First results of the French prospective cohort of colorectal cancers with microsatellite instability - COLOMIN2

[1]D. Tougeron, [2]V. Hautefeuille, [3]A. Zaanan, [4]K. Le Malicot, [5]V. Moulin, [6]R. Cohen, [7]T. Lecomte, [8]A. Aleba, [9]J. Viaud, [10]Y-H. Lam,
[11]P-L. Etienne, [12]L. Mosser, [13]M. Ramdani, [14]S. Le Sourd, [15]C. Ligeza Poisson, [16]G. Goujon, [17]C. Lepage, [18]O. Bouché

1 Poitiers, 2 Amiens, 3 Paris (HEGP), 4 Dijon, 5 Montpellier, 6 Paris (Saint-Antoine), 7 Tours, 8 Niort, 9 Saint Malo, 10 Cholet, 11 Plerin, 12 Rodez, 13 Beziers, 14 Rennes, 15 Saint Nazaire, 16 Paris (Bichat), 17 Dijon, 18 Reims

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Introduction

- **Colorectal cancers with microsatellite instability/deficient mismatch repair (dMMR/MSI CRC) are associated with particular outcomes**:
  - Good prognosis in adjuvant setting
  - Worse prognosis in metastatic setting
  - Adjuvant 5FU chemoresistance in stage II
  - A high sensitivity to immune checkpoint inhibitors (ICI)

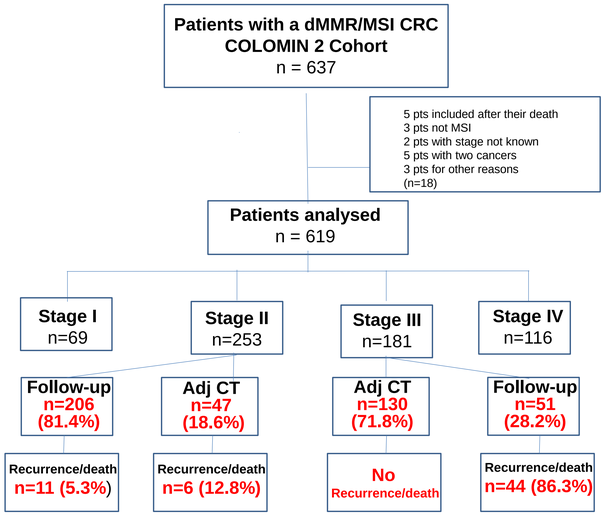
- There is no large prospective real-life cohort evaluating outcome and prognostic factors in dMMR/MSI CRC.

Methods

- **COLOMIN2 is a prospective, multicenter cohort designed to assess treatment and prognosis of dMMR/MSI CRC.**
- Key eligibility criteria included histologically proven CRC with a MSI (molecular biology) and/or dMMR (immunohistochemistry, IHC) status.
- **The primary endpoint is time to recurrence (TTR) for non-metastatic tumors and progression-free survival (PFS) for metastatic tumors.**

Results

- **Between March 2017 and October 2021, 637 patients were included by 37 centers.**
- **Most tumors had a MMR IHC (76.1%) and 23.9% had a MSI test alone.**



Results

Table 1. Patient and tumor characteristics according tumor stage.

		Stage I N=69	Stage II N=253	Stage III N=181	Stage IV N=116	All patients N= 619
Patients characteristics						
Age (Mean, SD)		69.2 (13.3)	71.8 (13.8)	68.8 (13.8)	66.8 (15.0)	**69.7 (14.1)**
Gender: Female		47 (68.1%)	147 (58.1%)	115 (63.5%)	63 (54.3%)	**372 (60.1%)**
WHO PS 0/1		33 (89.2%)	146 (87.9%)	114 (89.1%)	71 (79.8%)	**364 (86.7%)**
MMR gene mutation (proven Lynch syndrome)		33 (49.3%)	88 (35.6%)	83 (47.2%)	44 (38.9%)	**248 (41.1%)**
Tumor characteristics						
Tumor site	Ascending colon	49 (71.0%)	183 (72.6%)	131 (73.6%)	72 (64.3%)	**435 (71.2%)**
	Descending colon	12 (17.4%)	35 (13.9%)	21 (11.8%)	23 (20.5%)	**91 (14.9%)**
	Rect	6 (8.7%)	5 (2.0%)	4 (2.2%)	3 (2.7%)	**18 (2.9%)**
Grade: poor differentiation		6 (9.7%)	40 (17.9%)	57 (35.8%)	31 (34.1%)	**134 (25.0%)**
MMR loss	MLH1/PMS2	43 (62.3%)	164 (64.8%)	114 (63.0%)	59 (50.9%)	**380 (61.4%)**
	MSH2/MSH6	12 (17.4%)	33 (13.0%)	25 (13.8%)	11 (9.5%)	**81 (13.1%)**
	others	14(20.3%)	56 (22..2%)	42 (23.2%)	46 (39.6%)	**158 (25.5%)**
***BRAF* mutation**		16 (23.2%)	68 (26.9%)	52 (28.7%)	40 (34.5%)	**176 (28.4%)**
***RAS* mutation**		10 (14.5%)	33 (13.0%)	31 (17.1%)	22 (19.0%)	**96 (15.5%)**

Patients with metastatic disease (n=116)

- Most patients with stage IV disease had one metastatic site (76.6%).
- More frequent metastatic sites were liver (45.1%), peritoneum (37.2%) and lymph nodes (19.5%).
- Median PFS was 11.1 months
- **Most were treated by first-line CT +/- targeted therapy (63.8%) and few by ICI (11.2%). Median PFS were 11.1 [95%CI: 7.8-22.1] months and 29.2 [95%CI: 8.1-47.3] months for patients treated with CT and IO, respectively.**

Figure 4. Progression-free survival

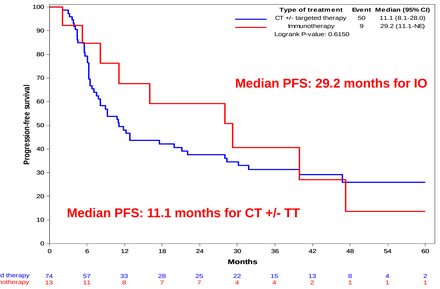


Figure 1. Time to recurrence

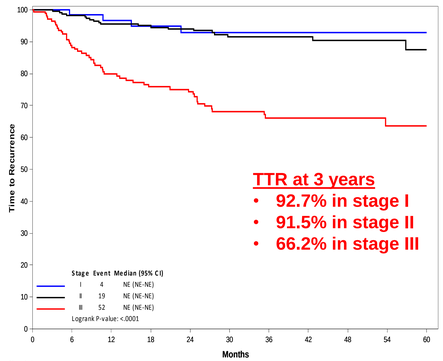


Figure 2. RFS according adjuvant chemotherapy

Median follow-up was 39.4 months

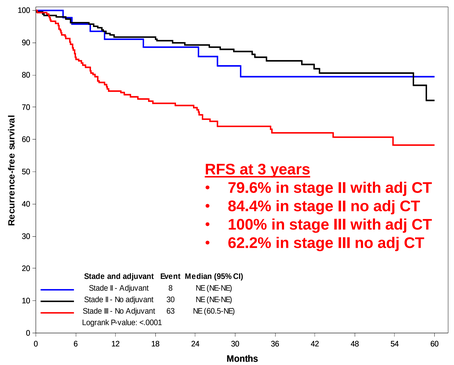
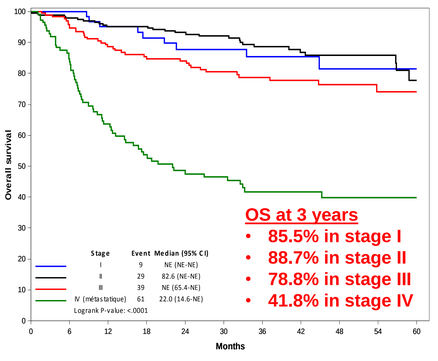


Figure 3. Overall survival



Discussion

This real-life cohort of dMMR/MSI CRC confirms:

- **Good prognosis at non-metastatic stage**, especially stage I and II but **high recurrence rate in stage III with no adjuvant chemotherapy**.
- **Poor prognosis at metastatic stage**, especially patients treated by chemotherapy +/- targeted therapy.
- Molecular analyses are currently explored to better determine the prognosis and chemosensitivty of dMMR/MSI CRC.

Conflicts of interests

- D. Tougeron is speaker and/or advisory board for Astra Zeneca, MSD, BMS and Roche.
- COLOMIN2 study was promoted by Fédération Francophone de Cancérologie Digestive (FFCD) and funded in part by Société nationale française de gastro-entérologie (SNFGE).

Contact information

david.tougeron@chu-poitiers.fr