THE INNATE KILLING ABILITY OF NATURAL KILLER CELLS

Dr. Patrick Soon-Shiong
Chairman & CEO
NantKwest

December 2, 2019
The Benjamin Hotel – New York City

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These slides and the accompanying oral presentation contain forward-looking statements within the meaning of the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, that are based on management's beliefs and assumptions and on information currently available to our management. Forward-looking statements include, but are not limited to:

- our ability to pioneer immunotherapy, harness the power of the innate immune system, implement precision cancer medicine and change the current paradigm of cancer care;
- our expectations regarding the potential benefits of our strategy and technology;
- our ability to utilize multiple modes to induce cell death;
- our beliefs regarding the benefits and perceived limitations of competing approaches, and the future of competing technologies and our industry;
- our beliefs regarding the success, cost and timing of our product candidate development activities and clinical trials;
- the timing or likelihood of regulatory filings or other actions and related regulatory authority responses, including any planned investigational new drug (IND) filings or pursuit of accelerated regulatory approval pathways or orphan drug status and breakthrough therapy designations;
- our ability to implement an integrated discovery ecosystem and the operation of that planned ecosystem;
- our expectations regarding our ability to utilize the Phase I aNK clinical trial data to support the development our other product candidates;
- our ability to produce an "off-the-shelf" therapy;
- our beliefs regarding the potential manufacturing and distribution benefits associated with our product candidates, and our ability to scale up the production of our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidate and not infringe upon the intellectual property of others;
- the ability and willingness of strategic collaborators, including certain of our affiliates, to share our vision and effectively work with us to achieve our goals;
- the ability and willingness of various third parties to engage in research and development activities involving our product candidates, and our ability to leverage those activities; and
- regulatory developments in the United States and foreign countries.

Factors that could cause our results to differ materially from those expressed in forward-looking statements include, without limitation:

- the fact that our business is based upon the success of aNK cells as a technology platform and the success of N-803 and the other product candidates;
- our aNK platform and other product candidate families, including genetically modified taNK, haNK and t-haNK product candidates, will require significant additional clinical testing;
- even if we successfully develop and commercialize our aNK product candidates or N-803, we may not be successful in developing and commercializing our other product candidates either alone or in combination with other therapeutic agents;
- we may not be able to file INDs, to commence additional clinical trials on timelines we expect;
- we will need to obtain substantial additional financing to complete the development and any commercialization of our product candidates; and
- risks associated with our ability to enforce intellectual property rights.

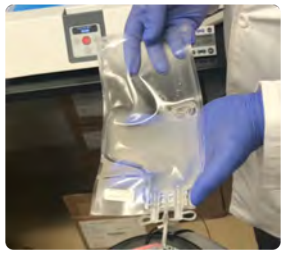
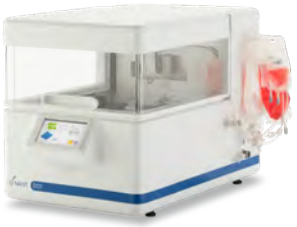
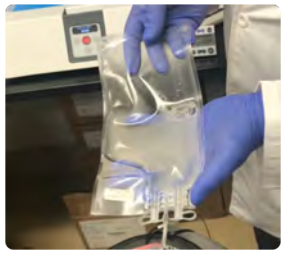
Forward-looking statements include statements that are not historical facts and can be identified by terms such as "anticipates," "believes," "could," "seeks," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should," "will," "would," or similar expressions and the negatives of those terms.

Forward-looking statements involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements.

These and other risks regarding our business are described in detail in NantKwest's Securities and Exchange Commission filings. We encourage you to review NantKwest's SEC filings in order to understand these risks. These forward-looking statements speak only as of the date thereof, and we disclaim any obligation to update these statements except as may be required by law. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this presentation.

Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. No representation or warranty, express or implied, is given as to the completeness or accuracy of the information or opinions contained in this document and we do not accept any liability for any direct, indirect or consequential loss or damage arising from reliance on such information or opinions. Past performance should not be taken as an indication or guarantee of future performance. You should read this presentation completely and with the understanding that our actual future results may be materially different from what we expect.

First in Human, First in Class
Clinical Path to Immunogenic Cell Death by Natural Killer Cell Activation

	NK Platforms	NK Products in Clinical Development
Cryopreserved Off-the-Shelf Engineered NK-92	 Cryopreserved NK →  Off-the-Shelf Engineered NK-92	= • haNK • PD-L1 t-haNK • HER2 t-haNK
Autologous Cytokine Induced Memory NK	 Apheresis →  GMP-in-a-Box →  Autologous Memory NK Cells	= • Autologous Memory NK Cell
Off-the-Shelf Engineered NK-92 + Endogenous Activation IL-15**	 Off-the-Shelf NK-92 +  IL-15 (N-803)	= • haNK + IL-15 (N-803) • PD-L1 t-haNK + IL-15 (N-803) • HER2 t-haNK + IL-15 (N-803)

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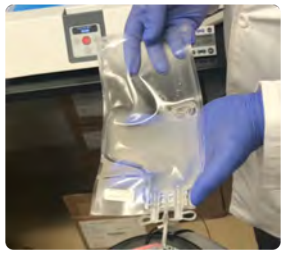
Cryopreserved Off-the-Shelf Engineered NK-92	 Cryopreserved NK →  Off-the-Shelf Engineered NK-92	= • haNK • PD-L1 t-haNK • HER2 t-haNK
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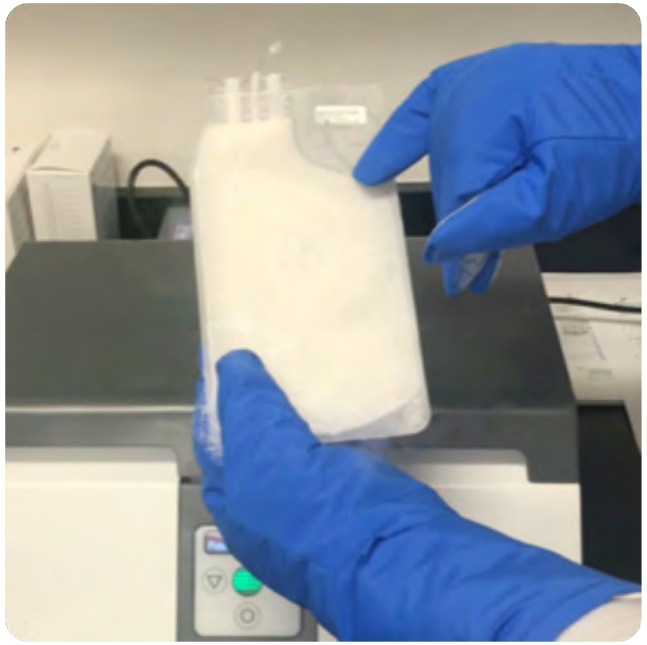
Cryopreserved Ready to Use Off-the-Shelf Natural Killer Cells



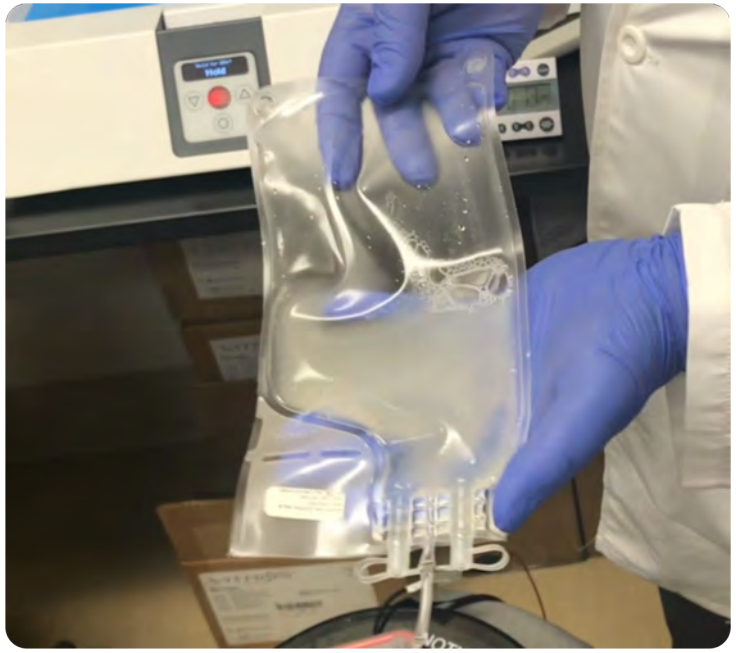
Cryopreserved / Ready-to-Use

Off-the-Shelf NK-92 Cells

2 Billion Cells ($2x10^9$)
Transfused as an Outpatient
Over 30 Minutes

First in Human Studies
2017 - 2019
Phase I / Ib
Exploratory Completed
Dec 2019

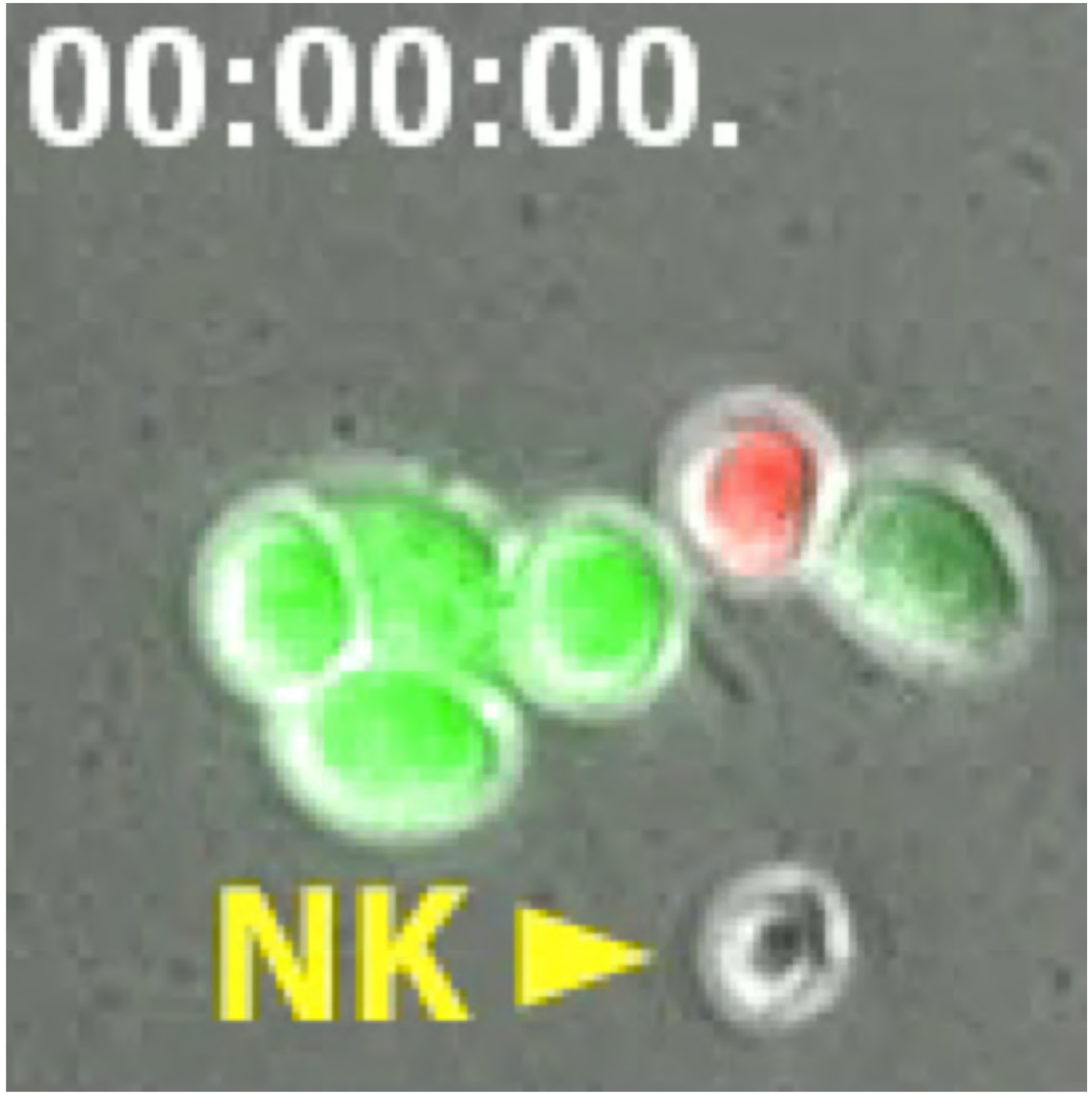
~600 NK Doses
($2x10^9$ Cells) Safely
Administered as
Outpatient

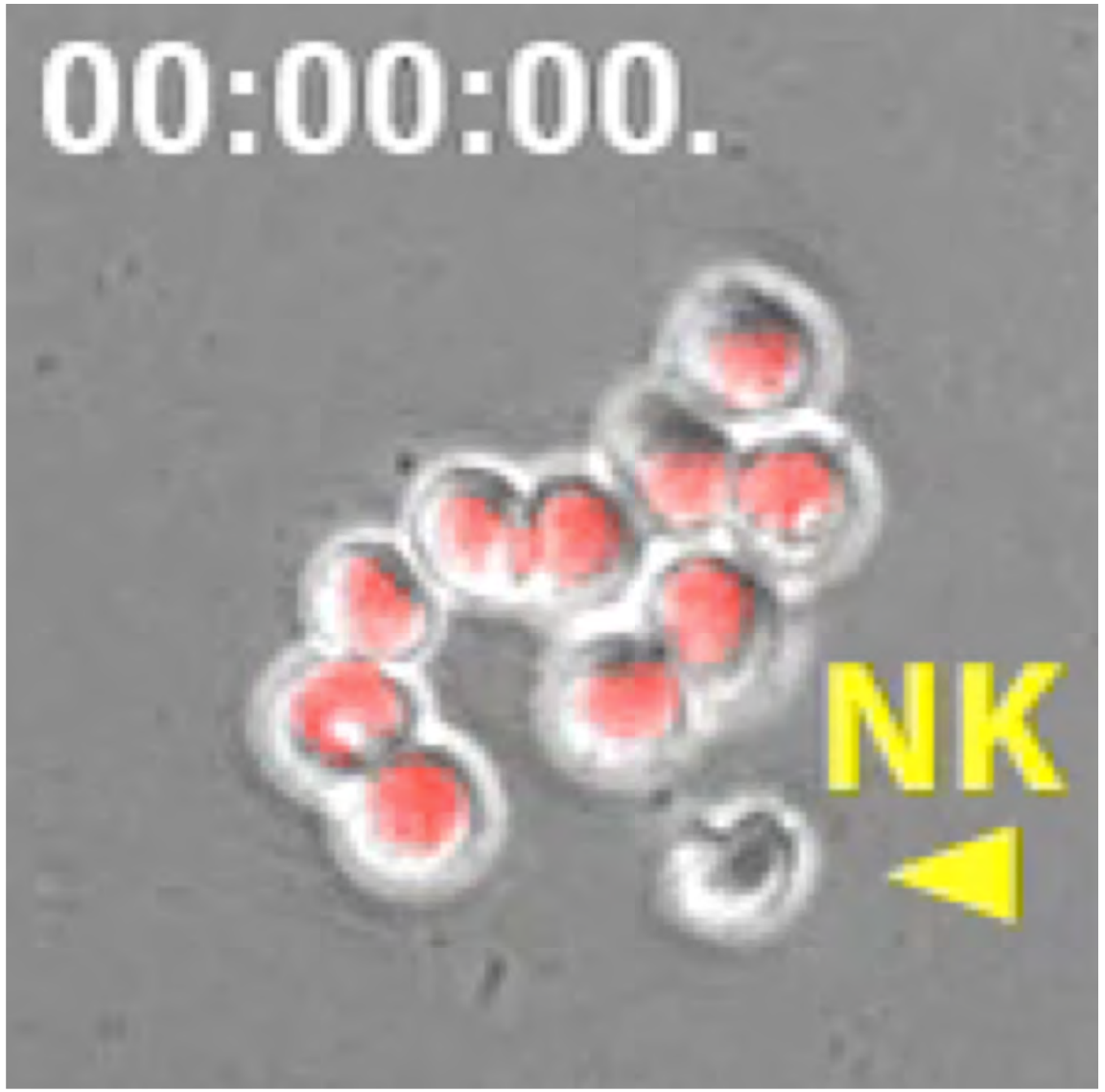


Natural Killer Cell Transfusion

NantKwest

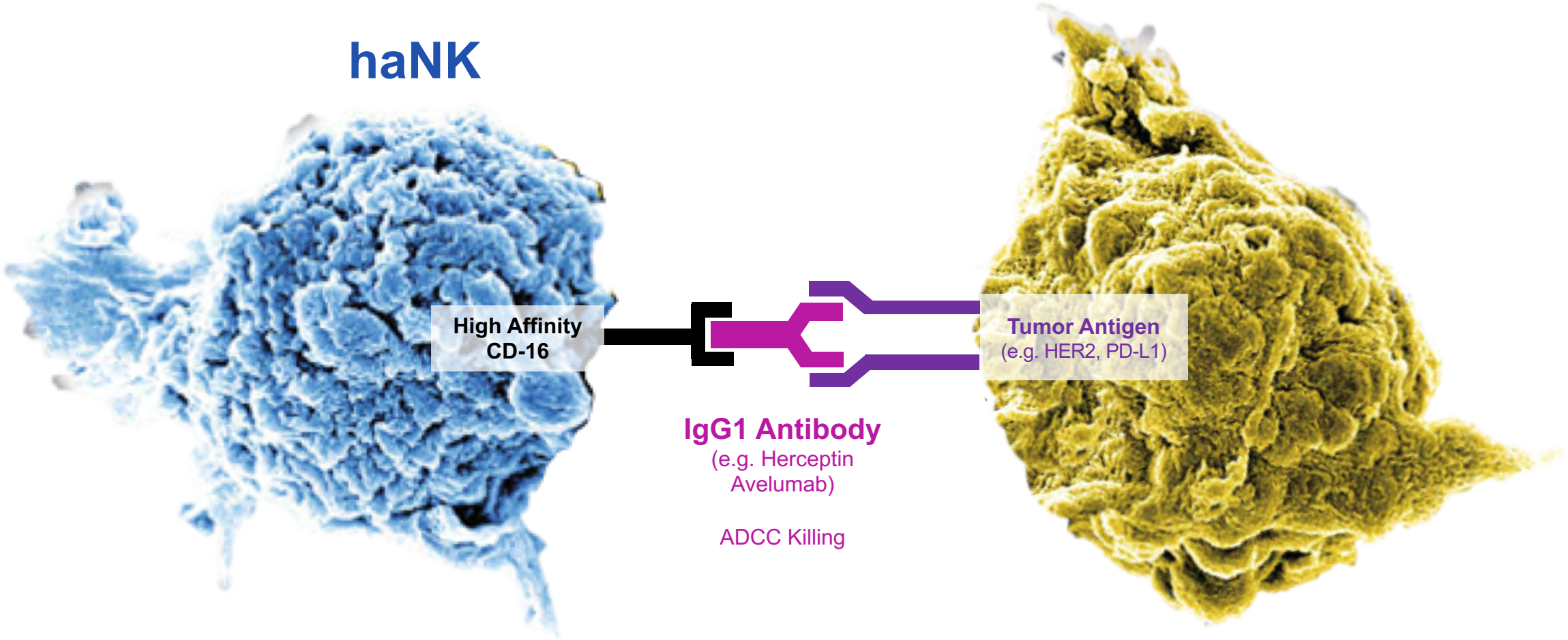
Off-the-Shelf Natural Killer Cells

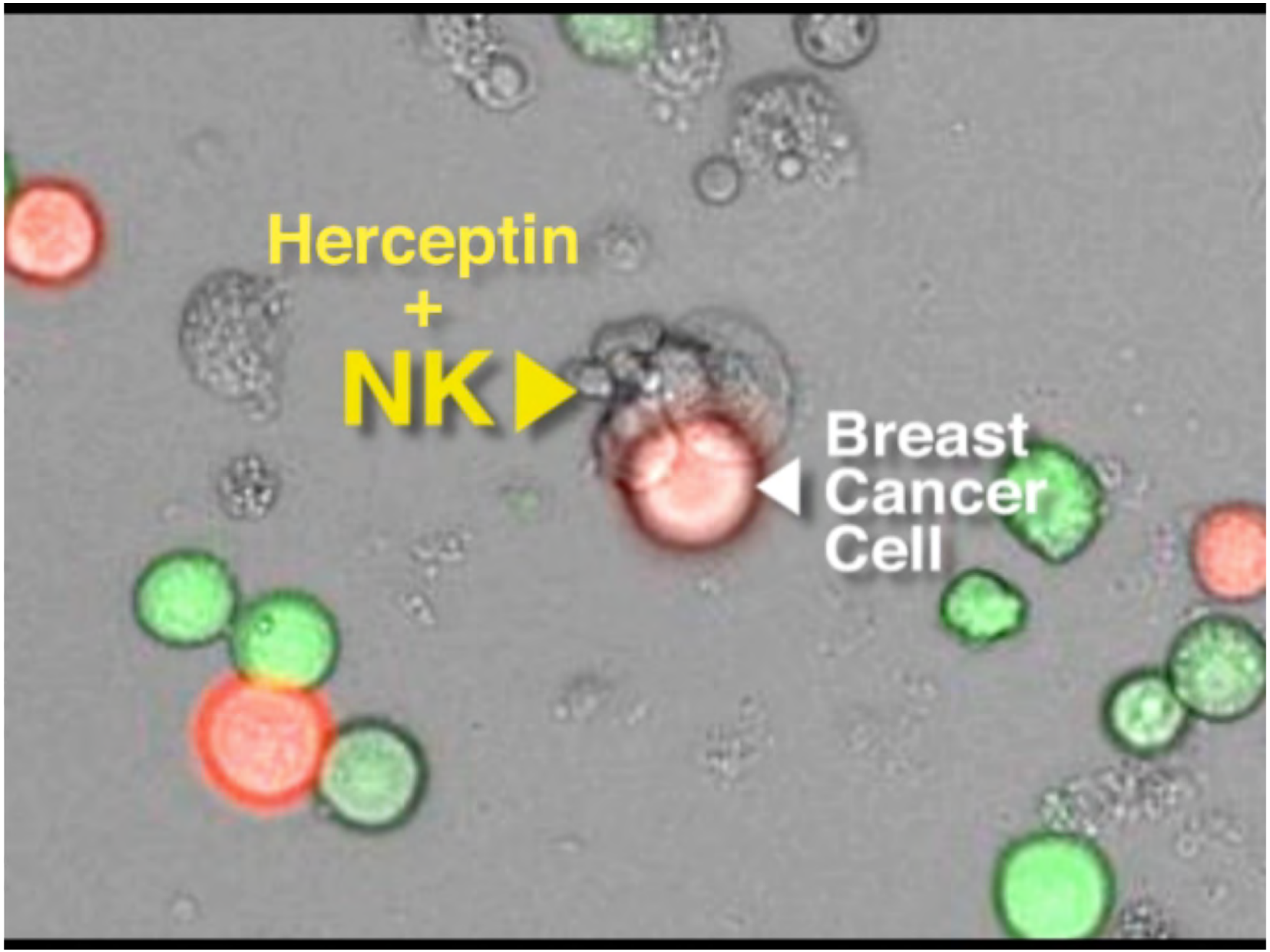




NantKwest

First in Human
First in Class Natural Killer Cell Immunotherapy at Clinical Stage

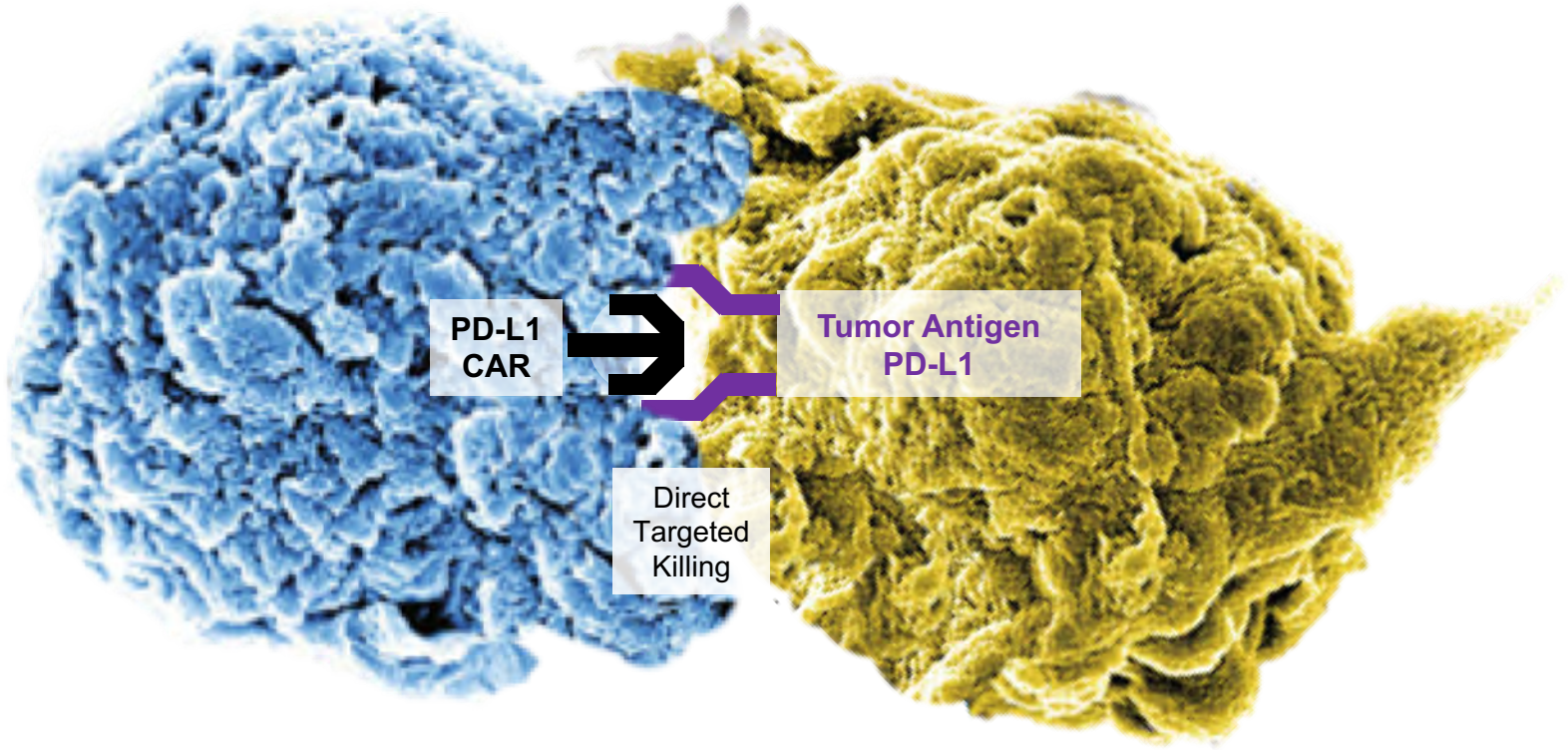




NantKwest

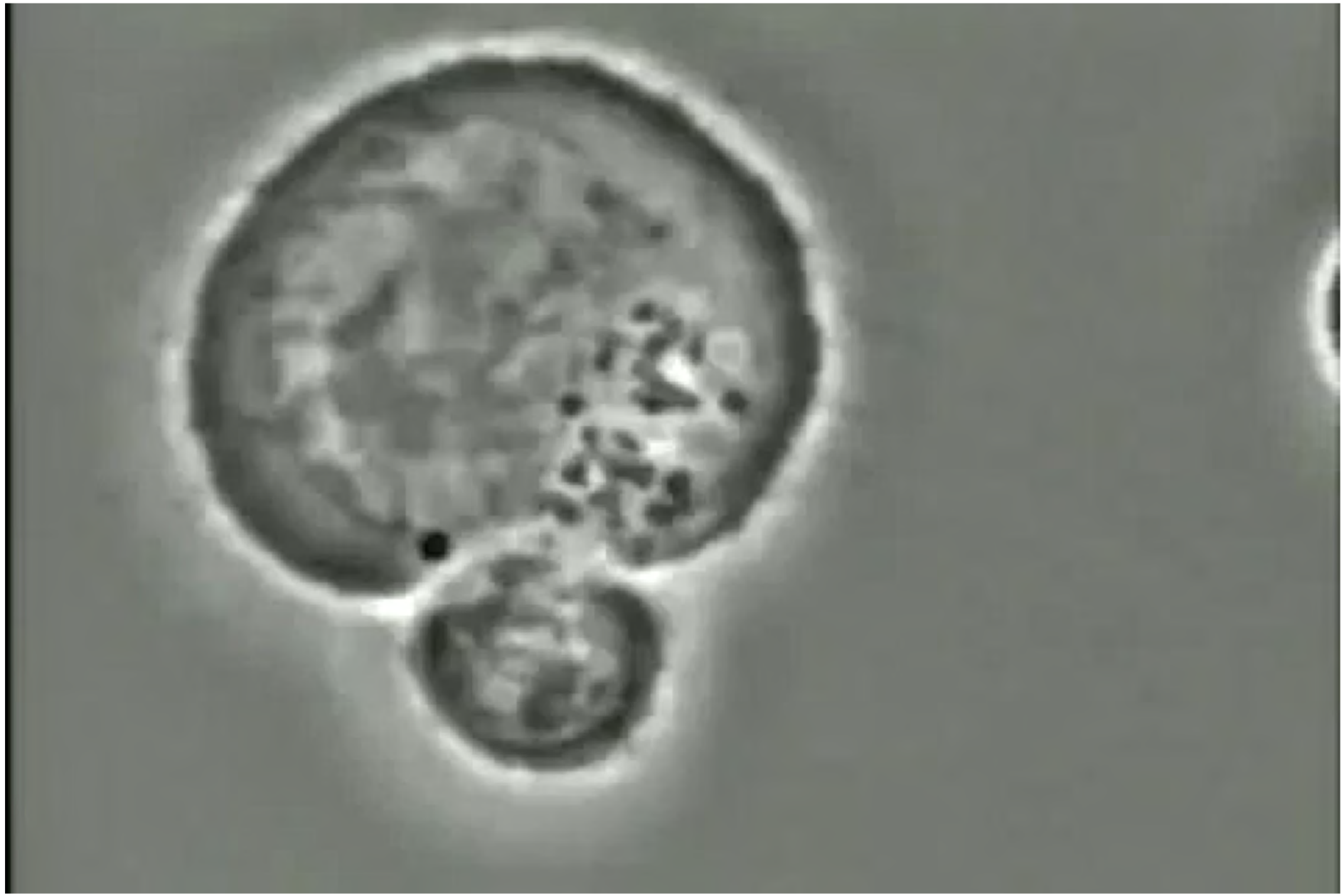
First in Human
First in Class Natural Killer Cell Immunotherapy at Clinical Stage

PD-L1 t-haNK



Off-the-Shelf Natural Killer Cell

Tumor Cell



First in Human, First in Class
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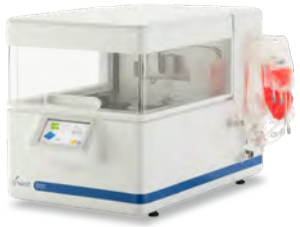
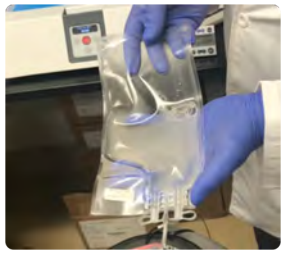
Autologous Cytokine Induced Memory NK	 Apheresis	 GMP-in-a-Box	 Autologous Memory NK Cells	= • Autologous Memory NK Cell
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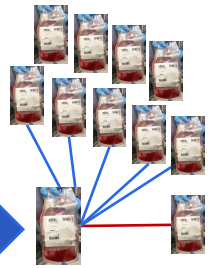
NantKwest Proprietary Method for Autologous (Cytokine Induced) Memory NK Cell Production in 17 Days

Day 1

Autologous Apheresis Patient White Cell Collection

Day 1

Autologous Apheresis White Cells



Single Aliquot For Enrichment

Aliquot One Bag into 10 Lots for Cryopreservation

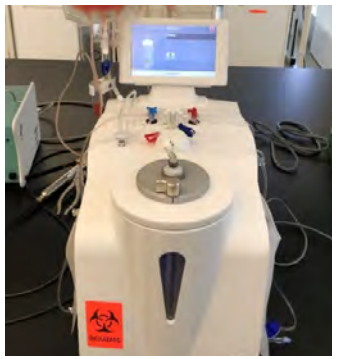
Day 1

Cryopreservation For Future Uses

Day 1-16
NK Enrichment

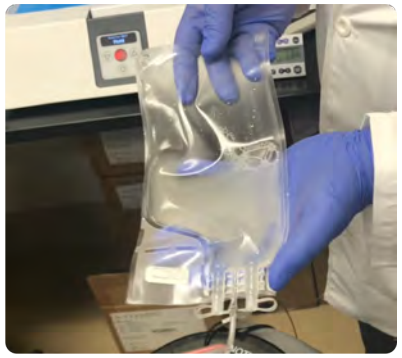
GMP-in-a-Box NK Cell Enrichment Cytokine Induced Proliferation

Day 17

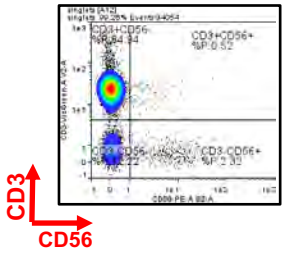


Concentrate
0.3 – 1.0 x 10^9 NK Cells

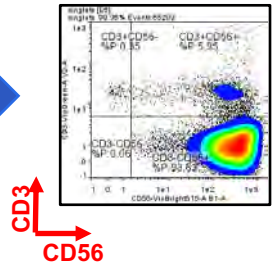
Day 17



Autologous Memory Natural Killer Cells for Transfusion
0.3 – 1.0 x 10^9 NK Cells



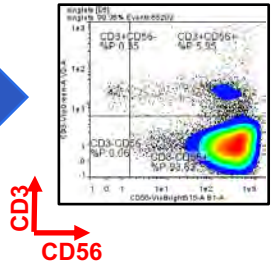
White Cells



Enriched NK Cells

GMP-in-a-Box

IND Ready



Memory NK Cells

First in Human, First in Class
Clinical Paths to Immunogenic Cell Death by Natural Killer Cell Activation

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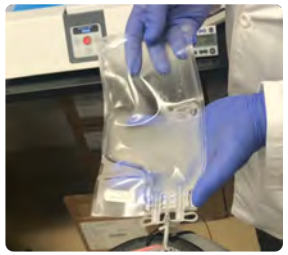
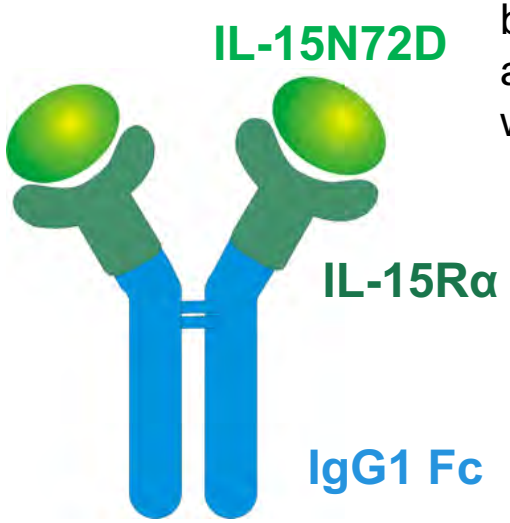
Autologous Cytokine Induced Memory NK	 Apheresis → GMP-in-a-Box → Autologous Memory NK Cells	= • Autologous Memory NK Cell
Off-the-Shelf Engineered NK-92 + Endogenous Activation IL-15**	 Off-the-Shelf NK-92 +  IL-15 (N-803)	= • haNK + IL-15 (N-803) • PD-L1 t-haNK + IL-15 (N-803) • HER2 t-haNK + IL-15 (N-803)

IL-15 (N-803)
First-in-Class IgG1-Fc IL-15 Cytokine Agonist



IL-15 N72D mutation enhances binding to IL-2Rβ, driving proliferation and activation of NK and T cells without expansion of Tregs

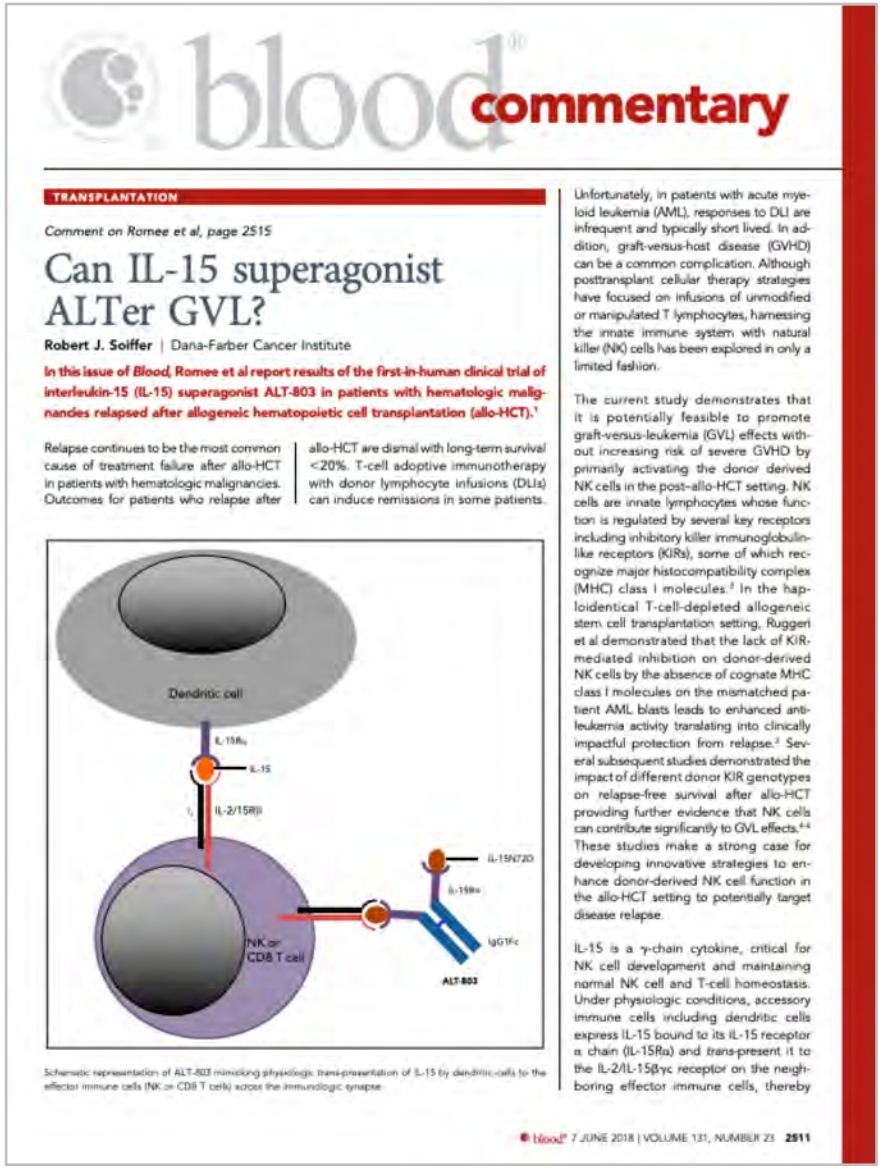
Allows transpresentation selectively to only IL-2Rβγ chain of NK and CD8+ T cells

Increases half-life and lymphoid recycling and distribution

N-803 promotes natural killer (NK) and CD8⁺ T-cell expansion and activation in vivo without expanding immunosuppressive regulatory T cells, with expansion of effector and central memory T cells

Key Features	
Composition	IL-15 / IL-15RαFc Fusion Protein
Mechanism of Action	Activation and expansion of NK and CD8⁺ T cells, without expansion of Tregs
Route of Administration	Subcutaneous (systemic) Intravesical (bladder)
Dose	SQ - 15 μg/kg, q 3 wks (cancer) Intravesical - 400 μg/dose, weekly
Key Indications	Early-stage bladder cancer (NMIBC) Checkpoint-relapsed solid tumors Lung cancer HIV
Number of patients who have received	Over 300
Potential Combinations	BCG PD1 & PD-L1 Checkpoints Herceptin, Rituxan, Cetuximab, haNK Adenovirus / Yeast Neoepitope Aldoxorubicin Radiation

Blood Commentary on First-In-Class IL-15 (N-803)



blood commentary

TRANSPLANTATION

Comment on Romee et al, page 2515

Can IL-15 superagonist ALTer GVL?

Robert J. Soiffer | Dana-Farber Cancer Institute

In this issue of *Blood*, Romee et al report results of the first-in-human clinical trial of interleukin-15 (IL-15) superagonist ALT-803 in patients with hematologic malignancies relapsed after allogeneic hematopoietic cell transplantation (allo-HCT).[1]

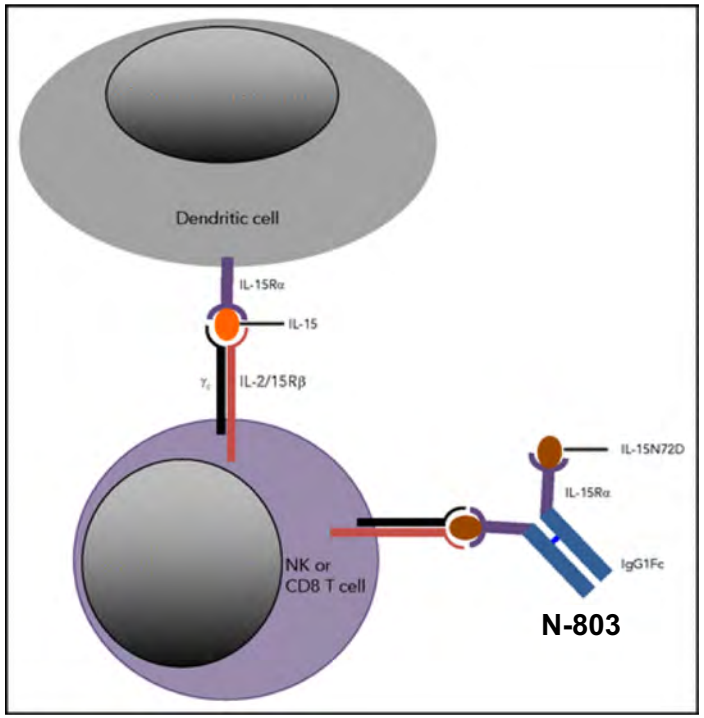
Relapse continues to be the most common cause of treatment failure after allo-HCT in patients with hematologic malignancies. Outcomes for patients who relapse after allo-HCT are dismal with long-term survival <20%. T-cell adoptive immunotherapy with donor lymphocyte infusions (DLIs) can induce remissions in some patients.

Schematic representation of ALT-803 mimicking physiologic trans-presentation of IL-15 by dendritic cells to the effector immune cells (NK or CD8 T cells) across the immunologic synapse.

Unfortunately, in patients with acute myeloid leukemia (AML), responses to DLI are infrequent and typically short lived. In addition, graft-versus-host disease (GVHD) can be a common complication. Although posttransplant cellular therapy strategies have focused on infusions of unmodified or manipulated T lymphocytes, harnessing the innate immune system with natural killer (NK) cells has been explored in only a limited fashion.

The current study demonstrates that it is potentially feasible to promote graft-versus-leukemia (GVL) effects without increasing risk of severe GVHD by primarily activating the donor derived NK cells in the post–allo-HCT setting. NK cells are innate lymphocytes whose function is regulated by several key receptors including inhibitory killer immunoglobulin-like receptors (KIRs), some of which recognize major histocompatibility complex (MHC) class I molecules.[2] In the haploidentical T-cell-depleted allogeneic stem cell transplantation setting, Ruggeri et al demonstrated that the lack of KIR-mediated inhibition on donor-derived NK cells by the absence of cognate MHC class I molecules on the mismatched patient AML blasts leads to enhanced anti-leukemia activity translating into clinically impactful protection from relapse.[3] Several subsequent studies demonstrated the impact of different donor KIR genotypes on relapse-free survival after allo-HCT providing further evidence that NK cells can contribute significantly to GVL effects.[4-6] These studies make a strong case for developing innovative strategies to enhance donor-derived NK cell function in the allo-HCT setting to potentially target disease relapse.

IL-15 is a γ-chain cytokine, critical for NK cell development and maintaining normal NK cell and T-cell homeostasis. Under physiologic conditions, accessory immune cells including dendritic cells express IL-15 bound to its IL-15 receptor α chain (IL-15Rα) and *trans*-present it to the IL-2/IL-15βγc receptor on the neighboring effector immune cells, thereby



N-803 Mimics an Activated Dendritic Cell

"…in the past, use of IL-15 in clinical trials has been hampered by the limited availability of recombinant human IL-15 (rhIL-15). Additionally, although IV rh1L-15 increased NK and CD8 T-cell numbers, its use was associated with a short half-life and was poorly tolerated by patients with advanced solid tumors in an early phase clinical trial.

N-803 is a high-molecular weight IL-15 superagonist molecule consisting of an IL-15 mutein (N72D) bound to IL-15Ra fused to IgG1Fc. This unique molecule aims to mimic the physiologic trans-presentation of IL-15 and significantly increase its half-life."

Current Clinical Development Status

2017 – 2019: First in Human Trials

2020+: Pivotal Trials

First in Human, First in Class
Clinical Paths to Immunogenic Cell Death by Natural Killer Cell Activation

NK Platforms	MOA	NK Product	Indication	Status of Development (2017 - 2020)
				IND / Phase I / Phase Ib
Cryopreserved Off-the-Shelf Engineered NK-92	CD-16 IgG1 Targeting	haNK	Solid Tumors	No DLTs
	PD-L1 Antibody + CD16 IgG1 Targeting	haNK + PD-L1*+ N-803	Metastatic 3L+ TNBC	78% DCR 66% ORR 22% CR
		haNK + PD-L1*+ N-803	Metastatic 2L+ Lung	50% ORR 25% CR
	PD-L1 CAR	PD-L1 t-haNK	Solid Tumors	No DLTs
	HER2 CAR	HER2 t-haNK	Solid Tumors	IND Ready
Autologous Cytokine Induced Memory NK	Memory Natural Killer Cell Activation	Memory NK Cell Apheresis + N-803	Solid Tumors	IND Ready

First in Human Studies 2017 - 2019
Phase I / Ib
Exploratory Completed Dec 2019

>600 NK Doses ($2x10^9$ Cells) Safely Administered as Outpatient

Pivotal Phase II / III Studies in 2020

Off-the-Shelf Engineered NK-92 + Endogenous Activation IL-15**	Off-the-Shelf Targeted Natural Killer + NK & Memory T Cell Activation by IL-15	haNK + N-803	Relapsed Merkel Cell	Pivotal Single Arm Phase II N = 43
		PD-L1 t-haNK + N-803	Neoadjuvant TNBC	Exploratory Randomized Phase II N = 58
		PD-L1 t-haNK + N-803	Metastatic 1L TNBC	Pivotal Randomized Phase III N = 404
		PD-L1 t-haNK + N-803	Metastatic 1L Lung	Pivotal Randomized Phase III N = 404

**October 2016, Exclusive Collaboration Agreement with ImmunityBio and NantKwest to combine N-803 with NK Platforms
*Supply Agreement with Pfizer for Avelumab (PD-L1 Antibody)

Key Opinion Leaders – December 2, 2019

Topic: Merkel Cell Carcinoma

George Ansstas, MD
Washington University of Medicine, St. Louis
Assistant Professor Department of Medicine, Medical Oncology

Topic: PD-L1 t-haNK

Clint Allen, MD
Johns Hopkins Otolaryngology Consult for the National Institutes of Health
Associate Professor of Otolaryngology - Head and Neck Surgery

Topic: Triple Negative Breast Cancer (TNBC)

Chaitali Nangia, MD
CSSIFM & Hoag Hospital Newport Beach
Medical Oncologist

First in Human, First in Class
Clinical Paths to Immunogenic Cell Death by Natural Killer Cell Activation

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Thank You

Key Opinion Leaders – December 2, 2019

Topic: Merkel Cell Carcinoma

George Ansstas, MD
Washington University of Medicine, St. Louis
Assistant Professor Department of Medicine, Medical Oncology

Merkel Cell Carcinoma - What is Next?

George Ansstas, MD

Associate Professor

Washington University School of Medicine

12/02/2019

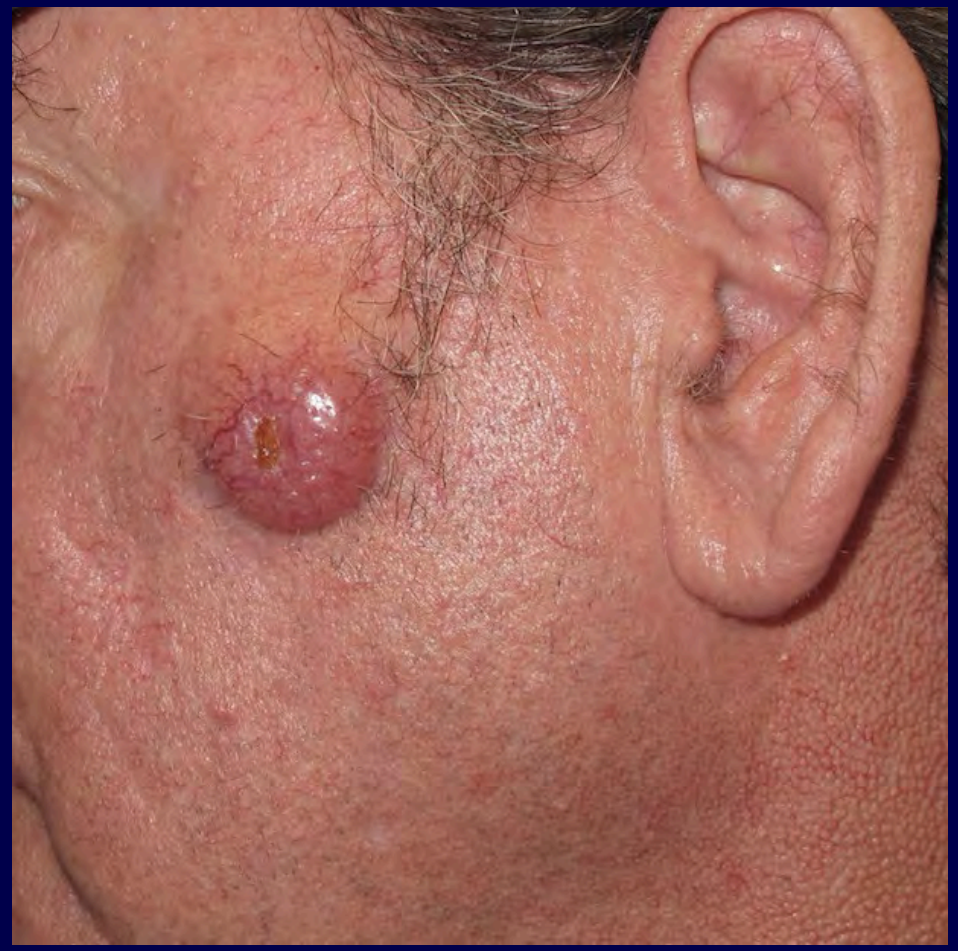
Lecture Outlines

- Disease overview
- Current treatment paradigm
- Unmet medical need
- Comments on NK recent data (N-803, haNK cells & avelumab in MCC)

Why Is MCC Important?

- ~2500 cases annually in the US; **incidence** is increasing.
- **Aggressive course** with a disease mortality rate ~45%.

  5-year OS for stage IV MCC is < 20%
- **Pathogenesis**:
  - MCC polyoma virus (MCPyV) in ~80% of MCC tumors
  - UV-induced damage



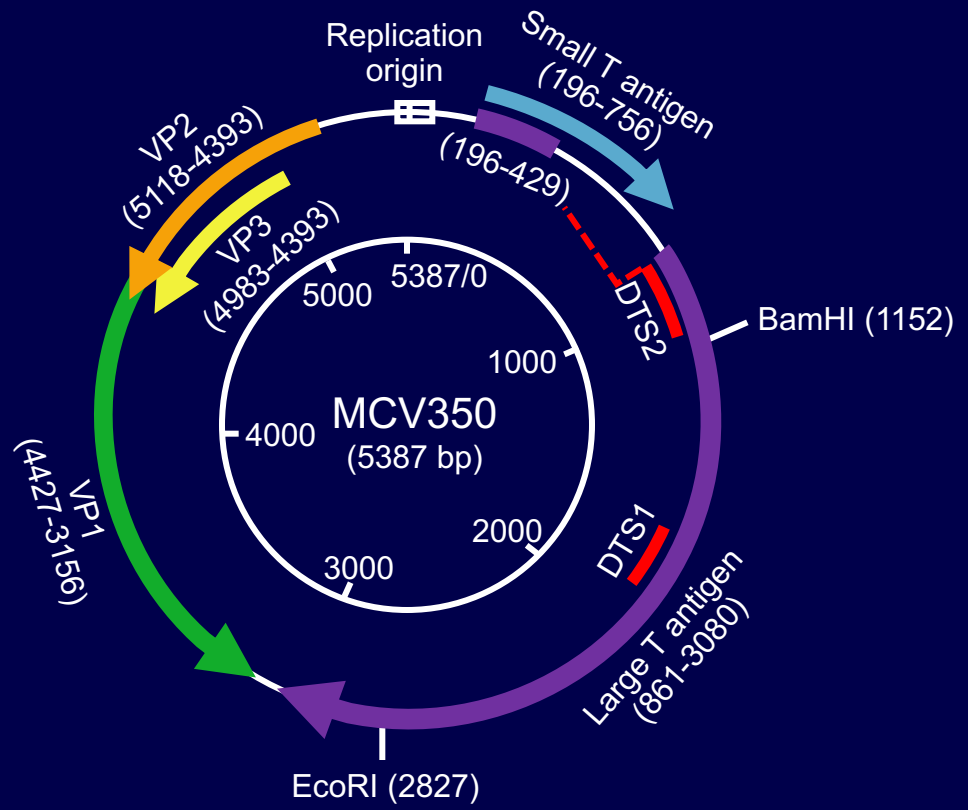
1. Bhatia S, et al. Curr Oncol Rep. 2011;13:488-497. 2. National Cancer Institute PDQ. Merkel cell carcinoma treatment. 3. Hughes MP, et al. Curr Dermatol Rep. 2014;3:46-53.

A New Human Virus That Causes Cancer Reported in 2008

Clonal Integration of Polyomavirus in MCC[1]

- Merkel cell polyomavirus identified by Moore and Chang (previously identified as KSHV)[1,2]
- Validated in multiple studies[3]
  - 80% of MCC related to virus
  - 20% of MCC independent of virus

Schematic of MCPyV Genome[1]

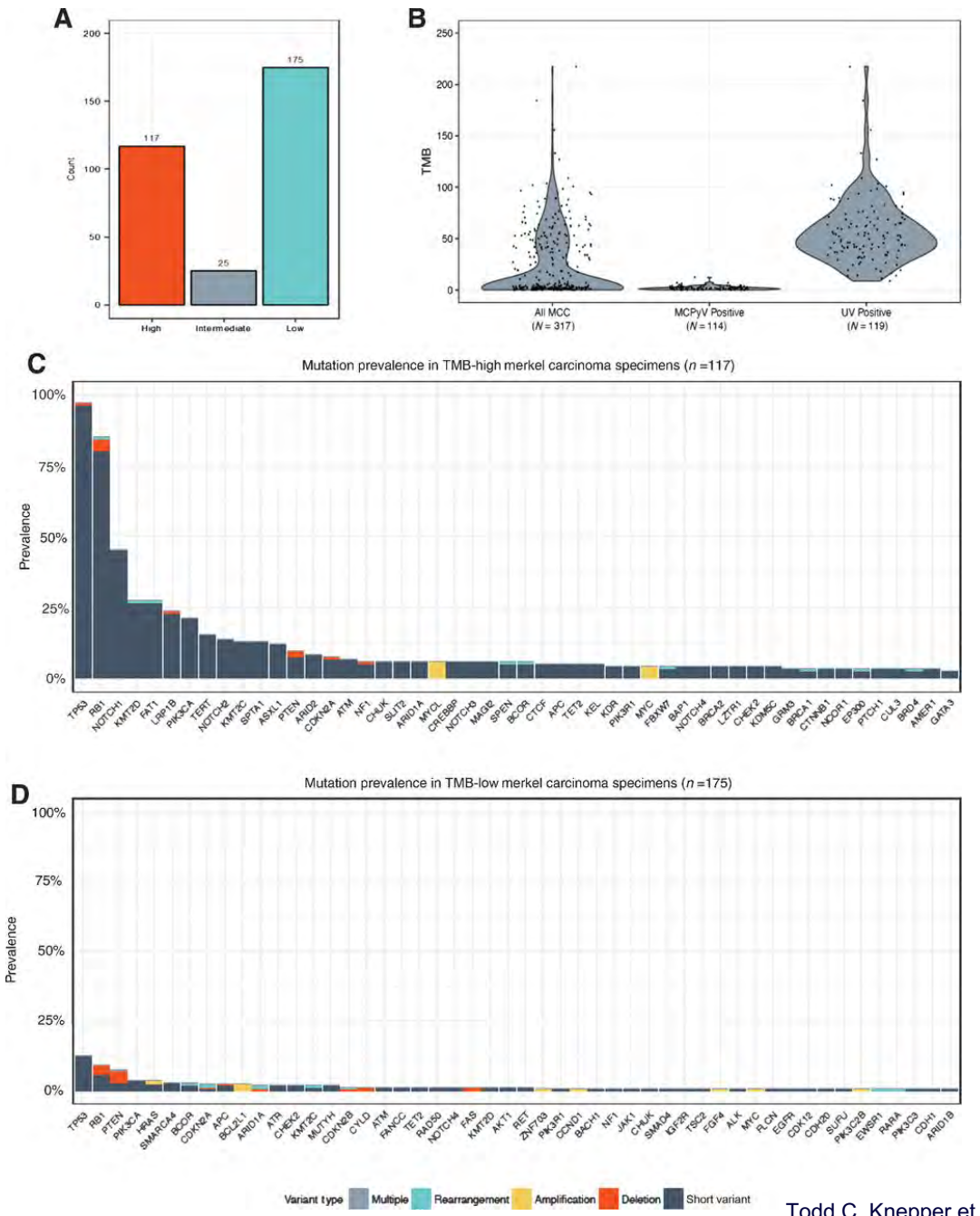


- **What are mutation patterns in virus-positive vs virus-negative tumors?**

1. From Feng H, et al. Science. 2008;319:1096-1100. Reprinted with permission from AAAS. 2. Chang Y, et al. Science. 1994;266:1865-1869. 3. Sihto H, et al. J Natl Cancer Inst. 2009;101:938-945.

Genomic Landscape of MCC

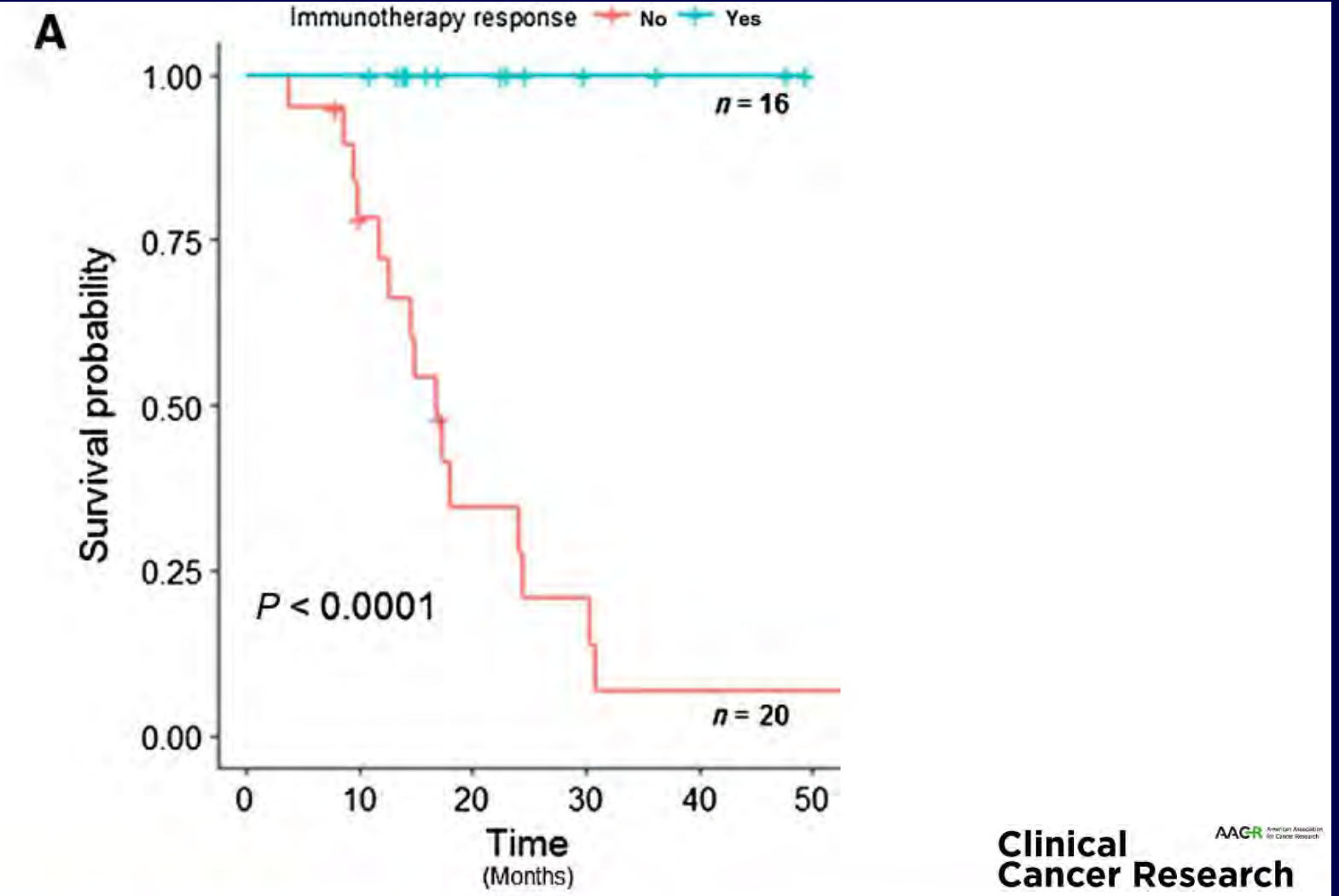
A, Distribution of MCCs with high intermediate, and low TMB (N = 317).



Clinical Cancer Research
AACR American Association for Cancer Research

Todd C. Knepper et al.
Clin Cancer Res 2019;25:596
1-5971

Patient Dichotomous Treatment with immune checkpoint inhibitors and patient survival.



Clinical Cancer Research

AACR American Association for Cancer Research

Todd C. Knepper et al. Clin Cancer Res 2019;25:5961-5971

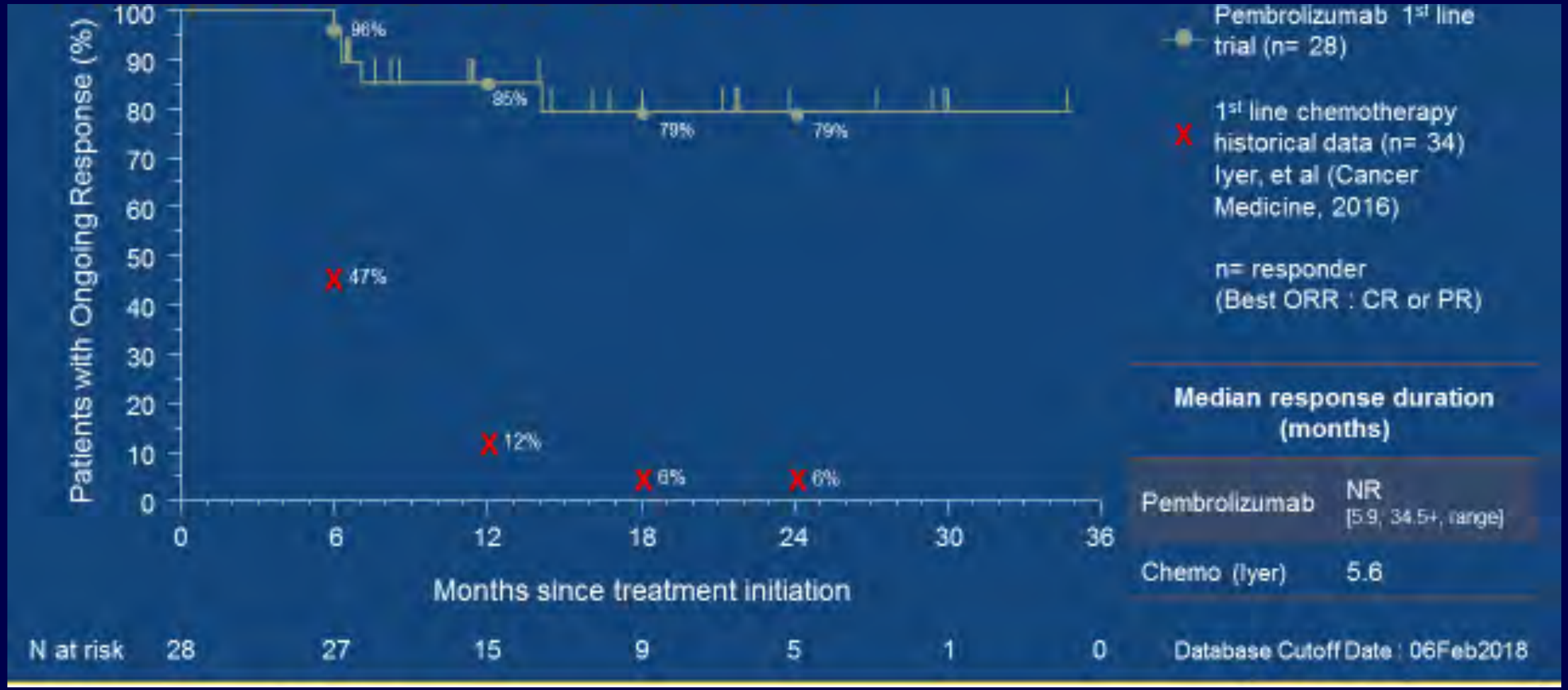
Radiologic tumor response to pembrolizumab in patients per viral status

MCPyV status:

- 45 evaluable patients
- Investigator-assessed exploratory end point
- Not an eligibility criterion

Response rate (%)	
MCPyV (+)	19/32 (59%)
MCPyV (-)	9/17 (53%)

Patients that Respond to Checkpoint have an approximate 80% durable response



Major Unmet Needs for MCC Pts

- PD-1 refractory pts: PD-1 blockade is effective only in a subset of pts (~ 50% of chemotherapy-naive pts[1] and ~ 30% of chemotherapy-treated pts[2])
- Immune-suppressed pts have limited options for treatment
- Effective systemic adjuvant therapy is needed for pts at high risk of recurrence

1. Nghiem PT, et al. N Engl J Med. 2016;374:2542-2552.
2. Kaufman HL, et al. Lancet Oncol. 2016;17:1374-1385.

Metastatic MCC

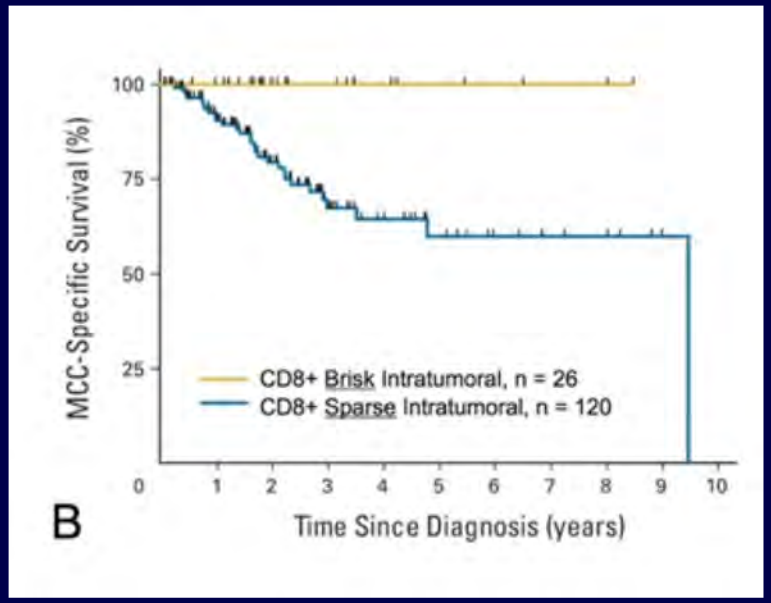
- There is a strong need for rational, biology-driven drug development in MCC for finding effective options in
  - Pts who do not respond optimally to PD-1 blockade
  - Pts who cannot receive immunotherapy due to autoimmune disease or systemic immune suppression

Merkel Cell Carcinoma (MCC): Immune evasion mechanisms

- Still significant **unmet needs** in advanced MCC
  - Intrinsic or acquired resistance to ICI (~50% OF MCC pts)
  - Ineligibility for ICI therapy (autoimmunity, immunosuppression etc).

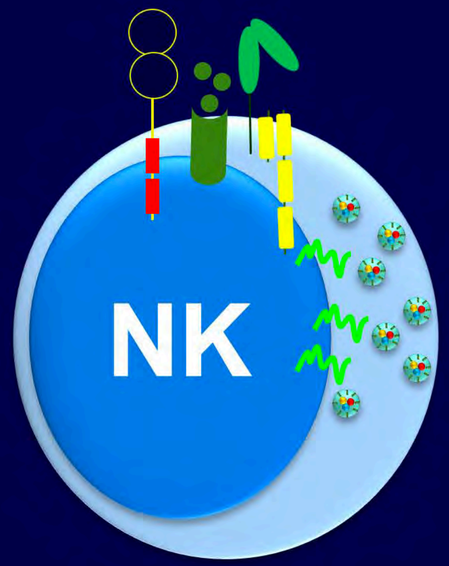
- Several **mechanisms of immune evasion**:
  - **Sparse T-cell infiltrates (~80% of MCC tumors)**
  - **Exhausted TILs**
  - **MHC-1 downregulation highly prevalent (84% of MCC)**
  - **MHC loss likely relevant to acquired resistance**

- **NK-cells** should recognize MHC-1 deficient cells; unfortunately, cancer patients have dysfunctional NK cells



{Paulson K *JNCCN* 2018; Paulson K *JCO* 2010; Paulson K *CIR* 2014; Paulson K *Nat Comm* 2018}

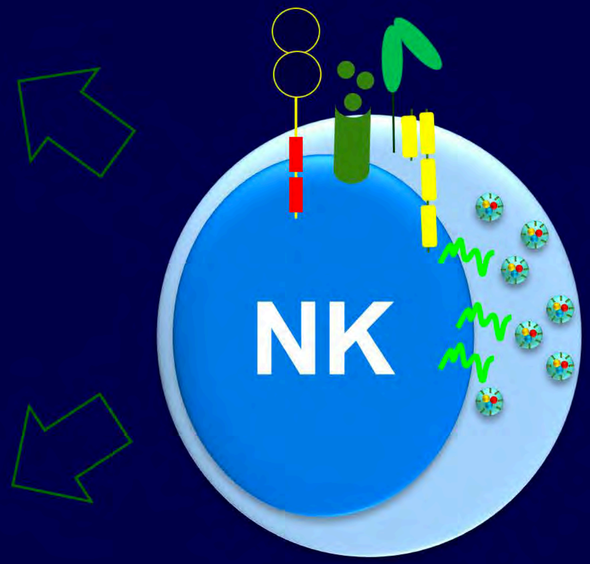
What are Natural Killer Cells?



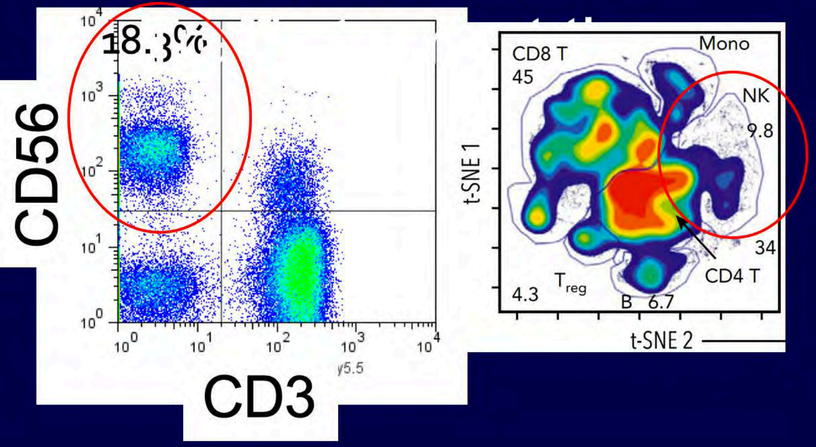
What are Natural Killer Cells?

Founding member of
Innate lymphoid cells

NK ILC1 ILC2 ILC3



5-20% of Blood
lymphocytes

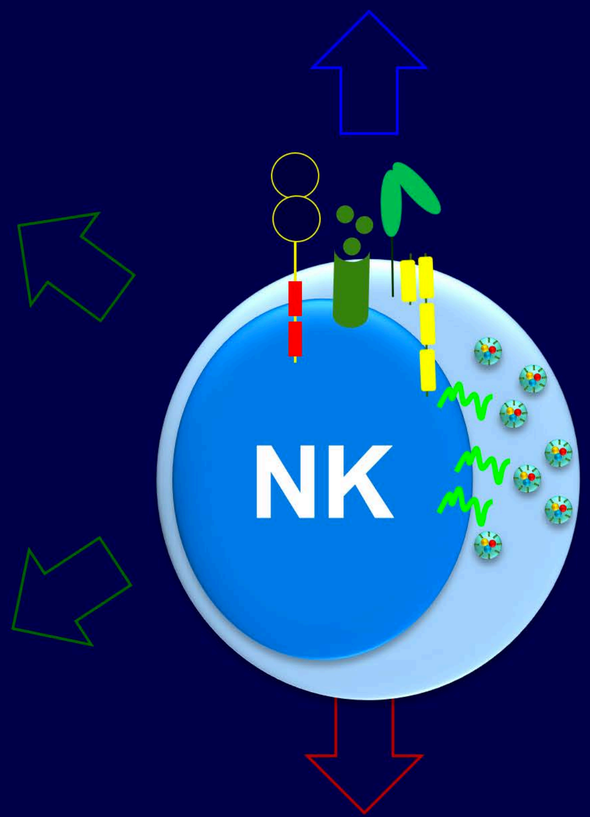


What are Natural Killer Cells?

Germline DNA encoded receptors:
inhibitory, activating, and cytokine

Founding member of
Innate lymphoid cells

NK ILC1 ILC2 ILC3



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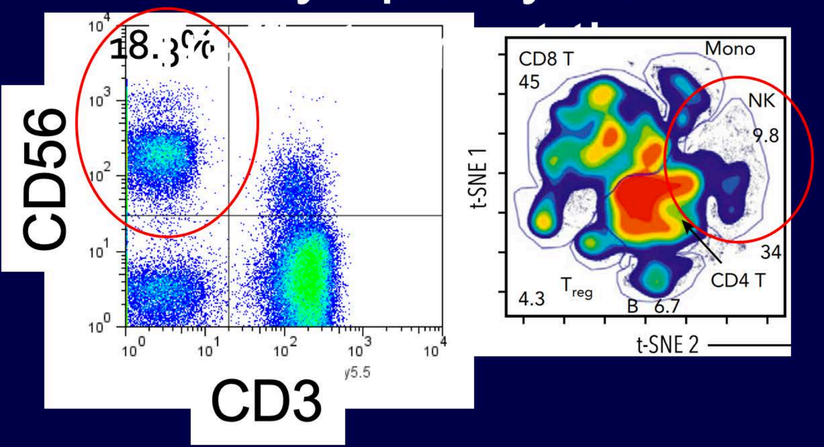
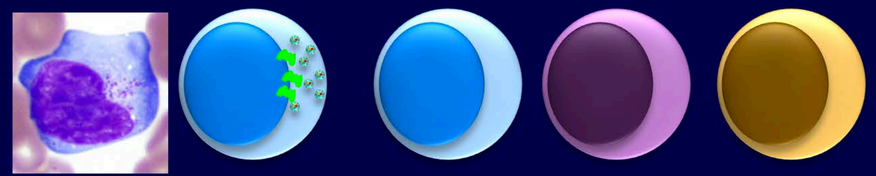


Different from T cells!
Do not have:
Recombined DNA for
antigen-specific activating receptor

What are Natural Killer Cells?

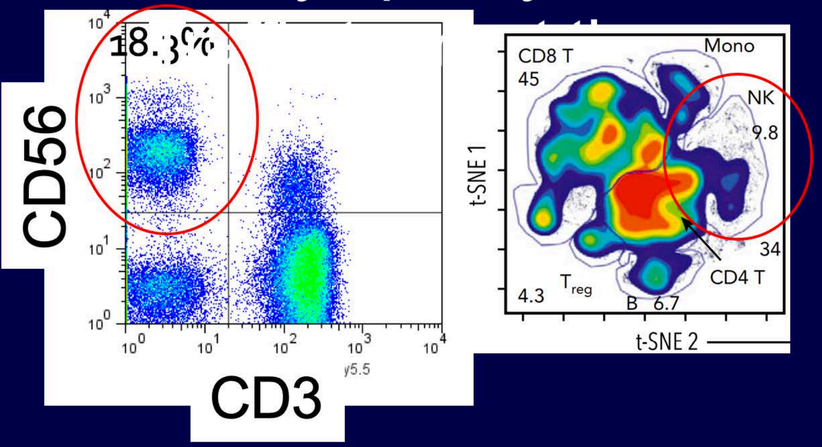
Germline DNA encoded receptors:
inhibitory, activating, and cytokine

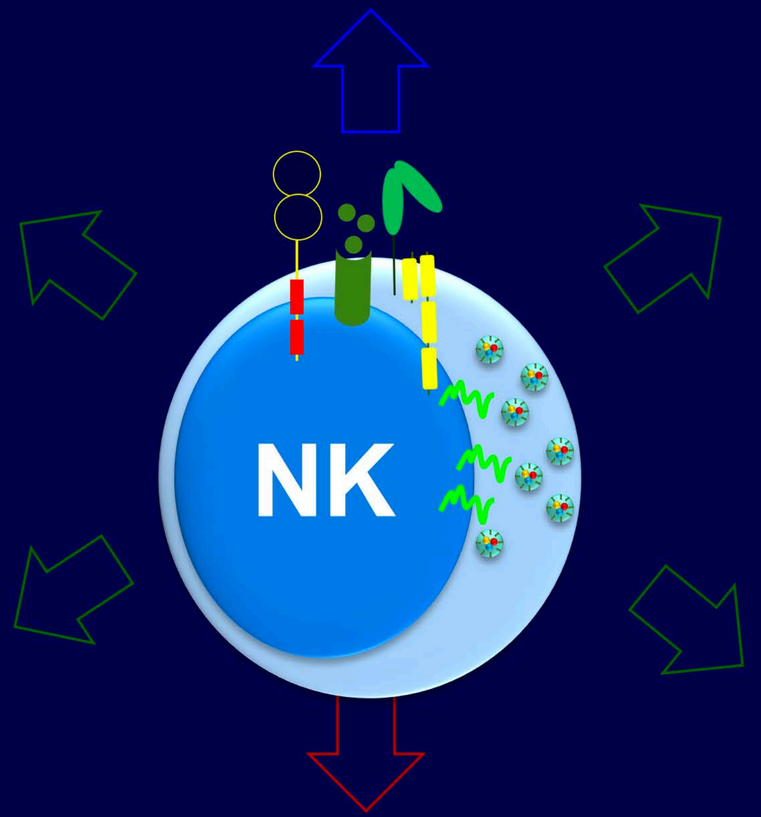
Founding member of Innate lymphoid cells



NK ILC1 ILC2 ILC3

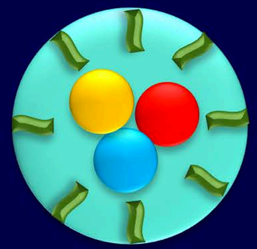
5-20% of Blood lymphocytes





Different from T cells!
Do not have:
Recombined DNA for
antigen-specific activating receptor

Cytotoxicity (Killing)



Granzymes

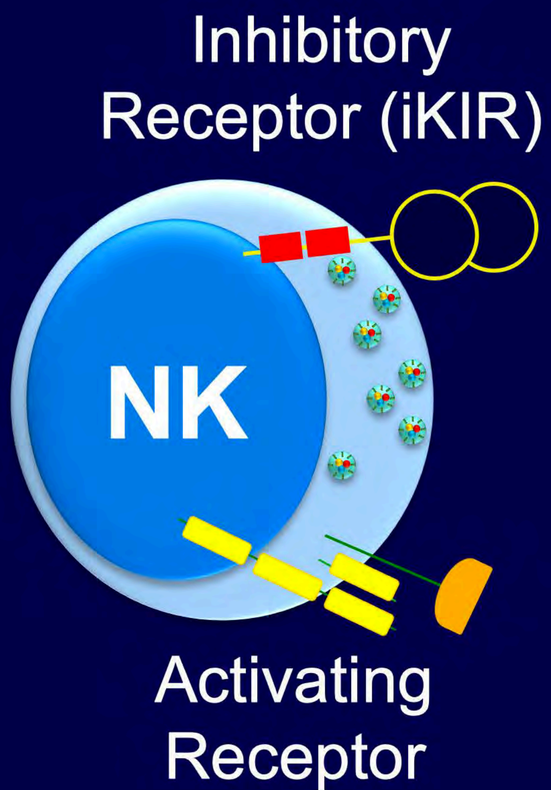
Perforin

LAMP-1 (CD107a)
Degranulation marker

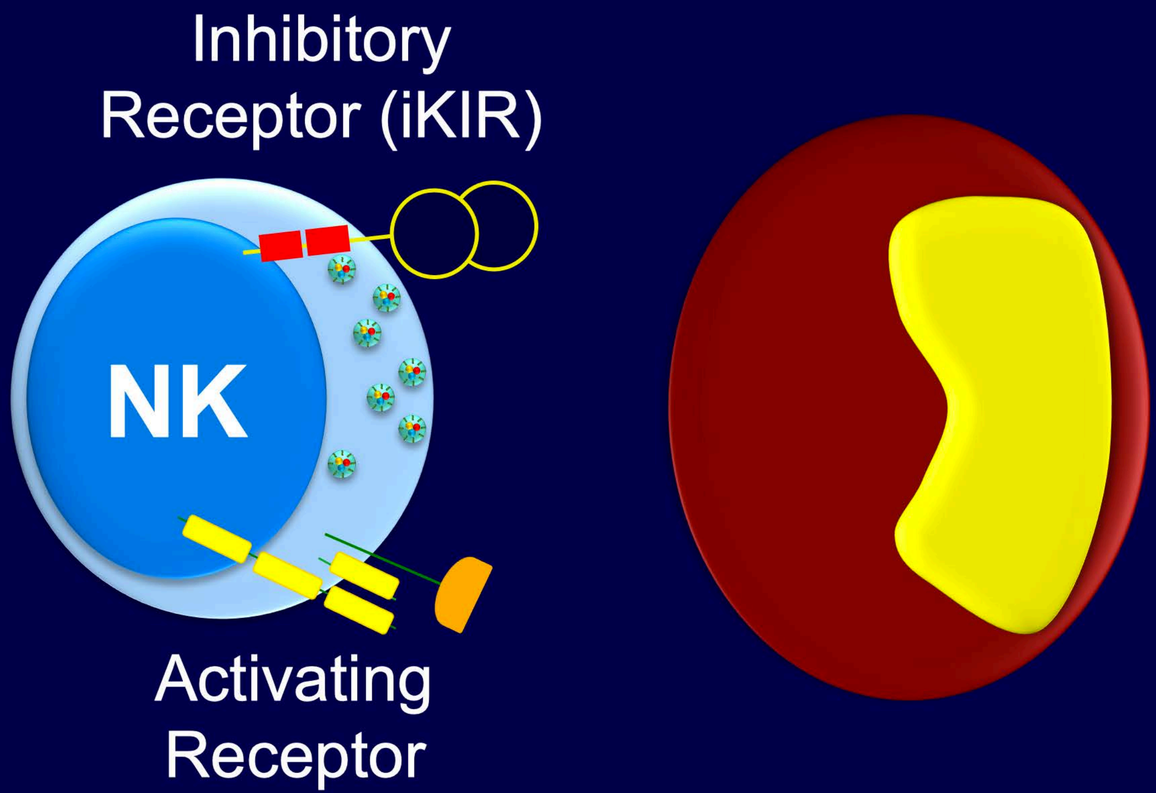
Cytokine and Chemokine Production

(Communication)

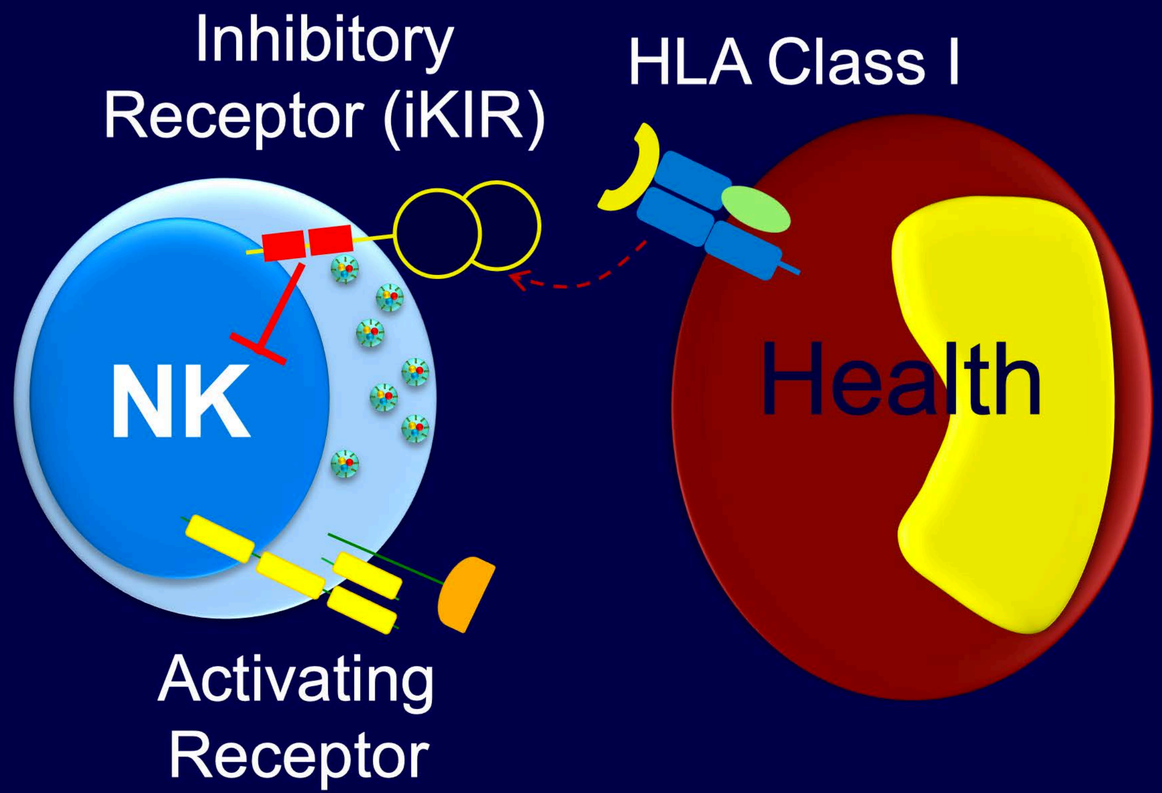
NK cell recognition by receptors



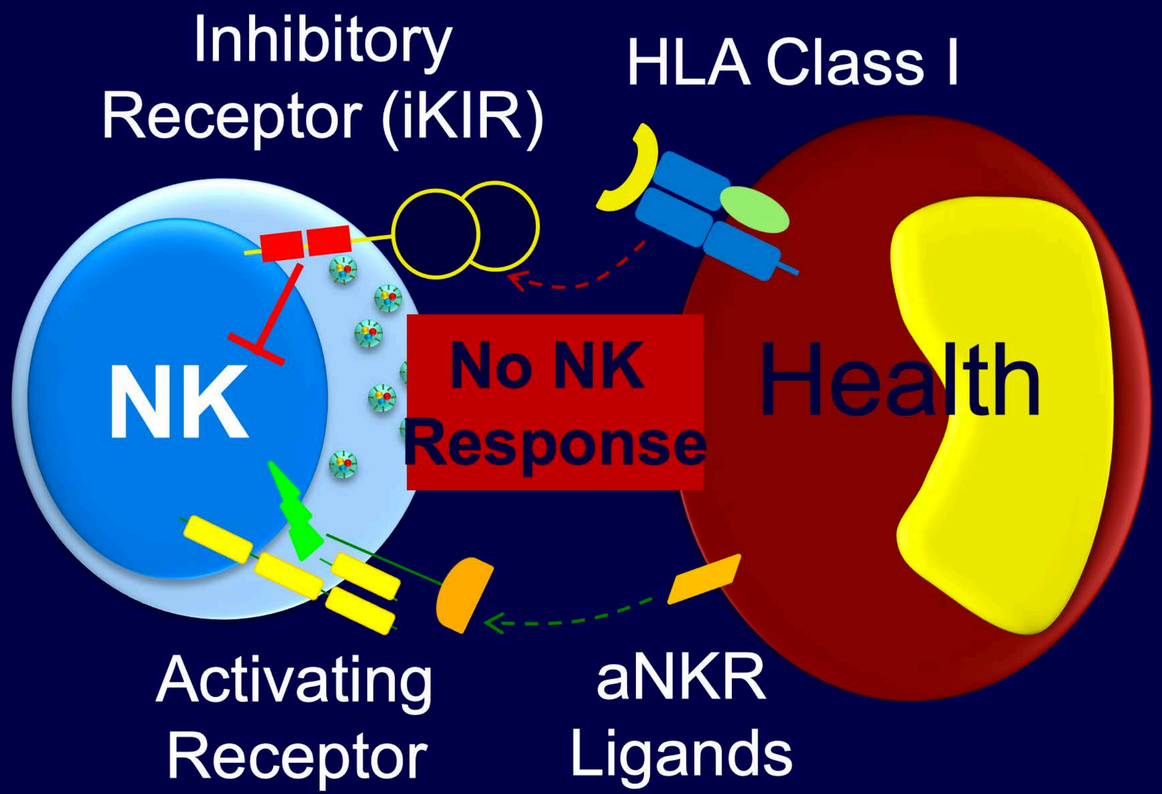
NK cell recognition by receptors



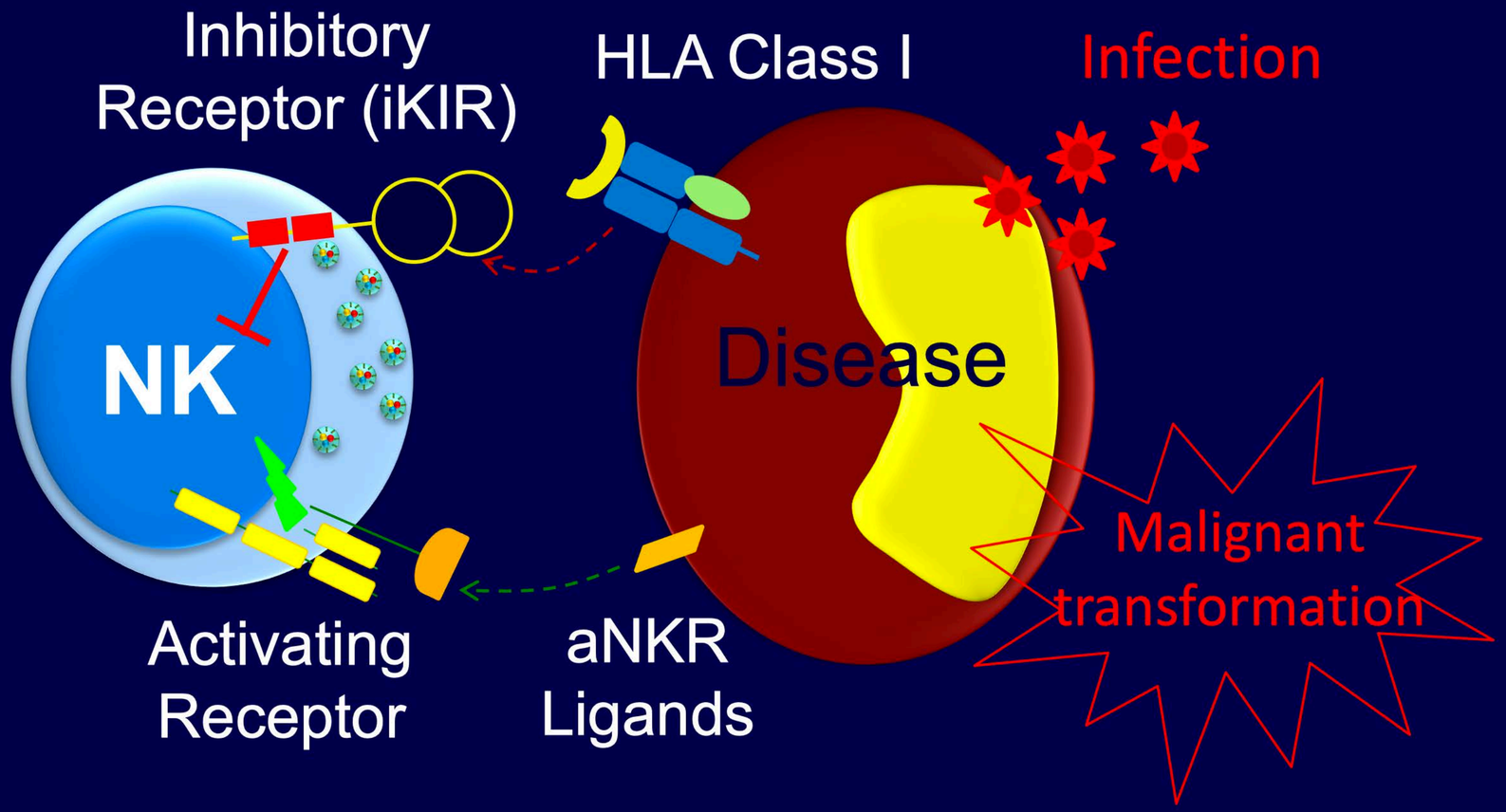
NK cell recognition by receptors



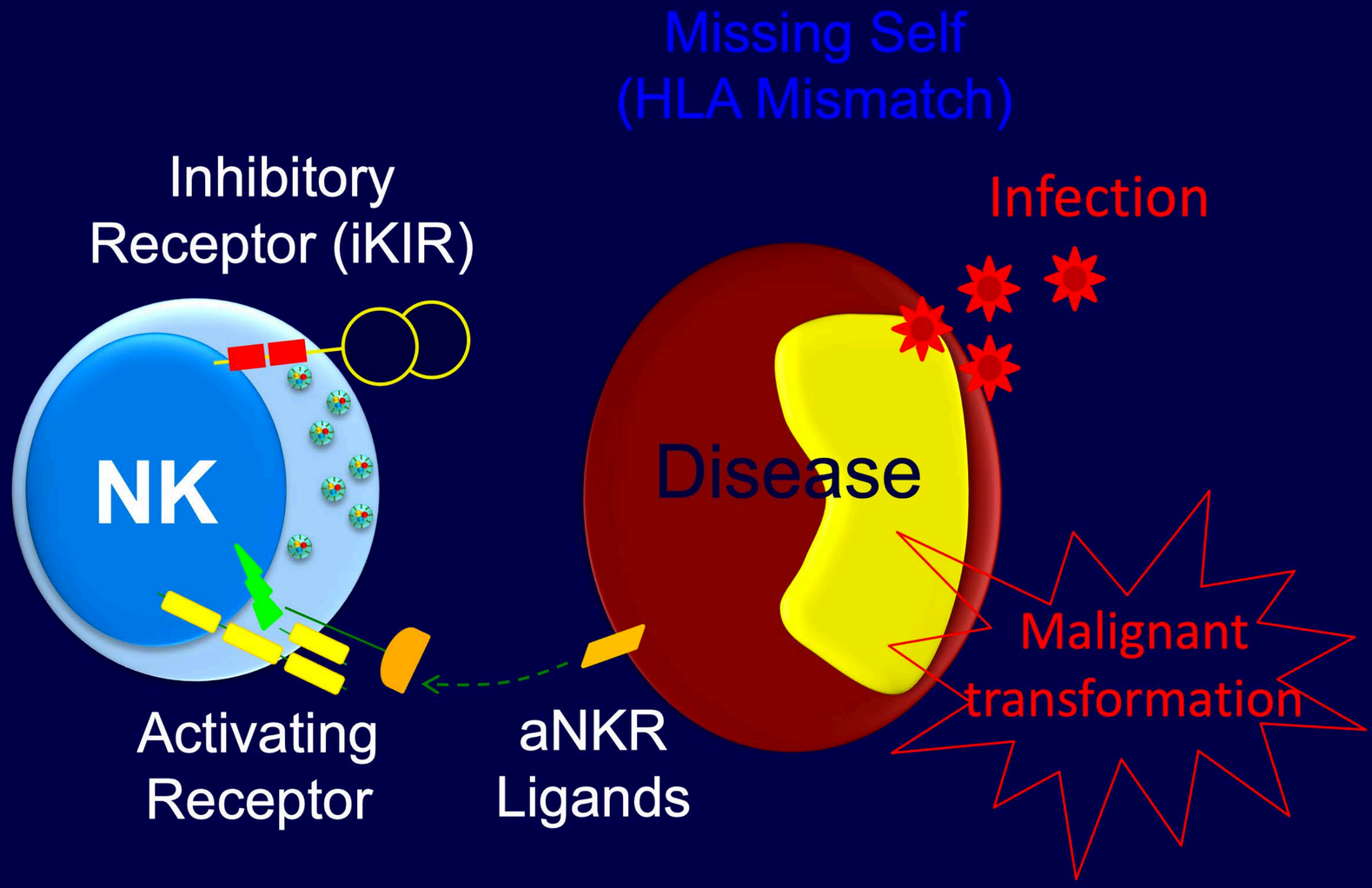
NK cell recognition by receptors



NK cell recognition by receptors



NK cell recognition by receptors



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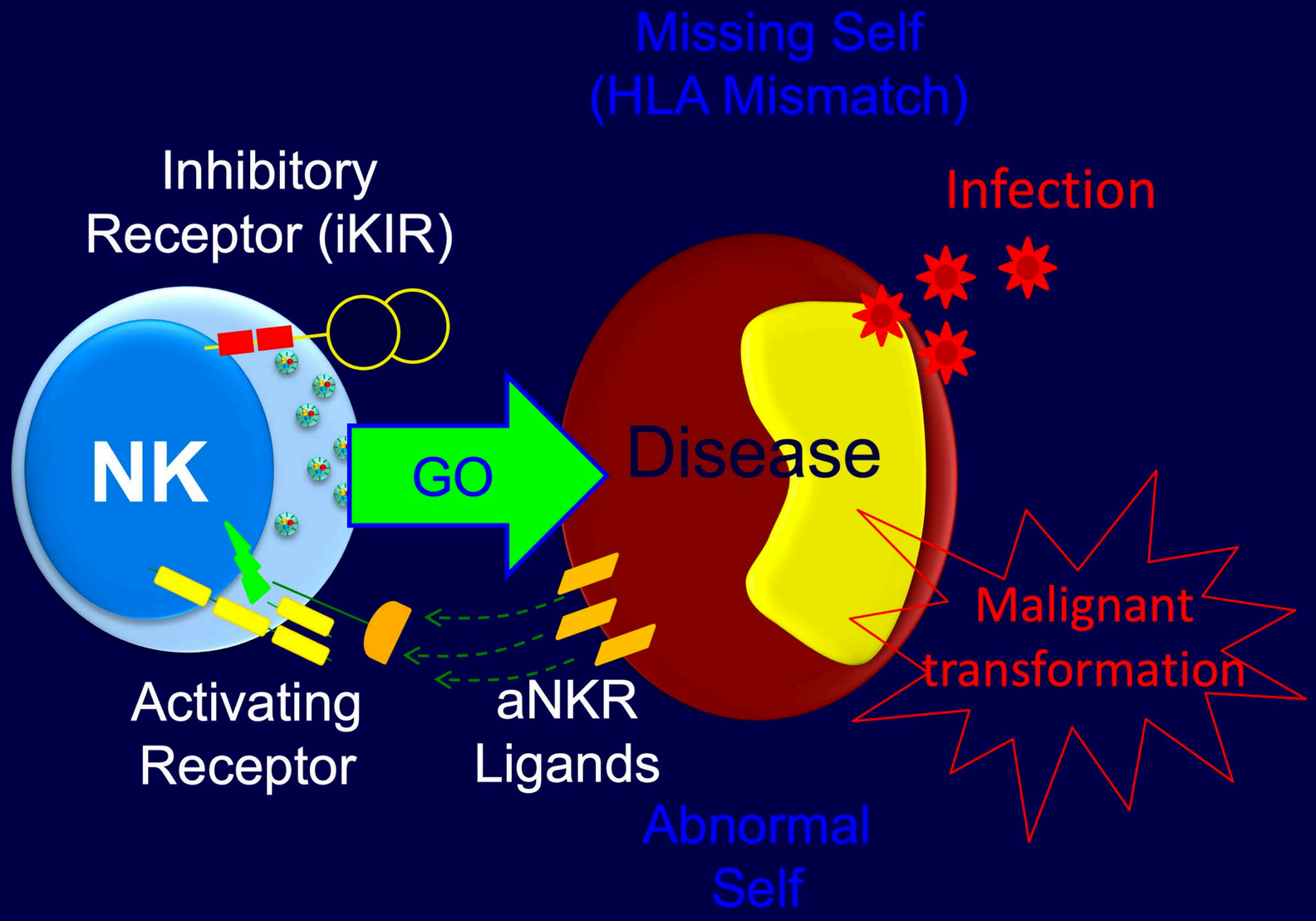
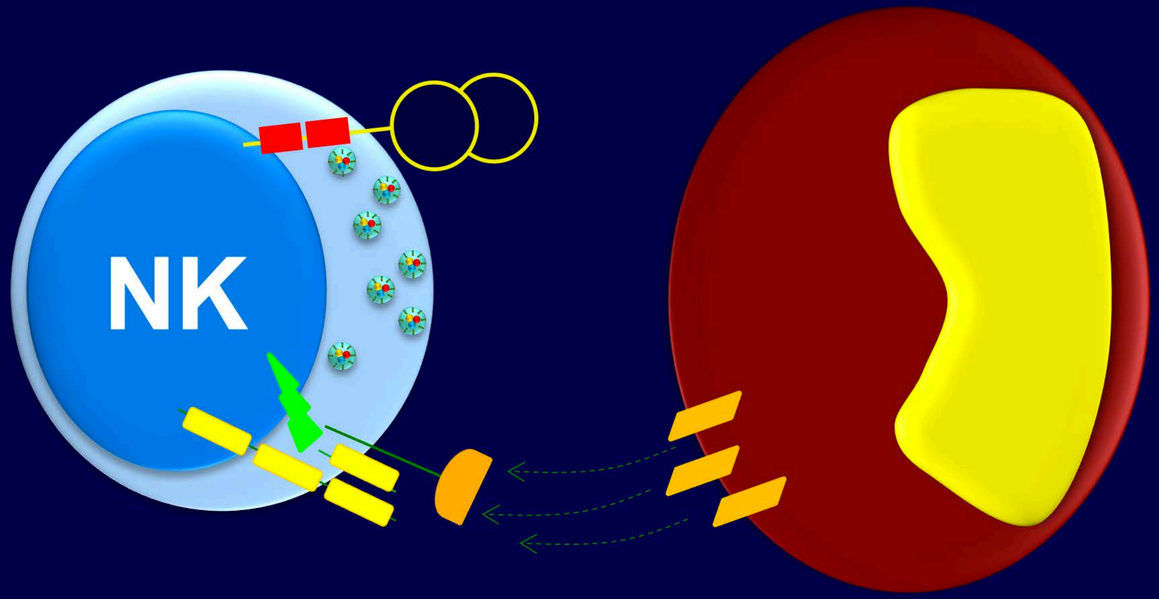
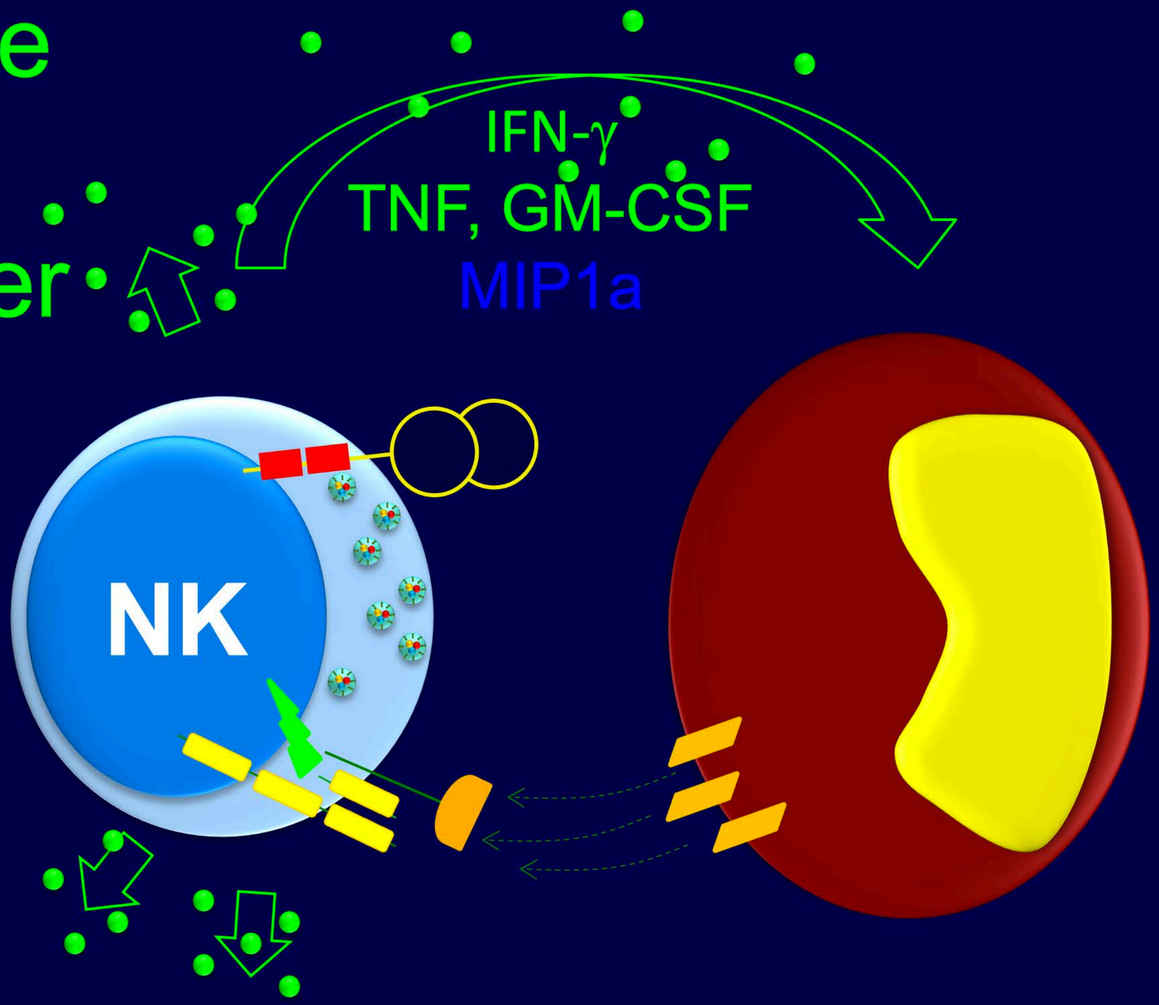


NK cell multipotential function



NK cell multipotential function

Communicate
Recruit
Signal Danger



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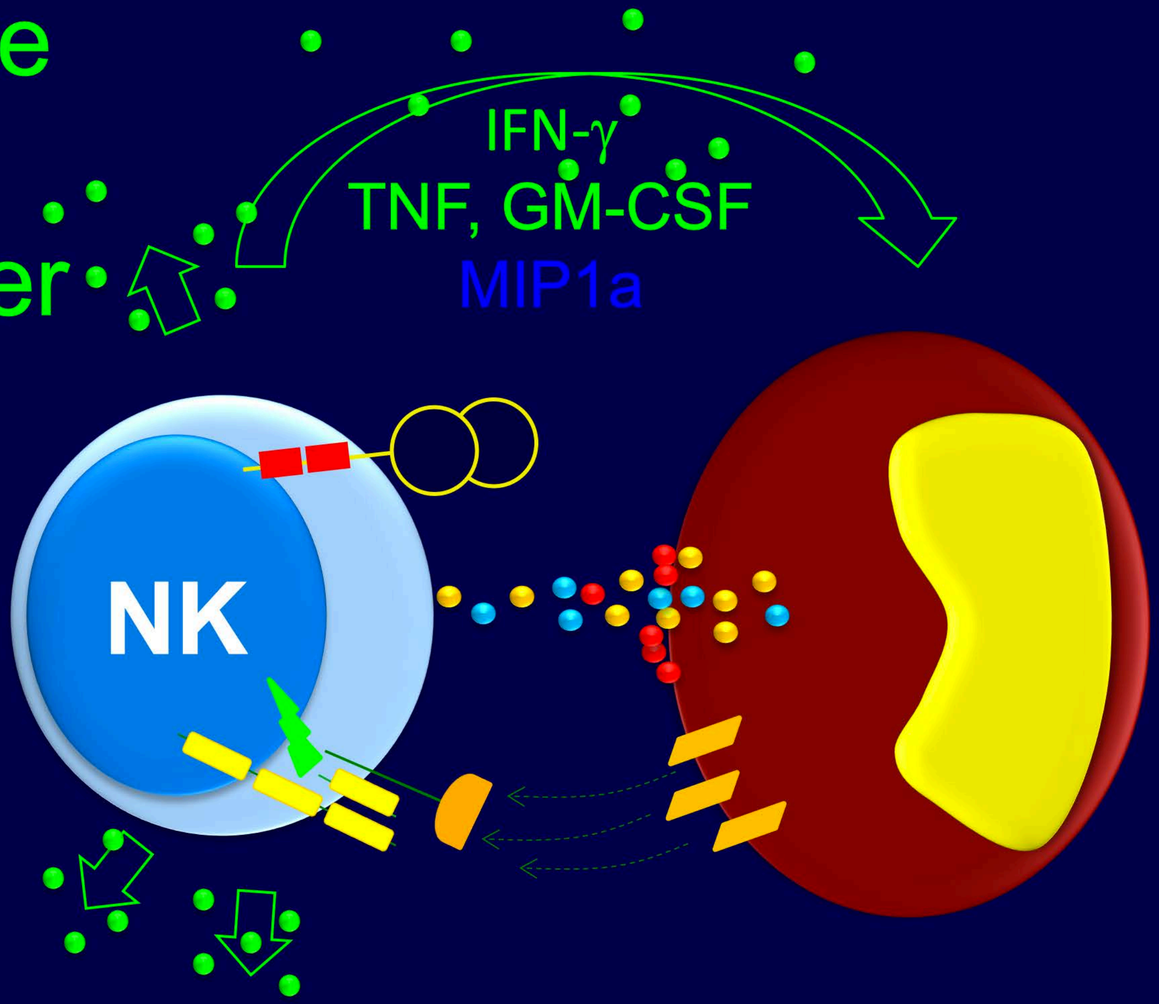

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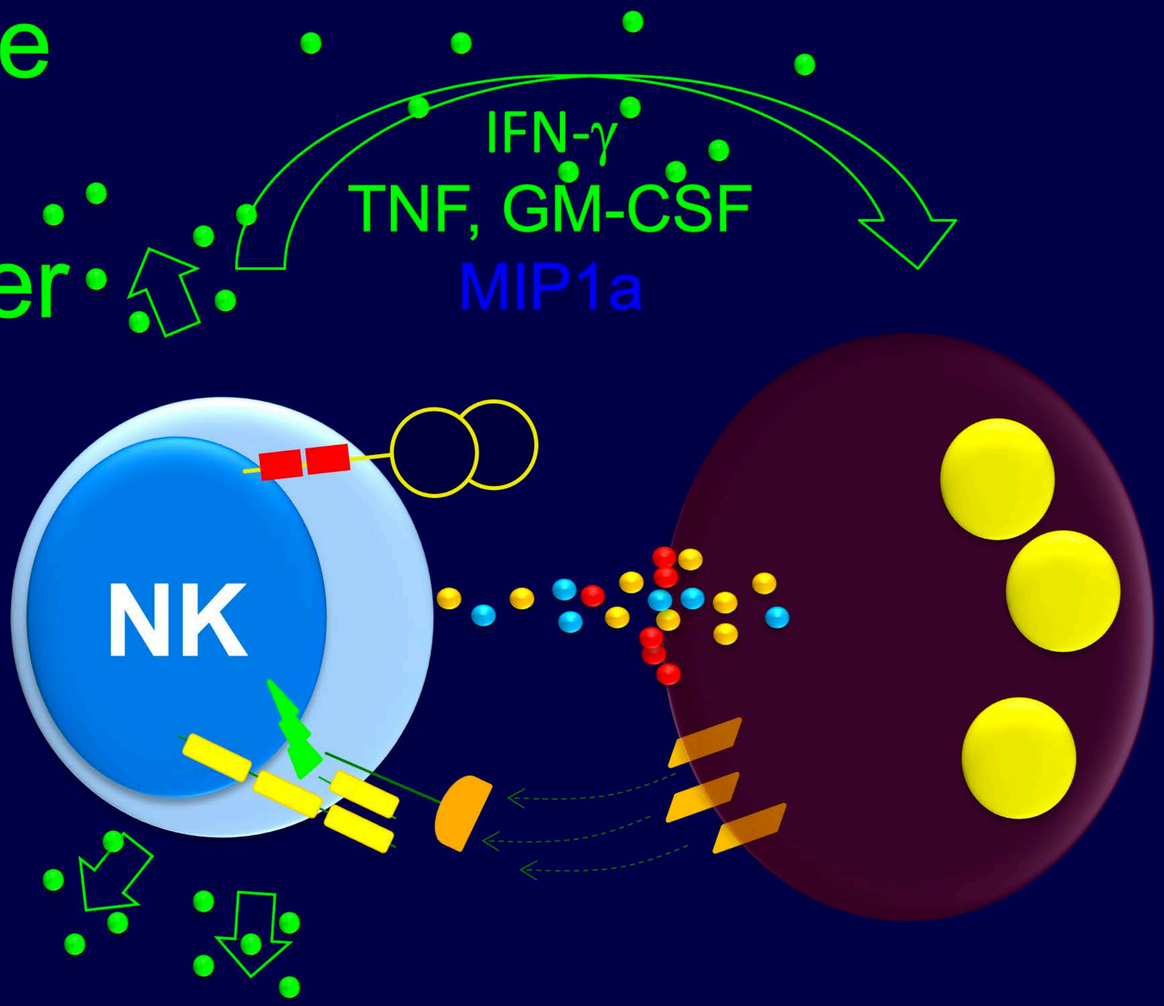

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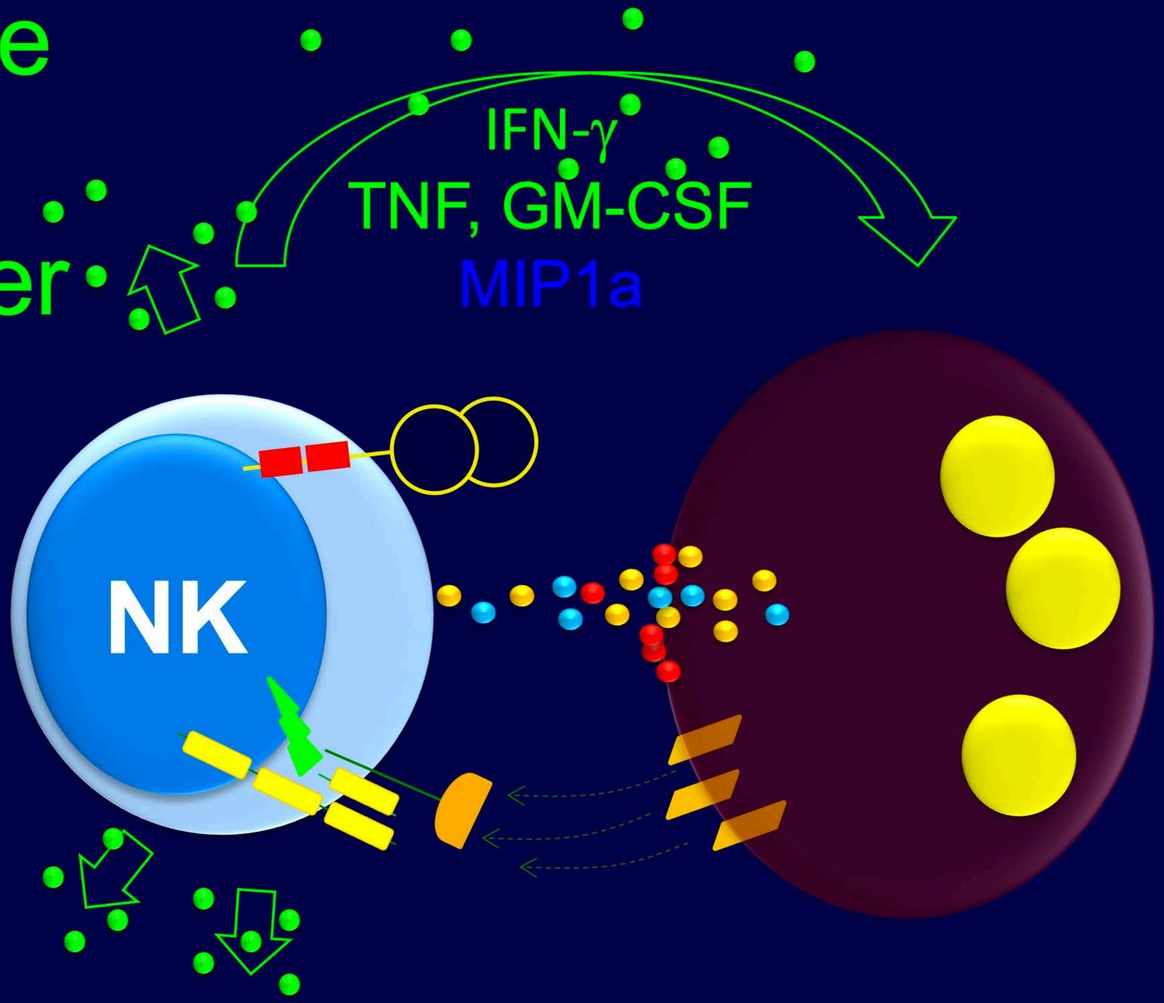
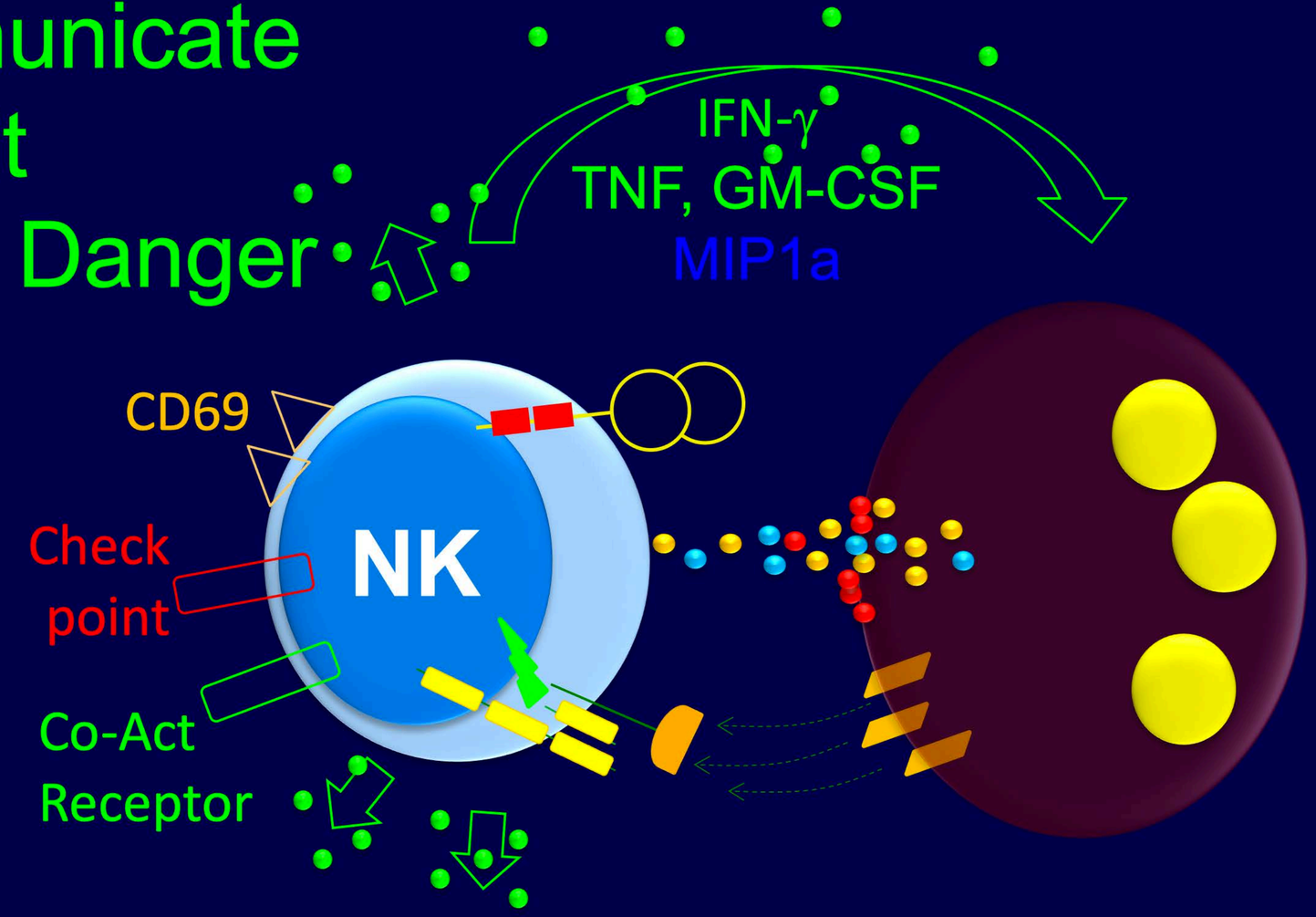


Kill Cancer
(Single Cell Killing)

NK cell multipotential function

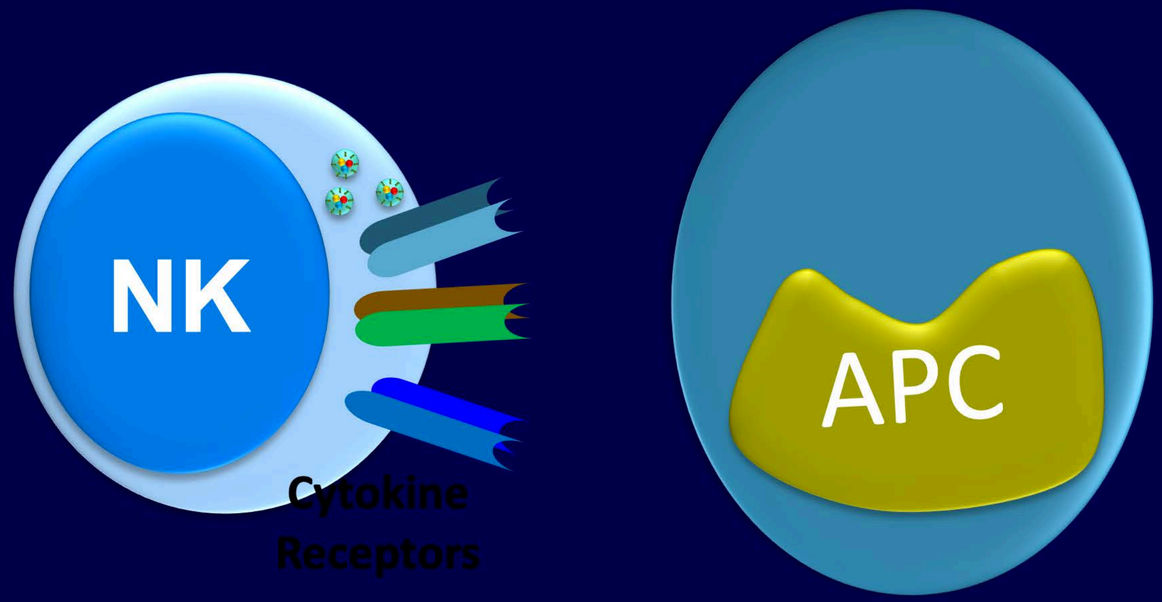
Communicate
Recruit
Signal Danger



Kill Cancer
(Single Cell Killing)

NK cells are function enabled by cytokines

enable functionality, survival, proliferation, metabolism, inhibitory/activating receptors



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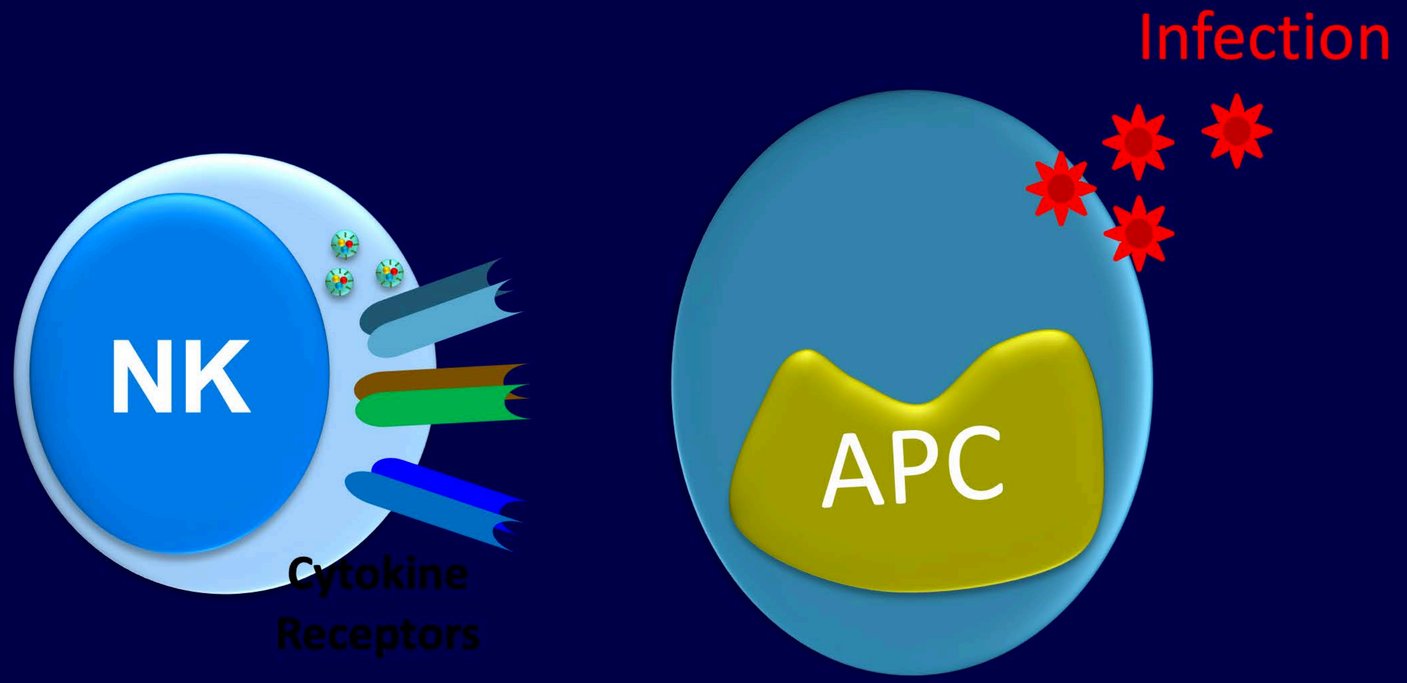

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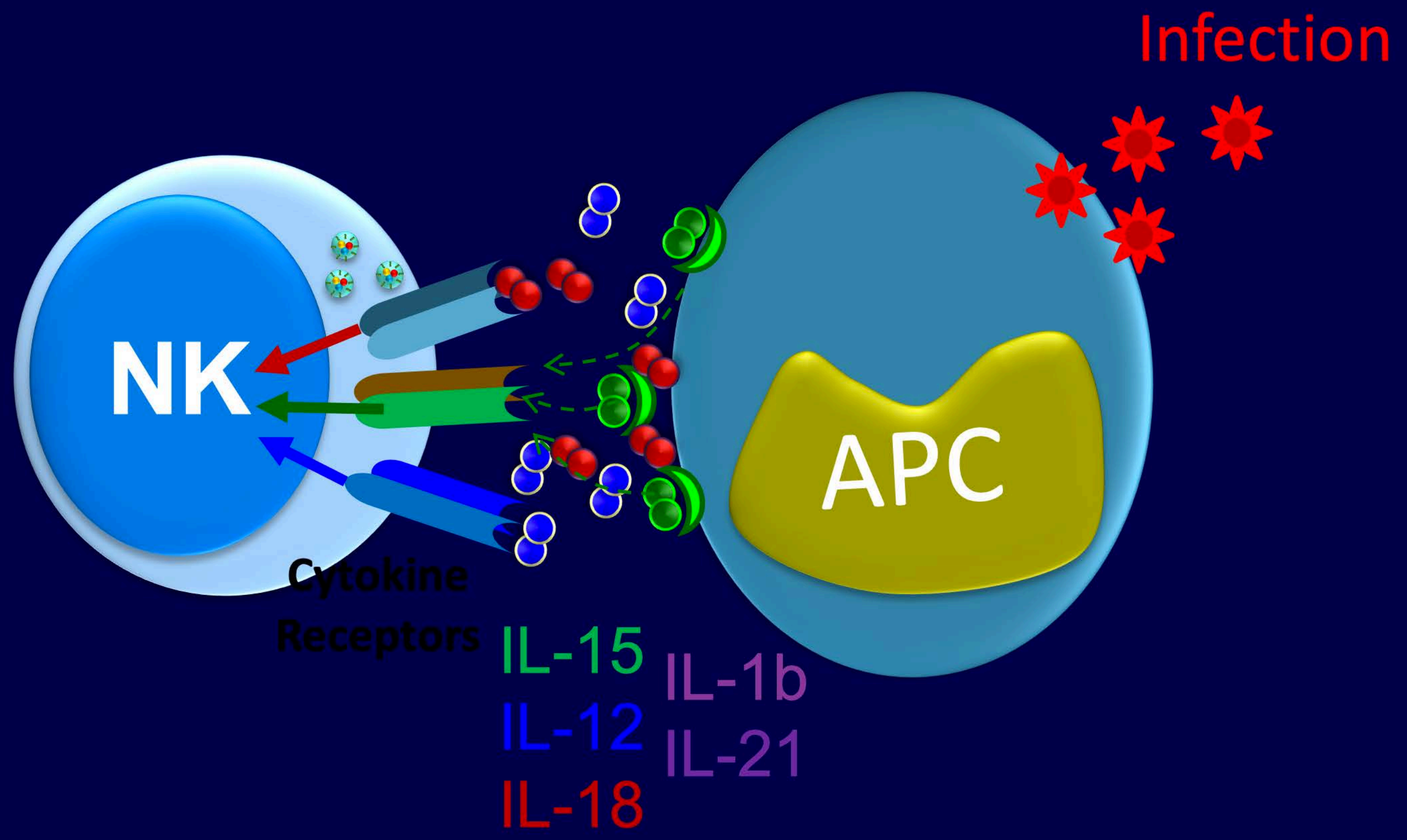

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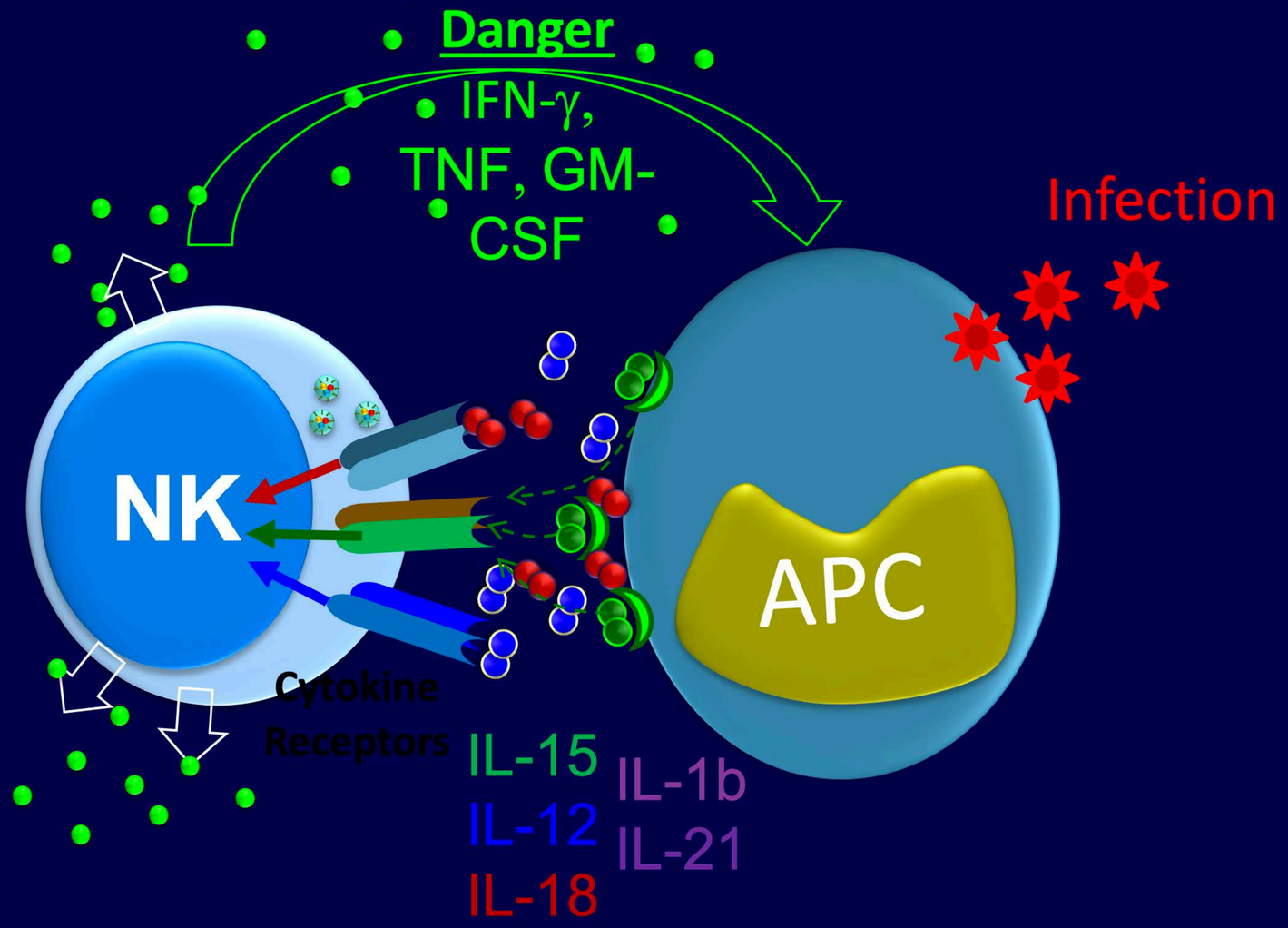

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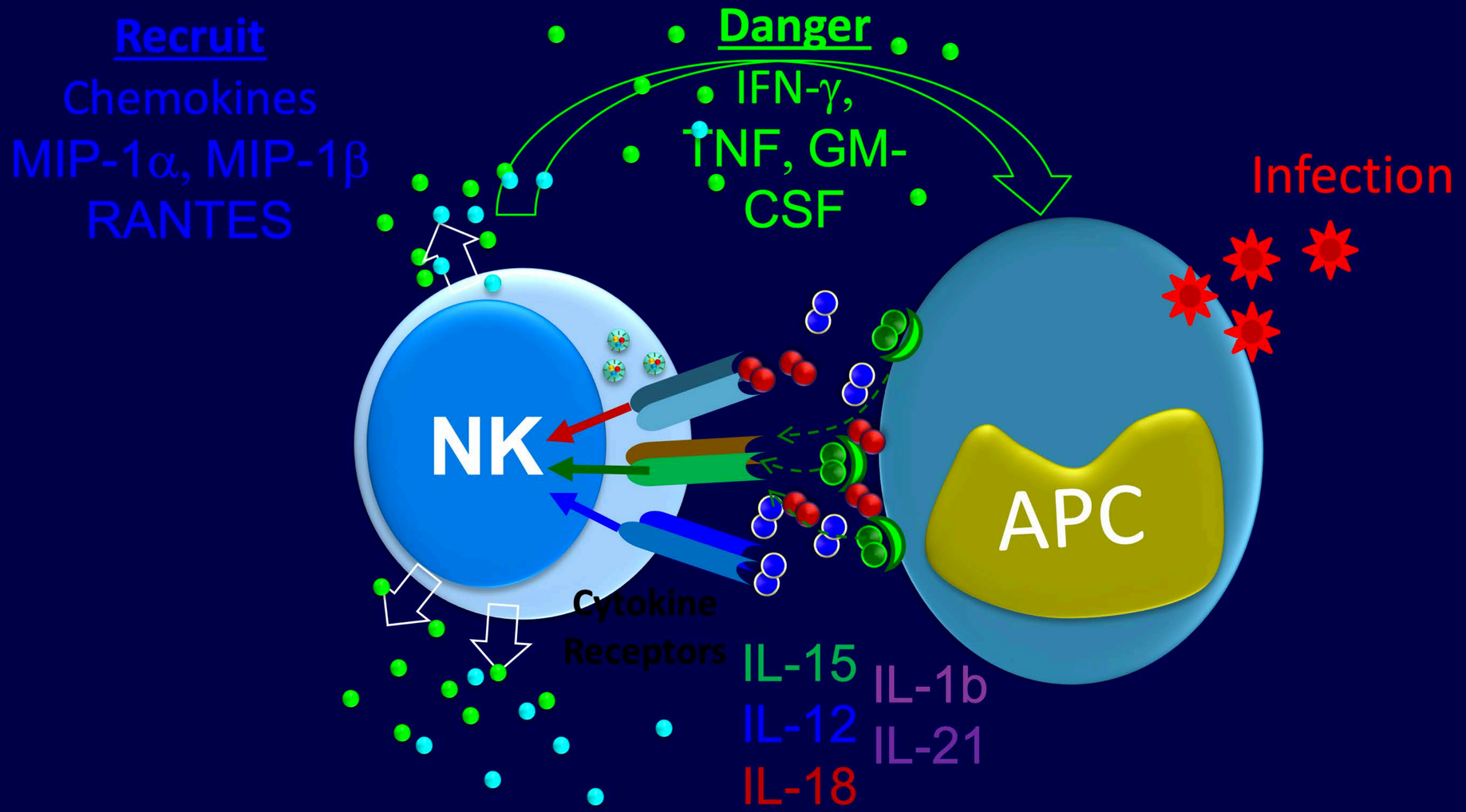

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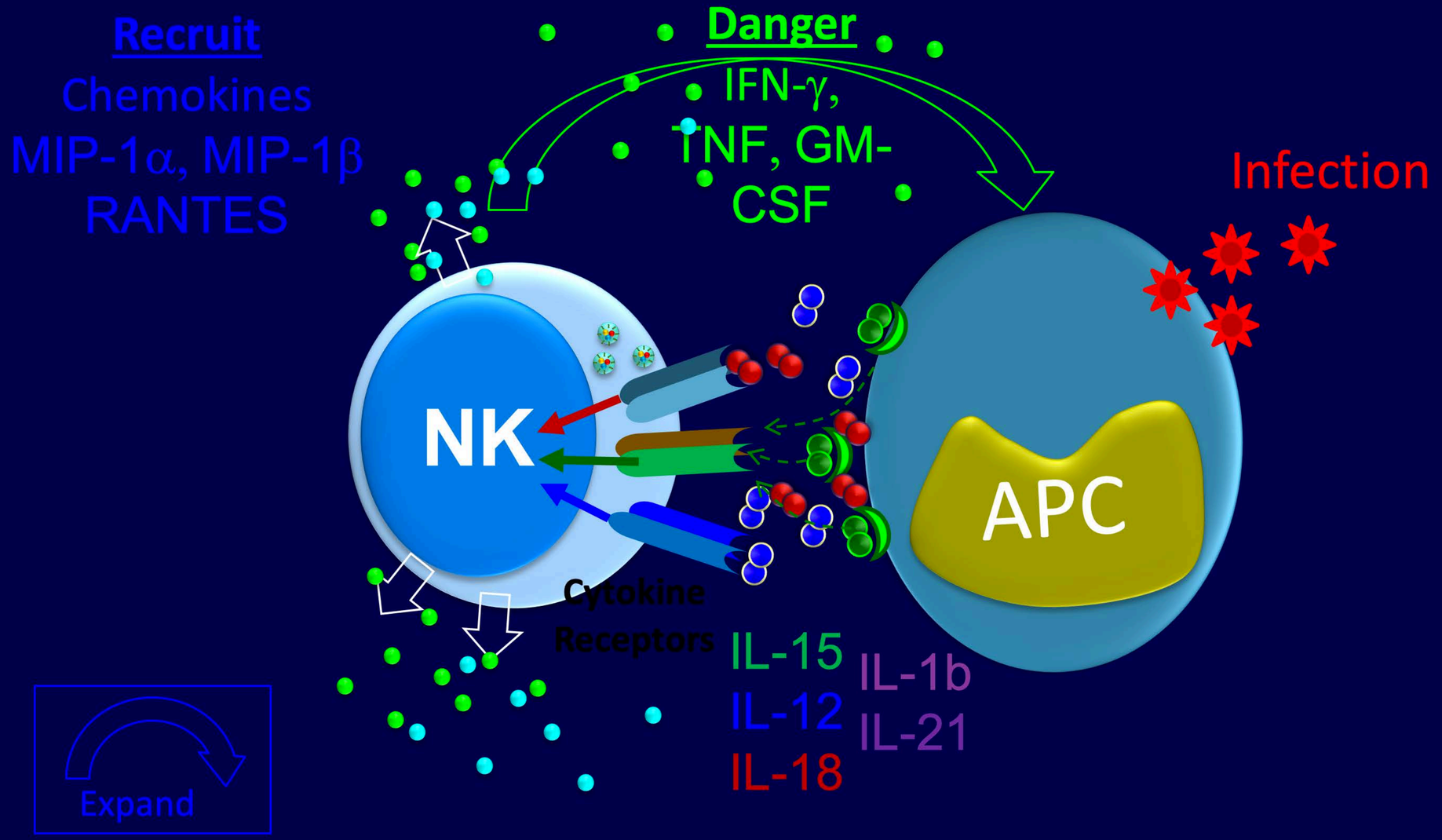

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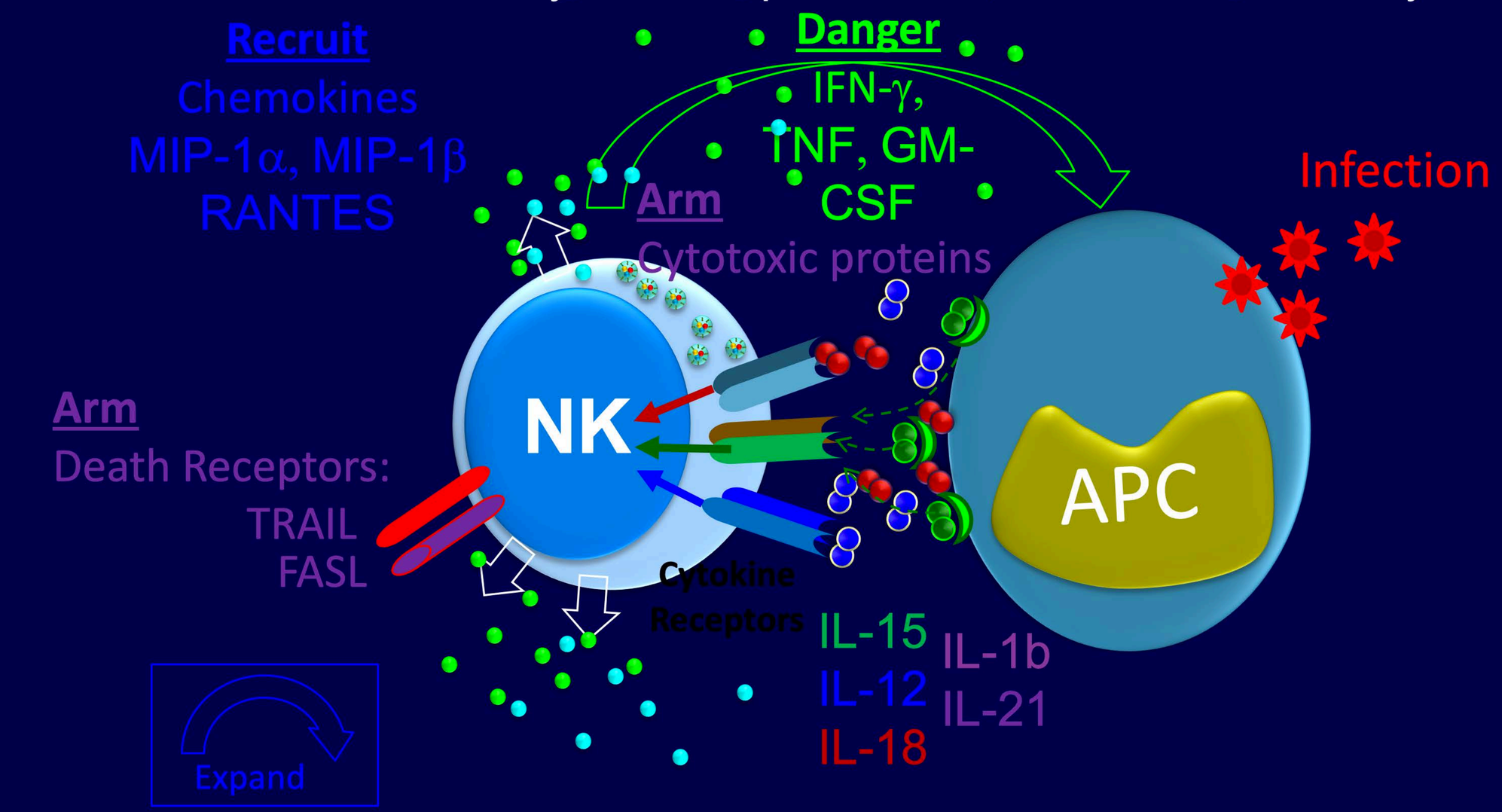

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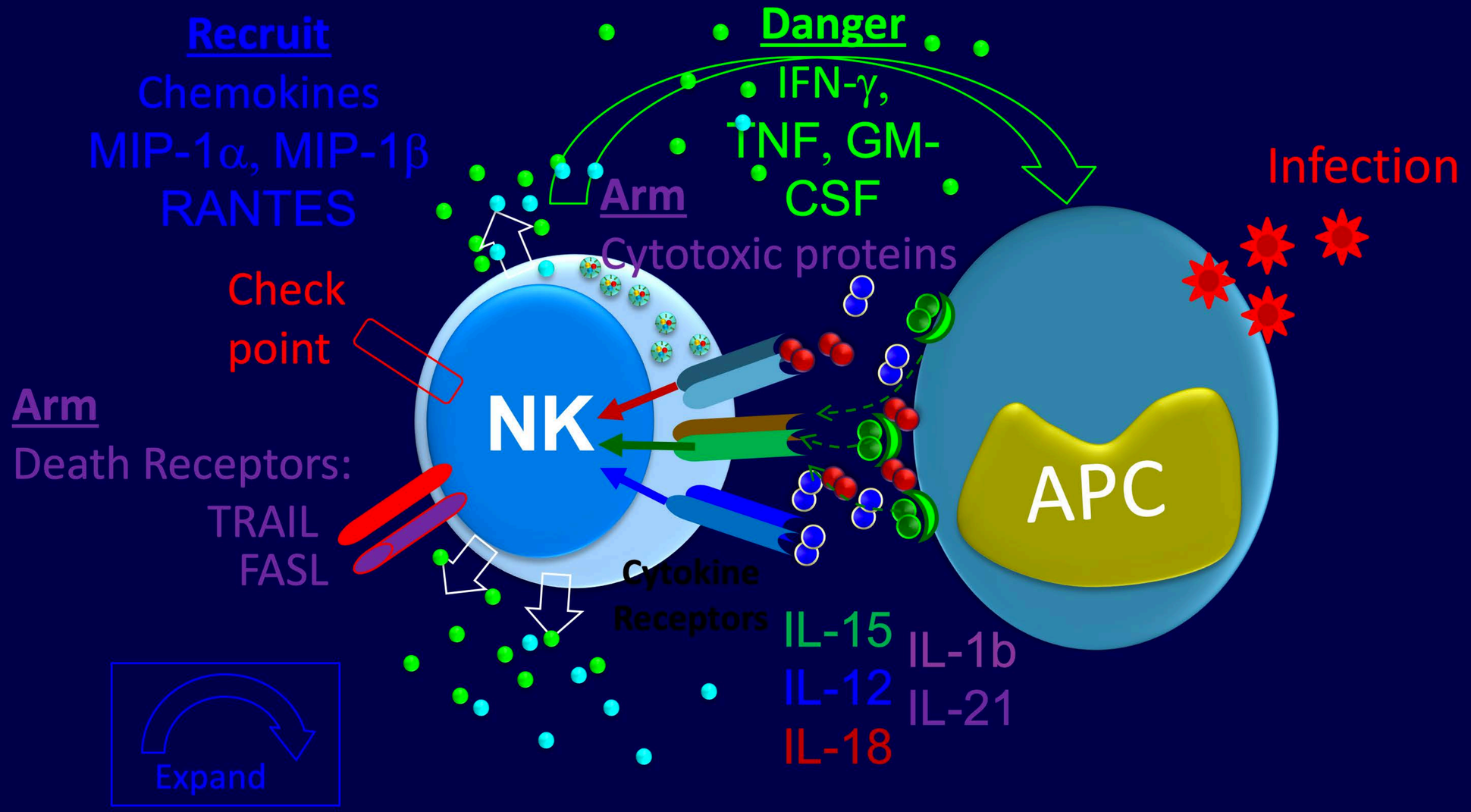
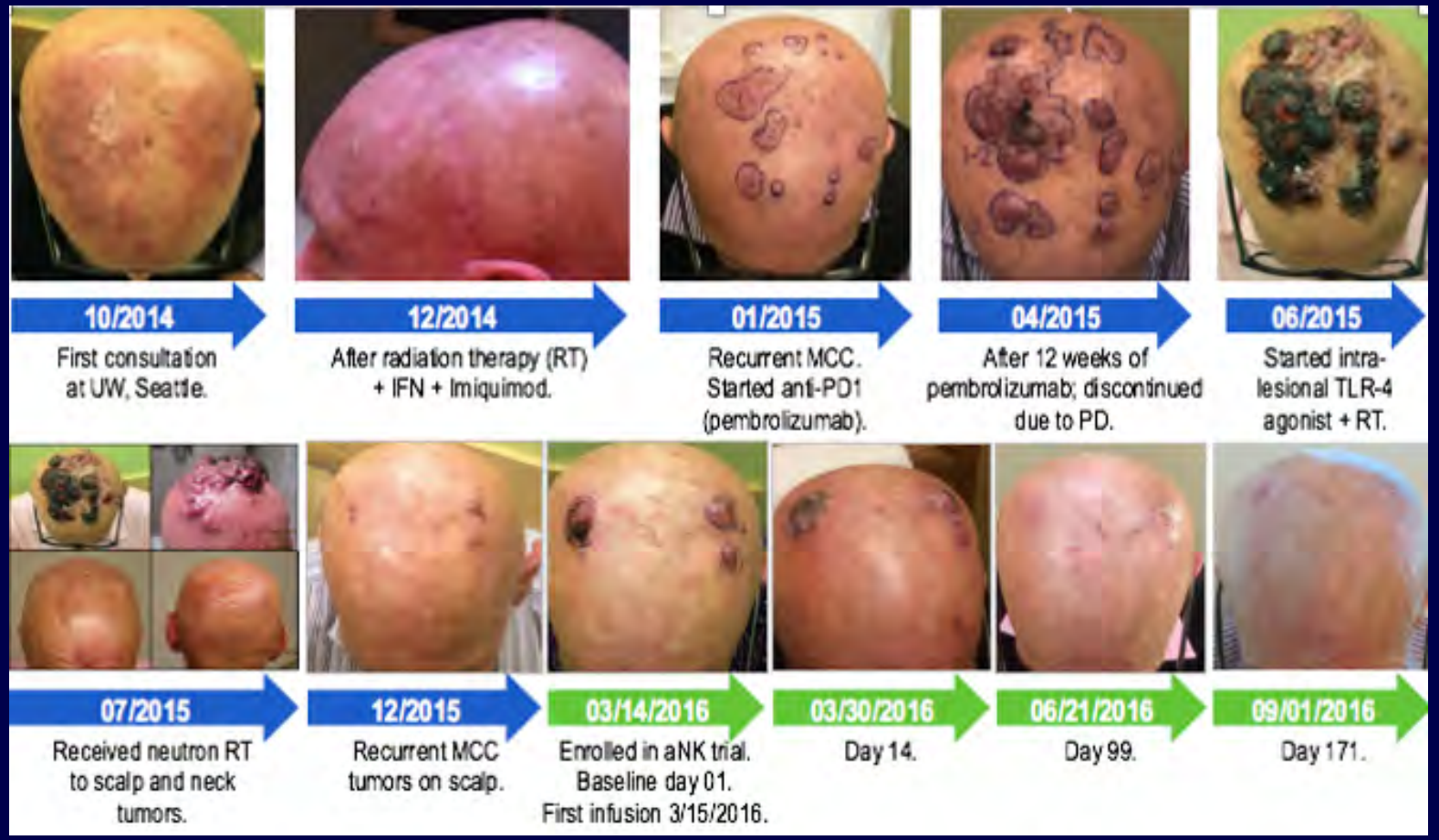


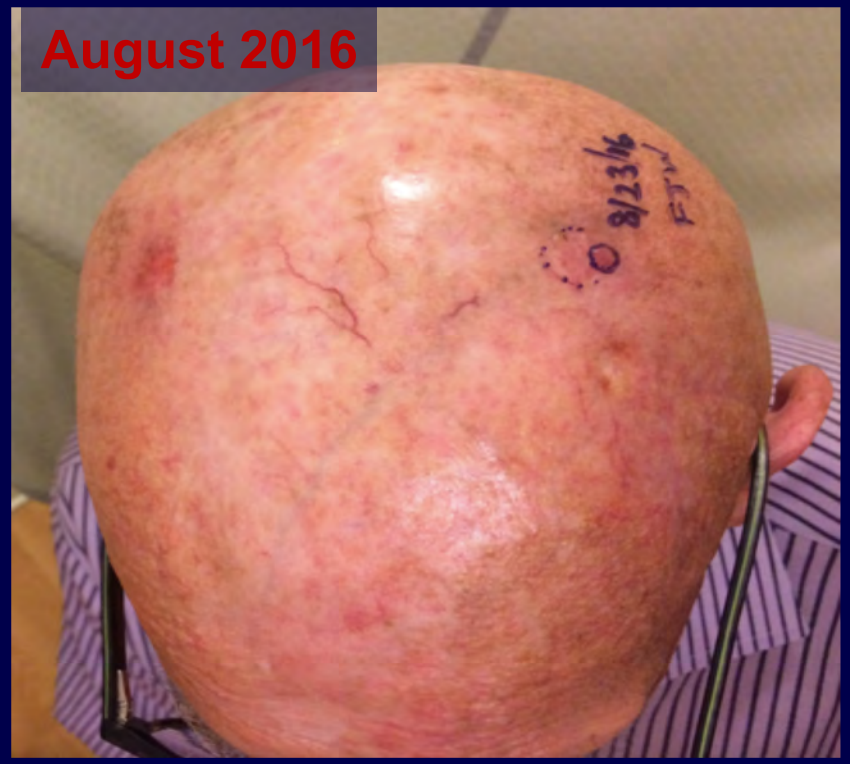
Innate Immunity: Phase II Trial of Activated Natural Killer Cells (NCT02465957)

Response With aNK Cell Therapy in a Pt With MCC Refractory to Chemotherapy, RT, and PD-1 Blockade

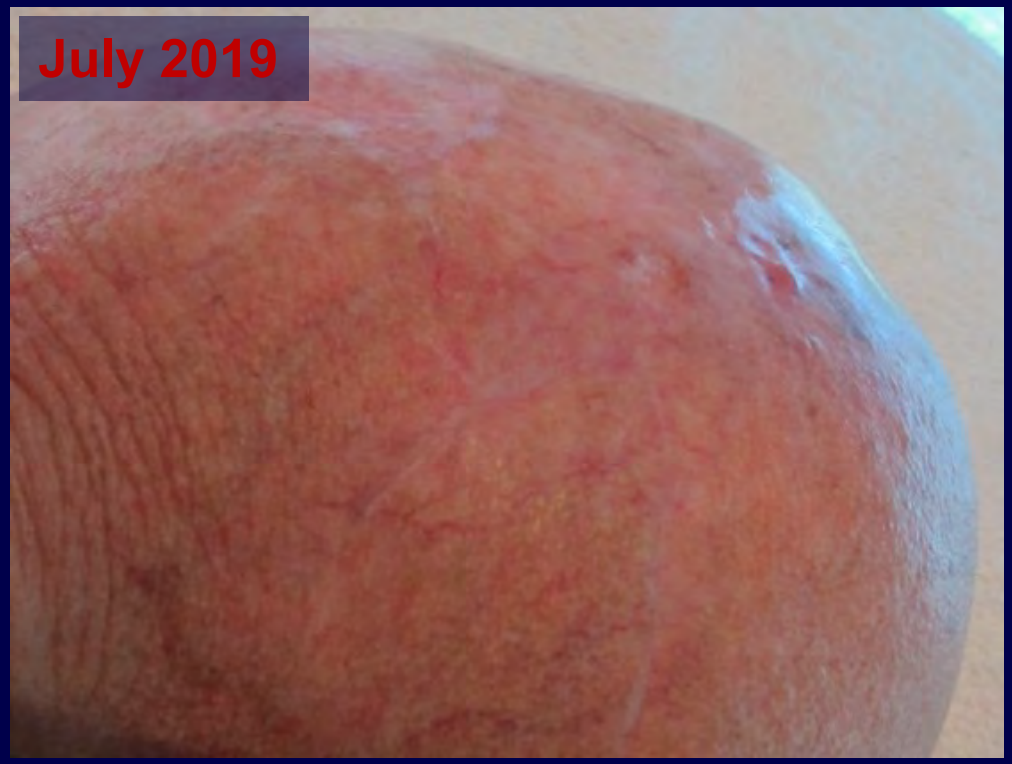


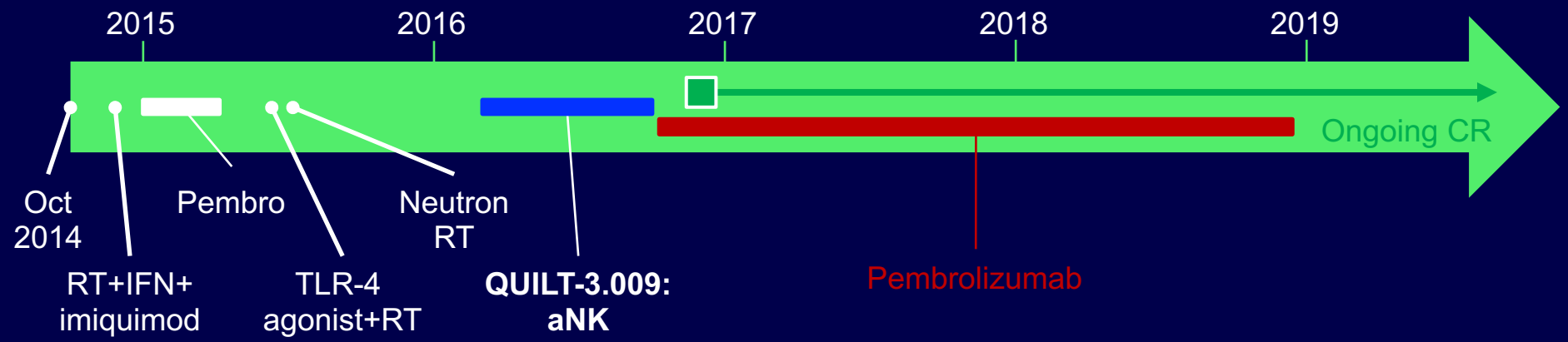
Bhatia S, et al. SITC 2016. Abstract 45.

Despite radiologic CR, residual MCC was detected on biopsy. Pembrolizumab re-challenge led to durable CR, ongoing at 3 yrs



Pembrolizumab

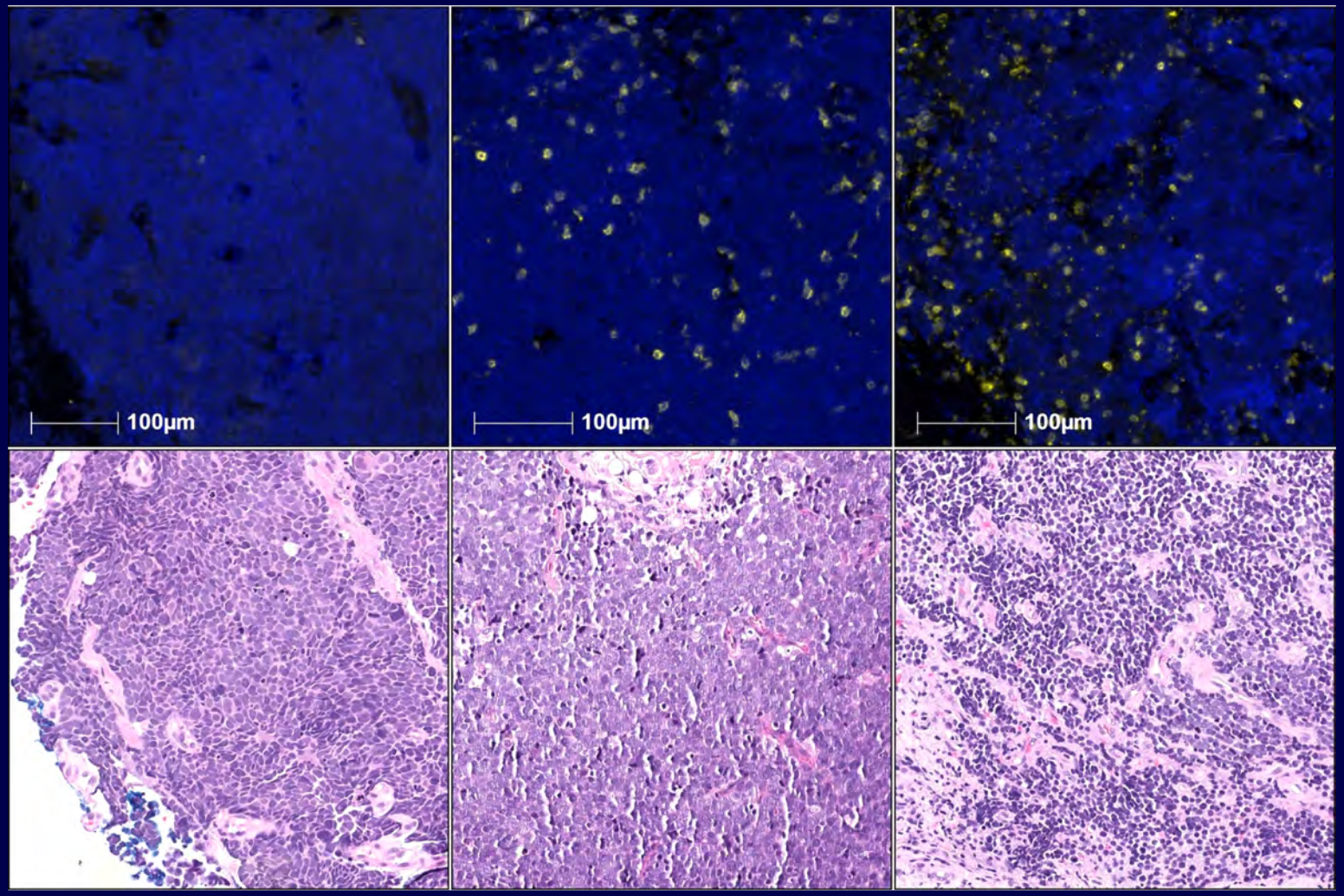




Patient 02-02: Immune cell infiltration in the TME is increased after aNK Monotherapy

Nuclei
CD8

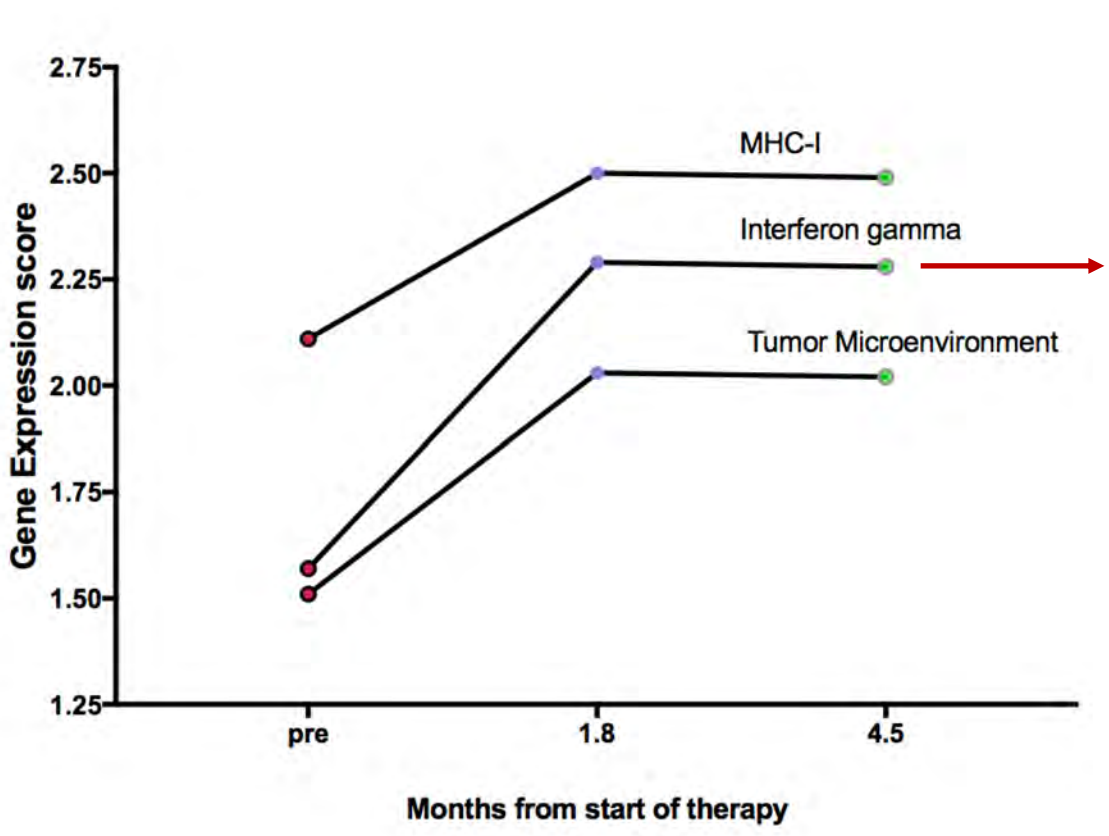
H&E

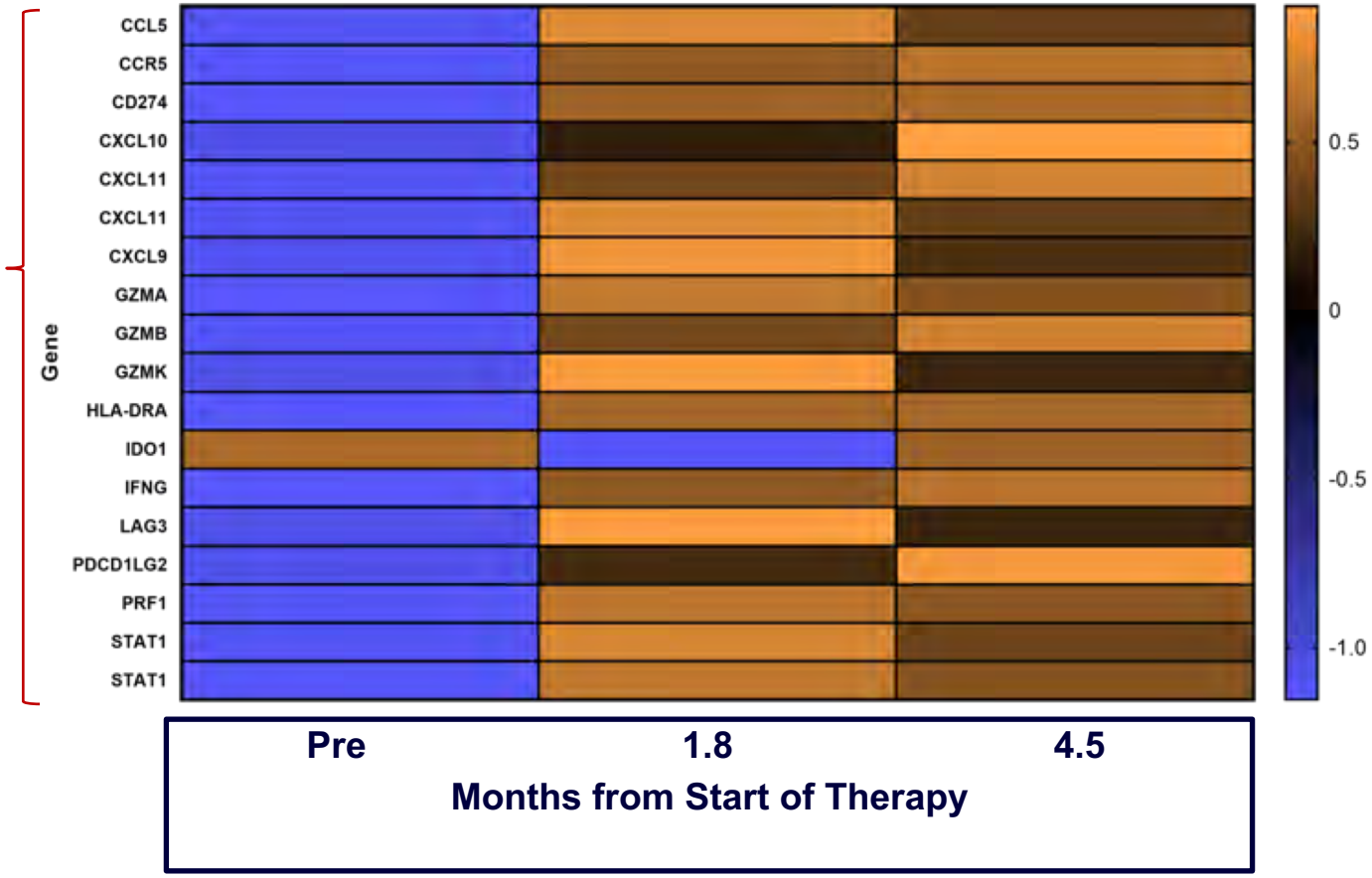


Pre 1.8 4.5

Months from Start of Therapy

Patient 02-02: Immune response-related gene expression is increased in the TME after aNK monotherapy





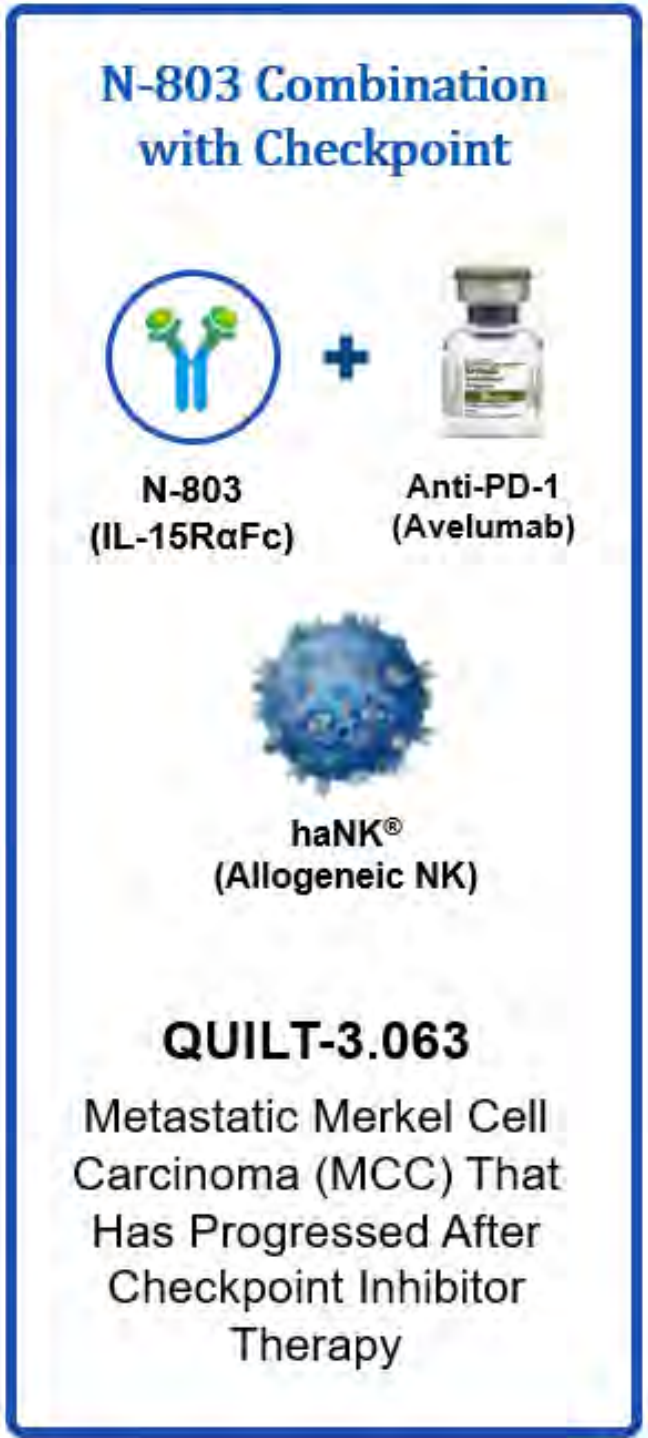
QUILT-3.009: Conclusions

- aNK monotherapy and aNK+N-803 were **well-tolerated**, with no treatment-related SAEs or grade ≥3 AEs.
- Promising **clinical activity** was observed with aNK monotherapy and with aNK+N-803 [ORR of 29% (2 of 7 patients); 1 pt with SD].
  - 1 patient (aNK monotherapy) experienced a radiologic CR; evidence for reversal of ICI refractoriness after aNK.
  - 1 patient (aNK + N-803) experienced a PR (ongoing after pseudo-progression)
  - Biologic activity observed even in patients with PD.
- Evidence of increased TILs and immune response-related gene expression after aNK in available biopsy samples.
- aNK-based therapeutic regimens need to be investigated further in patients with advanced MCC.

QUILT-3.063: A PHASE 2 STUDY OF COMBINATION THERAPY WITH AN IL-15 SUPERAGONIST (N-803), OFF-THE-SHELF CD16-TARGETED NATURAL KILLER CELLS (HANK), AND AVELUMAB WITHOUT CYTOTOXIC CHEMOTHERAPY IN SUBJECTS WITH MERKEL CELL CARCINOMA (MCC) THAT HAS PROGRESSED ON OR AFTER TREATMENT WITH A CHECKPOINT INHIBITOR

STUDY DESIGN:

- Phase 2, Single-Arm Combination Therapy of:
  - Investigational Products
    - N-803
    - haNK™
  - FDA Approved Product
    - Avelumab (BAVENCIO®)
- Subjects must have progressed on or within 6 months of checkpoint inhibitor therapy with a single-agent Avelumab or Pembrolizumab.
- The rationale for this study is based upon preclinical and clinical studies which have shown that N-803 enhances NK cell proliferation and anti-tumor responses in vitro and in vivo. Combining N-803 and haNK may potentiate cytotoxic activity of the NK and T cells, and the addition of N-803 also lead to an increased NK cell number and increased anti-tumor activity.



Study Objectives

- **Primary**
  - Evaluate safety of Avelumab, haNK™, and N-803 in subjects with progressed MCC on or after checkpoint inhibitor therapy.
  - Determine efficacy of Avelumab, haNK™, and N-803 in subjects with progressed MCC on or after checkpoint inhibitor therapy.
    - ORR using RECIST 1.1 based on BICR.
- **Secondary**
  - Additional measures of efficacy by PFS, OS, DSS, DOR, DCR, and QoL by Patient Reported Outcomes.
- **Exploratory**
  - PK and immunogenicity profile of N-803 in combination with haNK™ and Avelumab

Planned Enrollment

- 15-20 US sites.
- Up to 43 subjects.
  - Initially 18 subjects enrolled; ≤ 2 subjects confirmed response, enrollment terminated; otherwise additional 25 subjects enrolled in second stage.
  - 52 subjects screened to reach max target.
    - Number includes replacement subjects.
- Utilize Simon's two-stage optimal design for primary efficacy endpoint, ORR, evaluated using RECIST 1.1 based on BICR:
  - Clinically meaningful ORR > 10%; optimal ORR 25%

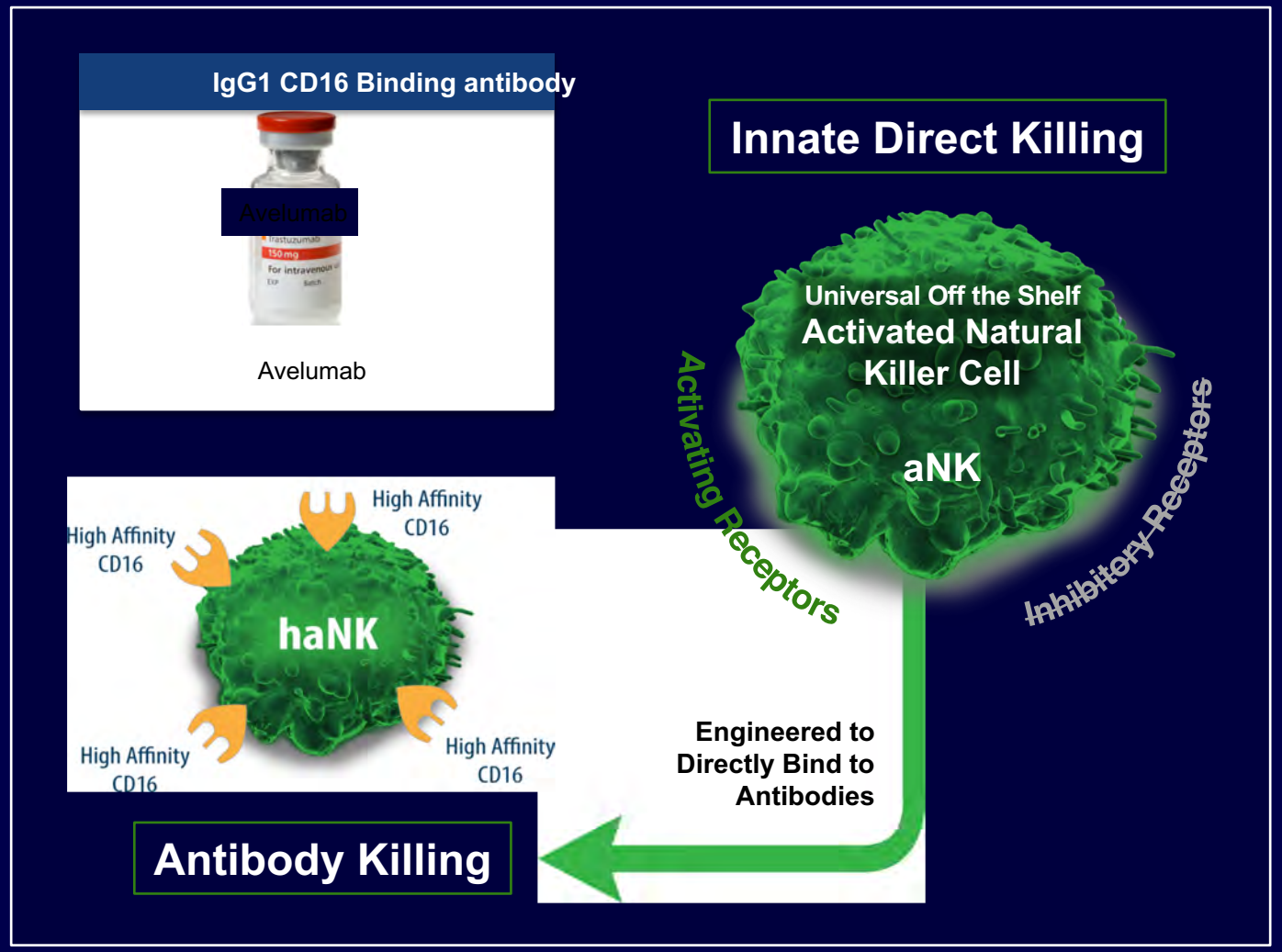
Study Treatment Schema

- Combination therapy administered:
  - Day 1, every 2 weeks: Avelumab via IV, haNK™ via IV
  - Day 1, every 3 weeks: N-803 SC injection.

Week	1	2	3	4	5	6	7	8	9	10	11	12	16	24	32	Up to 1 year	Months 12-24
Avelumab/haNK	▼		▼		▼		▼		▼		▼					Every 2 weeks	Every 2 weeks
N-803	▼			▼			▼			▼			▼			Every 3 weeks	Every 3 weeks
Response Evaluation								◆					◆	◆	◆	Every 8 weeks	Every 12 weeks

- Treatment for up to 2 years.
- Treatment discontinued if experience PD, unacceptable toxicity, withdraw consent, or not longer in patient's best interest.

haNK Program
Enhanced Antibody Killing (ADCC)



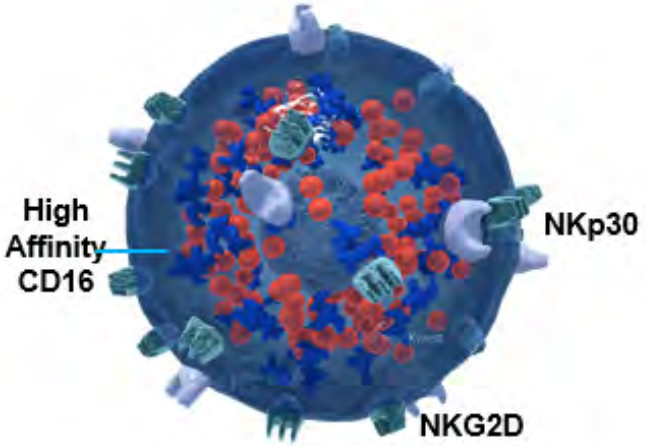
haNK Program

- Over 200 doses administered in combination with avelumab
- Cryopreservation storage
- Off the Shelf ready to use
- Bridging chemo is not required
- Lymphodepleting chemo is not required
- Studies to be completed in outpatient setting (as with previous studies)
- Cytokine release syndrome and neurotoxicity have not been seen with the product. Management of infusion reactions should be performed as per the study protocol (pg. 49).

Investigational Product – haNK™

NK-92 [CD16.158V, ER IL-2] haNK = HIGH AFFINITY NATURAL KILLER CELLS

- NK (Natural Killer) cells provide a rapid defense response to virus-infected cells and tumor cells.
- NK cells are activated and regulated by cytokines including IL-2 and IL-15.
- haNK Cells
  - NK cells with high-affinity CD16 receptor (v/v).
    - A plasmid encoding CD16 was transfected into the NK cells.
    - CD16 Receptor – mediates the direct killing of cancer cells by the NK cell.
  - Cells are continuously growing, unlike normal NK cells (which are irradiated before going into a patient so that they don't continuously grow inside of the patient).

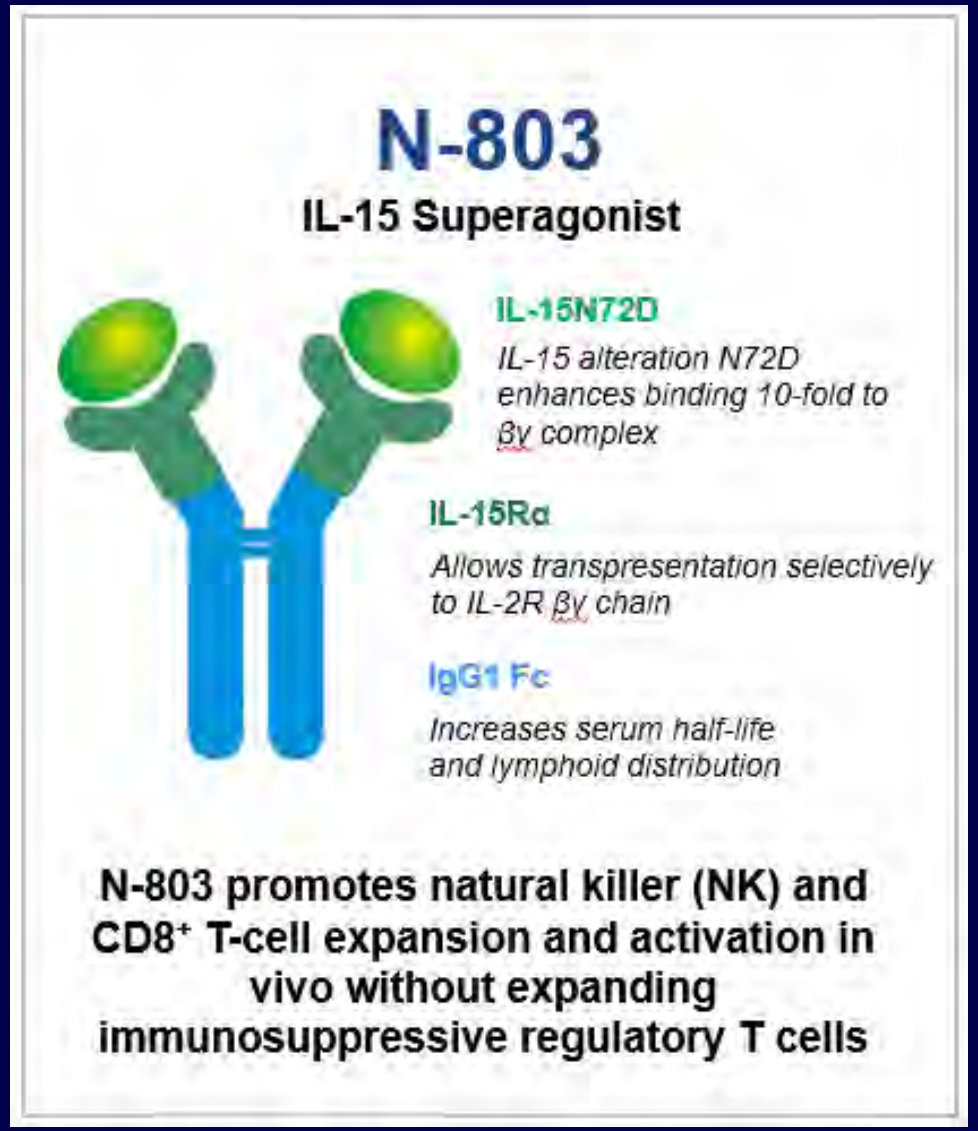


Cryopreserved/Ready-to-Use

Investigational Product – N-803

N-803; IL15 Superagonist Fusion Complex

- N-803 is an IL-15 stimulator (IL = interleukin → cytokine → brings about cell to cell communication)
- IL-15 promotes NK and T cell expansion and activation without expanding immunosuppressive regulatory T cells.
- Administered subcutaneously due to prolonged half life and decreased toxicity
- haNK along with N-803 identify invaders and create a response to eliminate cancer cells.



Combination Therapy Summary

	Composition	Intended Mechanism of Action in MCC	Route of Admin.	Approved or Investigational
N-803 (IL-15RαFc) 	**Protein Complex** Mutated IL-15 / IL-15Rα Fc	Activation and proliferation of NK and $CD8^+$ T cells, without proliferation of Tregs	SubQ	Investigational
haNK 	**Natural Killer** Cryopreserved NK cells with high-affinity CD16 receptor (v/v)	Direct cytotoxicity against tumor cells via recognition of NKG2D ligands, etc., as well as via ADCC (antibody-dependent)	IV	Investigational
Avelumab (Checkpoint) 	**Checkpoint** Anti-PD-L1 monoclonal antibody	Prevents tumor cell expression of PD-L1 from inhibiting T cells. Also allows for ADCC of PD-L1-expressing MDSCs and tumor cells	IV	FDA approved

Thank You

Key Opinion Leaders – December 2, 2019

Topic: PD-L1 t-haNK

Clint Allen, MD
Johns Hopkins Otolaryngology
Consult for the National Institutes of Health
Associate Professor of Otolaryngology
Head and Neck Surgery

Why we should be focused on developing NK cellular therapies

Clint T. Allen, MD, FACS

Chief, Translational Tumor Immunology Section, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bethesda, MD

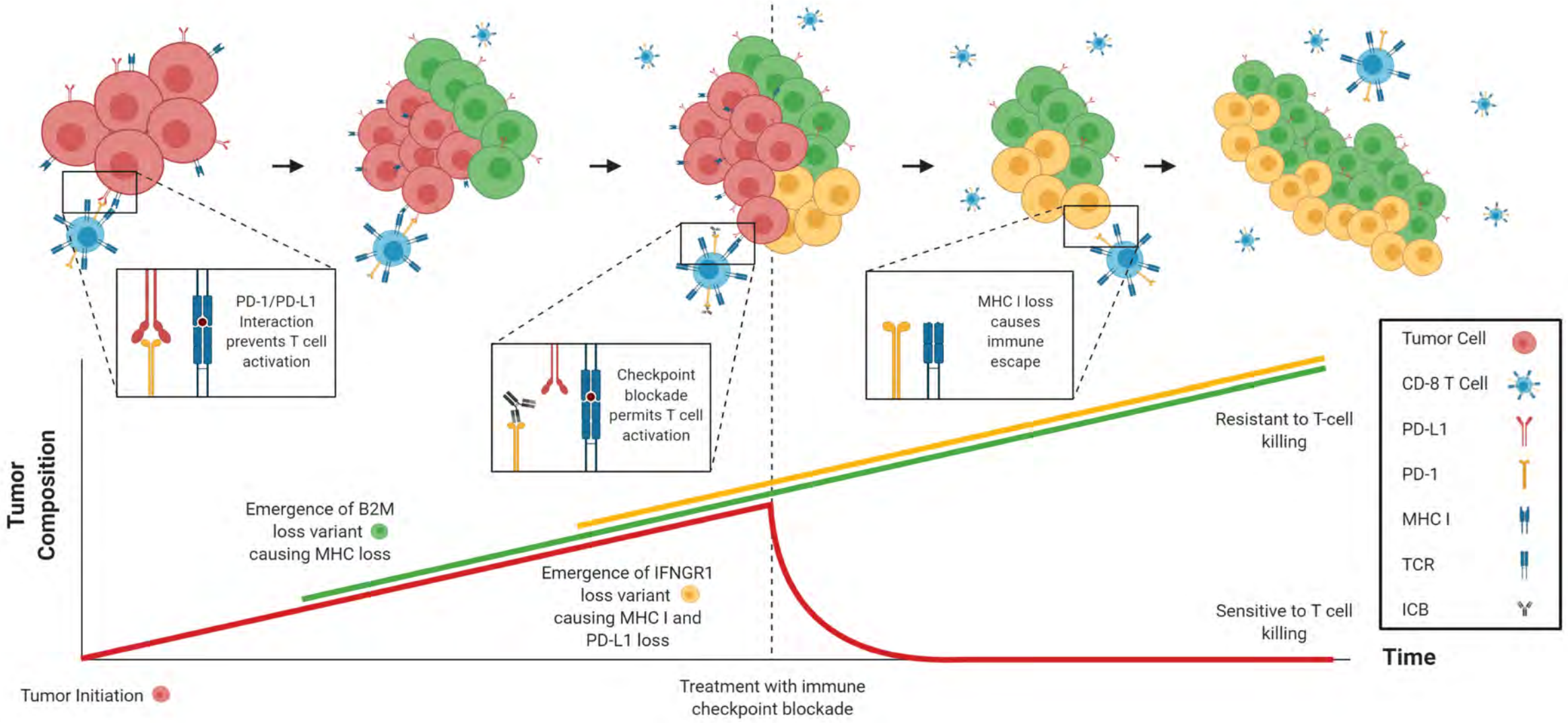
Associate Professor, Otolaryngology-Head and Neck Surgery, Johns Hopkins School of Medicine, Baltimore, MD

Discussion topics

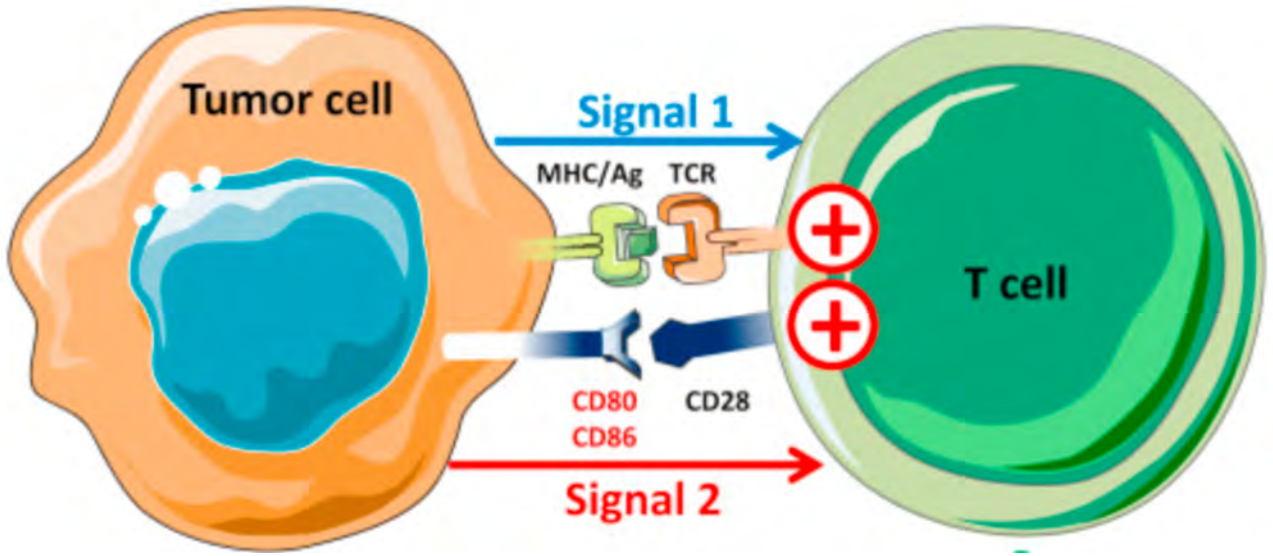
- What is the scientific rationale for the development of NK cell-based immunotherapy when we have so many options for T cell-based immunotherapy?

- What advantages might NK cellular therapy have over T cell-based cellular therapy?

Genomic instability leads to subclones of cells within a tumor that have different mutations



Subclones of tumor cells within an individual cancer lose genes required for T cell killing



Tumor cells require HLA expression and proper antigen processing to be detected and killed by T cells

<u>Examples of mutated or lost genes:</u>

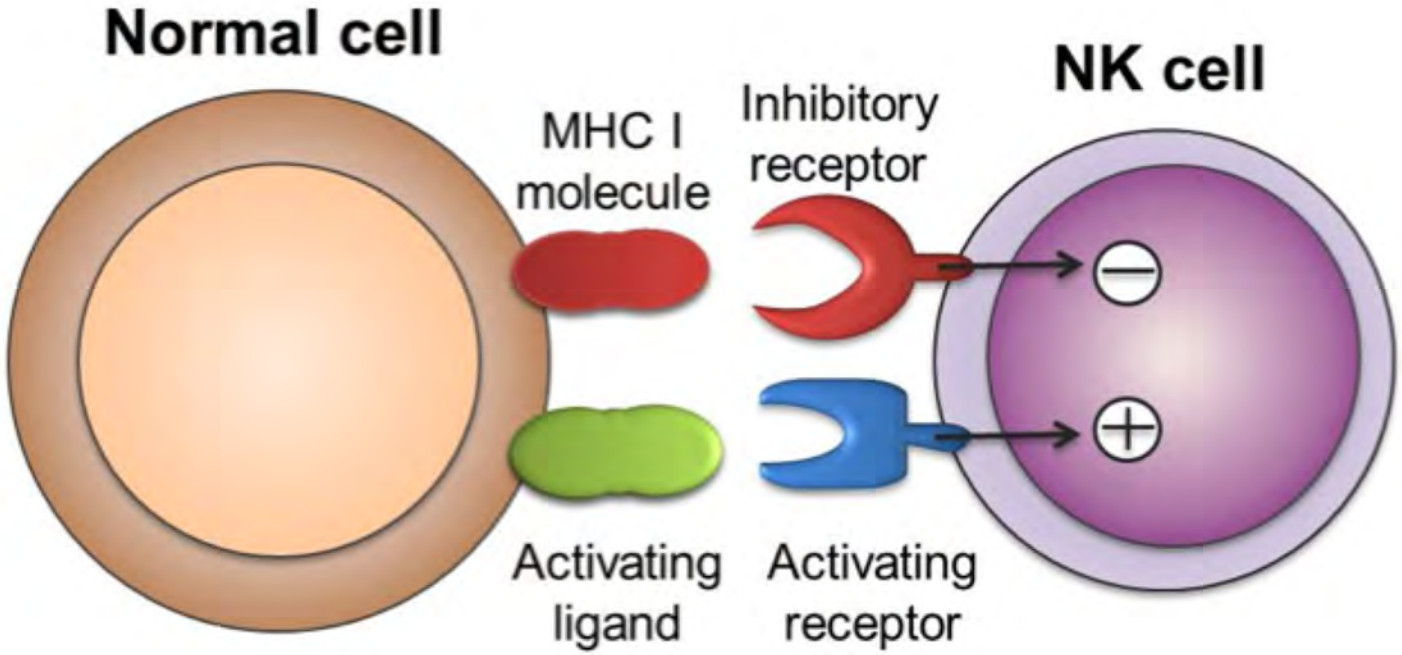
Class I or class II HLA alleles

Antigen processing machinery genes IFN response genes

Granzyme response (apoptosis) genes

Adapted from PMID: 27755997

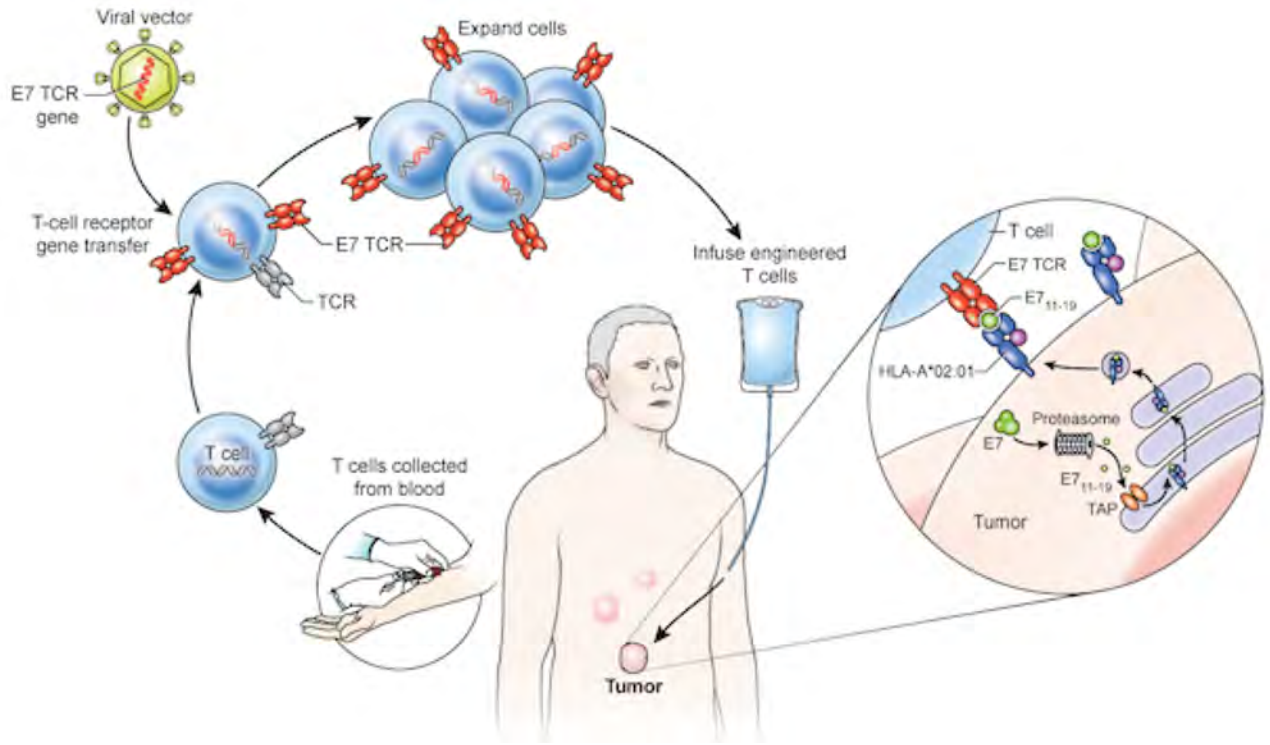
NK cells can still detect and kill tumor cells invisible to T cells



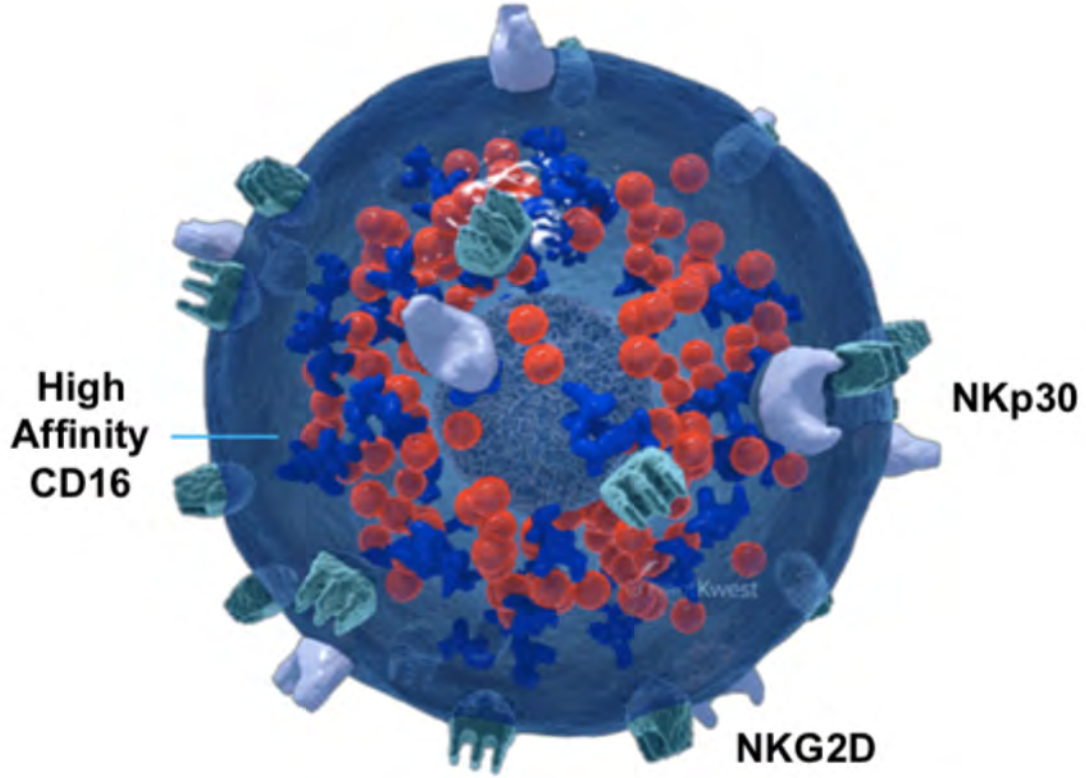
NK cells require neither HLA nor antigen to detect and kill a tumor cell

Figures adapted from PMID: 27755997

NK cellular therapy is feasible as an “off the shelf” product



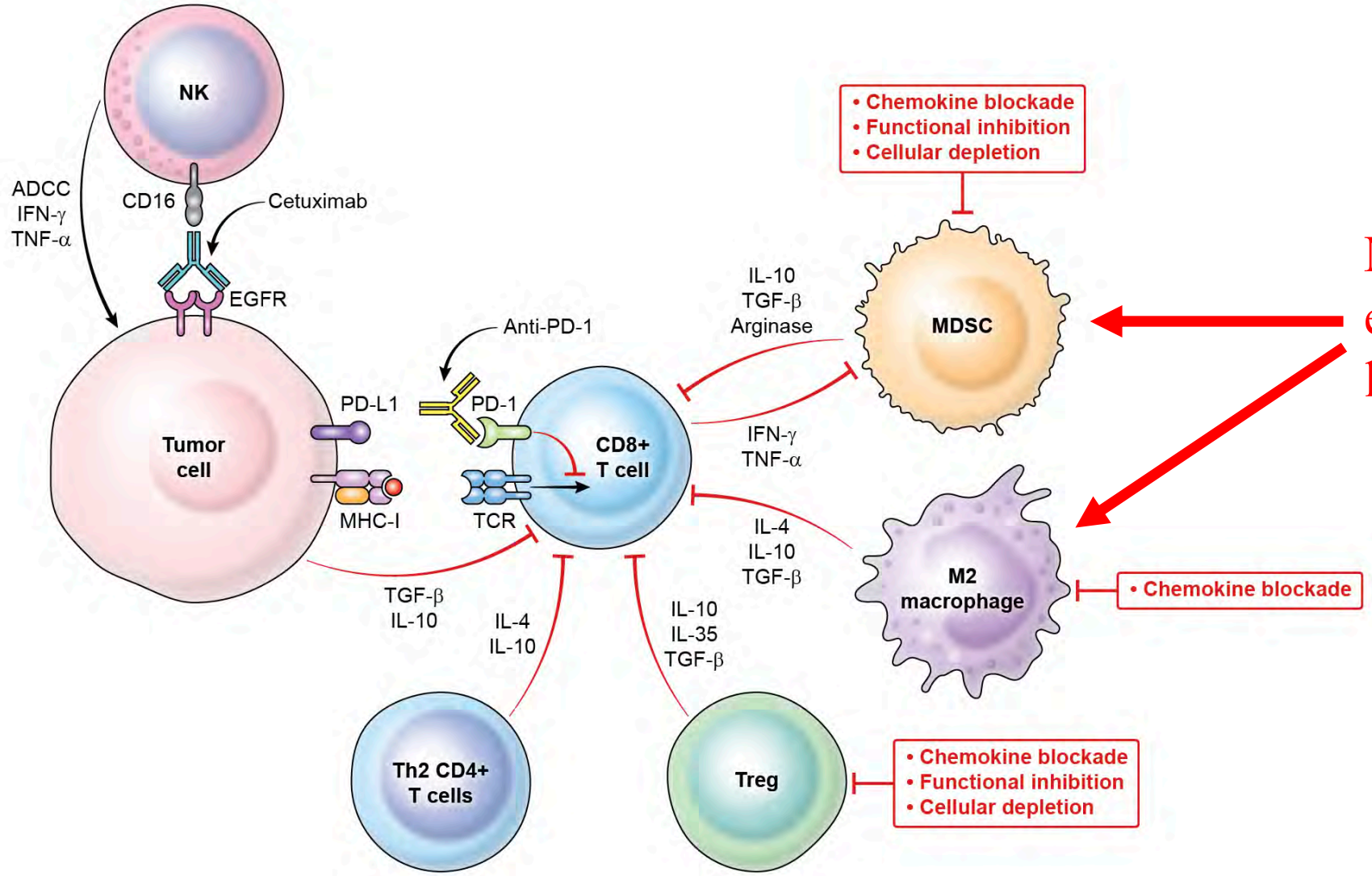
Engineered autologous T cells



haNK
(high-affinity NK cell)

Adapted from PMID 24329789

Another major mechanism of tumor immune escape: Immunosuppressive myeloid cells



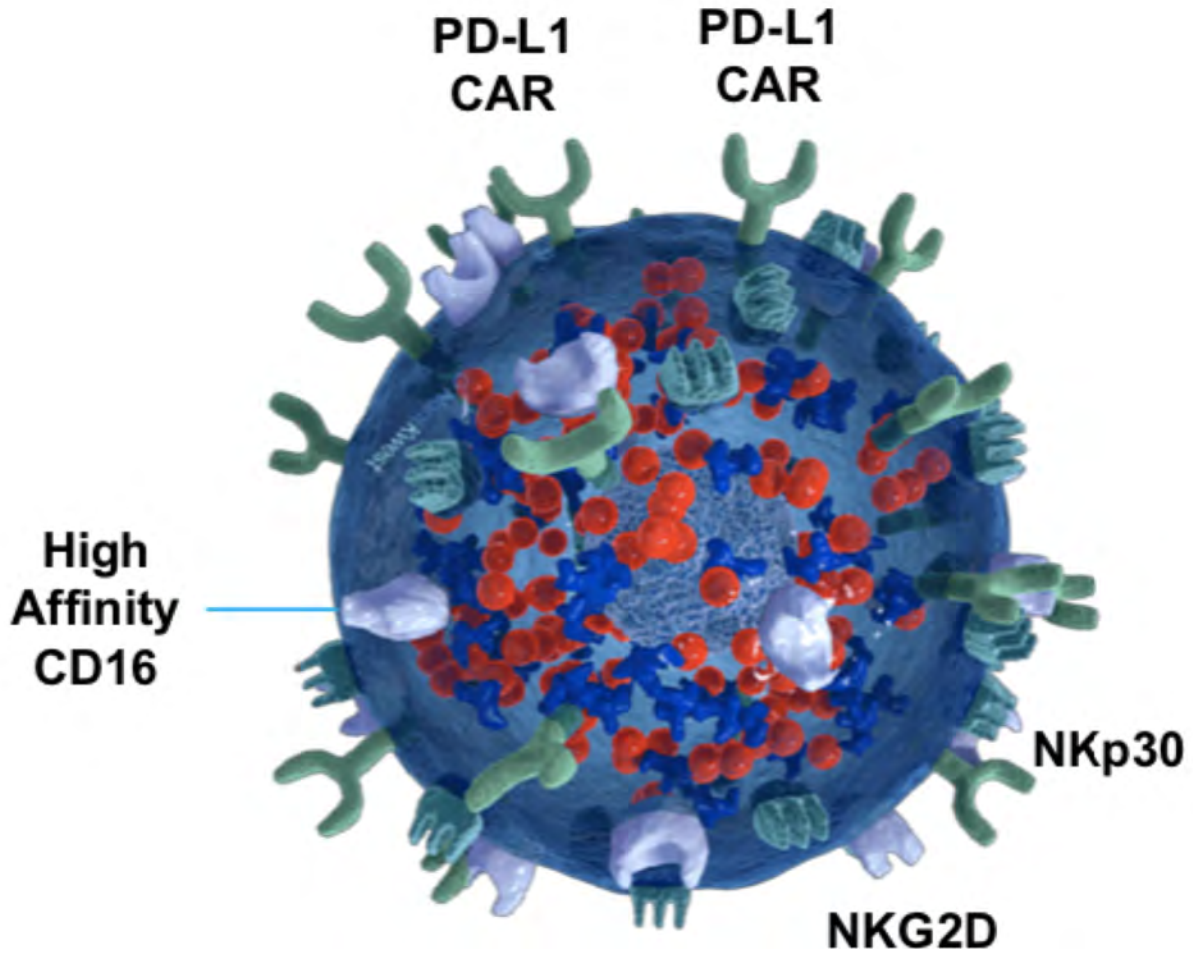
Myeloid cells express very high levels of PD-L1

The next NK cellular therapy product: PD-L1 t-haNKs

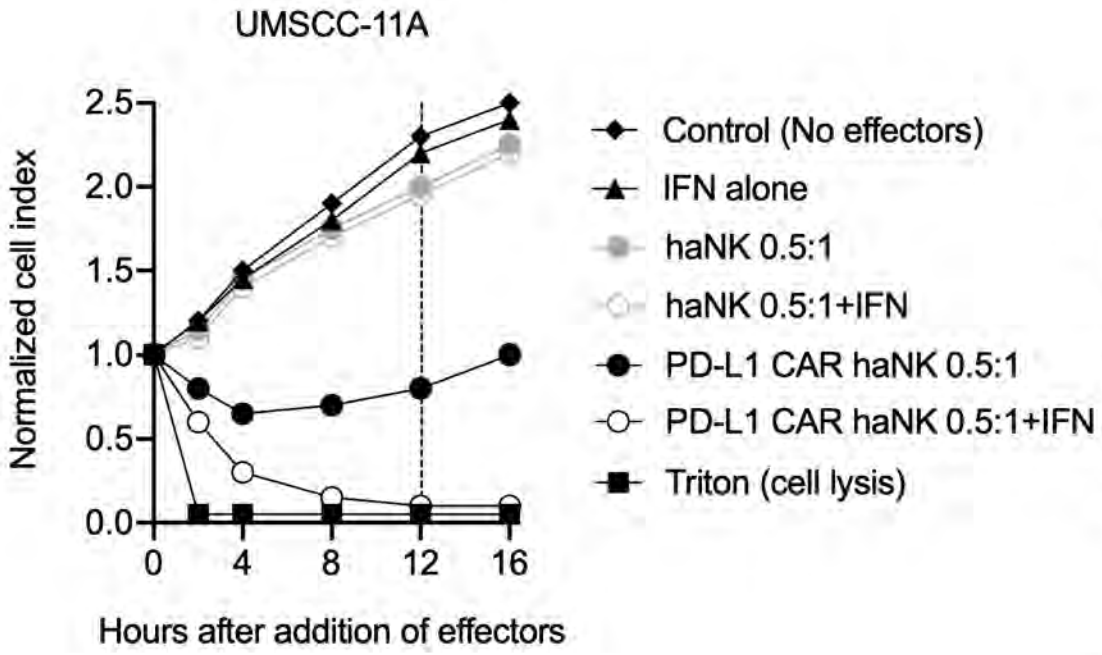
haNK cells that express a chimeric antigen receptor that targets PD-L1

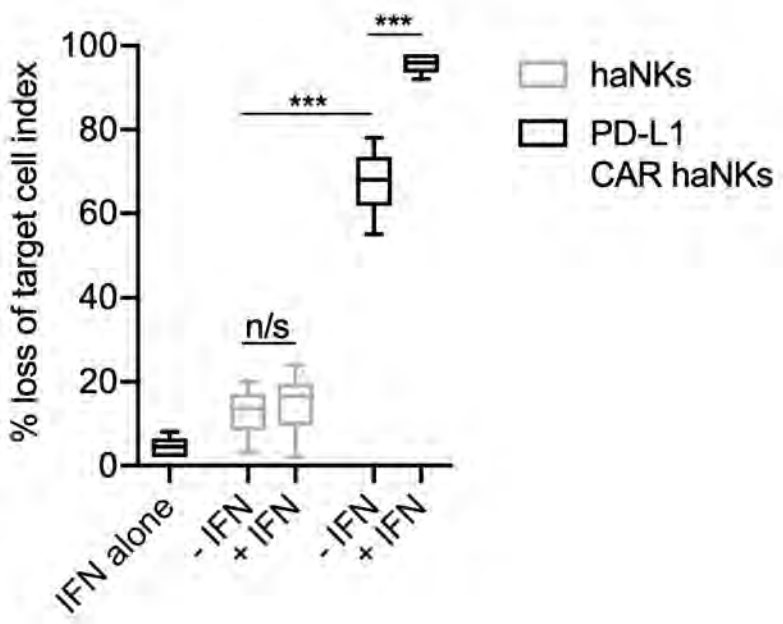
These cells have two major mechanisms of killing:

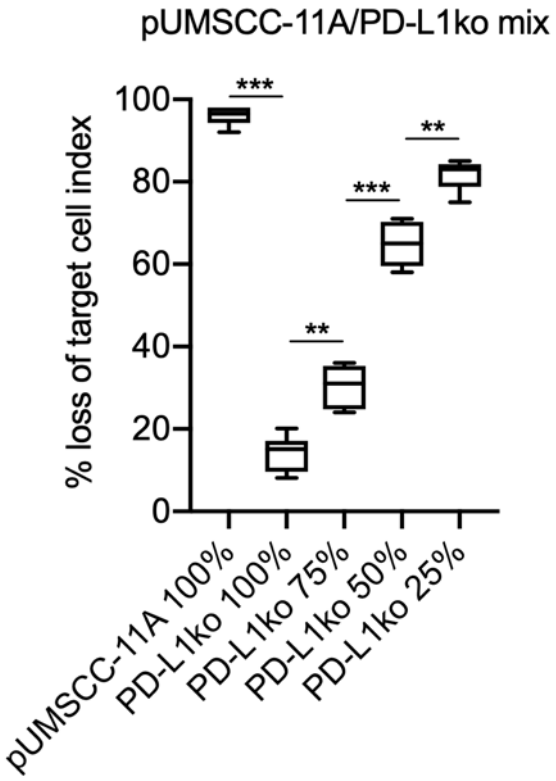
1) Direct NK killing
2) PD-L1 specific killing



PD-L1 t-haNKs efficiently kill PD-L1+ tumor cells

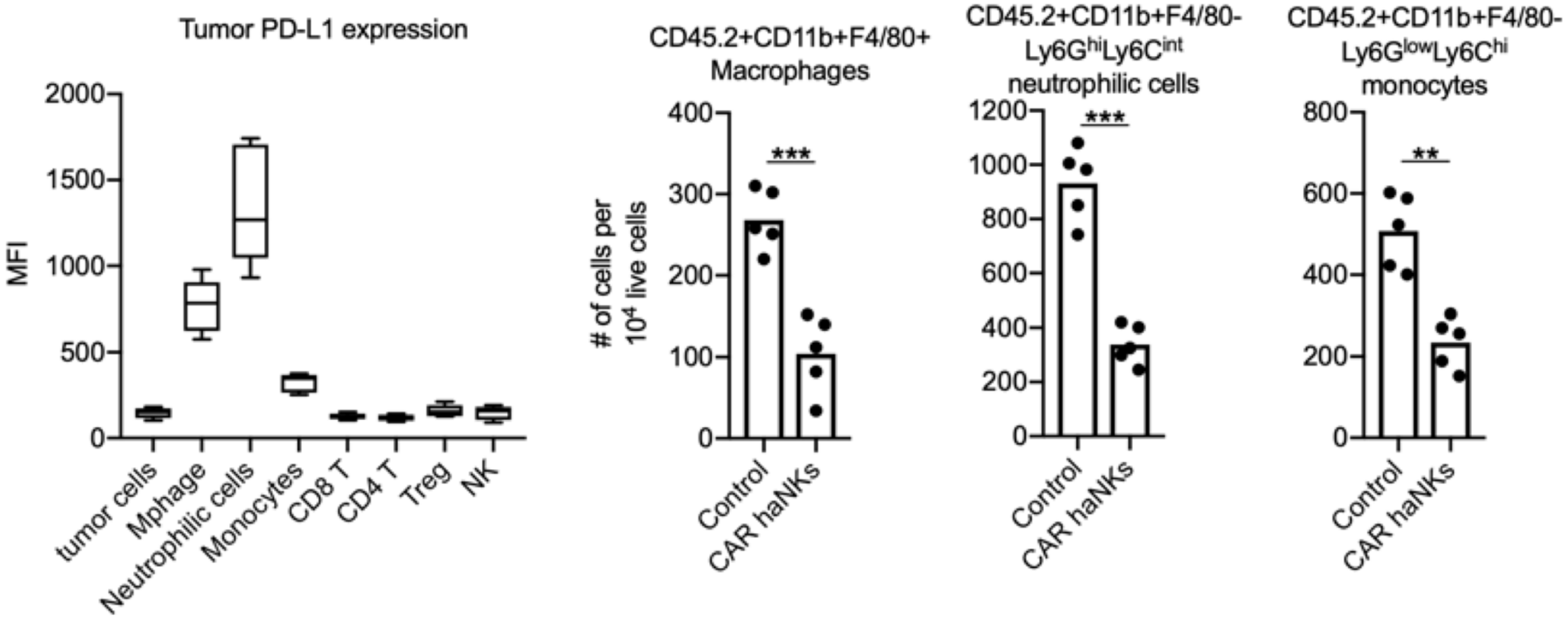






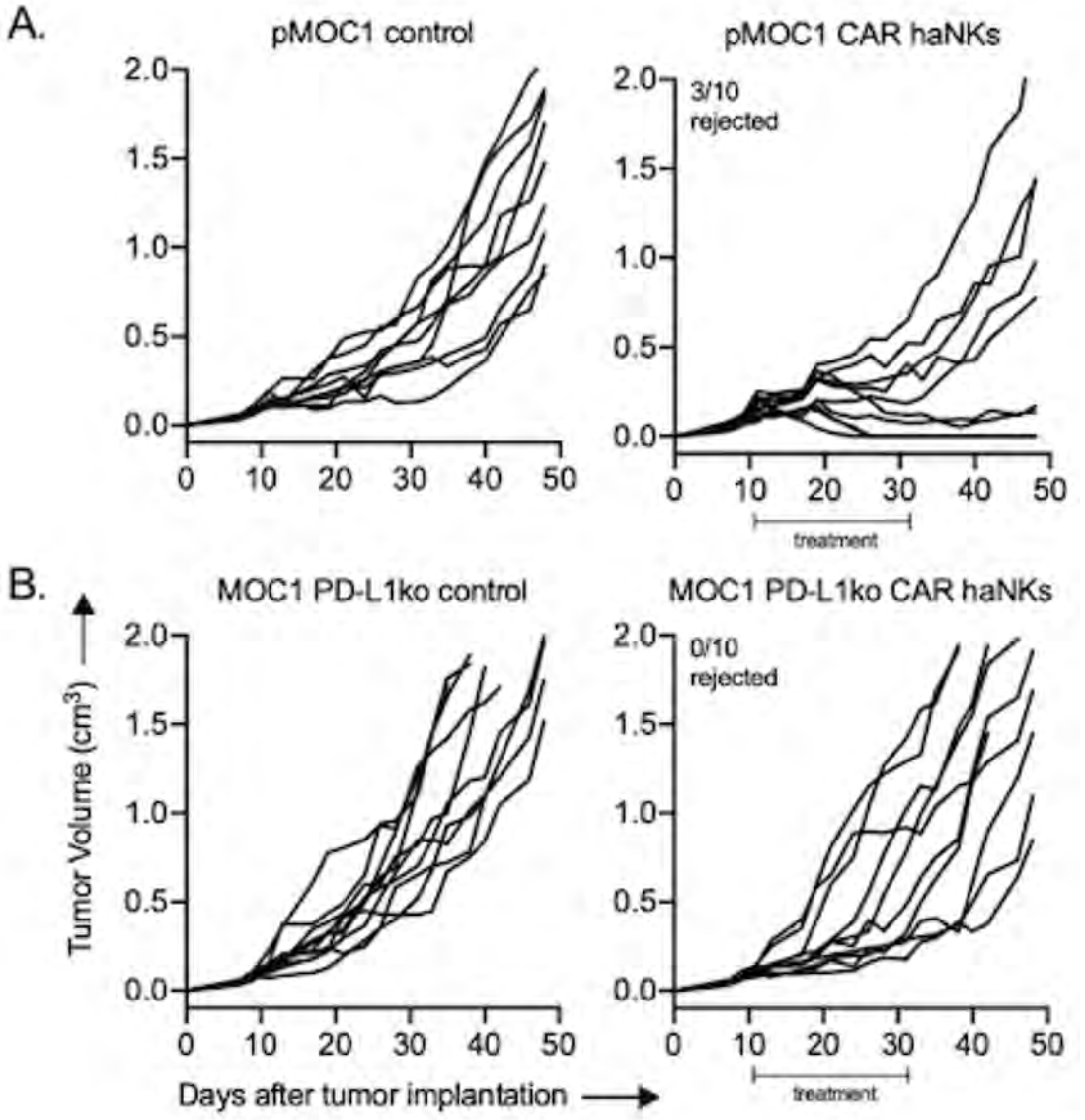
Tumor cell killing is increased when cell surface PD-L1 is increased and decreased by ~80% when PD-L1 is deleted.

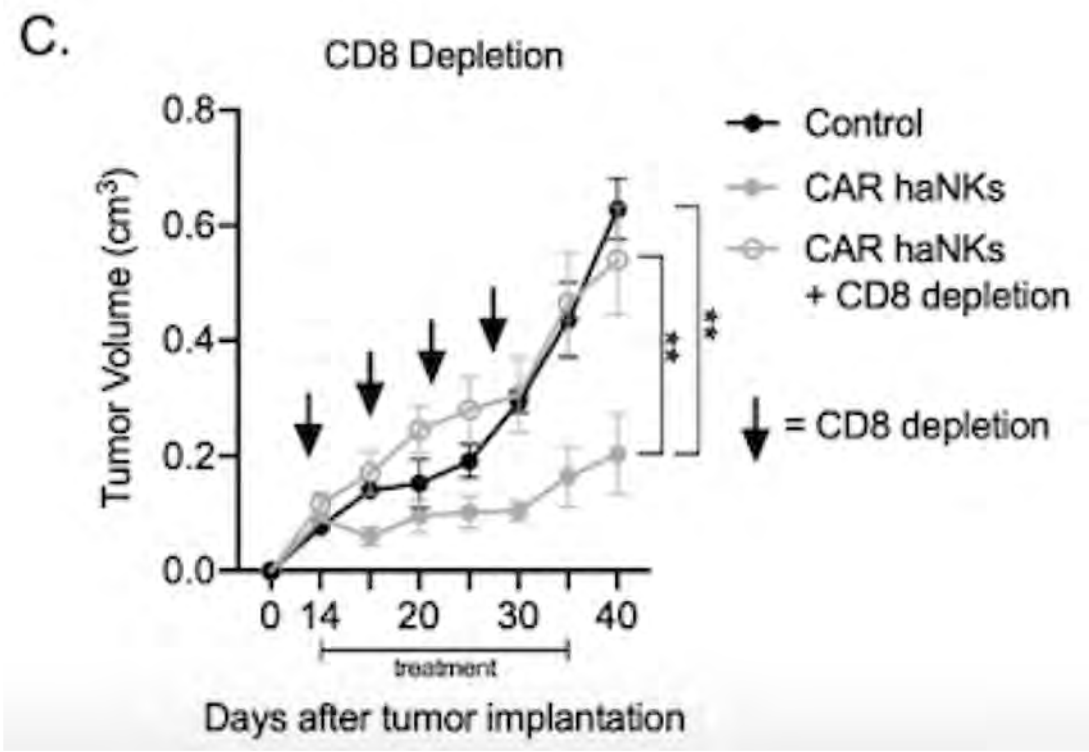
Treatment of tumor-bearing mice with PD-L1 t-haNKs depletes immunosuppressive cells



Immune cells within the tumor that have high PD-L1 expression (macrophages and MDSC) are selectively reduced and good effector immune cells are increased.

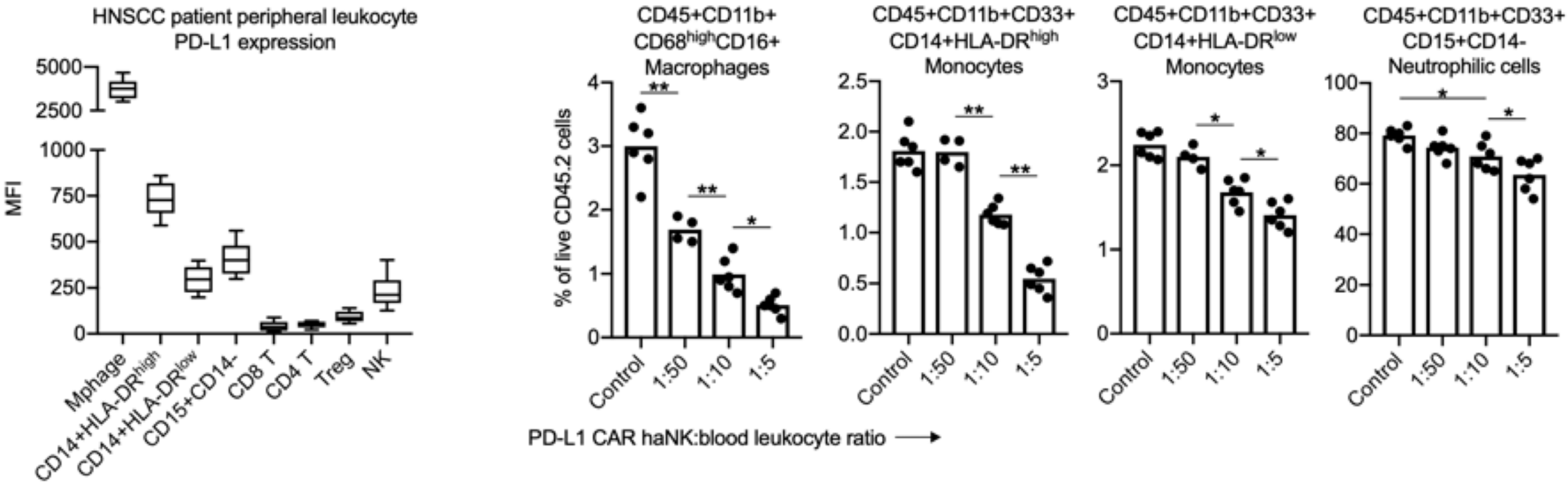
PD-L1 t-haNK treatment cured 30% of mice bearing resistant MOC1 tumors





Anti-tumor effect in mice is lost in PD-L1 knockout tumors or when T cells depleted

PD-L1 t-haNKs deplete immunosuppressive cells from the blood of cancer patients



Human immune cells that have high PD-L1 expression (macrophages and MDSC) are selectively reduced

First in Human Phase I PD-L1 t-haNK Safely Administered to First 6 Patients Without SAE or DLT as Outpatient

Patient	Cancer type	PD-L1 t-haNK infusions (2 billion/infusion)	Treatment status	Greatest Treatment related AE	Type of AE
001	HNSCC	9	Disease Progression	Grade 2	Tumor pain, fatigue
002	Breast	23	Disease Progression	Grade 2	Chills, vertigo
003	Colon	9	Disease Progression	None Reported	-
004	Colon	14	On Treatment	Grade 1	Infusion reaction
005	Glioblastoma	10	On Treatment	Grade 1	Fatigue, lightheadedness, ALT elevation
006	Bladder	12	On Treatment	Grade 1	Flu-like symptoms, Chills

Conclusions

- Curing most patients with heterogeneous tumors with T cell-based immunotherapy alone is unlikely
- NK-based immunotherapy is likely to be additive or synergistic with T cell-based immunotherapy
- The availability of NK cellular therapies such as haNKs or t.haNKs add a valuable tool to our immunotherapy menu for clinical trials

NIH Collaborators:
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Christian Hinrichs, MD (ETIB, NCI)
Claudia Palena, PhD (LTIB, NCI)
Jim Hodge, PhD (LTIB, NCI)
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Jason Redman, MD (GMB, NCI)
Julius Strauss, MD (GMB, NCI)
Margaret Gatti-Mays, MD (GMB, NCI)
Harris Floudas (GMB, NCI)
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Translational Tumor Immunology Program Team:
Paul Clavijo, PhD
Jay Friedman, PhD
Sreeni Gunti, PhD
Yvette Robbins, BS
Angel Huynh, BS

Thank you

Key Opinion Leaders – December 2, 2019

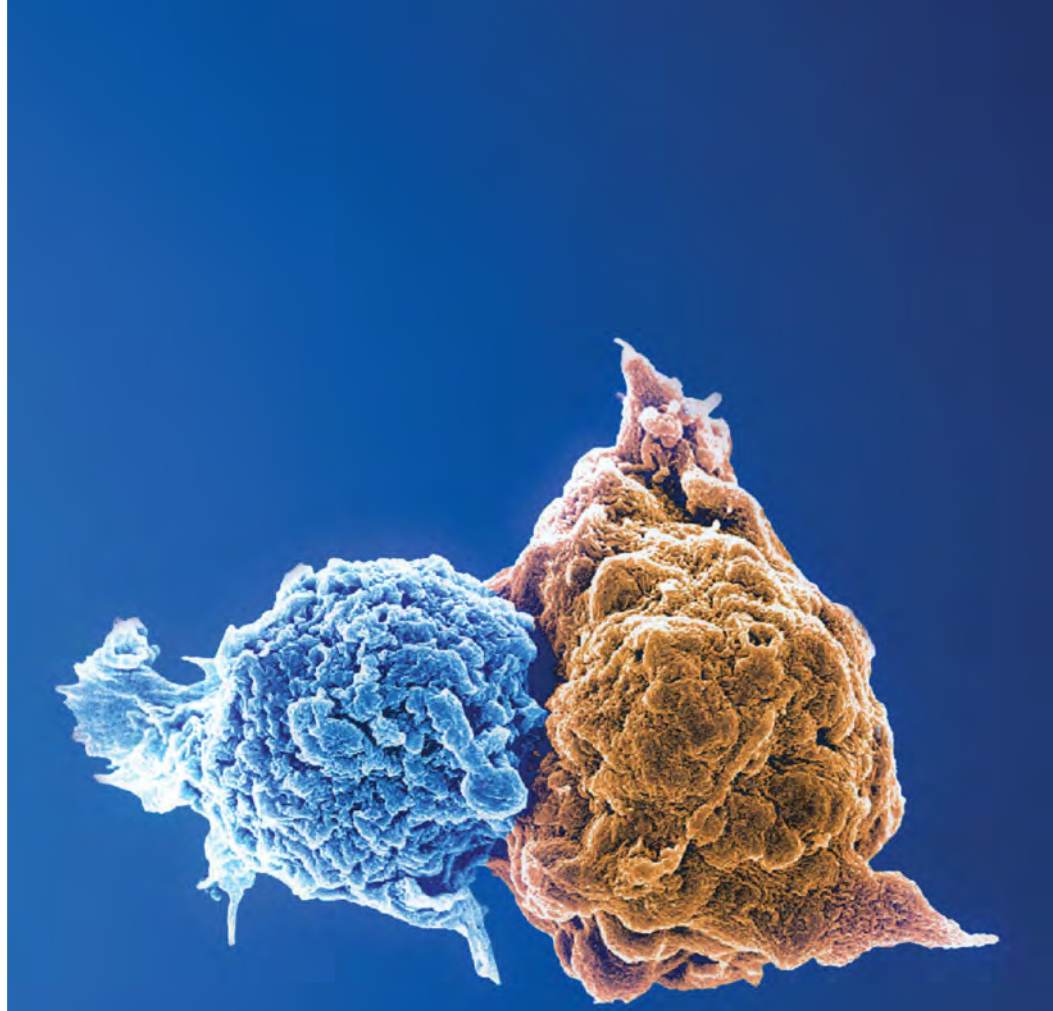
Topic: Triple Negative Breast Cancer (TNBC)

Chaitali Nangia, MD
CSSIFM & Hoag Hospital Newport Beach
Medical Oncologist

NANT Cancer Vaccine

Triple-Negative Breast Cancer

Chaitali Nangia MD Associate Professor
Chan Soon-Shiong Institute for Medicine (CSSIFM)
Immune Oncology Clinic



Study Design

Phase 1b Trial for patients with relapsed or refractory metastatic TNBC Beyond First line SOC therapy

- Low-dose metronomic chemoradiation therapy and immunotherapy activating NK and T-Cells
- haNK cells: off-the-shelf high-affinity natural killer cells
- Avelumab: Anti-PD-L1IgG1 antibody
- N-803: IL-15 Superagonist NK and T-Cell Activation
- Conducted at: Outpatient single center
- Response assessment by CT scans performed at 8 week intervals

Phase Ib Trial: Patient Population – Advance Disease

- 9 Patients enrolled between 3/2018 to present
- Most patients were third line of therapy or greater

Lines of Therapy Received	Patients Enrolled
1	1
2	4
3	2
4	2

Durable Efficacy Results in Advanced TNBC

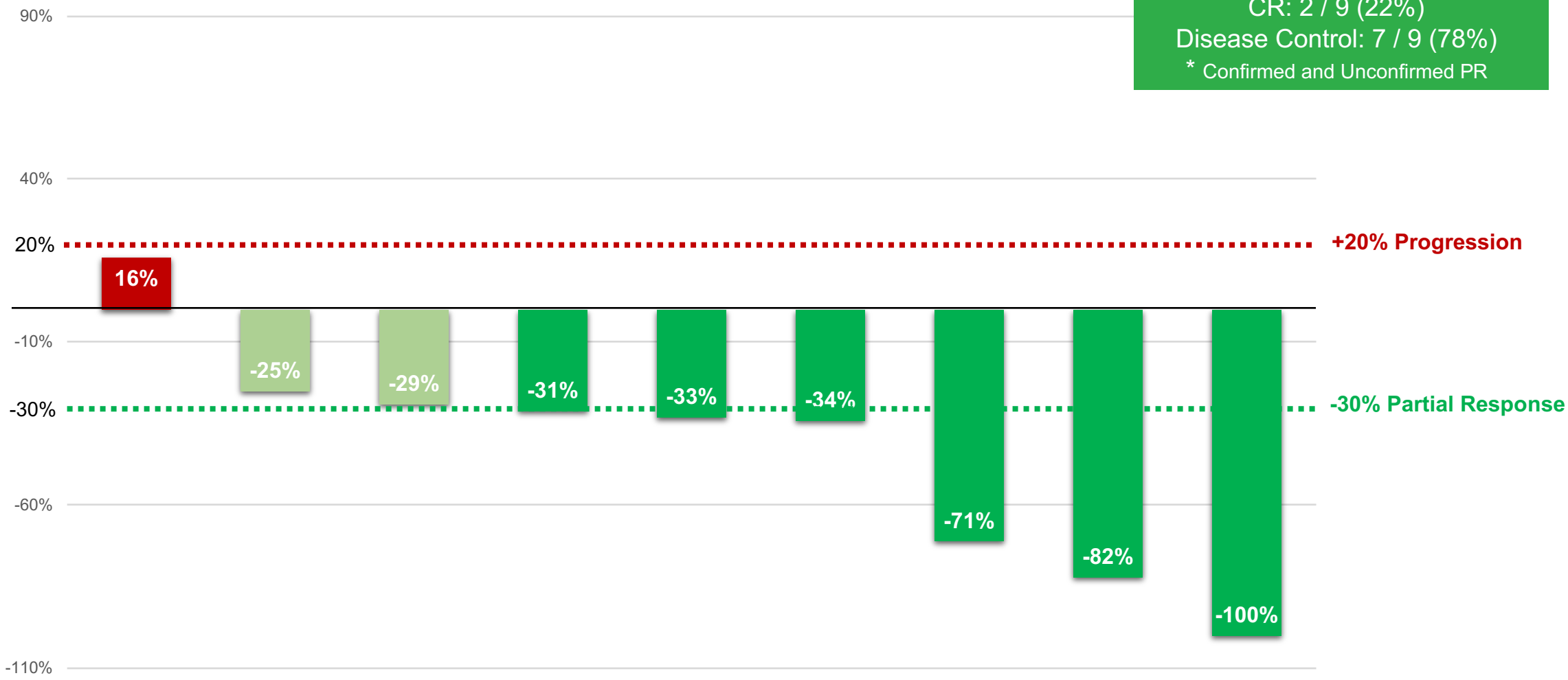
Early Efficacy:

- Median PFS **13.7 months** (Historical PFS in 2nd Line or Greater: 2-3 Months)
- 7 / 9 patients treated show a DCR, disease control rate (CR + PR* + SD) of **78%**
- 6 / 9 patients show overall response rate (PR + CR) of **67%**
- 2 / 9 patients show a complete durable response (CR) of **22%** (8 Months & 11 Months)
- 7 patients are alive, 4 patients remain on study to date (2 CR's, 2 PR, 1 SD)
- Duration of response ranges from 2 months to over 14 months

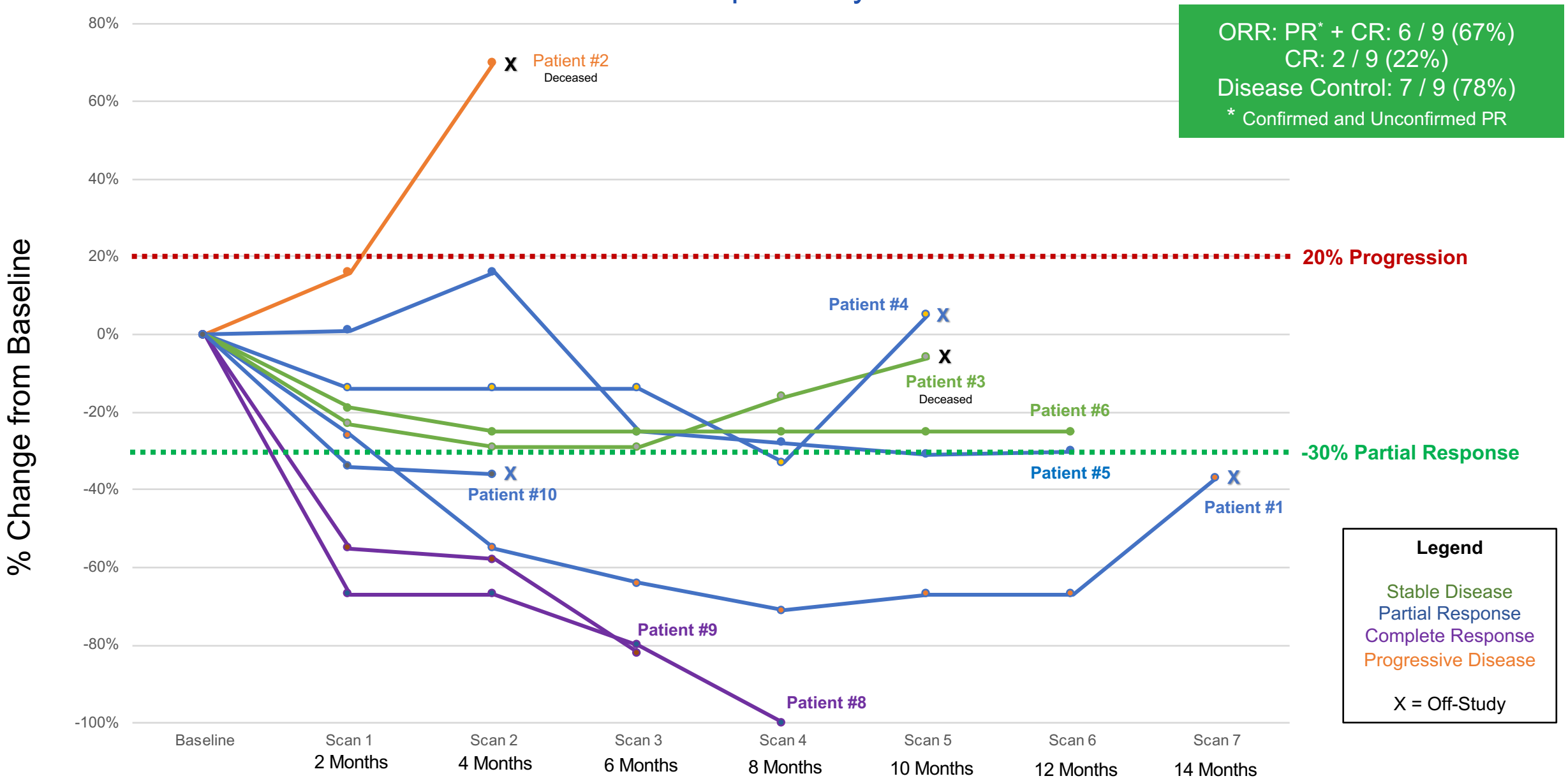
*Confirmed and Unconfirmed PR

Percent Change in Size of Target Lesion from Baseline

ORR: PR* + CR: 6 / 9 (67%)
CR: 2 / 9 (22%)
Disease Control: 7 / 9 (78%)
* Confirmed and Unconfirmed PR



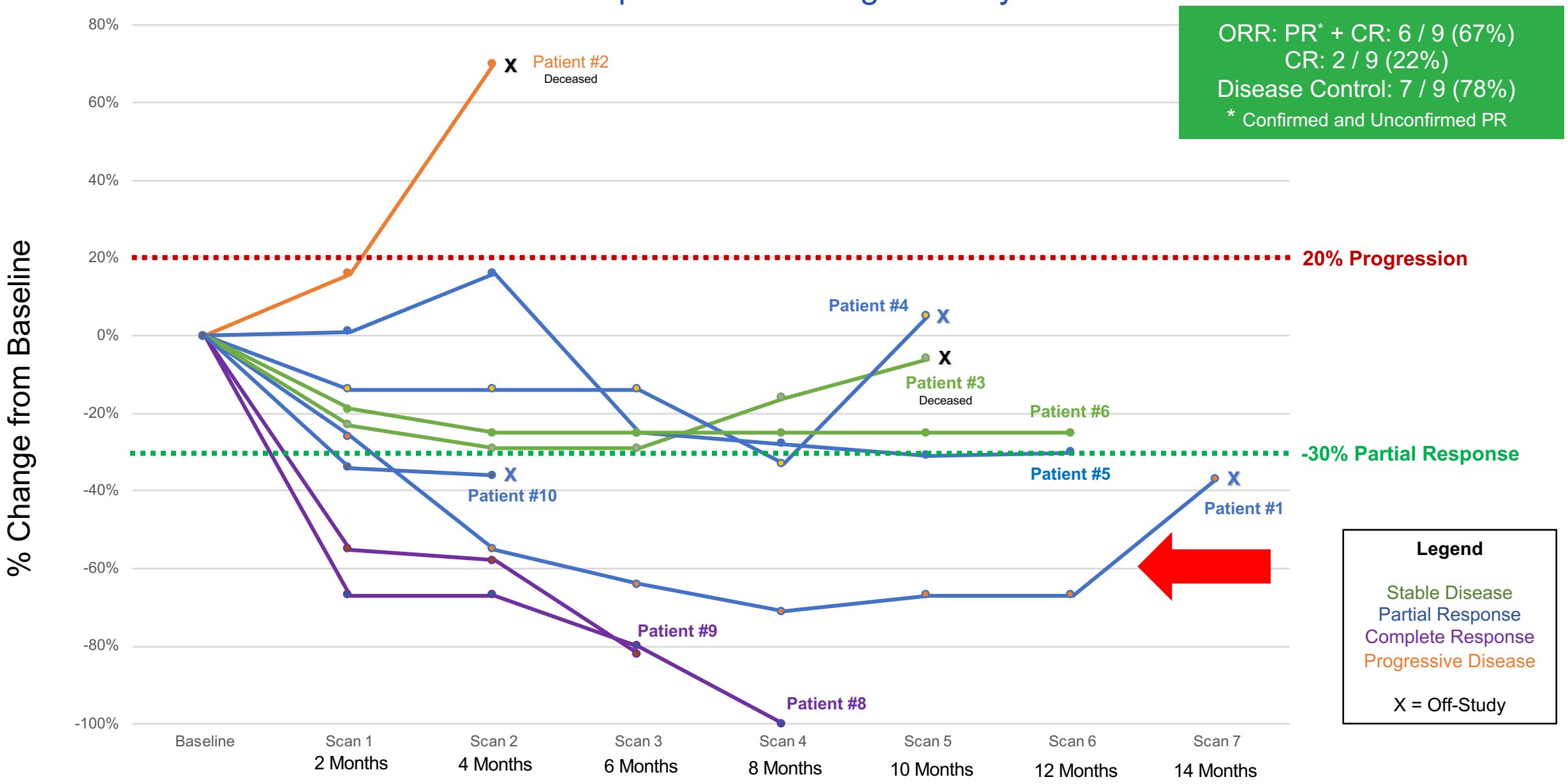
Early Signs of Efficacy in Relapsed (3rd line) Metastatic Triple Negative Breast Cancer
Best Response by Resist 1.1



Safety

- All patients received therapy in the outpatient setting
- No patients experienced cytokine release syndrome
- No SAE or hospitalizations attributable to immunotherapy
- All patients experienced at least 1 Grade ≥3 treatment related AE (mostly cytopenias due to chemotherapy)
- Grade 3 AEs for immunotherapy included fever, fatigue, and flu-like symptoms

Case Study #1: Patient 01: 57 Year-Old Female with 3rd Line TNBC Demonstrating Durable Partial Response Exceeding 400 Days



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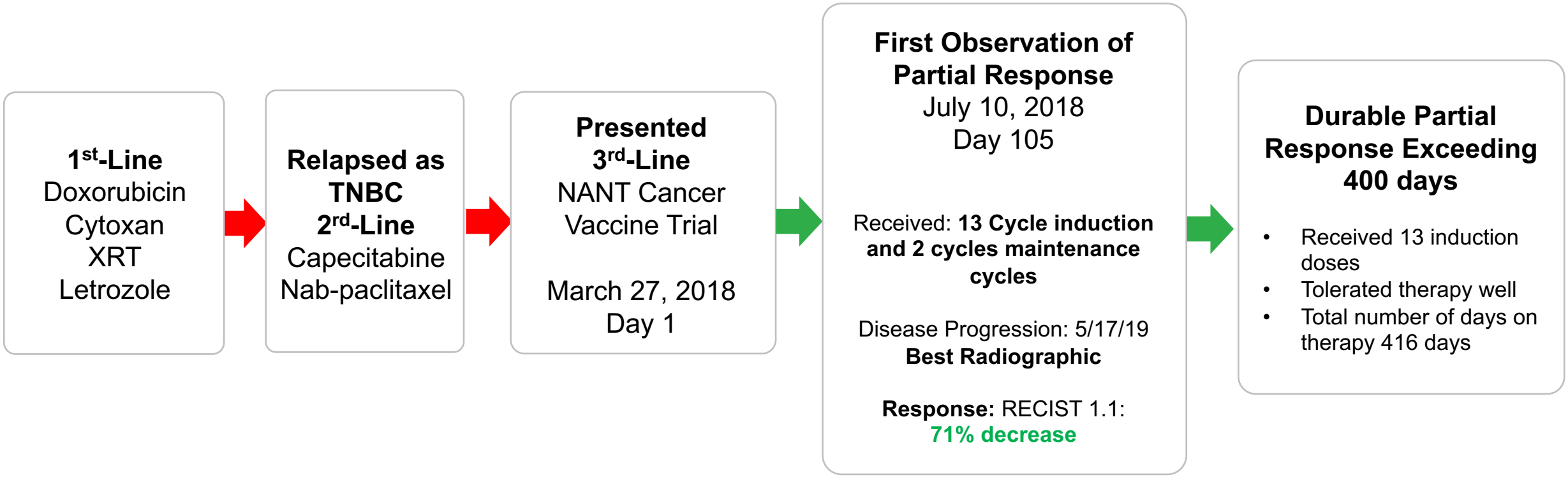

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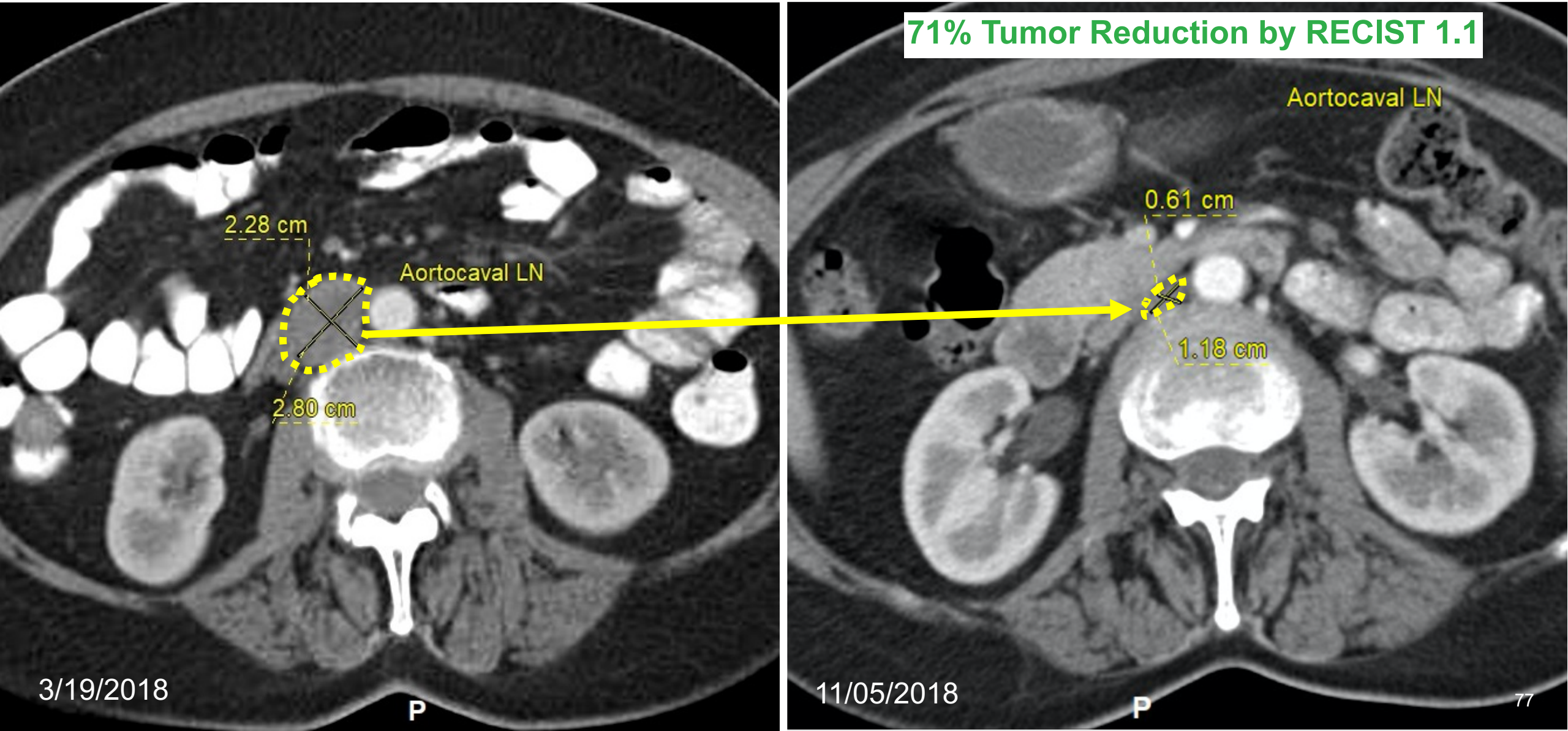
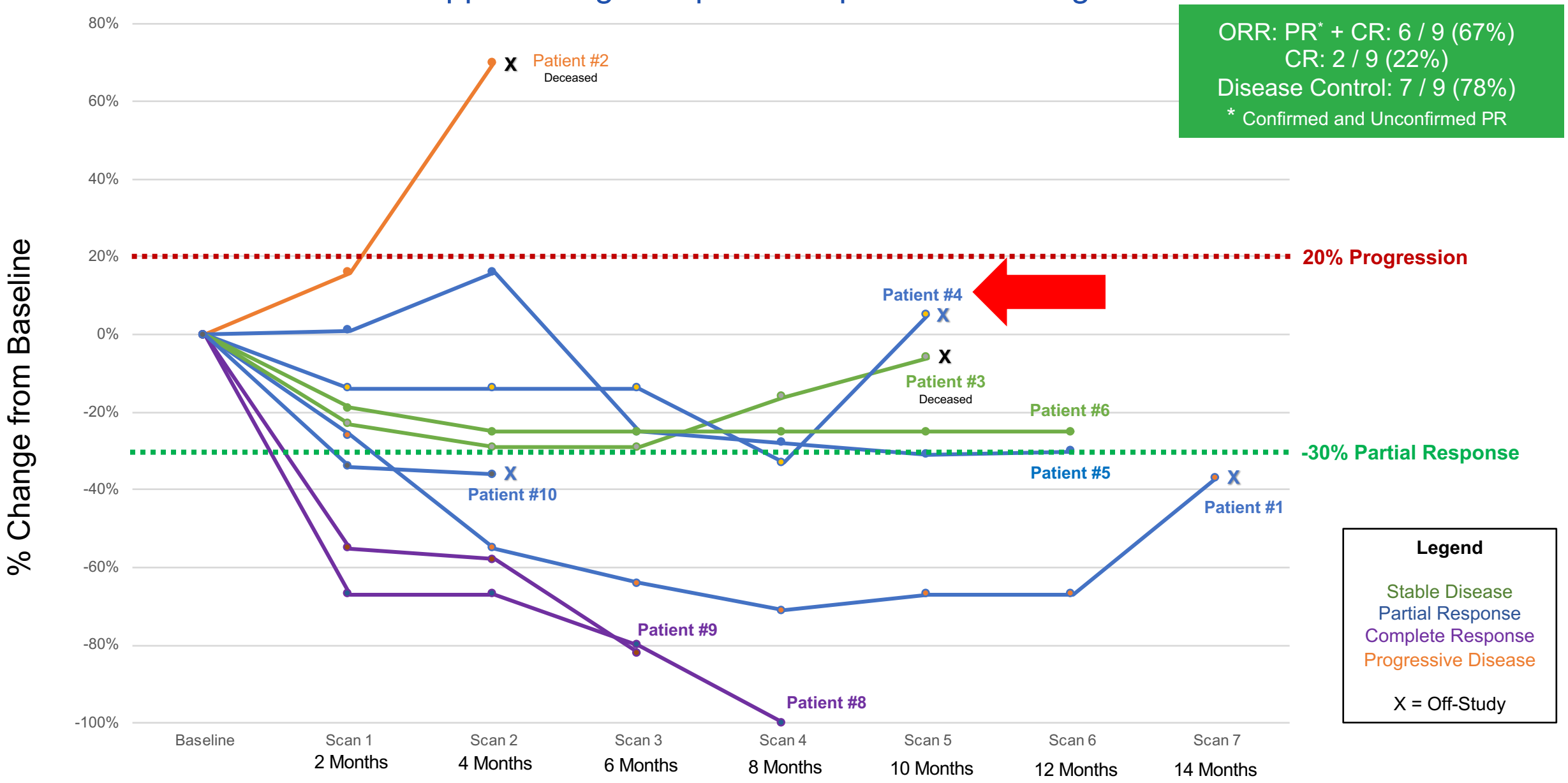


Case Study #2: Patient 04: 51 Year-Old Female with 3rd Line Metastatic TNBC Approaching Complete Response Post Progression



Case Study #2: Patient 04: 51 Year-Old Female with 3rd Line Metastatic TNBC Approaching Complete Response Post Progression

1st-Line
Doxorubicin
Cytoxan
Taxol

2rd-Line
Ibrance
Letrozole
Herceptin
Perjeta

3rd-Line
NANT Cancer Vaccine Trial

August 27, 2018
Day 1

First Observation of Partial Response

- Patient Had a 31% Partial response in target lesion masses
- Durable partial response of 292 days (9 months)
- Taken off study on 6/14/2019 for progression

Post Study Genomics analysis showed PIK3CA activating mutation patient treated with:

Alpelisib + Fulvestrant
Patient ongoing near CR

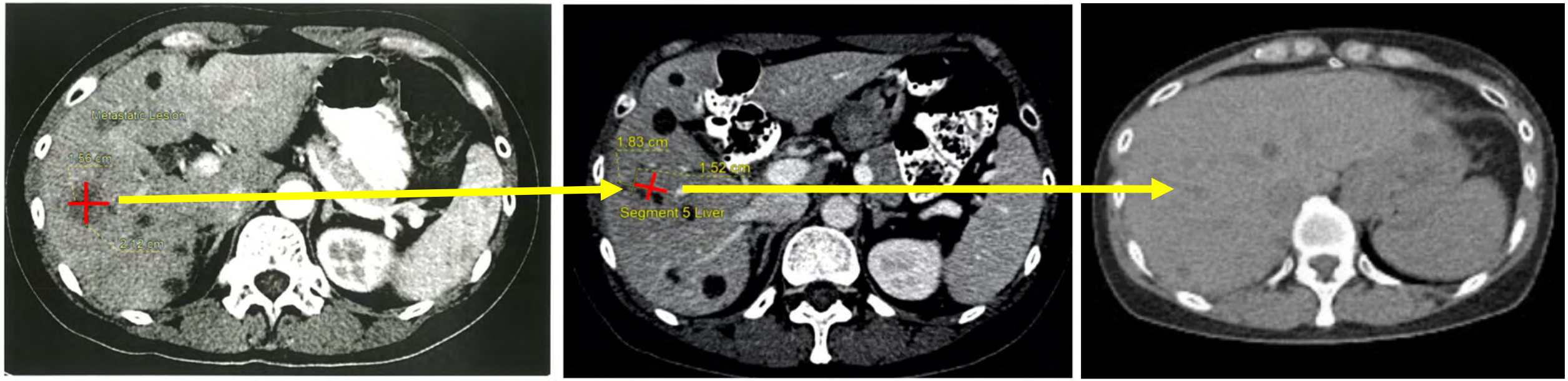
Anticipated to enter into PD-L1 t-haNK clinical study

Case Study #2: Patient 04: 51 Year-Old Female with 3rd Line Metastatic TNBC Approaching Complete Response Post Progression

Pre-Study Scan
1.56 cm by 2.12 cm

Partial Response
On Study
1.52 cm by 1.83 cm

Nearing
Complete Response
Off Study



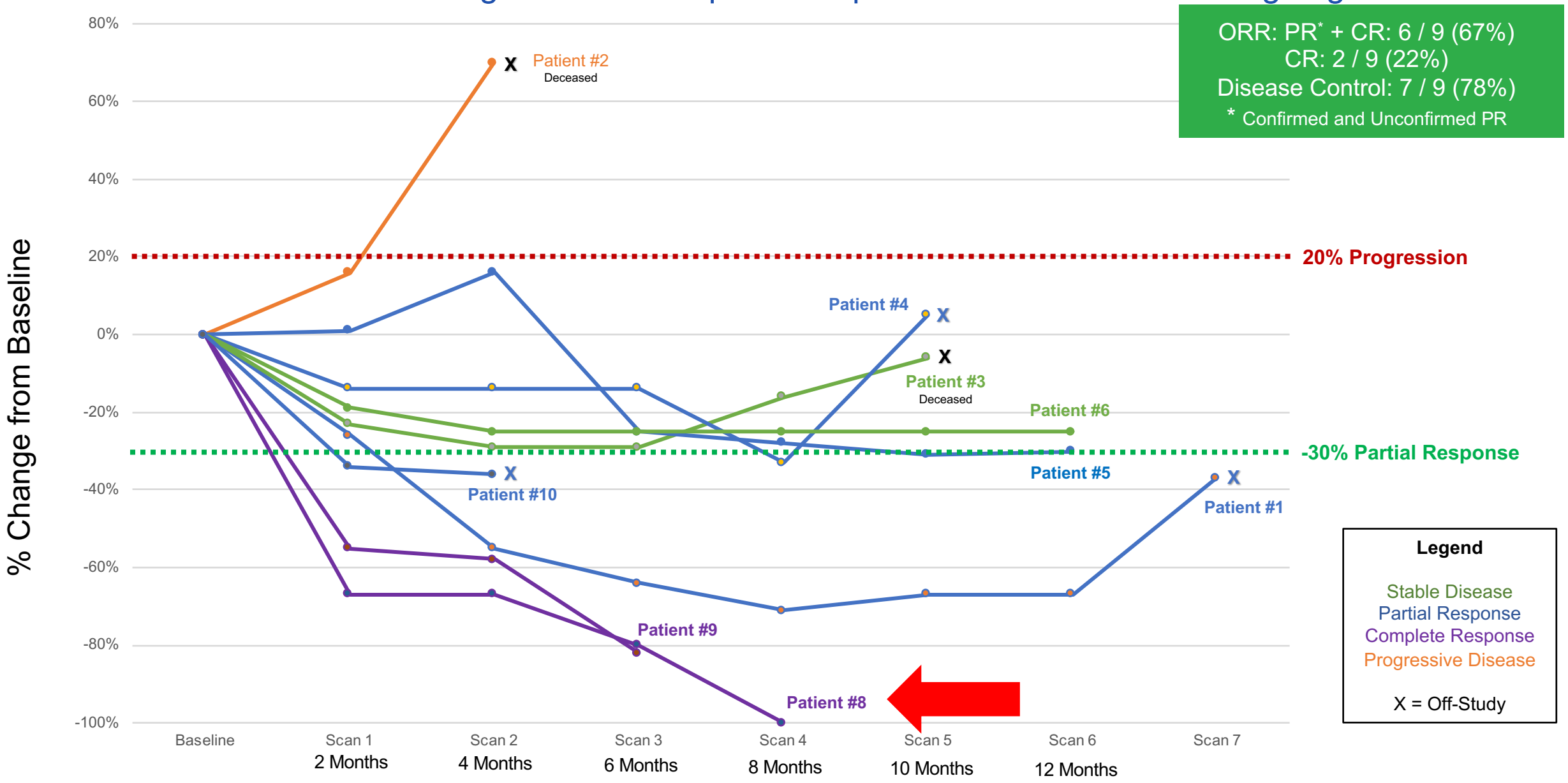
Sept 2018

Dec 2018

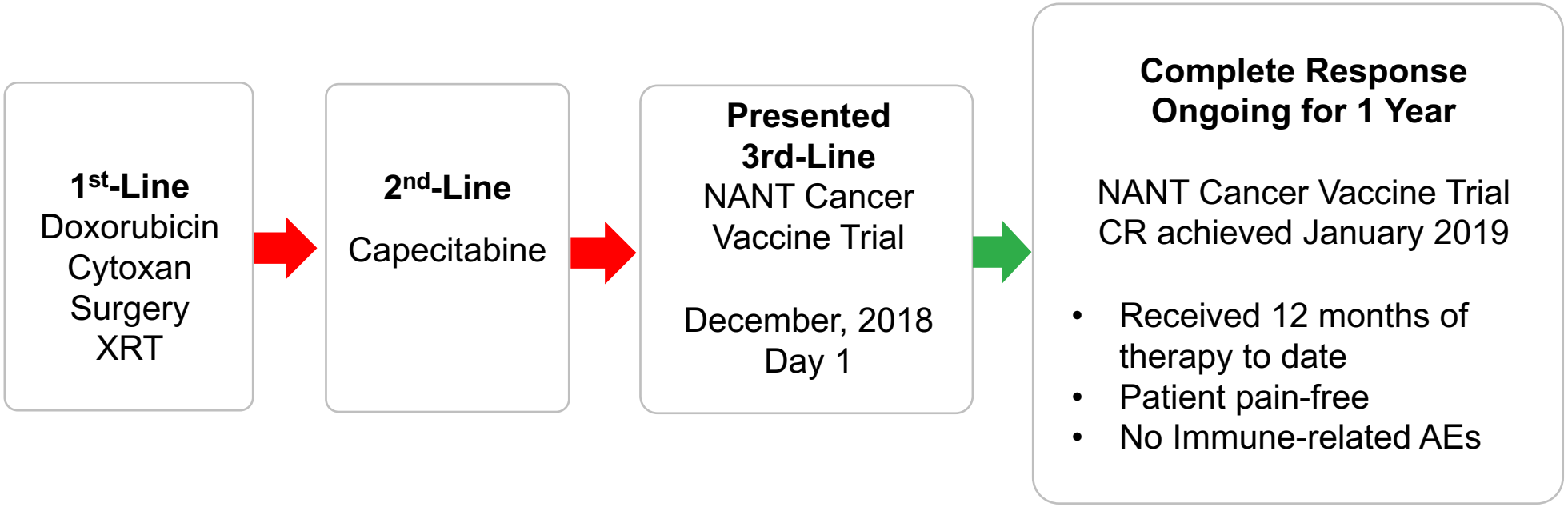
Sept 2019

Durable Partial Response – 292 Days (9 Months) → Near Complete Response (at 12 Months)

Case Study #3: Patient 08: 53-Year Old Female with 3rd-Line TNBC Demonstrating Durable Complete Response – 12 Months and Ongoing

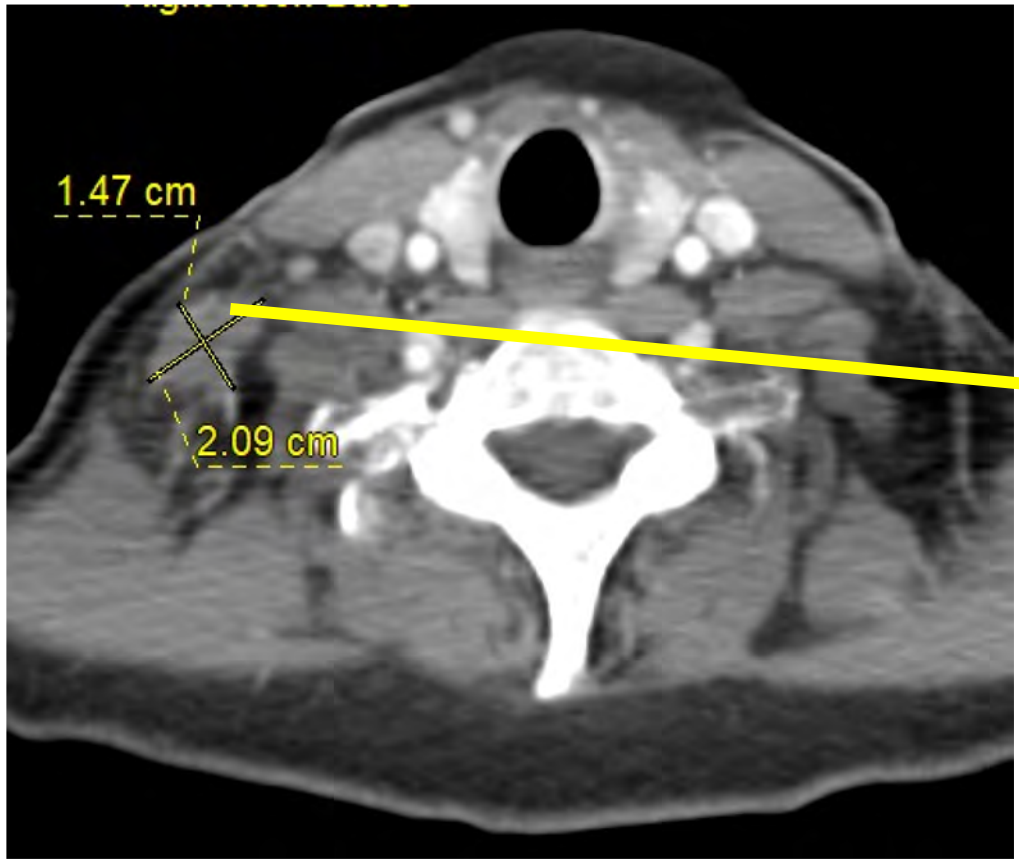


Case Study #3: Patient 08: 53-Year Old Female with 3rd-Line TNBC Demonstrating Durable Complete Response – 12 Months and Ongoing



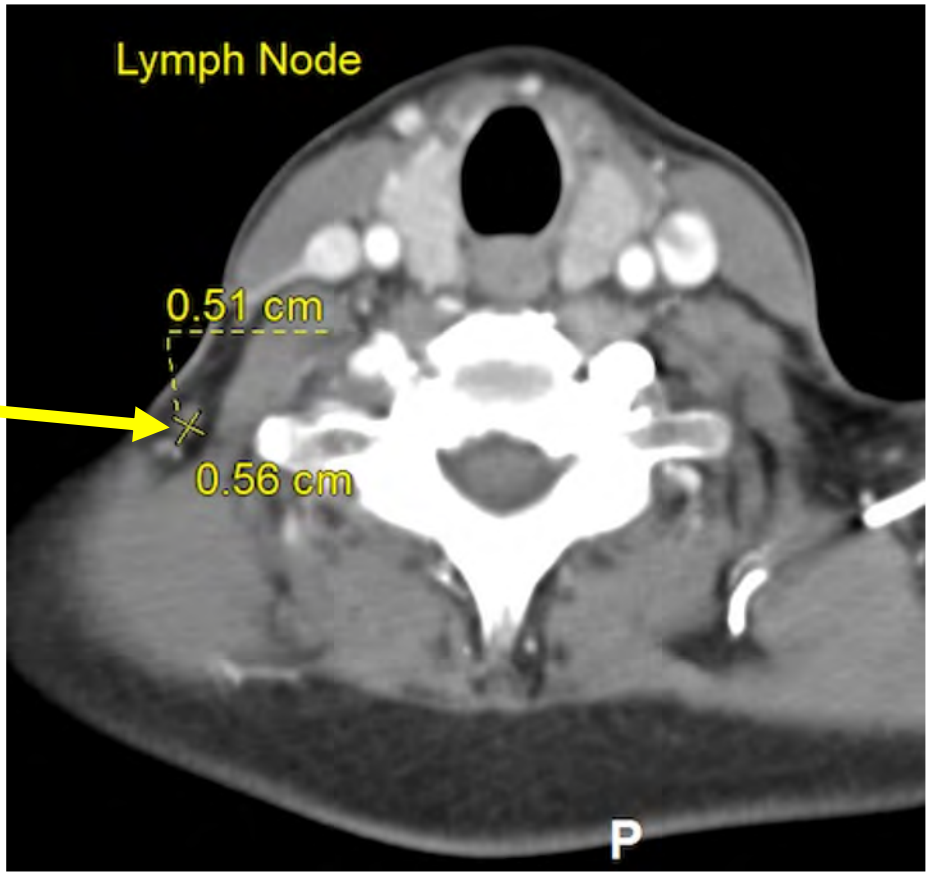
Case Study #3: Patient 08: 53-Year Old Female with 3rd-Line TNBC Demonstrating Durable Complete Response – 12 Months and Ongoing

Pre-Treatment Scan



Oct 2018

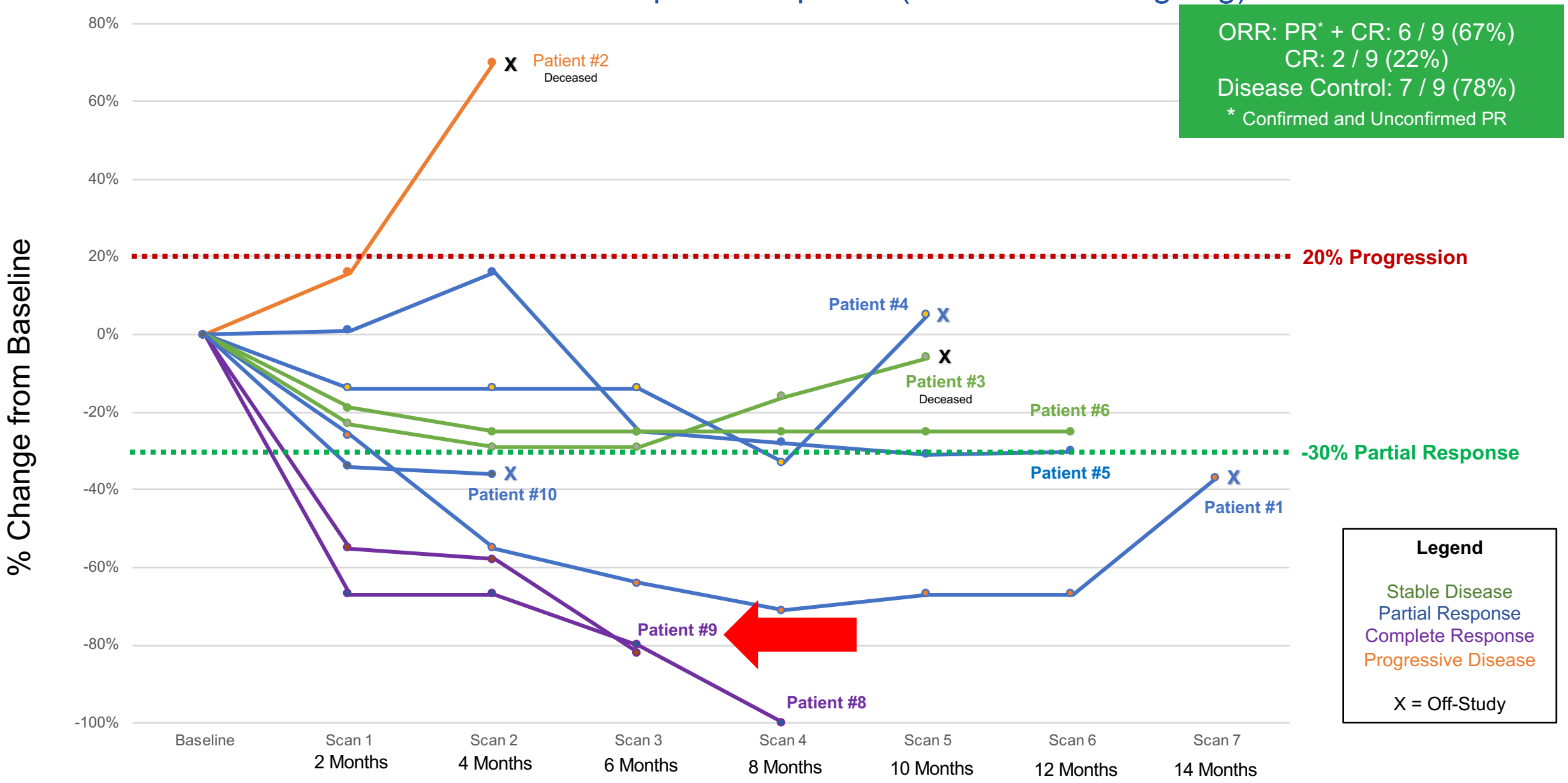
Complete Response



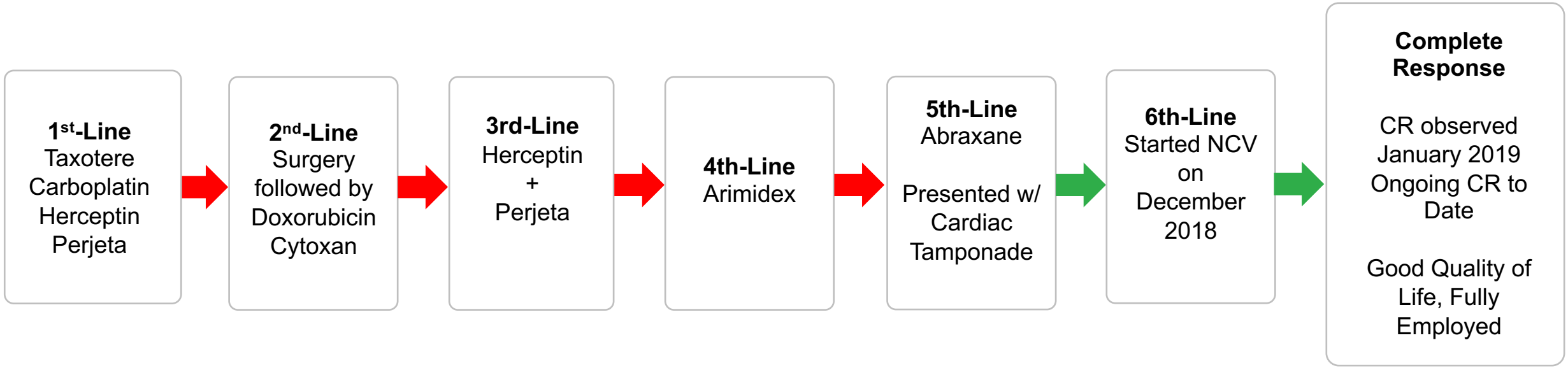
Dec 2018

Durable Complete Response (12 Months and Ongoing)

Case Study #4: Patient 09: 53 Year Old Female with 4th-Line TNBC With Durable Complete Response (11 Months & Ongoing)

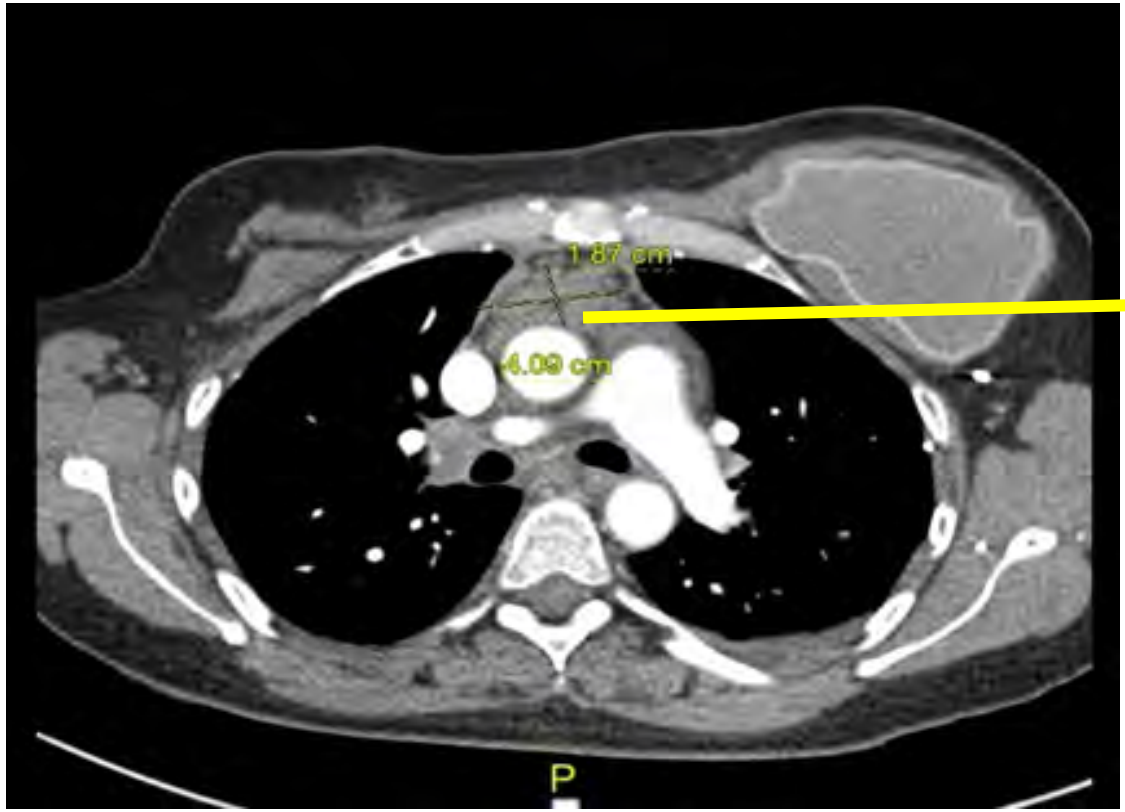


Case Study #4: Patient 09: 53 Year Old Female with 4th-Line TNBC With Durable Complete Response (11 Months & Ongoing)



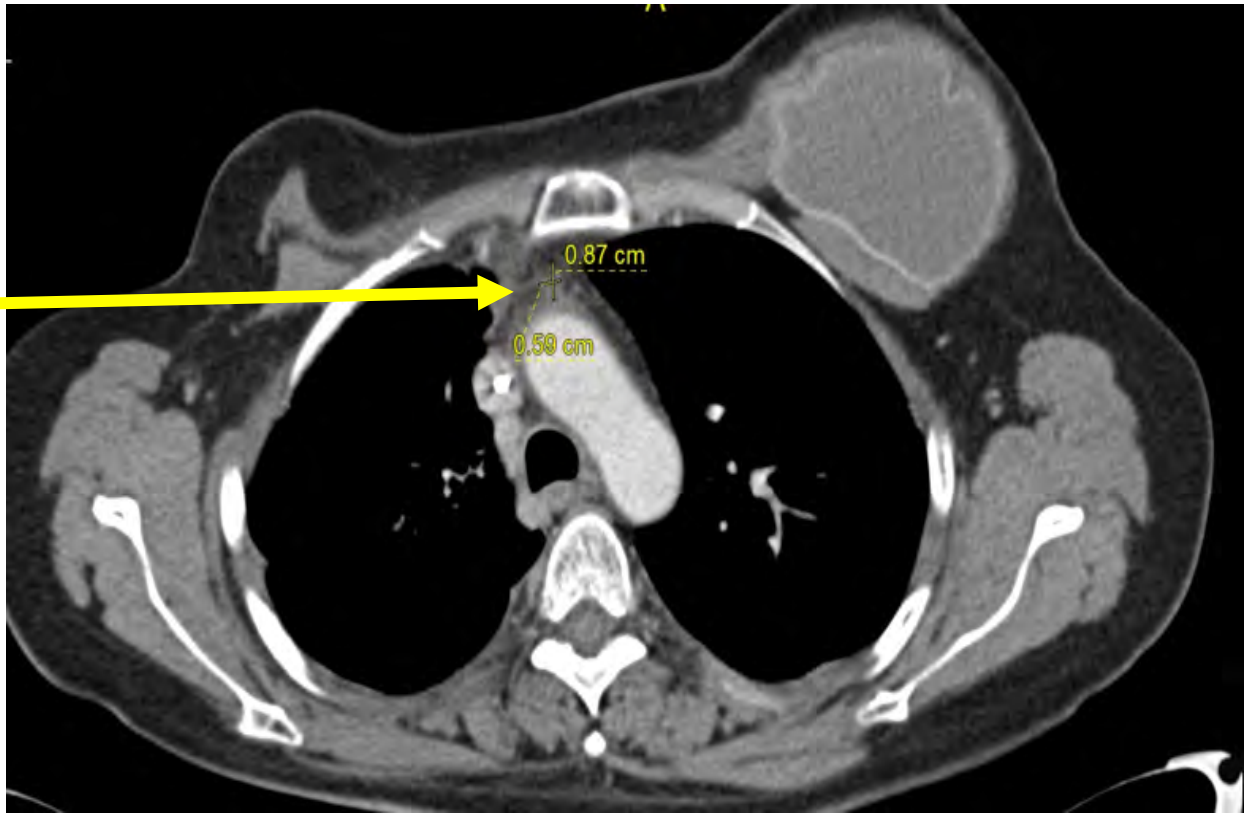
Case Study #4: Patient 09: 53 Year Old Female with 4th-Line TNBC With Durable Complete Response (11 Months & Ongoing)

Pre-Treatment Scan
Large Peri-Aortic Mass with Cardiac Tamponade



Nov 2018

Complete Response

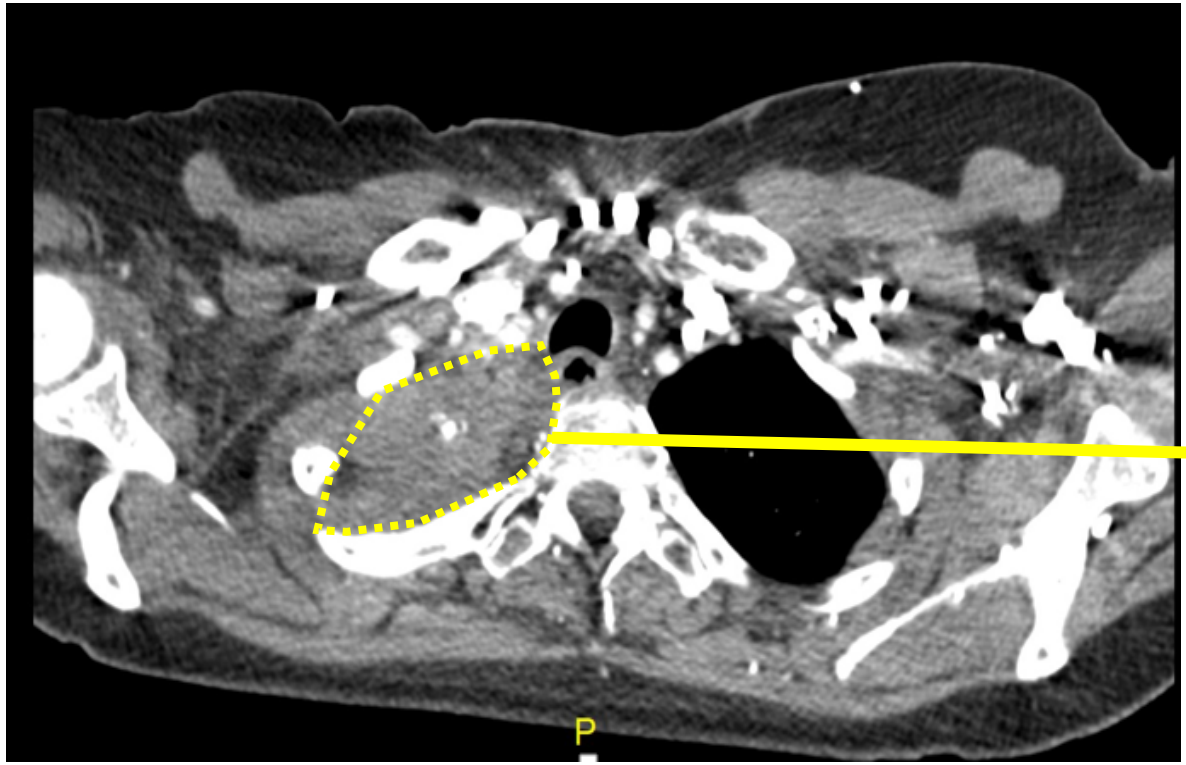


July 2019

Durable Complete Response (11 Months and Ongoing)

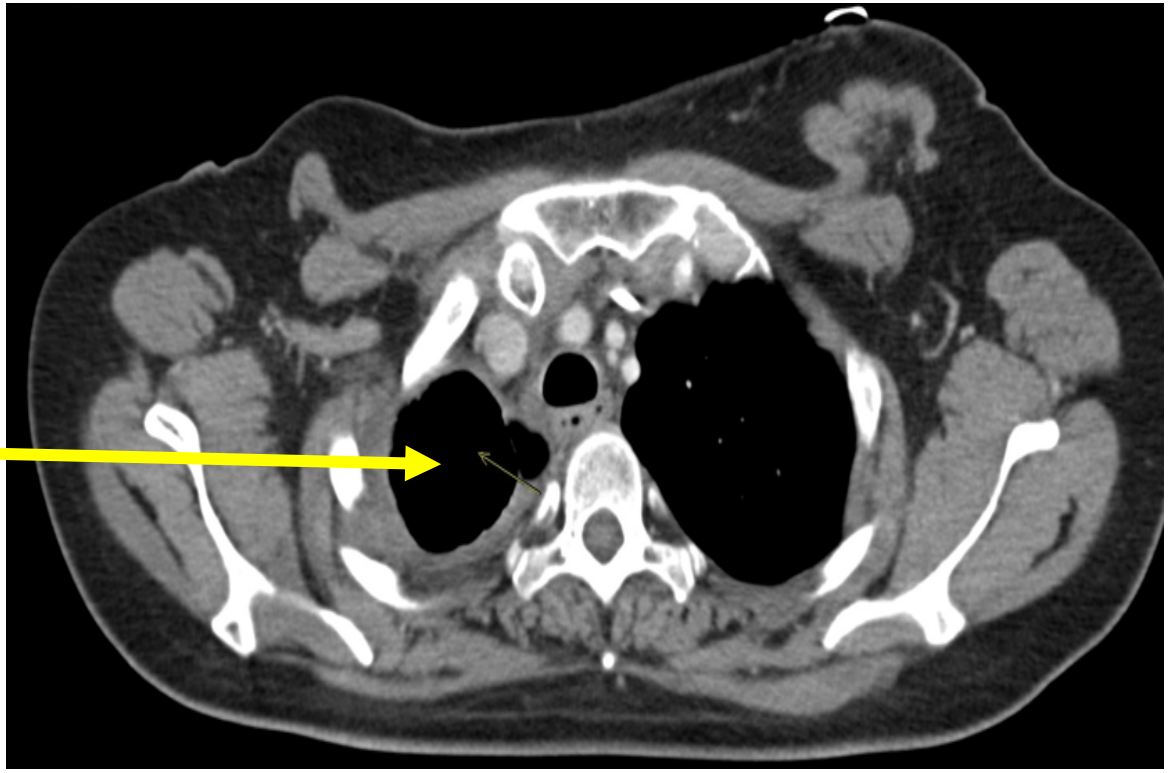
Case Study #4: Patient 09: 53 Year Old Female with 4th-Line TNBC With Durable Complete Response (11 Months & Ongoing)

Pre-Treatment Scan
Large Apical Lung Mass



Nov 2018

Complete Response



July 2019

Durable Complete Response (11 Months and Ongoing)

Natural Killer Cell
haNK Cell Infusion Experience

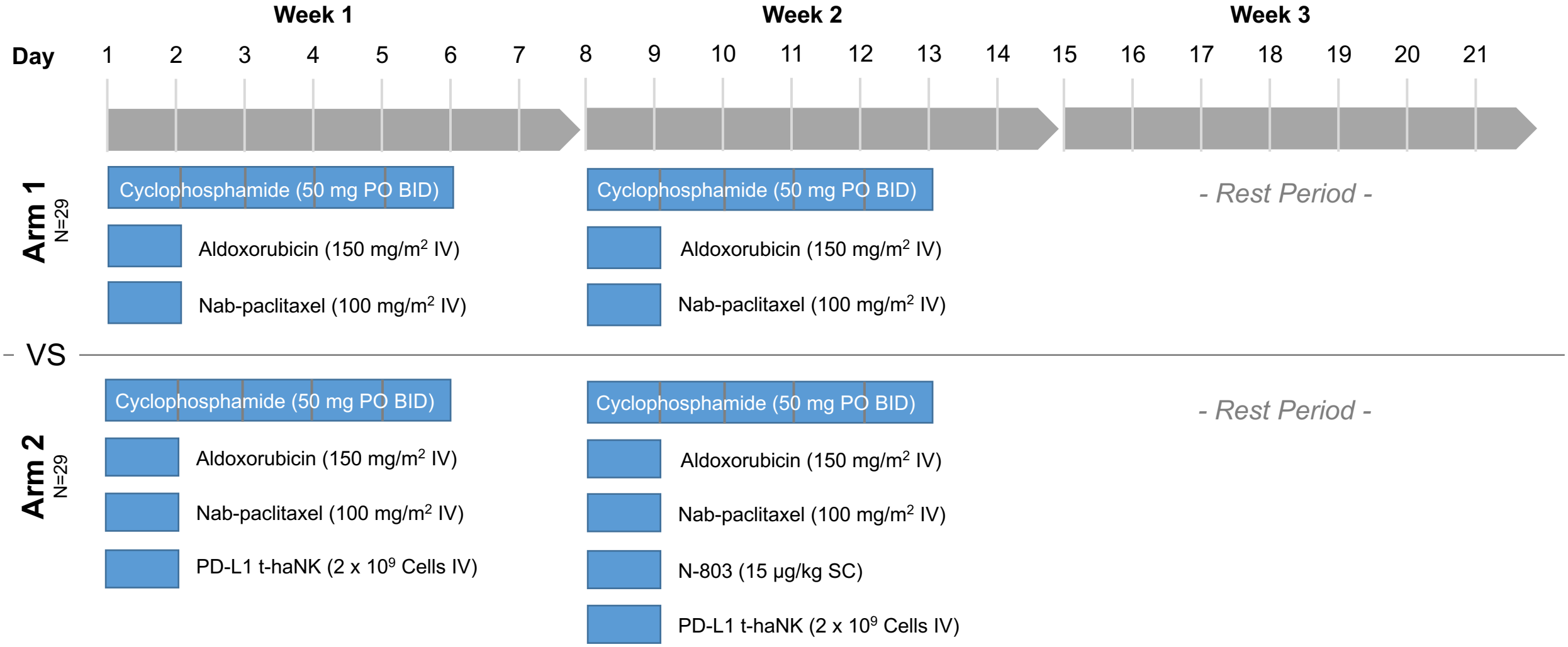
Total: 547 infusions of haNK given to date

TNBC: 224 haNK infusions given to date

- Early signs of efficacy with favorable PFS, ORR and Duration of Response
- Durable complete remissions
- All patients were in an outpatient setting
- Zero incidence of cytokine release syndrome
- No Grade 4 immune-related adverse events
- Most common immune related AE is fatigue and fever (Grade 1-3)
- Infusion reactions (Grade 1-2)

Future Direction: Phase II Exploratory Randomized TNBC Neoadjuvant Schema

Investigator Initiated Trial



December 2, 2019
The Benjamin Hotel – New York City

Q&A Session