Innovative Therapeutic Strategies For Metastatic Colorectal Cancer

Session No.: 6

Name: Philippe Rougier
Institution: L'Université Paris Descartes
Country: Paris, France
THERAPEUTIC STRATEGY IN CRC in 2015

Generalities

1. Surgery is safer, more efficient and must be integrated with other treatments

2. Surgery address primary tumors & selected metastasis

3. Radiotherapy is safer, more precise + better indications: (rectal cancer: prevention of local recurrences after TME)

4. Medical treatments are more efficient and allow secondary resection in 20 to 30% of cases

5. Multidisciplinary approach is mandatory to determine the optimal strategy in metastatic CRC.
Innovative therapeutic strategies metastatic (M) CRC

1. Chemotherapy + targeted therapies
2. Surgery of metastasis
3. Neoadjuvant approach for non (or marinally) resectable M
4. Local treatments in case of locoregional disease
5. Strategy in case of synchronous M CRC
6. Strategy in case of obstruction
7. Multidisciplinary meeting and Guidelines (ESMO, FFCD (tncd) & NCCTG)
### What is known in 2015 on palliative chemotherapy in mCRC:

1. Chemotherapy **increases survival** & quality of life. → **A**
2. Must be initiated **before symptoms** when possible (Glimelius, 1985) → **B**
3. Must be integrated in a **continuum of care**. → **D**
4. Must favor at maximum **secondary resection**. → **B**
5. Sequences of regimens must favor the chance to offer **all active drugs** to patients (5FU, Irinotecan, oxaliplatine). → **B**
6. **Elderly patients** in good PS and without severe comorbidity can be treated as younger patients with the same benefit (gr 1 of Balducci scale). → **A**
7. Combination with **targeted tt** improved its efficacy → **A**
1rst line treatments in CCRm since 50 years

1957–70: 5FU bolus: response 10%

1970: 5FU + folinic Ac, & prolonged perfusions: responses # 20%

Toxicity: haemato, diarrhoea, mucitis

1990 – 2004: FOLFOX = FOLFIRI
  - response rate: 45–55%
  - Tolerance Profile: different
    Neuropathy / oxaliplatin
    Alopecia & diarrhoea / irinotecan

> 2004: CT + Targeted tts
  1er antibody antiangiogenic
  1er antibody anti EGFR

2012–14: 3 new Targeted tts with antiangiogenic action

Métas non résécables

Survival < 6 m

5FU

Survival 10 – 12 m

Oxaliplatin

Survival 20 m

Irinotecan

Bevacuzimab

Survival > 24 m

Cetuximab

In 1rst time

panitumumab

Afibercept

Surviva 1 > 24 m

Regorfenib

28 – 36 m

ramucirumab

1\textsuperscript{rst} line: Efficacy of anti-VEGF (bevacizumab) + irinotecan => better survival (IFL + bev. vs IFL)

Median progression-free survival
6.2 vs 10.6 months
HR=0.54  p<0.0001

Median survival
15.6 vs 20.3 months
HR=0.66 p<0.001

+ 5 months MS
+ 12% 2-year OS

### 2<sup>nd</sup> line: efficacy of Anti-angiogenics on overall survival (ITT)

<table>
<thead>
<tr>
<th>Trials</th>
<th>Treatments</th>
<th>Control</th>
<th>RR, %</th>
<th>PFS (months)</th>
<th>OS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bevacizumab (CCR) = Ab anti VEGF-A</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E3200</td>
<td>Bev + FOLFOX4 (n=286)</td>
<td>FOLFOX4 (n=291)</td>
<td>22.7 vs 8.6 p&lt;0.0001</td>
<td>7.3 vs 4.7 HR=0.61 p&lt;0.0001</td>
<td>12.9 vs 10.8 HR=0.75 p=0.0011</td>
</tr>
<tr>
<td>TML</td>
<td>Bev + CT* (n=409)</td>
<td>CT * (n=411)</td>
<td>5 vs 4 p=0.31</td>
<td>5.7 vs 4.1 HR=0.68 p&lt;0.0001</td>
<td>11.2 vs 9.8 HR=0.81 p=0.0062</td>
</tr>
<tr>
<td>BEBYP</td>
<td>Bev + CT** (n=92)</td>
<td>CT** (n=92)</td>
<td>21 vs 18 p=0.71</td>
<td>6.7 vs 5.0 HR=0.66 p=0.0065</td>
<td>14.3 vs 15.9 HR=0.75 p=0.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Afiblercept (CCR) = anti VEGF A-B &amp; PDGF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VELOUR</td>
<td>Afiblercept+FOLFIRI (n=612)</td>
<td>FOLFIRI (n=614)</td>
<td>19.8 vs 11.1 p&lt;0.001</td>
<td>6.9 vs 4.7 HR=0.76 p&lt;0.0001</td>
<td>13.5 vs 12.1 HR=0.82 p=0.0032</td>
</tr>
</tbody>
</table>

EGFR signal transduction & TARGETED THERAPY

Patients with KRAS (2006) or NRAS (2013) Mutation are Resistant to anti-EGFR

Monoclonal antibodies anti EGFR: Cetuximab and panitumumab
PRIME STUDY: FOLFOX + PANITUMUMAB vs FOLFOX
Results on Overall Survival and RR according to KRAS codon 12 status

**WT KRAS**

- RR = 55% vs 48%
- P = 0.068

<table>
<thead>
<tr>
<th>Events n (%)</th>
<th>Median (95% CI) months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panitumumab + FOLFOX</td>
<td>106 (33)</td>
</tr>
<tr>
<td>FOLFOX</td>
<td>124 (37)</td>
</tr>
<tr>
<td>HR = 0.83 (95% CI: 0.64–1.08)</td>
<td>P-value = 0.16</td>
</tr>
</tbody>
</table>

**MT KRAS**

- RR = 40% vs 40%
- P = 0.98

<table>
<thead>
<tr>
<th>Events n (%)</th>
<th>Median (95% CI) months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panitumumab + FOLFOX</td>
<td>112 (51)</td>
</tr>
<tr>
<td>FOLFOX</td>
<td>84 (38)</td>
</tr>
<tr>
<td>HR = 1.53 (95% CI: 1.15 – 2.05)</td>
<td>P-value = 0.004</td>
</tr>
</tbody>
</table>

Douillard JY et al
Other RAS and KRAS mutation beside KRAS codon 12 mutation help to select better indications for Anti-EGFR

PRIME (KRAS exon 2)

- MT
- WT

Target Population

59.9%

n = 440/1,096 (40.1%)

PRIME study: RAS analysis (refinement of patient population by RAS mutation status)

MT KRAS (exon 3, 4)

n = 60/641 (9.4%)

MT NRAS (exon 2, 3, 4)

n = 48/641 (7.5%)

Target Population

48.3%

n = 512/1,060

PRIME study: effect of Panitumumab on overall survival

Non significant

Significant

MT KRAS exon 3 (codon 61) & exon 4 (codons 117/146);
MT NRAS exon 2 (codons12/13), exon 3 (codon 61) & exon 4 (codon117/146)
In 2014: Cetuximab + FOLFIRI in **KRAS and RAS wild-type**

### CRYSTAL STUDY: FOLFIRI + CETUX vs FOLFIRI Results on Overall Survival

**Results on Overall Survival (OS)**

**No significant benefit on OS in the whole population**

- **Population KRAS exon 2 wt**

  - NO selection on RAS

- **Population KRAS & RAS wt**

  - Significant benefit on OS

2d & ultimate LINE: PANITUMUMAB and CETUXIMAB ARE EFFICIENT In KRAS (and NRAS) wt

<table>
<thead>
<tr>
<th>Trials</th>
<th>treatment</th>
<th>control</th>
<th>Response (RR)</th>
<th>PFS (months)</th>
<th>OS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2d line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peters (ESMO 2009)</td>
<td>Pani + FOLFIRI (n=297)</td>
<td>2d -FOLFIRI (n=297)</td>
<td>35% vs 10% p&lt;0.001</td>
<td>5.9 vs 3.9 HR=0.73 p=0.004</td>
<td>14.5 vs 12.5 HR=0.85 p=0.012</td>
</tr>
<tr>
<td><strong>Ultimate line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amado (JCO 2008)</td>
<td>Pani (n=124)</td>
<td>BSC (n=119)</td>
<td>-</td>
<td>3 vs 1.7 HR=0.45 p&lt;0.0001</td>
<td>11.2 vs 9.8 HR=0.81 p=0.0062</td>
</tr>
<tr>
<td><strong>2-3d line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bond ph II (Cunnigham , N E J Med 2004)</td>
<td>Cetux + Irinotecan (n=218)</td>
<td>Cetux =&gt; iri (n=111)</td>
<td>23% vs 11% p=0.0074</td>
<td>4.1 vs 1.5 HR: 0.54 ; p=0.0001</td>
<td>8.6 vs 6.9 HR=0.91 p=0.48</td>
</tr>
<tr>
<td><strong>Ultimate line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jonker (N E J Med 2007)</td>
<td>Cetux + BSC</td>
<td>BSC</td>
<td>-</td>
<td>-</td>
<td>6.1 vs 4.6 HR: 0.77 , p=0.046</td>
</tr>
</tbody>
</table>

Panitumumab (Vectibix*)

Cetuximab (Erbitux*)
Importance of Drugs Exposure on overall survival

Overall Survival (OS) is better when all the active drugs are offered => strategy of utilisation +++

Grothey, JCO 2005
All These Progress have improved the Survival of patients suffering from metastatic CRC over decades (censored for patients with liver resection; in 2 specialized centers)

Kopetz S et al. JCO 2009
Strategy ? How to choose the best 1rst line trt?

- **Best quality of life ? (stepp up/top-down)**
  - Conservative approach when possible (low tumor burden)
  - Agressive when necessary (evoltive risk, resectability)

- **Most active ? 1rst line:**
  - 5FU monotherapy still use in # 10% & elderly
  - Bitherapies used in 80% FOLFIRI = FOLFOX < FOLFIRINOX
  - Iv 5FU # oral 5FU
  - Role of pharmacogenetics ? DPD, UGT1A determinations ?

- **Better adapted biologic in 1rst line according to biology**
  - RAS non mut: anti-EGFR > anti VEGF (FIRE3 & CALGB)
  - RAS mut: anti VEGF (Bevacizumab)
  - BRAF mutated : FOLFIRINOX +/- targeted tt
Strategy ? How to choose the following trts?

• Best sequence across time (continuum of care)
  • **Second line according first line**: change chemotherapy
    • And/or change biologic (beva => Aflib or Ramucirumab)
    • Beva => anti EGFR in RAS wt: Cetuximab or Ramucirumab
  • **Ultimate line according previous one**
    • Regorafenib
    • Cetuximab alone or + irinotecan or panitumumab alone
    • Radioembolisation ?

• Most active treatment when M resection is the goal
  • FOLFIRINOX (triplet) + biologic
  • Intra-arterial hepatic chemotherapy or chemoembolisation ?
  • Radioembolisation ?
Innovative therapeutic strategies for metastatic CRC

1. Chemotherapy + targeted therapies
2. Surgery of metastasis
3. Neoadjuvant approach for non (or marginally) resectable M
4. Local treatments in case of locoregional disease
5. Strategy in case of synchronous M CRC
6. Strategy in case of obstruction
7. Multidisciplinary meeting and Guidelines (ESMO, FFCD (tncd) & NCCTG)
The possibility of resections of liver metastases has modified the strategies. Resection is a new goal...

<table>
<thead>
<tr>
<th>Classification</th>
<th>Resectable</th>
<th>Borderline resectable</th>
<th>Never resectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strategy</td>
<td>Resection +/- preop CT</td>
<td>CT ± biologic</td>
<td>CT ± biologic</td>
</tr>
<tr>
<td>Aim of the treatment</td>
<td>Curative surgery</td>
<td>Overall Survival/ prolonged disease control/QcL</td>
<td></td>
</tr>
</tbody>
</table>

# 20-30% secondary resection
50% alive at 5-year but only 4% cured at 10y

25 – 40 months median OS

Importance of Responses to chemotherapy

Before CT

After 4 months CT

non resectable ➔ resectable!
Epilogus: ...this patient recurred 18 mths later and died 3 and half years later from extra-hepatic metastases...
<table>
<thead>
<tr>
<th>Group</th>
<th>Clinical presentation / chemot. (CT)</th>
<th>Treatment goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP 0</td>
<td>Clearly R0-resectable liver and/or lung metastases</td>
<td>Cure, decrease risk of relapse</td>
</tr>
<tr>
<td>GROUP 1</td>
<td>Not R0-resectable liver and/or lung metastases only, <strong>may become resectable</strong> =&gt; induction “aggressive” CT</td>
<td>Maximum tumor shrinkage</td>
</tr>
<tr>
<td>GROUP 2</td>
<td>Multiple metastases/sites, with <strong>rapid progression</strong> and/or tumor-related symptoms =&gt; “aggressive” CT</td>
<td>Clinically relevant tumor shrinkage as soon as possible, control PD</td>
</tr>
<tr>
<td>GROUP 3</td>
<td>Multiple metastases/sites, <strong>no option for resection</strong>, initially asymptomatic, less aggressive disease =&gt; less aggressive CT</td>
<td>Prevent further progression</td>
</tr>
</tbody>
</table>

ESMO guidelines (Experts/ESMO meeting): Patient groups

ESMO consensus – HJ Schmoll et al, Ann Oncology 2012
(A) Percentage of patients undergoing liver resection by date of diagnosis increased significantly for patients diagnosed in 1998 and stabilized around 20% for patients diagnosed in 2000 to 2006. Error bars represent SEM.

(B) Overall survival by landmark analysis of patients with metastatic colorectal cancer diagnosed between 1998 and 2006 and treated at the institutions. Of those patients alive at 12 months, median overall survival was 65 months in the population of patients who underwent liver resection during the first year. Error bars represent 95% CIs.

From:
Innovative therapeutic strategies for metastatic CRC

1. Chemotherapy + targeted therapies
2. Surgery of metastasis
3. Neoadjuvant approach for non (or marginally) resectable M
4. Local treatments in case of locoregional disease
5. Strategy in case of synchronous M CRC
6. Strategy in case of obstruction
7. Multidisciplinary meeting and Guidelines (ESMO, FFCD (tncd) & NCCTG)
Locoregional Strategy

- **Patients with liver metastasis**
  - Intra-arterial hepatic chemotherapy (IAHC)
    - in first line
    - Or after failure of systemic treatments
  - Radio-embolization (loaded microspheres)

- **Patients with peritoneal carcinomatosis**
  - Hyperthermic Intra Peritoneal Chemotherapy
    - HIPEC

- **Combined with active systemic treatments**

Dual liver blood supply
- Portal Vein: 75%
- Hepatic Artery: 25%

Tumor blood supply
- portal vein < 5%
- hepatic artery: 95%
### Intra-Arterial Hepatic CT (IAHC) + active IV CT = High Response Rates (RR) & Secondary Resections

<table>
<thead>
<tr>
<th>Study</th>
<th>IAHC iv CT (1rst line)</th>
<th>RR</th>
<th>2d Resection.</th>
</tr>
</thead>
<tbody>
<tr>
<td>N Kemeny*</td>
<td>FUDR IRI-LOHP</td>
<td>92%</td>
<td>39%</td>
</tr>
<tr>
<td>N=49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D Malka**</td>
<td>LOHP LV5FU2s + cetuximab</td>
<td>83%</td>
<td>48%</td>
</tr>
<tr>
<td>N=36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# 85% Response & 45% secondary resections of LM!

(*) JCO 2009; 21: 3465-71; (** JCO 2010, 28, 15s # 3558)
Chemo-Emboliisation IAH: DEBIRI* vs FOLFIRI
Randomized Phase II Trial (DC beads loaded with irinotecan)

<table>
<thead>
<tr>
<th></th>
<th>OS</th>
<th>RR</th>
<th>PFS</th>
<th>Toxicité</th>
<th>Amélioration QOL*</th>
<th>Coût</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Aiguë (G2/3)</td>
<td>Tardive (G2)</td>
<td></td>
</tr>
<tr>
<td>DEBIRI (n = 34)</td>
<td>22 m</td>
<td>69%</td>
<td>7 m</td>
<td>70%**</td>
<td>20%</td>
<td>5000 € (2 D)</td>
</tr>
<tr>
<td>FOLFIRI (n = 35)</td>
<td>15 m</td>
<td>20%</td>
<td>4 m</td>
<td>25%</td>
<td>80%</td>
<td>18000 € (8 CT)</td>
</tr>
</tbody>
</table>

Suivi médian : 50 mois (extrêmes : 26-64)
* Score d’Edmonton en % par rapport au baseline
** Douleurs, vomissements, asthénie malgré prophylaxie (hydratation, morphine, lidocaïne, antibiotiques, corticoides, sétrons)

=> Ongoing phase III in first line CT...

Fiorentini G., et al. ASCO GI 2012; abstr. 587
Radio-embolisation IAH (SIR sphere Y$^{192}$)

Eligible Patients
Liver-limited mCRC refractory to chemotherapy

Stratification
Institution
Interval to progression on chemotherapy

Random Assignment

Arm A
5FU protracted IV infusion (300 mg/m² D1-14 q3w)
Until progression

Arm B
Y resin microspheres D1 cycle 1
5FU protracted IV infusion (225 mg/m² D1-14, cycle 1; 300 mg/m² D1-14 q3w thereafter)
Until progression

Eligible Patients
Liver-limited mCRC refractory to chemotherapy

Best Overall Hepatic Response

<table>
<thead>
<tr>
<th>Response</th>
<th>FU Alone (n=23)</th>
<th>Radioembolisation + FU (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Partial response</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stable disease</td>
<td>8</td>
<td>35</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>14</td>
<td>61</td>
</tr>
<tr>
<td>Nonevaluable</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

NOTE. Comparison of response rates: 0 of 23 versus two of 21, $P=.22$ (95% CI for the difference between arms B and A ranging from -0.10 to 0.32). Comparison of stabilization rates: eight of 23 versus 18 of 21, $P=.001$ (95% CI for the difference ranging from 0.19 to 0.71).

=> improvement in Time to Liver Progression, Time to Progression Overall but not in OS

=> Ongoing phase III in first line...  

Peritoneal Carcinomatosis: Total Excision + HIPEC

Overall and disease free survival
median follow-up: 27.4 months (18.3-49.6)

HIPEC
hyperthermic
Intra
Peritoneal
Chemotherapy

Elias D Ann Surg and JCO
Innovative therapeutic strategies for metastatic CRC

1. Chemotherapy + targeted therapies
2. Surgery of metastasis
3. Neoadjuvant approach for non (or marinally) resectable M
4. Local treatments in case of locoregional disease
5. Synchronous M CRC: resection of primary?
6. Strategy in case of obstruction
7. Multidisciplinary meeting and Guidelines (ESMO, FFCD (tncd) & NCCTG)
Resection of the primary is questioned

Retrospective studies in favor of the resection of the primary first

- ACCORD 13: +13%
- ML 16987: +10%
- FFCD 2000-05: +19%
- Absolutes benefit at 24 months

Faron M et al., Eur J Cancer 2015
1 French ongoing Randomized Trial: PRODIGE 30 - CLIMAT

Main O: overall survival at 2-year

Secondaries O:
- QoL / complications / tolerance chemo-biotherapy
- post-op complications / response rate / PFS / R0 resection

2 other randomized studies on progress on the same topic...
- Netherlands: Cairo 4
- German trial: Synchronous

But no studies evaluates colonic stenting in the strategy…
Innovative therapies for metastatic (M) CRC

1. Chemotherapy + targeted therapies
2. Surgery of metastasis
3. Neoadjuvant approach for non (or marinally) resectable M
4. Local treatments in case of locoregional disease
5. Strategy in case of synchronous M CRC
6. Strategy in case of obstruction: Surgery or Stenting
7. Multidisciplinary meeting and Guidelines (ESMO, FFCD (tncd) & NCCTG)
Which strategy for synchronous metastatic CRC?
standard rules (experts opinion & ESMO and French guidelines)

- In absence of occlusion: no indications for colonic stent... even in symptomatic patients.
- Active chemotherapy: > 2-year survival in stage IV CRC, responses > 50% on the primary
- Secondary resection of metastases in # 20%.
- Curative resection of the primary must be emphasized (patients in good PS and liver limited metastasis...)
- Strategy determined in multidisciplinary staff and never by gastroenterologists or surgeons alone ...

Expert discussion ESMO/WCGIC Barcelona june Van Cutsem E et al; Ann Oncology - 2010
Stent & Chemotherapy +/- targeted therapy

- Few studies (retrospective, heterogeneous, sub-groups)
- No precisions on the proportion of pts who received chemotherapy according to complications ... 25% ?
  => Higher « theoretical» risk of local complications :
    - Tumor Response → stent migration
    - hematological Toxicity (Neutropenia) → increased risks for local infections (abcedation)
    - Perforations in case of bevacizumab... 17%-50%, (x 3)
  => RISKS MUST BE CONSIDERED WHEN THE STRATEGY is DISCUSSED alternatives to stent must be favored.

Innovative therapeutic strategies for metastatic CRC

1. Chemotherapy + targeted therapies
2. Surgery of metastasis
3. Neoadjuvant approach for non (or marinally) resectable M
4. Local treatments in case of locoregional disease
5. Strategy in case of synchronous M CRC
6. Strategy in case of obstruction
7. Multidisciplinary meeting and Guidelines (ESMO, FFCD (tncd) & NCCTG)
Multidisciplinary approach and personnalised medicine

Patients

Comorbidities
PS
Age
Symptoms

Tumor

TNM Stage
Volume / extension
PS
Comorbidities
Nbr of sites
Possibilities of Surgical resection

Biology

WBC
Plat.
LDH
AP
RAS
BRAF
MSI
DPD
UGT1A1

Treatment Choice

Possibilities of Surgical resection
Personalized Cancer Medicine

A Sample

Biological samples
- Tumor type (FFPE vs. fresh frozen)
- Tumor origin (primary tumor vs. metastatic deposits)
- Time of analysis (archival vs. contemporary)
- Surrogates for tumor tissue (ctDNA and CTCs)

Biomarker identification as novel targets
- Prognostication
- Therapy selection
- Pharmacodynamic assessment

Genomic analysis
- Time of genomic analysis
- Bioinformatics
- Tumor board

Platforms
- Gene expression/microarray
- Gene copy number analysis
- Targeted massive parallel sequencing
- Proteomics

C Targeted Therapy

Drug development process
- Preclinical
- Clinical (phase I, II, III)

Molecular targeted agent access
- FDA approved
- Clinical trial
- Compassionate use

Endpoints
- Tumor growth kinetics
- Tumor growth ratio
- PFS1/PFS2

D Clinical Trial

Clinical trial/drug access
- Series of patients
- Single center
- Multicenter
THERAPEUTIC STRATEGY IN CRC has benefited from 25 YEARS OF INNOVATION.....

1. Surgery must be integrated with other treatments for treatments of primary tumors & selected metastasis

2. Radiotherapy is presently evaluated for treatments of selected metatases (stereotaxic / radiosurgery).

4. Medical treatments are efficient but must be adapted to patients / tumors / and biology.

5. Multidisciplinary approach is mandatory to determine the optimal strategy and best personnalized treatment for each patient.
We are no more in Middle Age ...

Colorectal Cancers are no more a fatality... because we have benefited from a lot of innovations

THANK YOU!