

Colonic stents, contra

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QUALITY IN ENDOSCOPY

COLONOSCOPY &
COLONIC NEOPLASMS

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Introduction management of colo-rectal cancer (CRC) in occlusion

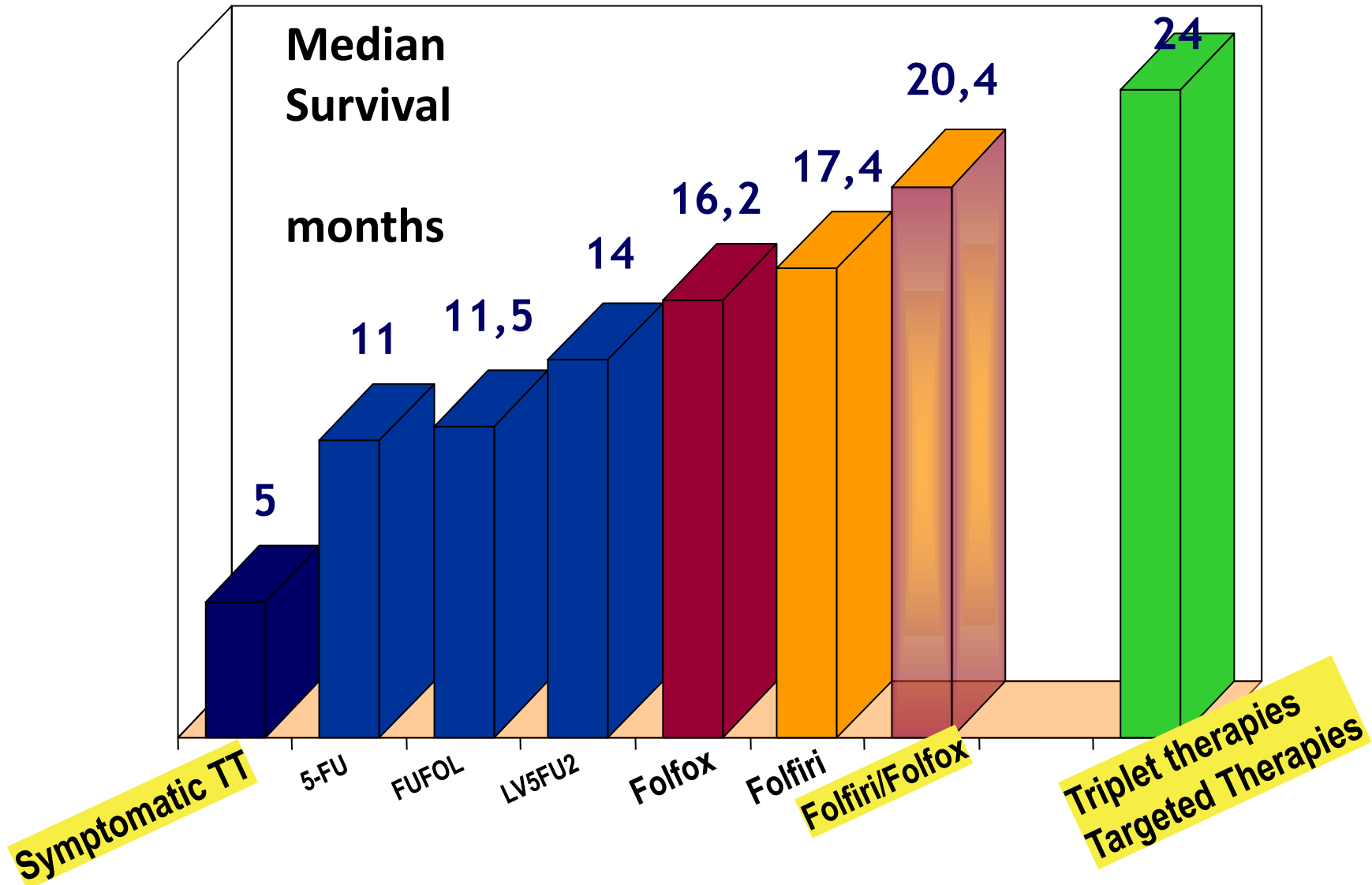
- **70% of colonic stenosis are related to cancer and # 10% of colonic cancer are revealed by an occlusion.**
- **Two different clinical presentations:**
 - Acute occlusion with an « a priori » curable CRC
 - Occlusion by a metastatic CRC (+/- palliative situation).
- **Therapeutic options in emergency:**
 - Immediate surgery (resection or colostomy) or Colonic stent
 - Medical management and early start of active chemotherapy

Management of colo-rectal cancer (CRC) in occlusion: Optimal treatments ?

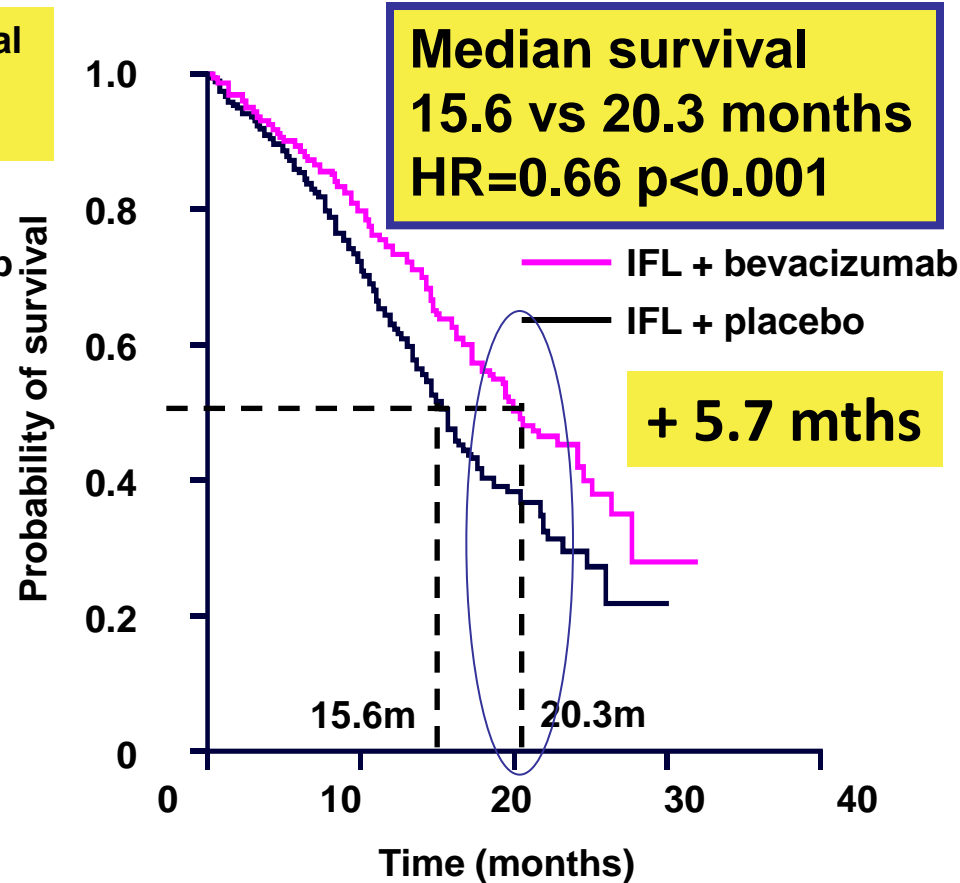
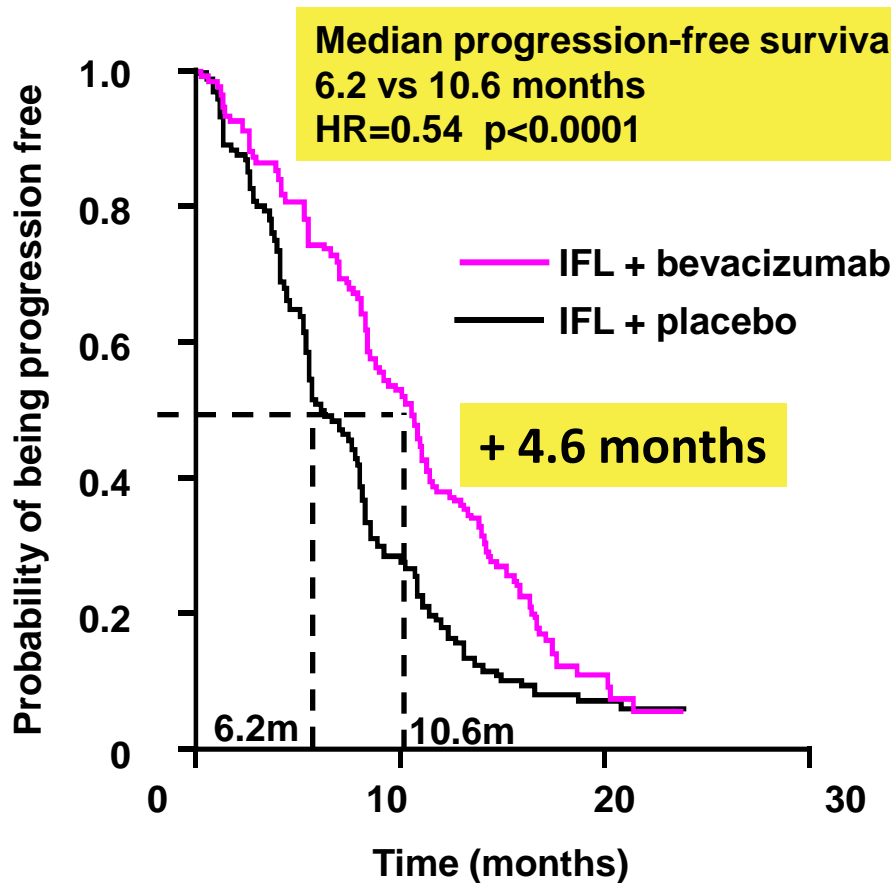
- **Stage IV (synchronous metastases) => best Palliation**
 - Must allow early chemotherapy administration in patients who are candidates.
 - Must preserve chances of secondary resections
 - In elderly patients, PS 3-4, etc to favor quality of life
- **Locally advanced CRC: Optimal curative treatment**
 - Must favor chances of curative resection in 1 or 2 time.
 - and chance to receive combinations of active antitumoral tts: surgery & chemotherapy +/- radio-chemotherapy

Always justify a multidisciplinary approach

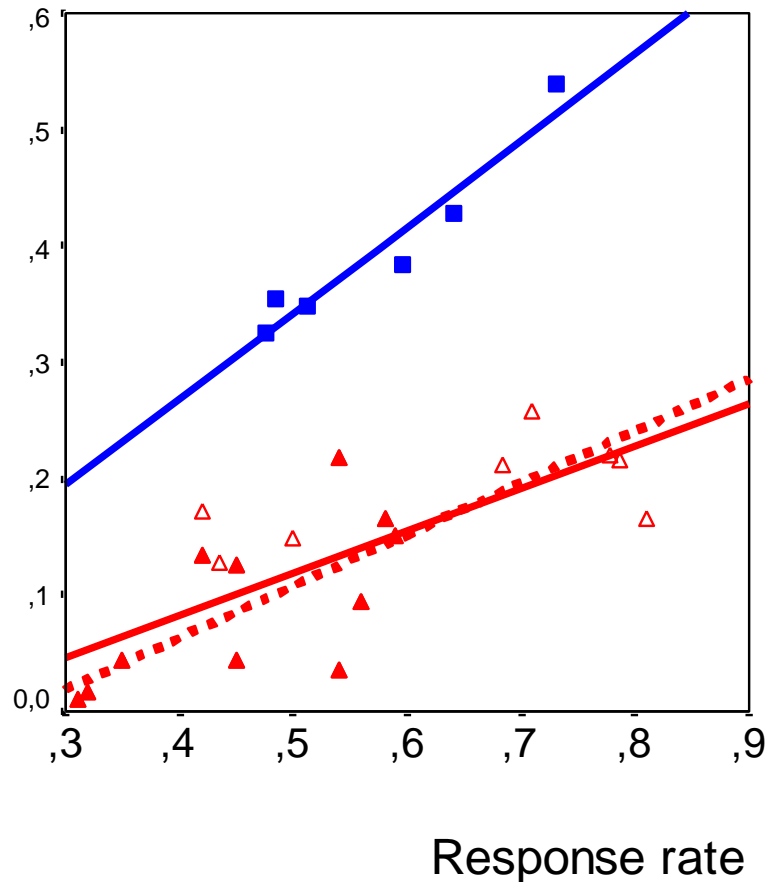
We have done progresses in systemic chemotherapy for metastatic CRC



With an additional benefit using antiangiogenic : bevacizumab + irinotecan resulting in a significant increase in PFS + OS In 1rst line (IFL + bev. vs IFL)



And ... possibilities for secondary resection of metastases are related to tumor response to chemotherapy +++



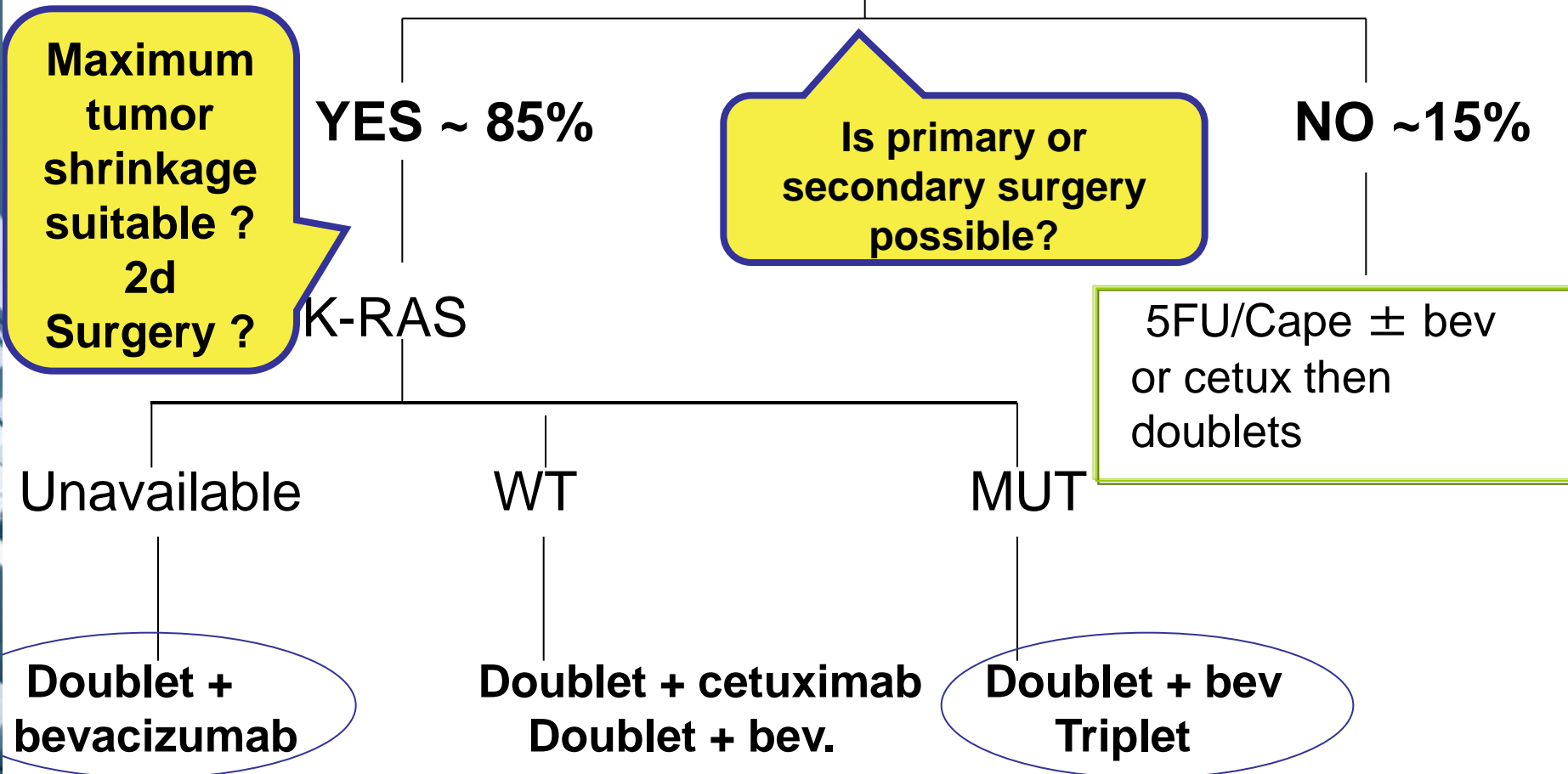
■ **Studies including selected patients**
(liver metastases only, no extrahepatic disease)
($r=0.96$; $p=0.002$)

△ ▲ **Studies including all patients with mCRC**
(solid line)
($r=0.74$; $p<0.001$)

▲ **Phase III studies including all patients with mCRC**
(dashed line)
($r=0.67$; $p=0.024$)

First line strategy of metastatic CRC

Does the patient need (or desire) aggressive therapy?



Strategy in case of large bowel obstruction ?

- **Obstruction (occlusion ; subocclusion) in CRC # 10 %**
- **High morbidity & mortality after surgery in emergency:**
 - 30 days mortality: 10- 25 % *Law, Br J Surg 2003*
 - But mortality is less after stoma
 - High rate of colostomy : 30-50 %
 - But most are transient and not definitive (2 time surgery)
- **Stent are discussed in 2 very different situations**
 - **palliation : in presence of metatasis or inoperability**
 - **Curative intent : bridge to the curative resection**

I - Colorectal stent in palliative situation:

to avoid colostomy or resection ?

I- Which strategy for synchronous metastatic CRC?

standard rules (experts opinion & ESMO and French guidelines)

- In absence of occlusion there is no clear indications for colonic stent... even in symptomatic patients .
- Active chemotherapy regimens
 - have a significant anti tumoral effect on the primary in 70%.
 - allows secondary resection of metastases in # 20%.
- Curative resection of the primary must always be discussed specially in patients in good PS and liver limited metastasis...
- Strategy must be determined in mutidisciplinary staff and never by gastroenterologists or surgeons alone

...BECAUSE...

Expert discussion ESMO/WCGIC Barcelona june Van Cutsem E et al; Ann Oncology - 2010

In case of « obstruction » there are significant results of colonic stent ...

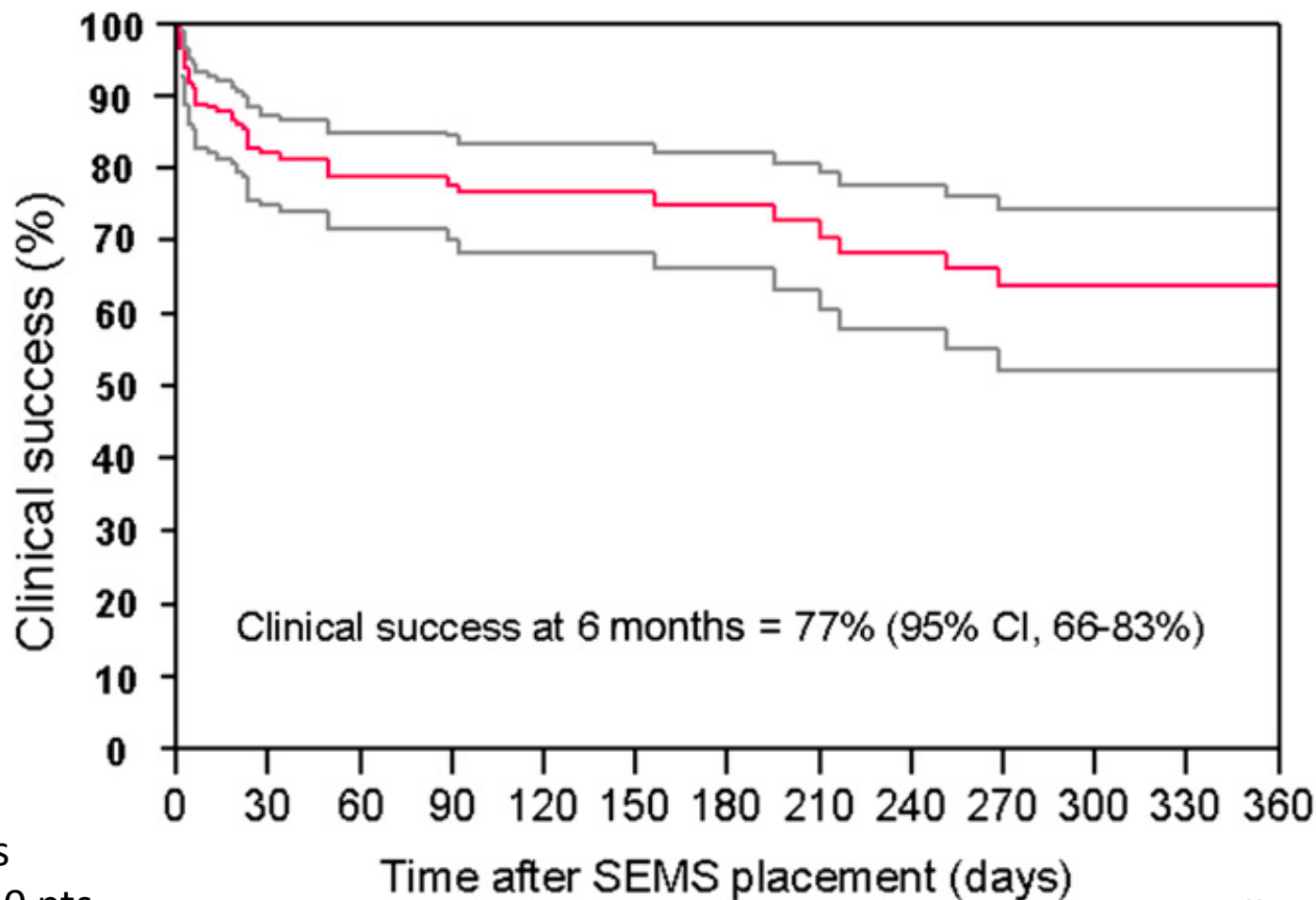
Systematic review of 15 « comparative » studies*

- **Technical Success** > 90 %
- **Clinical Success at 3 months** # 75%
- **Hospitalisation stay: shorter** 8j
- **Less definite stoma**
better**
- **cost- «efficacy » ratio
better**
- **Difference of mortality vs Surg. NS**

•Watt AM et al. *Ann Surg* 2007 ; 246: 24-30. ; **Law et al *Dis Col Rect* 2004 ;
•Karoui, *Arch Surg* 2007

Colonic stent in palliative situation: NY experience*

only 77% clinical success at 6 months



N = 168 pts
CCR N = 120 pts
Age moyen : 73 ans

Small, GIE 2011

And ... Long Term Complications are frequent

Colorectal stent in palliative situation

- **Complications rates: 25 - 50 %**

- Perforation : **5-10 %**
- Obstruction : **10-15 %**
- Migration : **5-20%**
- Ulceration : **< 5 %**

50% of complications are observed after the 1^{rst} week

*Fernandez-Esparrach, Am J Gastro 2010
Small, GIE 2011; Ceze, JFHOD 2007*

Risk Factors :

complete occlusion ; distal CC

dilation of the stenosis when the STENT is placed

STENT diameter < 22 mm

Endoscopist/radiologist skill and experience

Chemotherapy/bevacizumab

Colorectal stents vs Colostomy: NS

Two small randomised studies with low power

1- N = 15 pts in each arm.

Xinopoulos, Surg Endosc 2004

Fiori, Anticancer Res 2004

- « immédiat » success rates : 93 % ; until death : 53 %
- OS median : 21,4 (STENT) vs 20,9 months (colostomy)
- Hospital stay duration : mean 28 vs 60 d

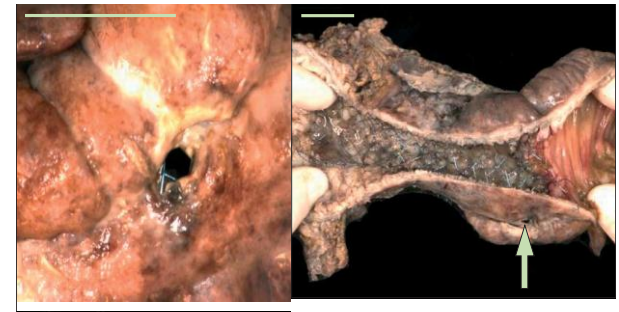
2- N= 21 pts: Dutch Stent-in I – multicentric:

– Study stopped (nb pts: 10 stents vs 11 surgery)

for overmortality in STENT arm

– 6 perforations → 3 deaths

– Related to stent type ?



van Hooft, Lancet 2006; van Hooft, Endoscopy 2008

And many questions on stent & Chemotherapy

- Few studies on chemotherapy efficacy after stenting (retrospective, heterogeneous, sub-groups)
- Feasibility of the association STENTS & chemotherapy is reported in retrospective series & pts sub-groups but without precisions on the proportion of pts who didn't receive chemotherapy related to complications ... 25% ?

And there is a higher « theoretical » risk of local complications :

- Tumor Response → stent migration
- hematological Toxicity (Neutropenia) → increased risks for local infections (abcedation)

⇒ RISKS MUST BE CONSIDERED WHEN THE STRATEGY is DISCUSSED

Risk +++ when bevacizumab in presence of stent

- **Intestinal Perforation & bevacizumab in pts with CC metastasis**
 - Meta-analysis (17 trials) : RR X 3
 - Risk Factors:
 - recent ATCD of colonoscopy, radiotherapy *Saif, Ann Surg Oncol 2007*
 - Stents ?

Manes, Arch Surg 2011;

Small, GEI 2010

Cennamo V, Clin Gastroenterol Hepatol 2009

- **In case of colic stent** :many case reports (delay 1 – 9 months)
 - Increased risk of perforation ? But few data reported (low power) ... => **perforation rates : 17.5 – 50 %**
 - bevacizumab must be used with great caution (stent is a relative contre-indication)
 - alternatives to stent must be favored.
 - Risk with other anti-angiogenics unknown

And always in mind the fact that secondary surgery may be done after initial chemotherapy in case of efficacy...

Bajwa A et al : (Eur Surg Oncol 2009 ; 35 : 164-7) (Univ Col London hospital, UK)

67 asymptomatic primary, and unresectable M CRC=> Chemotherapy

• surgery of primary		32 (48%)	
(stabilisation, bleeding or obstruction)			
• Prolonged Survival			OR
	p		
– Surgery			0.26
	0.00013		
– Clinical response primary		0.53	0.0012
• Poor outcome			
– Proximal tumors		2.61	0.0075
– Multiple primary		3.37	0.002

=> resection of the primary in absence of occlusion is not mandatory ?

=> secondary resection may improve survival in case of response ?

Stent may also prevent from... Initial resection of the primary which is an acceptable strategy...

Suported by studies on strategies performing surgery of the primary as first treatment in synchronous stage IV CRC with Better outcome if secondary chemotherapy may be administered...

(Verhoef C et al Eur J Cancer 2011 ; 47: S61-66 ; Eisenberg A et al. Int J Colorectal Dis 2008 ; 23: 559-68).

Strategy with immediate resection of the primary

- **Kaufman: 115 pts out of 185 had palliative surgery:**
=> Better survival if surgery ($p < 0.0001$)
And if surgery + chemo (30 mths vs 15) ($p < 0.0004$)
(Kaufman et al. Colorectal Dis 2008 ; 10: 498-502).
- **Karoui: 208 pts with synchronous unresectable M CRC.**
=> better survival (univariate):
 - **1ary colectomy*** ($p = 0.031$) ; **2ary curative surgery*** ($p < 0.001$)
 - well differentiated tumor* ($p < 0.001$) ; exclusive liver metastases* ($p < 0.027$)
 - **absence of need for colonic stent** ($p = 0.009$) ;
 - addition of antiangiogenic* ($p = 0.001$) or anti EGFR ($p = 0.013$)(Karoui M et al. Dis Colon Rectum 2011 ; 54: 930-8).
* positive in multivariate analysis

Then ... Stents cannot be an alternative to surgery in stage IV CRC because they may limit the other active treatments and have their own multiple limits...

Poor results (and/or high morbidity)

- **low / mid rectum (rectal syndrom) or proximal colon**
- **stenosis > 10 cm ; angulated or complete stenosis**
- **failure of contrast to pass through the stenosis**
- **Extracolonic stenosis (peritoneal carcinomatosis)**

Technic plays a major role especially in emergency:

- **Unexperienced opererators (<20 procedures)**
- **Type of prothesis (SEMS ?)**

Contre-indication :

- **Colonic distension (risk of diastatic perforation)**

Colorectal stent in palliative situation: to avoid colostomy or resection ?

Conclusion : CONTRA

The need of stenting appears limited...to few very palliative indications...

- because other active treatments are available
- because the results are not so good !
- because there are few well powered randomized trials

II - Which strategy for non metastatic CRC ?

Colorectal stent in curative situation: « bridge to surgery »

- **Aim: to avoid transient colostomy**
- **Feasibility established near 20 years ago**
(*Tejero, Dis colon rectum 1994*)
- **But a potential high « carcinological » risk ...?**
 - Risk of tumor manipulation (carcinologic surgical rule) and risk of silent perforation.
 - Risk of tumor dissemination
 - No clear clinical data
 - **Increase in the number of circulating tumor cells** (*Maruthachalam, Br J Surg 2007*)

Colorectal stent as bridge to surgery: Korean exp*.

- **35 pts in occlusion (1999-2007) surgery after stenting (SEMS) compared to 35 matched pts with immediate resection (out of 350 pts with non obstructing tumors):**
- **Univariate analysis for complications**
 - **Less stoma in the stent group**
 - => Adverse effect of stent**
 - **On 5-y overall survival: 38.4% vs 65.5%**
p=0.025
 - **On 5-y disease free survival : 48.3% vs 75.5%**
p=0.024

*Yonsei University College; Kim JS et al ; World J Surg 2009; 33:1281-6

Stenting in the management of left-sided colon cancer obstruction may be associated with adverse oncological results compared to non obstructing elective surgery ?

Randomized studies on colorectal stent as « bridge to surgery » (1)

two positives studies with a low level of
evidence...

1- STENT followed by laparoscopic surgery vs classical» surgery (25 pts in each arm) (*Cheung, Arch Surg 2009*)

- STENT Success rate : 83 %
- One session surgical excision 67 % vs 38% (p = 0,04)

2- STENT followed by surgery (n=15 pts) vs surgery (n = 13 pts) (*Alcantara, World J Surg 2011*)

- Hypothesis: decrease hospitalisation stay: 21 pts per arm
- Early stop related to a high rate of morbidity in the surgery arm: 53,8 % vs 13,3 % (p = 0,042)

Randomized studies on colorectal stent as « bridge to surgery » (2)

And two negative trials with a better methodology
! ...

1- Surgery in emergency (n=30) compared to delayed after STENT placement (n=30) (*Pirlet, Surg Endosc 2011*)

- Early stop, need colostomy : 57 % vs 43 % in STENT arm (ns)
- Failure in STENT placement : 53 % !

2- Surgery in emergency (n = 51) vs delayed after STENT placement (n = 47) (*Van Hooft, Lancet Oncol 2011*)

- Aim : Q of life for a 6 mths period (60 pts per arm)
- **Stopped (interim analysis): morbidity at D30 in STENT arm**
- Success rate for STENT : 70 %; perforation rate : 20 %
- Colostomy rate during follow up : 66 vs 58 % (NS)

CONCLUSIONS

STENT for CRC in « obstruction » ?

Benefits of colonic stent in palliative situation

« benefits does not counterbalance drawbacks »

- **It prevents surgery ...But in only few situations:**
 - Left colon, unique and short tumoral stenosis (<10 cm)
 - in absence of complete stenosis and colon dilation.
 - with a risk of perforation (5-20%)
 - Require expert endoscopist (> 20 procedures)

Fernandez-Esparrach G et al Am J Gastroenterol 2010 ; 105: 1087-93

- **And... restrict the possibility of other treatments**
 - limits the use of antitumoral treatments (risks +++)
 - Prevents the possibility of using bevacizumab,

This correspond to a lack of chance in most the cases.

Colonic stent in curative situation

« benefits does not counterbalance drawbacks »

Facilitate one-time surgery (# 70%) and decrease the risk of stoma.

But ...

- Risk of perforation (10-20%) especially in case of complete obstruction and colon dilation...which is the « indication»**
- Need expert endoscopist (> 20) often not present in emergency.**
- Require a short delay between stenting and curative surgery... not possible in # 25% of pts related to complications**
- Not supported by trials: one negative meta-analysis, 3 negative randomized trials and no long term follow-up data...**

And with a potential risk of dissemination of tumoral cells.

Stent must be avoid at maximum because ... the aim is not to prevent 2 time surgery and stomy but to give the best chance of cure...

Perspectives for a consensus ?

- **Indication of stent placement must always be discussed in a multidisciplinary staff and according to:**
 - Patients conditions and prognostic factors
 - Therapeutical objectives
 - Other treatments indications (chemotherapy)
- If chemotherapy +/- bévacizumab is planed stent has to be avoided at maximum
- New studies built with specialists in digestive oncology and surgeons are required +++