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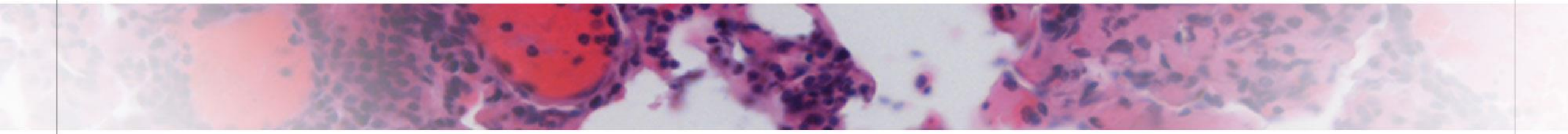

A Phase 1/2 Study of Lentiviral-Mediated Ex-Vivo Gene Therapy for Pediatric Patients with Severe Leukocyte Adhesion Deficiency-I (LAD-I): Interim Results

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Abstract # 2932

Disclosure

- Employee of Rocket Pharmaceuticals, Inc.

Leukocyte Adhesion Deficiency-I (LAD-I)

LAD-I

- Mutations affecting the common chain (CD18) of the beta2-integrin family (*ITGB2* gene) prevent functional CD18/CD11 heterodimer expression on leukocyte cell surfaces - essential for cell adhesion and subsequent migration.
- Severe LAD-I is characterized by ultimately fatal disseminated infections.
- <u>Current Treatment Option</u>: Allogeneic HSCT - limited by donor availability, infections, frequent GvHD and graft failure.

LAD-I Disease Spectrum

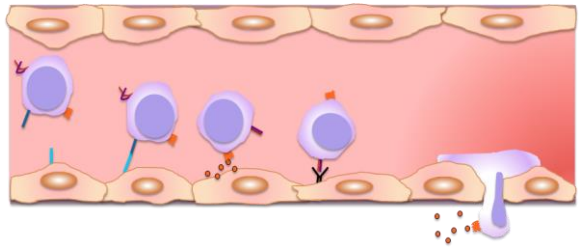
Moderate:
2-30%
CD18+ PMN

Severe:
<2%
CD18+ PMN

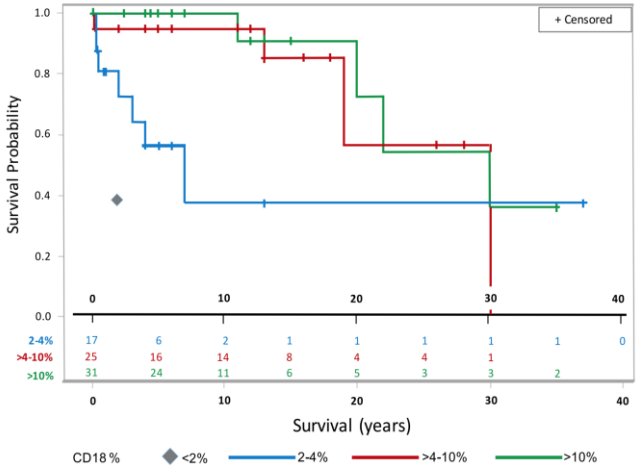
PMN: polymorphonuclear leukocytes

LAD-I Clinical Prognosis

- Patients suffer from recurrent infections; fatal in majority
  - 60-75% pts with severe LAD-I: death **prior to age 2**
  - >50% pts with moderate LAD-I: death **prior age 40**



Kaplan-Meier Survival Estimates by Neutrophil CD18 Expression



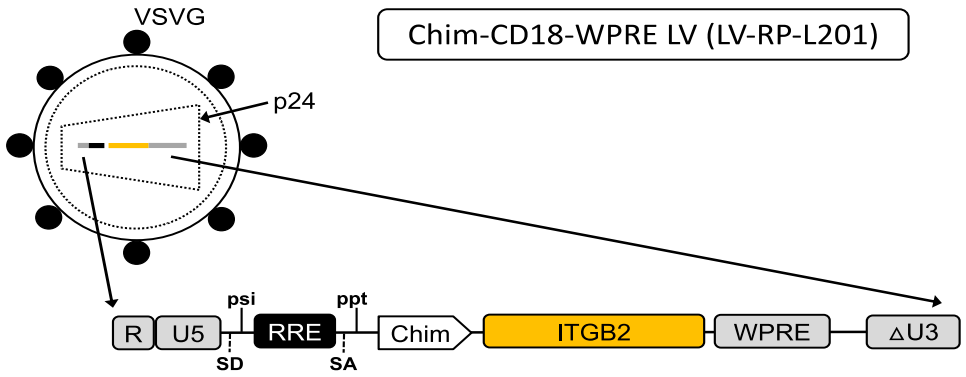
Patients with severe & moderate LAD-I not receiving allogeneic HSCT

◆: 39% survival to age 2 years for 66 evaluable patients with severe LAD-I not receiving HSCT

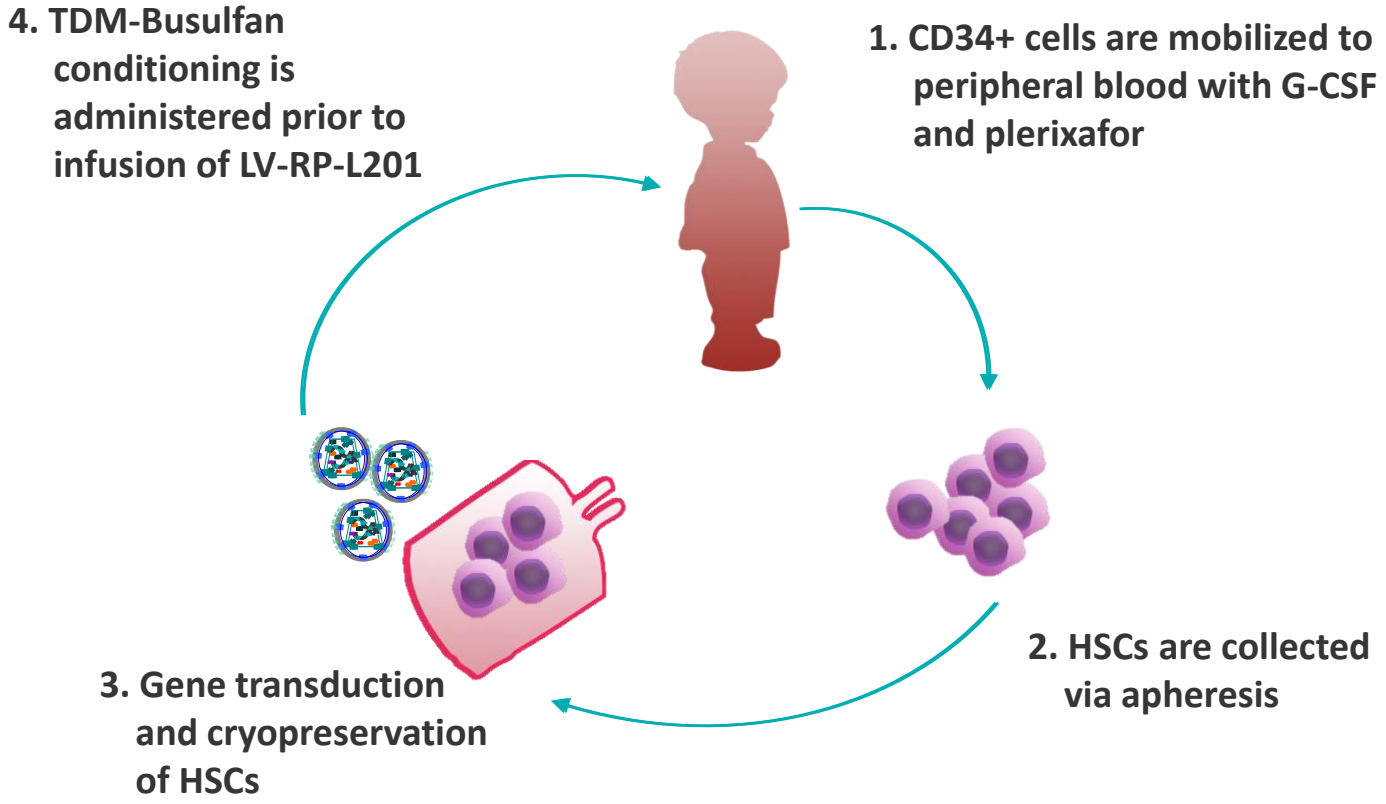
Almarza Novoa E et al. J Allergy Clin Immunol Pract. 2018 July-August (6) 1418-1420.

Gene Therapy for LAD-I: RP-L201

Ex-vivo lentiviral vector gene therapy consists of autologous CD34+ cells transduced with a lentiviral vector (Chim-CD18-WPRE LV) encoding for the CD18 (β-subunit) component of β2-integrin



Developed at CIEMAT, in partnership with UCL



RP-L201 Clinical Trial Design & Outcome Measures

Trial Design

Non-Randomized Global Phase 1/2 Study (n=9)

Primary Outcomes

- **Phase 1:**
  - Safety & preliminary efficacy
- **Phase 2:**
  - Survival: proportion of patients alive at age 2 and at least 1-year post infusion (& not requiring alloHSCT)
  - Safety

Secondary Outcomes

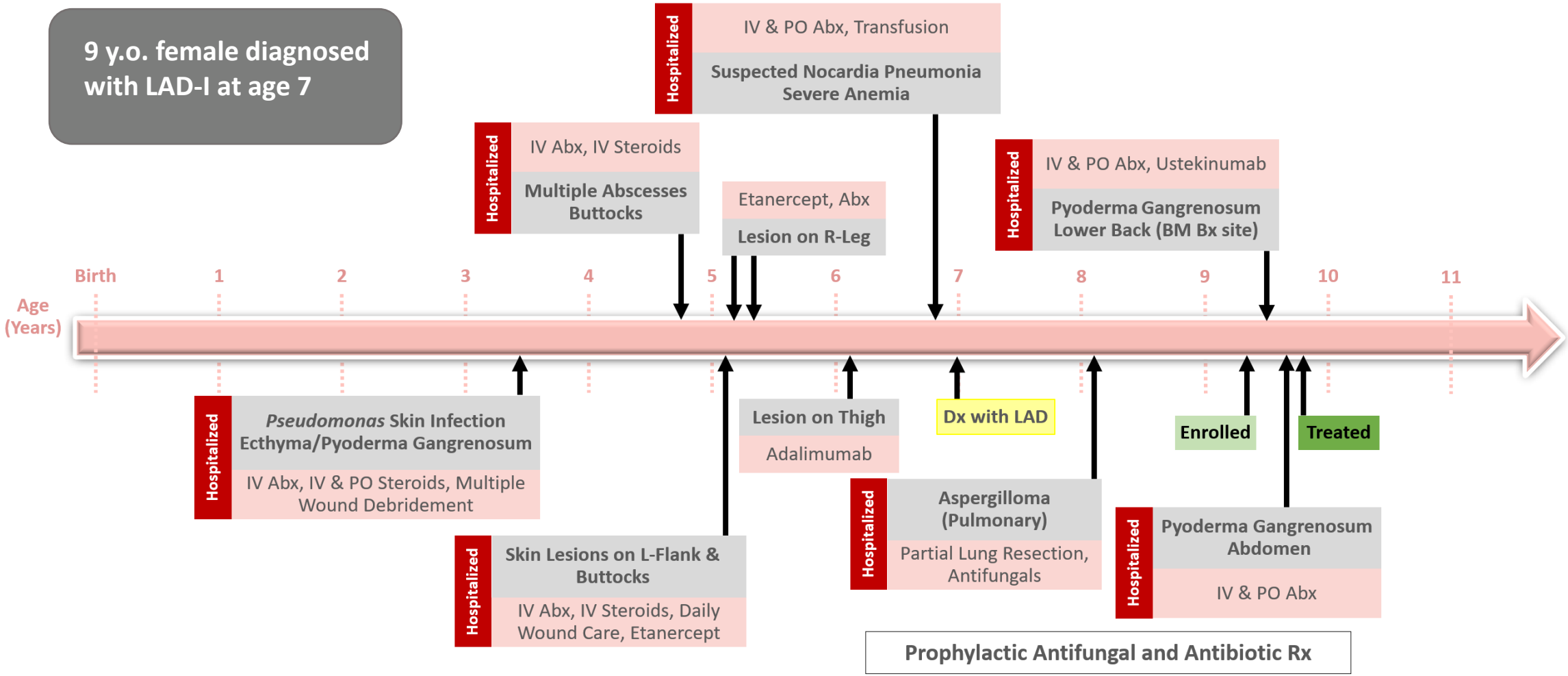
- **Incidence and severity of infections** (e.g., infection hospitalization-free survival, frequency of antimicrobial prophylaxis discontinuation)
- % of pts **w/neutrophil CD18 expression at least 10% of normal**
- % of pts w/neutrophil **VCN** of at least 0.1 copies/cell at 6m post-infusion
- Improvement/**normalization of neutrophilia**
- Resolution (partial or complete) of underlying **skin rash or periodontal abnormalities**

Patient	Sex	Age at enrollment	Drug Product VCN	CD34+ Cell Dose
L201-003-1001	F	9 yrs.	3.8	4.2×10^6 cells/kg
L201-003-1004	F	3 yrs.	2.5	2.8×10^6 cells/kg
L201-003-2005	F	3 yrs.	1.8	6.5×10^6 cells/kg
L201-003-2006	M	7 mo.	2.9	4.3×10^6 cells/kg
L201-003-2007	M	3 mo.	3.6	5.0×10^6 cells/kg
L201-004-2008	M	5 mo.	3.8	3.3×10^6 cells/kg
L201-004-2009	M	3 yrs.	2.0	4.5×10^6 cells/kg
L201-003-2011	F	2 yrs.	3.8	3.8×10^6 cells/kg
L201-002-2010*	F	4 yrs.	3.5	10×10^6 cells/kg

As of December 2021: Data reported from 8 of 9 patients; 3–24m follow-up. *Recent RP-L201 infusion

Clinical Outcome Data

Medical History of Subject L201-003-1001



Historical patient records collected by UCLA Mattel Children's Hospital

Clinical Outcome Data

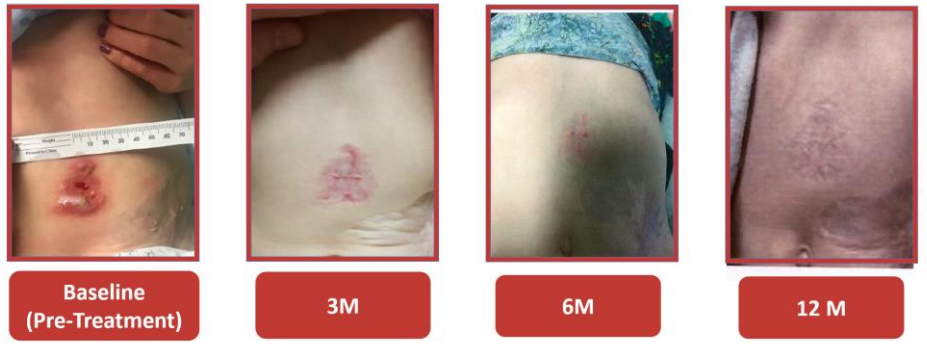
Subject L201-003-1001: 24 Month Follow-Up

Key Drug Product Metrics

CD34+ Cell Dose: 4.2 x 10^6 /kg
Drug Product VCN: 3.8

RP-L201: Skin Lesions Improvements Post-Treatment

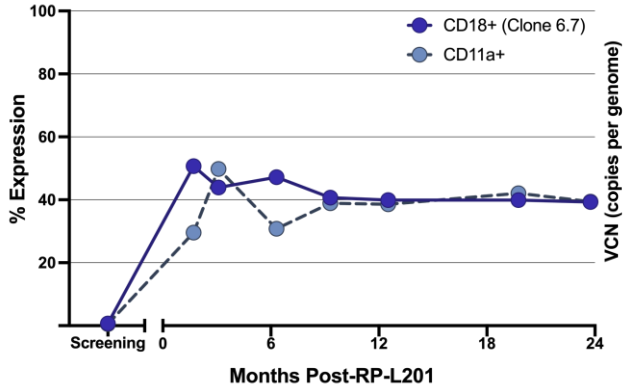
Spontaneous Abdominal Skin Lesion

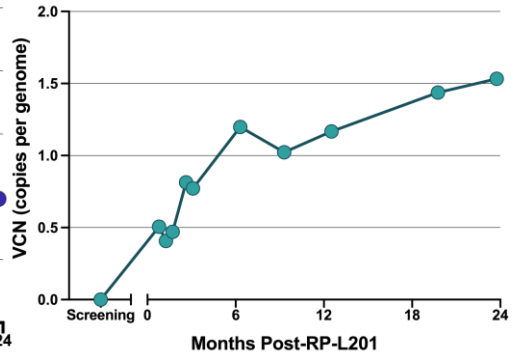


Baseline (Pre-Treatment) | 3M | 6M | 12 M

UCLA Mattel Children's Hospital Data

% CD18 and %CD11a Expression (PMN) In Peripheral Blood and VCN (PBMC)

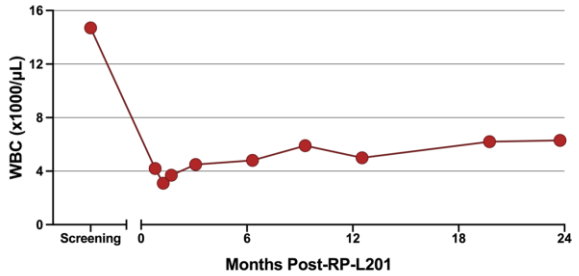




PMN: polymorphonuclear leukocytes

PBMC: peripheral blood mononuclear cell

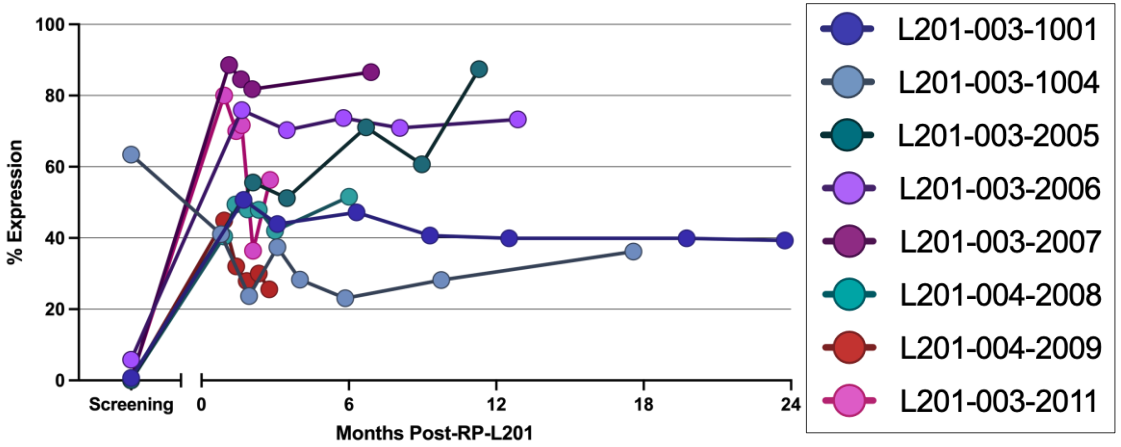
WBC in Peripheral Blood



WBC: White Blood Cells

Clinical Efficacy Overview

% CD18 Expression (PMN) In Peripheral Blood

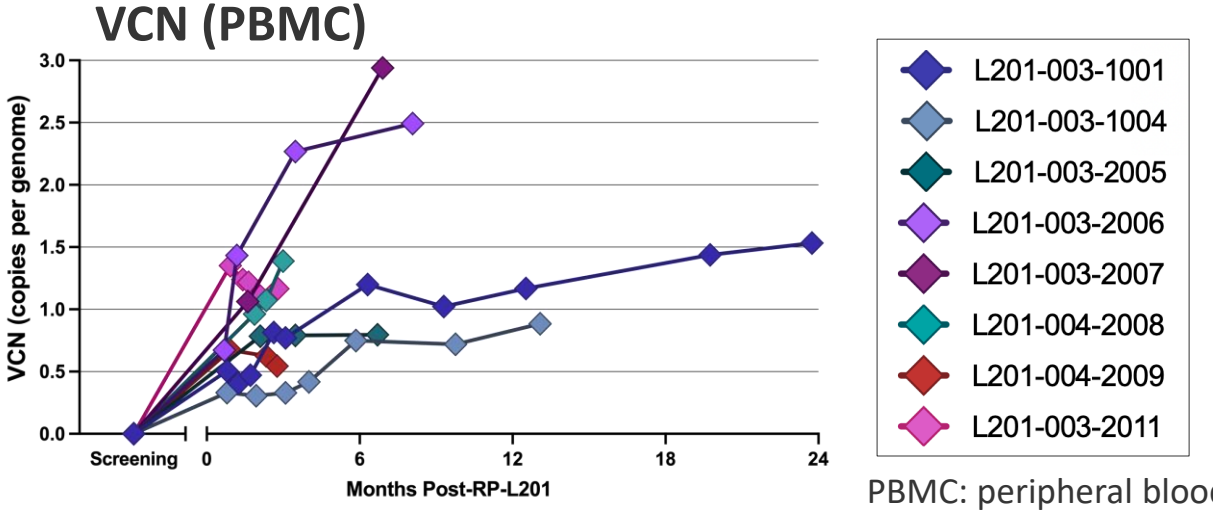


Dim/weak CD18 expression reported at baseline for subject L201-003-1004 in ~63% of cells

PMN: polymorphonuclear leukocytes

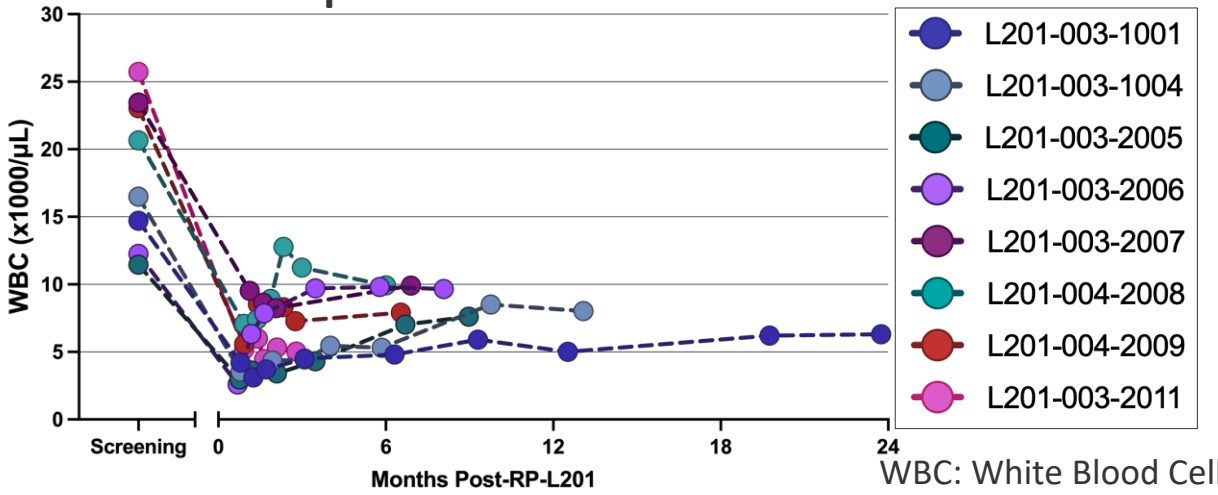
- As of December 2021: Data reported 8/9 patients; 3-24m follow-up
  - One (1/9) subject recently received RP-L201 infusion: L201-003-2010
- Sustained %CD18 expression, VCN integration and leukocytosis resolution

VCN (PBMC)



PBMC: peripheral blood mononuclear cell

WBC in Peripheral Blood



WBC: White Blood Cells

Clinical Safety Overview

As of December 2021, a total of **nine** severe LAD-I patients have been successfully treated with RP-L201. **Data** reported **8/9** patients with 3-24m follow-up available. One (1/9) subject recently received RP-L201 infusion.

- **Neutrophil engraftment** achieved in 8 of 8 reported subjects (<34 days post-infusion)
- A **conditioning-related SAE** reported: Veno-occlusive disease (**VOD**), resolved with no subsequent complication
- A grade 4 **drug-product-unrelated SAE** reported: pulmonary arterial hypertension (**PAH**), considered secondary to busulfan in the context of damaged pulmonary milieu due to severe pre-treatment pneumonias. In addition to severe LAD-I, patient had given double aortic arch associated with tracheal compression.
  - PAH medically improved and given **immune reconstitution,** patient is now scheduled to undergo **surgical correction of double aortic arch**.

RP-L201 Clinical Safety & Efficacy Overview

- **Nine** (9/9) severe LAD-I patients have successfully received RP-L201.
- Infusion has been **well tolerated**; no drug product-related SAEs.
- **Eight** (8/9) reported patients with at least 3 months of follow-up
  One (1/9) patient recently received RP-L201
- Safety profile of RP-L201 appears favorable
- Efficacy evident in **8 of 8** evaluable patients, including **4** patients with **≥ 12 months** of follow-up
  - **Patient L201-003-1001** with durable CD18 (and CD11) PMN expression ~40% at 24 months and PB VCN of 1.53 copies/genome at **24 months** post-infusion, resolution of pre-existing skin lesions, no infections/hospitalizations after hematopoietic reconstitution post RP-L201.
  - **Sustained** >10% **CD18 PMN expression**, >0.1 copies/cell **VCN** integration and leukocytosis resolution across the cohort

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