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Evidence-Based Series #4-20: Section 1

Chemotherapy for Recurrent, Metastatic, or Persistent Cervical Cancer: A Clinical Practice Guideline

*H. Hirte, J. Strychowsky, T. Oliver, M. Fung-Kee-Fung, L. Elit, A. Oza,
and the Gynecology Cancer Disease Site Group*

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Question

What are the front-line chemotherapeutic options for women with recurrent, metastatic, or persistent cervical cancer? Outcomes of interest include response rate, survival, toxicity, and quality of life (QOL).

Target Population

These recommendations apply to women with metastatic, recurrent, or persistent cervical cancer for whom first-line treatment with chemotherapy is indicated.

Recommendations

- It is recommended that all patients, particularly those who have been previously treated with cisplatin as a radiosensitizer, be offered the opportunity to participate in randomized trials, if available, that evaluate the efficacy and toxicity of other single-agent or combination chemotherapy regimens.
- Until further evidence becomes available, it is recommended that cisplatin in combination with topotecan should be offered to patients on the basis of improvements in response and survival outcomes when compared with single-agent cisplatin alone.
 - The improvement in outcomes must be weighed against significant increases in adverse events, especially hematological toxicities, and the degree of the clinical benefit. Despite the increase in toxicity, no significant differences in quality of life were detected. Severe hematological toxicities were managed by dose modification and the use of granulocyte-colony-stimulating factors (G-CSFs) in subsequent cycles.

Key Evidence

- Fifteen randomized trials provided the evidence basis for this report.
- One trial reported statistically significant improvements in response rates (27% versus [vs.] 13%, $p=0.004$), progression-free survival (4.6 vs. 2.9 months, $p=0.014$), and median survival (9.4 vs. 6.5 months, $p=0.017$) in patients who received 50 mg/m² cisplatin on day 1 and 0.75

mg/m² topotecan on days 1 to 3, repeated every three weeks, when compared with patients treated with single-agent cisplatin.

- In that trial, 57% of patients had been previously treated with cisplatin as a radiosensitizer.
 - As part of a subgroup analysis, median survival among patients not previously treated with cisplatin as a radiosensitizer was 15.4 months for patients treated with cisplatin and topotecan versus 8.8 months among patients treated with cisplatin alone. In those previously treated with cisplatin as a radiosensitizer, median survival was 7.9 months versus 5.5 months, respectively (p-values not reported).
- In the remaining trials, where reported, the majority of patients did not receive chemotherapy as a radiosensitizer.
 - Three of these trials detected statistically significant improvements in overall response rates with cisplatin in combination with paclitaxel, BEM (bleomycin, vindesine, and mitomycin-C), or ifosfamide when compared with single-agent cisplatin.
 - Two trials reported a statistically significant progression-free survival advantage for patients receiving cisplatin in combination with paclitaxel or ifosfamide when compared with patients receiving single-agent cisplatin.
- Significant increases in Grade 3 and 4 adverse events, especially severe hematological toxicities, were detected among patient treated with combination cisplatin-based chemotherapy when compared with patients who received cisplatin alone.
- Of the two trials that reported QOL data, no statistically significant differences were detected in patients treated with cisplatin in combination with topotecan or paclitaxel versus patients treated with single-agent cisplatin.

Future Research

Further randomized trials are needed to inform the role of single-agent or combination chemotherapy regimens, particularly in patients who have been radiosensitized with prior cisplatin. Trials comparing single-agent (i.e., cisplatin or topotecan) with other single-agent or combination chemotherapy regimens, or comparing various combination chemotherapy regimens are needed.

Related Guidelines

PEBC Practice Guideline #4-5: *Primary Treatment for Locally Advanced Cervical Cancer: Concurrent Platinum-Based Chemotherapy and Radiation.*

EVIDENCE-BASED SERIES #4-20

Contact Information

For further information about this series, please contact:

Dr. Michael Fung-Kee-Fung, Chair, Gynecology Cancer Disease Site Group; Ottawa General Hospital, 501 Smyth Road, Ottawa, Ontario; Telephone: 613-737-8560, FAX: 613-737-8828

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