Results of a Phase 1 Trial of GDA-201 Nicotinamide-Expanded Allogeneic Natural Killer Cells (NAM-NK) in Patients with Refractory Non-Hodgkin Lymphoma (NHL) and Multiple Myeloma (MM)

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Phase 1 Study: Disclosures

- **ClinicalTrials.gov Identifier:** NCT03019666
- **IND sponsor:** V. Bachanova
- Supported by Gamida Cell, Ltd

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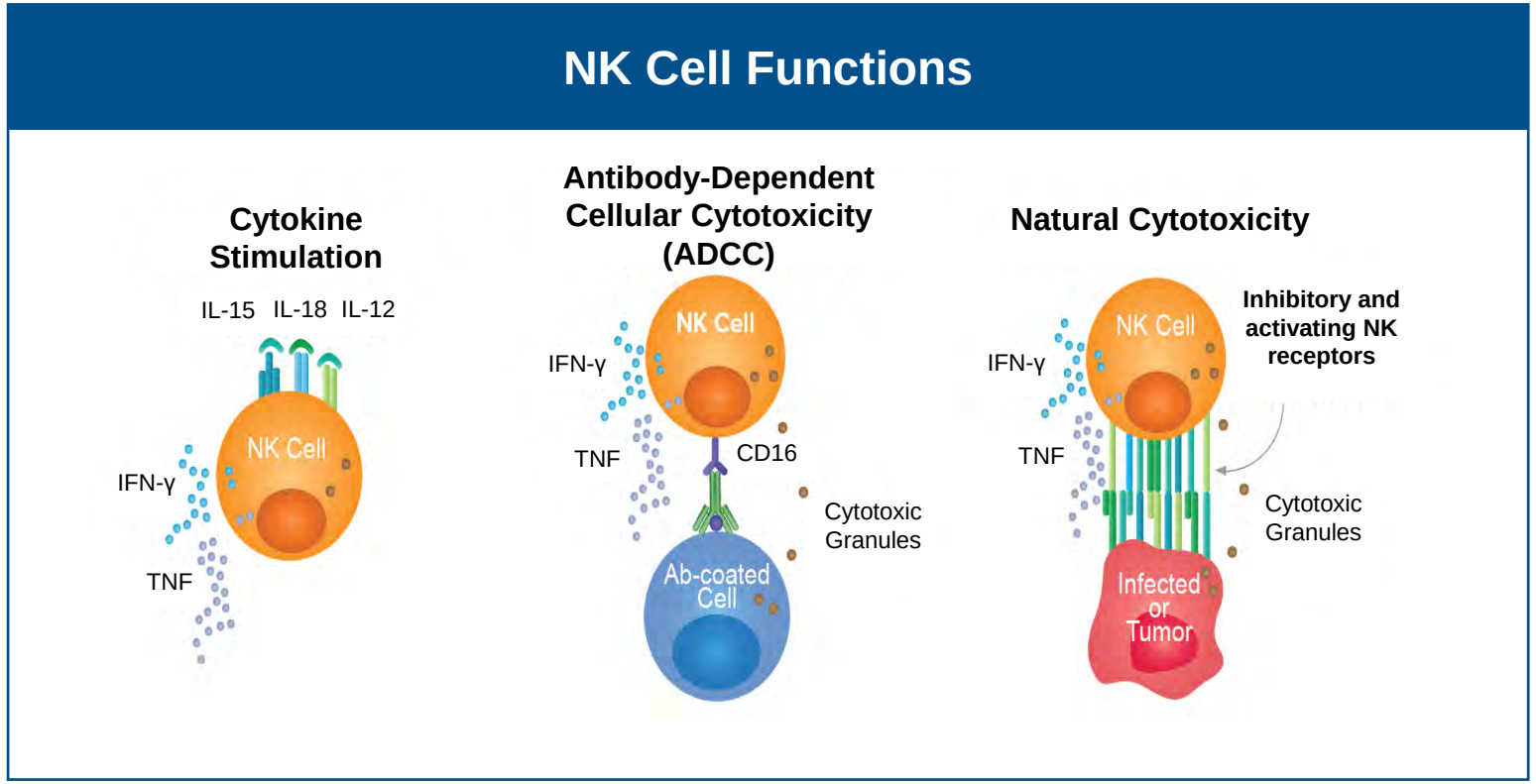
Background: Natural Killer (NK) Cells

- Adoptive transfer of cytolytic NK is an attractive immunotherapeutic approach to the treatment of lymphoma and other malignancies.
- Previous clinical success has been modest due to limited in vivo persistence of NK cells and their impaired effector function.

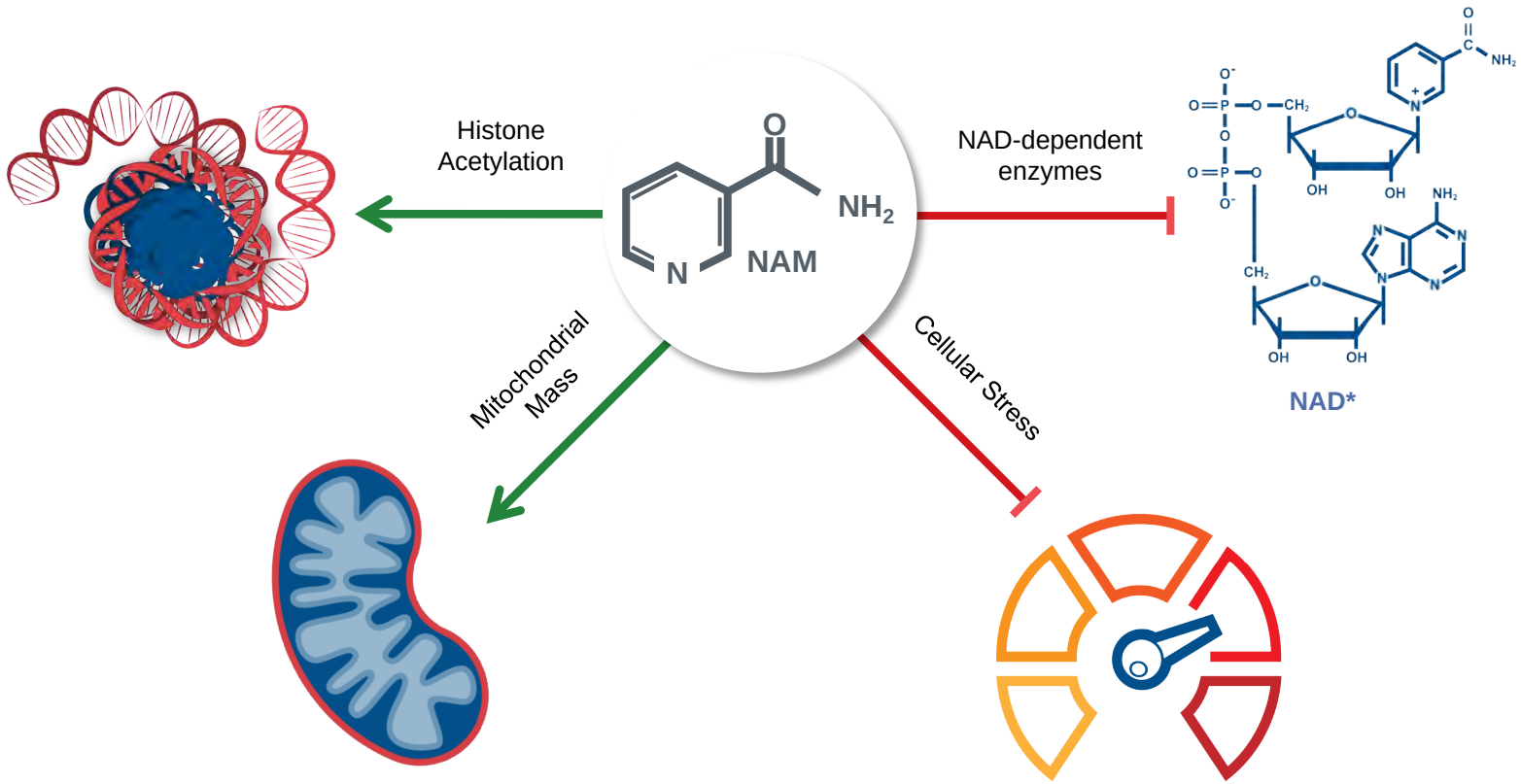


Technology Platform Designed to Enhance the Number and Functionality of Donor Cells in Culture

NAM can expand any cell type, including stem cells and natural killer (NK) cells

Importance of NAM

- Plays a key role in metabolic reprogramming of cells
- Is a master regulator of NAD-related signaling pathways
- Preserves cellular functionality and phenotype during expansion



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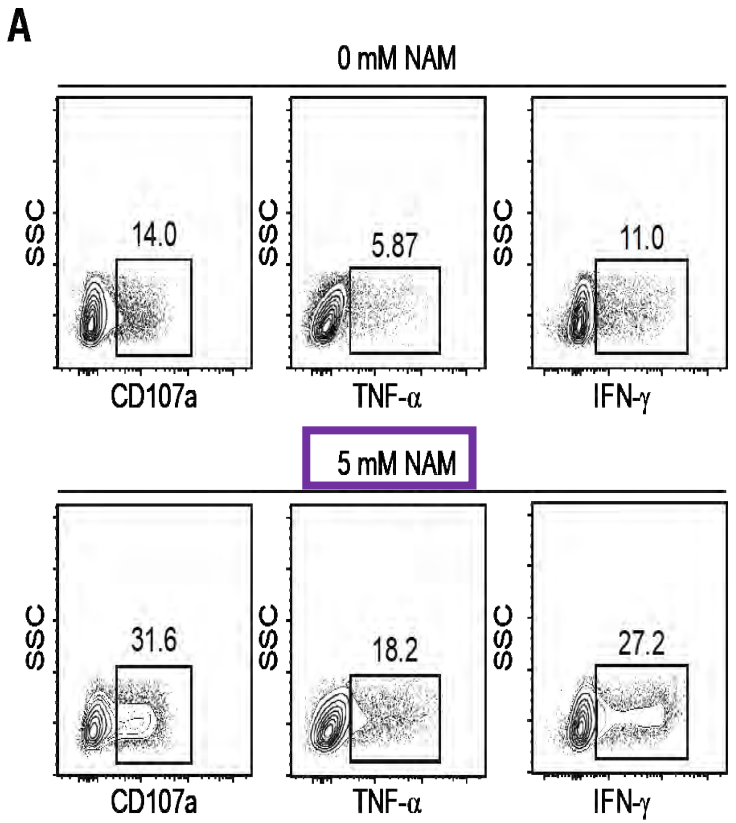
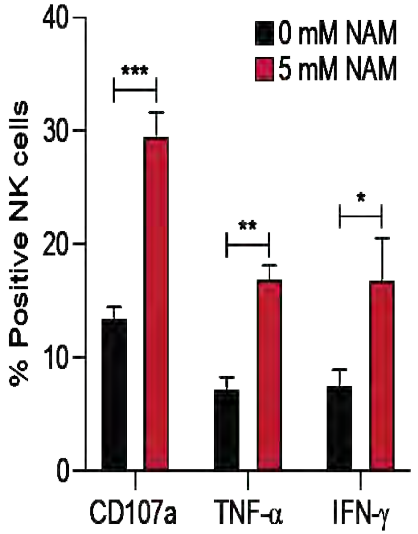
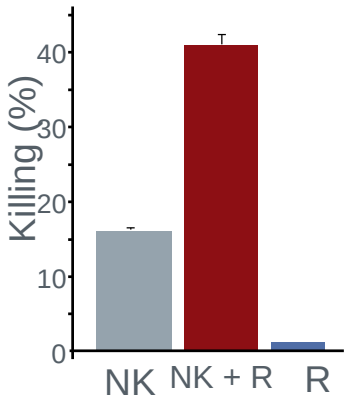
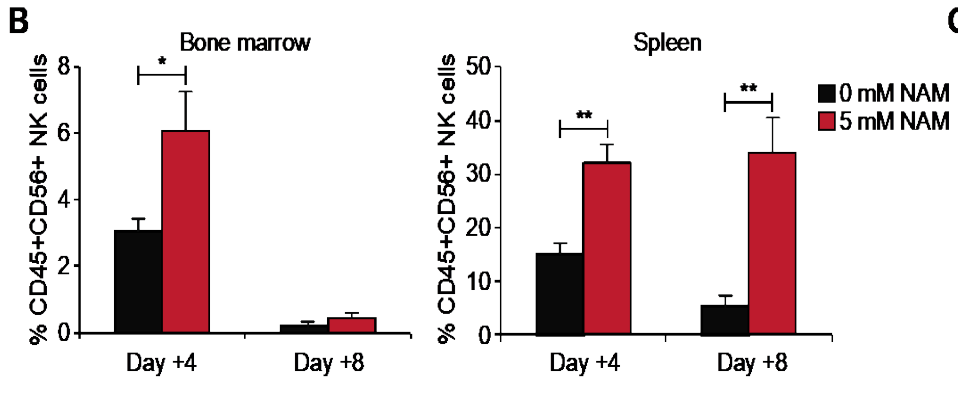
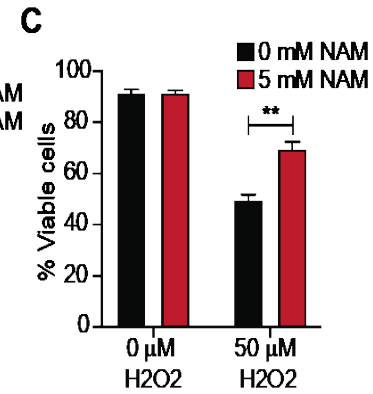
NAM Significantly Enhances Anti-tumor Function of Ex Vivo Expanded NK Cells









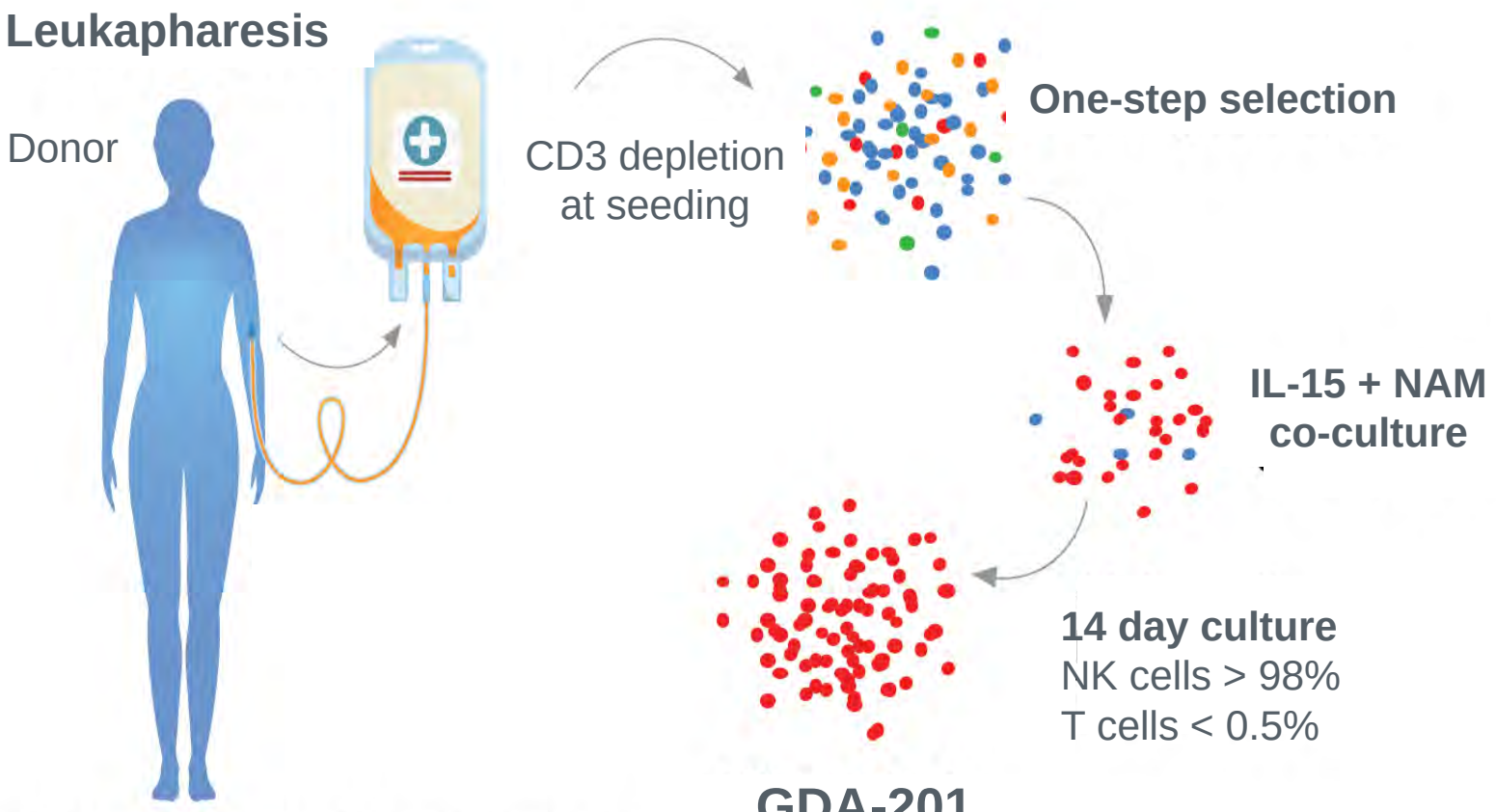


NAM supplementation promotes:

- NK cell function
- Antibody mediated killing
- In vivo persistence in pre-clinical model
- Tissue trafficking in animal model
- Tolerance to oxidative stress

Peled, T., Brachya, G., et al: Blood 2017, 130:657.

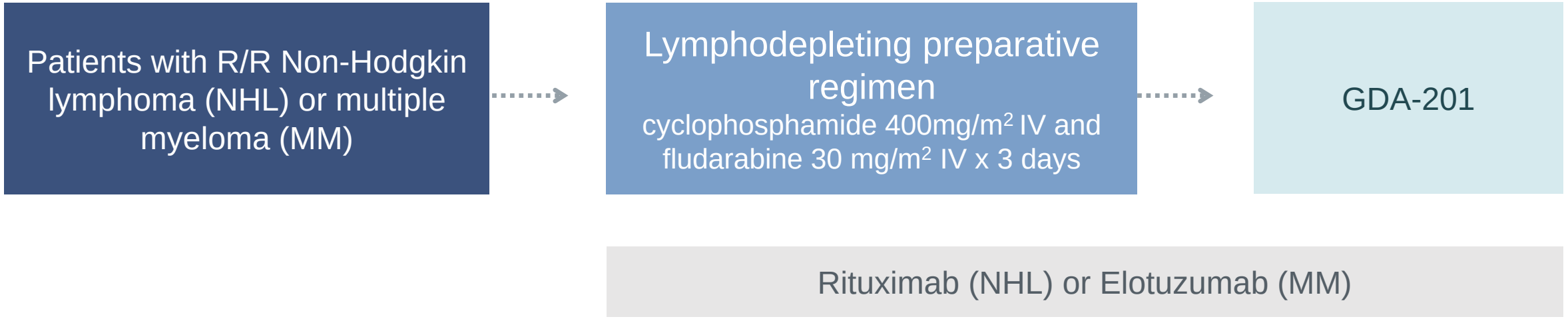
GDA-201 Manufacturing



Donor NK cells obtained from HLA-haploidentical or mismatched related donor

Highly functional NK cells:
~50 - 100 billion, purity >98%

Phase 1 Study of GDA-201 in Patients with Non-Hodgkin Lymphoma or Multiple Myeloma



Primary endpoint:
Determine maximum tolerated dose of NAM-NK.

Secondary endpoints:
Overall disease response, toxicity.

ClinicalTrials.gov Identifier NCT03019666

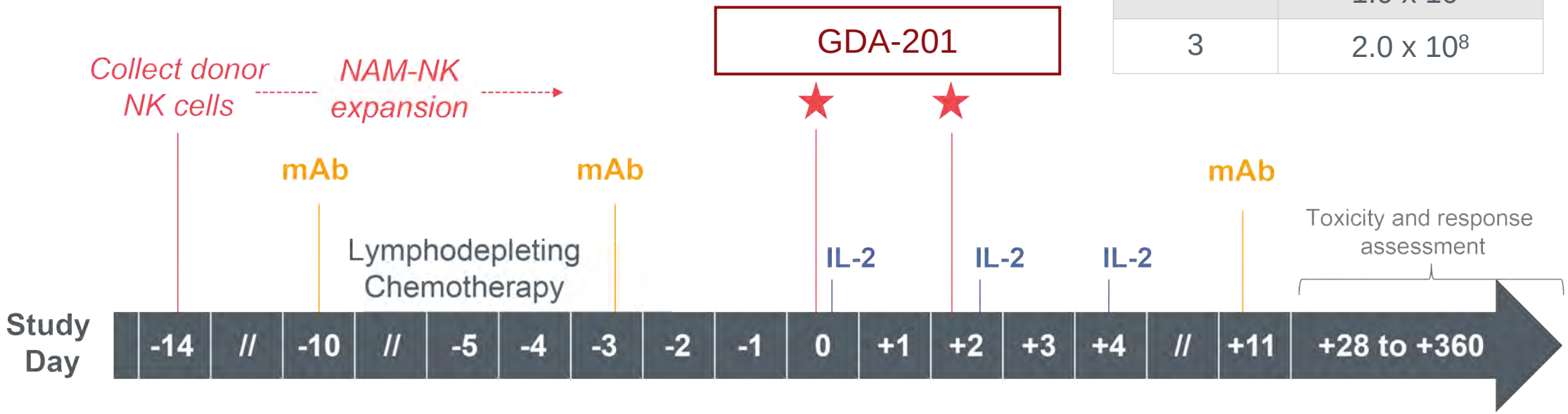
Phase 1 GDA-201 Study Schema and Dose Cohorts

Monoclonal antibodies (mAb): Elotuzumab (10 mg/kg IV) for multiple myeloma, rituximab (375 mg/m2 IV) for B-cell lymphoma

Lymphodepleting chemotherapy: Cyclophosphamide (400 mg/m2 IV) x 3d and fludarabine (30 mg/m2 /d IV x 3d)

IL-2: 6 million units sc

GDA-201 Cohort	Target TNC Dose (cells / kg)
1	2.0×10^7
2	1.0×10^8
3	2.0×10^8

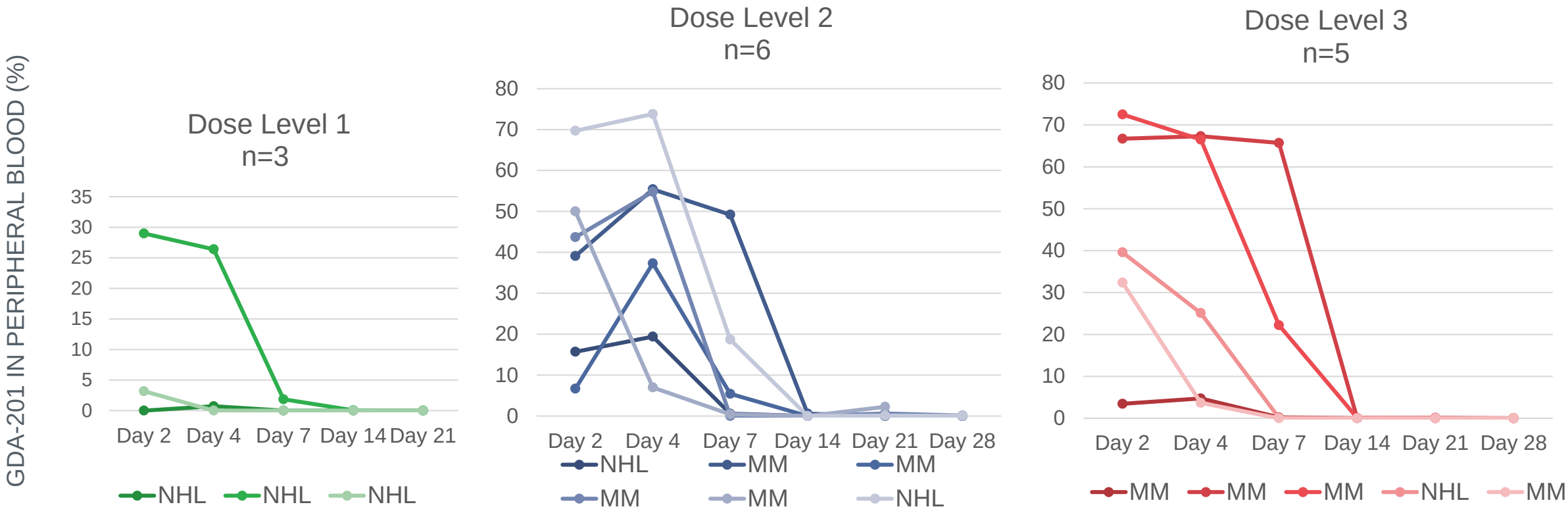


Phase 1 GDA-201 Study: Patient Demographics

Patient and Disease Characteristics	Number of Patients (N = 22)
Age [median (range)]	62 (47-76 years)
Gender: male/female	13/9
Dg: Non-Hodgkin lymphoma	9 (43%)
Diffuse large B cell lymphoma	4
Follicular lymphoma	4
Mantle Cell lymphoma	1
Dg: Myeloma	13 (57%)
Disease status	
Relapsed	13 (63%)
Refractory	9 (37%)
Stage III-IV (NHL only)	8 (90%)

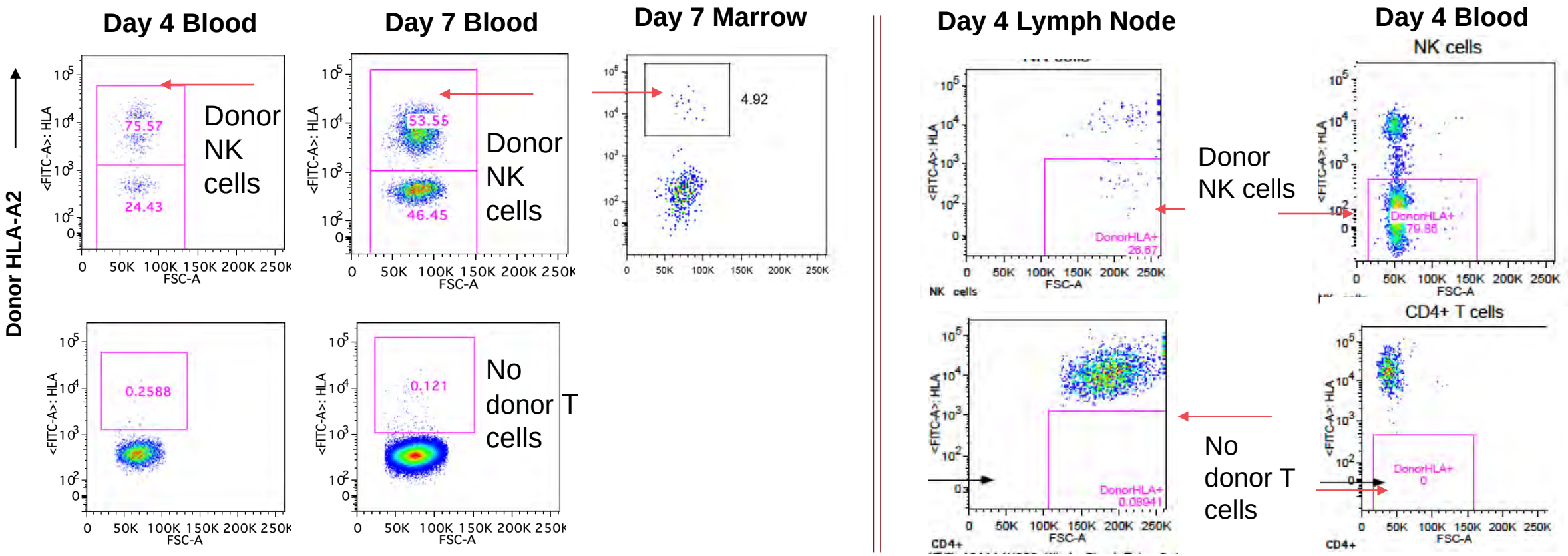
Patient and Disease Characteristics	Number of Patients (N = 22)
Number of lines of Therapies	
NHL (Median, range) Myeloma (Median, range)	4 (2-8) 7 (3-11)
Prior autologous transplant	8
Prior allogeneic transplant	1
KPS equal or < 80 %	13 (63%)
Time from diagnosis to treatment [median; range]	4.5 (1-26 years)
Median follow-up [median; range]	167 (21-678 days)

Persistence and Expansion of GDA-201 (% donor NAM-NK cells)



- GDA-201 detected by flow cytometry using donor HLA-specific antibodies.
- Day 7 range 2-68% donor derived NK cells
- NK cells persistence appears to be dose dependent.

GDA-201 Cells Traffic to Marrow and Lymph Nodes



GDA-201 detected in blood and lymph node by flow chimerism (Donor is HLA-A2+).
Flow plots are gated on CD56+CD3- NK and T Cells.

Safety Results: Grade 3-5 Adverse Events

EVENT	GRADE 3/4 EVENTS (N=22)
Neutrophil count decreased	7
Electrolyte abnormalities	5
Hypertension	4
Generalized body aches	4
Febrile Neutropenia	2
Anemia	3
Thrombocytopenia	3
Fever	2
Dyspnea	2
Hypophosphatemia	2
Hypoxia	2
Hypotension	1
Upper respiratory infection	1
Sepsis	1
Sinus bradycardia	1

EVENT	GRADE 3/4 EVENTS (N=22)
Hyponatremia	1
Abdominal pain	1
Cytokine release syndrome	1
Congestive Heart Failure	1
Confusion	1

Grade 5 toxicity: n=1
E coli pneumonia/sepsis in non-neutropenic patient

- Most non-hematologic toxicities were attributed to cyclophosphamide/ fludarabine.
- Bradycardia gr 3 reported in one patient, attributed to elotuzumab.

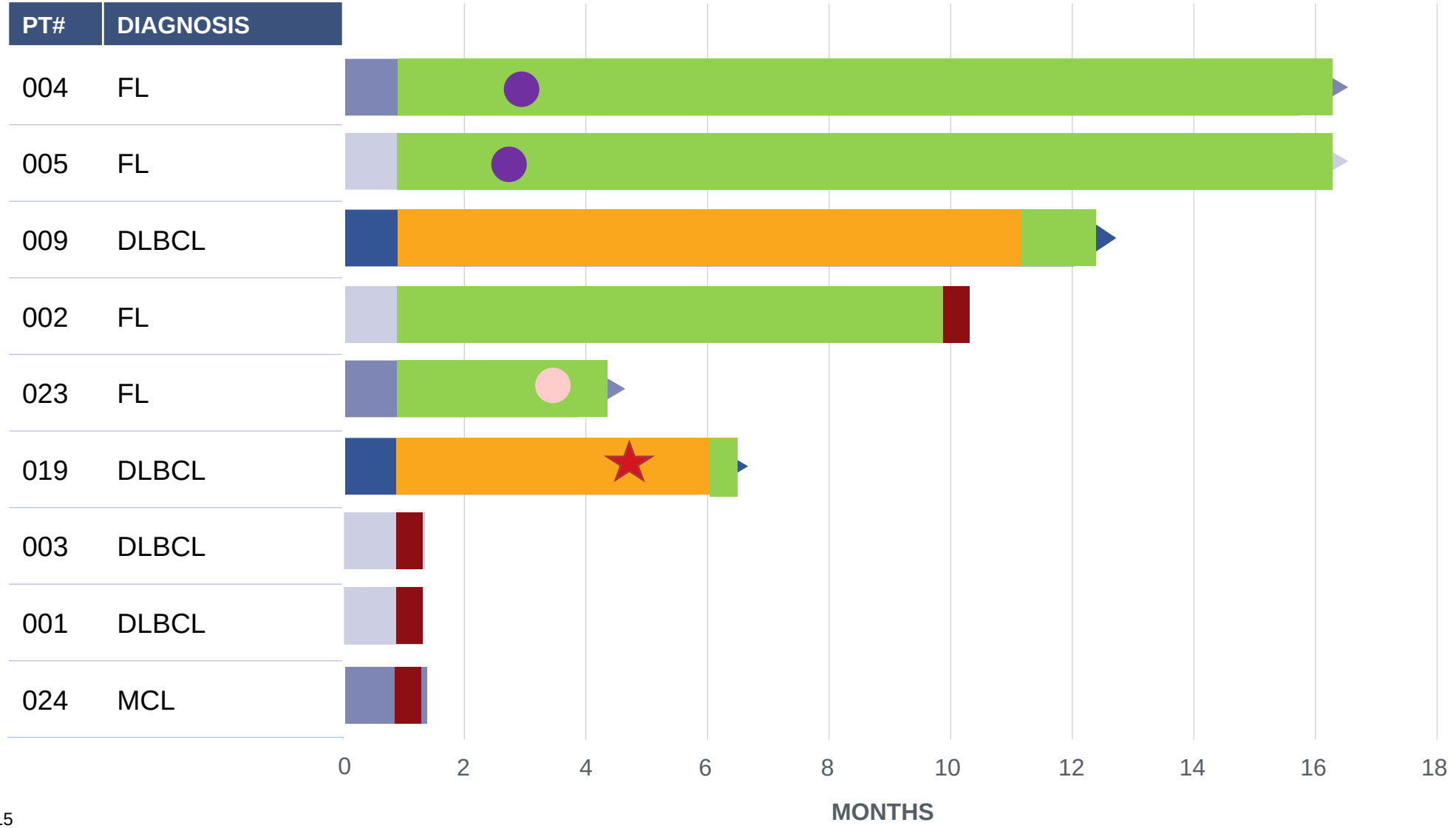
DLTs and Events of Special Interest

- No dose limiting toxicities.
- No GVHD, tumor lysis syndrome.
- No neurotoxicity reported, no marrow aplasia.
- 1 patient with possible CRS (grade 3) at d18 with fever, hypoxemia and hypotension, promptly responded to tocilizumab; IL6 level at 258 pg/ml; patient later died due to E. coli pneumonia/sepsis.

Phase 1 Study Efficacy Results: Best response (21 evaluable)

NHL	N=9	Myeloma	n=12
ORR	67% (n=6)	ORR	8%
CR	56% (n=5)	CR	8% (n=1) (extramedullary myeloma)
PR	11% (n=1) (90% TMV reduction)	SD PR	42% (n=5) 0
PD	33% (n=3)	PD	50% (n=6)

Phase I GDA-201 Study: Duration of Response in NHL patients



LEGEND

Cohort /Dose Level

1 **2** **3**

Complete response

Partial response

Progressive disease

Continued response

Allogeneic transplant

Autologous transplant

2nd GDA-201 infusion

FL: Follicular lymphoma;
DLBCL: diffuse large B cell lymphoma

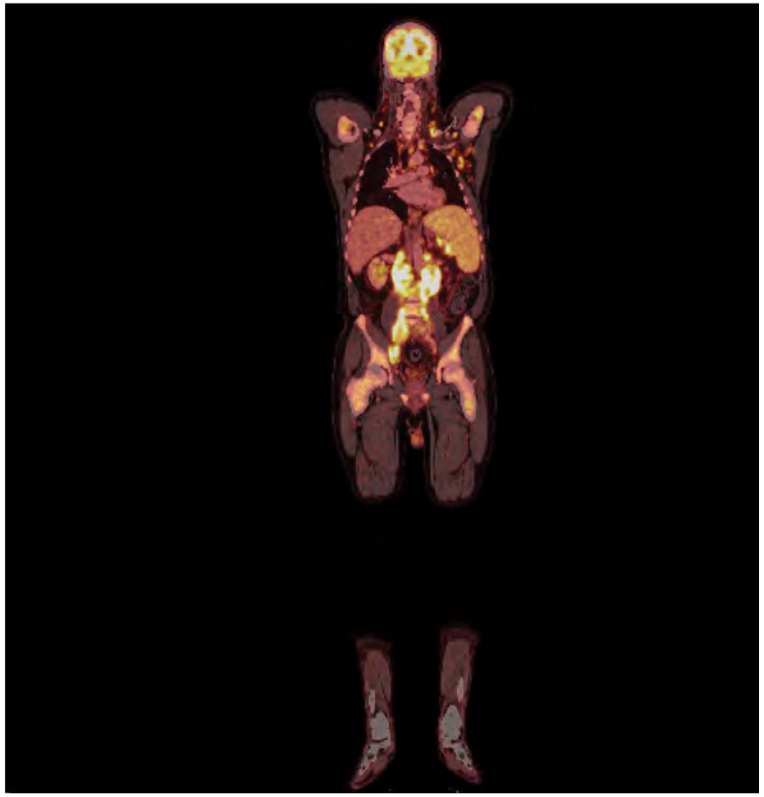
Patient 004

- 60-year-old man with Stage IV follicular lymphoma diagnosed in 2015

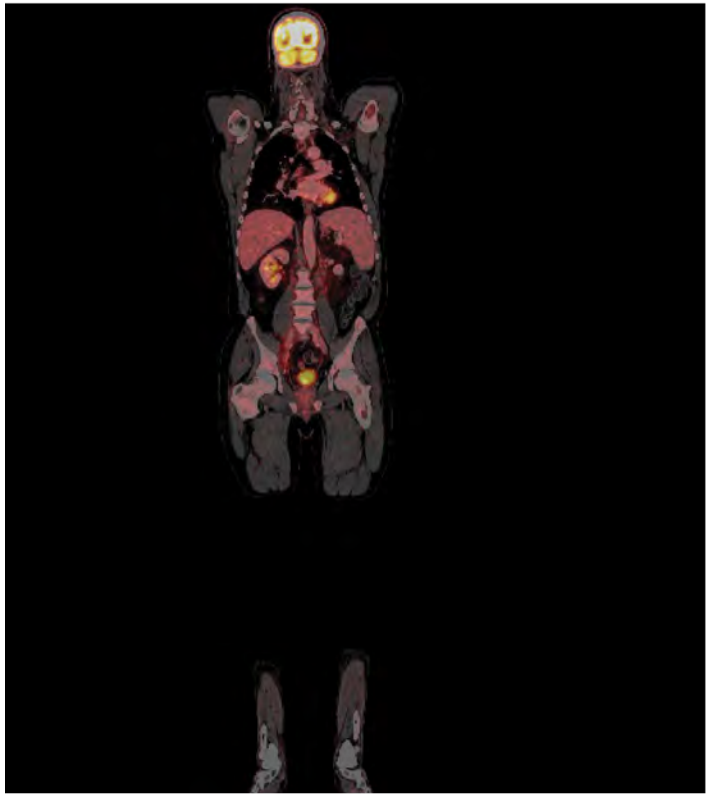
- Prior therapy: R-bendamustine,
- Relapse R-CHOP, and R-ICE – no response

- Day 28 post GDA-201: Complete response

Baseline



1 month post GDA-201

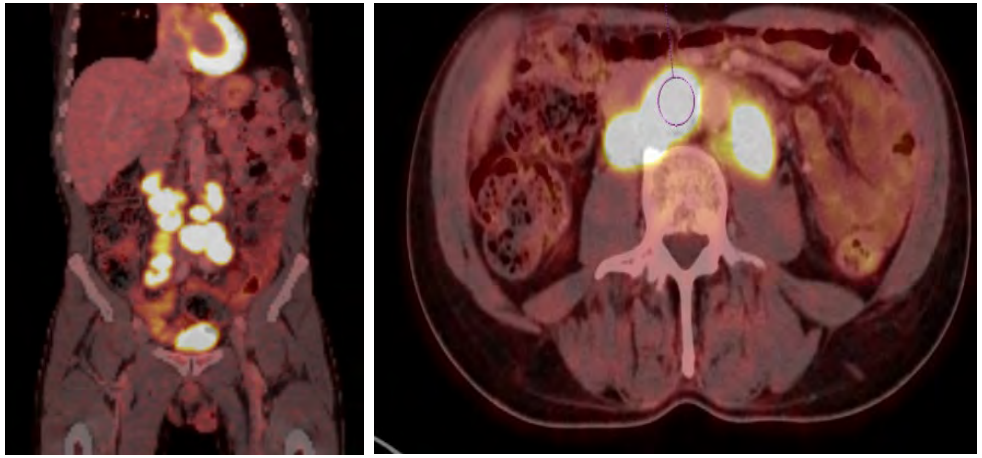


Patient 004: Radiographic Complete Response

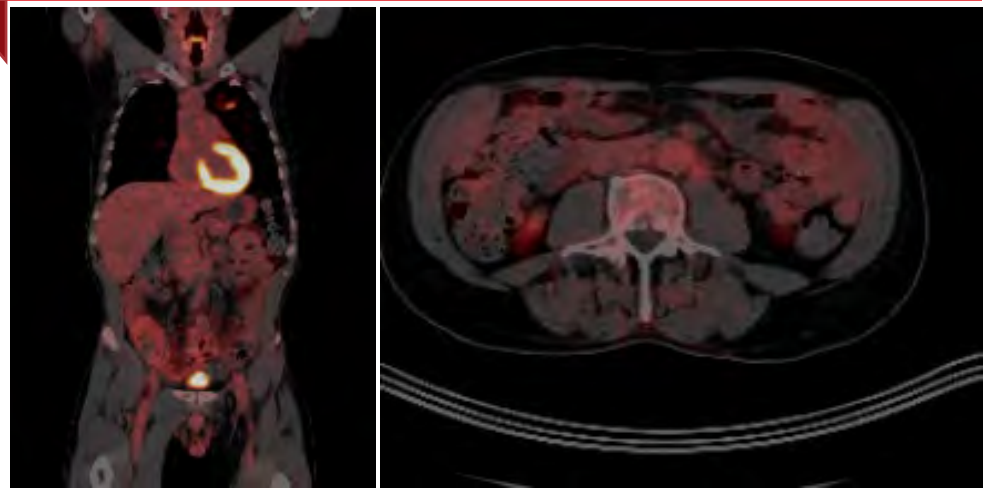
Patient 009

- 57-year-old man with history of CLL and Richter's transformation - large cell lymphoma, measurable retroperitoneal lymph nodes at baseline
- Prior therapy: FCR-light, Rituximab/Bendamustine Ibrutinib/Revlimid, R-CHOP, Venetoclax/Rituximab
- Allogeneic HSCT (matched sib)
- Relapse at 6 months
- Treated with GDA-201
- 28 day response- tumor shrinkage
- 6 months: PR with continued tumor shrinkage
- 12 months: Complete response

Pt 009: Baseline



Pt 009: 6 month post GDA-201



Phase 1 GDA-201 Study: Conclusions

- GDA-201 (NAM enhanced haplo-NK cells) was well-tolerated without infusion toxicity or DLTs.
- Maximum target dose of 2 x 10^8 cells/kg was achieved.
- GDA-201 cells were detectable in blood, bone marrow and lymph node, and exhibited proliferative phenotype and cytotoxic function.
- Clinical activity was observed, including complete responses in patients with lymphoma and myeloma.
- Future directions include cryopreservation and exploration of multiple treatment cycles.
- Protocol was amended to add pomalidomide to MM arm to improve anti-tumor efficacy and NK cell persistence

Data support multi-center Phase 1/2 study in 2020.

Acknowledgments

- Patients and their families
- University of Minnesota BMT and Cellular Therapy Program

Masonic Cancer Center
University of Minnesota
Comprehensive Cancer Center designated by the National Cancer Institute

gamida cell

NIH

American Society of Hematology

Marrow on the Move