NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

Faith E. Davies, MD, MBBCh, MRCP, FRCPath
Professor of Medicine
NYU Grossman School of Medicine
Perlmutter Cancer Center, NYU Langone
New York, NY

1

WELCOMING REMARKS

NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

Lizette Figueroa-Rivera, MA
Sr. Director, Education & Support
The Leukemia & Lymphoma Society

LEUKEMIA & LYMPHOMA SOCIETY®

2

FACULTY
NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

Faith E. Davies, MD, MBBCh, MRCP, FRCPath
Professor, Medicine
NYU Grossman School of Medicine
Perlmutter Cancer Center, NYU Langone
New York, NY

LEUKEMIA & LYMPHOMA SOCIETY®

3

DISCLOSURES
NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

Faith E. Davies, MD, MBBCh, MRCP, FRCPath, has the following disclosures; BMS, Janssen, Takeda, Sanofi, GSK, Regeneron *(Ad Board)*; BMS, Janssen, Takeda, Sanofi *(Consultant).*

LEUKEMIA & LYMPHOMA SOCIETY®

4

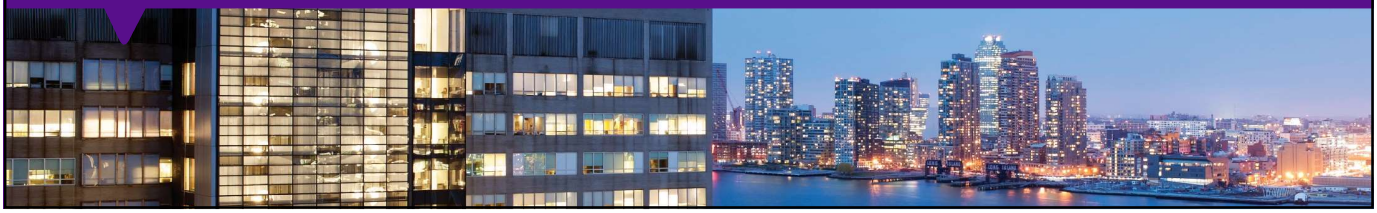
NYU Langone Health

Perlmutter Cancer Center

NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

Faith Davies

Professor of Medicine NYU Langone Health



5

Acknowledgements

- I have ‘borrowed’ a number of the images used in this talk - I thank the ‘internet artists’ who drew them.
- I pray I haven’t broken any copyright laws

- Advisory boards: BMS/Celgene, GSK, Janssen, Regeneron, Sanofi, Takeda

6

Talk Outline

- Clinical trials
  - Why are they important
  - What are they
- New and emerging therapies
  - Targeted treatment approaches
  - Immune therapies

7

In order for a drug to be prescribed in the clinic we need to:-

- Have laboratory data to show how the drug works (mechanism of action)
- Have data from animal studies to show how the drug is handled by the body and how safe it is (what side effects may occur)
- Have data from humans showing how the drug is handled by the body, how effective the drug is at killing cancer cells, what side effects occur

Clinical trials provide this information

8

Clinical trial phases

Phase 1 → Phase 2 → Phase 3 → Phase 4

Studies at each phase differ in the aims and size

9

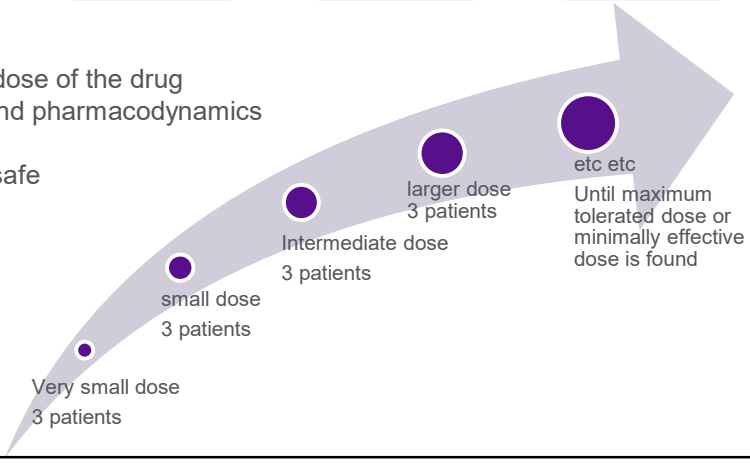
Clinical trial phases

Phase 1 → Phase 2 → Phase 3 → Phase 4

To determine the correct dose of the drug
pharmacokinetics and pharmacodynamics

To determine the drug is safe

Usually 30-50 patients



10

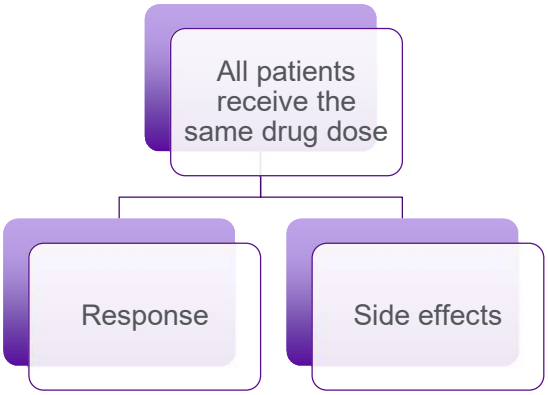
Clinical trial phases

Phase 1 → **Phase 2** → Phase 3 → Phase 4

To determine how effect the drug is

To determine the drug is safe

Usually 50-100 patients



11

Clinical trial phases

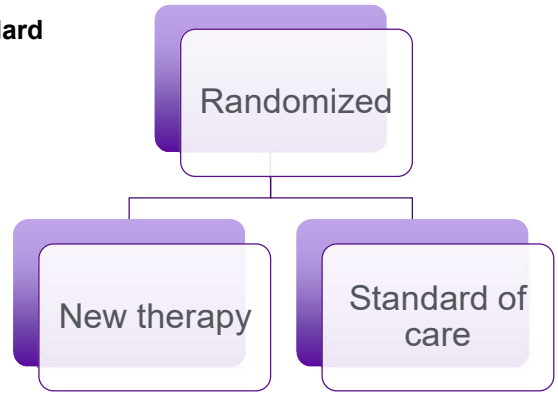
Phase 1 → Phase 2 → **Phase 3** → Phase 4

To compare the drug to previous gold standard therapies

To determine the drug is safe

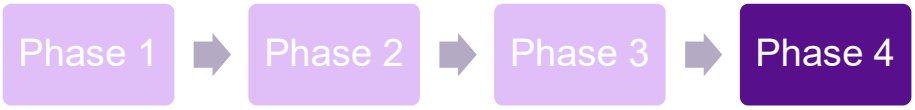
Randomized
- **By chance**
- **Rarely contain an ineffective / placebo**

Usually 100-1000 patients



12

Clinical trial phases



Drug will usually get approval from phase 2 or phase 3 studies

Phase 4 studies;-

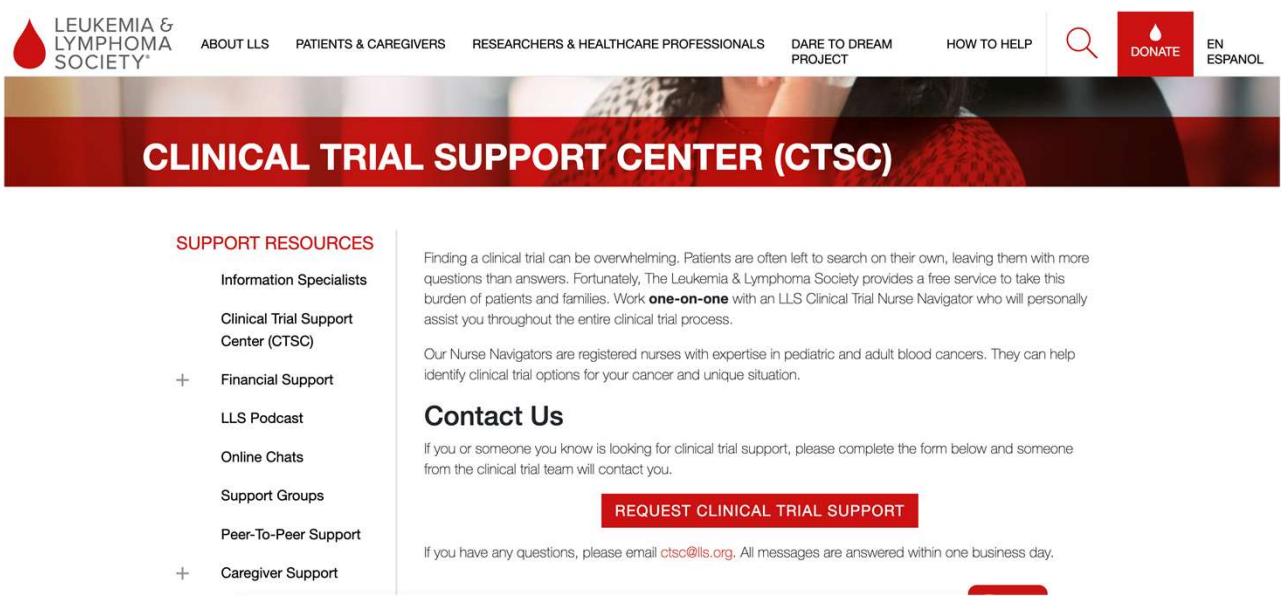
Post approval / marketing

Continue to ensure the drug is safe and no unexpected side effects occur.

13

Where in the disease course do studies take place

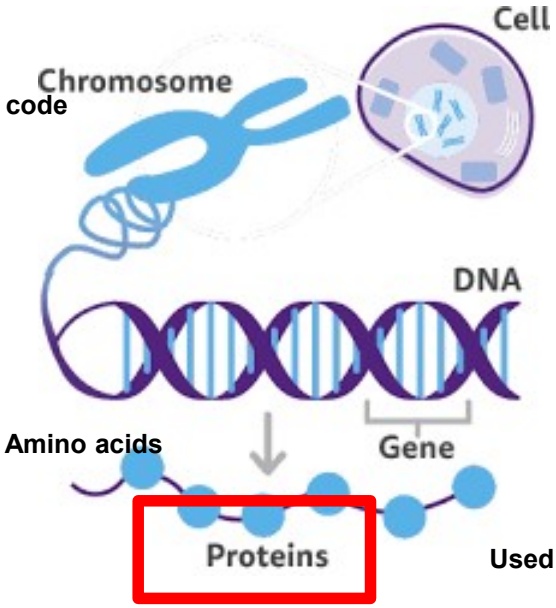
14



15

Biology of a cancer cell

A way to package the genetic code
- **46 chromosomes**
- **23 pairs**



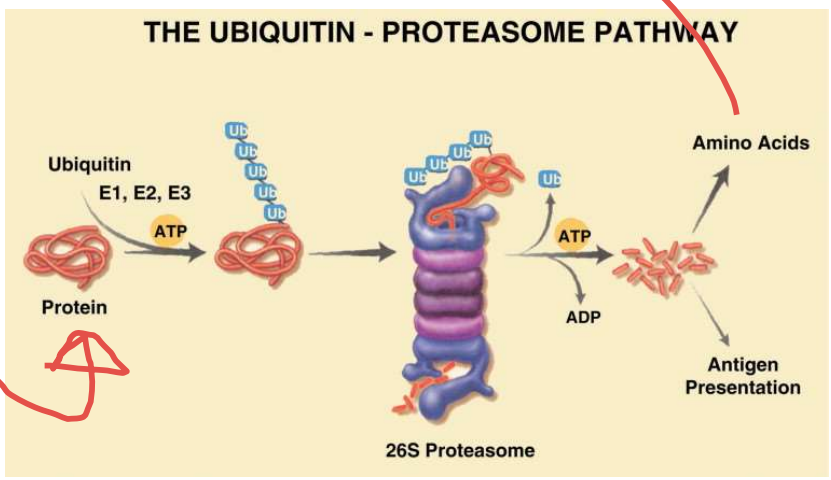
Cancer cell

The genetic code

Used to make proteins
- **The building blocks of a cell**

16

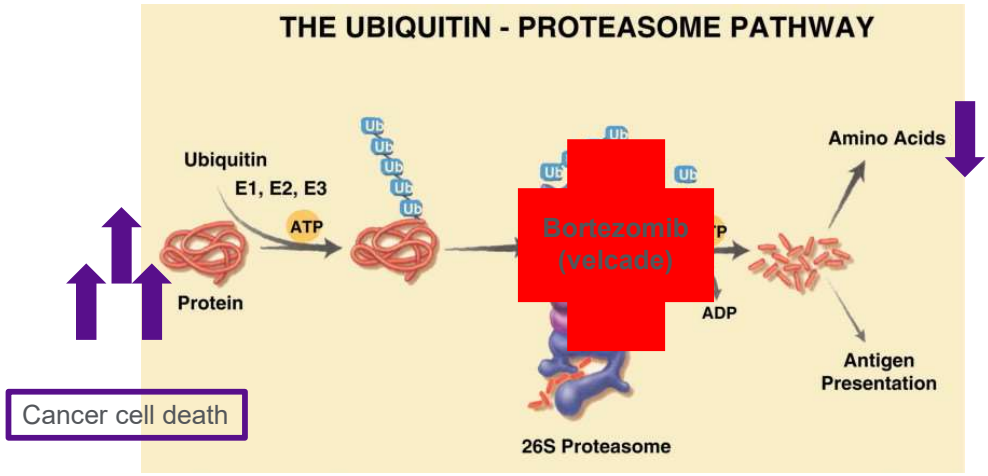
All cells have a recycling machines



Kisselev *et al* Cell Chemical Biology 2001

17

The recycling process can be a target for drugs

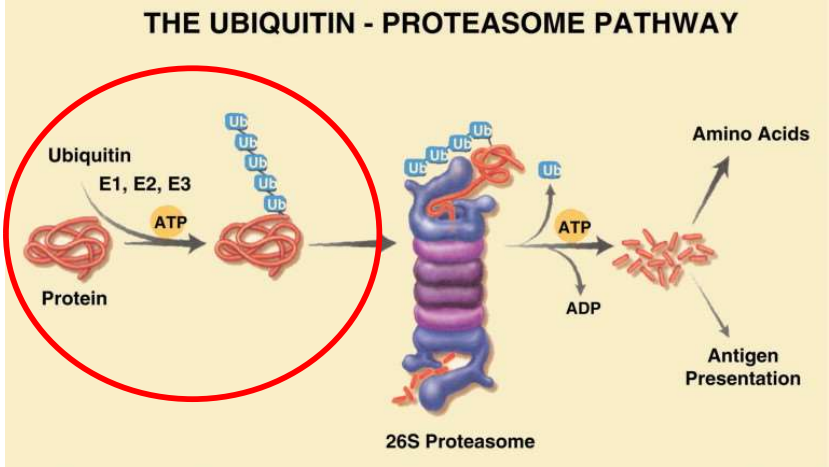


Adapted from Kisselev *et al* Cell Chemical Biology 2001

18

New ways to target the recycling process

target proteins key for cancer cell growth

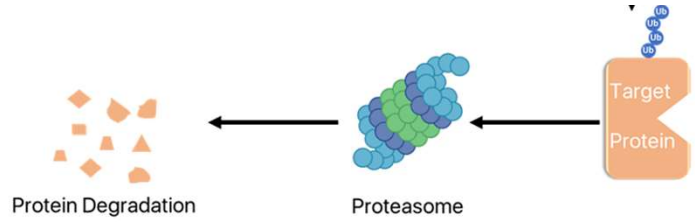


Kisselev *et al* Cell Chemical Biology 2001

19

Protacs / Degraders

Degrade the protein essential for cancer cell survival – cancer cell dies



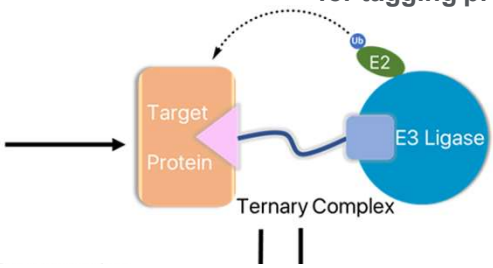
Tag the protein essential for cancer cell survival

Dr. Jin Wang, Baylor College of Medicine

20

Protacs / Degraders

E3 ligases are responsible for tagging proteins

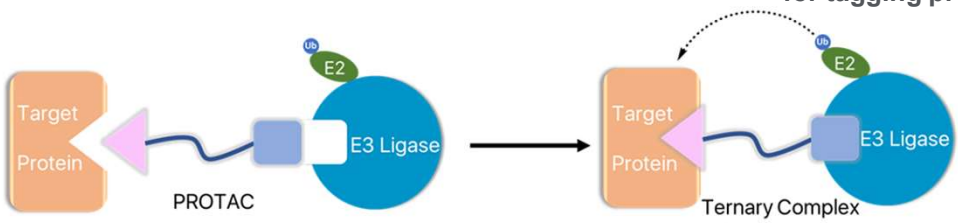


Dr. Jin Wang, Baylor College of Medicine

21

Protacs / Degraders

E3 ligases are responsible for tagging proteins

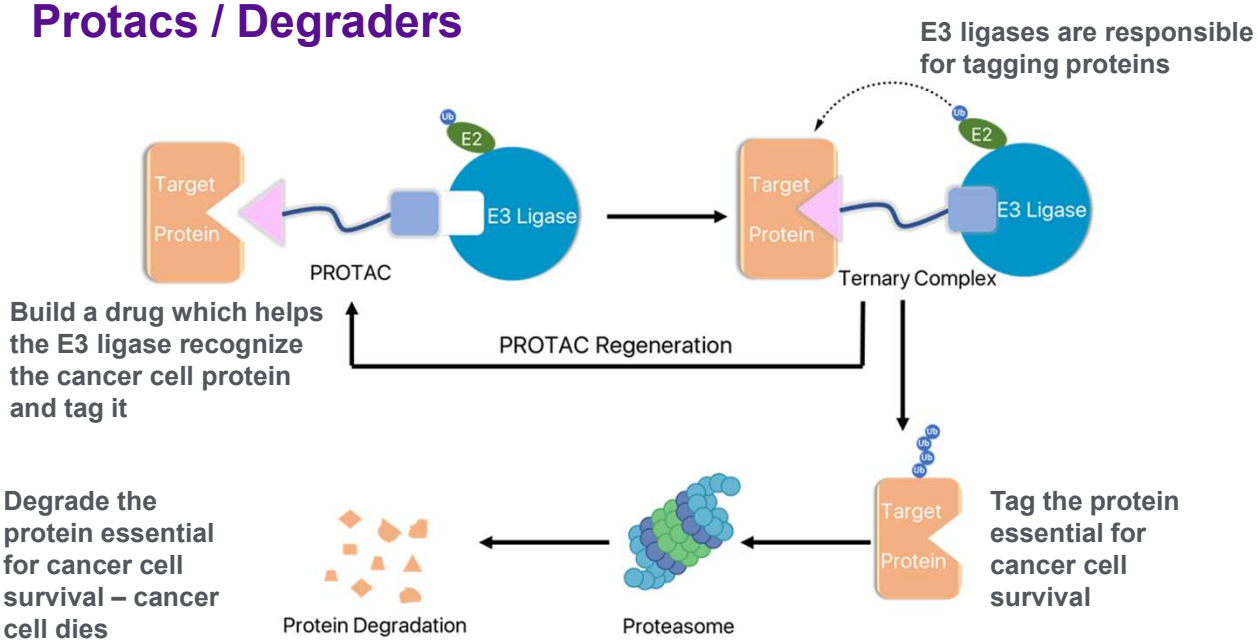


Build a drug which helps the E3 ligase recognize the cancer cell protein and tag it

Dr. Jin Wang, Baylor College of Medicine

22

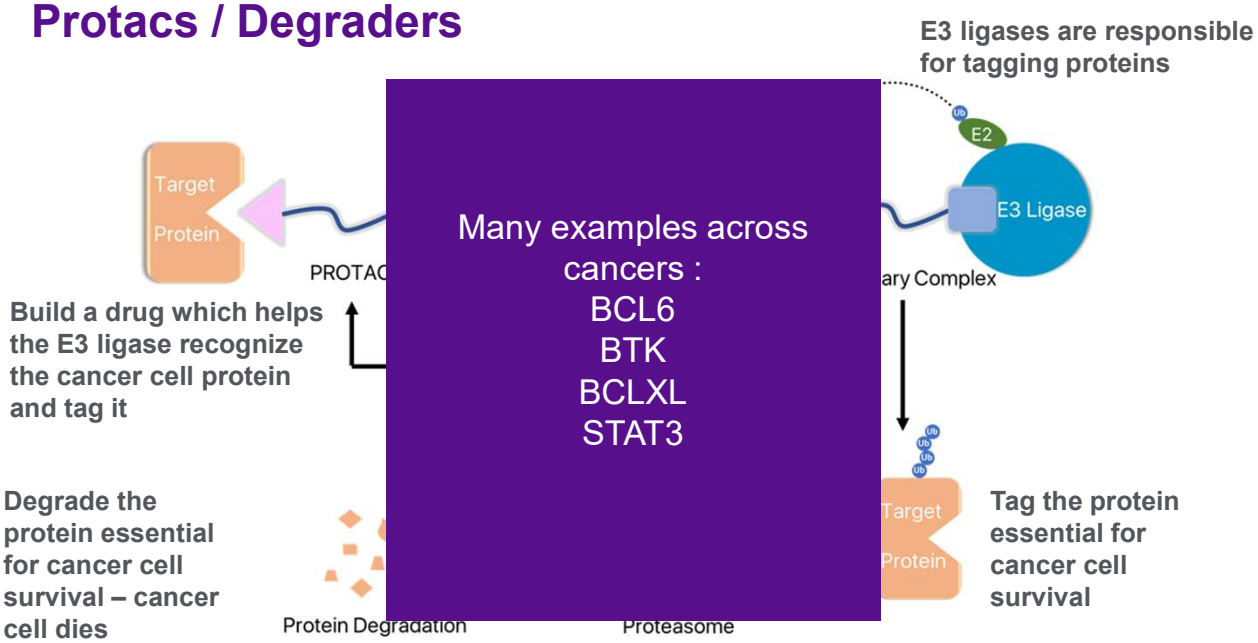
Protacs / Degraders



Dr. Jin Wang, Baylor College of Medicine

23

Protacs / Degraders



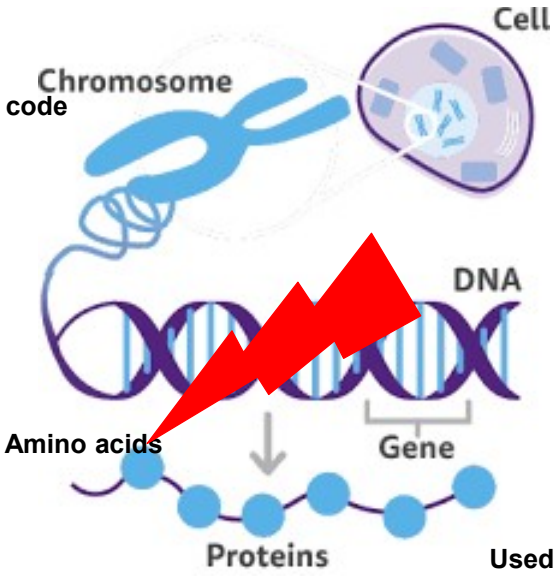
Dr. Jin Wang, Baylor College of Medicine

24

Biology of a cancer cell

A way to package the genetic code
- 46 chromosomes
- 23 pairs

Mutation
Translocation
Copy number



Cancer cell

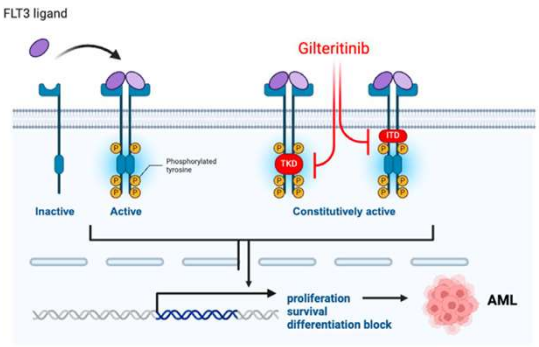
The genetic code

Used to make proteins
The building blocks of a cell

25

Other targeted treatment approaches

FLT 3 inhibitors

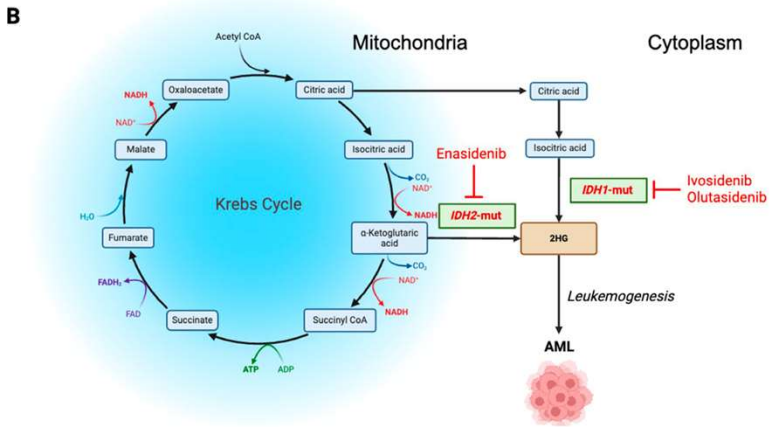


Gutierrez Moore et al American Journal of Hematology 2025

26

Other targeted treatment approaches

IDH2 inhibitors

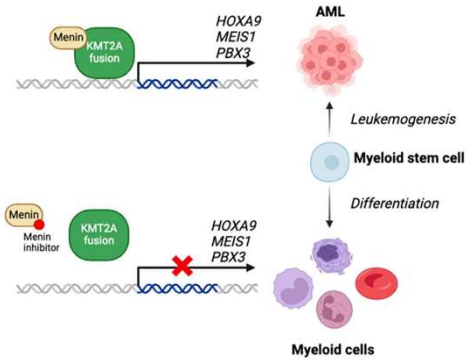


Gutierrez Moore et al American Journal of Hematology 2025

27

Other targeted treatment approaches

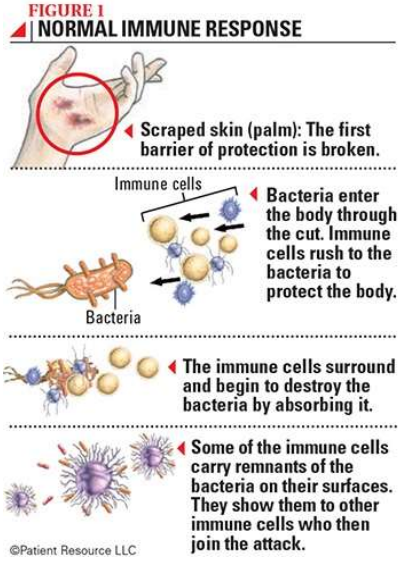
Menin inhibitors



Gutierrez Moore et al American Journal of Hematology 2025

28

Harnessing a Patients Immune System



A cancer cell should be considered as 'foreign' by the body and destroyed.

Instead the cancer cell manages to hide, survive and grow.

Newer approaches to treating cancers aim to reinvigorate the immune system to kill the cells.

29

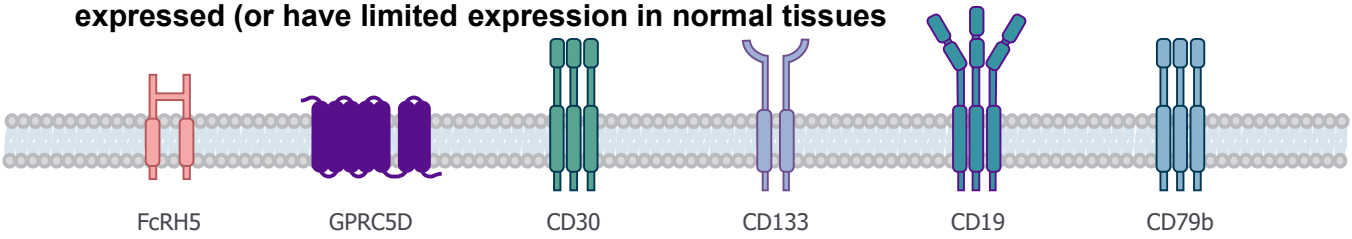
Immunotherapy Landscape

Cancer cells have proteins on their cell surfaces which help the cell survive by communicating with the environment

These proteins can be used to deliver drugs
Well recognized examples include Rituximab, Daratumumab

New approaches to targeting these proteins are being developed

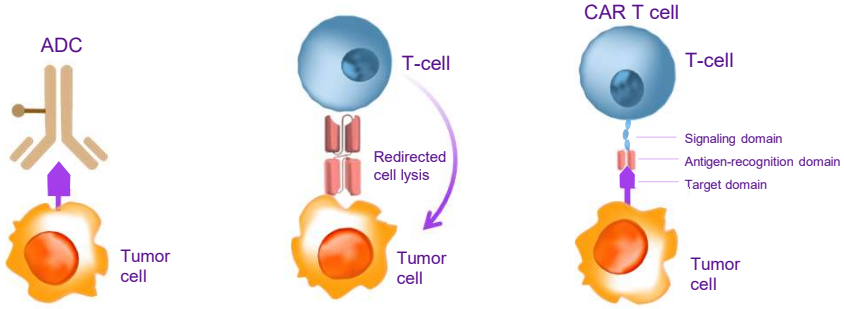
Ideally a good target protein will be highly expressed on the cancer cell and not expressed (or have limited expression in normal tissues



Adapted from Braunstein M, et al. Expert Rev Hematol. 2021;14:377-389

30

Novel immune active therapeutic agents



ADC

Once bound to antigen-expressing target cells, ADCs are internalized and the toxic payload is released to induce DNA damage and cell death[1]

Bispecific

Facilitate cell-to-cell interactions between the patients' own T cells and malignant cells expressing tumor-specific antigens[1]

CAR-T

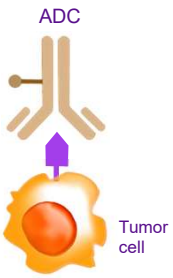
Genetically modified T cells that express a CAR targeted against a specific antigen, which upon binding initiates T-cell activation in a human leukocyte antigen–independent manner[1]

ADC, antibody-drug conjugates; BCL-2, B-cell lymphoma 2; CAR-T, chimeric antigen receptor T-cell therapy; MOMP, mitochondrial outer membrane permeabilization; TAA, tumor associated antigen; TAA, tumor-associated antigen.

1. Shah N, et al. *Leukemia.* 2020;34(4):985-1005; 2. Seiller C, et al. *Cell Death Dis.* 2020;11(5):316.

31

Antibody Drug Conjugate (ADC)



ADC

Once bound to antigen-expressing target cells, ADCs are internalized and the toxic payload is released to induce DNA damage and cell death

Antibody with its payload recognizes a marker on the surface of the cancer cell.

Payload is internalized and activated to kill the cancer cell.

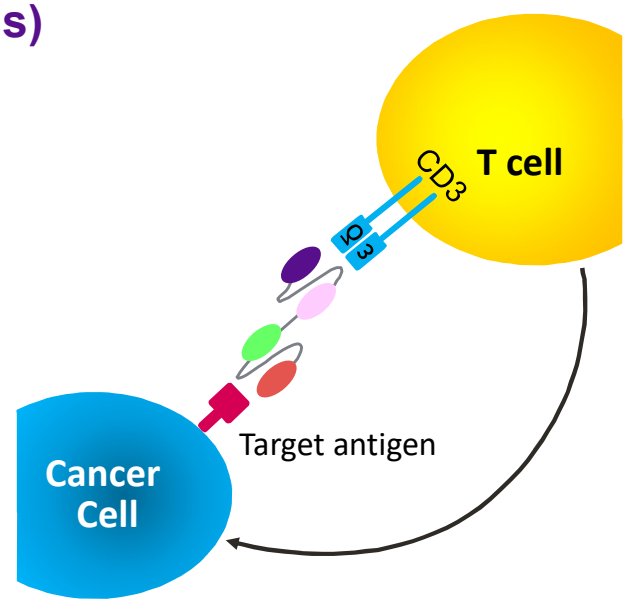
Large number of different cell surface targets
- Examples include - CD33, CD123, CD117

Large number of different payloads
- Radiation, chemotherapy - monomethyl auristatin F (mafodotin), monomethyl auristatin E (MMAE)

32

Bispecific Antibodies (T cells)

- Potential to overcome the limitations of immunosuppressive tumor microenvironment by redirecting T cells to kill cancer cells
- Off the shelf
- T cell redirecting bispecific antibody that binds to CD3 on T cells and surface marker of on cancer cells to mediate T cell activation and subsequent lysis of target expressing cancer cells
  - BCMA, GPRC5D, FcRH5
  - CD19, CD20, CD22



Engineered so that one end binds to cancer cell, the other end binds to T cell

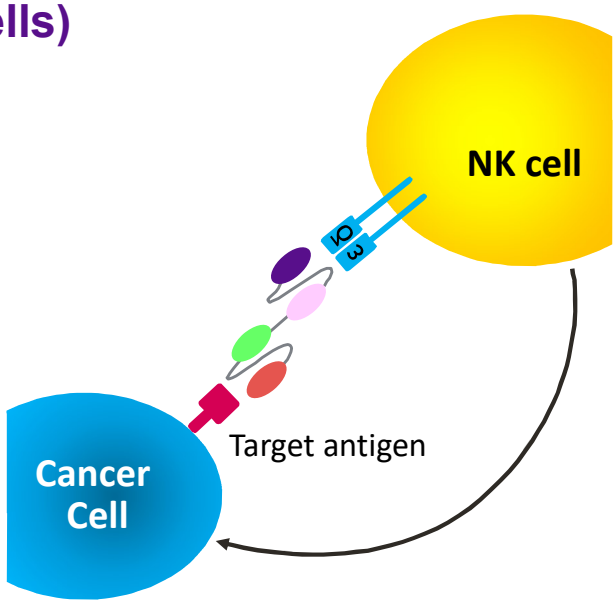
33

Bispecific Antibodies (NK cells)

Potential to overcome the limitations of immunosuppressive tumor microenvironment by redirecting NK cells to kill tumor target cells

Off the shelf

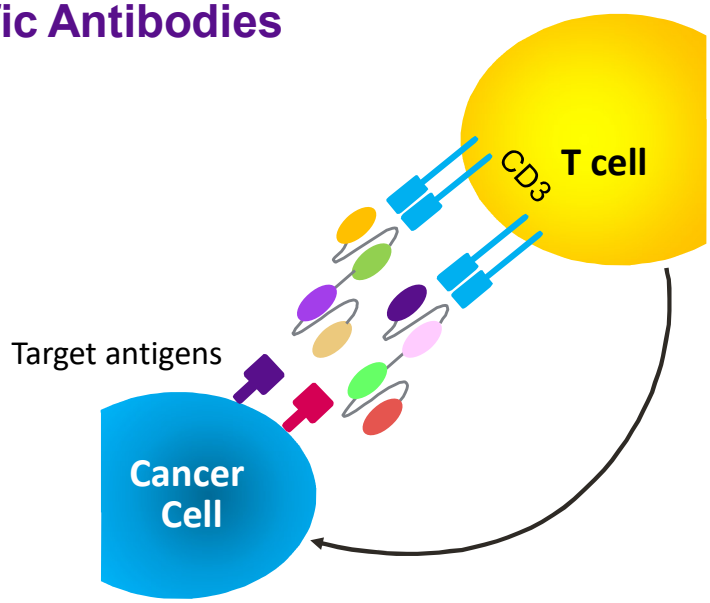
NK cell redirecting bispecific antibody that binds to NK surface cell protein and surface marker of on cancer cells to mediate NK cell activation and subsequent lysis of target expressing cancer cells



Engineered so that one end binds to cancer cell, the other end binds to NK cell

34

Trispecific Antibodies



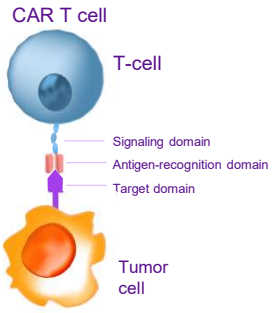
Engineered so that two end bind to cancer cell, the other end binds to T cell

35

CAR-T

a type of genetically engineered immune cell (specifically a T cell) that has been modified in the lab to recognize and attack cancer cells by expressing a special receptor called a chimeric antigen receptor (CAR) on its surface

Essentially, it's a patient's own T cell that has been reprogrammed to better fight cancer.

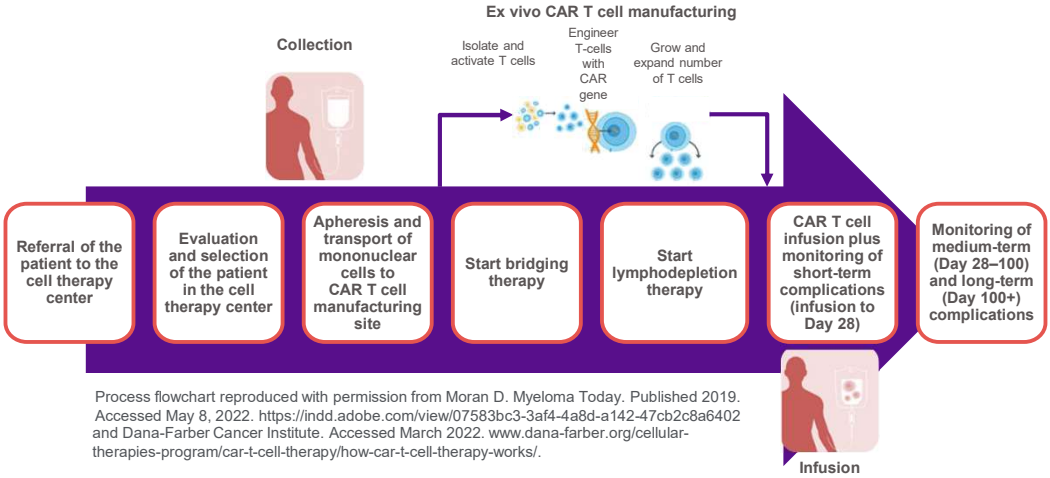


CAR-T

Genetically modified T cells that express a CAR targeted against a specific antigen, which upon binding initiates T-cell activation in a human leukocyte antigen–independent manner[1]

36

CAR T cell therapy process



Process flowchart reproduced with permission from Moran D. Myeloma Today. Published 2019. Accessed May 8, 2022. https://indd.adobe.com/view/07583bc3-3af4-4a8d-a142-47cb2c8a6402 and Dana-Farber Cancer Institute. Accessed March 2022. www.dana-farber.org/cellular-therapies-program/car-t-cell-therapy/how-car-t-cell-therapy-works/.

CAR, chimeric antigen receptor.

1. Moran D. The potential of CAR T-cell therapy and the myeloma patient journey. Myeloma Today. Published 2019. Accessed May 8, 2022. https://indd.adobe.com/view/07583bc3-3af4-4a8d-a142-47cb2c8a6402. 2. Raje N, et al. *N Engl J Med*. 2019;380(18):1726-1737. 3. Turtle CJ, et al. *Sci Transl Med*. 2016;8(355):355ra116. 4. Yakoub-Agha I, et al. *Haematologica*. 2020;105(2):297-316.

37

Clinical results for immune therapies

RESPONSES

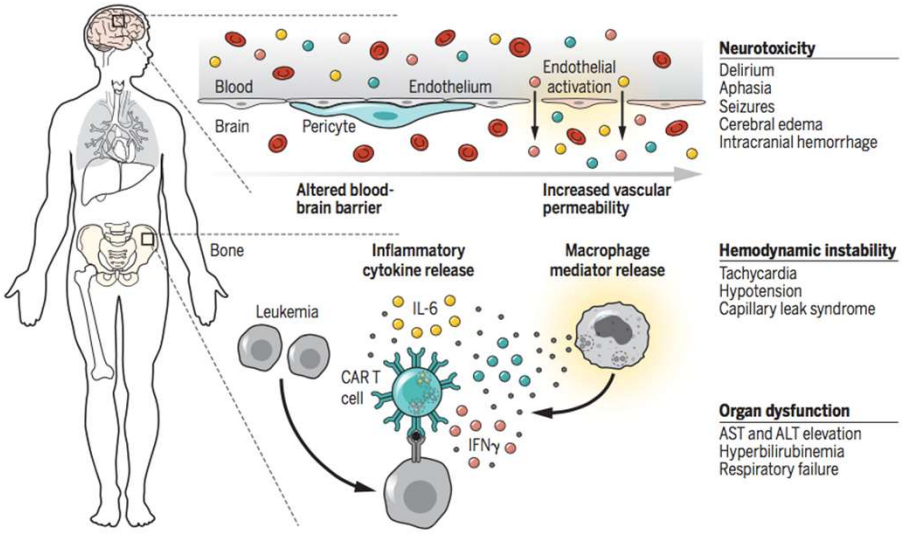
- Dramatic responses in patients who have received most available therapies
- 70% of patients respond, many with deep responses (complete responses)

SIDE EFFECTS

- Unique set of side effects
- CRS, cytokine release syndrome
- ICANS, immune effector cell-associated neurotoxicity syndrome
- Infections

38

Pathophysiology of CRS and ICANS

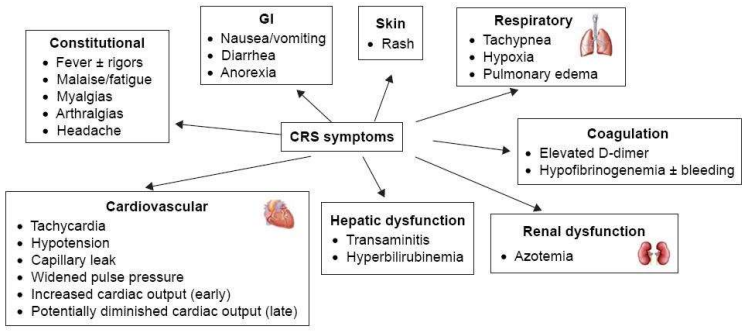


June CH, et al. *Science.* 2018;359 (6382):1361-1365. doi: 10.1126/science.aar6711

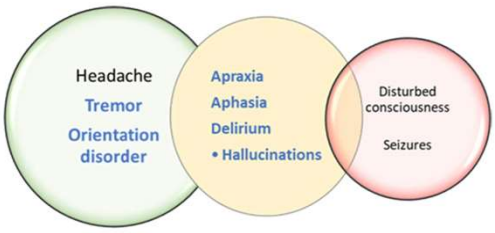
39

Unique Side Effects

CRS signs and symptoms[1]



ICANS signs and symptoms[2]



May occur in first 1 – 2 weeks. Require close monitoring

CRS, cytokine release syndrome; GI, gastrointestinal; ICANS, immune effector cell-associated neurotoxicity syndrome.
1. Riegler LL, et al. *Ther Clin Risk Manag.* 2019;15:323-335. 2. Möhn N, et al. *Neurol Res Pract.* 2022;4(1):1. doi:10.1186/s42466-021-00166-5

40

Conclusions

- Many different ways of killing cancer cells
- Majority of ways rely on finding a process or target that is different on the cancer cell compared to normal cells to selectively kill the cancer cells whilst doing as little damage as possible to the normal cells
- Clinical trials are ongoing and the future looks bright

41

THANK YOU

NYU Langone Health

42

ASK A QUESTION

NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

Ask a question by phone:

Press star (*) then the number 1 on your keypad.

Ask a question by web:

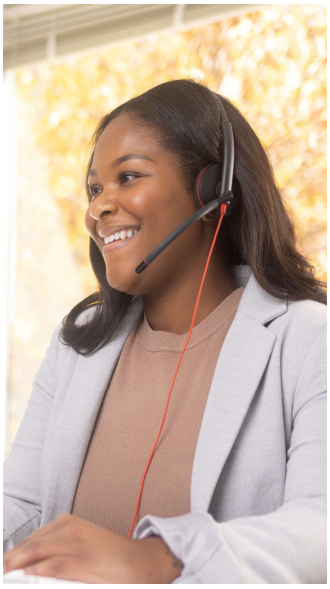
Click "Ask a question"
Type your question
Click "Submit"

Due to time constraints, we can only take one question per person. Once you've asked your question, the operator will transfer you back into the audience line.

LEUKEMIA & LYMPHOMA SOCIETY®

43

LLS EDUCATION & SUPPORT RESOURCES

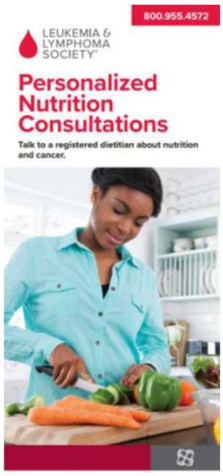


HOW TO CONTACT US:

To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:
www.LLS.org/InformationSpecialists

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
Email: www.LLS.org/ContactUs
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation

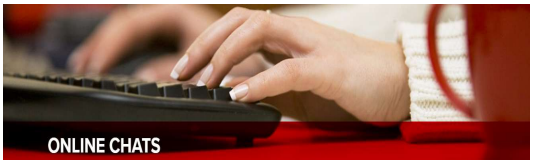


NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLSNutrition.org

LEUKEMIA & LYMPHOMA SOCIETY®

44

LLS EDUCATION & SUPPORT RESOURCES



Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit **www.LLS.org/Chat**

Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit **www.LLS.org/EducationVideos**

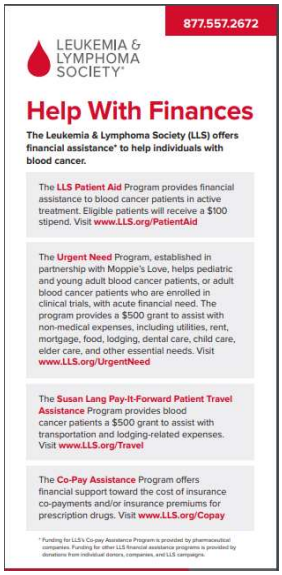
Patient Podcast

The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit **www.TheBloodline.org**

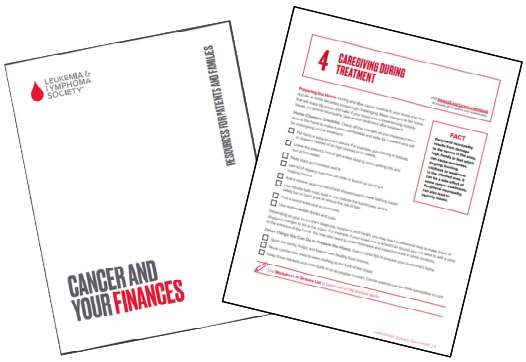
LEUKEMIA & LYMPHOMA SOCIETY®

45

LLS EDUCATION & SUPPORT RESOURCES



The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers: **www.LLS.org/Finances**



To order free materials: **www.LLS.org/Booklets**

LEUKEMIA & LYMPHOMA SOCIETY®

46


THANK YOU
PLEASE PROVIDE US WITH FEEDBACK:
LLS.ORG/NEWTHERAPIESEVAL
We have one goal: A world without blood cancers
LEUKEMIA & LYMPHOMA SOCIETY®

47