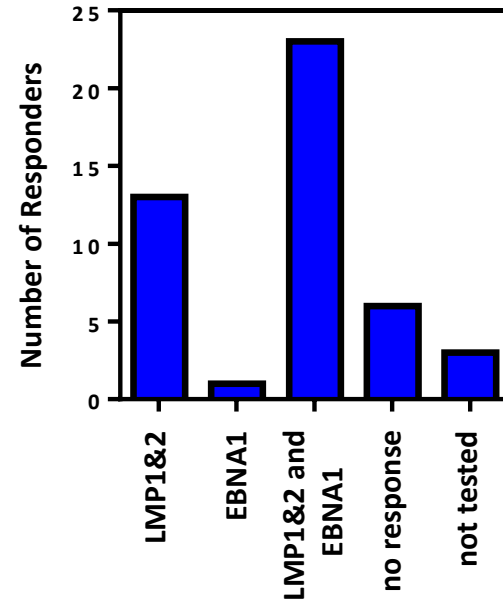
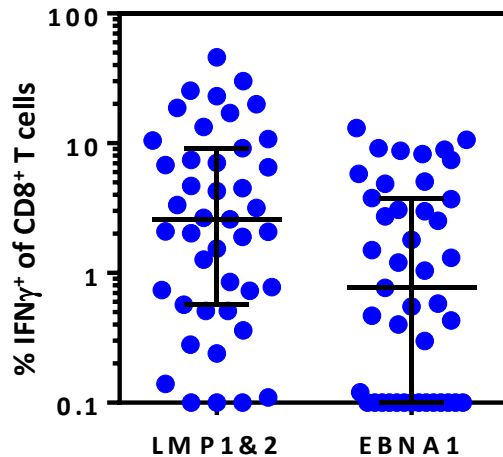
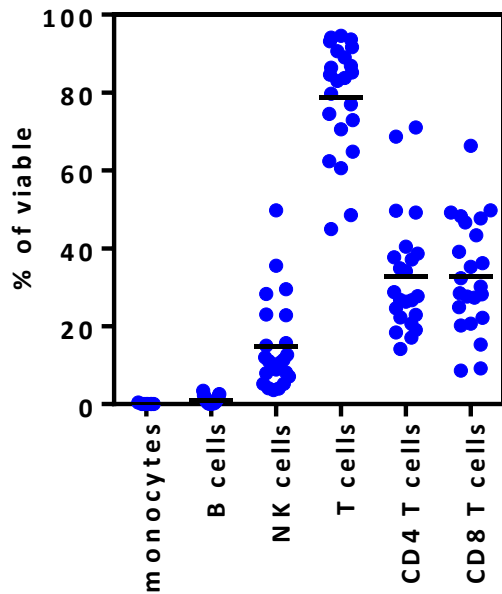
- Lost to follow-up (n=0)
- Discontinued intervention (n=1)

Analysis

- Analysed (n=29)
 - 20 Active Refractory Disease (Active)
 - 9 No Radiographic Disease/Minimal Residual Disease (N/MRD)

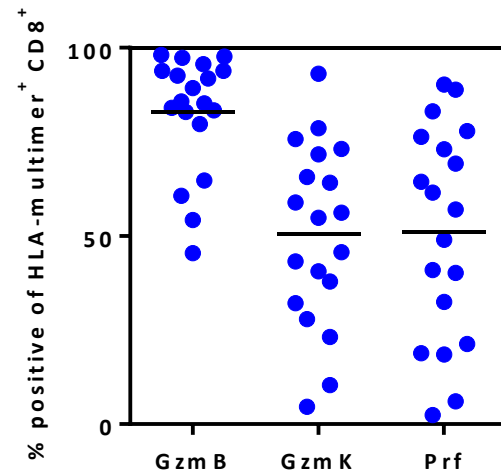
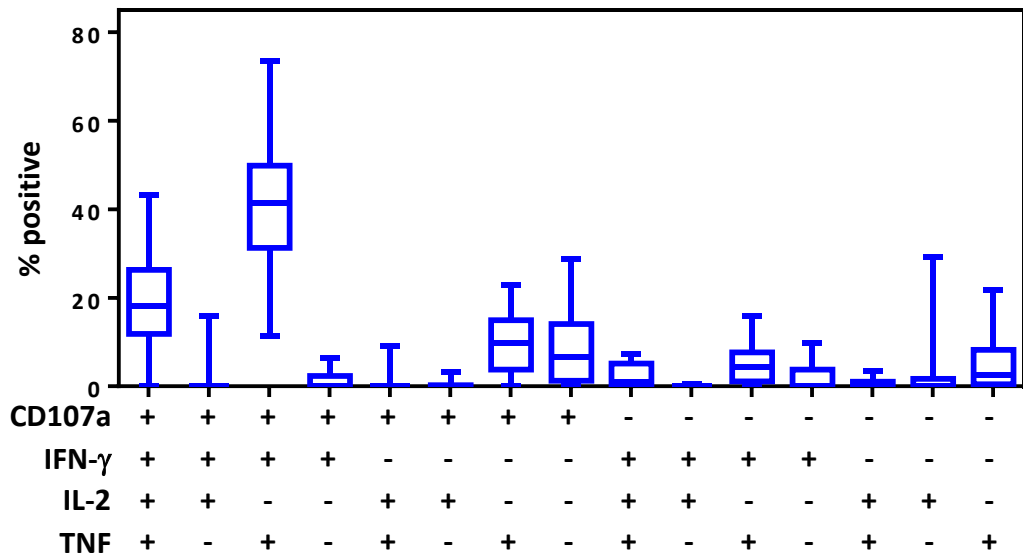


E1-LMPpoly is efficient in expanding LMP1/2 and EBNA1-specific T cells from NPC patients



34/46 (74%) successful T cell expansions

E1-LMPpoly expanded T cells are functionally competent



Treated patient characteristics

	Active	N/MRD
Number of Patients	20	9
Age	Median: 46 (range:34-68)	Median: 49 (range: 22-66)
Sex		
Female	2	1
Male	18	8
Stage on Diagnosis		
I	2	2
II	4	1
III	6	4
IV	8	2
Pre-CTL Chemotherapy Regimes	Median: 3 (range:1-5)	Median: 2 (range:1-4)
History of Recurrent Disease	20	7
Disease at Treatment		
No Radiological disease		9
Local/Neck Nodes	14	
Distal Nodes	3	
Lung Metastases	8	
Liver Metastases	5	
Bone Metastases	5	
Pre-CTL EBV Plasma Load	Median: 2.3×10^3 (range: 0 - 6.3×10^6)	Median: 0

Safety Profile on E1-LMPpoly T cell therapy

Adverse Event	Attribution**		
	Possible	Probable	Definite
Grade 1: Mild			
Fatigue (malaise)	1	0	0
Dry cough	1	0	0
Fever	3	0	0
Chills	1	0	0
Chest pain	1	0	0
Throat pain	1	0	0
Hyperbilirubinaemia	1	0	0
Auditory - other (distorted hearing)	1	0	0
Grade 2: Moderate			
Fever	2	0	0
Fatigue	1	0	0
Dyspnea	1	0	0
Headache	1	0	0
Vomiting	1	0	0
Grade 3: Severe			
Lung abscess	2	0	0

** Number of patients who experienced an adverse event in each attribution category



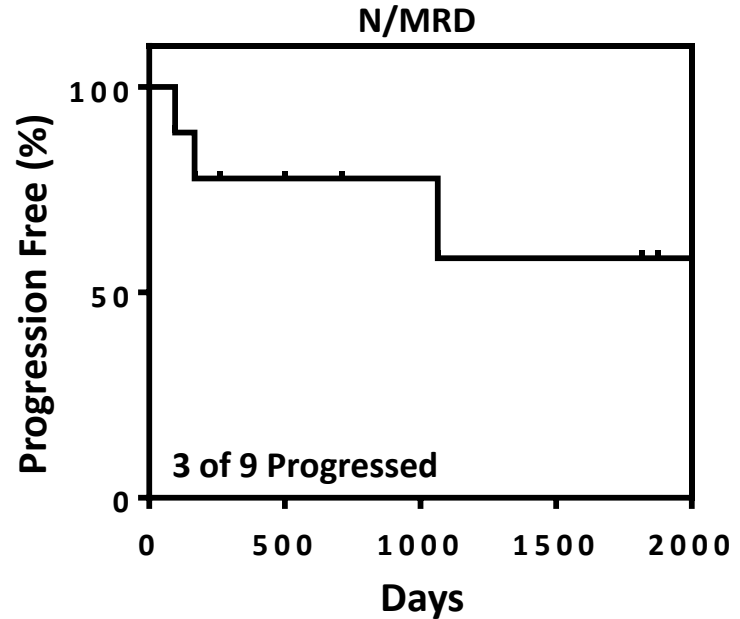
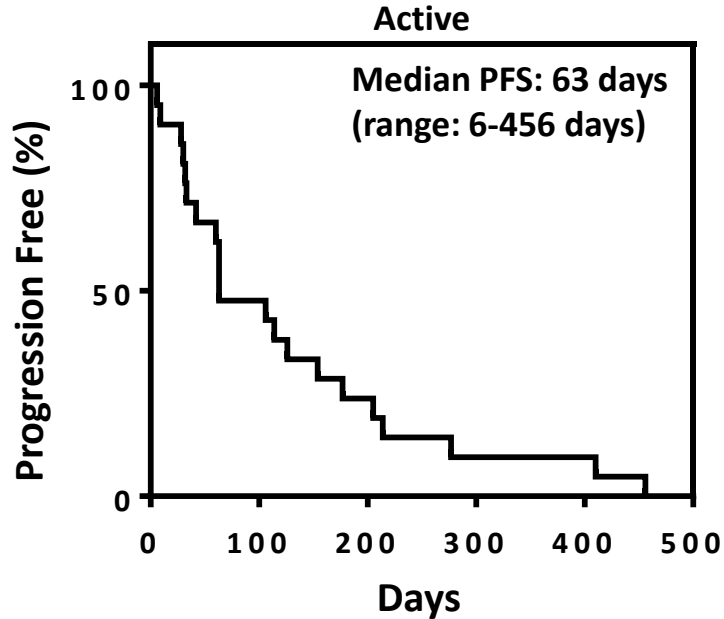
T cell Characteristics and Response to Therapy

	Active	N/MRD
T cell frequency		
LMP1 and 2	Median: 2.08% (range: 0-45.95%)	Median: 7.265% (range: 0.73-23.08%)
EBNA1	Median: 0.470% (range: 0-13.08%)	Median 2.285% (range: 0-8.94%)
Number of Doses	Median: 4 (range:2-6)	Median: 6 (range: 4-6)
Total CTL Dose	Median: 9.2×10^7 (range: 4.9×10^7 - 2.4×10^8)	Median: 1.5×10^8 (range: 1.0×10^8 - 2.4×10^8)
Response to Therapy		
Stable Disease	58%	
Progression Free/Overall Survival		
at 6 months PFS (OS)	24% (90%)	78% (100%)
at 12 months PFS (OS)	10% (70%)	78% (100%)
at 36 months PFS (OS)	0% (19%)	58% (100%)

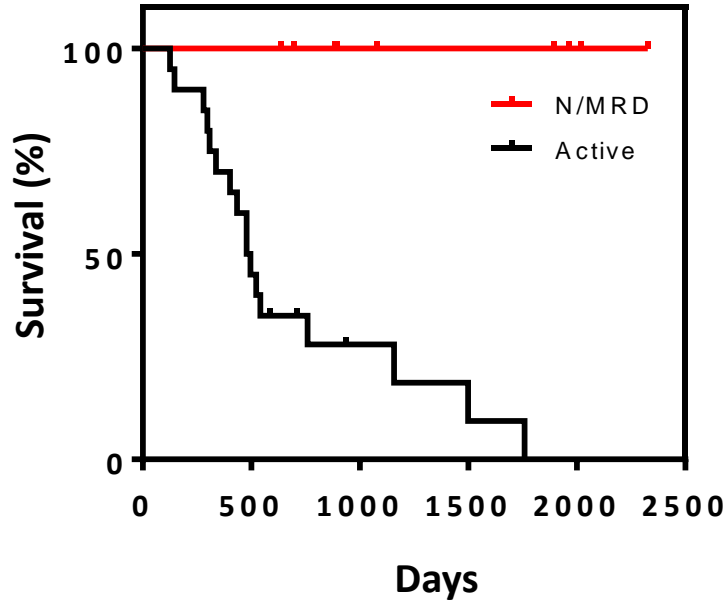
PFS: Progression Free Survival; OS: Overall Survival



Post EBV-specific T cell therapy and Progression-free survival



Post EBV-specific T cell therapy and Overall survival



Active Disease Patients

Median OS: 479 days
(range: 126-1759 days)

The median overall survival for a corresponding active disease cohort during the study period from the same institute was 309 days

Future Directions

- Combination therapy with standard chemotherapy for relapsed metastatic disease (tumour debulking and lymphodepletion)
- Early intervention using EBV plasma DNA monitoring for disease burden monitoring
- “Off the shelf” products to increase patient coverage and maximize T cell frequency and effector function
- E1-LMPpoly as a therapeutic vaccine platform



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