

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

Peter G. Rose, M.D., Brian N. Bundy, Ph.D., Edwin B. Watkins, M.D., J. Tate Thigpen, M.D., Gunther Deppe, M.D., Mitchell A. Maiman, M.D., Daniel L. Clarke-Pearson, M.D., and Sam Insalaco, M.D. *N Engl J Med* 1999; 340:1144-1153

[April 15, 1999 DOI: 10.1056/NEJM199904153401502](https://doi.org/10.1056/NEJM199904153401502)

# 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.

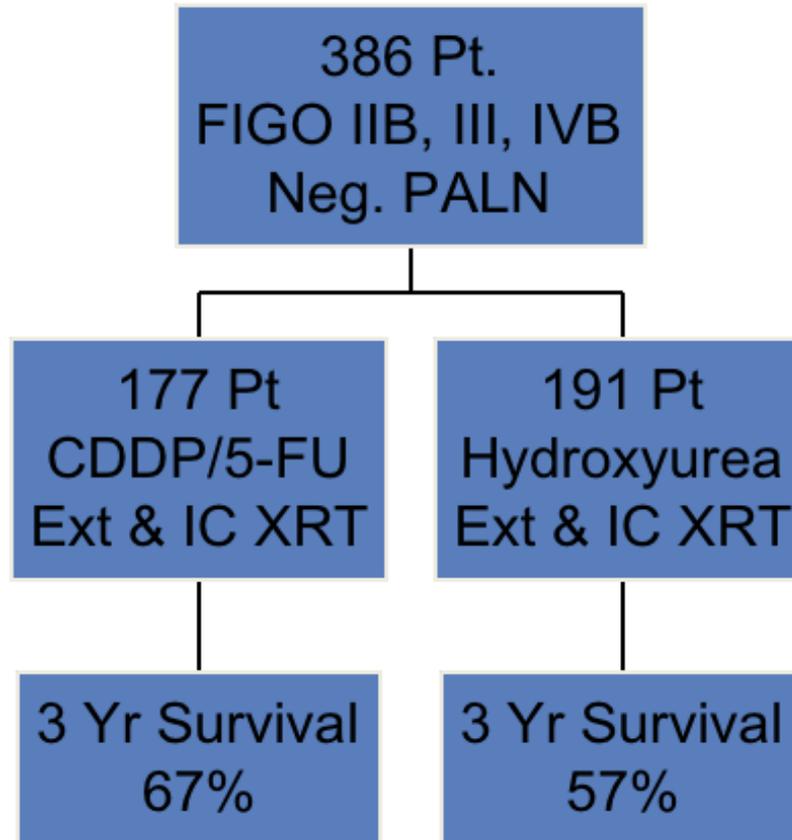
# Theory

- 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

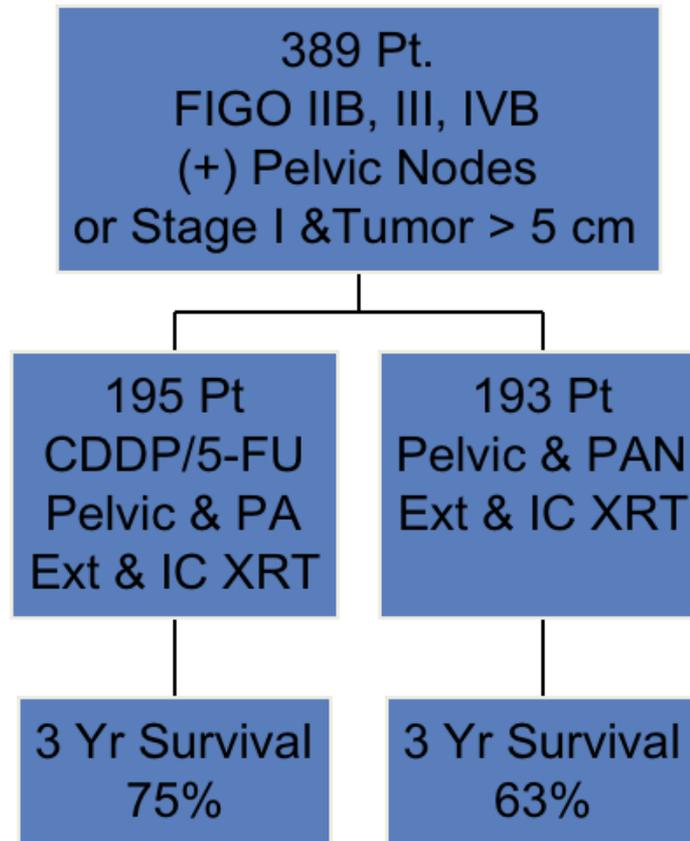
- Multiple randomised studies had demonstrated benefit of adding chemotherapy concurrently to radiation in advanced cervical cancer.
- Which was the superior regimen?

# GOG 85 / SWOG 8695



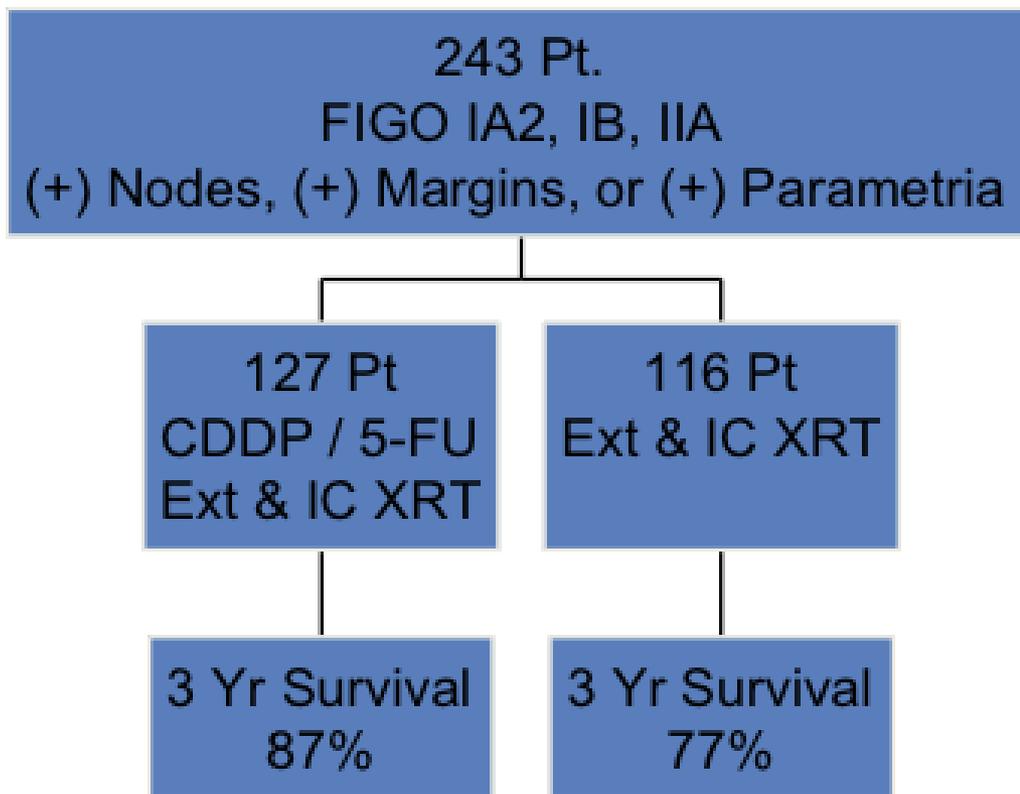
Whitney C, Sause W, Bundy B, Malfetano J, et al. A randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic nodes. A Gynecologic Oncology Group and SWOG Study. J Clin Oncol

# RTOG 9001



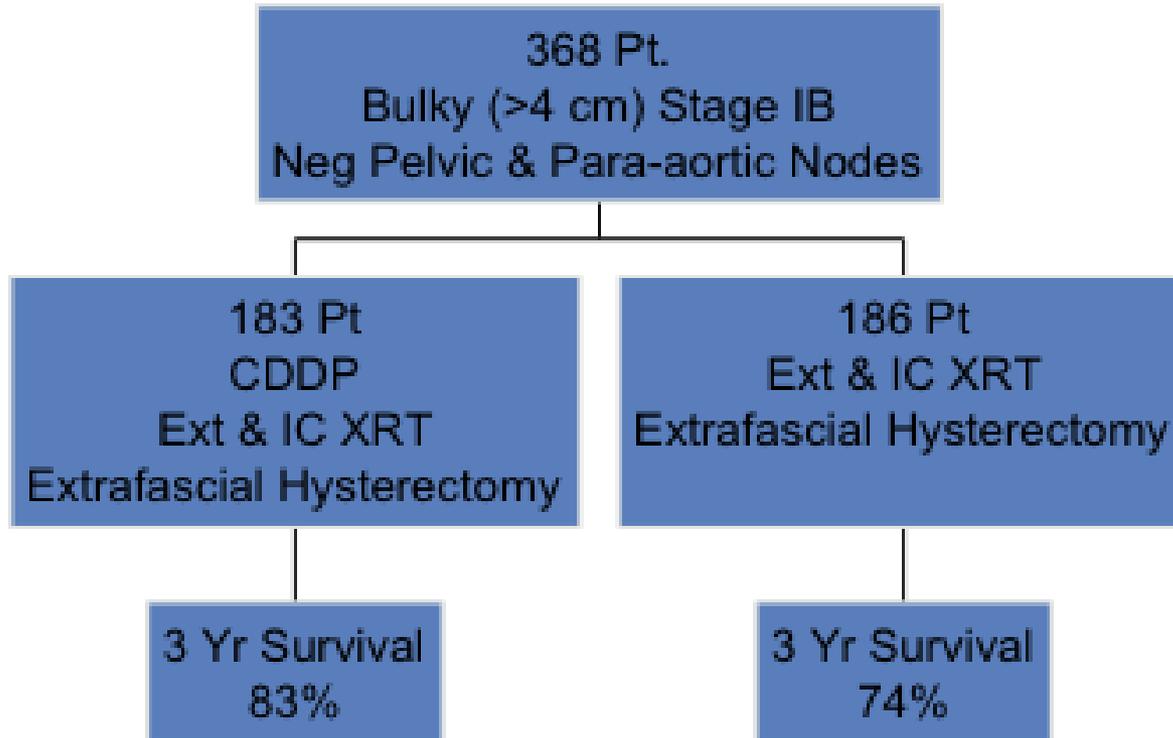
Morris M, Eifel P, Lu J, Grigsby P, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high risk cervical cancer. NEJM, 1999;340:1137-43.

# SWOG 8797 / GOG 109 / RTOG 9112



Peters W, Liu P, Barrett R, Gordon W, et al. Cisplatin and 5-fluorouracil plus radiation therapy are superior to radiation as adjunctive in high-risk early stage carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: report of a phase III intergroup study.

# GOG 123



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

# Participants

- Stage IIB, 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
- 10week 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
- The total dose delivered to point B (the pelvic wall) was 55.0 Gy

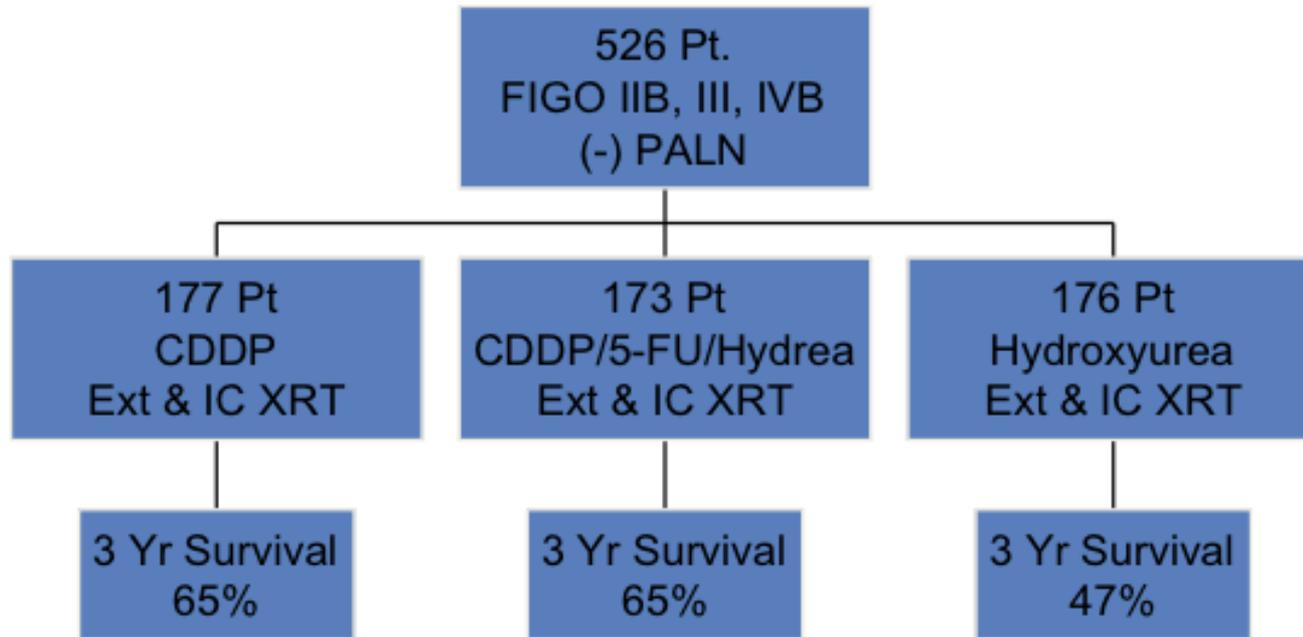
# Stage III or IV A

- 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



Rose P, Bundy B, Watkins E, Thigpen J, et al. Concurrent cisplatin based radiotherapy and chemotherapy for locally advanced cervical cancer. NEJM, 1999;340:1144-53.

# GOG 120

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