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Sterotactic ablative radiotherapy in the treatment of patients with oligometastatic to the lung colorectal cancer: efficacy and toxicity

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Background

~25% of newly diagnosed CRC present with metastases

~50% of patients will develop metastases (liver, lung,..)

Stage IV median survival for untreated patients is 4-6 months

Surgical metastasectomy of liver and lung can achieve a 5-year survival rate of 30-50%*

Despite the widespread use for 50 years, no prospective controlled or randomized trials are available to affirm the evidence-based benefit of lung surgery

*Pfannschmidt J, et al Ann Thorac Surg 2007
Fiorentino F, et al Br J Cancer 2011

Lung Metastases From Colorectal Cancer: Analysis of Prognostic Factors in a Single Institution Study

2014

Maria Giulia Zampino, MD, Patrick Maisonneuve, Eng, Paola Simona Ravenda, MD, Elena Magni, MD, Monica Casiraghi, MD, Piergiorgio Solli, MD, Francesco Petrella, MD, Roberto Gasparri, MD, Domenico Galetta, MD, PhD, Alessandro Borri, MD, Stefano Donghi, MD, Giulia Veronesi, MD, and Lorenzo Spaggiari, MD, PhD

199 patients with CRC treated with lung metastasectomy
Median survival for R0 patients was 4.4 years with a 5years OS of 47%, while
Median survival for R1 patients was 1.44 years and the 5-years OS was 14%

The Prognosis of Pulmonary Metastasectomy Depends on the Location of the Primary Colorectal Cancer

2014

Jong Ho Cho, MD, Masatsugu Hamaji, MD, Mark S. Allen, MD, Stephen D. Cassivi, MD, MS, Francis C. Nichols, III, MD, Dennis A. Wigle, MD, PhD, K. Robert Shen, MD, and Claude Deschamps, MD

697 patients with CRC underwent 952 pulmonary metastasectomy (626 patients available for statistical analysis)
5-years OS of 55.6% (regardless the primary location)
5-years DFS 64.1% (better for colon patients)

Background

- Patients with oligometastatic disease (1-5 metastases) may benefit from local curative treatments, even achieving longer survival than other stage IV patients
- In the last few years some retrospective studies analyzed the effectiveness of the SABR for the treatment of oligometastatic CRC

Kim MS, et al. Oncology (2009)

Milano MT, et al. Int J Radiat Oncol Biol Phys (2011)

Salama JK, et al. Cancer (2012)

Thibault I, et al. Clin Oncol (R coll Radiol) (2014)

Filippi, et al. Int J Radiat Oncol Biol Phys (2015)

Qiu H, et al. Am J Clin Oncol (2015)

Background

- Oligometastatic CRC patients treated with SABR, had a 1y-, 2y- and 5-years OS of 90-95%, 42.5-75.5%% and 30-60%
- Median survival time widely ranged from 20.3 to 46 months

Filippi, et al. Int J Radiat Oncol Biol Phys (2015)
Qiu H, et al. Am J Clin Oncol (2015)

End-points

Retrospective analysis:

selected series of oligometastatic/oligorecurrent CRC patients with lung metastasis treated with SABR to all active sites



Response
Local control
Time to progression
Survival
Toxicity rate

Materials and Methods

62 lung metastases in 38 patients with CRC

Inclusion criteria:

- Controlled primary tumor with complete response or stable disease after surgery/radiotherapy/combined therapy
- ≤ 4 synchronous or metachronous lung metastasis at the time of treatment
- No other active sites of distant metastasis.

<i>Patient's characteristics</i>	
Mean Age	70 (52-90)
Sex	
Male	28 (74)
Female	10 (26)
Location of Primary Cancer	
Colon	20 (52)
Rectum	18 (48)
Sites of disease	
1	20 (53)
2-4	18 (77)
Site	
Central	6 (20.5)
Peripheral	23 (79.5)

Primary CRC Stage	
I	2 (5)
II	11 (29)
III	14 (37)
IV	9 (24)
Unknown	2 (5)

Previous first line CHT	
Yes	23 (60)
No	15 (40)

Materials and Methods

Treatment's characteristics

4DCT + IGRT

Single fraction 51 (85)

Multiple fraction 9 (15)

62 lung metastases in 38 patients with CRC

Median time to oligometastasis: 48 mo

Fractionation

23 Gy / 1fr
Multiple lesions 18 (30)

30 Gy / 1 fr
Peripheral or small
tumors (< 30cc) 33 (55)

45 Gy / 3 fr
Central or big
tumors (>30 cc) 9 (15)

Mean PTV volume: 10.65 cc (1.6 – 78.5 cc)

Results – Response

Response in 62 metastases:

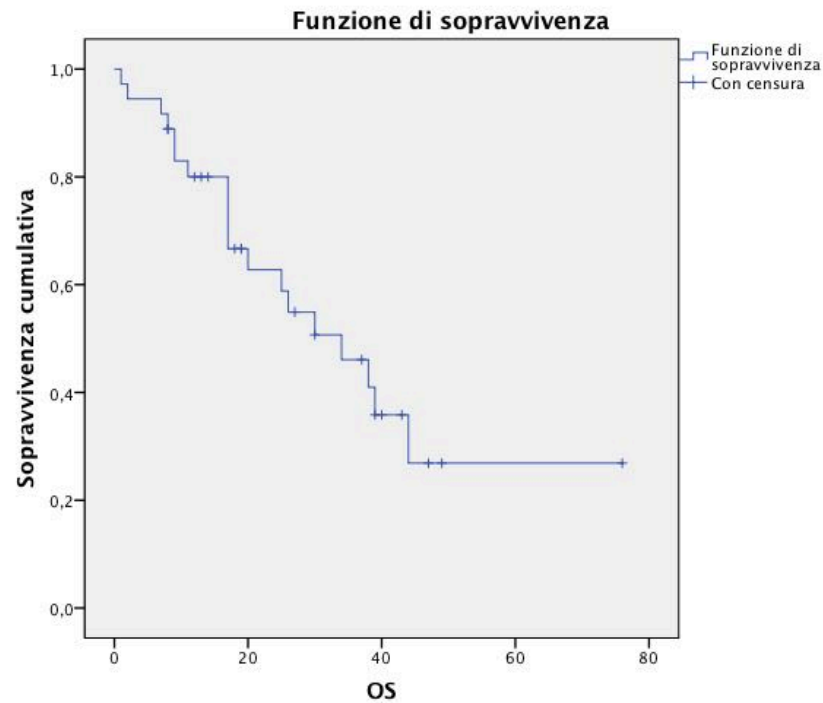
- Complete response (CR) 36.6%
- Partial response (PR) 40%
- Stable disease (SD) 20%
- Progressive disease (P) 3.4%

Overall local control was 96.6 % (58/60).

Distant failure occurred in 24 patients (40%) after a median time of 10 months

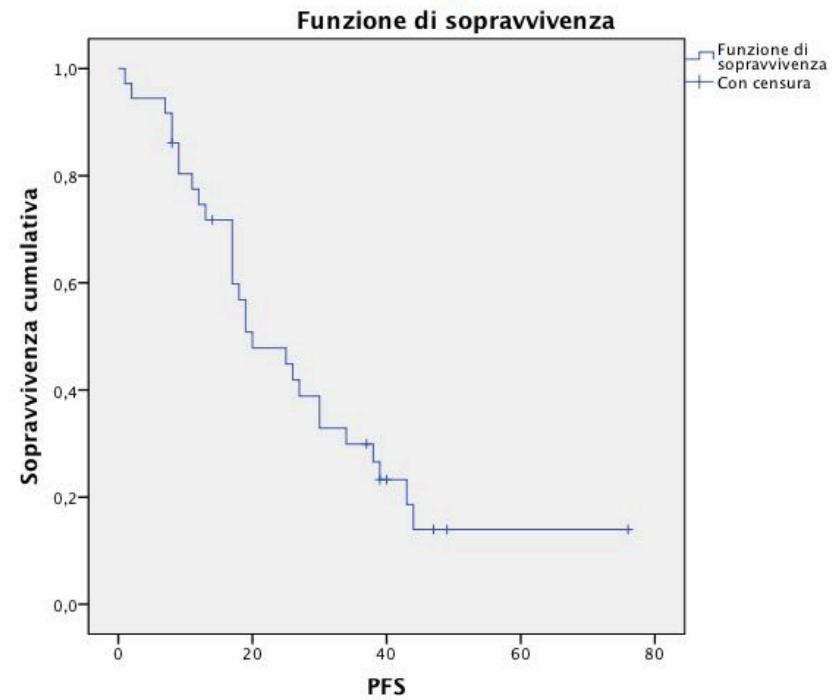
Results – Survival

Median OS: 34 mo



1 year: 80%
2 years: 50.7%
5 years: 26.9%

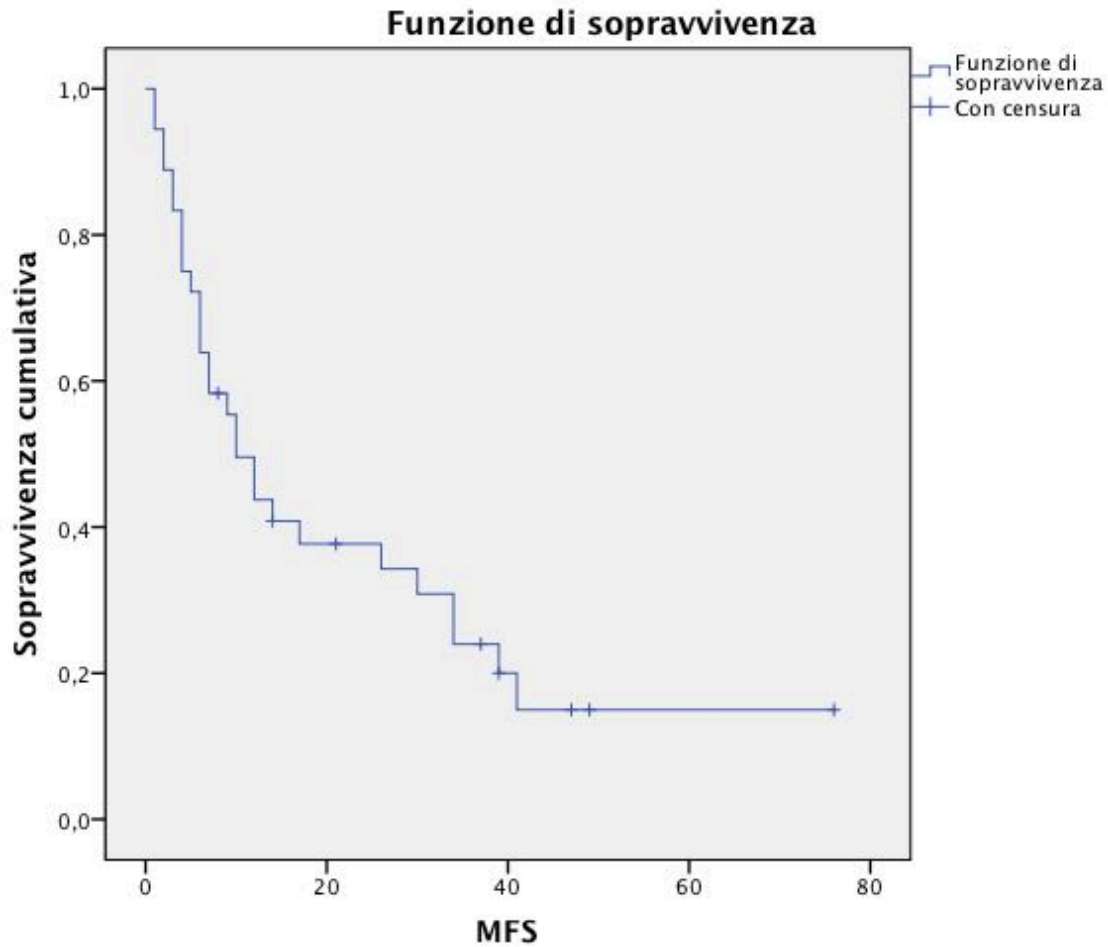
Median PFS: 20 mo



1 year: 74.6%
2 years: 47.8%
5 years: 14%

Results – Survival

Median MFS: 10 mo



1 year: 43.8%
2 years: 37.7%
5 years: 15%

Results – Prognostic factors

CR correlated with higher survival (as compared with PR and SD)

CR patients:

1-, 2- and 5-years OS of 100%, 90.9% and 67.3%

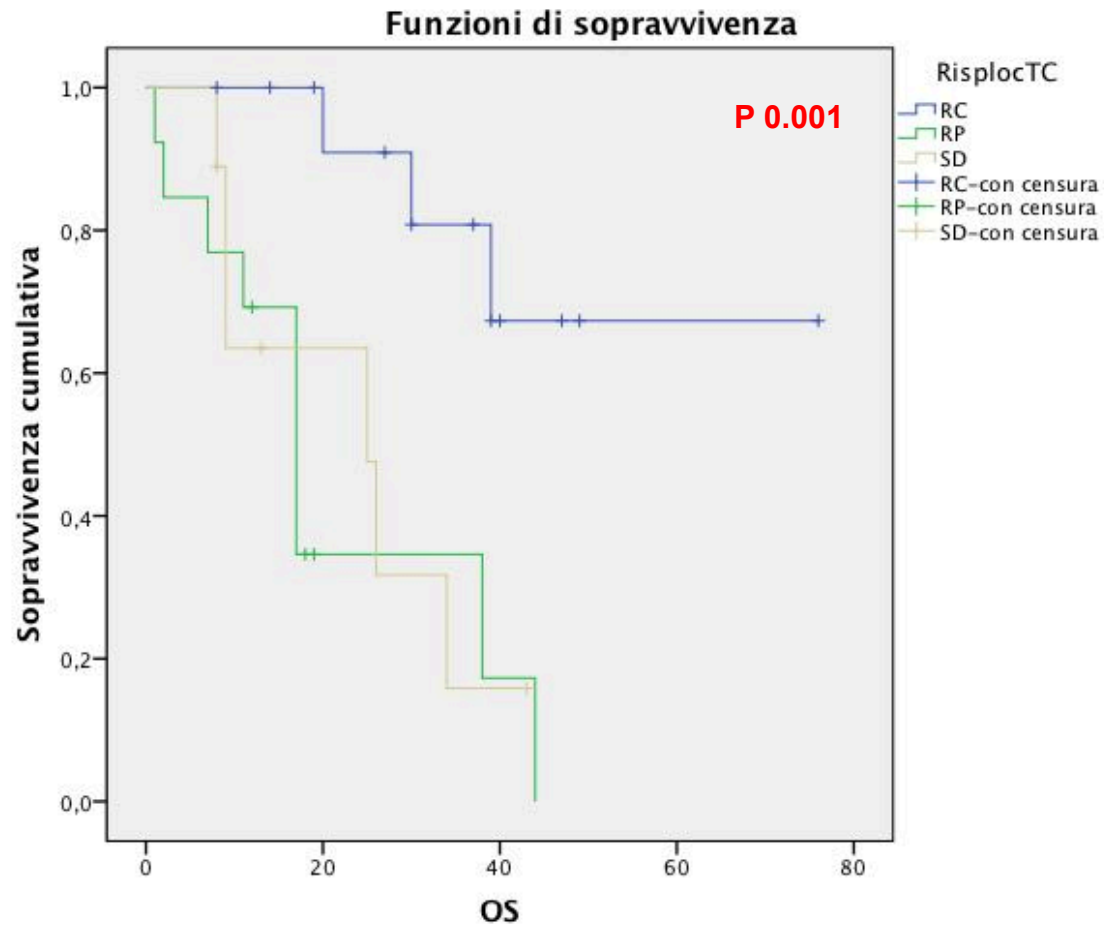
PR patients:

1-, 2- and 5-year OS of 69.2%, 34.6% and 0%

SD patients:

1- and 2-years OS of 63.5% and a 5-years OS of 15.9%

Results – Prognostic factors



Median OS

RC: nr

RP: 17 mo

SD: 25 mo

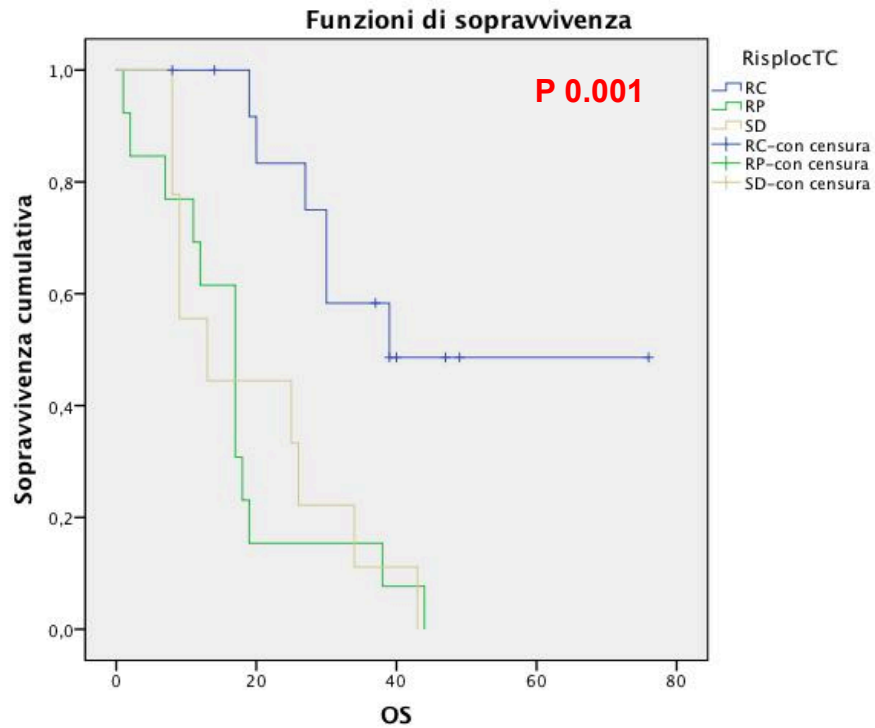
Results – Prognostic factors

PFS (response)			
	CR (median 39 mo)	PR (median 17 mo)	SD (median 13 mo)
1 year	100%	83.3%	48.6%
2 year	61.5%	44.4%	0%
5 year	55.6%	15.4%	0%

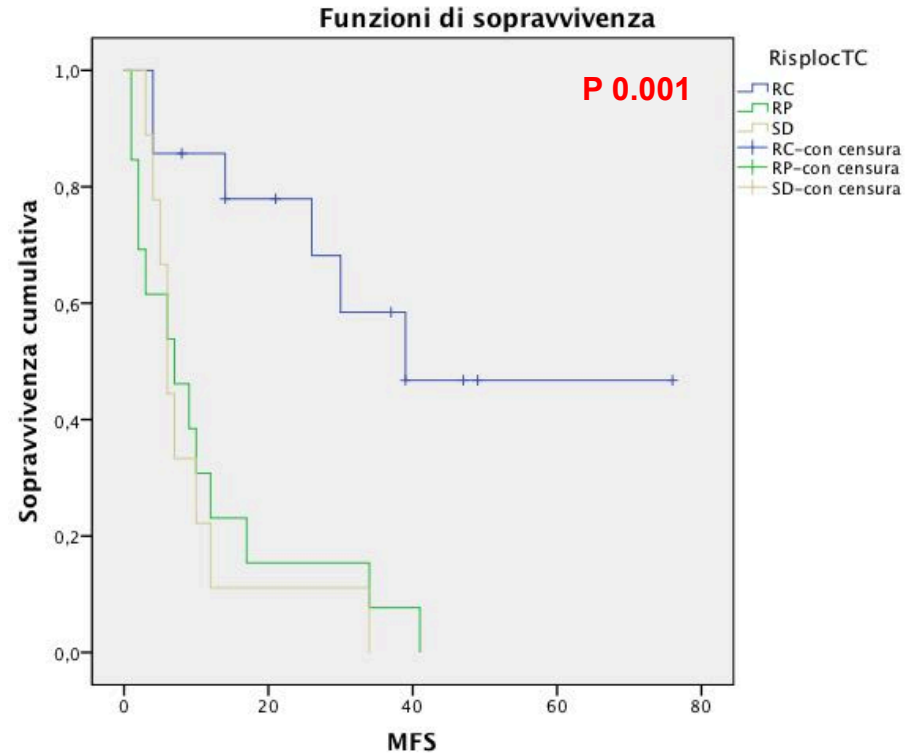
MFS (response)			
	CR (median 26 mo)	PR (median 6 mo)	SD (median 6 mo)
1 year	85.7%	77.9%	58.4%
2 year	23.1%	15.4%	0%
5 year	11%	0%	0%

Results – Prognostic factors

PFS (response tailored)



MFS (response tailored)

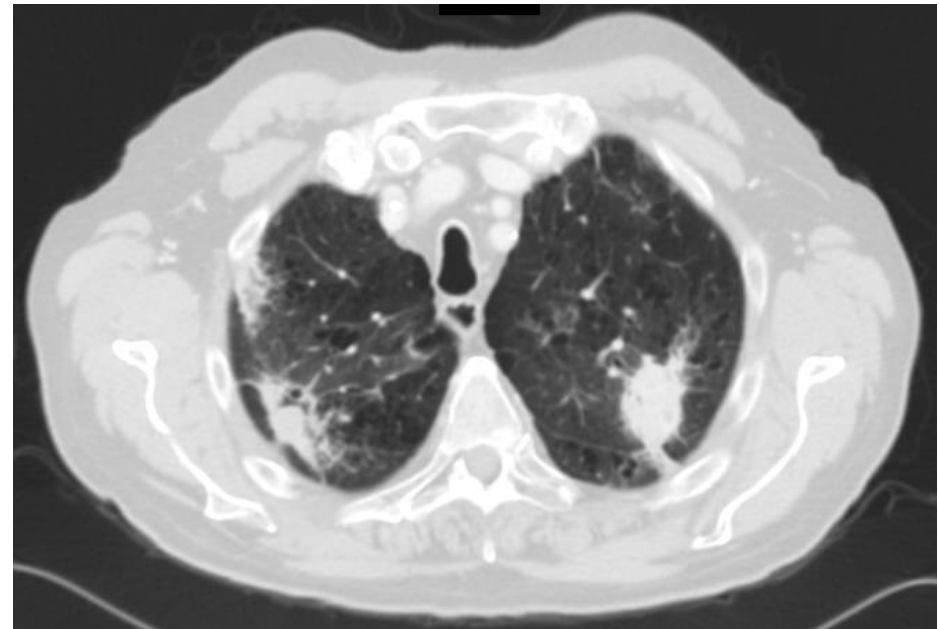
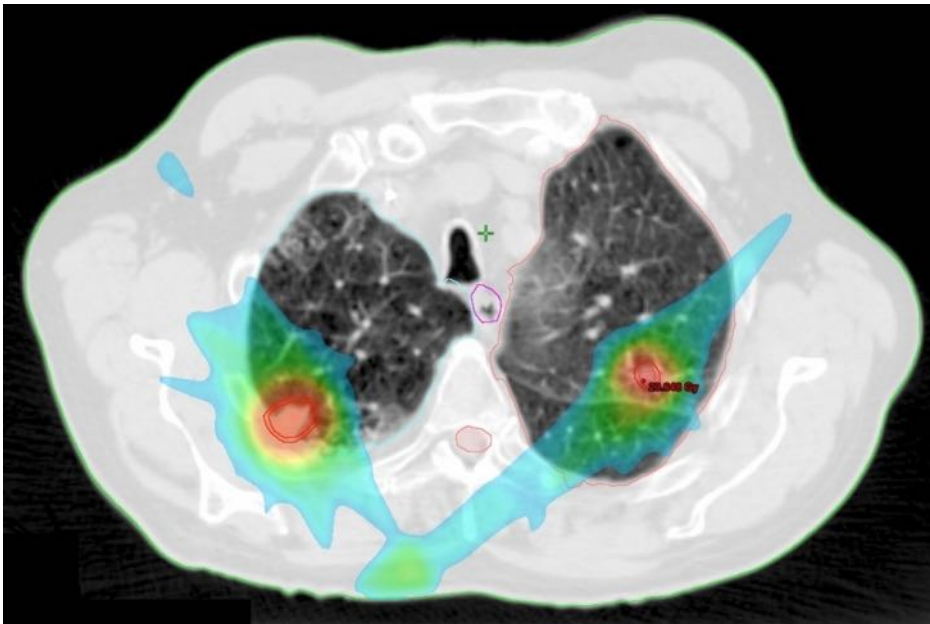


Results – Toxicity

6 pts (10%) developed G1-2 pneumonitis

1 pts (1.6%) had G3 pneumonitis

15 pts (25%) developed G1-2 late toxicity



Fibrosis after 1 year

Limits of this study?!

Small number of patients

Retrospective study

Consider the role of systemic therapy

Conclusions

Long term results rely on an exact and shared definition of oligometastatic disease

Higher survival for CR patients and in some cases even long-term survival

High rate of local control, well tolerated

Local ablative treatment is a feasible option in this well-selected setting of disease

Need for larger series of patients and phase III randomized trial

Thanks for your attention