Alliance A031102: A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed By High-dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment Of Germ Cell Tumors (TIGER)

Darren R. Feldman, MD

Memorial Sloan Kettering Cancer Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Please use the headings above to navigate through the different sections of the poster

Rationale

- Germ cell tumors (GCT) represent the most common malignancy affecting adolescent and young adult men in both Europe and the United States. [1]
- Up to 30% of pts with advanced GCT are not cured with first-line chemotherapy and require salvage treatment, consisting of either conventional-dose chemotherapy (CDCT) or high-dose chemotherapy (HDCT).
- The optimal initial salvage approach (HDCT vs. CDCT) is not clear; retrospective studies consistently report superior outcomes with HDCT but the one prior RCT (IT-94) found no improvement with HDCT. [2]
- IT-94 had several shortcomings including:
  - Only 1 high-dose cycle in the HCT arm (most effective regimens use 2 or 3)
  - Exclusion of pts with incomplete response to first line chemotherapy (only allowed relapsing pts)
  - >25% of pts assigned to HDCT arm never received the high-dose cycle
- The current TIGER study aims to determine whether HDCT or CDCT is the optimal initial salvage approach.
- Collaboration between Alliance, EORTC, ECOG, SWOG, COG, ANZUP
- Open in 13 countries across 3 continents (North America, Europe and Australia)

References: 1. Feldman *JAMA* 299:672-84, 2008; 2. Pico *Ann Oncol*16:1152–59, 2005

Alliance A031102: A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed By High-dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment Of Germ Cell Tumors (TIGER)

Darren R. Feldman, MD

Memorial Sloan Kettering Cancer Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Please use the headings above to navigate through the different sections of the poster

Endpoints

Primary

Overall Survival (OS)

Sample size = 420 patients (expected deaths = 232)

- 168 patients from US Cooperative Groups; 252 patients from EORTC
- Cure rate model: 35% of patients will be cured with TIP (median OS 1.5yrs)
- Power 81%, 1-sided type I error rate = 0.05 where TI-CE will reduce the hazard by 29% (θ =0.71)
  - Efficacy & futility analyses regularly per Alliance policy
- Formal toxicity analysis for early stopping (90% CI for one-sided difference in treatment-related mortality > 16%)

Secondary

- Progression-free survival (PFS)
- Favorable response rate
  - CR and PR-negative markers
- Treatment-related mortality
- Toxicities by CTCAE v4.0
- Validation of the IPFSG risk model [3]

Correlative Studies

- Quality of life assessment of TIP vs. TI-CE using EORTC QLQ-C30 and the QLQ-TC26
- Pharmacogenomics: correlation of SNP rs1649942 (associated with platinum response) with PFS in the entire study population
- Tumor whole exome analysis assessing for the association of genetic alterations with OS
  - DNA Repair genes (TP53) [6]
  - PI3K/RAS/RAF genes[7]

References: 3. Lorch *J Clin Oncol* 28:4906-11, 2010; 6. Feldman *J Clin Oncol* (Epub 2016); 7. Feldman. *Clin Cancer Res* 20 (14); 3712–20, 2014

Alliance A031102: A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed By High-dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment Of Germ Cell Tumors (TIGER)

Darren R. Feldman, MD

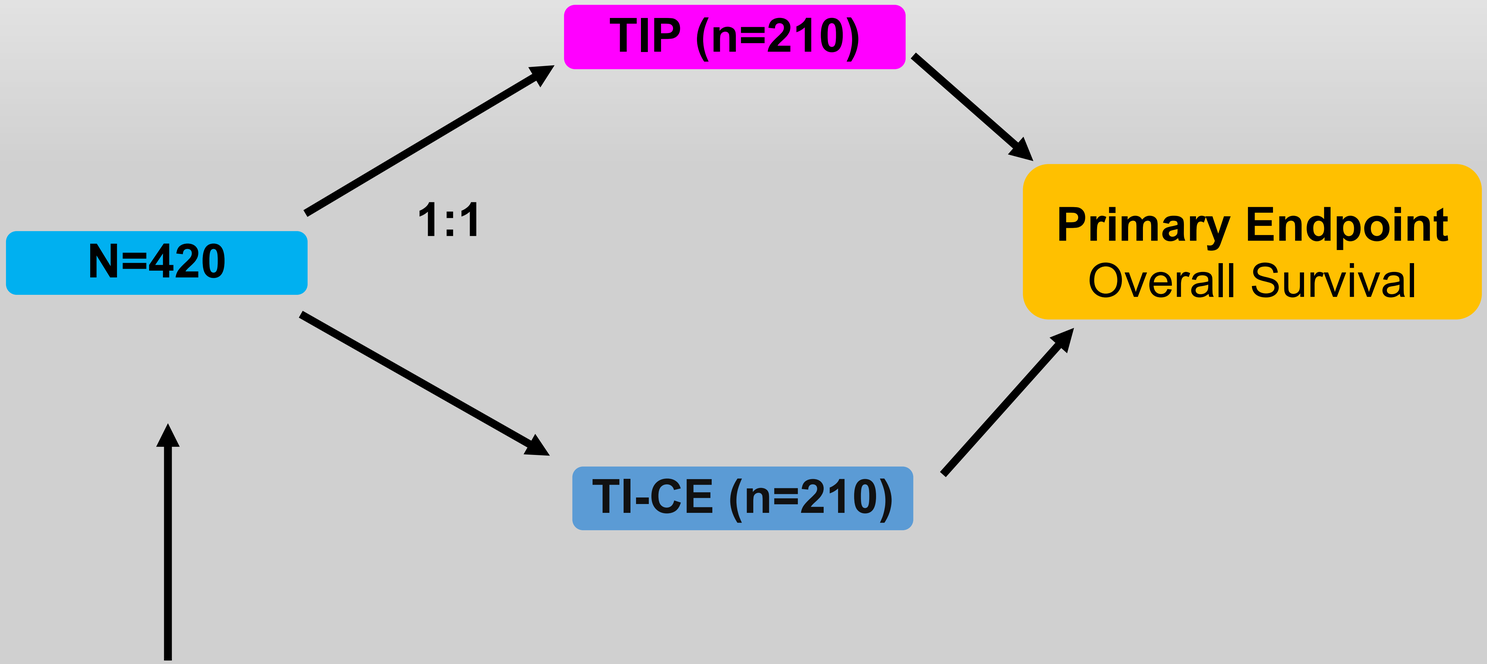
Memorial Sloan Kettering Cancer Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Study Schema



Please use the headings above to navigate through the different sections of the poster

Stratification Factors:

1. International Prognostic Factor Study Group (IPFSG) risk class[3]
2. Continent of enrollment

Alliance A031102: A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed By High-dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment Of Germ Cell Tumors (TIGER)

Darren R. Feldman, MD

Memorial Sloan Kettering Cancer Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

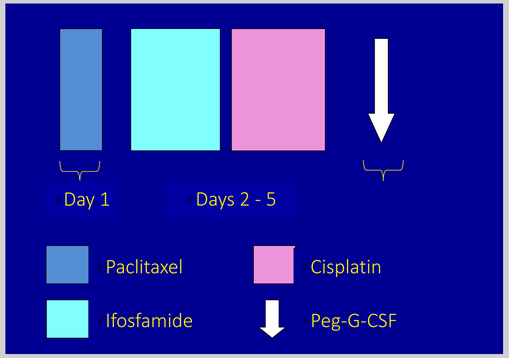
NCI National Clinical Trials Network
a National Cancer Institute program

Please use the headings above to navigate through the different sections of the poster

Treatment Plan

ARM A (CDCT): TIP[4]

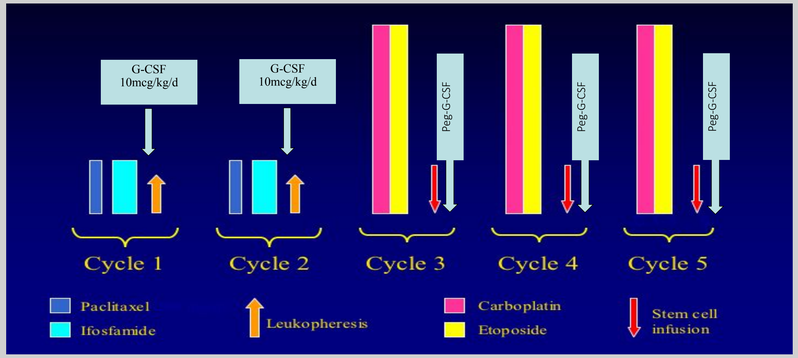
Drugs and Doses	Infusion Time	Days
Paclitaxel 250mg/m^2	24 hours	1
Ifosfamide 2000mg/m^2	1-2 hours	2-5
Mesna	1-2 hours	2-5
Cisplatin 25mg/m2	0.5 – 1 hour	2-5



- 4 cycles given every 21 days
- Exact infusion time at discretion of investigator and institution
- Levofloxacin 500mg daily given as prophylaxis from day 7 to 13 of each cycle

ARM B (HDCT): TI-CE[5]

Cycle #	Cycle Duration	Drugs and Doses	Days
1-2	14 days	Paclitaxel 200mg/m^2	1
		Ifosfamide 2000mg/m^2/d	2-4
3, 4, 5	21 days	Etoposide 400mg/m^2/d	1-3
		Carboplatin AUC 7-8/d	1-3



References: 4. Kondagunta J Clin Oncol 23: 6549–55, 2005; 5. Feldman *J Clin Oncol* 28:1706-13, 2010

Alliance A031102: A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed By High-dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment Of Germ Cell Tumors (TIGER)

Darren R. Feldman, MD

Memorial Sloan Kettering Cancer Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Please use the headings above to navigate through the different sections of the poster

Key Eligibility Criteria

- Male
- Age ≥ 14 years
- ECOG 0 - 2
- Histologic confirmation of GCT diagnosis
- Evidence of progressive disease after one line of cisplatin-based chemotherapy including:
  - Biopsy of new/growing mass consistent with non-teratomatous GCT
  - Rising HCG or AFP
  - New or enlarging lesions in the setting of elevated (even if not rising) HCG or AFP
- Received 1 prior line of cisplatin-based chemo (3 – 6 cycles)
- No prior treatment with TIP or HDCT
- GFR ≥ 50ml/min by 2 methods or ≥ 70ml/min by 1 method
- ANC ≥ 1,500/mm3, PLT ≥ 100,000/mm3
- T bilirubin ≤ 2.5 x ULN and AST/ALT ≤ 2.5 x ULN
- Negative serology for HIV, HTLV, Hep B, and Hep C
- No secondary somatic malignancy arising from teratoma

Alliance A031102: A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed By High-dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment Of Germ Cell Tumors (TIGER)

Darren R. Feldman, MD

Memorial Sloan Kettering Cancer Center

TAP TO RETURN TO KIOSK MENU

Please use the headings above to navigate through the different sections of the poster

Funding Support

Alliance A031102 is funded by the National Institutes of Health through National Cancer Institute grant awards.

Contact Us

Study Chair: Darren R. Feldman, Memorial Sloan Kettering Cancer Center
E-mail: feldmand@mskcc.org
Phone: 212-639-7202

Protocol Coordinator: Colleen Watt
E-mail: cboyle@uchicago.edu
Phone: 773-702-4670