大腸直腸癌防治介紹

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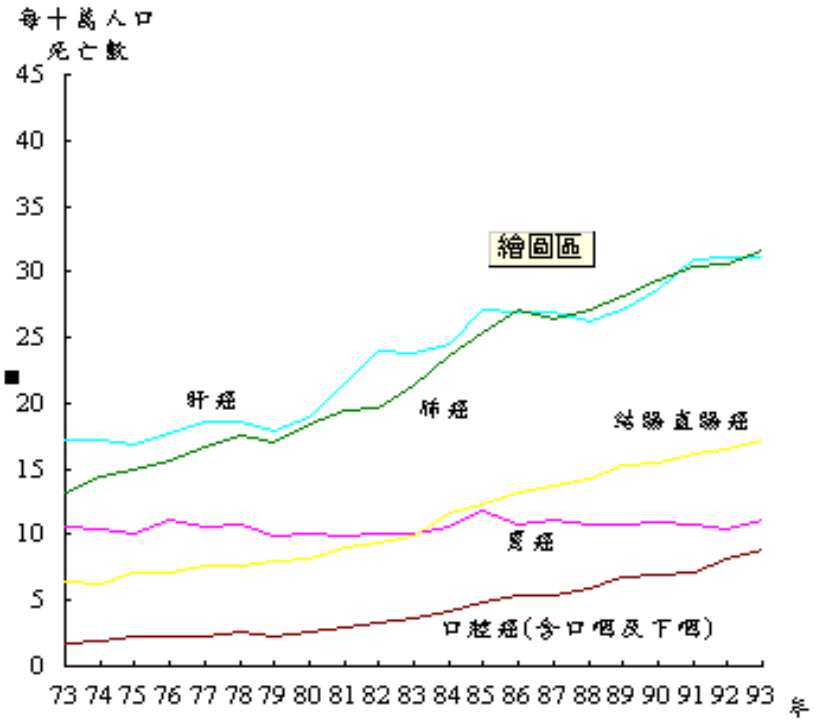
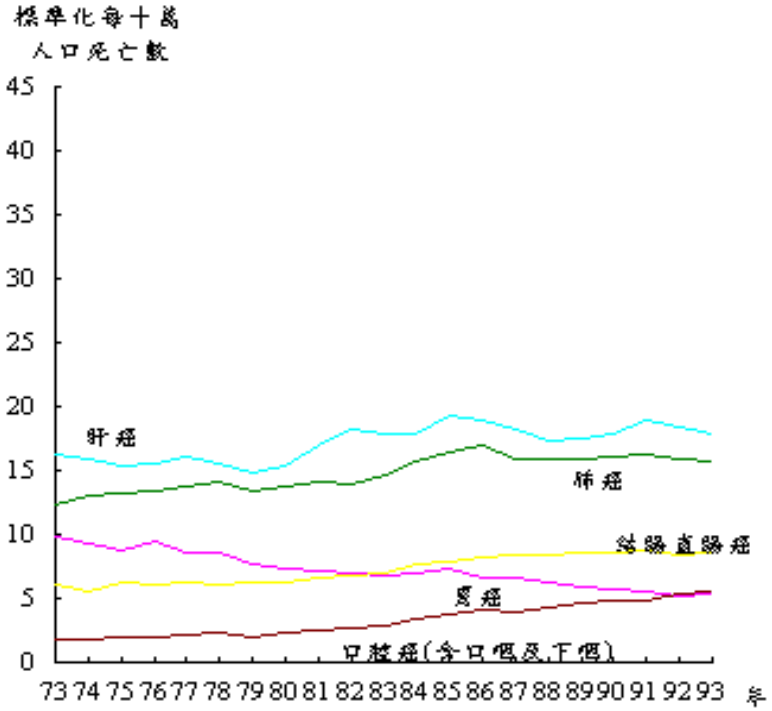
臺灣地區主要癌症死亡率趨勢圖

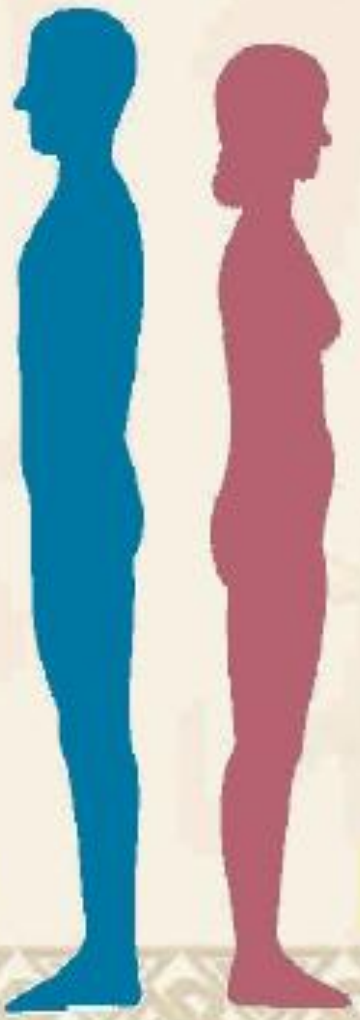




註：標準化死亡率係以民國七十年臺灣地區男性年中人口年齡結構為基準。

台灣男女性10大癌症發生分率，民國95年

男性		女性	
(7,167人)肝	17%	22%	乳房 (6,895人)
(5,793人)結腸及直腸	14%	14%	結腸及直腸(4,455人)
(5,756人)肺	14%	9%	肝(2,925人)
(4,879人)口腔	12%	10%	肺(2,992人)
(3,073人)攝護腺	7%	6%	子宮頸(1,828人)
(2,455人)胃	6%	4%	胃(1,339人)
(1,624人)食道	4%	4%	甲狀腺(1,257人)
(1,406人)膀胱	3%	4%	子宮體(1,159人)
(1,328人)皮膚	3%	4%	皮膚(1,129人)
(1,116人)鼻咽	3%	3%	卵巢(1,000人)
(7,420人)其他癌症	17%	20%	其他癌症(6,297人)
男性共42,017人		女性共31,276人	



註：口腔癌含下咽及口咽

General consideration

- Originate from epithelium
- Anatomy:Rectosigmoid
- Colorectal malignancy

  Adenocarcinoma 95%

  Carcinoid

  GISTs

  Lymphoma

Epidemiology

- Second leading cause of cancer death in America and England, third in Taiwan
- Prevalence:20/100,000
- Gender:male>female in rectal cancer, equal in colon cancer
- Etiology: Genetics and Environmental

  1.First degree relative

  2.HNPCC/FAP

  3.Diet

RISK FACTORS

1.Family history
2.Familial adenomatous polyposis;FAP/HNPCC
3.History of CRC
4.History of colorectal polyps
5.Age
6.Inflammatory bowel disease;IBD
7.Diet
8.Exercise
9.Hormone
10.Others

Natural course of untreated FAP patients

- Age of appearance of adenomas 25 y/o
- Age of onset of symptoms 33 y/o
- Age of diagnosis of adenomas 36 y/o
- Age of diagnosis of carcinoma 39 y/o
- Age of death from carcinoma 42 y/o

Amsterdam criteria for HNPCC

- At least three relatives with histologically verified colorectal cancer, one of which is a first-degree relative of another
- Involvement of at least two generations
- At least one colorectal cancer diagnosed before the age of 50 years

Pathogenesis

Multifactorial

Fearon ER and Vogelstein B 1990

*Mutational activation is initiated by oncogenes (c-myc, ras----etc)

*Mutational inactivation of multiple suppressor genes (p53, DCC, MCC---etc)

*Normal epithelium→Epithelial transposition→Polyp(Adenoma)→Carci-noma in situ→Invasive cancer

Symptomatology

1.Bowel habit change

2.Rectal bleeding

3.Tenesmus

4.Mucoid diarrhea

5.Small caliber stool

6.Abdominal pain and abdominal mass

7.Anemia

8.Poor appetite and body weight loss

Diagnosis

1.Rectal digital examination

2.Rigid proctoscopy

3.Flexible sigmoidoscopy

4.Colonoscopy

5.Barium enema examination

6.Tumor marker(CEA)

7.Sonography, CT scan, MRI

Role of CEA

1. Useful for early diagnosis?
2. Useful for prognosis?
3. Useful to detect recurrence?
4. Can second-look operation be based on CEA?
5. Useful to follow treatment response?
6. Non-malignant condition?

Useful for early diagnosis?

No. Few patients (5%) with localized disease have elevated levels

Useful for prognosis?

Yes. Higher levels have poorer prognosis.

Useful to detect recurrence?

Yes. 67-79% of patients have elevated serum levels prior to or at the time of recurrence.

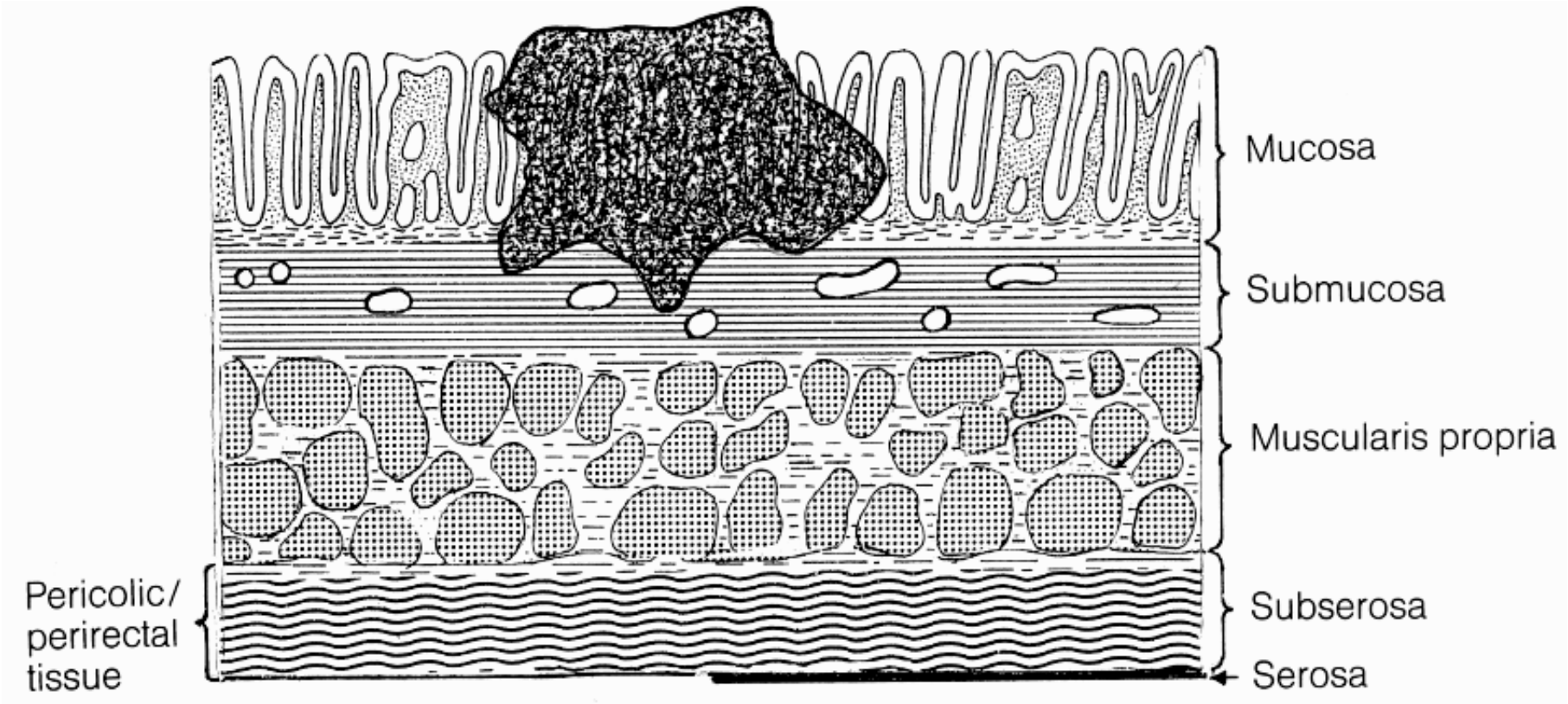
Useful to follow treatment response?

Yes. In 90% of patients, serum CEA levels accurately reflect disease progression or regression.

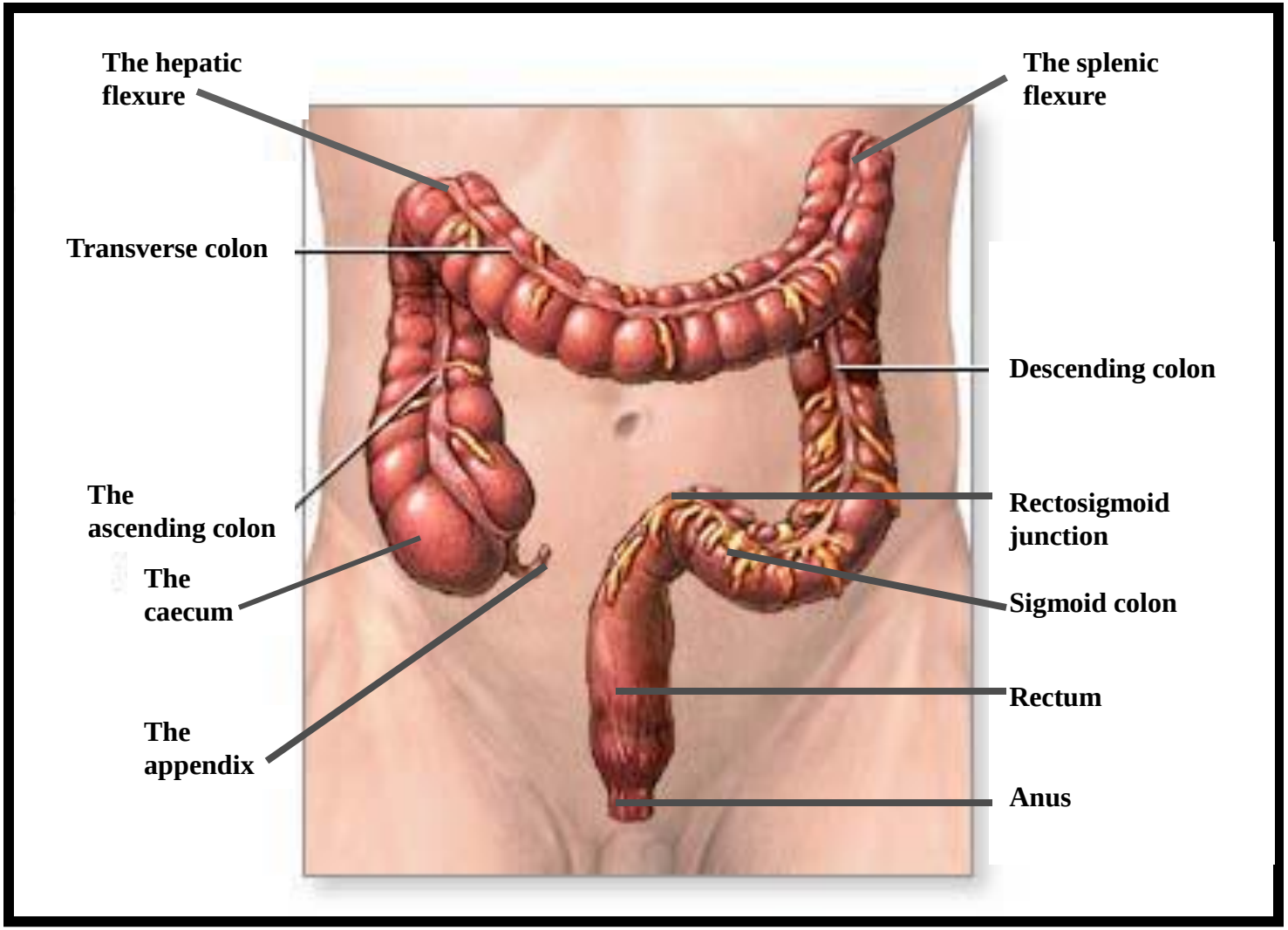
Staging of colorectal cancer

1. Dukes classification
2. Astler-Coller classification
3. TNM system
4. AJCC/UICC system

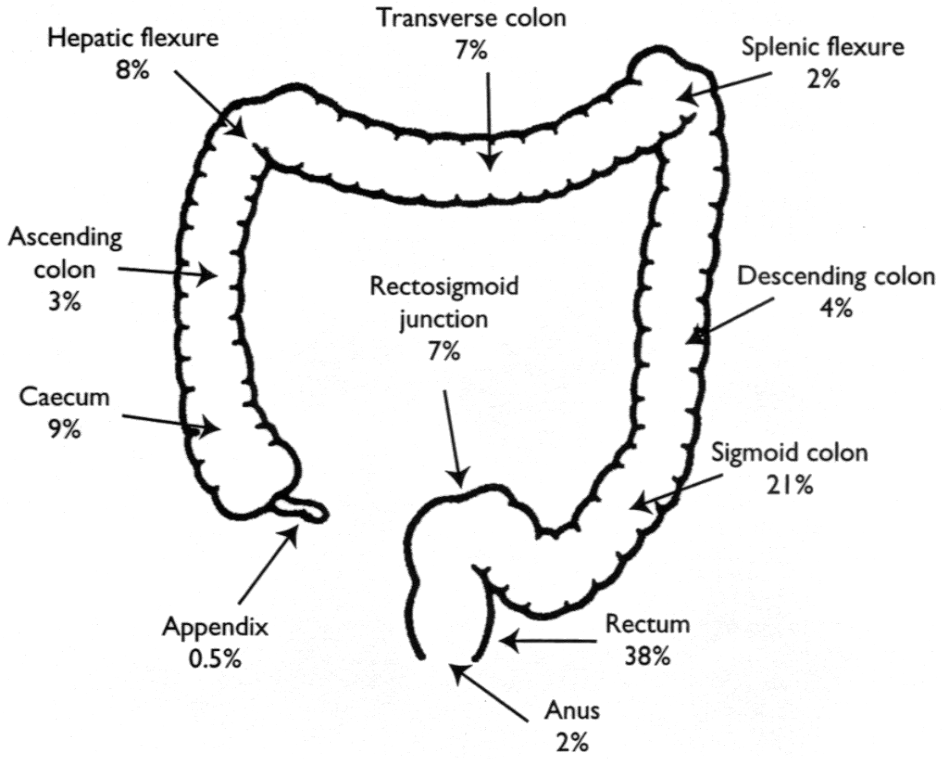
DIAGRAM TO SHOW THE VARIOUS LAYERS OF THE WALL OF THE LARGE INTESTINE



THE LARGE INTESTINE



TOPOGRAPHY AND MORPHOLOGY OF COLORECTAL CANCER



The subdivisions of the large intestine, showing the percentage of all intestinal tumours that occur at each site

Most colorectal malignancies arise in the membrane lining the bowel wall. As this is glandular tissue the majority of tumours are:

- **ADENOCARCINOMAS**
  - **Mucin secreting >80%**
  - **Mucinous 15%**
  - **Signet ring cell 2%**
- **CARCINOIDS (<1%)**
  Arising from neuroendocrine cells
- **MALIGNANT LYMPHOMA (<1%)**

Tumours may also arise in the muscle wall of the intestine. They may be described as:

- **Gastrointestinal stromal tumours (GIST), which may be of uncertain malignancy (borderline), or invasive.**
- **Leiomyosarcoma, a malignant tumour of smooth muscle.**

PROGNOSTIC FACTORS FOR COLORECTAL CANCER

DUKES STAGE is the most widely accepted and used staging system for colorectal cancer. It was originally introduced as a pathological grade *(i.e. taken from the surgical specimen).*

- **DUKES STAGE A** **Tumour confined to bowel wall**
- **DUKES STAGE B** **Tumour penetrated bowel wall**
- **DUKES STAGE C** **Regional lymph nodes involved**

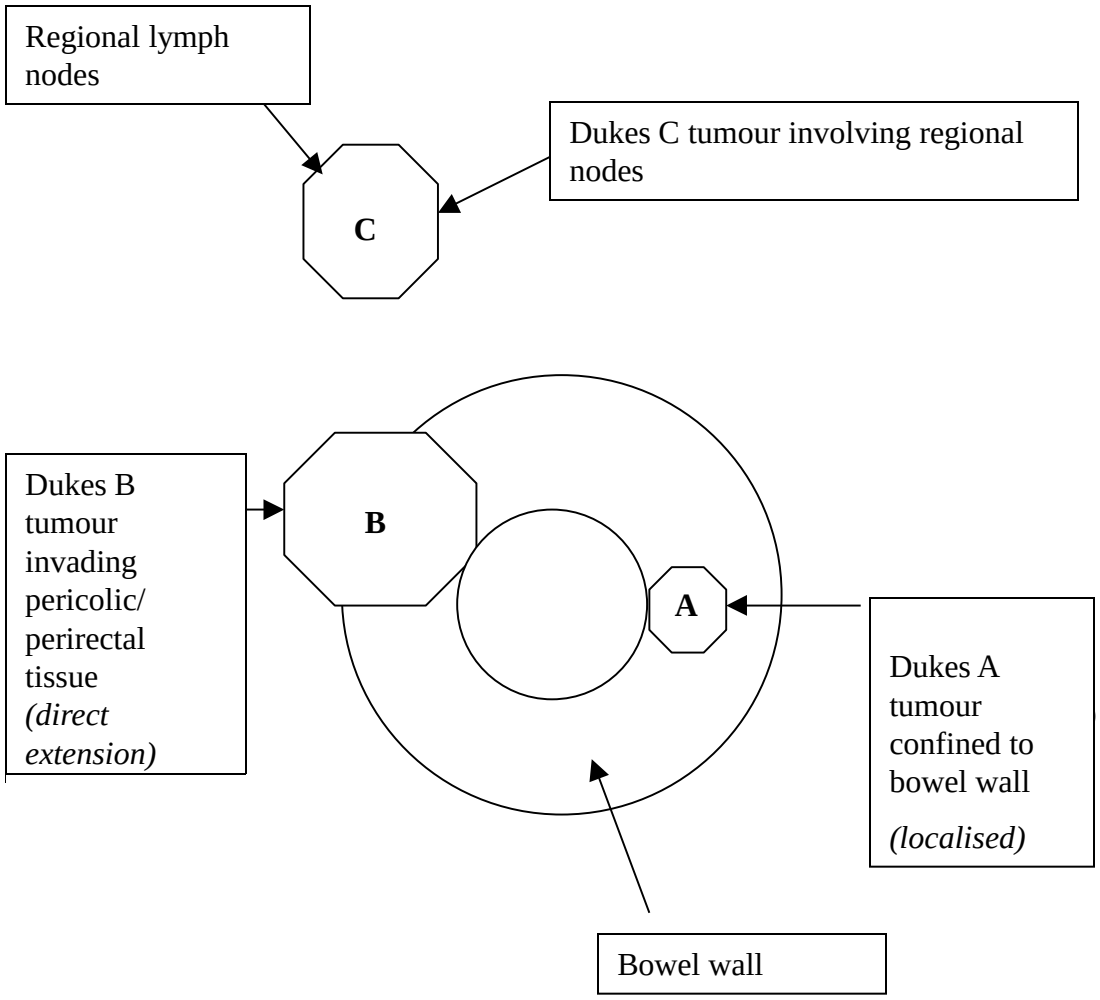
- **DUKES STAGE D has been added more recently to show that metastases are present.*(Not possible to tell this from a colectomy specimen)***

Stage B may be divided according to whether the tumour has just penetrated the outer surface of the bowel wall (B1) or the surrounding tissues are involved (B2), and stage C according to whether the apical nodes are involved (C2) or not (C1).

The ASTLER-COLLER system is based on Dukes but the values:
A, B1, B2, C1, C2, D1, D2 have slightly different definitions.

DUKES CLASSIFICATION OF COLORECTAL TUMOURS

Diagram



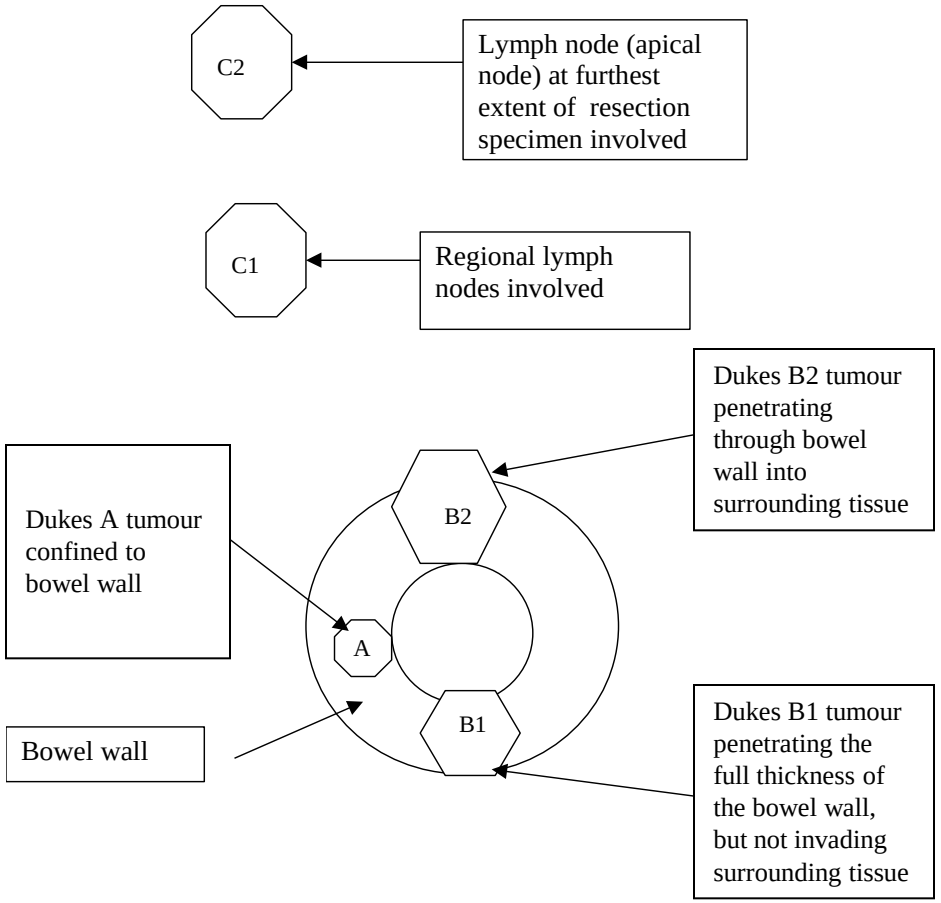
THE CANCER REGISTRY STAGING SYSTEM

Cancer registries use a simplified staging system for all tumour sites which indicates how far a tumour has spread at diagnosis:

- **LOCALISED - confined to the organ of origin.**
- **DIRECT EXTENSION - spread to tissue next to the organ of origin.**
- **REGIONAL LYMPH NODE INVOLVEMENT – lymph nodes nearest to the organ of origin involved.**
- **DISTANT METASTASES present – tumour cells have been carried to another part of the body via the blood stream, or to distant lymph nodes.**

Duke's B can be divided between B1, where the tumour has not penetrated beyond the bowel wall – localised disease, and B2 where it has – direct extension.

MODIFIED DUKES CLASSIFICATION OF COLORECTAL TUMOURS



OTHER PROGNOSTIC FACTORS FOR COLORECTAL CANCER

Other, more sophisticated staging and grading systems have been introduced, e.g. JASS, which deals with a number of different prognostic factors, but DUKES is the most important being the most widely accepted and used.

- **Classical STAGE is derived from UICC TNM has the following values:**

  stages 0, 1, 2A, 2B, 3A, 3B, 3C, 4

N.B. Cancer registries record how far the patient's tumour has spread (i.e. the tumour stage) AT DIAGNOSIS.

TNM cancer classification system

Primary tumor(T)

Tx Primary tumor cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma in situ

T1 Tumor invades submucosa

T2 Tumor invades muscularis propria

T3 Tumor invades through the muscularis propria into the subserosa or into nonperitonealized pericolic or perirectal tissue

T4 tumor perforates the visceral peritoneum or directly invades other organs or structures

TNM cancer classification system

Regional lymph node (N)

Nx Regional lymph nodes cannot be assessed

N0 No regional lymph nodes metastasis

N1 Metastasis to 1 to 3 pericolic or perirectal lymph nodes

N2 Metastasis to 4 or more pericolic or perirectal lymph nodes

N3 Metastasis to any lymph nodes along the course of a named vascular trunk

TNM cancer classification system

Distant metastases (M)

Mx Presence of distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis

The stage of the TNM system

Stage I : T1 or T2, N0, M0

Stage II : T3 or T4, N0, M0

Stage III: Any T, N1-N3, M0

Stage IV: Any T, Any N, M1

Treatment

Depends on preoperative evaluation and clinical presentations

1. Surgical treatment
2. Systemic chemotherapy
3. Radiation therapy

Complication of colorectal cancer

- Obstruction
- Perforation
- Bleeding
- Septicemia

Obstruction

- Carcinoma is the most common cause of large bowel obstruction, constributing to 60% of cases in the elderly
- Left colon
- Incidences range from 7% to 29%
- A nonspecific type of colitis may develop proximal to an obstructing carcinoma of the colon
- Diminished survival

Perforation

- Incidence is in the 6% to 12% range
- In conjunction with obstruction in about 1% of patients with colorectal carcinoma
- Site of perforation: carcinoma itself or cecum

Bleeding

- Bleeding is a very common symptom of colorectal carcinoma, but massive bleeding is an uncommon presentation

Septicemia

- With or without endocarditis, septicemia caused by Streptococcus bovis may be associated with an occult colonic malignancy
- All patients with endocarditis caused by S. bovis should be evaluated for concomitant colon cancer

Treatment Strategies

It's not just about chemotherapy

SCREENING:- prevention better than cure

SURGERY:- TME & rectal cancer; Liver resection

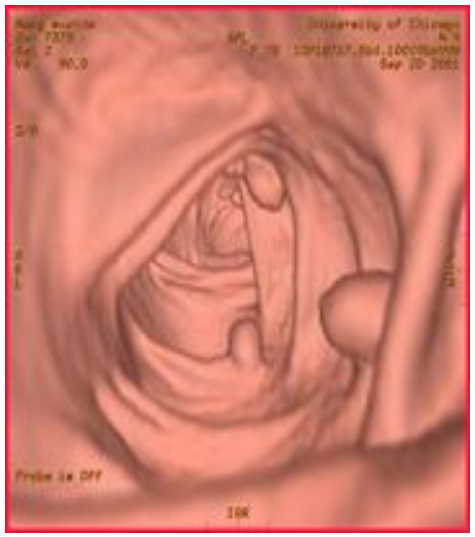
RADIOTHERAPY:- improvements in rectal cancer

CYTOTOXIC CHEMOTHERAPY :-
what to give, when and to whom

NOVEL AGENTS:- a new horizon but
can we afford it

TO BOLDLY GO

FOBT Screening



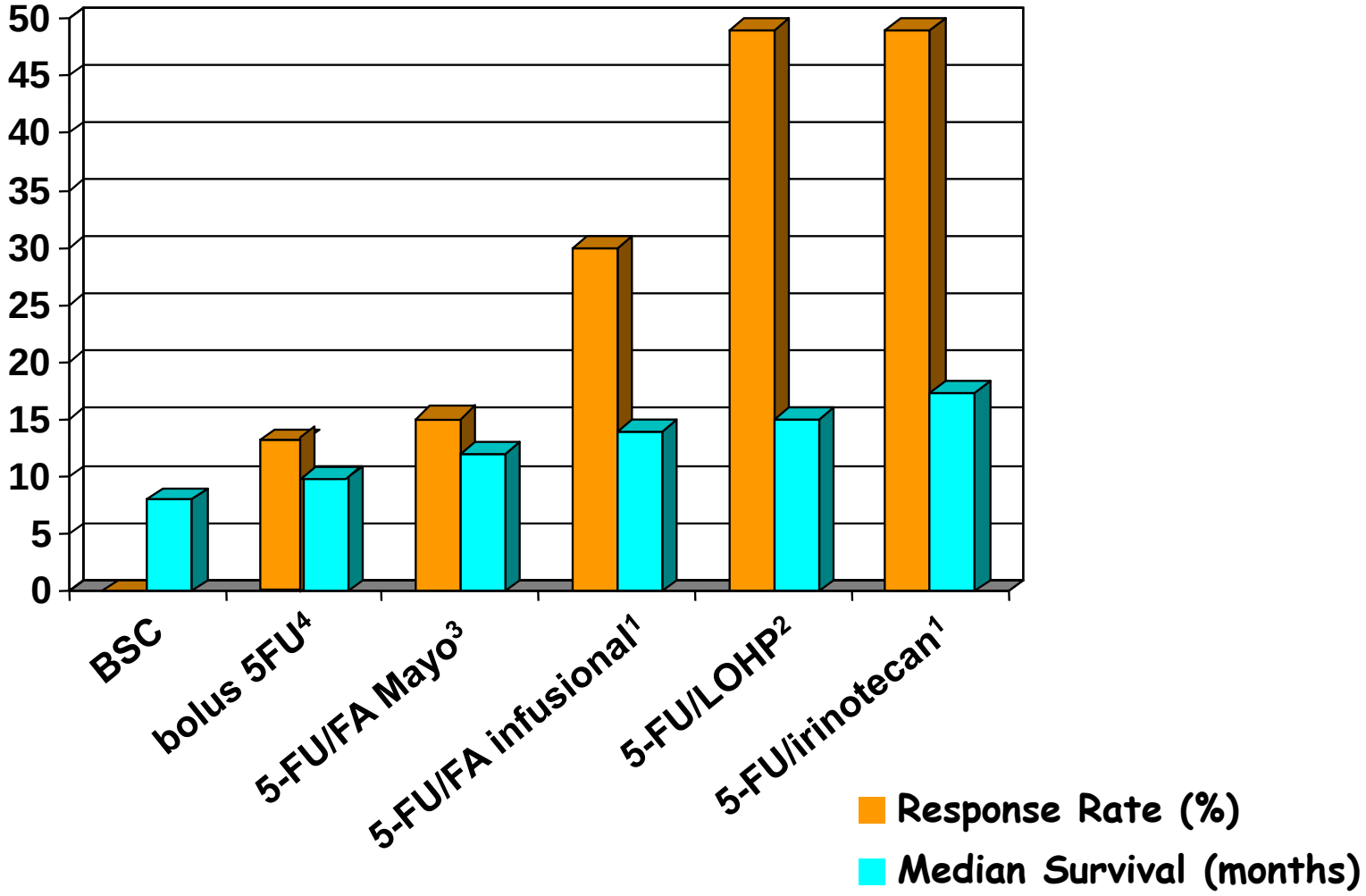
<u>化學法(gFOBT)</u>來偵測大便潛血 紅血球內含的酵素可以催化過氧化氫，進而產生氧化及顏色變化。Guaiac零陵香木試驗可偵測任何的血色素，包括動物血、藥物及某些水果蔬菜，因含有過氧化酶，因此會得到假陽性

<u>免疫化學方法(iFOBT)</u>來偵測血紅蛋白，它只對人類血紅素、球蛋白、及一些早期的分解物有反應，理論上應可達到較高的特異性。

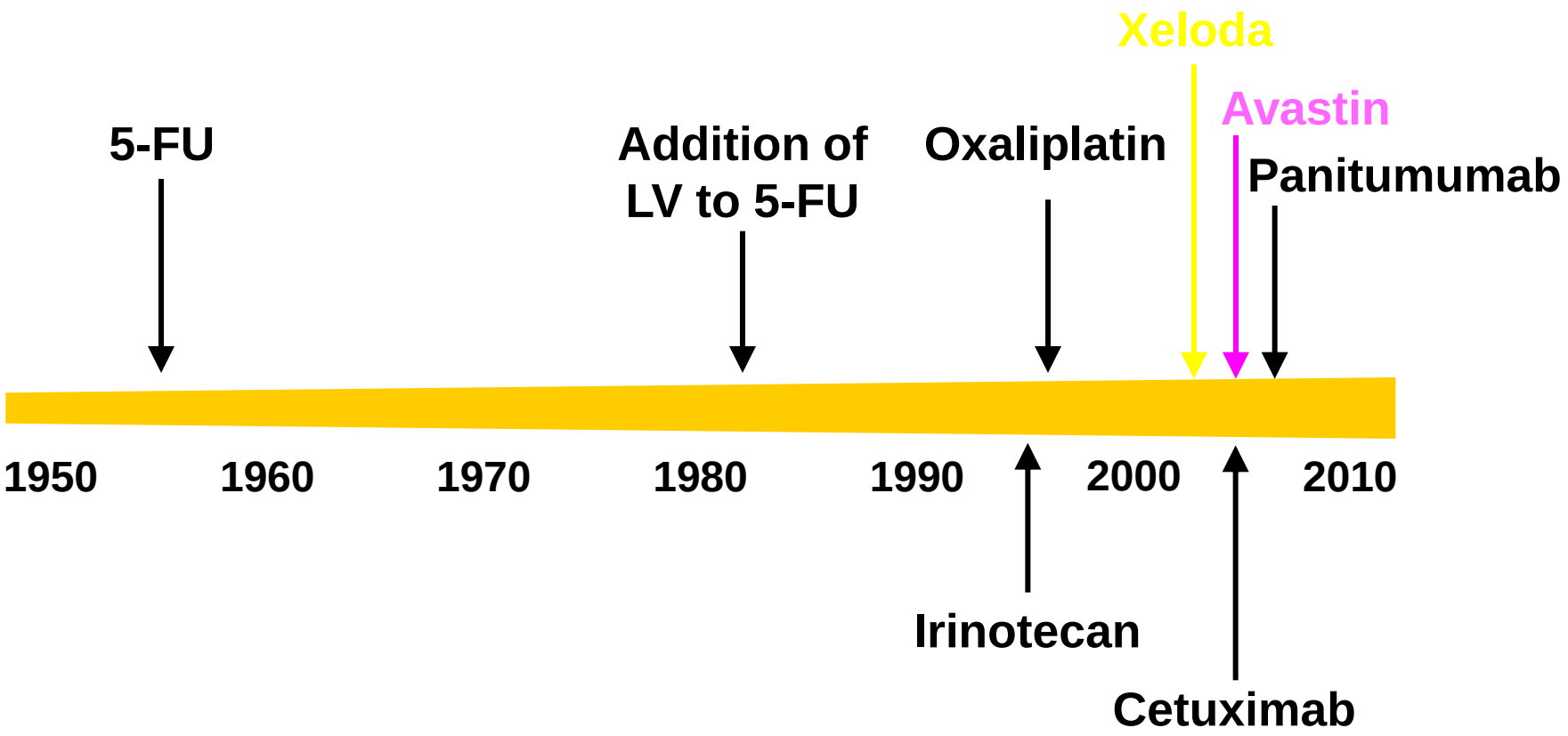
Terminology

* Monotherapy: oral, IV(bolus or infusional)
* Combination therapy
  1) Doublet: Folfox, Folfiri, Xelox, Xeliri
  2) Triplet : Folfoxiri
  3) Target therapy: Avastin+C/T or Erbitux+C/T
* Metronomic, Adjuvant, Neoadjuvant, Palliative, CCRT(concurrent chemoradiotherpay) etc.

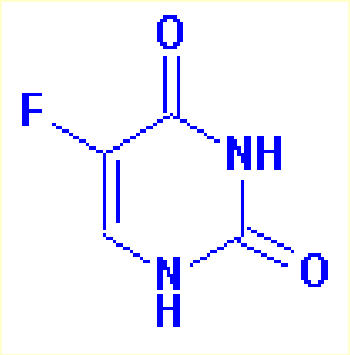
First line chemotherapy in CRC: the evolution of benefit



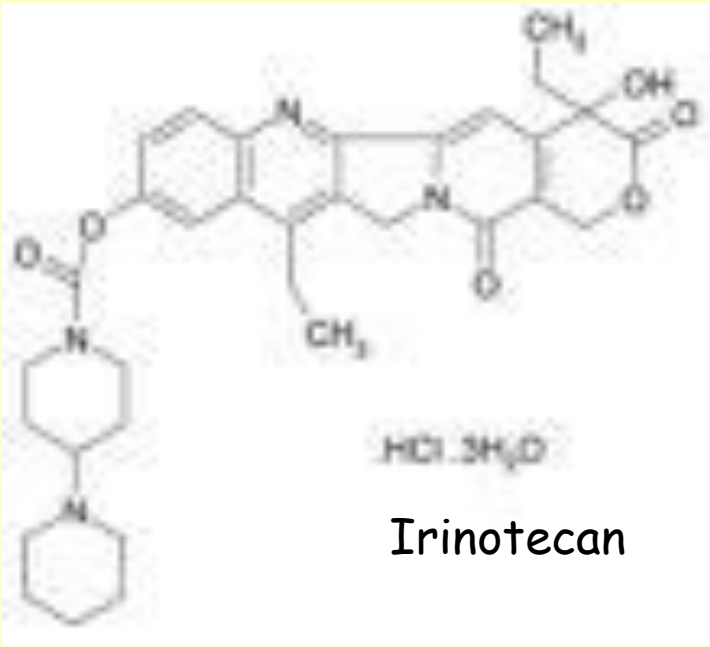
CRC treatment landscape

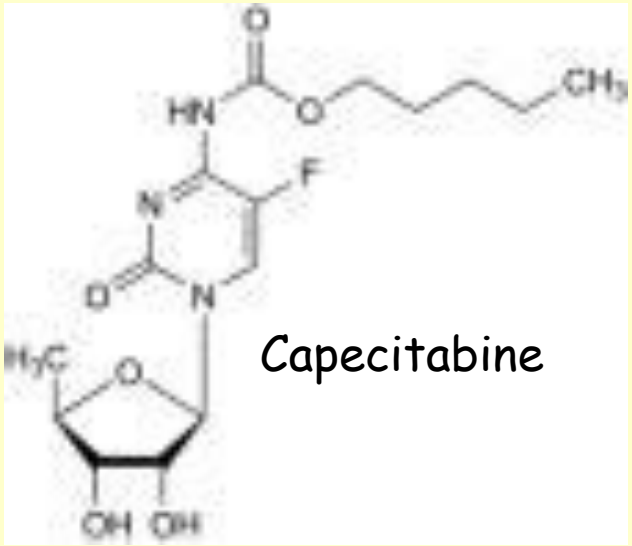


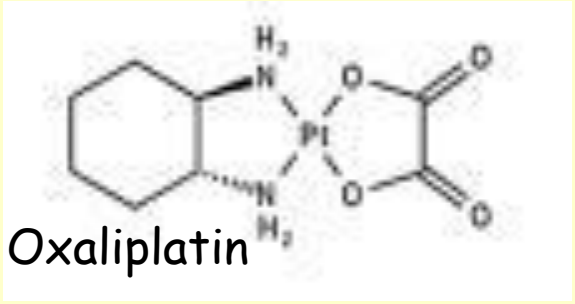
Active Cytotoxics in Colorectal Cancer



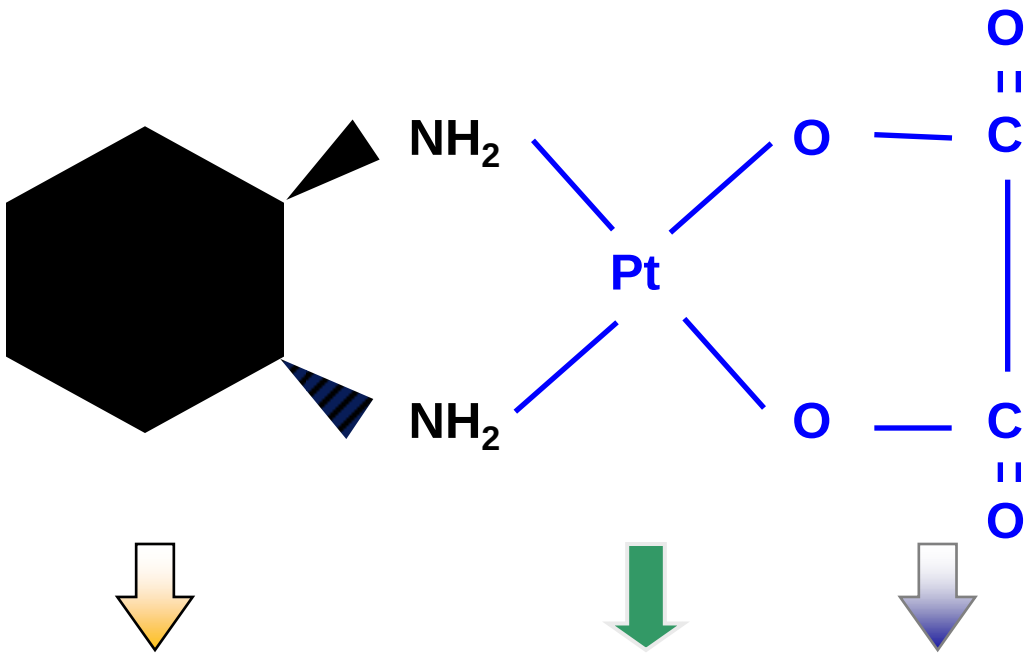
5 - Fluorouracil







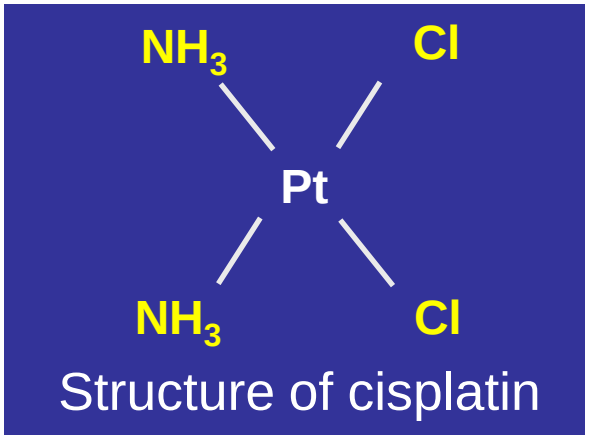
Oxaliplatin



DiAminoCycloHexane
DACH
carrier ligand

Platinum

Oxalate
hydrolysable
ligand



Structure of cisplatin

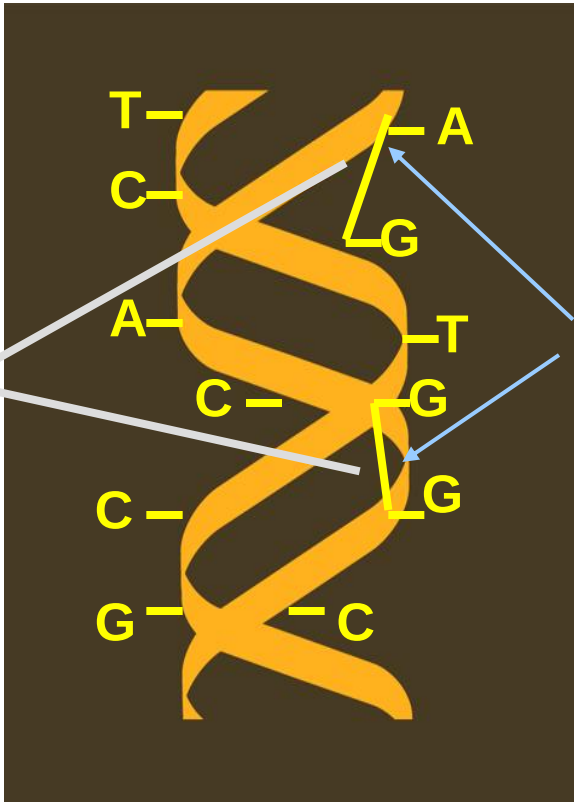
Oxaliplatin is a water soluble platinum derivative with an oxalate ligand and a 1, 2-diaminocyclohexane (DACH) carrier

trans-1-dach (1R, 2R-dach) oxalatoplatinum

Platinum Cytotoxicity

- **Formation of platinated inter- and intrastrand adducts,leading to inhibition of DNA synthesis**

Oxaliplatin

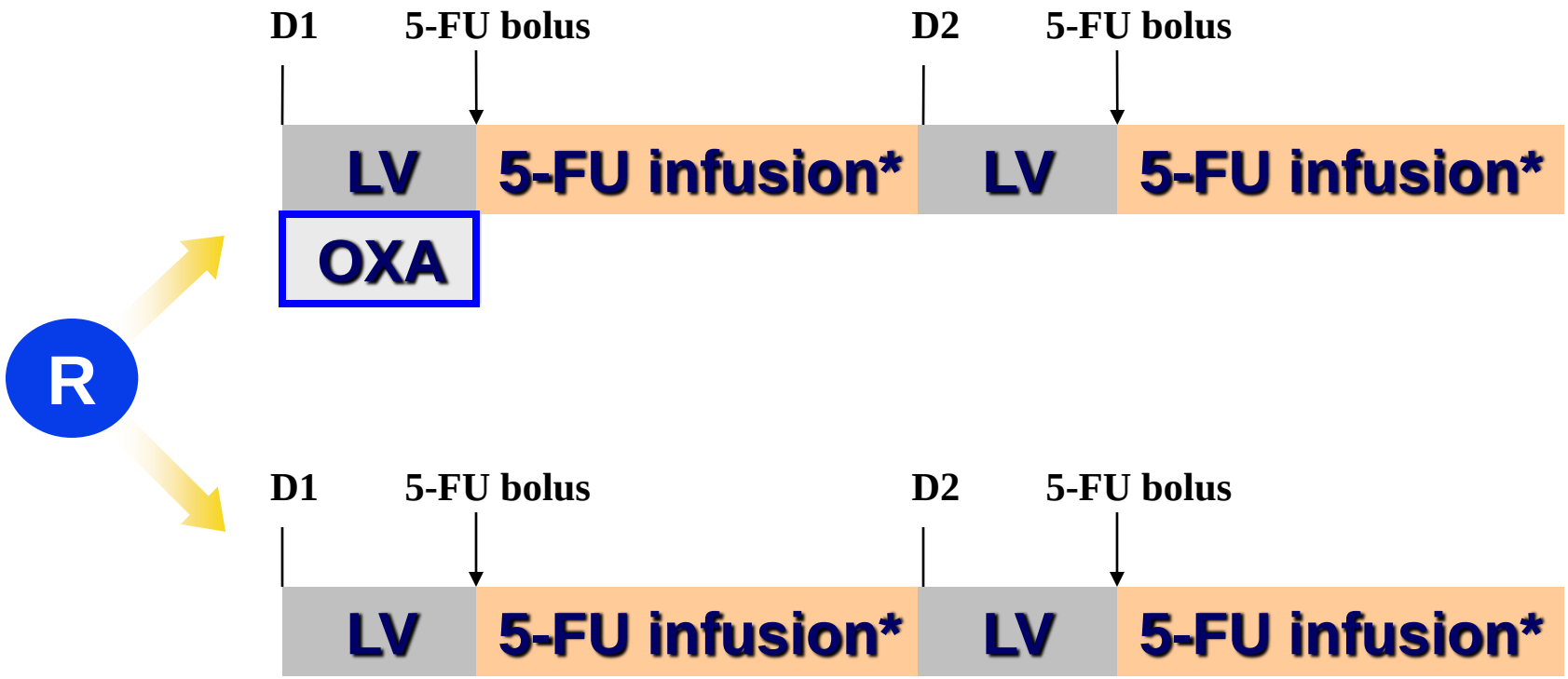


Platinated intrastrand adducts

. Cvitkovic, BJC 1998; 77 (suppl.4): 8-11

MOSAIC: Treatment arms

FOLFOX4: LV5FU2 + Oxaliplatin 85 mg/m2



Every 2 weeks, 6 months treatment (12 cy)

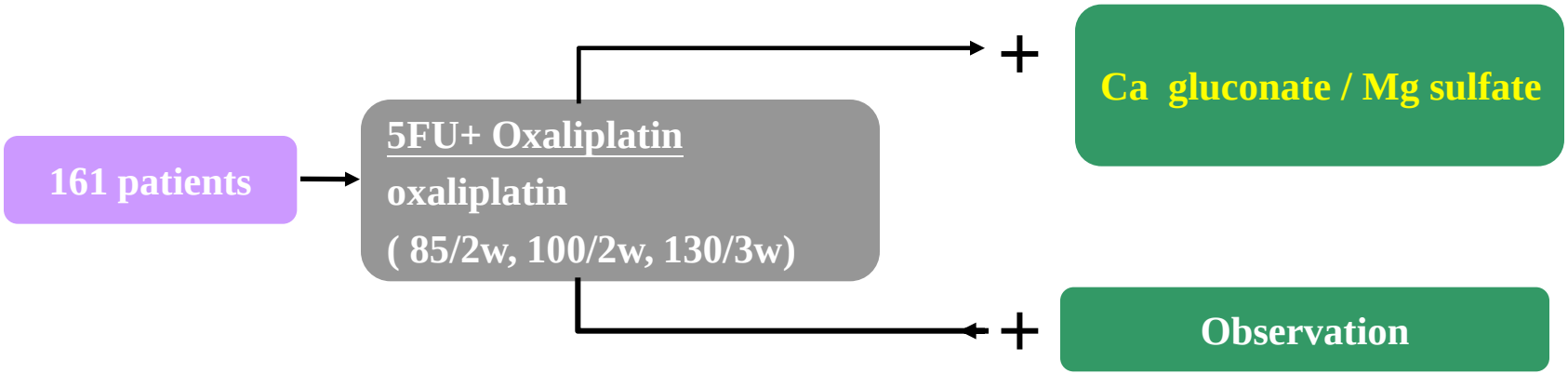
**Baxter LV5 infusors*

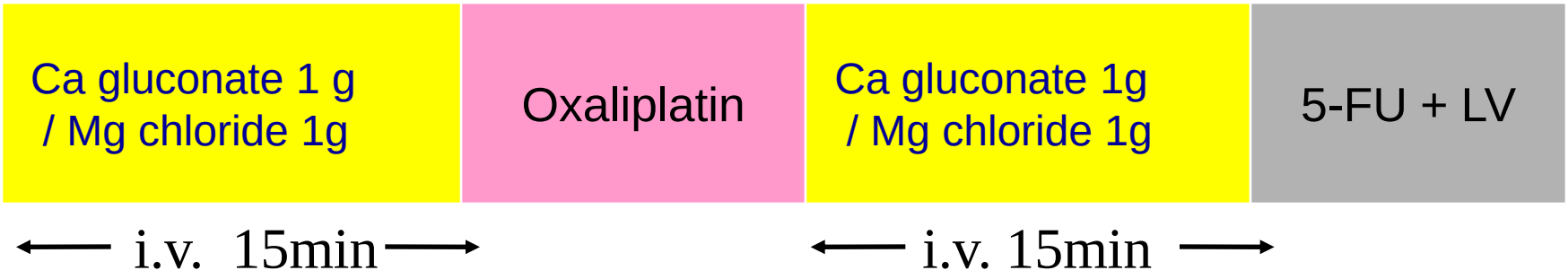
Neurotoxicity Grading

Gr 1.	P/D that do not interfere with function
Gr 2.	P/D interfering with function, but not ADL
Gr. 3	P/D with pain or interference with ADL
Gr. 4	Persistent PD that are disabling or life-threatening

Ca^{2+} / Mg^{2+}

Schema





Laurence Gamelin, Clin Can Res; 2004

CAMPTO® (irinotecan HCl) Prescription Information

CAMPTO® irinotecan

Irinotecan - Pharmacokinetics

- Irinotecan has a mean terminal elimination half-life of 6 to 12 hours
  - The mean terminal elimination half-life of the active metabolite SN-38 is 10 to 20 hours
- Over the recommended dose range (50 to 350 mg/m^2) the AUC of irinotecan increases linearly with dose
- Maximum concentrations of the active metabolite SN-38 are generally seen within 1 hour following a 90-minute infusion

Recommended Dosage and Administration

- In **combination therapy with 5FU and FA** (Folfiri regimen):
  - 150 -180 mg/m² administered once every 2 weeks as an intravenous infusion over a 90-minute period, followed by infusion with FA and 5-FU.

Important Considerations

- Both early and late forms of diarrhea can occur:
  - Late diarrhea should be managed promptly with loperamide and supportive care including antibiotics as needed.
- Use of a colony-stimulating factor may be considered in patients with significant neutropenia.

Oral Fluoropyrimidines

Strategies;

Prodrug activation within tumour cells: CAPECITABINE

Inhibition of 5FU metabolising enzymes to improve bioavailability

UFT (tegafur:uracil – 1:4);
S1 (tegafur, CDHP, oxonic acid)

Oral 5-FU in Adj Study:
NSABP C-06 and X-ACT

	NSABP C-06	X-ACT
Patients No.	1,608	1,987

Efficacy	UFT	5-FU	P value	Xeloda	5-FU	P value
3-yr DFS	74.5%	74.5%	NS	64.2%	60.6%	P=0.0528
3-yr RFS	-	-	-	65.5%	61.9%	P=0.0407
3-yr OS	85%	84%	NS	81.3%	77.6%	P=0.0706

NS= Not significant

N Engl J Med 352;26-30, 2005; J Clin Oncol 24:2059-2064 2006

Oral 5-FU in Adj Study:
NSABP C06 and X-ACT

	NSABP C-06		X-ACT	
G3/4 Toxicity	**UFT**	**5-FU**	**Xeloda**	**5-FU**
Granulocytopenia	1%	1%	NA	NA
Thrombocytopenia	<1%	<1%	NA	NA
Diarrhea	29%	28%	12%	14%
Stomatitis	1%	1%	1%	8%
HFS	0%	0%	18%	1%
N&V	<4%	3%	4%	3%

N Engl J Med 352;26-30, 2005; J Clin Oncol 24:2059-2064 2006

Safety of Tegafur/Uracil

Summary of Adverse Events with Tegafur/Uracil and 5-FU

Adverse Event	Tegadur/Uracil (n=21,762) 300-600mg/d		SWOG : 8904			
			5FU bolus (n=88) 500mg/m2/d x 5 q5w		5FU CI (n=85) 300mg/m2/d d1-28 q5w	
	No.	%	No.	%	No.	%
Diarrhea	390	1.8	43	49	26	31
Anorexia	957	4.4	NR		NR	
Nausea	597	2.7	NR		NR	
Stomatitis	119	0.6	44	50	40	47
Vomiting	301	1.4	27	31	24	28
Leukopenia	723	3.3	58	66	10	12
Granulocytopenia	29	0.1	58	66	7	8
Thrombocytopenia	240	1.1	23	26	4	5

J Clin Oncol 1998, 16:2877-85

Hand-foot syndrome

- 手足症候群

(Hand-Foot Syndrome)

手足症候群為最常見的Xeloda的副作用，特徵如下：

- 手、足部發紅，局部麻木感或感覺異常為第一級手足症候群。
- 出現疼痛性紅斑及手部、足部腫大，或影響到病患每日活動之不適感則定義為第二級。

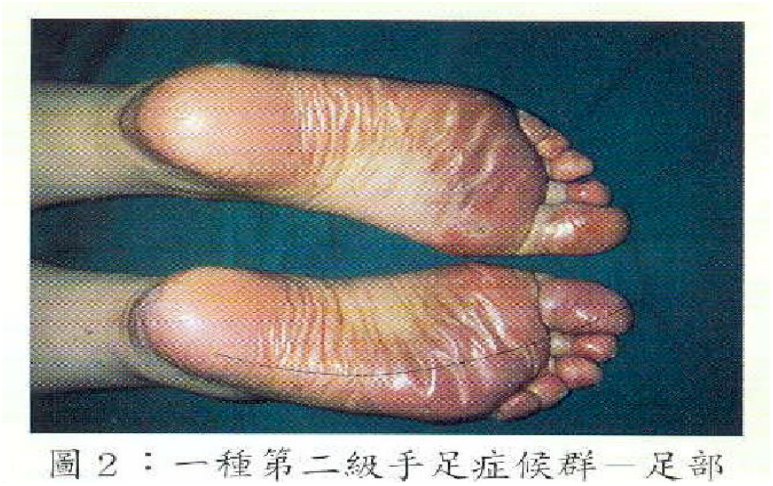


圖 2：一種第二級手足症候群—足部

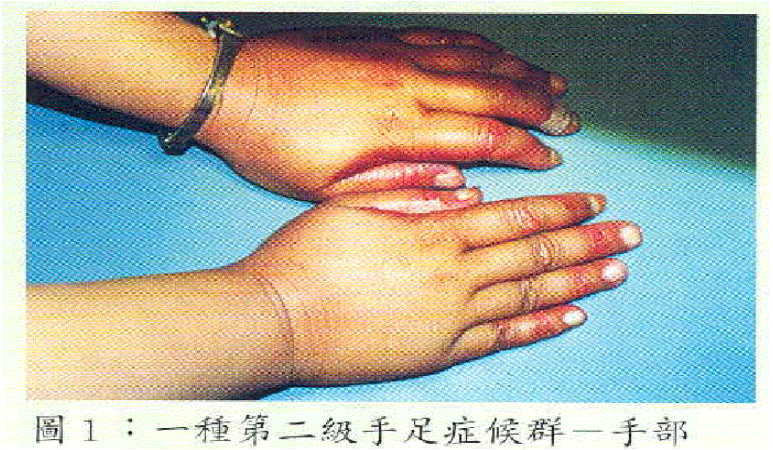


圖 1：一種第二級手足症候群—手部

Hand-foot syndrome

- 第三級手足症候群的定義為濕性脫屑、潰爛、起水泡及手或足部之嚴重疼痛，或造成病患無法工作或從事日常活動的嚴重不適感。

- 當發生第二級手足症候群時一定要先停藥，並請求醫師協助，直到恢復第一級或是完全正常，才可重新服藥 。如果這時候不先停藥，症狀一定會更嚴重，便成第三級的手足症候群.

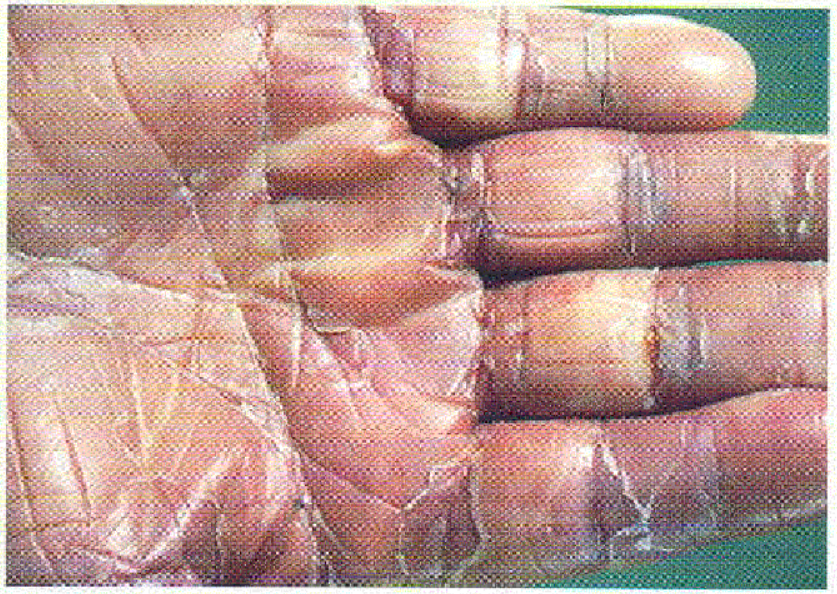
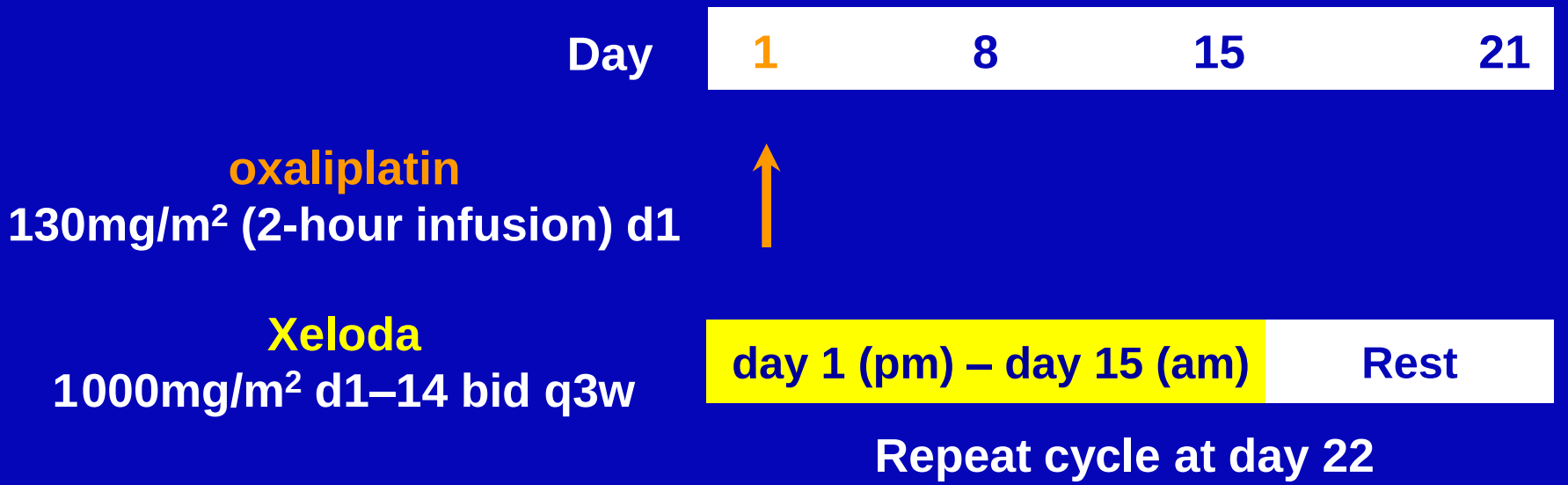


圖 3：一種第三級手足症候群

藥物健保給付規範

	UFUR/UFT	Xeloda
主成分	Tegafur-Uracil	Capecitanine
T1/2	7~13hr	45 minutes
Contraindication	Sorivudine, Phenytoin	Sorivudine, Phenytoin, Coumarin
健保給付價格	77/71	131
健保給付規範	3.大腸癌、結腸癌第Ⅱ、Ⅲ期患者之術後輔助性治療，且使用期限不得超過2年(94/10/1)	3.Xeloda可作為治療轉移性結腸直腸癌的第一線用藥 4. 第三期結腸癌患者手術後的輔助性療法，以八個療程為限（96/9/1)

XELOX Phase I study: recommended regimen in mCRC



- Grade 3/4 AEs: diarrhoea (26%), thrombocytopenia (22%), neutropenia (17%), paraesthesia (13%)
- ORR: 26%, response duration: 4.9 months

Díaz-Rubio et al. Ann Oncol 2002

Targeted Therapies

EGFR

Overexpression associated with poor prognosis in colorectal cancer

Strategies;
MAb binding to & innactivation of receptor
Small molecule inhibition of active TK site

ANGIOGENESIS

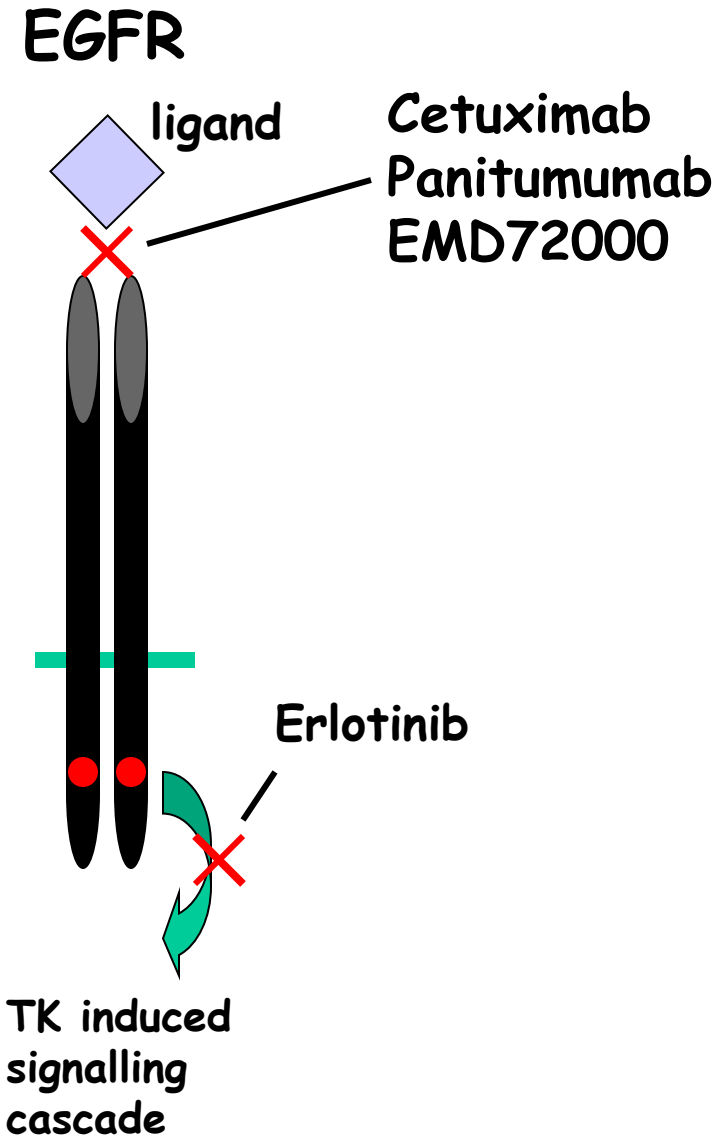
Microvessel density & VEGF expression correlate with worse prognosis in colorectal cancer.

Strategies;
MAb innactivators of ligands & receptors
Small molecule TKI

“Targeted” Therapy: Examples

Growth Factor Inhibitors:

- **Anti-EGFR (Epidermal Growth Factor Receptor)**
- **Anti-VEGF (Vascular Endothelial Growth Factor)**



CETUXIMAB

Chimeric IgG1 Mab for EGFR

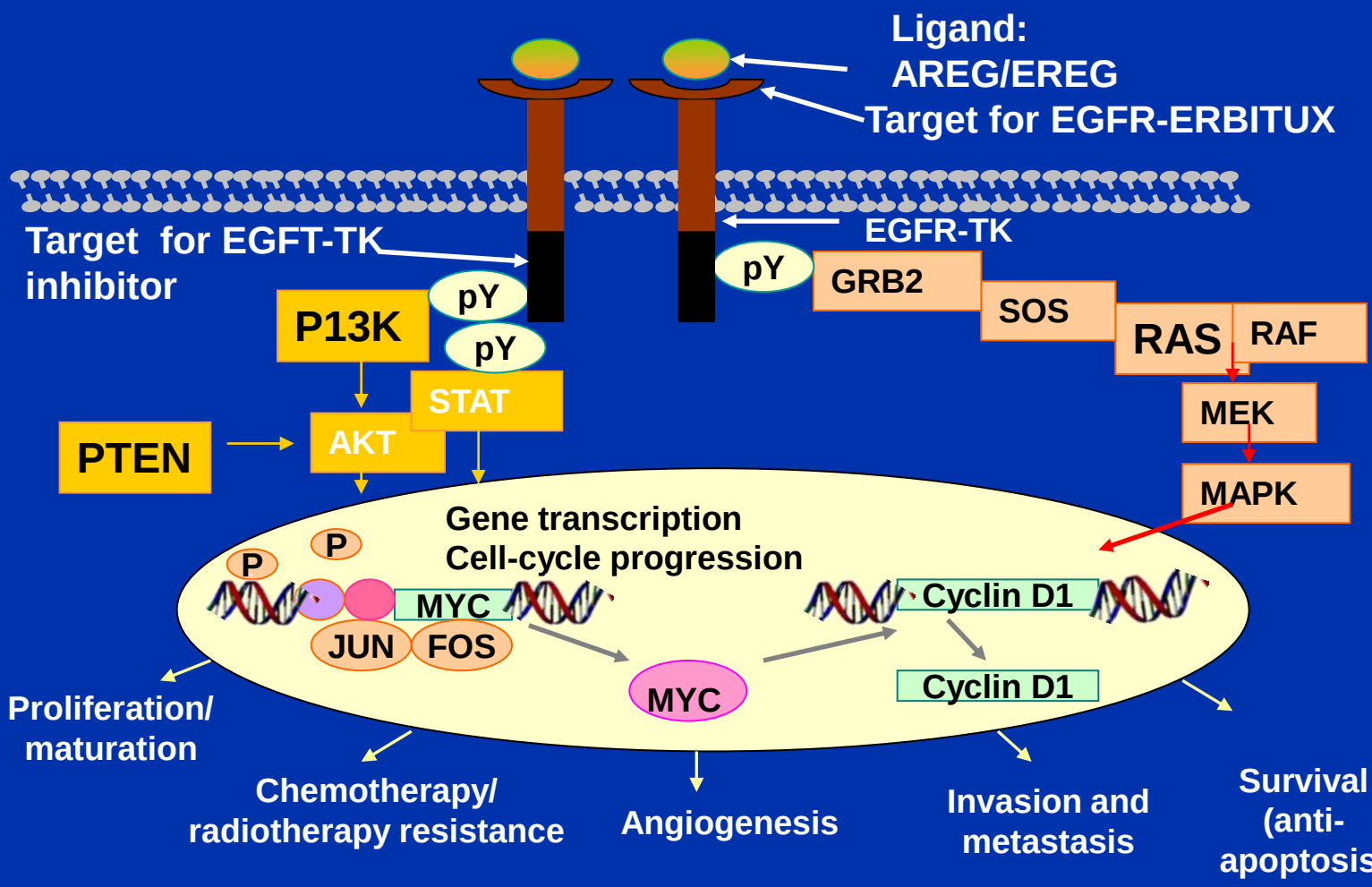
Phase II study data

BOND study;

≥1 prior regime
(Ir/5FU)
EGFR +ve

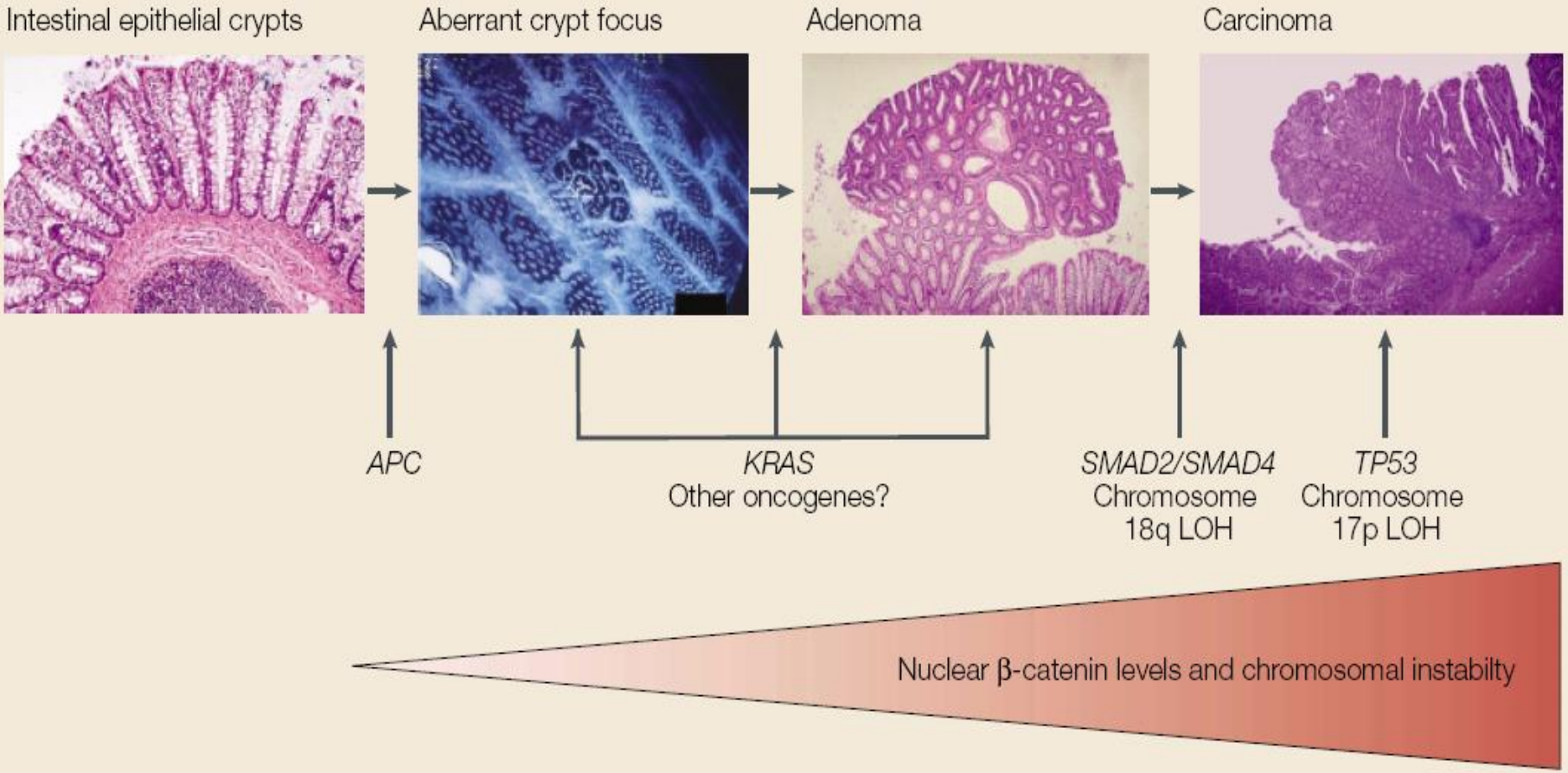
Cetuximab	Cetuximab + Irinotecan
(n=111)	(n=218)
OR – 10.8%	OR – 22.9%
mTTP = 1.5month	mTTP = 4.1month

EGF receptor signaling pathway: A rationale for personalized therapy



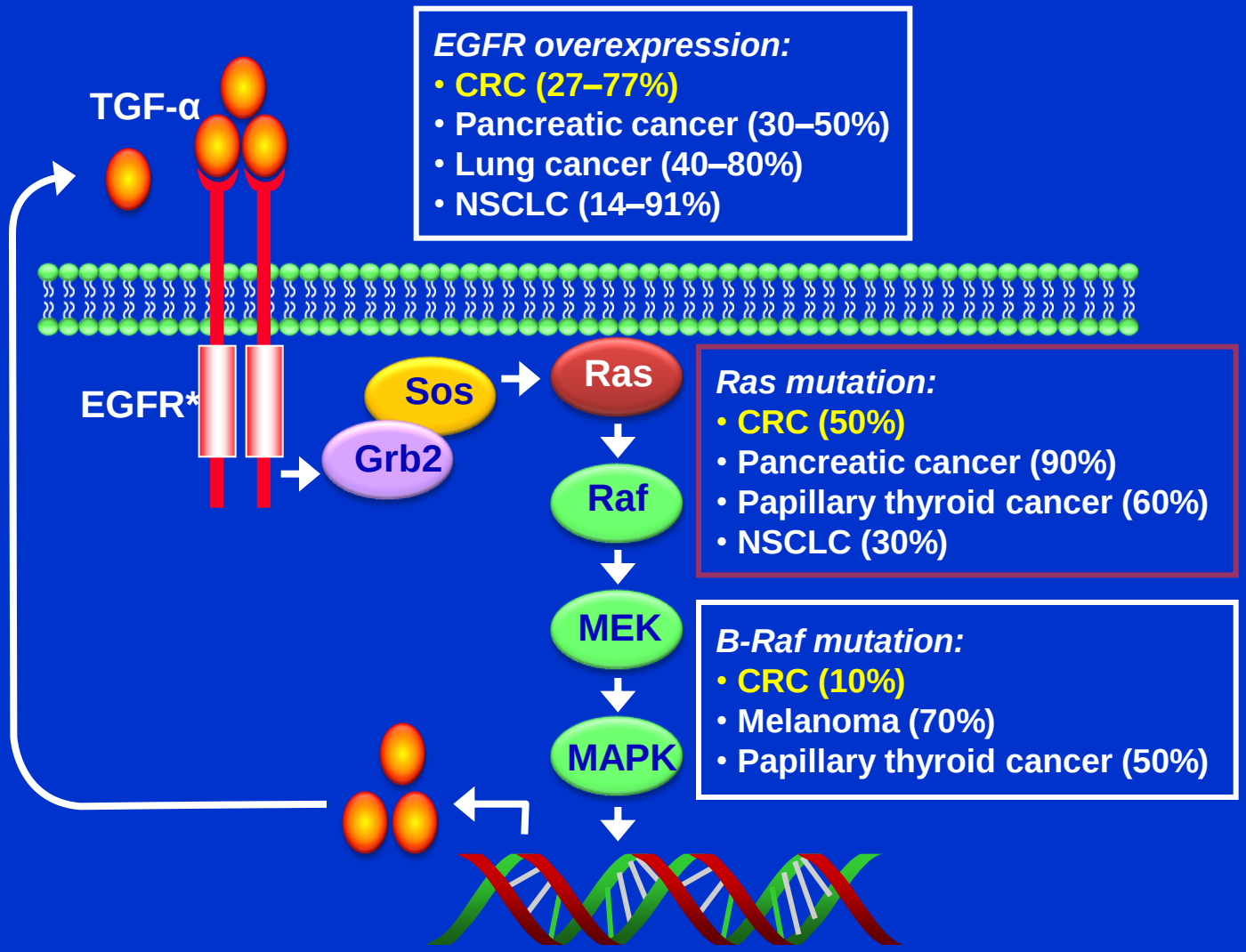
Yarden Y, Sliwkowski MX. Nat Rev Mol Cell Biol 2001;2:127–137; Chakravarti A, et al. Cancer Res 2002;62:4307–4315; Baselga J. Eur J Cancer 2001;37(Suppl. 4):S16–S22; Kawanaka H, et al. Life Sci 2001;69:3019–3033

KRAS mutations: Occur in 40% of colorectal cancer tumors – an early event



Fodde R, et al. Nature Rev Cancer 2001;1:55–67

Targeting the EGFR pathway: *K-Ras* mutations



Adapted from Roberts Der. Oncogene 2007

ERBITUX® (cetuximab)

Safety and tolerability

ERBITUX safety and tolerability (1)

- ERBITUX is generally well tolerated as monotherapy and in combination with irinotecan-, oxaliplatin- and platinum-based chemotherapy
- ERBITUX does not increase the toxicity of cytotoxic chemotherapy or radiotherapy
- The most common adverse events related to ERBITUX are skin reactions, particularly an acne-like rash
  - which may develop in approx. 80% of patients
  - 85% of these reactions are mild-to-moderate
- There is a strong correlation between development of acne-like rash and response to treatment

ERBITUX safety and tolerability (2)

Other adverse events observed with ERBITUX include:

- **Nail disorders, e.g. paronychia**
- **Eye disorders**
- **Respiratory disorders**
- **Infusion-related reactions (IRRs)**
  - mild to moderate reactions occur in more than 10% of patients with severe reactions occurring in 1 - 10% of patients
  - in a post hoc analysis of the MABEL study only 1% of patients treated with antihistamines and corticosteroids as prophylactic medication had grade 3/4 IRRs

EGFR inhibitor-related skin reactions

ERBITUX
Skin reactions

- **Skin reactions are a common feature of treatment with many EGFR inhibitors**
- **Skin reactions are seen in approx. 80% of patients treated with ERBITUX**
  - 85% are mild-to-moderate
- **Skin reactions typically present as acne-like rash**
- **Pruritus, dry skin and nail disorders (e.g. paronychia) are observed less frequently**
- **Skin reactions are generally manageable and should rarely be a reason for discontinuing treatment**

ERBITUX
Management of skin reactions

Acne-like rash

MILD/MODERATE RASH
Clindamycin
Erythromycin
Benzoyl peroxide
Metronidazole
Topical retinoids may be used sparingly

Itching

Antihistamines
Treat dry skin if necessary

Fissures

Topical emollients + salicylic acid
Hydrocolloid dressing
Steroid tape
Topical antibiotic if required

Paronychia

Topical antibiotic creams or soaks

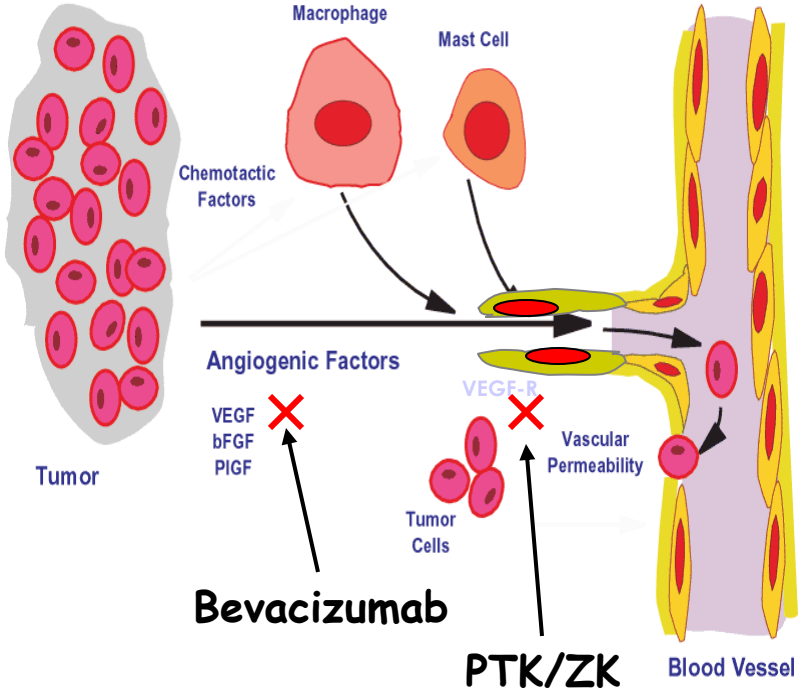
MODERATE/ SEVERE RASH
Topical treatment as before, plus systemic treatment
Second generation tetracyclines (doxycycline, minocycline)
Treat for at least 12 weeks. Possible adverse effects

Segaert et al. J Dtsch Dermatol Ges 2005;8:599-606

Correlation between skin reactions and response to treatment with ERBITUX

- The presence and/or intensity of skin reactions correlates strongly with response to ERBITUX and survival
- This relationship has been observed in different tumor types, including CRC and SCCHN
- However, patients not developing skin reactions may also respond to treatment with ERBITUX

Anti-angiogenic agents



Bevacizumab

Humanized anti VEGF monoclonal antibody

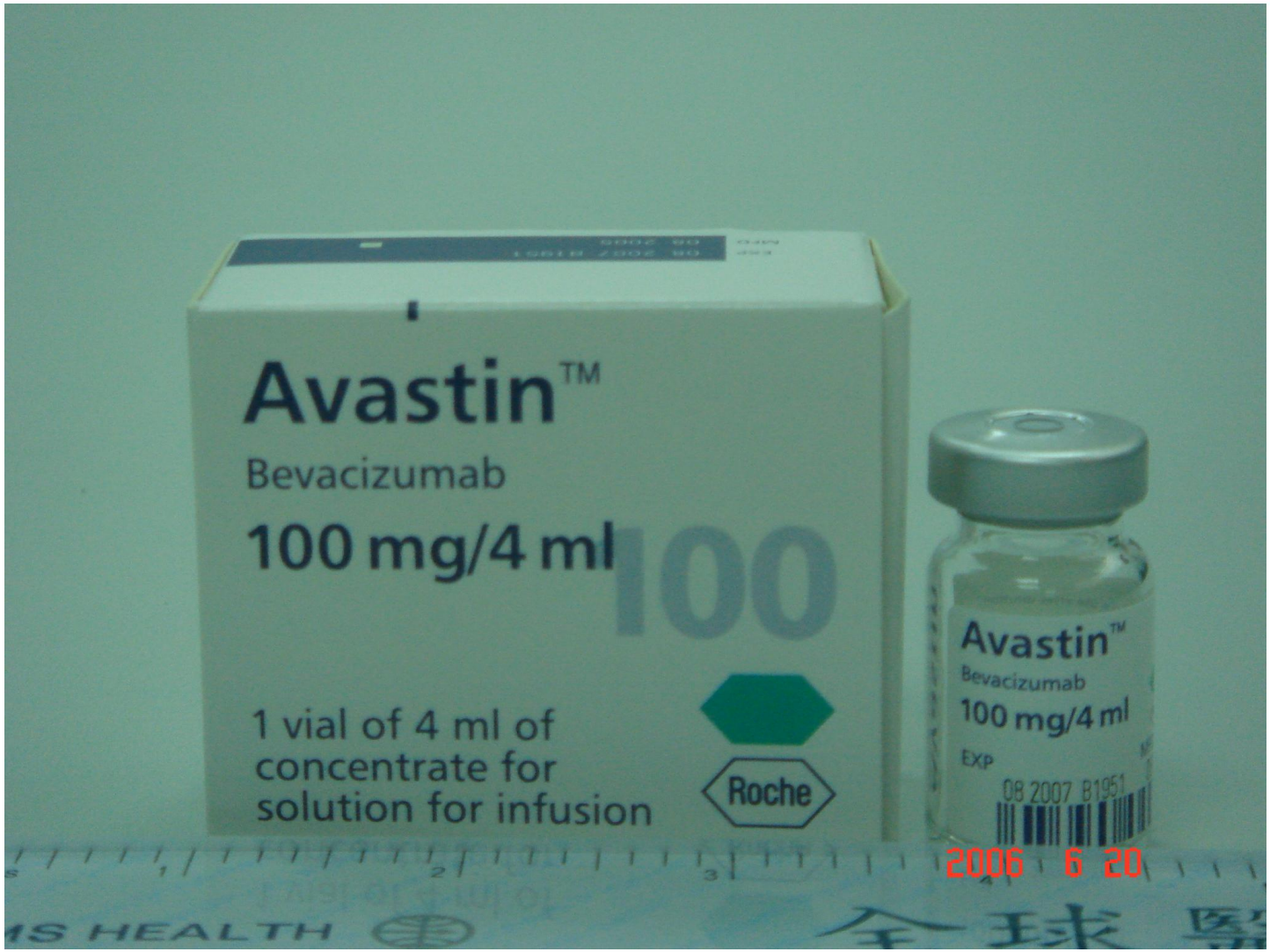
Inhibits angiogenesis

Registration trial; Phase III

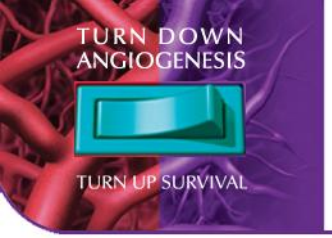
1st line advanced colorectal cancer

	IFL/placebo (n=412)	IFL/bevacizumab (n=403)
RR	35%	45%
mTTP	6.2	10.6
mOS	15.6	20.3

Toxicity – hypertension / perforation



AVASTIN
bevacizumab
Leading angiogenesis inhibition



什麼是VEGF?

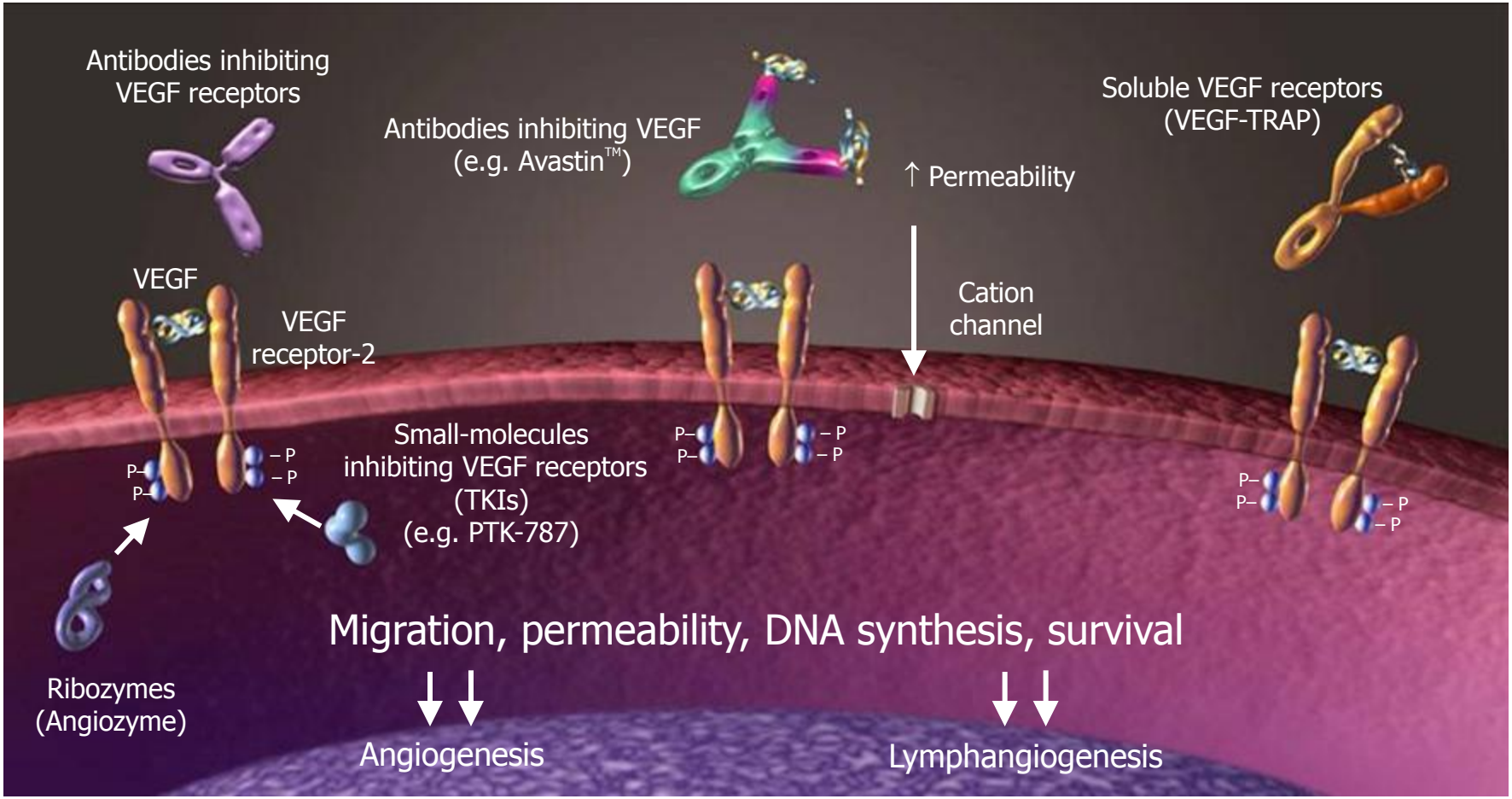
- VEGF 全名是vascular endothelial growth factor，中文是血管內皮生長因子，是腫瘤細胞分泌促使血管新生的重要因子。當VEGF和它位於血管內皮細胞上的接受器結合，會促使新血管的生成，幫助腫瘤細胞生長。

AVASTIN® (bevacizumab)

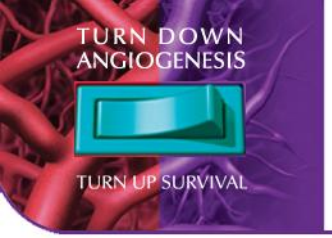
TURN DOWN ANGIOGENESIS

TURN UP SURVIVAL

Agents targeting the VEGF pathway



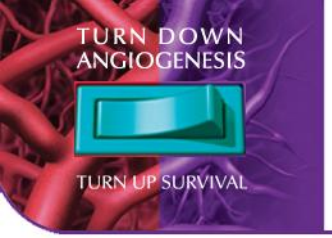
AVASTIN® (bevacizumab)



什麼是癌思停(Avastin)？

- 癌思停(Avastin)是第一個抑制血管新生(anti-angiogenesis)的單株抗體(monocolonal antibody)，可以和血管內皮生長因子(vascular endothelial growth factor, VEGF)結合，藉由抑制血管的新生，而抑制癌細胞的生長。

AVASTIN® (bevacizumab)



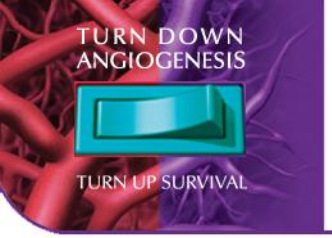
使用癌思停(Avastin)有哪些需要特別注意的事項?

- **胃腸穿孔**：轉移性大腸或直腸癌患者在使用癌思停(Avastin)及化學療法時，會有發生胃腸穿孔的危險，發生的機率約1.5%。

- **高血壓**：以癌思停(Avastin)治療之患者的高血壓發生率較高。建議在治療期間，每二個星期定期監測患者的血壓。如果高血壓無法以藥物治療控制，應永久停用癌思停(Avastin)的治療。

- **傷口癒合** ：重大手術後至少28天或手術傷口完全癒合後，再開始進行癌思停(Avastin)的治療。

AVASTIN® (bevacizumab)



使用癌思停(Avastin)有哪些需要特別注意的事項?

- **動脈血栓栓塞** ：有動脈血栓栓塞病史或年齡超過65歲的患者，在癌思停(Avastin)治療期間發生動脈血栓栓塞的危險性會增加。

- **出血** ：在癌思停(Avastin)治療期間出現3級或4級出血的患者應永久停用癌思停(Avastin)。

AVASTIN® (bevacizumab)

癌思停(Avastin)—注射劑—儲存2~8°c

- 100mg / 4 ml : 17750元
- Q2w : 5 mg / kg ；Q3w : 7.5 mg / kg
- 稀釋至100 c.c 0.9%生理食鹽水調配時不可以用力搖晃。
- 第一次90分鐘在化學治療之後
- 若耐受性良好第二次60 分鐘在化學治療之前或後
- 若耐受性良好第三次以後30 分鐘在化學治療之前或後
- 稀釋後在室溫可保持12小時安定 ； 在2~8°c可保持24小時安定

AVASTIN® (bevacizumab)

適應症

Avastin (bevacizumab) 與含有irinotecan/5-fluorouracil/leucovorin 或5-fluorouracil/leucovorin 的化學療法合併使用，可以作為轉移性大腸或直腸癌患者的第一線治療。

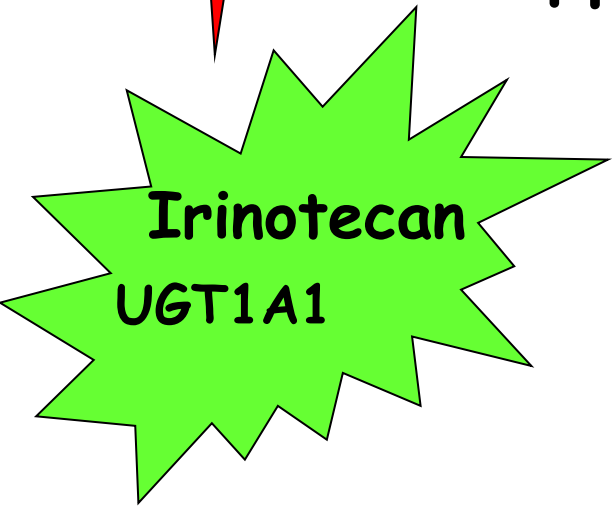
Avastin 與含有5-fluorouracil/leucovorin/oxaliplatin 的化學療法合併使用，可以作為先前接受過以fluoropyrimidine 為基礎的化學療法無效且未曾接受過Avastin 治療的轉移性大腸或直腸癌患者的治療。

AVASTIN bevacizumab
Leading angiogenesis inhibition

The pharmacogenomic revolution

Genetic polymorphisms & drug metabolism / effect

Prognostic & Predictive markers



Individualisation of treatment