
iSBTc Mini-symposium: Biologics Effects of Targeted Therapeutics

Michael B. Atkins, MD

Beth Israel Deaconess Medical Center

Louis Weiner, M.D.

Fox Chase Cancer Center

Evolution of Cancer Therapy

- ◆ 1800s- Surgery
- ◆ 1920- Radiation Therapy
- ◆ 1970s -Cytotoxic chemotherapy
- ◆ 1985 - Immunotherapy

NOVEMBER 25, 1985

FORTUNE

CANCER BREAKTHROUGH

SPECIAL REPORT
GORBACHEV VS.
THE SOVIET ECONOMY

INTERLEUKIN-2, Human
(des-alanyl, serine-125)

Lyophilized Preparation
— For single use
with sterile Water for

INANT INTERLEUKIN-2, Human
(des-alanyl, serine-125)

Lyophilized Preparation
2-8°C — For single use
with sterile Water for

Cetus Corp.'s
tumor-zapping
Interleukin-2

COMPACT DISCS: A SONIC BOOM

Newsweek

December 24, 1992 \$5.95

CANCER AND INTERLEUKIN-2

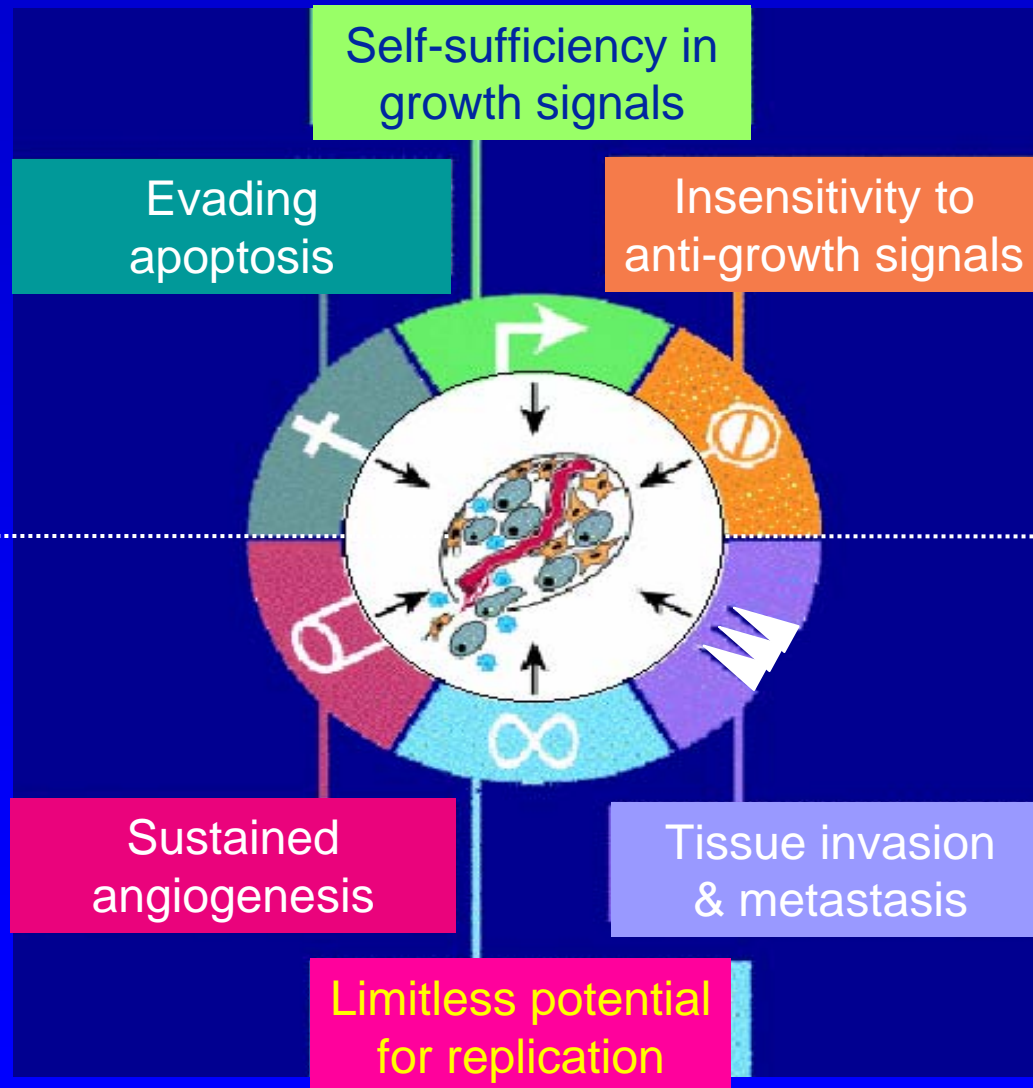
The Search for a Cure

Dr. Steven Rosenberg
at the National Cancer Institute

Evolution of Cancer Therapy

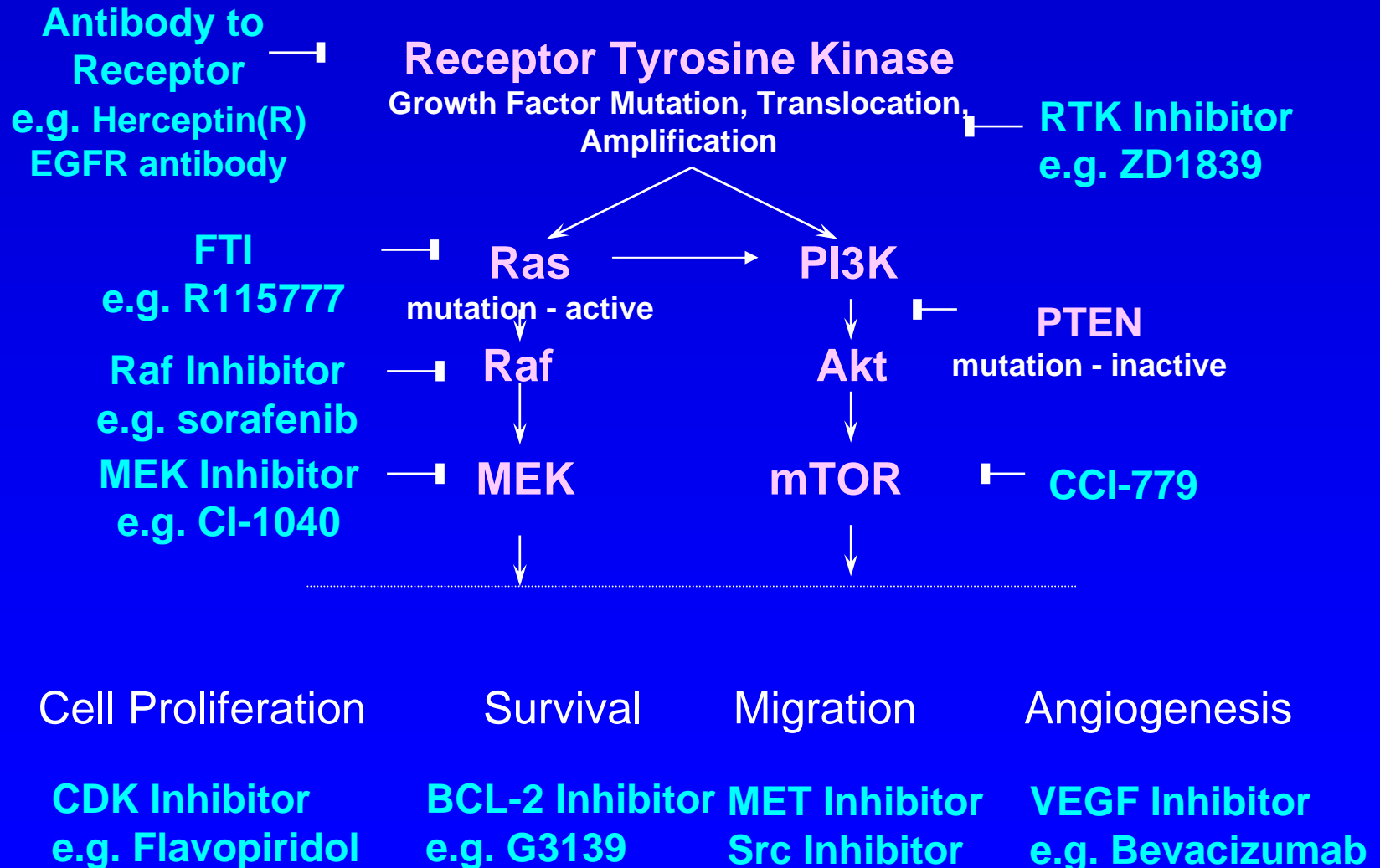
- ◆ 1880- Surgery
- ◆ 1920- Radiation Therapy
- ◆ 1970s -Cytotoxic chemotherapy
- ◆ 1985 - Immunotherapy
- ◆ 2000 – Targeted Therapy

Essential Alterations in Cell Physiology in Malignancy



*Hanahan & Weinberg,
Cell 100:57 (2000)*

Targets and Tools



Targeted Therapy: Promise and Progress

◆ Antibodies

- trastuzumab, bevacizumab, rituximab, cetuximab

◆ Small molecules

- C-Kit- imatinib
- VEGFR: sunitinib, sorafenib
- EGFR: gefitinib, erlotinib
- mTOR: Temsirolimus

◆ Demethylating agents

- decitabene

Having a target is good



"Bummer of a birthmark, Hal"

Targeted Therapy: Issues (1)

- ◆ Pathways are relevant to more than just tumor cells
 - Endothelium
 - Pericytes
 - Immune cells- DCs, Tcells, Tregs
- ◆ Small molecule RTK inhibitors are less selective than originally anticipated
 - Sorafenib, sunitinib
 - Herceptin- VEGF
- ◆ Blocking some targets may produce pro-survival effects
 - GSK3 β activation
 - Compensatory increases in upstream molecules -
 - HIF related proteins with VEGFR inhibition
 - AKT with mTOR blockade
- ◆ Cell death may trigger distinct biologic pathways

Targeted Therapy: Issues

Off target biologic effects of targeted therapies may influence the tolerability, activity duration of benefit, and ability to combine these agents

Targeted Therapy: Issues (2)

- ◆ Treatments are largely non-curative
- ◆ Durable complete responses will likely require tumor specific immune activation
- ◆ Push for combination targeted therapy and biologic therapy

Mini-Symposium: Goals

- ◆ Describe the current knowledge regarding various off-target effects of current therapies
- ◆ Identify most relevant issues and current gaps in knowledge base
- ◆ Discuss optimal means of obtaining necessary information
- ◆ Use above information to -
 - Inform and influence basic science efforts and discussions
 - Rationally design combination treatment regimens
 - Optimally design most relevant correlative studies in the context of current and future treatments



Save the Date

21st Annual Meeting

October 26-29, 2006

Hyatt Regency Century Plaza
Century City, Los Angeles, California

International Society for Biological Therapy of Cancer





22ND ANNUAL MEETING

NOVEMBER 1-4, 2007 • BOSTON, MASSACHUSETTS

Seaport World Trade Center

iSBTc
Save
the Date

www.isbtc.org

INTERNATIONAL SOCIETY FOR BIOLOGICAL THERAPY OF CANCER