CHOP vs GEM-P

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Clinical trials in PTCL
The Issues

- This a group of rare diseases with clinical and biological heterogeneity
- Historically patients with PTCL have been treated on the same protocols as those used for high grade B cell NHL but the small numbers have often made meaningful sub-group analyses untenable
- There have been no previous UK prospective randomised controlled Phase III clinical trials in PTCL
- Most clinical trial activity in the UK has been based on relatively small, usually single centre, often retrospective, studies
- Data calculated from pooled case reports are influenced by publication bias and often poorly defined and inconsistent response criteria
- The purpose behind conducting clinical trials is to provide an evidence-base for management guidelines and to evaluate the role of novel treatments

CANCER RESEARCH UK

The Royal Marsden NHS
NHS Foundation Trust

CHOP versus GEM-P in the first line treatment Of T-cell Lymphoma, a multicentre randomised phase II study

CHEMO-T

NCRI
National Cancer Research Institute

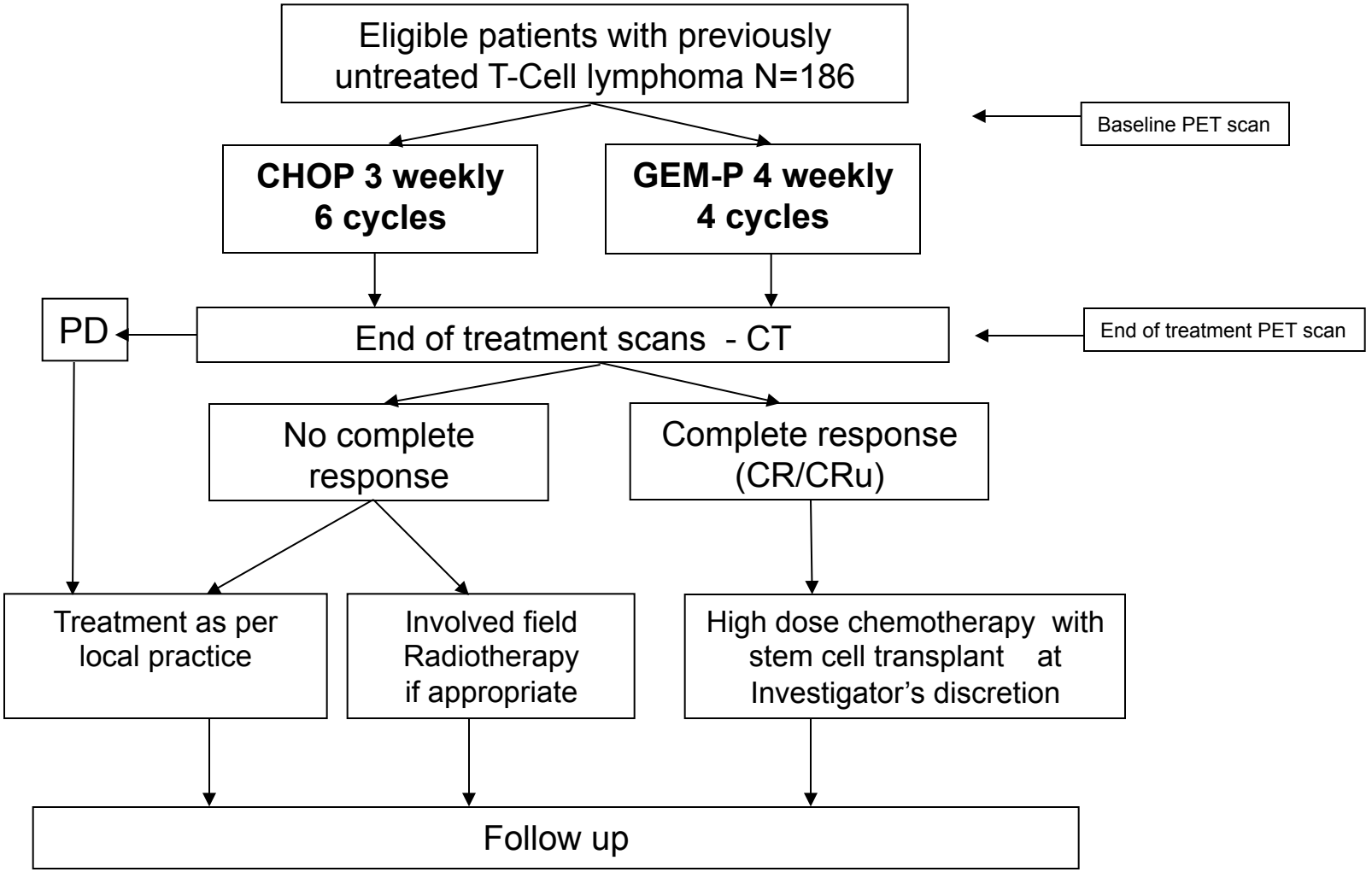
PI: Professor David Cunningham

Why CHEMO-T ?

- CHOP-based regimens are the most frequently used
  - CR rate with CHOP alone approximately 39-60%[1,2]
  - 5-yr OS ~36%[2]
- Urgent need for a better first-line chemotherapy regimen
- Gemcitabine and Cisplatin have demonstrated activity in several small series and are well tolerated [3-6]
  - OR rate 80% first-line, 73% relapsed
  - CR rate 40% first line, 45% second line
- Difficult to evaluate newer agents without an optimal chemo backbone
- Fit patients considered for high-dose treatment + ASCT

1. Simon et al, Br J Haem 2010 2. Pautier et al, Leukaemia and Lymphoma 1999 3. Ng et al, Br J Cancer 2005
4. Arkenau et al, Haematologica 2007 5. Emmanouilides et al, Clin Lymphom 2004 6. Yim et al, JCO suppl abstract 8052 2010

CHEMO-T Study Design and Schema (N=186)



Primary endpoint CR+CRu

PI: David Cunningham

Trial Endpoints

- Primary Endpoint:
  - To compare the complete response rate (CR + CRu) of GEM-P with CHOP chemotherapy in the first line treatment of patients with T–cell Lymphoma (as assessed on end of treatment CT scan)

1999 IWG criteria

Trial Endpoints

- Secondary endpoints:
  - Metabolic complete and partial response at the end of treatment as seen on the FDG-PET scan
  - Overall response rate
  - Toxicity of treatment
  - Overall survival (OS)
  - Progression Free Survival (PFS)
- Exploratory
  - Investigate impact of International Prognostic Index (IPI) on the outcomes response rate, PFS and OS

Main Inclusion criteria

- Histologically proven T-cell lymphoma of the following subtypes:
  - Peripheral T-cell lymphoma NOS
  - Systemic Anaplastic large cell lymphoma (ALCL) ALK negative cases only
  - Angioimmunoblastic T-cell lymphoma
  - Hepatosplenic gamma/ delta T-cell lymphoma
  - *Enteropathy-associated T-cell lymphoma (EATL)*
- Bulky Stage I, Stage II, III or IV
- No prior chemotherapy regimen
- Patients aged 18 years or over.
- WHO performance status 0,1 or 2
- Adequate organ function
- No CNS or leptomeningeal involvement with lymphoma
- No known HIV, Hepatitis C or active Hepatitis B viral infection

Main Exclusion Criteria

- Documented or symptomatic CNS involvement or leptomeningeal disease.
- Any other clinically significant co-morbidity which may adversely affect the safe delivery of treatment within the trial
- Any other malignancies diagnosed or treated within the last 5 years (other than curatively treated BCC of the skin and/or in situ carcinoma of the cervix)
- Treatment with another investigational agent within 30 days of commencing study treatment
- Patients with poorly controlled diabetes mellitus

Statistics and Sample Size

- Planned total study accrual n= 186

- With 93 patients per arm, we will be able to detect a difference in complete response rate from 50% in the CHOP arm to 70% in the GEM-P arm with 80% power and 2-sided alpha of 5%

- Interim Analysis built into the protocol after 42 patients treated on the GEM-P arm have been assessed for response. If response in the GEM-P arm is lower than the pre specified level, IDMC will review responses in

Use of Steroids

- Ideally not instituted prior to PET
- Permitted if required for lymphoma symptoms
- If given prior to PET:
  - → Stop 24 hrs pre PET
  - → Glucose ≤8.0mmol/l immediately prior to PET
  - → Dose should not exceed 100mg prednisolone (or equivalent)/day for 7 days

Study Treatment

Arm A: CHOP	Dose	Day of cycle
Cyclophosphamide	750 mg/m^2 IV	D1
Doxorubicin	50 mg/m^2 IV	D1
Vincristine	1.4 mg/m^2 IV	D1
Prednisolone	100mg PO	D1

Arm B: GEM-P	Dose	Day of cycle
Gemcitabine	1000 mg/m^2 IV	D1, D8, D15
Cisplatin	100 mg/m^2 IV	D15
Methylprednisolone	1000 mg IV/PO	D1-D5

Investigations

- CT scans:
  -
  -
  -
- PET scans:
  -
  -
    analysis of response by PET scan
- Archival tissue sample, Biomarker blood (for translational studies)

Follow-up

- Clinical follow up:
  - 3 (+CT), 6, 9, 12 (+CT), 18, 24 months
  - Then annually to 5 years

  - Patients with relapse/PD

    →Phone calls/GP contact for survival only.

CHEMO-T: Current Status

- 42 centres open of 50 planned in UK
- 48 patients recruited (out of 186), below target
- Plan:
  - Increase number of centres
  - Extend recruitment period by further 2 years
  - Explore international collaboration
  - Amendment to add EATL
  - Additional blood samples for circulating tumour DNA
  - Interim analysis after 42 patients randomised to GEM-P