Cancer cells show heterogeneity in metabolic patterns, no one borad therapy.

Cancer cells reconstruct the metabolic pathway, have characteristics

- Upregulated biosynthetic pathways, increased oxidative glycolysis
- Subset of cells highly dependent on glutamine

Personalised medicine: analyse the genetic sequence of leision, design medicine targeting specific metabolic profile

Chemotherapies targeting specific metabolic enzymes:

- 5-fluorouracil targets thymidylate synthase (TYMS), which generate dNMP required for DNA synthesis
- Methotrexate inhibit dihydrofolate reductase: inhibit tetrahydrofolate synthesis, affect homeostatic pathway
- Hexokinase convert glucose into G-6-P, HEX2 function in tumour can be targeted.

Types of tests to detect tumour and assess its profile

- Physical examination
- DNA/RNA - detection for antigen
- Biopsy - sampling of tissues, detection for cell type
- Imaging (X-ray, MRI)
- PET scan

PET (Position emission tomography) scan:

- identification of tumour via metabolic activity using Fluorine-18 labelled glucose
- F-glucose taken in via GLUT1, become phosphorylated in the cell by HEX2, causing it to become trapped
- Radioactive half-life of 2 hours, decay releasing positron, collide with electron = gamma radiation, detected and imaged.
- Tumour contains upregulated glucose transport, allow locating.

Targeting receptor tyrosine kinase RTK: due to its well defined pathway

- RTK pathway in tumours are constitutively active, monoclonal antibody and RNAi therapies are developed to shut off signalling.
- EFGR inhibitors:
    - 1st Gen: Gefitinib - competitive inhibitor of ATP binding to RTK
    - 2nd Gen: Afatinib - Covalent inhibitor of RTK - cancer develop resistance, tyrosine mutated to methionine
    - 3rd Gen: Osimertinib, bind EFGR even with mutation, pressure cancer to develop further mutation
    - Possible resistance mechanisms: bypass signalling, expression amplification, EFGR mutation, downstream activation
- EFGR monoclonal antibody:
    - Trastuzumab: bind to EGFR, promote degradation
- Anti-angiogenesis therapy:
    - Binding of VEGF molecule and VEGFR

Strategies to overcome mutagenic environment

- Two hit strategy: Allosteric site + active site, small possibility for two simultaneous mutations
- Different pathways drugs at the same time