



ILLINOIS
CANCERCARE, P.C.

Specializing in Cancer and Blood Disorders

CANCER THERAPIES FACTS, FIGURES AND THE FUTURE



HOPE
WE

WE
HELP

WE
CARE

The Facts

- **1 in 3** people will be diagnosed by cancer in their lifetime.
- **10** million Americans are living with cancer today.
- Each day, more than **1,500** Americans lose their lives to cancer.
- This year alone:
 - **1.4** million Americans will be diagnosed with cancer.
 - **560,000** will lose their lives to this disease.
 - Cancer will cost our economy more than **\$400** Billion dollars.

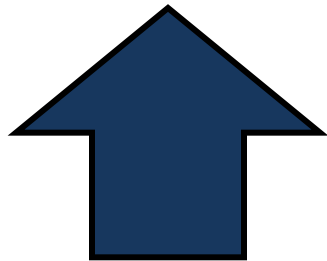
HOPE
WE

WE
HELP

WE
CARE

The Trends

- The 5-year relative survival rate for all cancers diagnosed between 1996 and 2003 is 66%, up from 50% in 1975-1977.
- The improvement in survival reflects progress in diagnosing certain cancers at an earlier stage and improvements in treatment.



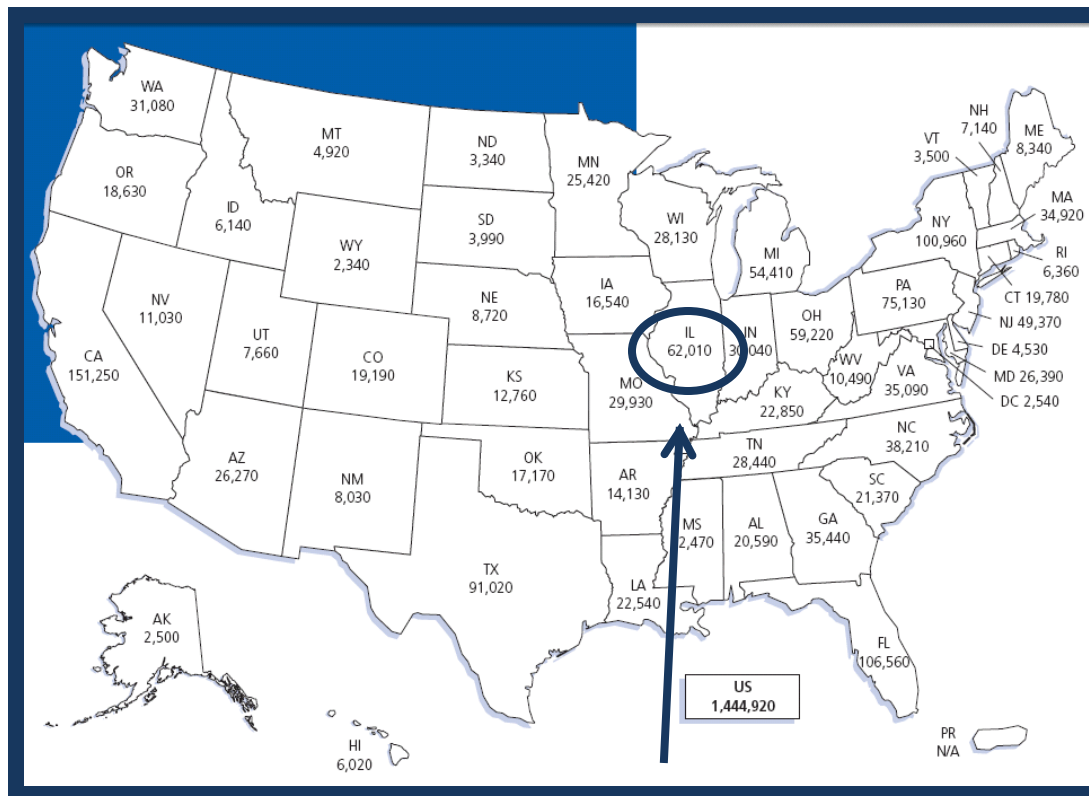
Survival rates are on the rise, thanks to clinical cancer research trials

HOPE
WE

WE
HELP

WE
CARE

Cancer Incidence by State



Illinois 6th highest in the nation

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

1940 to 1970

HOPE

WE

WE

HELP

WE
CARE

Cancer Drug Development

- Ft. Detrick, Maryland 1940
- Biological Division of the Army
- Animal studies with dogs receiving Nitrogen Mustard
- Cause of death- topical, inhaled, and intravenous
- First patient treated



ILLINOIS
CANCERCARE, INC.

Specializing in Cancer and Blood Disorders

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

- Early years – mechanisms not known primitive understanding of cell biology
- Melphalan or phenylalanine mustard was thought to be a potential building block in the formation of melanin and was first tried in melanomas.
- Amethopterin
- Actinomycin-D
- 5-fluorouracil

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

1970 to 2000

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

- Ames assay
- National Cancer Institution cell culture panel
- Tumor models
- Small animals
- Large animals
- Man

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

- Two types of Phase-I studies
- Dose escalation per group
- Dose escalation in an individual
- Looking for “ Maximum Dose”
- Starting dose one level below the max dose or “maximum tolerated dose” also called the “MTD”

Cancer Drug Development

- Phase-II studies used the MTD as a single agent in various cell types i.e. breast cancer, colon cancer, lung cancer, etc.
- Usual study was 0 of 15 responses and the study was closed, 1 of 15 and the study would be held open until 34 patients were entered.

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

- A drug could be given in a different schedule, e.g. day one every three weeks, weekly, Monday/Wednesday/Friday
- Route could be changed (i.e. IV, PO subcutaneous)
- Given as bolus or timed infusions

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

- Phase-III studies test a new drug(s) against “best” therapy.
- Chop vs. R-Chop

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

2000 to Present

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

- Dr. Drucker changed the way we think about cancer.
- CML is a disease with one major pathway that is abnormal.
- CML has a 9-22 translocation
- This causes some of the DNA on 9 to be fused with DNA on 22 to produce a fusion molecule called BCR/ABL.
- BCR/ABL is stuck in the on position. It is folded in a way that allows a tyrosine kinase to fit and so doing fuels the protein. Drucker looked at this site and developed an inhibitor to fit in this site and by robbing it of energy shut off this signal.



ILLINOIS
CANCERCARE, PC
Specializing in Cancer and Blood Disorders

HOPE
WE

WE
HELP

WE
CARE

Cancer Drug Development

- We now know that cancers have key pathways that are regulated up or down and this gives the cancer its special characteristics.
- We are now looking for the inhibitors of these pathways.

HOPE

WE

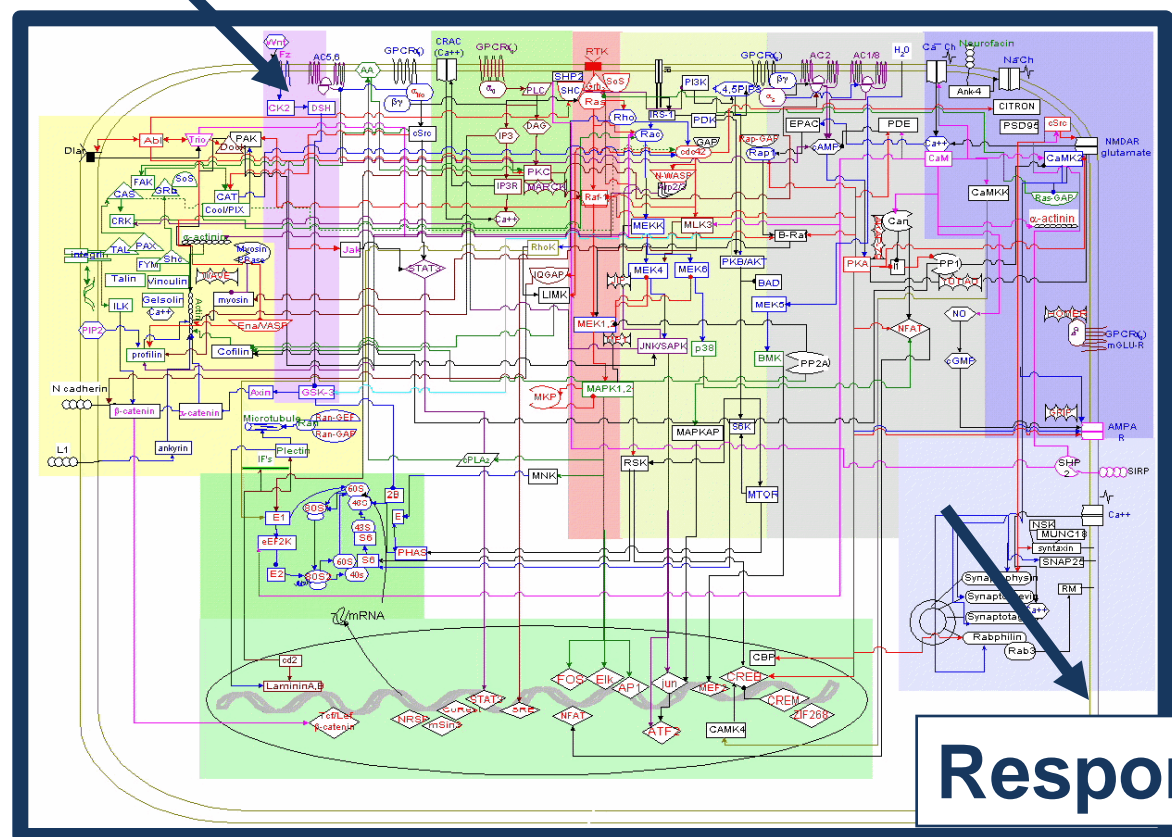
WE

HELP

WE

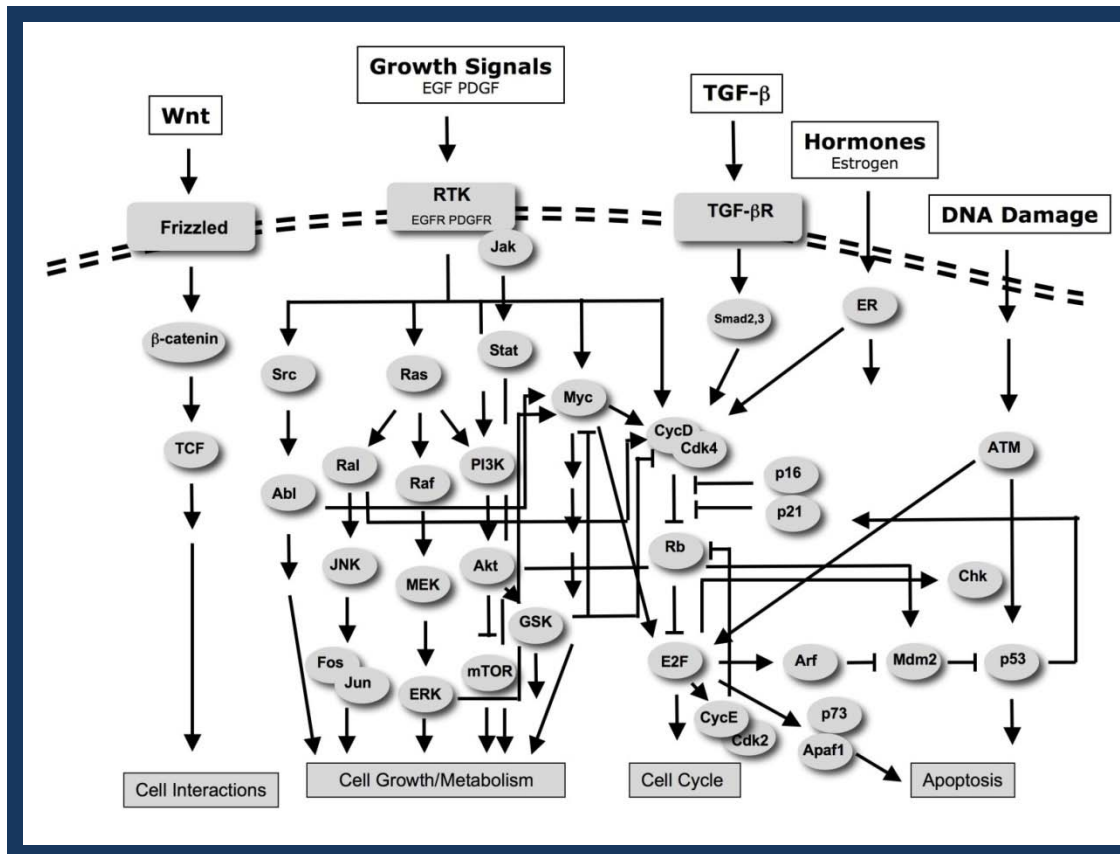
CARE

Sense (input)



Respond (output)

Surrogate Signatures - A Link with Pathway Activation

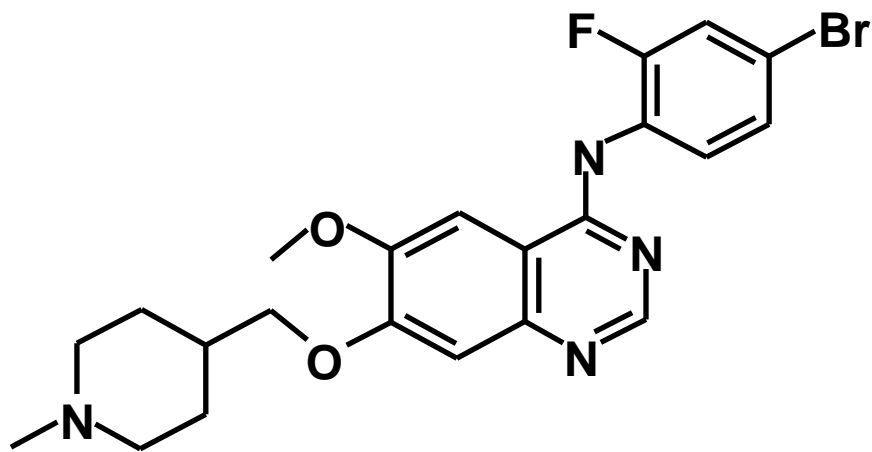


HOPE
WE

WE
HELP

WE
CARE

Vandetanib Selectively Targets VEGFR, EGFR, and RET Tyrosine Kinase Activity



Kinase	IC₅₀ (μM)
VEGFR-2 (KDR)	0.04
VEGFR-3 (Flt-4)	0.11
RET	0.13
EGFR	0.50
VEGFR-1 (Flt-1), PDGFR-β, Tie-2, FGFR1	>1
MEK, CDK2	>10
c-kit, erbB2, FAK, PDK1	>20
AKT	>100
IGF-1R	>200



HOPE
WE

WE
HELP

WE
CARE

Agents Targeting the VEGF Pathway

