

# cancer answers

Cancer Answers is a series of free public lectures, presented by *Cancer Care Nova Scotia*, on a variety of cancer-related topics. The lectures, delivered by cancer experts, are designed to raise awareness and educate participants about issues related to prevention, screening, early diagnosis, treatment, survivorship and palliative care.

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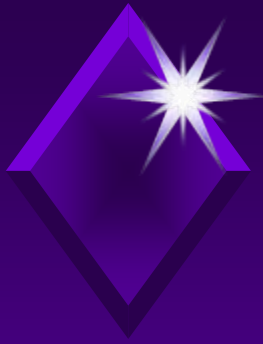


# ***New Treatment Options for Colorectal Cancer: Advances and Access***



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# ***Why Aren't All Patients Cured After Surgery?***

- ◆ **Early spread of microscopic cancer cells through the blood or lymph system**



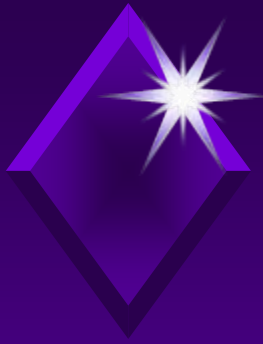
## ***Colon Cancer Risks of Recurrence with Surgery Alone at 5 Years***

- ◆ **Node - :** ~ 25-30%
- ◆ **Node + :** ~ 50-70%



# *Patterns of Recurrence*

	<b>Local</b>	<b>Distant</b>
<b>Colon</b>	<b>3-8%</b>	<b>90-95%</b>
<b>Rectal</b>	<b>20-40%</b>	<b>80-95%</b>



## ***Goal of Adjuvant (Post-Surgical) Therapy***

- ◆ **Elimination of microscopic metastases**
- ◆ **Increase chance of surgical cure**



# *Adjuvant Therapy: Colon Cancer*

- ◆ Stage III (+ lymph nodes)
- ◆ High risk stage II (clear lymph nodes) **BUT**
  - ◆ obstruction
  - ◆ perforation
  - ◆ < 6 nodes sampled

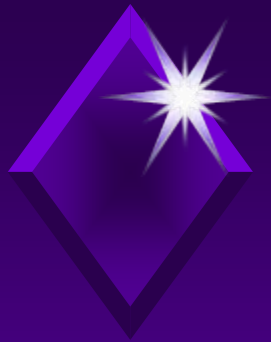


## ***Standard Since 1990: FUFA***

- ◆ 2 drugs given daily x 5 days; once a month x 6 months

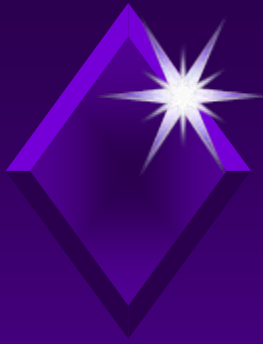
FUFA    |||||    |||||    |||||    |||||    |||||    |||||

- ◆ 40% relative risk reduction for recurrence
- ◆ 33% relative risk reduction for death



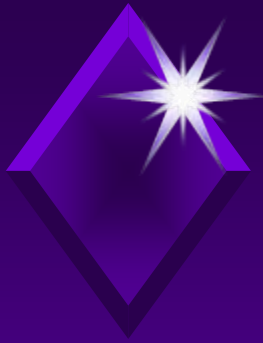
# ***New Adjuvant Options***

- ◆ **Capecitabine x 6 months**
- ◆ **FUFA + Oxaliplatin**

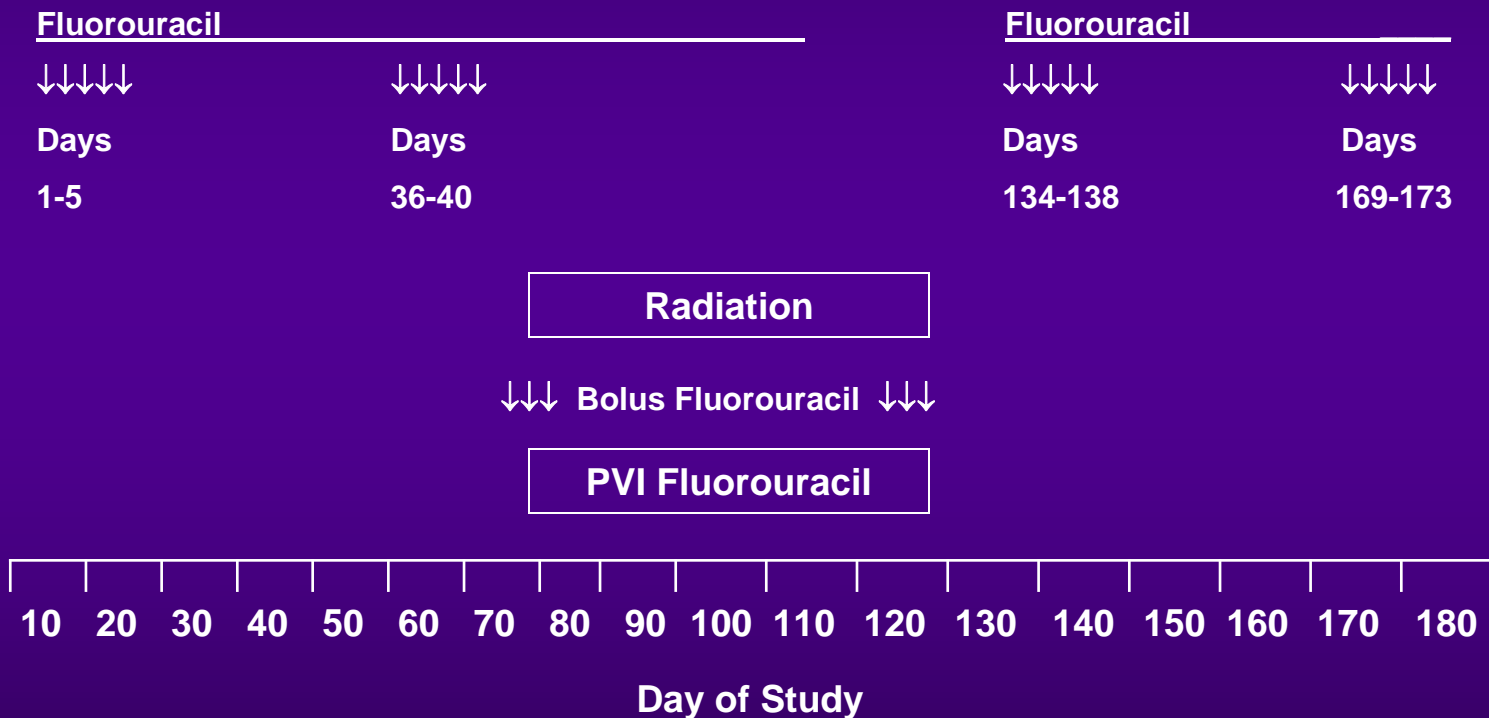


# ***Adjuvant Therapy: Rectal Cancer***

- ◆ **Stage III (+ lymph nodes)**
- ◆ **Stage II (disease penetrating through full wall of rectum, clear lymph nodes)**



# Schedule of Chemotherapy and Radiation Therapy for Rectal Cancer

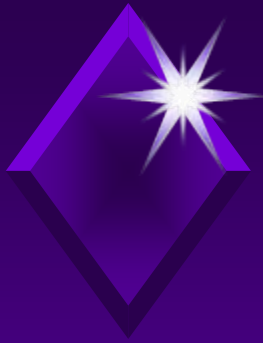


Bolus denotes the administration of fluorouracil by rapid intravenous injection and PVI its administration by protracted venous infusion. Fluorouracil was given in a dose of 500 mg per square meter of body-surface area on days 1-5 and days 36-40, and 450 mg per square meter on days 134-138 and days 169-173. Semustine was given in a dose of 130 mg per square meter on day 1; and 100 mg per square meter on day 134. Radiation therapy began on day 64; the total dose was 4500 cGy. For other details of therapy, see the Methods section.



## *Progress in Adjuvant Therapy of Rectal Cancer: 5-Year Survival (in %) on NCCTG Studies*

<b>Study</b>	<b>79A</b>	<b>79B</b>	<b>86A</b>	<b>86B</b>	<b>86C</b>	<b>86D</b>
Regimen MAC Stage	<b>RT</b>	<b>RT + FU, Me</b>	<b>RT + Bolus 5-FU, Me</b>	<b>RT + PVI 5-FU, Me</b>	<b>RT + Bolus 5-FU</b>	<b>RT + PVI 5-FU</b>
<b>B + C</b>	<b>48.0</b>	<b>56.5</b>	<b>51.7</b>	<b>63.9</b>	<b>56.5</b>	<b>64.3</b>
<b>B</b>	<b>63.6</b>	<b>68.8</b>	<b>56.3</b>	<b>80.8</b>	<b>70.3</b>	<b>83.4</b>
<b>C</b>	<b>40.3</b>	<b>50.0</b>	<b>50.3</b>	<b>58.9</b>	<b>52.0</b>	<b>58.4</b>



# ***Importance of Distinction Between Colon and Rectal Cancers***

- ◆ **Patterns of failure**
- ◆ **5-FU used as sole systemic therapy for rectal cancer; combined with leucovorin for colon cancer**
- ◆ **Radiation therapy is part of standard adjuvant therapy for rectal cancer; not for colon cancer**
- ◆ **Protracted venous infusion of 5-FU is part of standard adjuvant therapy for rectal cancer, not for colon cancer**
- ◆ **Adjuvant therapy recommended for all T<sub>3</sub> lesions in rectal cancer, even if node negative**
- ◆ **Adjuvant therapy for colon cancer largely restricted to node positive disease**



## ***New Options***

- ◆ **Pre-operative radiotherapy**
- ◆ **Capecitabine instead of 5-FU**
- ◆ **New drugs**



# ***Improvements 1990 → 2005***

	<b>Incidence</b>	<b>Mortality</b>
<b>Males</b>	<b>-1.4%</b>	<b>-13.3%</b>
<b>Females</b>	<b>-9.4%</b>	<b>-20.7%</b>

CCS 2005.



# ***Advances in Metastatic Disease***

## Median Survivals

**FUFA (1980-2000)**

**~ 10-12m**

**IFL (Irinotecan – 2000-)**

**~ 15m**

**FOLFIRI ↔ FOLFOX (2004-)**

**~ 21m**

**IFL + Bevacizumab (2004-)**

**~ 20m**

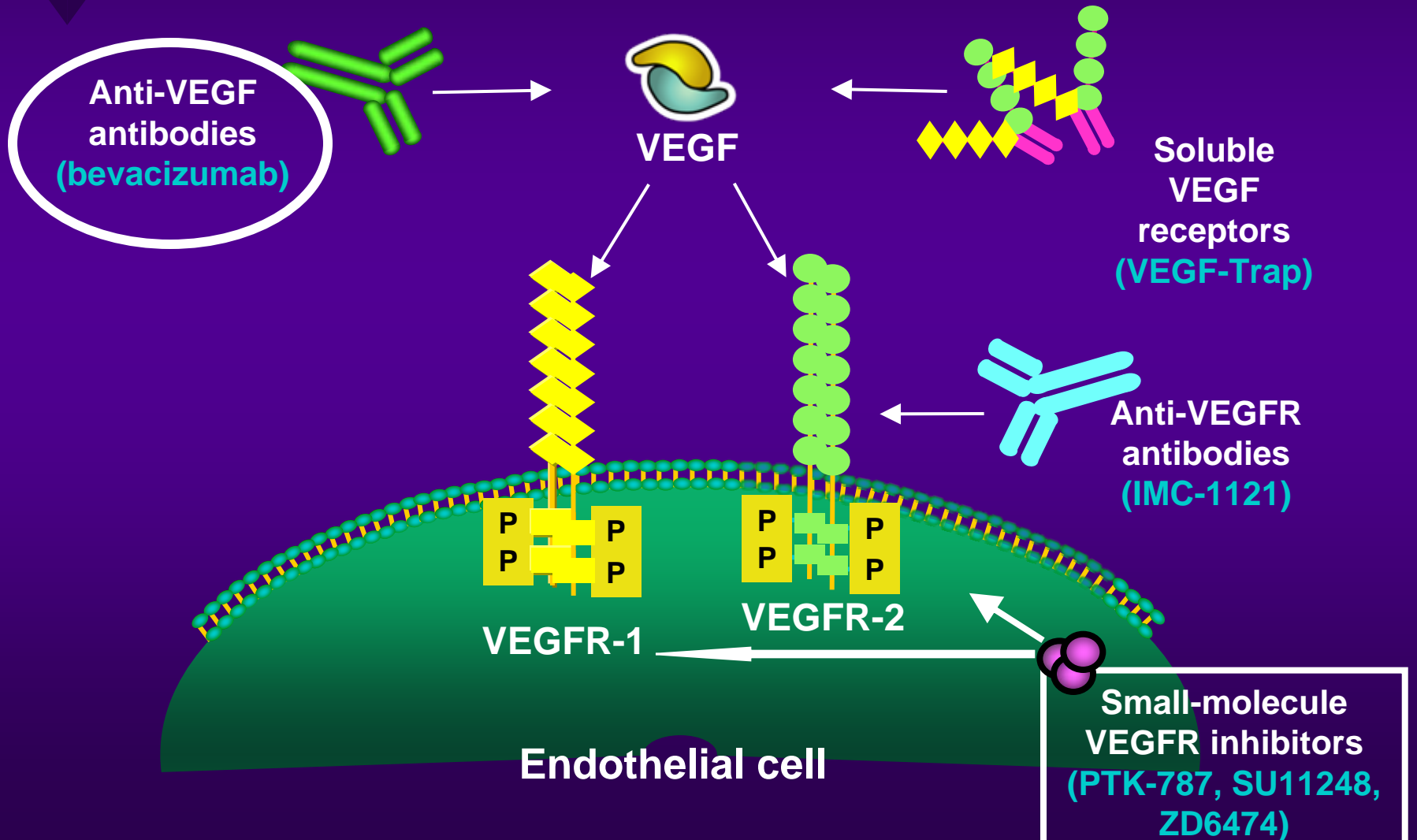
**vs.**



# ***Bevacizumab and VEGF***

- ◆ **Monoclonal antibody to the VEGF antigen**
- ◆ **VEGF: naturally occurring molecule promoting blood vessel growth (angiogenesis)**
- ◆ **Blocking VEGF reduces new blood vessel formation and inhibits cancer growth**

# Agents Targeting the VEGF Pathway





# *Targeted Therapy for Breast and Colon Cancer*

	RR	OS
<b>CTX</b>	<b>36%</b>	<b>20.9m</b>
<b>CTX + H</b>	<b>62%</b>	<b>25.4m</b>
<b>CTX</b>	<b>35%</b>	<b>15.6m</b>
<b>CTX + A</b>	<b>45%</b>	<b>20.3m</b>

Hurwitz et al. NEJM 2004.

Slamon D et al. NEJM.



***BUT ...***

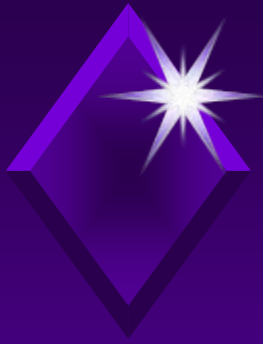
- ◆ **More aggressive therapies potentially lead to increased toxicities**
- ◆ **Most cases of metastatic colorectal cancer are incurable**
- ◆ **Treatment goals are palliative**



# ***Palliative Equation***

- ◆ **Minimization of treatment-induced toxicity and disease-related morbidity =**

**Prolongation of  
Good Quality Survival**



# ***New Barriers to Access for Novel Therapies***

- ◆ **Pharmaceutical company practices**
  - ◆ i.e.: Oxaliplatin
- ◆ **Cost**
  - ◆ typical course of Avastin: **\$35,000**
- ◆ **Government**