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Drugs, Diagnostics & Delivery

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Cancer Treatment: Diagnosis & Clinical Trials

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School of Cancer Studies
University of Birmingham

What Is Cancer?

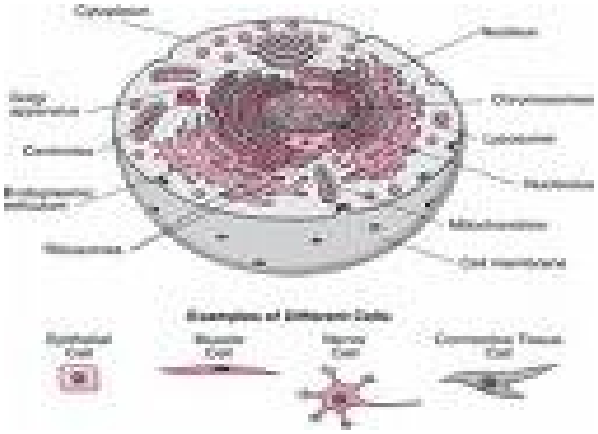
Cancer is a disease of cells

The DNA of cells is damaged

Inherited Predisposition

Environmental

Cells proliferate too fast or don't die when they should



Too many cells 'a tumour'

Benign

Malignant tumours (cancer) kill because they can spread

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Into nearby normal tissues

INVASION

Around the body

METASTASIS

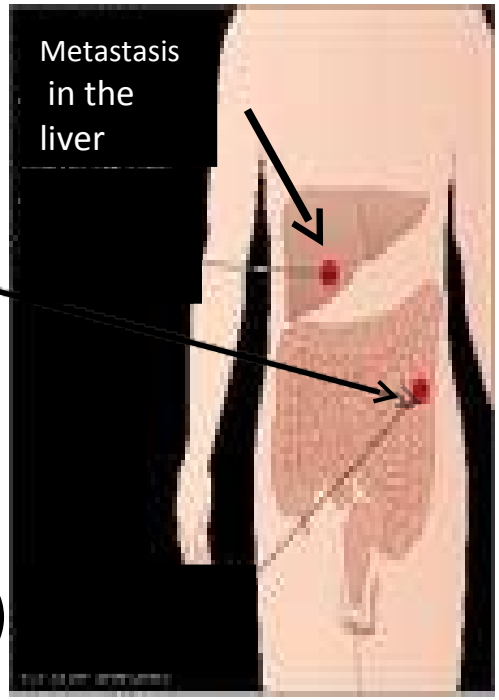
Naming of Cancers

Cancers are named after the ***primary*** site

i.e. the organ in which the cancer starts

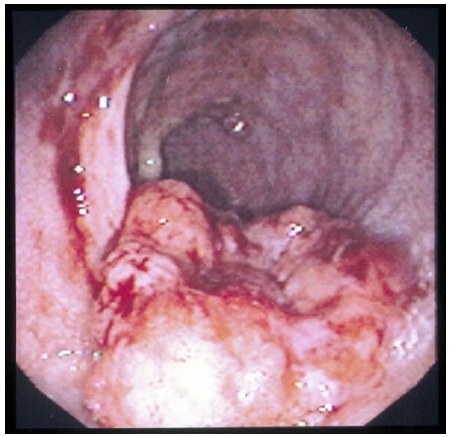
The organ to which the cancer spreads

is known as the ***secondary*** site (a ‘metastasis’)



Examples Of Cancer Metastasis

Curable → **Incurable**



Cancer of the bowel

Primary

Secondary (metastases)

Cancer of the bone

Cancer –The Fundamental Problem

We are very good at treating/curing cancer when it is small/early and has not spread

We are much less adept at treating cancer once it has spread – 'metastasised' - & is at an advanced stage

What's in the cancer treatment tool box?

Tools for Cancer Treatment

The Aim

For primary disease

- Surgery
- Radiotherapy

} Cure

For metastatic disease

- Drugs (Chemotherapy)

Cure or prolongation of survival

When cure/survival extension is not an option

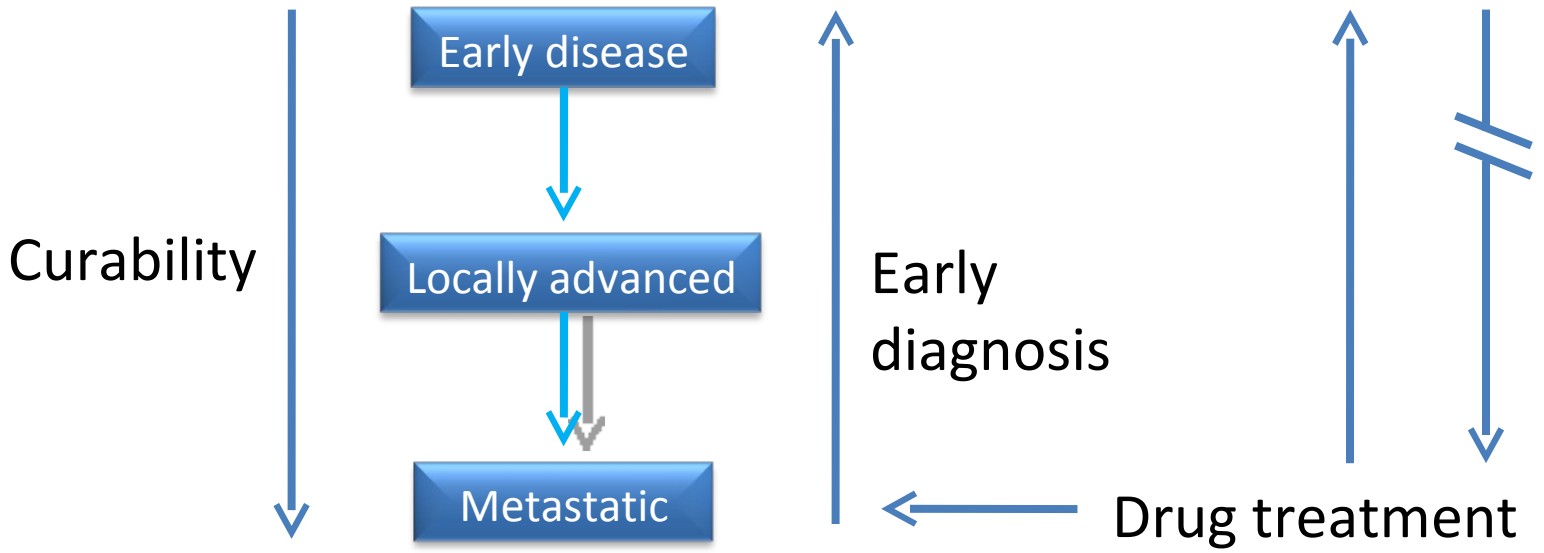
- Palliation

Control of Symptoms

What other cancer control strategies do we have and how are drugs used?

Other Strategies For Cancer Control & The Role Of Drugs

Prevent it starting in the first place!



What kind of drugs do we have to implement this strategy?

Drug Treatment of Advanced Cancer

20th Century Approach To Treatment
Cytotoxic drugs

21st Century Approach to Treatment
Targeted drugs

Not rationally designed
Often discovered by serendipity or 'fishing'
Non-specific - hit rapidly dividing cells
Renowned for nasty side effects
Cause intellectual indigestion

BUT

Cheap
Can cure some cancers, even without knowing how they work

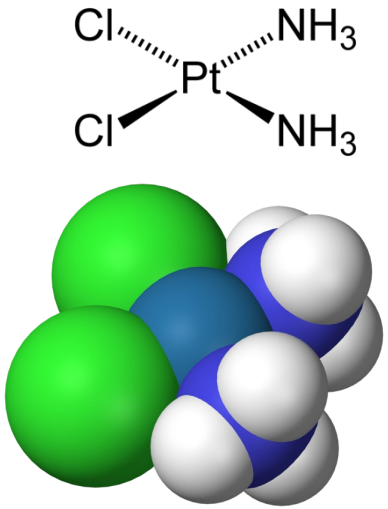
Rationally designed
Target relevant biochemical pathways
Intellectually satisfying
Less side-effects are expected

BUT

Their modest benefit for great expense poses a 'NICE' problem

Cisplatin - The Most Widely Used Cytotoxic Drug

Serendipity & Inspiration & Perspiration



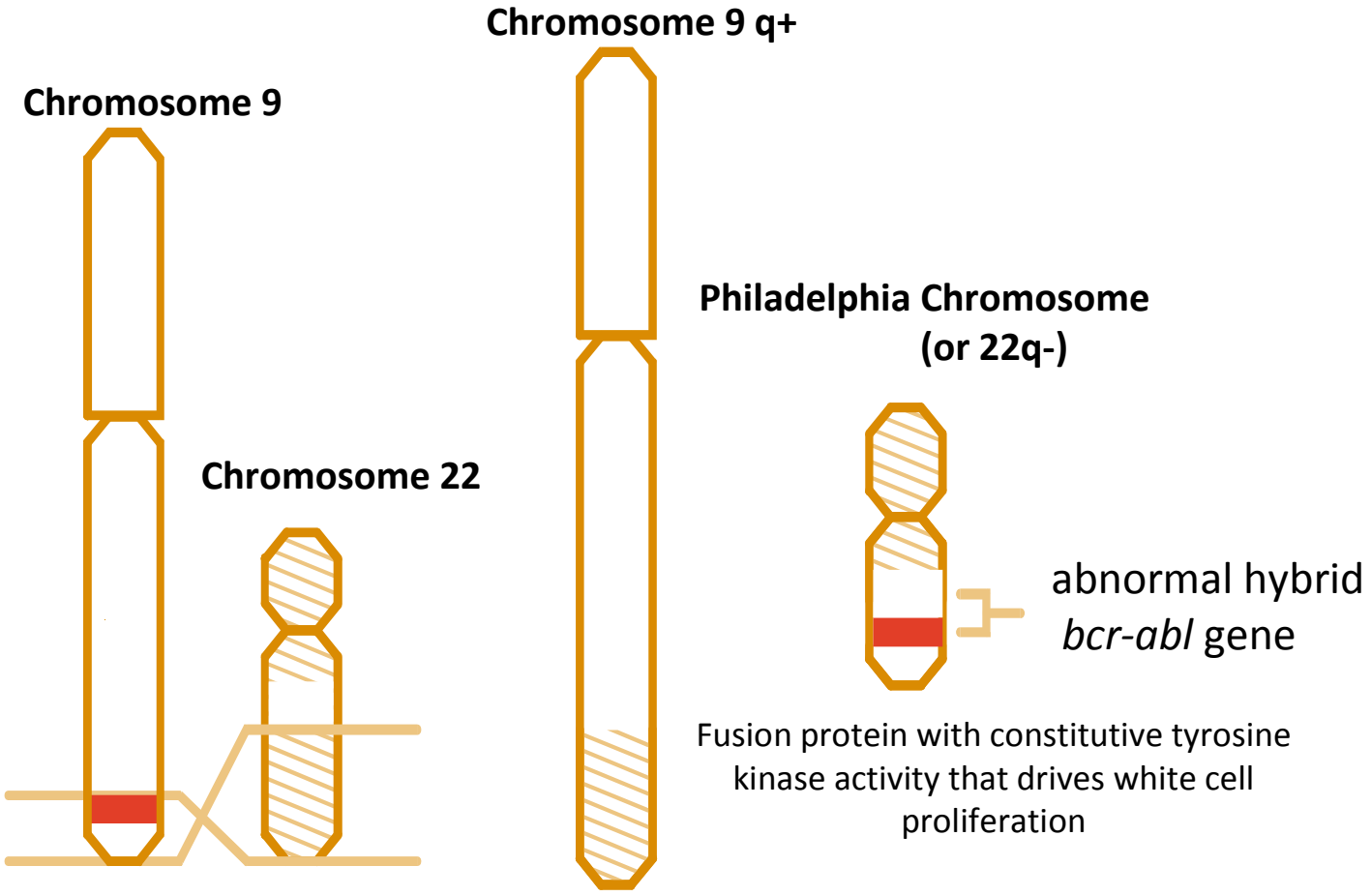
Researchers found that an electric current inhibited growth of bacterial cell division

Would it inhibit growth in mammalian cells – Yes!, But why?..

Electrolysis products from the platinum electrodes! And that it could cure cancers in animal models

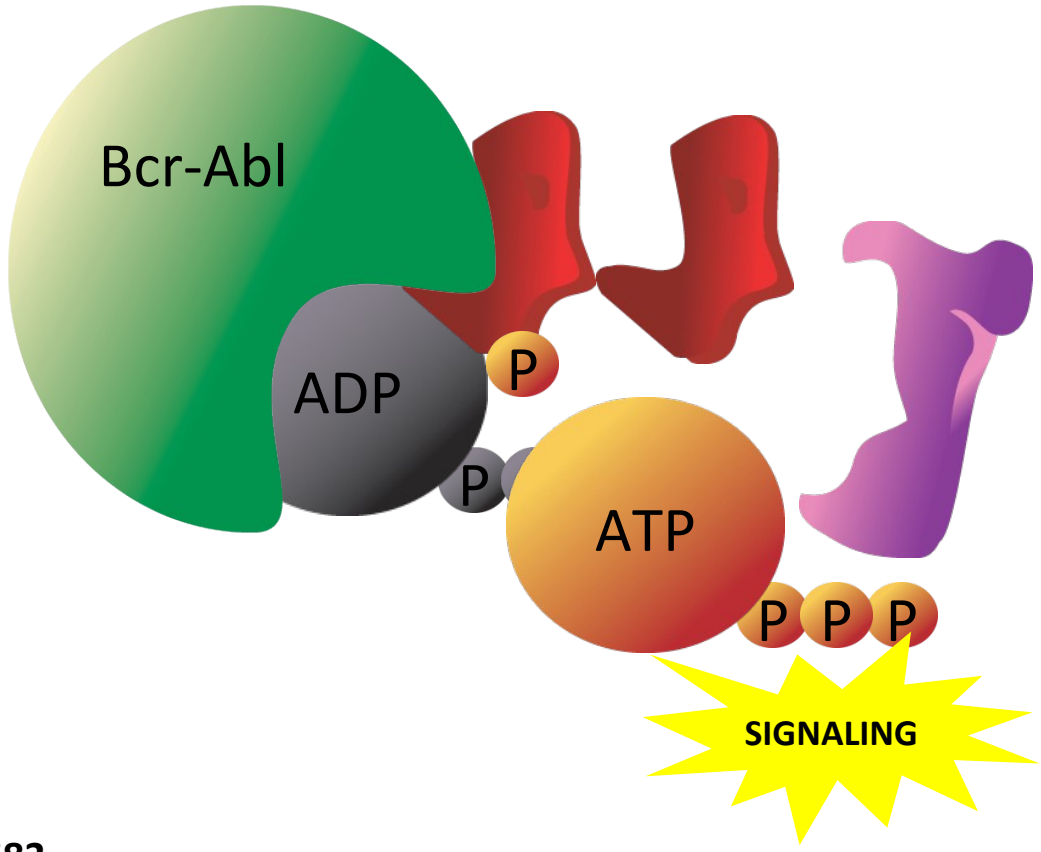
Barnett Rosenberg, Loretta van Camp, Thomas Krigas “Inhibition of Cell Division in Escherichia coli by Electrolysis Products from a Platinum Electrode” Nature 1965, Vol 205, page 698

Imatinib & Chronic Myeloid Leukaemia
The Appliance Of Science



Normal Bcr-Abl Signaling

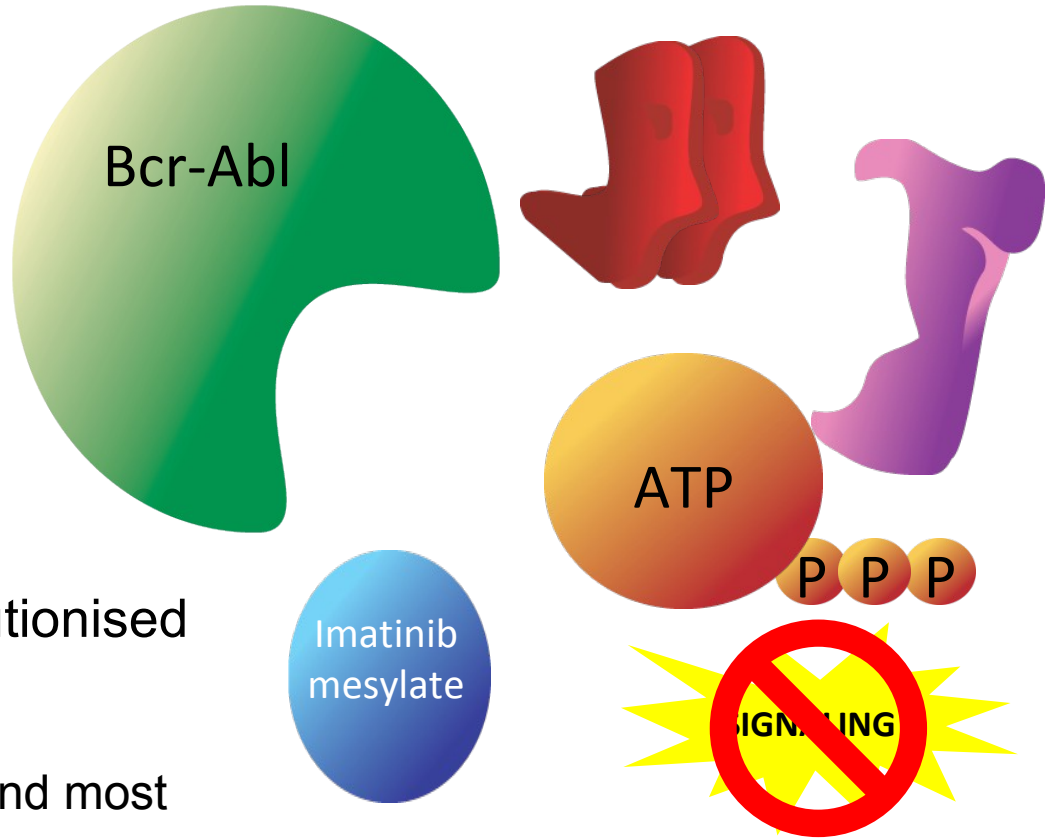
Once activated by phosphorylation, the signaling that results in the leukemia is initiated



Savage and Antman. *N Engl J Med.* 2002;346:683
Scheijen and Griffin. *Oncogene.* 2002;21:3314.

Imatinib, In Theory And In Practice, Treats The Leukaemia

- Imatinib occupies the ATP binding pocket of the Abl kinase domain
- prevents substrate phosphorylation and signaling
- And the treatment of Chronic Leukaemia is revolutionised



But most cancers aren't so simple, and most targeted drugs aren't so effective...!

Savage and Antman. *N Engl J Med.* 2002;346:683.

More Typical Examples Of Targeted Drugs

Both subject of a negative assessment by NICE, on grounds of limited cost-effectiveness

Avastin* (Bevacizumab) *for advanced colon cancer

When added to conventional cytotoxic therapy improved survival from 15 to 20 months

Cost- around £25,000 per patient

Nexavar (Sorafenib) for Liver cancer

First agent to show benefit in advanced disease.... from about 8 to 11 months

Cost – around £25, 000

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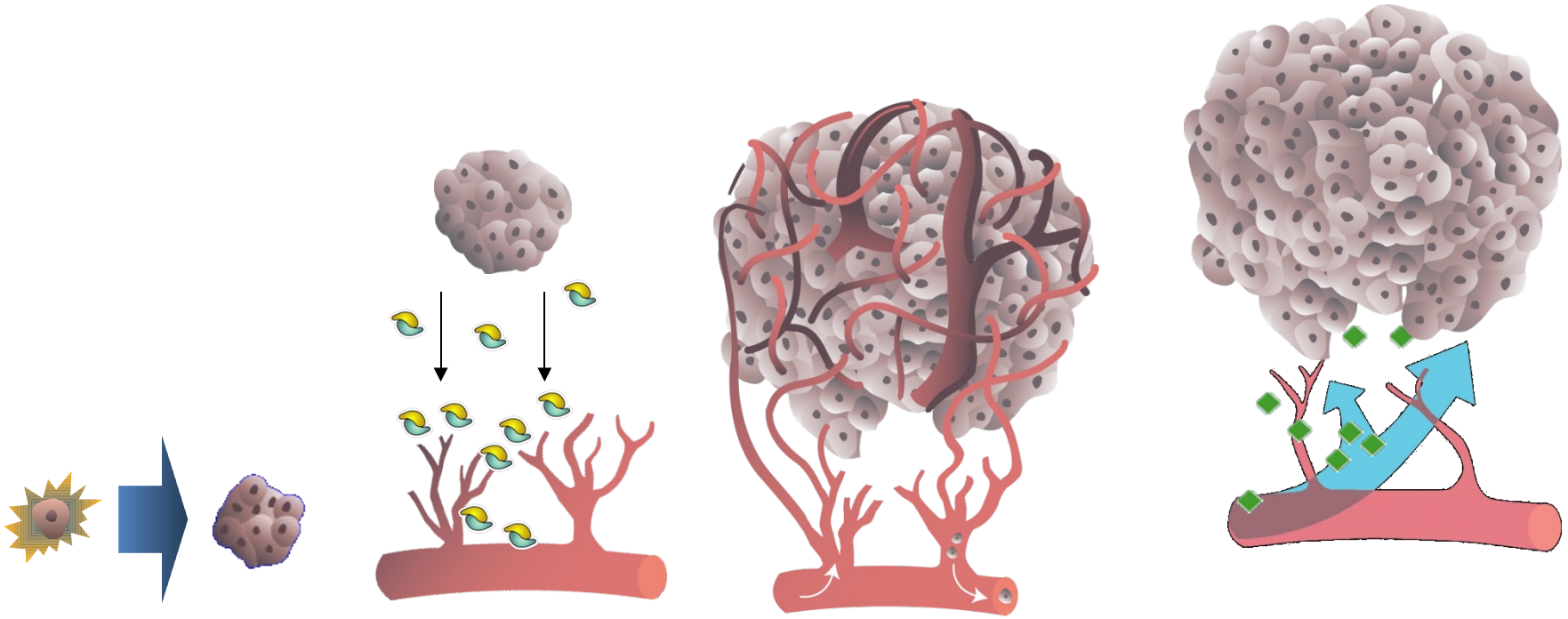
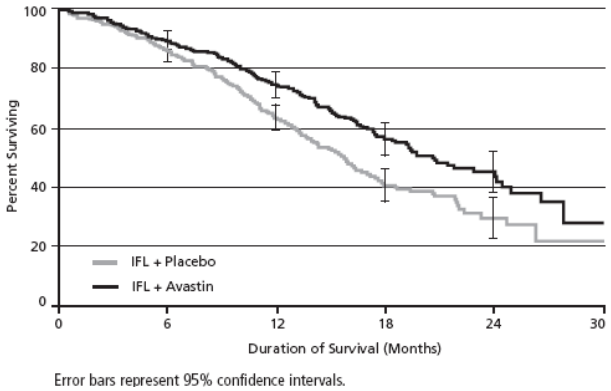
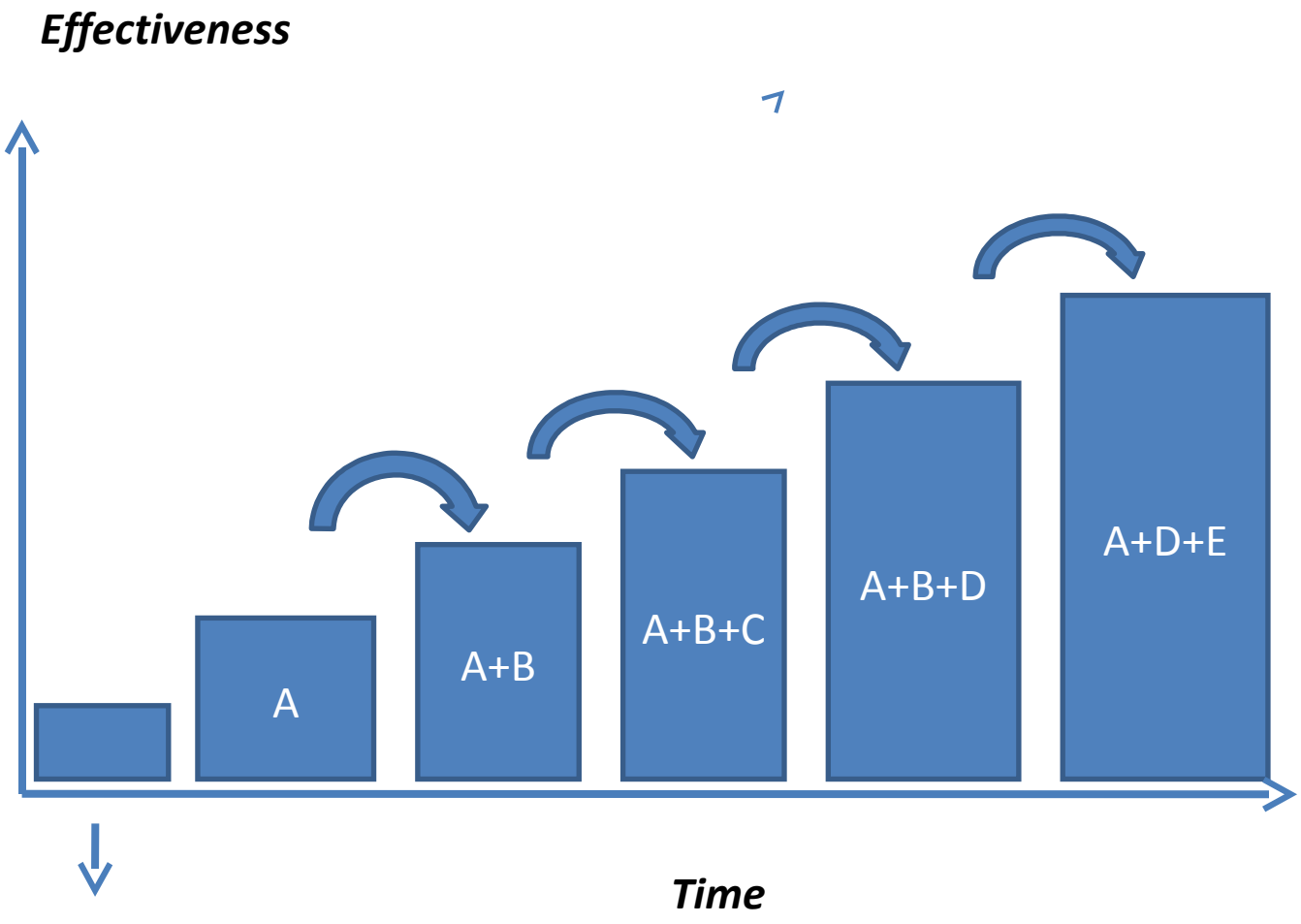
Avastin (Bevacizumab) For Colon Cancer



Cancers need their own blood supply
Inhibition of blood vessels is a major therapeutic area
Avastin was designed to do this &
Increases survival from 15 to 20 months



Trajectory Of Cancer Treatment Progress is Incremental

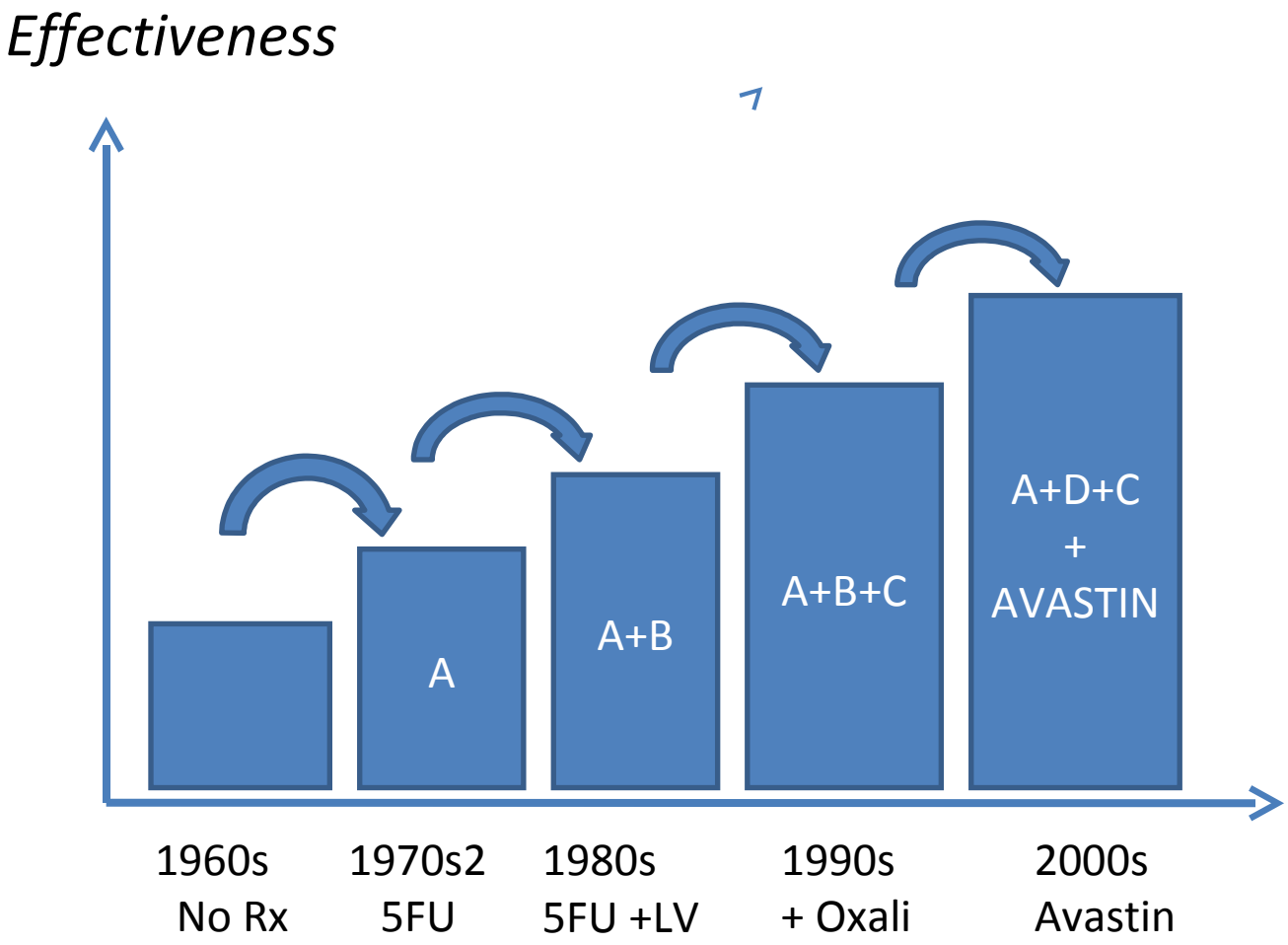


Benefit from 'A' maybe trivial

Benefit from A+D+E is valuable

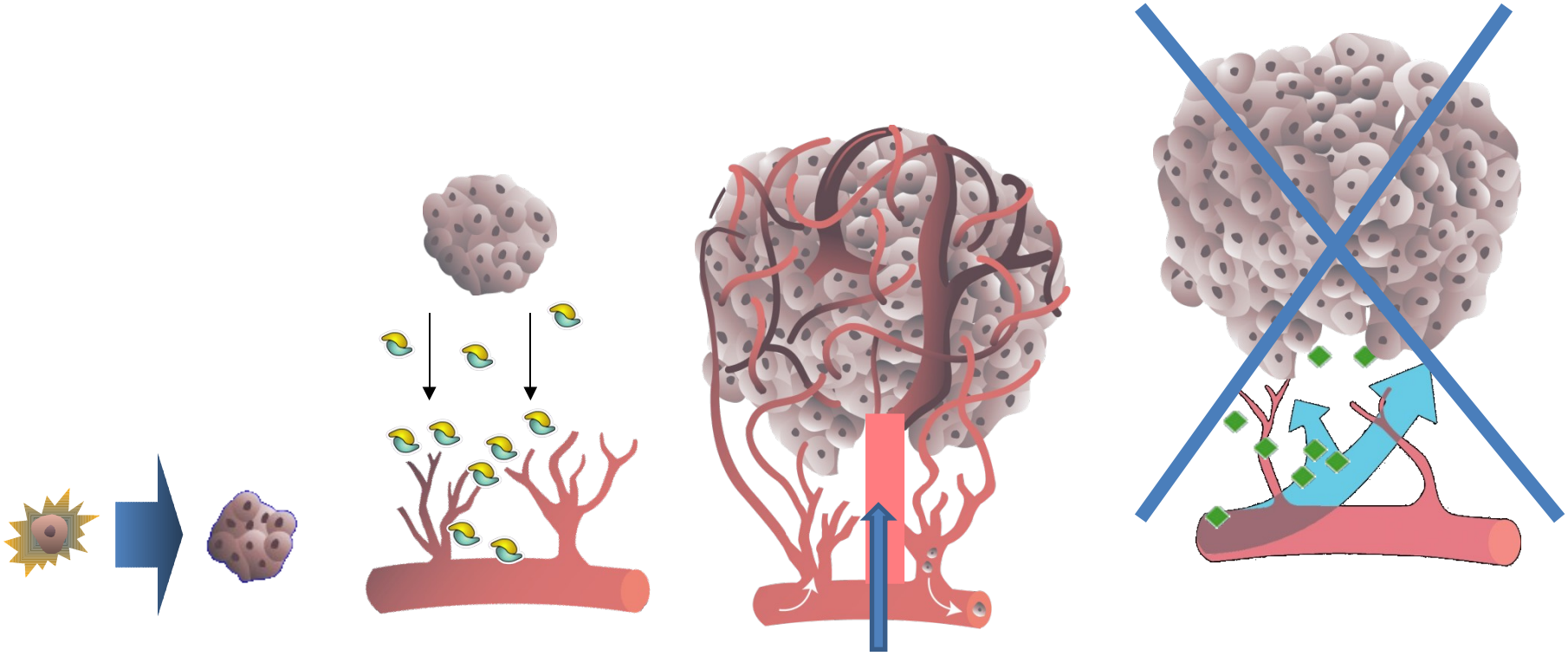
But you can't get to A +D+E without going through A

Trajectory Of Cancer Treatment Progress In Advanced Colorectal Cancer



Each step is small, but over 50 years we've gone from 3 months survival to nearly 2 years

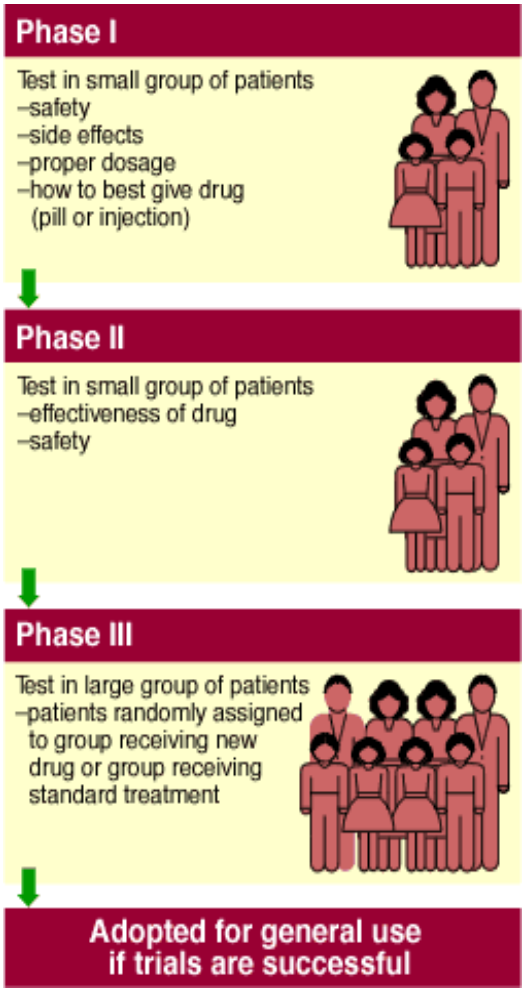
Avastin For Colon Cancer



Stabilises chaotic cancer related blood vessels

improves access of conventional cytotoxic agents

The Clinical Trial Process



Is it safe?

Yes, but more side -effects than expected

Does it do 'what is says on the tin' Usually, shrink the tumour

No, it did not shrink tumours

By shrinking the tumour does it make people live longer, than current best therapy

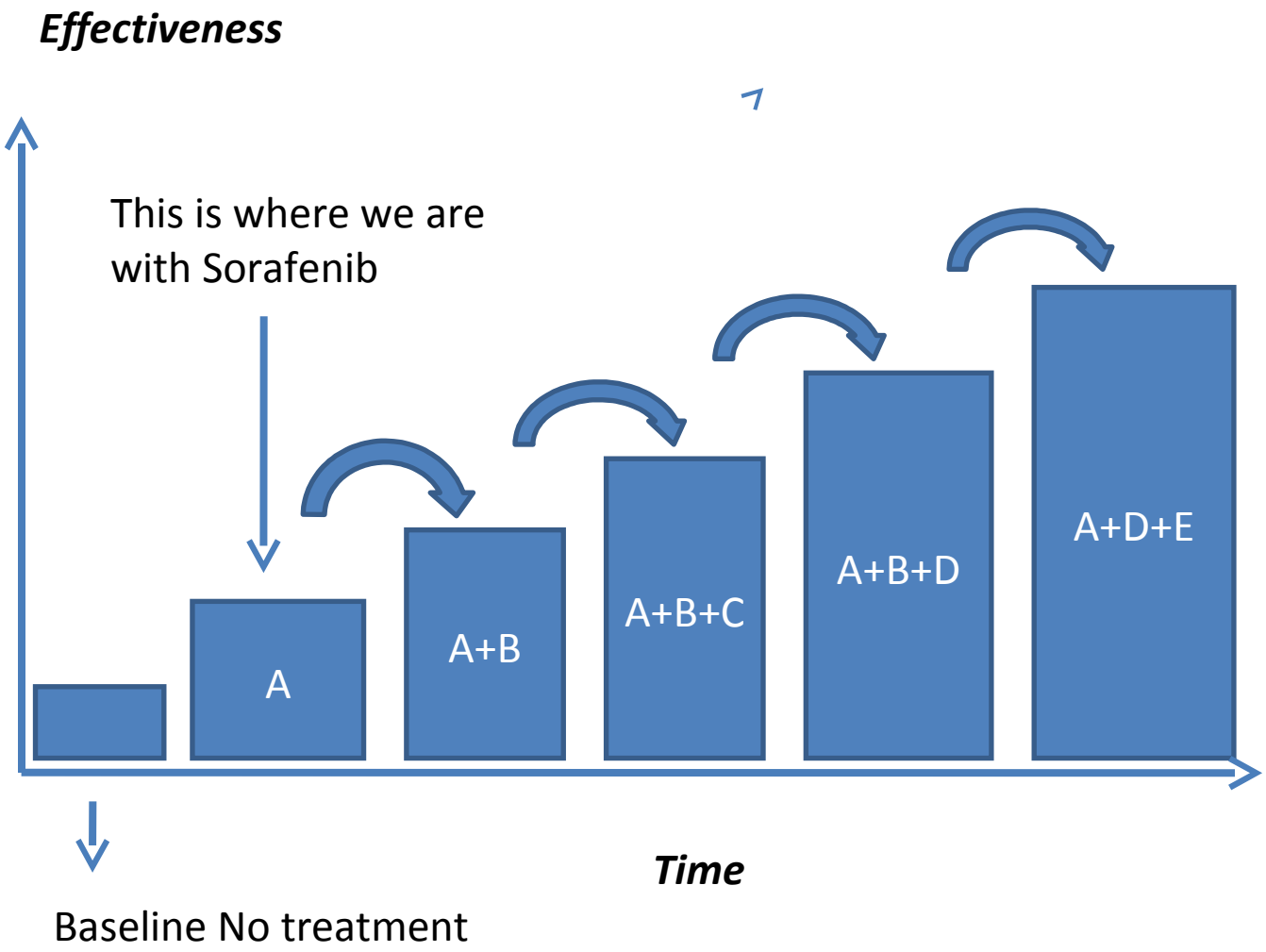
Yes, people taking the drug live longer

The Sorafenib pathway

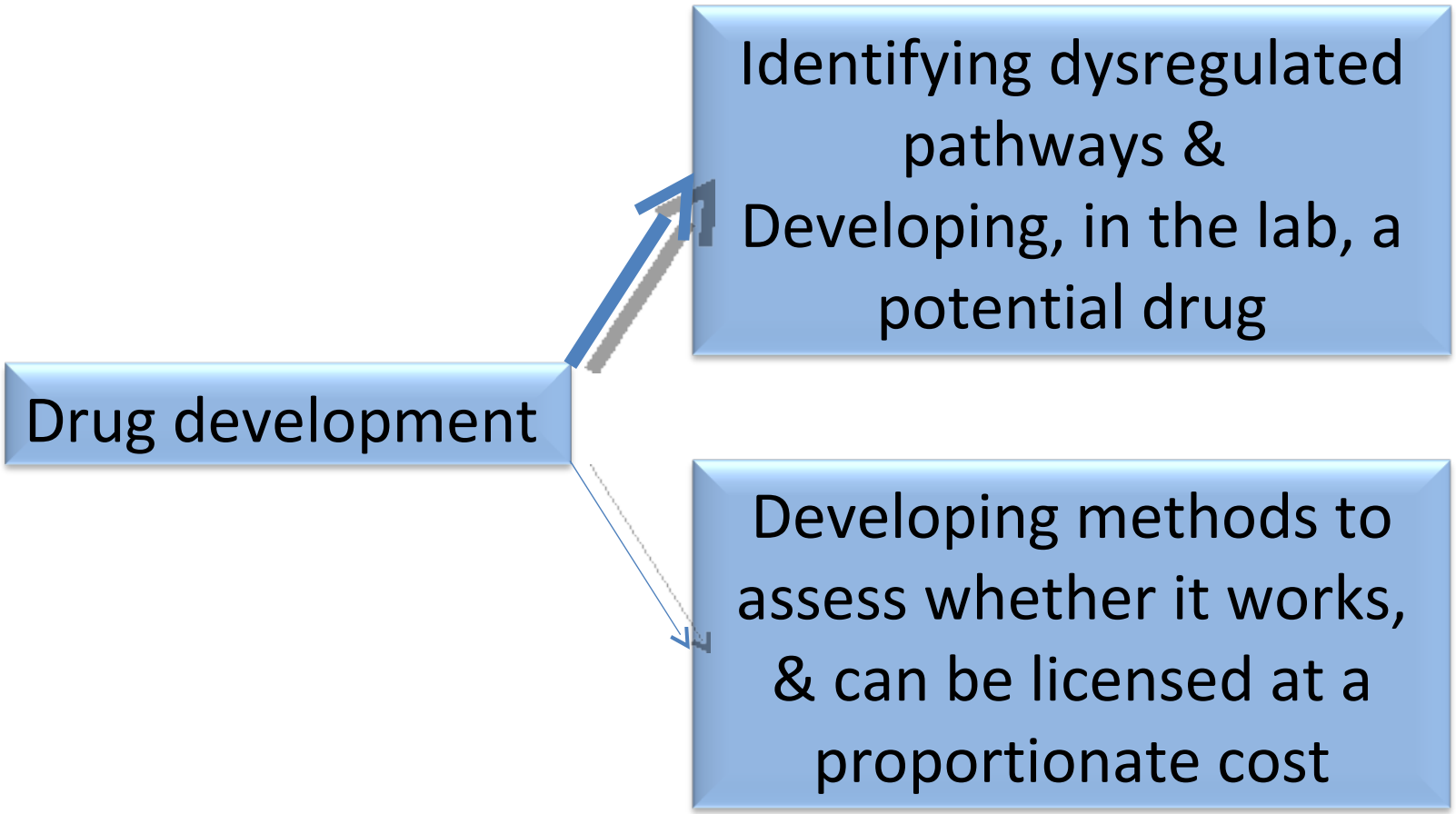
$100M

So we don't know the best signal to move, at a cost of millions of pounds, to phase III

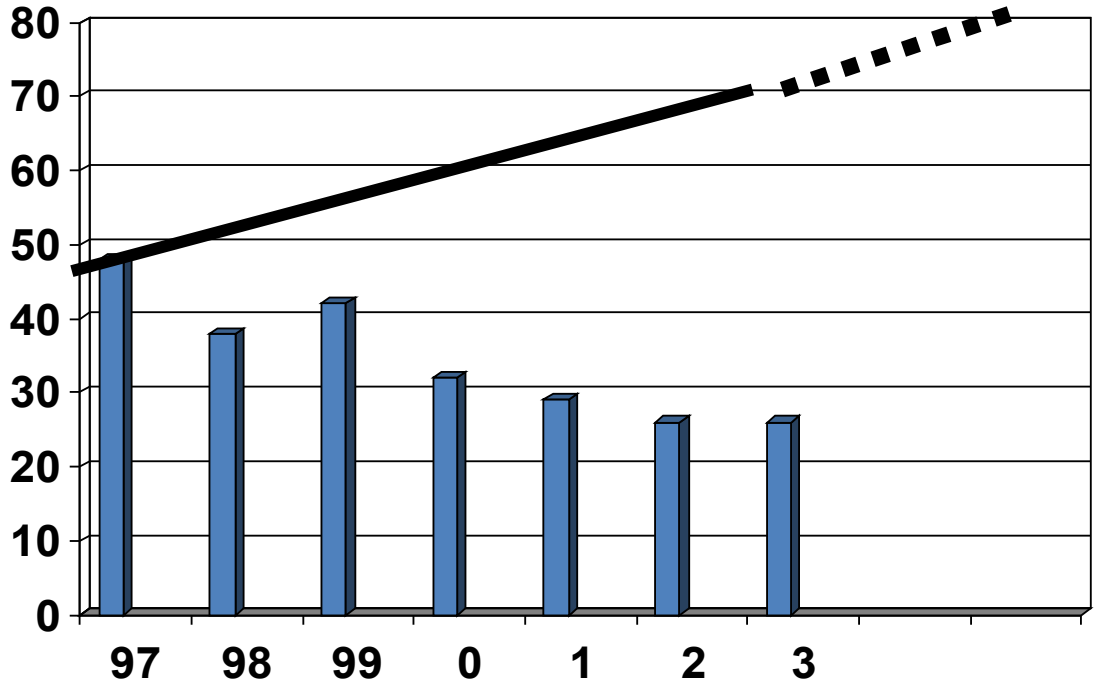
Trajectory Of Cancer Treatment
Progress is Incremental



It’s Not Just About Making A Drug!



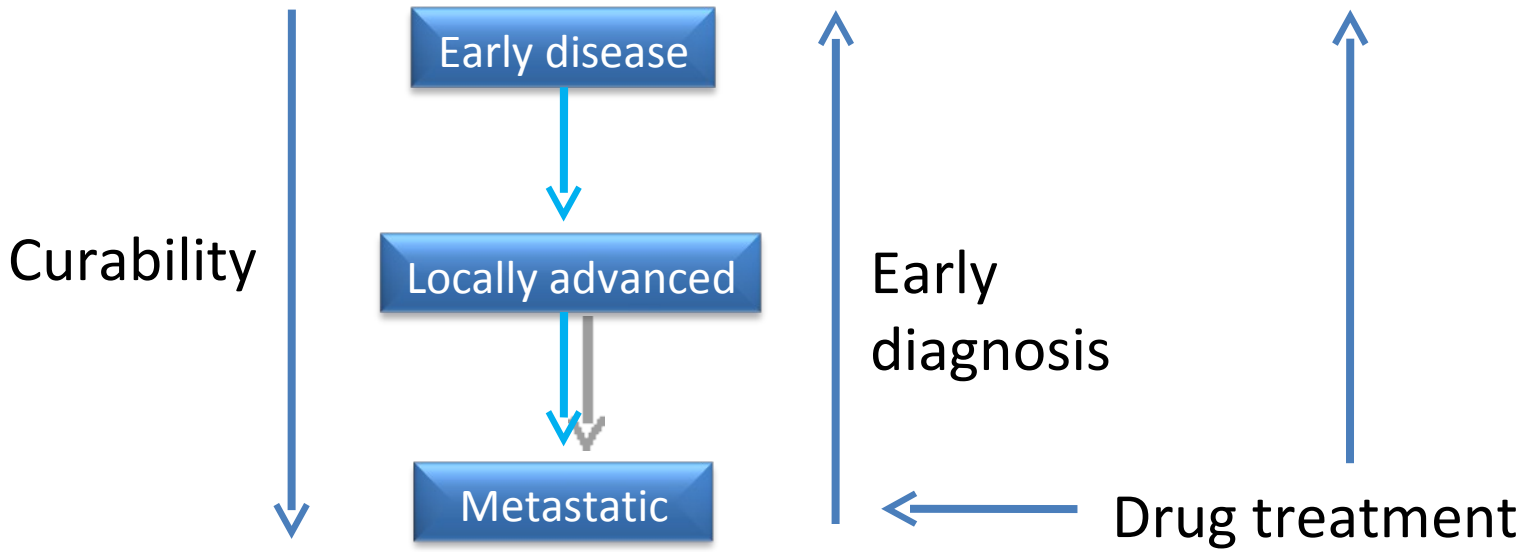
Spending More – Getting Less
Looking Into The Crocodile's Mouth



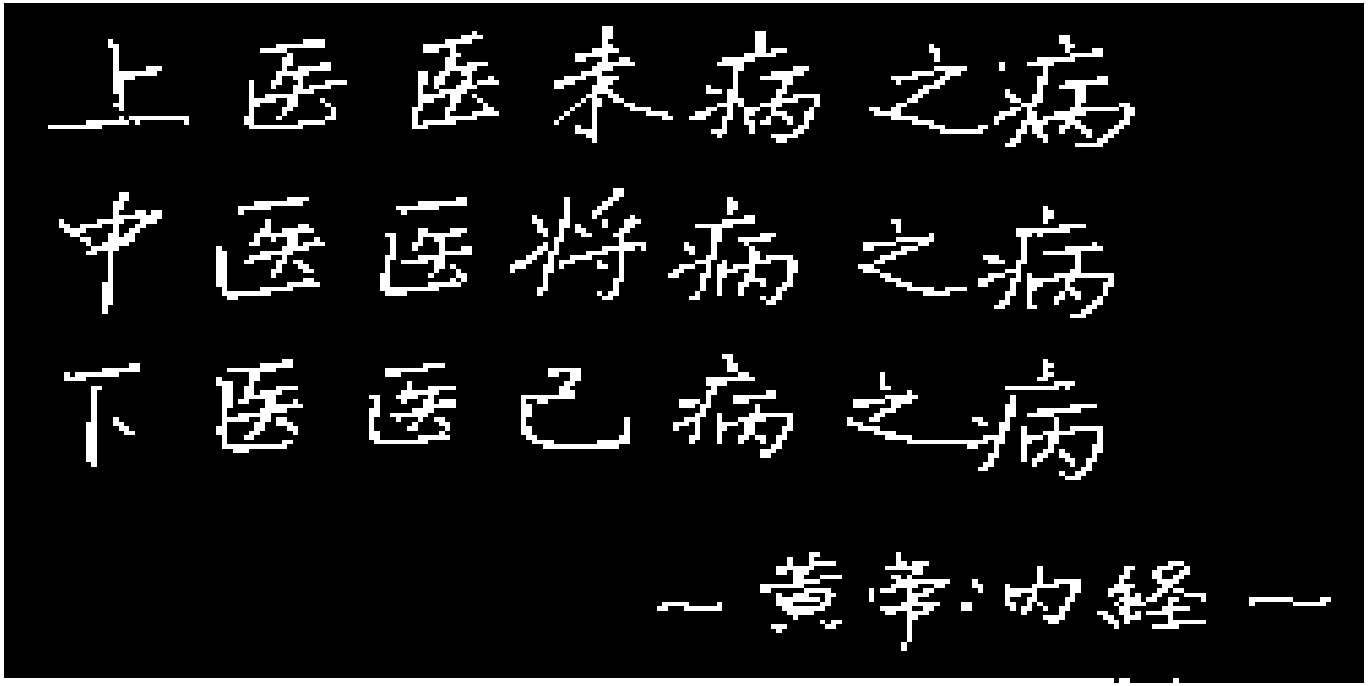
CMR international

For Any Given Cancer Type....
The Medical Options

Prevent it starting in the first place!



And Finally An Historical Note.....



Translation: "Superior doctors prevent the disease. Mediocre doctors treat the disease before evident. Inferior doctors treat the full blown disease." Huang Dee Nai-Ching (2600 BC, 1st Chinese Medical Text).