How do we dose Chemotherapy?

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How does chemotherapy work?

- Targets dividing cells in a number of ways
- Some normal tissues have rapidly dividing cells that may be affected by chemotherapy e.g. bone marrow cells
- Therapeutic window
- Risk of infection, diarrhoea, occasional deaths fro toxicity

Metabolism

- Most chemotherapy drugs metabolised by the liver
- Smaller number excreted by the kidney
- Differences between patients in their ability to clear drugs related to genetic factors
- Slower clearance may lead to greater toxicity

How assess adequacy of chemotherapy

- Survival
- Quality of life for non-curative therapies

How are chemotherapy doses determined?

- Phase I trials: dose finding studies
- Phase II: validation on various tumour types
- Phase III: validation against current "best practice" protocols

Chemotherapy dosing

- mg/kg
- mg/M2 (BSA)
- Fixed dosing
- AUC (plasma concentration over time, related to renal function)

Patients Factors

- Age
- Co-morbidity
- Extent of disease
- Performance status

Selection of Patients

- Curative treatment (lymphomas, leukaemia, testicular cancer)
- Adjuvant therapy (breast cancer, ovarian cancer, colorectal cancer)
- Palliation (that is to improve quality of life by tumour control)
- Symptomatic measures only

Levels of Evidence

- I-Evidence from at least one randomized controlled trial,
- II1-Evidence from at least one well designed cohort study or case control study, i.e. a controlled trial which is not randomized
- II2-Comparisons between times and places with or without the intervention
- III-Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

Chemotherapy Dosing: Breast Cancer (eviQ)

- Breast Metastatic AC (DOXOrubicin and CYCLOPHOSPHamide)
- Breast Metastatic Anastrozole
- Breast Metastatic Capecitabine
- Breast Metastatic Capecitabine and Lapatinib
- Breast Metastatic cARBOplatin and Gemcitabine
- Breast Metastatic CMF Classical (CYCLOPHOSPHamide Methotrexate Fluorouracil)
- Breast Metastatic CYCLOPHOSPHamide and Methotrexate (Low Dose Oral)

- Breast Metastatic DOCEtaxel and Trastuzumab Three Weekly
- Breast Metastatic DOCEtaxel Pertuzumab Trastuzumab
- Breast Metastatic DOCEtaxel Three Weekly
- Breast Metastatic DOXOrubicin
- Breast Metastatic DOXOrubicin Weekly

- Breast Metastatic EC (Epirubicin and CYCLOPHOSPHamide)
- Breast Metastatic Eribulin
- Breast Metastatic Everolimus and Exemestane
- Breast Metastatic Exemestane
- Breast Metastatic FEC (Fluorouracil Epirubicin CYCLOPHOSPHamide)
- Breast Metastatic Fulvestrant
- Breast Metastatic PACLItaxel Weekly and Trastuzumab Three Weekly

- Breast Metastatic Pegylated Liposomal DOXOrubicin
- Breast Metastatic Tamoxifen
- Breast Metastatic Trastuzumab Emtansine
- Breast Metastatic Trastuzumab Three Weekly
- Breast Metastatic vinORELBine (IV)
- Breast Metastatic vinORELBine (IV) and Trastuzumab Three Weekly
- Breast Metastatic vinORELBine (Oral)

- Breast Metastatic Goserelin (Zoladex)
- Breast Metastatic Letrozole
- Breast Metastatic Nab PACLItaxel Three Weekly
- Breast Metastatic Nab PACLItaxel Weekly
- Breast Metastatic PACLItaxel Weekly
- Breast Metastatic PACLItaxel Weekly and Pertuzumab and Trastuzumab Three Weekly

Doxorubicin

- Breast Metastatic DOXOrubicin
- ID: 000048 (V.3) Approved: 21 Apr 2008 Last Modified: 10 Oct 2016 Review Due: 30 Jun 2019
- All chemotherapy drugs (includes both cytotoxic and non-cytotoxic) included in the treatment schedule of this protocol are included on the World Health Organisation (WHO) Model List of Essential Medicines (19th List April 2015). The WHO Model List of Essential Medicines may be found here.
- Treatment Schedule Summary
- Drug Dose Route Day
- DOXOrubicin 60 mg/m^2* IV 1
- * Doxorubicin dose can vary from 60 mg/m^2 to 75 mg/m^2. It is the consensus of the reference committee that a starting dose of 60 mg/m^2 is more appropriate for this patient population unless fit or being treated in the first line.
- Frequency: 21 days
- Cycles: Continuous until disease progression or unacceptable toxicity (up to 6 cycles)

Local Experience

- Sydney Cancer Centre (RPAH, Concord Hospital)
- Published 2009
- (patients with NSCLC) over 14 months
- Assessed eligibility for receiving treatment according to SWOG9509, TAX326 and E1594

Local Experience

- Only 35% met eligibility criteria for E1594
- Only 28% met eligibility for TAX326 or SWOG9509
- Reasons for ineligibility included co-morbidities, poor performance status, symptomatic brain metastases
- Only 1 in 3 patients could be treated according to published protocols

The Real World

- Older patients
- May have significant co-morbidity
- Generally more extensive disease
- Poor performance status
- Treatment needs to be tailored to the individual patient