Changing Paradigms for evaluating costs and benefits of drug treatments

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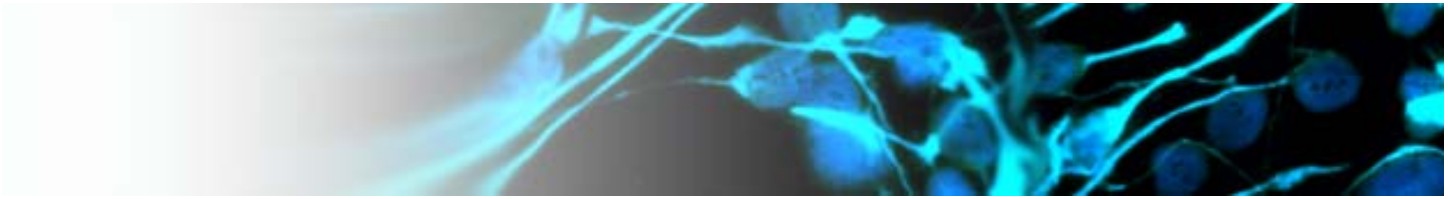
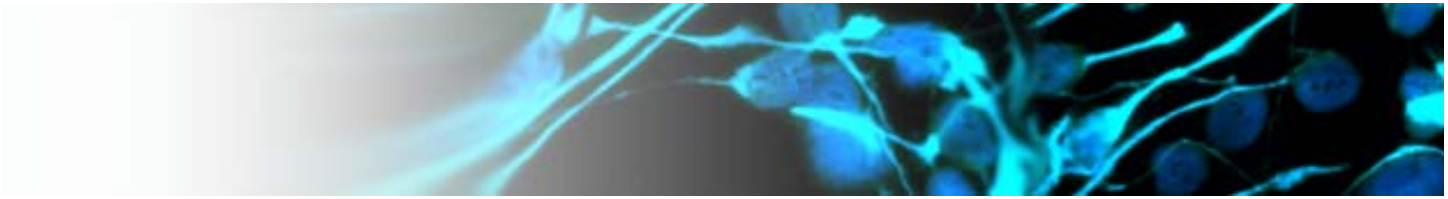
What do we mean by changing paradigms?

- Elevating pharmaceutical costs has led payers to attempt to target treatment at patients more likely to benefit
- Pharmacogenetics provides a framework for this to be achieved
- There are benefits for patients, payers and companies
- However the relationships between the genetics and outcomes is not always straightforward



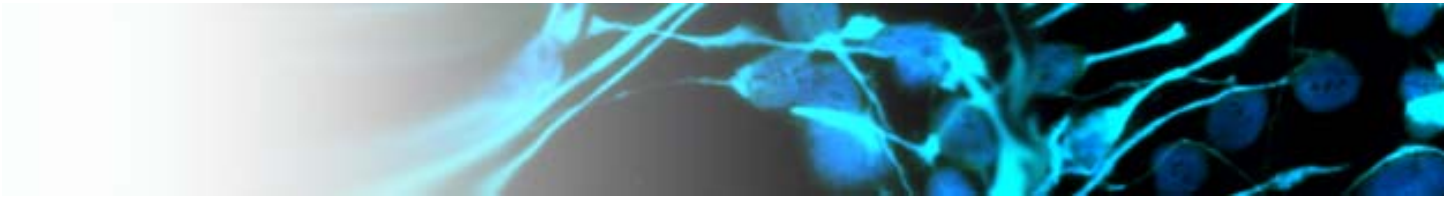
Agenda

1. pharmacogenetic testing
2. where is the extra value?
   - Example of Centoxin
   - Example of Herceptin
   - Example of Iressa/ Tarceva
3. conclusion



Potential impact of pharmacogenetic testing

- identifies patients genotypes in order to target drugs
- avoid treating patients no benefit / harm
  - ApoE gene re treatment for Alzheimer's
  - B1 variant of the CETP gene for statins
  - CystLT1 receptor for cysteinyl leukotriene antagonists in asthma
- payers will adopt if the savings exceed costs
- for drug companies, lower patient volumes
- could be socially beneficial but reduce incentives unless
  - offsetting cost reductions, e.g. in cost of R&D
  - price increases reflecting the greater specificity



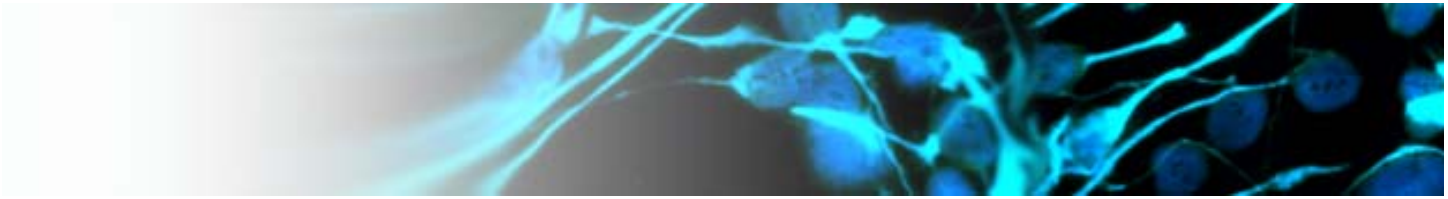
Payer perspective

- testing is beneficial to the payer:
  - **if the savings** i.e. non-responders N_2 (cost of adverse reactions a + price of drug P_d)

    are greater than the costs i.e. number of responders N_1 x change in price of the drug ΔP_d + Total number of patients N x price of the test P_t
- if a is zero, (no side effects) and the price of the drug is unchanged, then $N_2 / N > P_t / P_d$, and testing is worthwhile from the payer perspective if the ratio of non-responders to the total population exceeds the ratio of the cost of the test to the cost of the drug

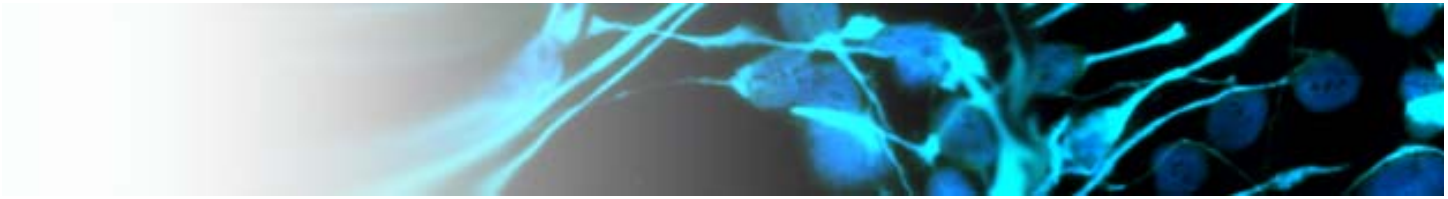
An increase in price?

- The societal benefit constitutes 3 elements
  - the increment in expected health benefit per patient treated
  - adverse effects of the drug on non-responders,
  - cost of testing for the population, amortized over the number of responders
- ability of company to obtain price premium depends on the three factors and also the resistance of the payers
- However if prices not adjusted, treatments could no longer be commercially viable



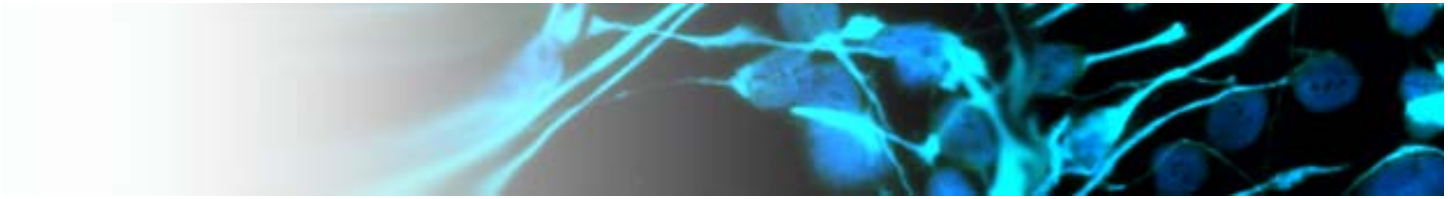
The example of Centoxin

- Centoxin (Nebacumab) launched in 1991 in Europe
- treatment for gram negative bacteraemia (gnb) sepsis. However,
  - Only one third of all sepsis cases are gnb
  - $4,000 per patient cost
  - 1,000 patients treated meant $2.67m wasted
  - Centoxin was harmful to patients without gnb
- Centocor withdrew the product and FDA filing
- what would the value of a bedside test have been?



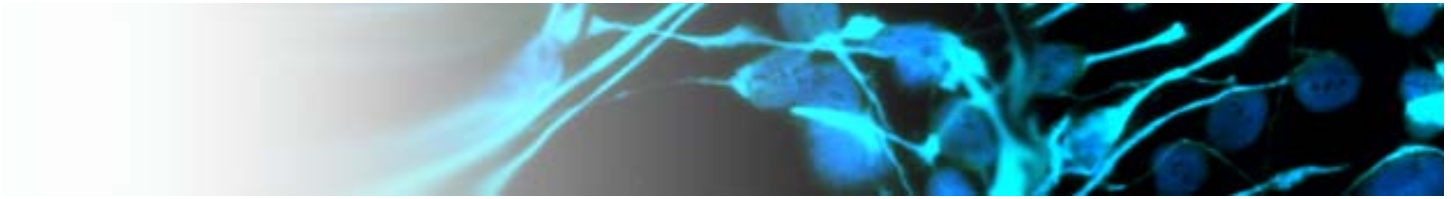
Value of a bedside test (i)

- Gain of 19% in 28-day survival of gnb group
- Increase in mortality of was 11% in the others
- The following assumptions can be made
  - Each death costs 20 QALYs
  - Cost per QALY threshold of $10,000
  - ignore extra treatment costs
  - Price of drug with and without test would be the same i.e. $4,000



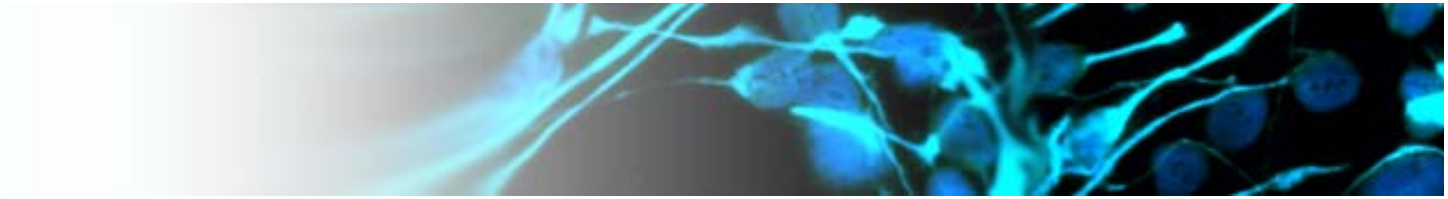
Value of a bedside test (ii)

- Without a test the product was not cost-effective or safe
- However given that 33% of patients have gnb and the assumptions then:
  - with bedside diagnostic test cost up to $11,000 Centoxin would have been cost-effective at a price of $4000
  - or alternatively with a bedside test of $1000 a drug price of $34,000 would have been cost-effective
- without the test would it have been profitable for the company?



Example of Herceptin (i)

- Genentech/Roche product for breast cancer
- benefits only those patients with HER-2
- around 25% of patients
- three diagnostic tests FDA approved
- each costs less than $100 per test
- no adverse reactions in non responders
- US price is $1,382 for a 440mg injection



Example of Herceptin (ii)

Would the testing lead to benefit?

- say treatment costs are $7000 per patient

  $[N_2 / N] > P_t / P_d$

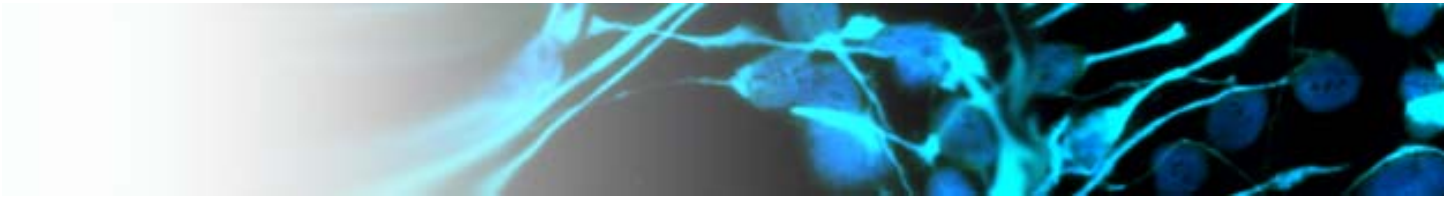
  $[N_2 / N] > 100/7000$

  $[N_2 / N] > 0.015$ or 1.5%

- Proportion of non-responders ≈ 75%

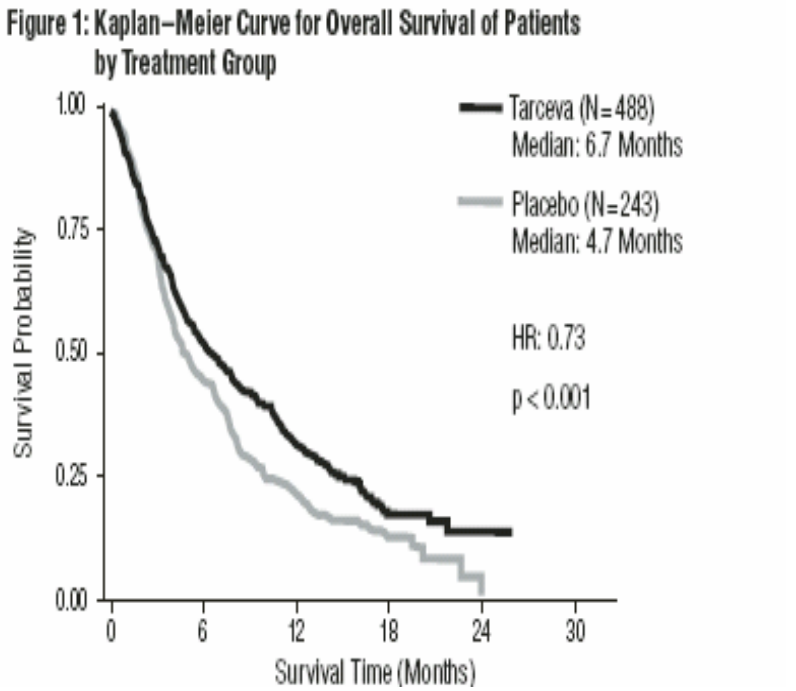
Example of Iressa/ Tarceva

- Iressa and Tarceva are orally administered epidermal growth factor tyrosine kinase (EGFR-TK) inhibitors.
- **May 2003-** Iressa (Geftinib) approved for marketing in the US for non-small-cell lung cancer patients
- **Nov 2004-** Tarceva (erlotinib) approved for marketing
- **Dec 2004-** Phase 3 trial was published which compared Iressa to placebo (ISEL trial). Did not reach statistical significance
  - the ISEL data suggested however that patients of oriental origin or who had never smoked benefited in terms of overall survival
- there have been a few papers published showing that patients who have a mutation on the gene that leads to over-expression of EGFR



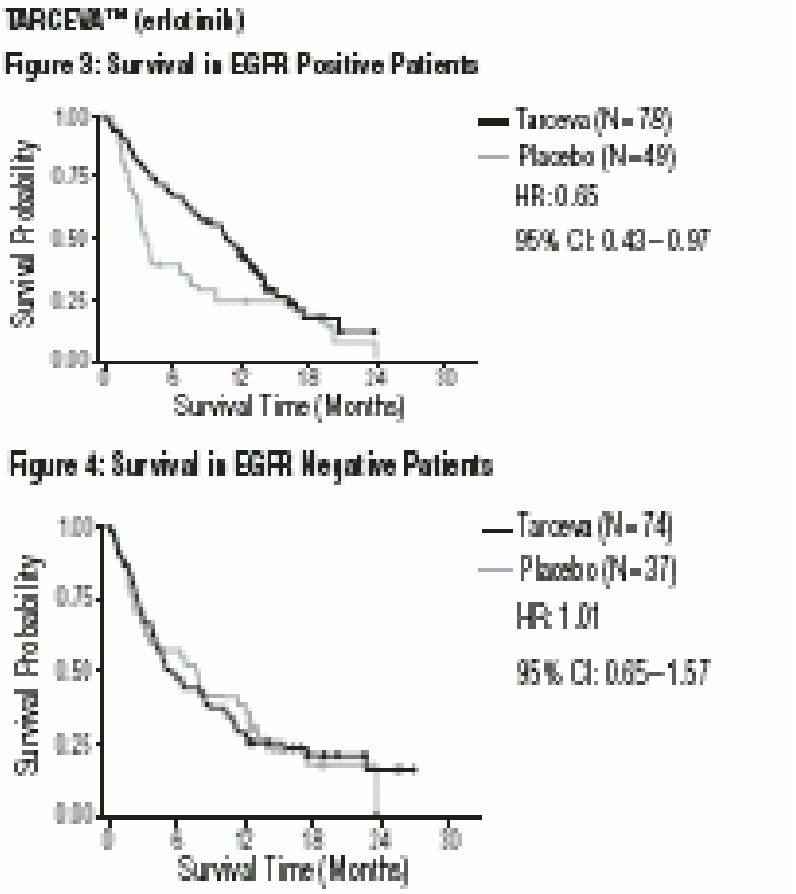
Overall Cost-effectiveness of Tarceva

- 2 month survival increase ≈0.15 QALY gain.
- Tarceva costs $2000 per month therefore total costs are $14,000
- Crudely cost/ QALY gained for NSCLC patients may be **$93,000.**
- If smokers excluded, the increase in survival of non-smokers may be 2.5 months assumed to be a 0.2 QALY gain
- If average survival for these patients is about 7.5 months then total costs are $15,000
- Crudely cost/ QALY gained for never smoking NSCLC may be **$75000.**



Cost-effectiveness of Tarceva if EGFR expression tested

- No improvement in survival in the EGFR negative group
- EGFR positive group 7 month survival increase≈ 0.6 QALYs
- If smokers excluded, the increase in survival of non-smokers could be 8 months and 0.7 QALYs
- If average life expectancy for these patients is about one year then total costs are $24,000
- Crudely cost/ QALY gained for EGFR positive patients may be **$34,000.**



Conclusion

- “personalised/ targeted medicine” may be socially optimal if
  - the proportion of non-responders is high
  - serious adverse reactions can arise
  - cost of the test is inexpensive relative to drug price
  - High specificity/ sensitivity of test
- In some cases beneftis difficult to demonstrate
- prices should reflect benefits of targeting