Concurrent Cisplatin-Based Radiotherapy and Chemotherapy for Locally Advanced Cervical Cancer

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Theory

• Ability of radiotherapy to cure locally advanced cervical cancer is limited by the size of the tumor, because the doses required to treat large tumors exceed the limit of toxicity in normal tissue.

• Radiation therapy not able to treat systemic disease spread.
Theory

• Concurrent chemotherapy
  – Inhibits the repair of sub-lethal damage from radiation
  – Synchronizes cells to a particularly radiosensitive phase of the cell cycle
  – Cytotoxic in vitro
Background

• Multiple randomised studies had demonstrated benefit of adding chemotherapy concurrently to radiation in advanced cervical cancer.

• Which was the superior regimen?
RTOG 9001

389 Pt. FIGO IIB, III, IVB (+) Pelvic Nodes or Stage I & Tumor > 5 cm

195 Pt CDDP/5-FU Pelvic & PA Ext & IC XRT
3 Yr Survival 75%

193 Pt Pelvic & PAN Ext & IC XRT
3 Yr Survival 63%

Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. NEJM, 1999; 340:1154-61.
Participants

• Stage IIIB, III or IVA
• Excluded if extra pelvic disease, + Para-aortic LNs or intra-peritoneal disease

• Primary end points were survival and progression-free survival
Radiation Therapy

- Standardised fields
- Dose schedule set
- 10 week treatment window
- External Beam followed by brachytherapy
Stage IIB

- 24 fractions totaling 40.8 Gy
- One or two intracavitary implants were inserted, totalling 40 Gy
- The total dose delivered to point A (a reference location 2 cm lateral and 2 cm superior to the cervical os) was 80.8 Gy
disease
- The total dose delivered to point B (the pelvic wall) was 55.0 Gy
Stage III or IV A

- 30 fractions totaling 51.0 Gy
- One or two intracavitary implants were inserted, totalling 30 Gy
- The total dose delivered to point A (a reference location 2 cm lateral and 2 cm superior to the cervical os) was 81.0 Gy
- The total dose delivered to point B (the pelvic wall) was 60.0 Gy
Chemotherapy

• Randomised to one of 3 arms
  – 40 mg of cisplatin per square meter of body-surface area per week for six weeks (group 1)
  – 50 mg of cisplatin per square meter on days 1 and 29, followed by 4 g of fluorouracil per square meter given as a 96-hour infusion on days 1 and 29, and 2 g of oral hydroxyurea per square meter twice weekly for six weeks (group 2)
  – 3 g of oral hydroxyurea per square meter twice weekly for six weeks (group 3).
GOG 120

• Similar improvement in PFS in cisplatin containing regimens
• Increased toxicity in 3 drug regimen