Tumore del colon retto : update nella prevenzione , Diagnosi e trattamento

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1 Prevenzione e diagnosi precoce

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- Il quadro generale
- Una prima fonte di speranza
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A PREVENTABLE EPIDEMIC

DIET

Many foods have been linked with increased (animal fat, sugars) or decreased (garlic, fibre, calcium) risk of colorectal cancer[3], but the most compelling evidence for increased risk relates to the consumption of red and processed meats[4,5].

GENETICS

Having a first-degree relative with colorectal cancer increases the risk of the disease by 80%. By the age of 40, almost all adults with familial adenomatous polyposis[7] will have colorectal cancer, and *BRCA1* mutations may also increase risk.

OBESITY

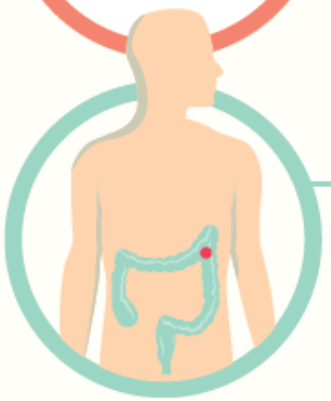
Closely linked to diet and physical inactivity, obesity also increases the risk of colorectal cancer. One 2013 study[10] found that obese people have a 33% higher risk of colorectal cancer than people of healthy weight.

AGE

One of the most crucial factors for colorectal cancer is age. Up to 90% of all colorectal cancers occur in people aged 50 years and over[6].

EXERCISE

The World Cancer Research Fund and the American Institute for Cancer Research both identify exercise as protective against colorectal cancer. Colorectal cancer risk is 17–24% lower in the most physically active people compared with the least physically active[8,9].



SCREENING

Screening finds precancerous polyps that can be removed before they become cancerous. The problem is ensuring access. In the United States, for example, one-third of adults over 50 have not been screened appropriately.

Screening per CCR

Rettosigmoidoscopia
(una volta nella vita
tra i 55 e i 64 anni)

Riduzione mortalità
~ 20-30%

Ricerca sangue
occulto fecale
(ogni due anni
tra i 50 e i 69 anni)

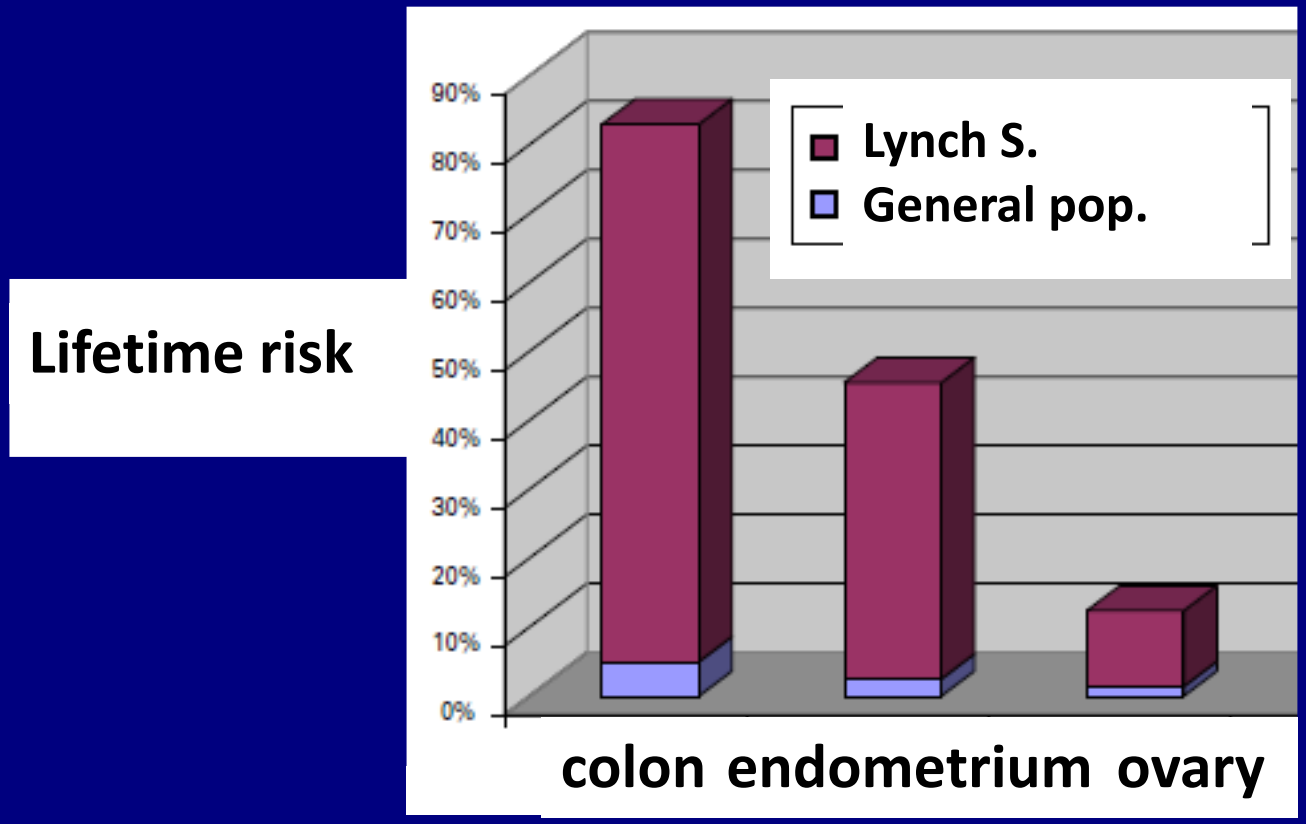
Riduzione mortalità
~ 10-20%

Colonscopia
(?)

No prove di
riduzione mortalità
da studi di fase 3

Hoff, BMJ 2009; Atkin, Lancet 2010; Segnan, JNCI 2011;Zorzi, Gut 2015; Brenner,BMJ 2014

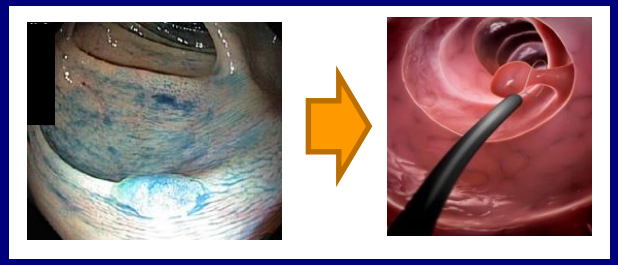
Lynch S.
Increased lifetime incidence of cancer

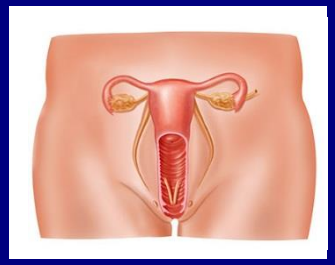


JNCI, sept 2010

Surveillance for Lynch S. relatives

ASCO-ESMO guidelines *Stoffel, JCO 2015*





Colonoscopy q 1-2 yrs,
from 20-25 yoa

Gyn ex + US + asp.bx annually, from 30-35 yoa.
Consider proph. surgery

Aspirin?

Mortality Reduction 60-70%

Jarvinen, JCO '09; Vasen, Gastroenterology '10; Møller, Gut '15 ;Movahedi, JCO '15; Brown, Cochran Rev '16

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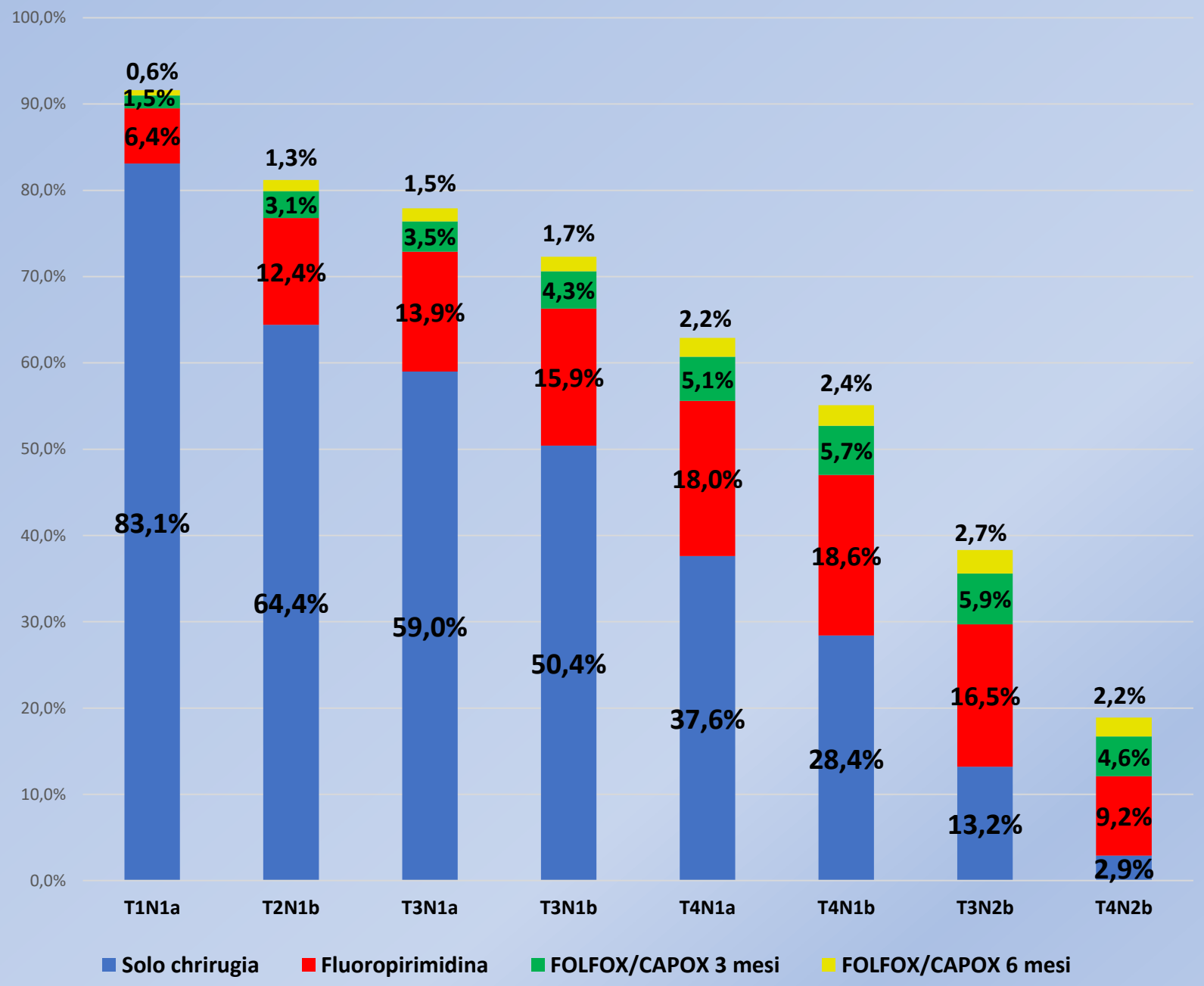
100,0%
90,0%
80,0%
70,0%
60,0%
50,0%
40,0%
30,0%
20,0%
10,0%
0,0%
0,6%
1,5%
6,4%
83,1%
1,3%
3,1%
12,4%
64,4%
1,5%
3,5%
13,9%
59,0%
1,7%
4,3%
15,9%
50,4%
2,2%
5,1%
18,0%
37,6%
2,4%
5,7%
18,6%
28,4%
2,7%
5,9%
16,5%
13,2%
2,2%
4,6%
9,2%
2,9%
T1N1a
T2N1b
T3N1a
T3N1b
T4N1a
T4N1b
T3N2b
T4N2b
Solo chrirugia
Fluoropirimidina
FOLFOX/CAPOX 3 mesi
FOLFOX/CAPOX 6 mesi

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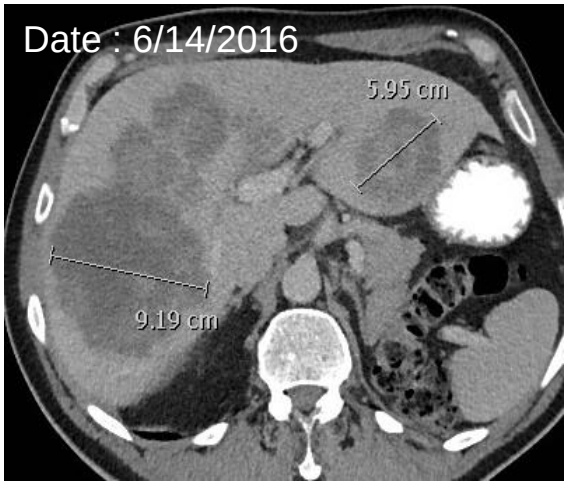
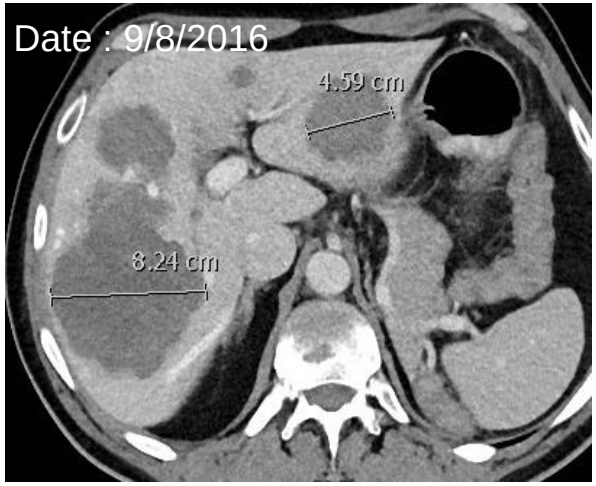
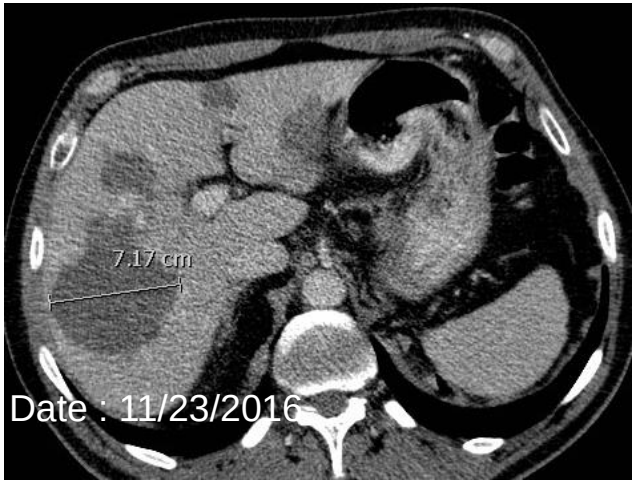
Simplification of the incremental overall benefit of the antineoplastic agents in advanced CRC (34 trials)

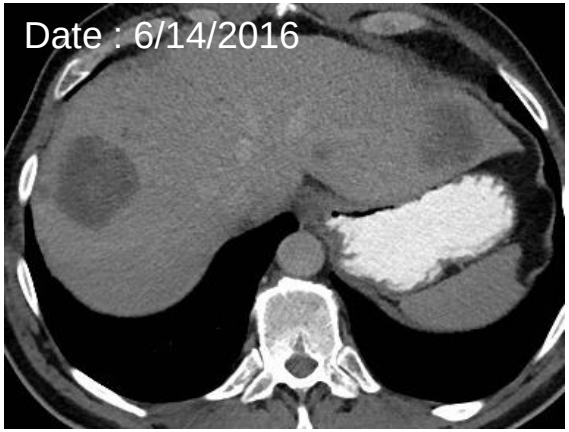
Agent	gain in median OS
FU	6 mo +
Oxali irino	6 mo
Anti VEGF	6 mo
Anti EGFR	6 mo +

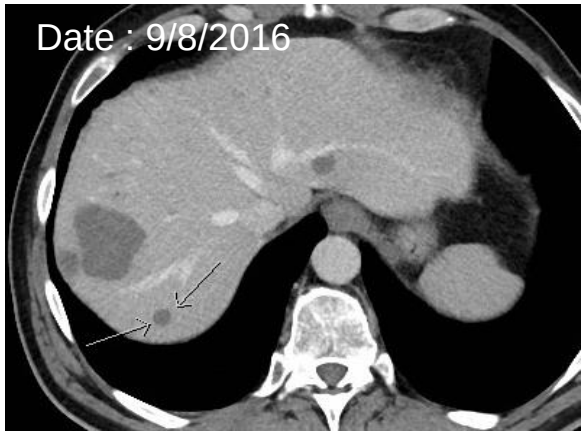
baseline	4 cycles	8 cycles











Alk. Phosphatase	667	239	182	(ULN 12)
LDH	624	190	232	(ULN 248)
CEA	402	247	34	(ULN 5.5)

Significant improvement in general condition

VOLUME 25 · NUMBER 29 · OCTOBER 10 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Actual 10-Year Survival After Resection of Colorectal Liver Metastases Defines Cure

James S. Tomlinson, William R. Jarnagin, Ronald P. DeMatteo, Yuman Fong, Peter Kornprat, Mithat Gonen, Nancy Kemeny, Murray F. Brennan, Leslie H. Blumgart, and Michael D'Angelica

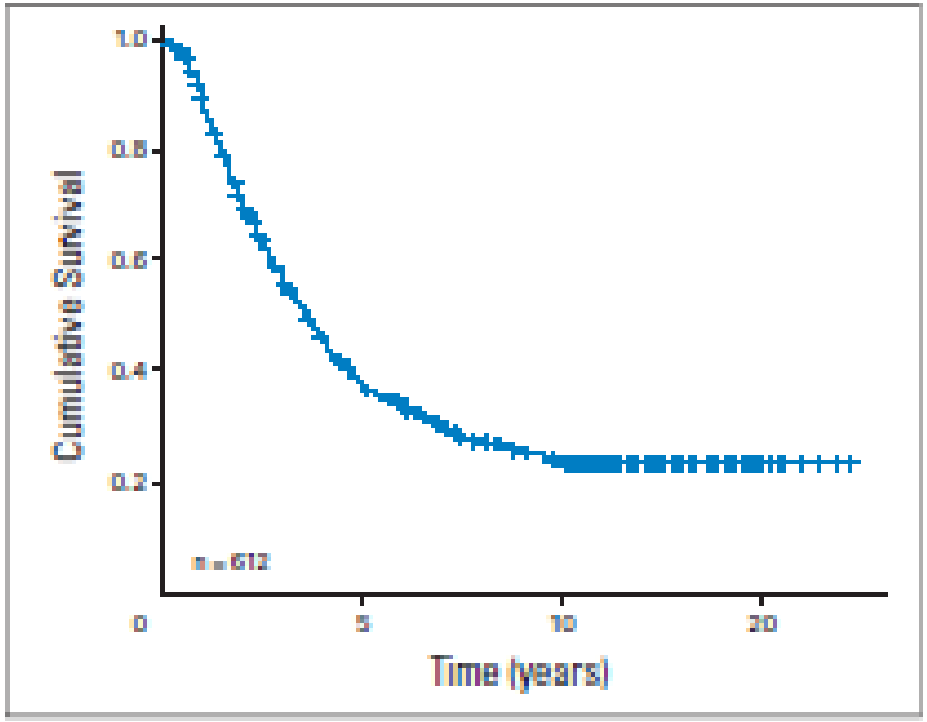


Fig 1. Kaplan-Meier plot of disease-specific survival for 612 patients with potential 10-year follow-up who underwent resection of colorectal liver metastases from 1985 to 1994 at Memorial Sloan-Kettering Cancer Center.

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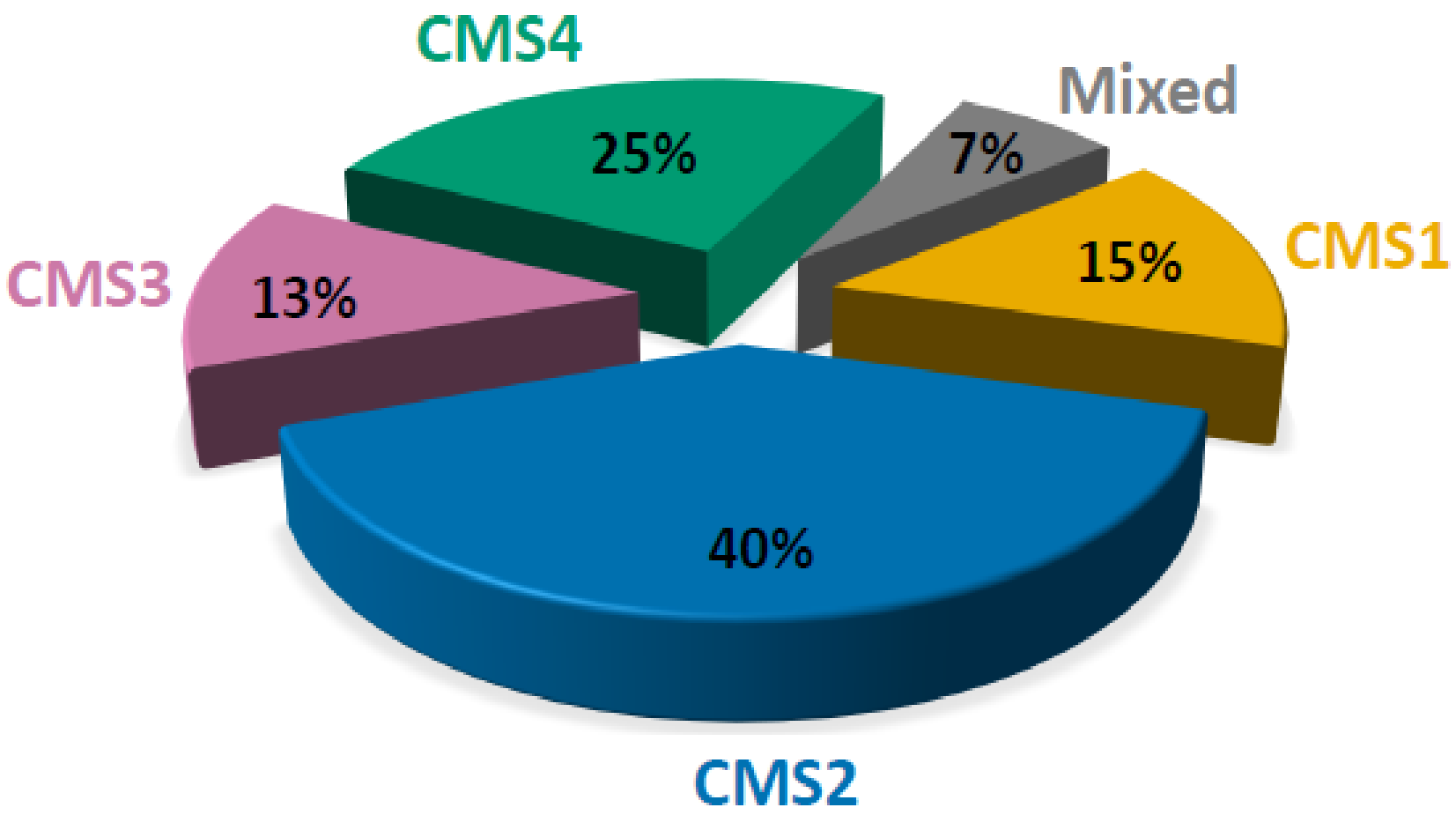
Transcriptomic classification



Microenvironment of CRC

Immune-activated

CMS1
MSI immune

dMMR – MSI
Hypermutation

Th1 cells
Cancer cell
Th1 cells
IFNγ
PDL1
IFNγ
CXCL9/10/13
Cytotoxic T cells
Macrophages
NK cells

Immune-tolerant Inflamed

CMS4
Mesenchymal

Inflammation
TGFβ
Complement
Stromal cells
Monocytes
Cancer cell
IL-17
CCL2
MDSC
Th17 cells
Stromal cells
TGFβ
CCL2
IL-23
Cytotoxic T cells
Macrophages
NK cells

Immune-ignorant

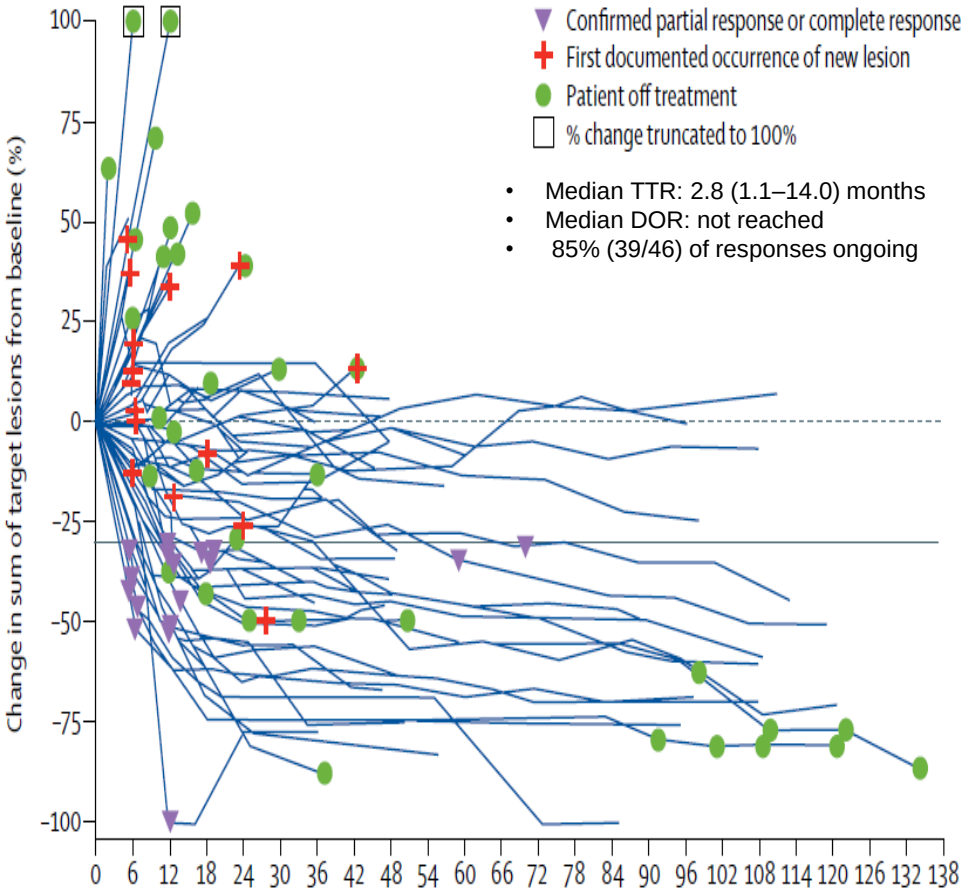
CMS2
Canonical

CMS3
Metabolic

Cancer cell

Changes in Tumor Burden

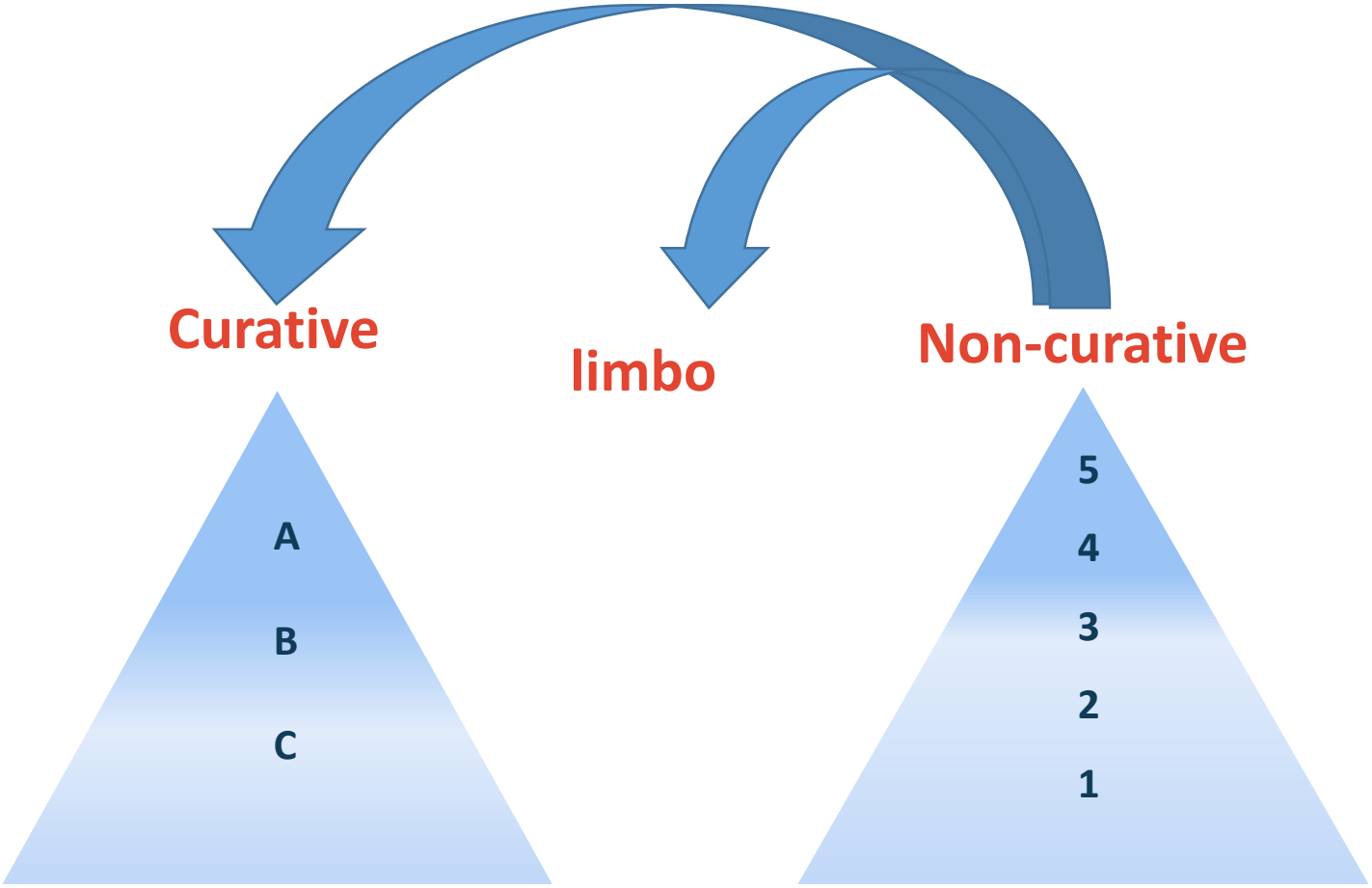
CheckMate 142 Nivolumab alone



Tt discontinuations
38 pts(51%) :
27 (36%) for PD
6 (8%) Toxicity
5 (7%) other

Overman M, Lancet Oncol 2017

ESMO-MCBS



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