
# The management of IBD patients with cancer history

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*Roma*

# *Background risk of new or recurrent cancer after a first cancer*

The lifelong risk of cancer is progressively rising due to increased life expectancy and increased incidence of various cancers.

Data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program suggest that patients with a history of cancer have an overall excess risk (16 %) of developing a second malignancy compared to the general population.

First cancer during childhood or adolescence increases the lifelong risk of a second malignancy 6-fold.

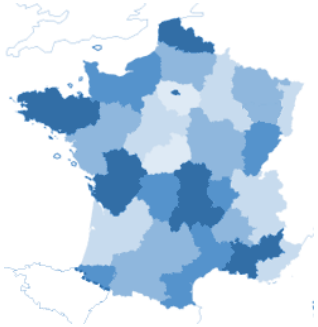
However, there is no excess risk of second cancer in patients who develop their first cancer after 70 years of age.

Quinn MJ, et al. Ann Oncol 2003
Curtis RE, et al. National Cancer Institute 2006
Altekruse SF, et al. National Cancer Institute, 2010

# *IBD patients with a history of cancer*


- **Which is the risk of developing new or recurrent cancer ?**
- **Does IBD therapy predispose to new or recurrent cancer ?**
- **How to manage these patients ?**

# Risk of new or recurrent cancer in patients with IBD and previous cancer



**17,047 IBD pts of the CESAME cohort**
**405 pts with a prior diagnosis of cancer**

***Incident cancer rates during follow-up (2.9 yrs):***

***21.1/1000 pt-yrs (pts with a cancer history)***
***6.1/1000 pt-yrs (pts without a cancer history)***

***HR of incident cancer :***

***1.9 (95% CI 1.2-3.0, p = 0.003) in pts with prior cancer compared to pts without prior cancer***

**IBD patients with prior cancer have a doubled risk of developing any (new or recurrent) cancer, compared to IBD patients who have never had cancer**

Laurent Beaugerie
for the CESAME Study Group *Gut* 2014

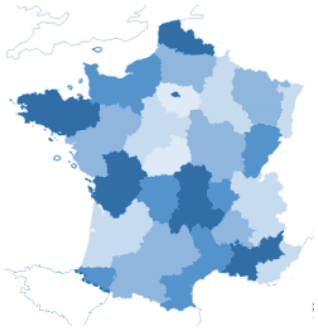
# *IBD patients with a history of cancer*


❖ Which is the risk of developing new or recurrent cancer ?

❖ **Does IBD therapy predispose to new or recurrent cancer ?**

❖ How to manage these patients ?

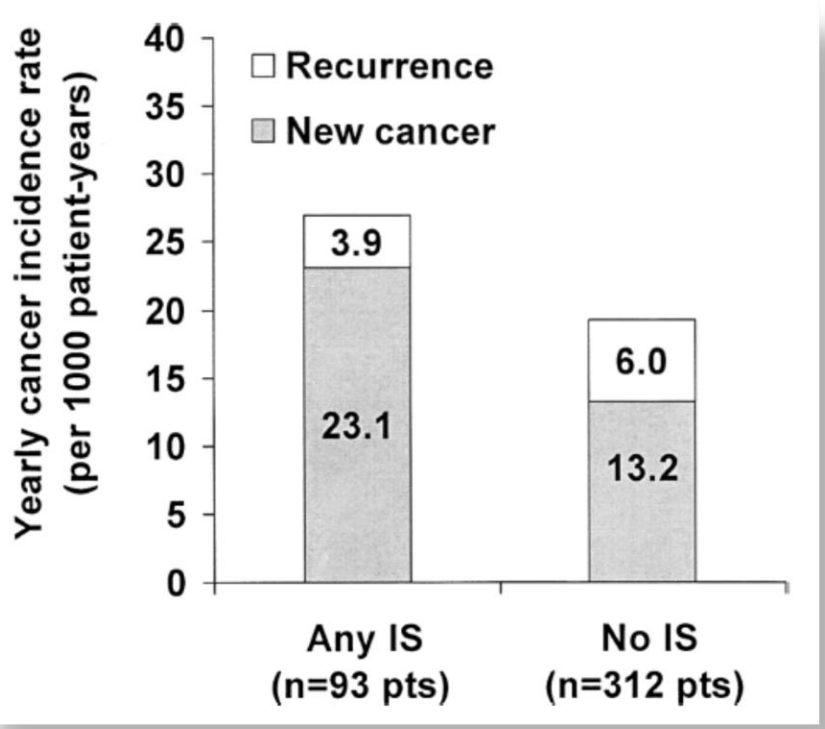
# Risk of new or recurrent cancer under immunosuppressive therapy in patients with IBD and previous cancer



**17,047 IBD pts of the CESAME cohort**

**405 pts with a prior diagnosis of cancer**

Rate of new and recurrent cancer in patients (pts) with previous cancer according to immunosuppressant (IS) status at entry




Laurent Beaugerie
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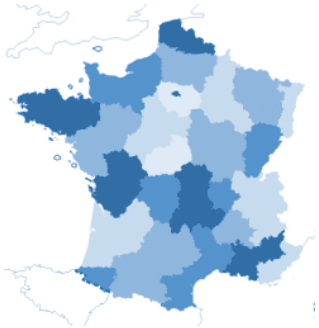
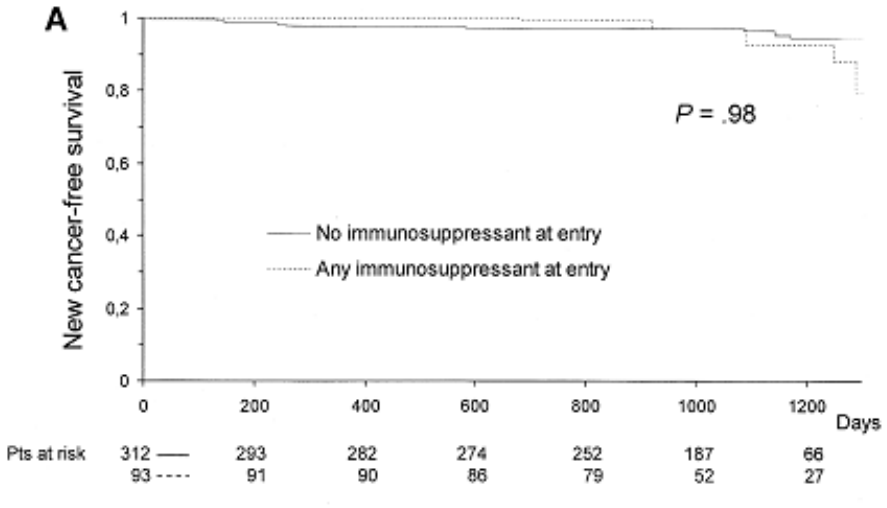
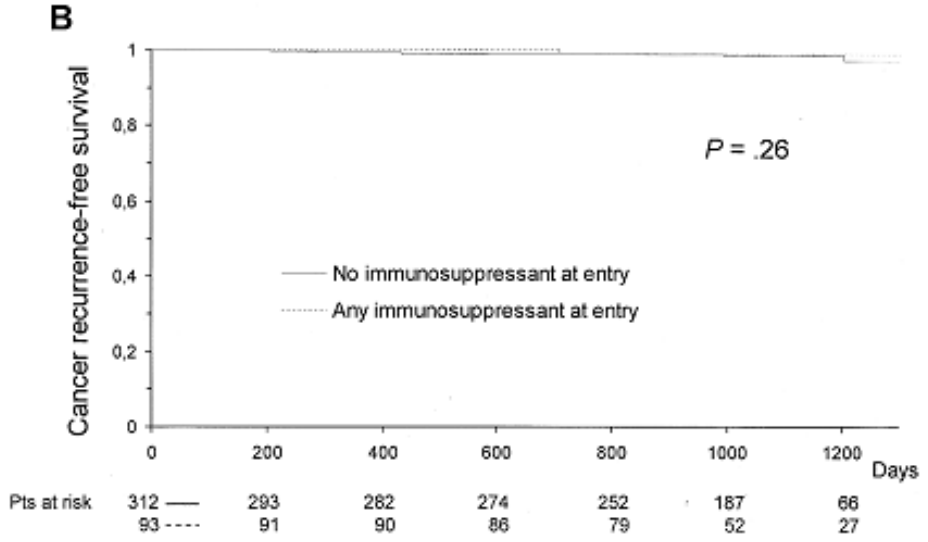
# Risk of new or recurrent cancer under immunosuppressive therapy in patients with IBD and previous cancer



**The CESAME cohort**

**405 pts with a prior diagnosis of cancer**




***New cancer-free survival*** ***Cancer-recurrence free survival***

**Probability of remaining free of new or recurrent cancer between patients exposed or not exposed to any immunosuppressant**

Laurent Beaugerie
for the CESAME Study Group *Gut* 2014

# Risk of New or Recurrent Cancer in Patients With Inflammatory Bowel Disease and Previous Cancer Exposed to Immunosuppressive and Anti-Tumor Necrosis Factor Agents

## Incident Cancer Outcomes

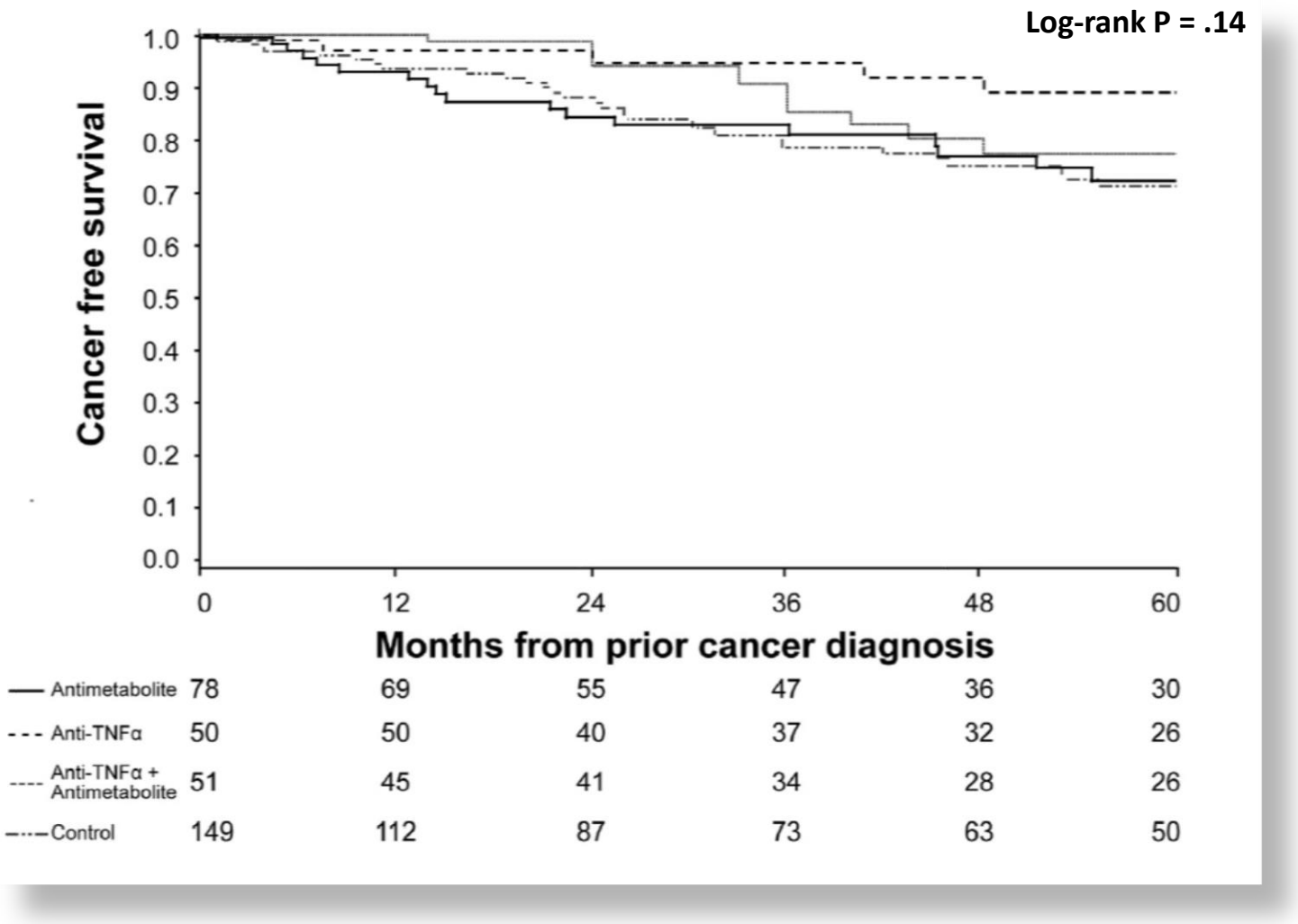
| | Anti-TNF-$\alpha$ | Anti-TNF-$\alpha$ + antimetabolite | Antimetabolite | Control | *P* value |
|---|---|---|---|---|---|
| No. of patients (*% of total*) | 55 (16.5) | 51 (15.3) | 78 (23.4) | 149 (44.7) | |
| Median duration of follow-up (*mo*) | 57.1 | 71 | 58.7 | 44.3 | .0671 |
| Incident cancer | 7 (13%) | 15 (29%) | 22 (28%) | 46 (31%) | |
| New | 1 (2%) | 5 (10%) | 13 (17%) | 25 (17%) | |
| Recurrent | 6 (11%) | 6 (12%) | 7 (9%) | 19 (13%) | |
| New and recurrent | 0 (0%) | 4 (8%) | 2 (3%) | 2 (1%) | .0712 |
| Incident cancer category | | | | | |
| Gastrointestinal | 0 (0%) | 4 (24%) | 5 (18%) | 10 (20%) | |
| Hematologic | 0 (0%) | 1 (6%) | 1 (4%) | 1 (2%) | |
| Skin | 3 (43%) | 6 (35%) | 10 (37%) | 11 (23%) | |
| Solid | 4 (57%) | 6 (35%) | 11 (41%) | 27 (55%) | .6165 |
| Incident cancer recurrence risk type[22] | | | | | |
| High | 5 (72%) | 7 (54%) | 7 (35%) | 17 (39%) | |
| Intermediate | | | | 10 (23%) | |
| Low | | | | 2 (4%) | |
| Undetermined | | | | 15 (34%) | .6143 |
| Incident cancer rate | | | | 5.4 | |
| 100-person years (*r* | | | | (852) | |

| | Anti-TNFα | Anti-TNFα + antimetabolite | Antimetabolite | Control |
|---|---|---|---|---|
| **Incident cancer rate per 100-person years** *(no. of person-years)* | **2.46 (285)** | **3.63 (414)** | **5.75 (383)** | **5.42 (852)** |

**Median time to anti-TNF initiation after cancer diagnosis: 14.5 months (0-704 months; average, 74.5 months)**

Axelrad J, et al. Clin Gastroenterol Hepatol 2016

# *Cancer-free survival between groups at 5 years*




Axelrad J, et al. Clin Gastroenterol Hepatol 2016

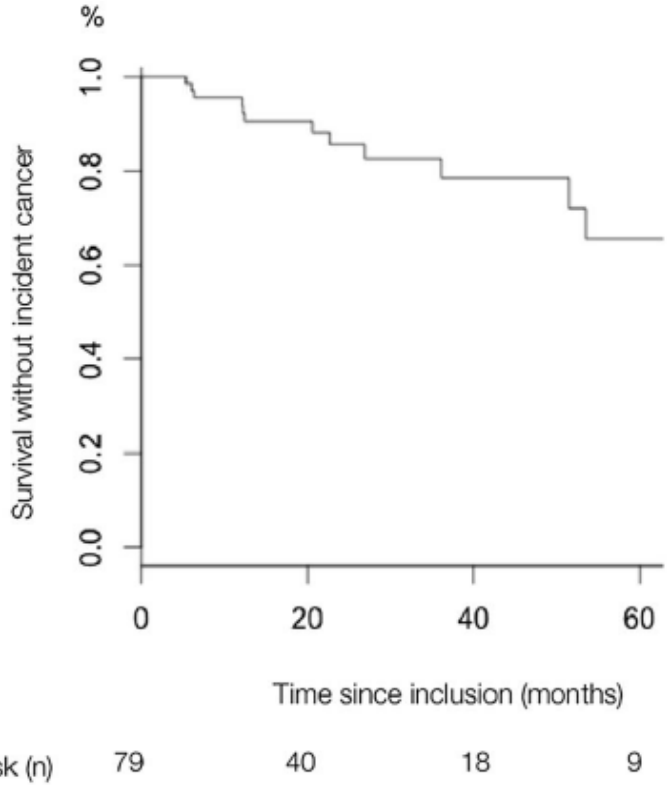
# Risk of incident cancer in IBD patients starting anti-TNFα therapy while having recent malignancy (GETAID survey)

Poullenot F, et al. IBD 2016

**79 IBD pts**
**with previous cancer < 5 years**
**(median 17 months, range 1-65)**
**before starting anti-TNFα therapy**

**During follow-up**
**(median: 21 months, 1-119)**
**15 (19 %) pts developed an incident cancer**
**(8 recurrent and 7 new cancers)**

**Incidente rate: 84.5 (95% CI, 83.1-85.8)**
**1000 pts-years**




Kaplan-Meier curve of survival without incident cancer during follow-up

**Survival without incident cancer:**
**96% at 1 year**
**86% at 2 years**
**66% at 5 years**

# Thiopurines and anti-TNFs after a diagnosis of cancer in patients with inflammatory bowel disease

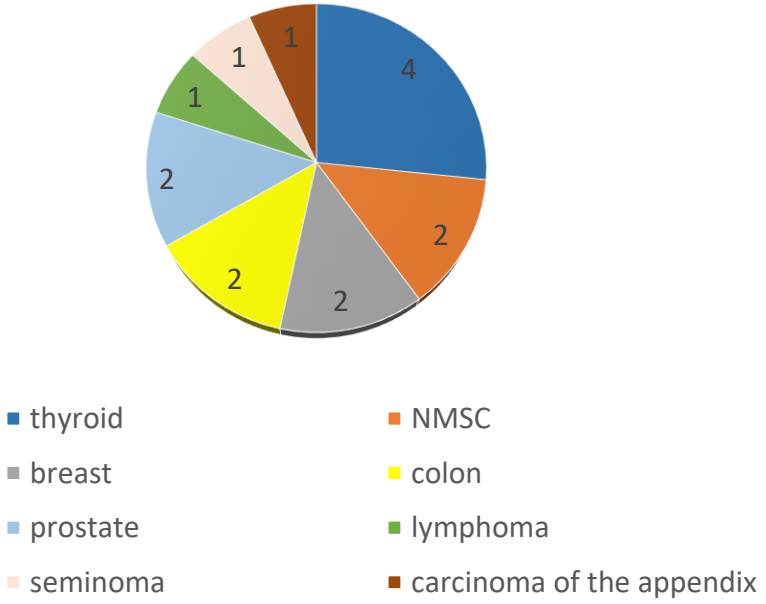
S. Onali*, C. Petruzziello, G. Condino, M. Ascolani, E. Calabrese, E. Lolli, A. Ruffa, F. Pallone, L. Biancone

**2000-2013: 82 IBD pts with cancer**

**15 (18.2%) pts subsequently received:**
***thiopurines (12 pts)***
***anti-TNF (3 pts)***

**Time interval between cancer diagnosis and IMM:**
**6 yrs (range 1-26)**

**Median follow-up after cancer diagnosis:**
**10 yrs (range 3-30)**




**Cancer locations**

**None of the 15 IBD pts showed recurrence of cancer**

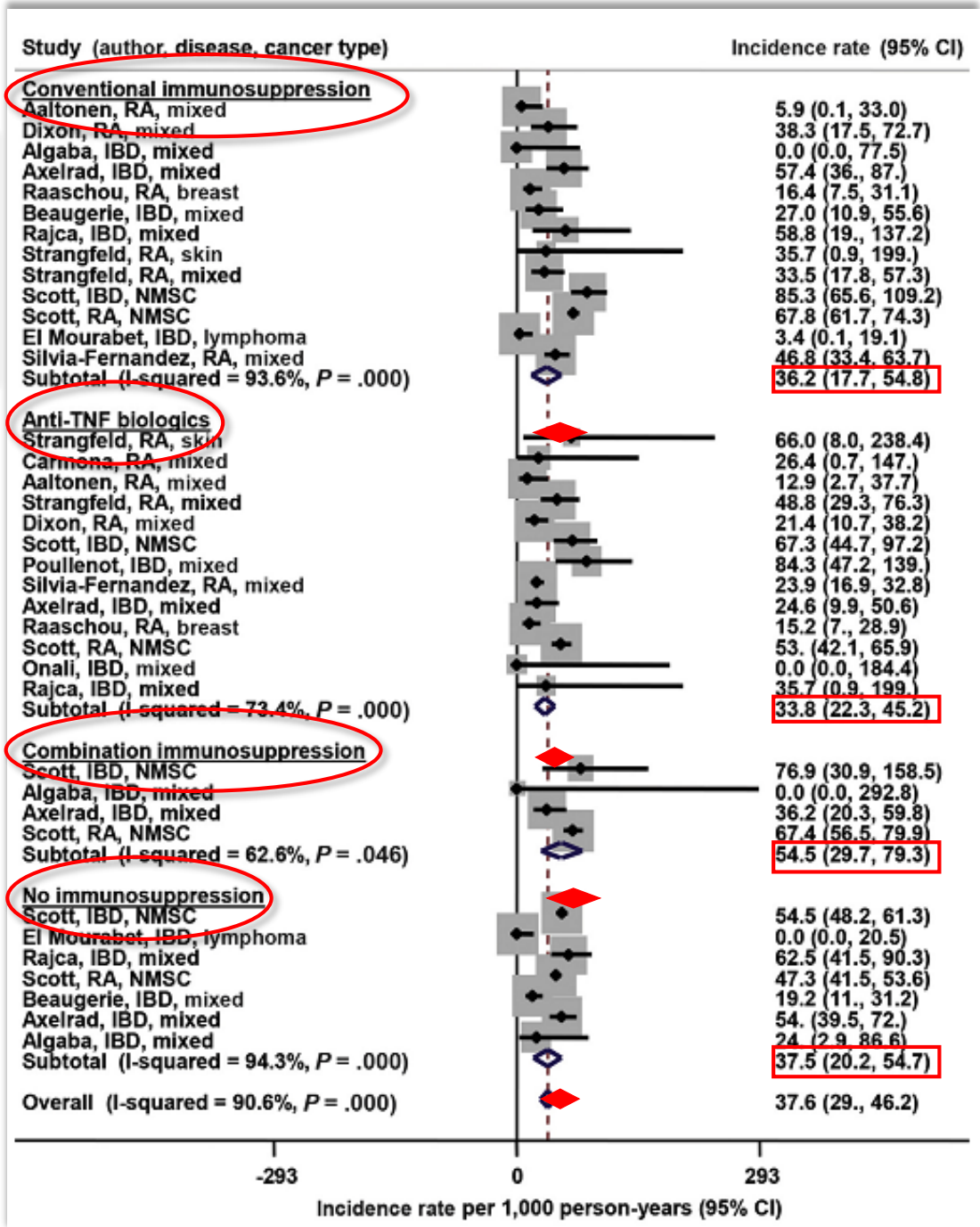
Onali S, et al. ECCO 2014

# New/recurrent cancer following ISS and anti-TNF therapy in patients with immune-mediated diseases and cancer history

**16 studies ***

**11.702 pts with cancer history**
**(median interval between index cancer and ISS/anti-TNF therapy: 6 yrs)**

**1.698 new/recurrent cancers**

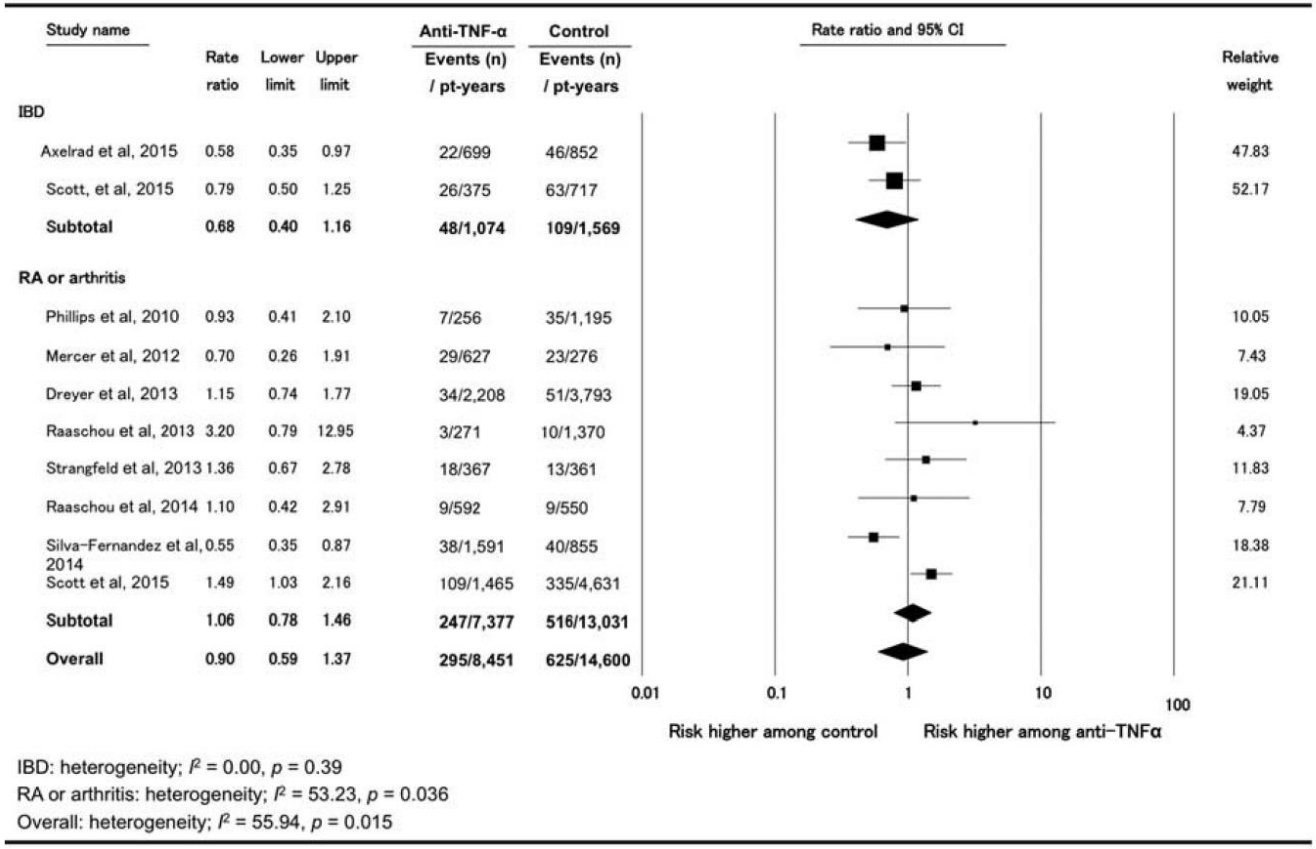



* *7 of pts with IBD*
*7 of pts with rheumatoid arthritis (RA)*
*1 of pts with IBD and pts with RA*
*1 of pts with psoriasis*

Shelton E, et al. Gastroenterology 2016

# Risk of Cancer Recurrence Among Individuals Exposed to Antitumor Necrosis Factor Therapy

## *A Systematic Review and Meta-Analysis of Observational Studies*




***9 studies***
***(2 on IBD pts)***

***11.679 pts with cancer history***
***3.707 pts exposed to anti-TNF therapy following cancer***

Micic D, et al. IBD 2017


- Randomized controlled trials of anti-TNFα therapies in IBD patients usually exclude patients with a cancer history, consequently there are no randomized prospective data in this population
- Relatively small sample size of IBD patients with previous cancer included in the studies
- Most results are based on retrospective studies
- Significant heterogeneity between the studies included in the meta-analysis
- Most physicians avoid ISS/anti-TNFα drugs in patients who survive to a life-threatening cancer or who have a high risk of cancer recurrence

Beaugerie L, et al. Gut 2014; Axelrad J, et al. Clin Gastroenterol Hepatol 2015; Poullenot F, et al. IBD 2016; Shelton E, et al. Gastroenterology 2016; Micic D, et al. IBD 2017; Rajca S, et al. JCC 2014

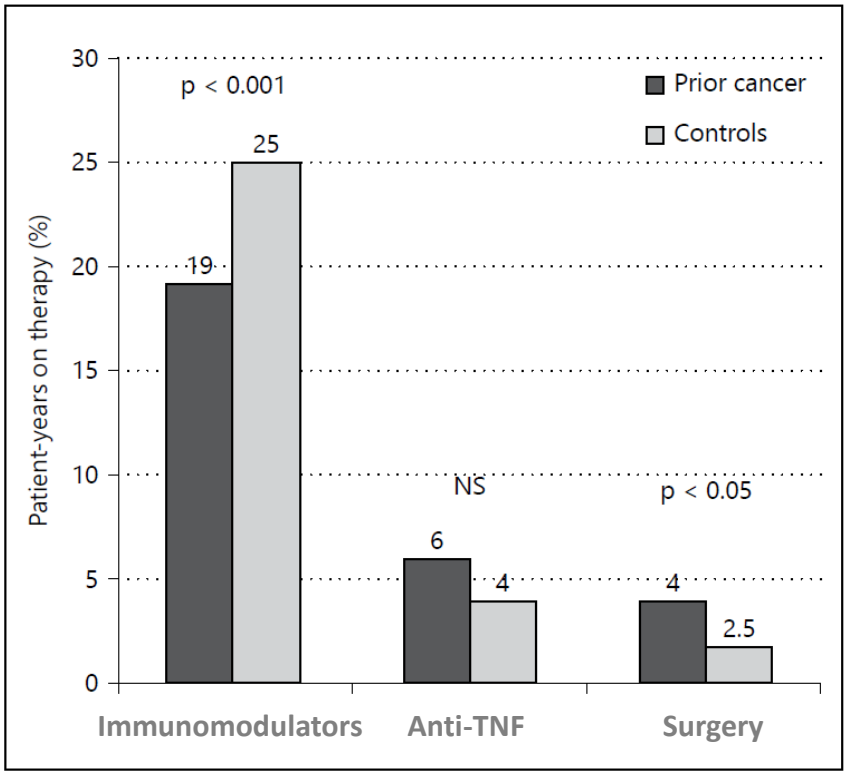
# Impact of the diagnosis and treatment of cancer on the course of inflammatory bowel disease

S. Rajca, P. Seksik, A. Bourrier, H. Sokol, I. Nion-Larmurier, L. Beaugerie, J. Cosnes*

JCC 2014

**MICISTA registry**

*Database of 7.158 IBD pts*




***Choise of therapy in 50 IBD pts with prior cancer compared to 150 matched controls***

*(629 vs. 2,121 patient-years, respectively)*

adapted from Cosnes J. Dig Dis 2017

# *IBD patients with a history of cancer*


## *Considerations:*

- ***The prior cancer may be completely eradicated, theoretically eliminating the risk of recurrence under immunosuppression.***
- ***The prior cancer may be dormant due to treatment and ongoing immunosurveillance and might therefore have a risk of recurrence under immusuppression.***
- ***A new cancer might arise due to immunosuppression.***

adapted from Bernheim O, et al. Gut 2013

# How should IBD therapy be managed for patients with a history of cancer ?


*Gastroenterologist* *Oncologist*

*Quality of life*

***Thorough knowledge***

***C Appropriate***
***(I***
***d communication***
***n with the patient***
***factors…***
***Cancer type and stage…)***

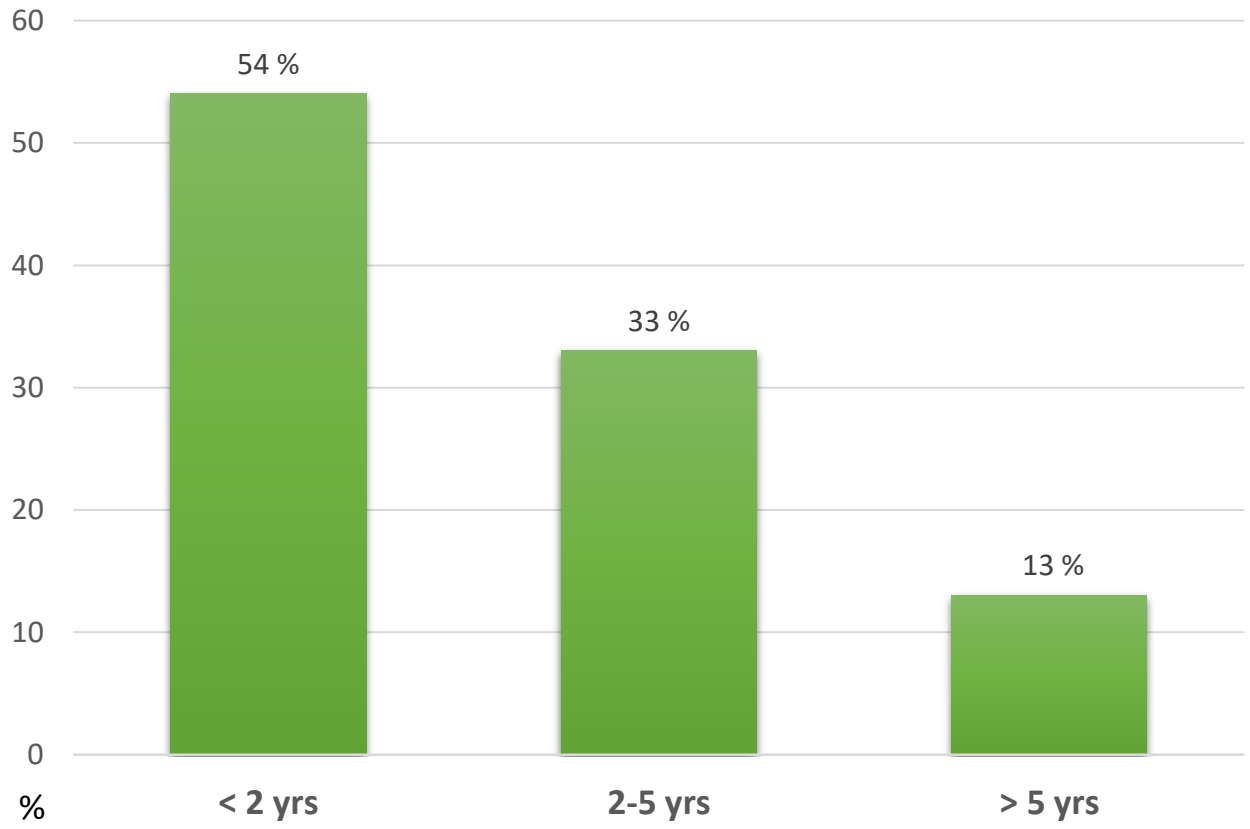
# *Risk of recurrence of pre-existing cancers under post-transplant immunosuppressive therapy*

| Risk level | Organ |
|---|---|
| Low (≤ 10%) | Incidentally discovered renal tumours |
| | Lymphomas |
| | Testicle |
| | Uterine cervix |
| | Thyroid |
| Intermediate (11-25%) | Uterine body |
| | Wilms' tumour |
| | Colon |
| | Prostate |
| | Breast |
| High (> 25%) | Bladder |
| | Sarcomas |
| | Melanomas |
| | Non-melanoma skin cancers |
| | Myelomas |
| | Symptomatic renal carcinomas |

adapted from Penn I. Transplantation 1993

# *Risk of recurrence of pre-existing cancers in renal transplant patients on immunosuppressive therapy*

***The longer the interval from cancer to renal transplant, the lower the risk of cancer recurrence***




Penn I. Ann Transplant 1997

# *Safe interval for starting ISS/anti-TNF after successful treatment of malignancy*

**ECCO Statement 6G**

Based on data in transplant recipients, physicians should consider delaying the resumption of immunosuppressant therapy for IBD in patients being treated for cancer, because of the risk of recurrent neoplastic disease, for 2 years following the completion of cancer treatment [EL 3]. The delay can be extended to 5 years if the cancer is associated with an intermediate or high risk of recurrence [EL 3]

ECCO consensus on IBD and malignancy. Annese V, et al. JCC 2015

# *Management of IBD patients with past history of malignancy*

**ECCO Statement 6F**

In patients with active IBD and a history of malignancy, 5-aminosalicylates, nutritional therapies, and local corticosteroids can be safely used [EL 3]. In more severe flares that do not respond to these treatments, the use of anti-TNF, methotrexate, short-term systemic corticosteroids, and/or surgery should be considered on a case-by-case basis [EL 5]

ECCO consensus on IBD and malignancy. Annese V, et al. JCC 2015

# Immunosuppressant/anti-TNF therapies to use or avoid in IBD patients with a cancer history according to the type of cancer

| Type of cancer | Avoid | Use with caution | Can be used |
|---|---|---|---|
| Lymphoma | Thiopurines | Anti-TNF, methotrexate, steroids | |
| Acute myeloid leukaemia and severe myelodysplastic disorders | Thiopurines | Anti-TNF | Methotrexate, steroids |
| Melanoma | Anti-TNF | Thiopurines, steroids | Methotrexate |
| Non-melanoma skin cancer | Thiopurines | Anti-TNF, steroids | Methotrexate |
| Urinary tract cancer | Thiopurines | Anti-TNF | Methotrexate, steroids |
| Other tumours | | Thiopurines, anti-TNF | Methotrexate, steroids |

ECCO consensus on IBD and malignancy. Annese V, et al. JCC 2015

adapted from Beaugerie L. Curr Drug Targets 2014

# *Management of IBD patients with past history of malignancy*

**ECCO Statement 6B**

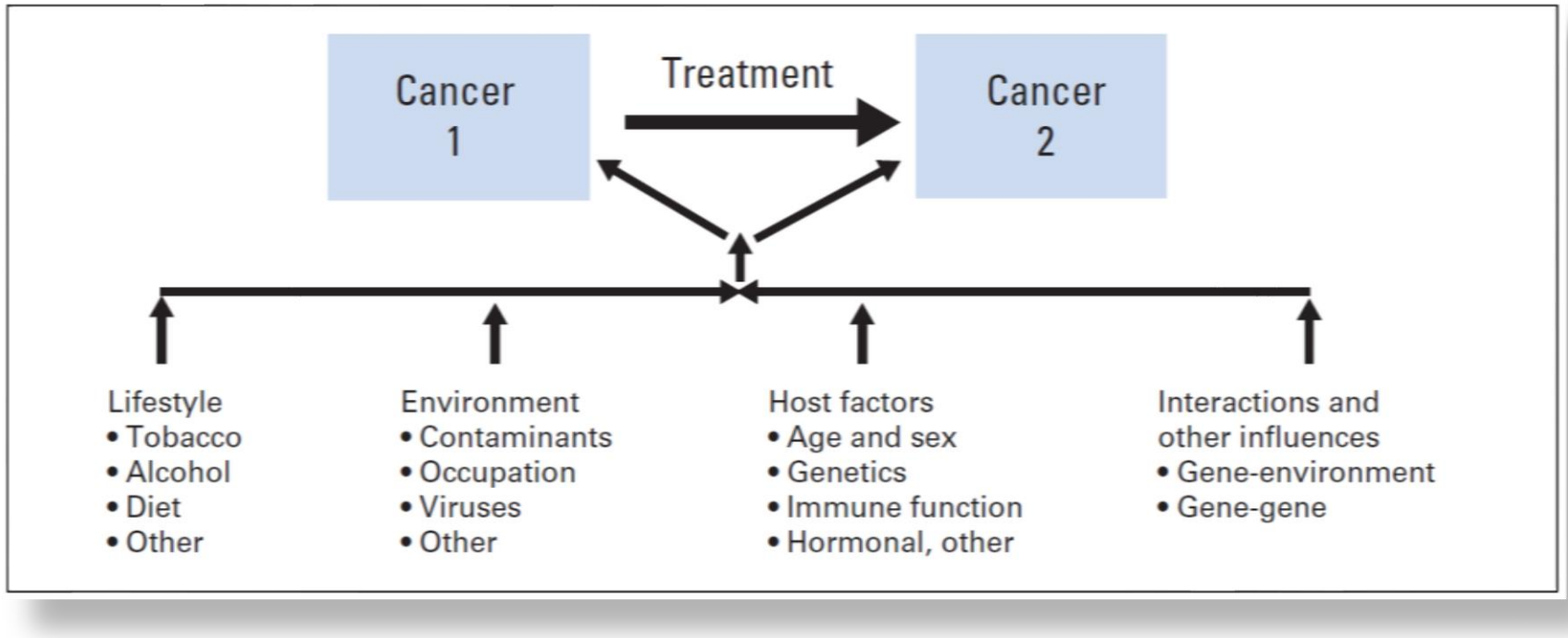
Physicians must be aware of the potential impact of immunosuppressants on cancers and on the risk of developing a second malignancy in cancer survivors [EL 3]

**ECCO Statement 6C**

Preliminary data on immune-mediated inflammatory diseases and IBD demonstrate no obvious excess risk of developing a second [new or recurrent] cancer while being treated with anti-TNF therapy [EL 4]

ECCO consensus on IBD and malignancy. Annese V, et al. JCC 2015

# *Multiple risk factors for second malignant neoplasms*




Wood ME, et al. J Clin Oncol 2012

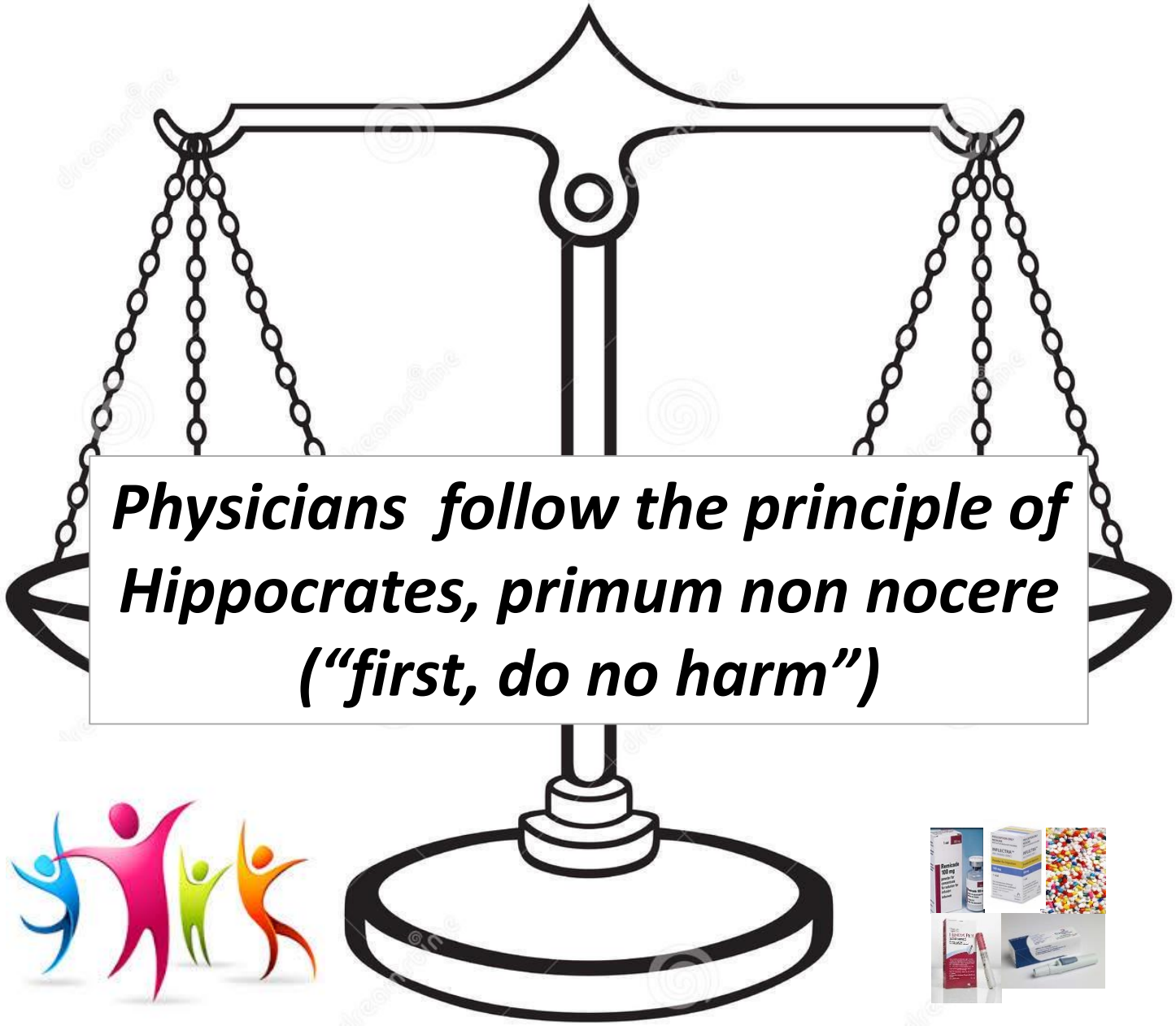
# Conclusions

## Multidisciplinary management with the oncologist

***Case-by-case decision making:***

- **Characteristics of the previous cancer**
  - Type, stage…
  - Risk of recurrence
  - Time from successful completion of cancer treatment
- **IBD activity…**
- **Impact of IBD therapy on the risk of new/recurrent cancer**
- **Other risk factors**
- **Patient quality of life**

***More studies are needed***



***Physicians follow the principle of Hippocrates, primum non nocere ("first, do no harm")***