Concomitant radiotherapy and TKI in EGFR-mutant or ALK positive metastatic non-small cell lung cancer.

M.L. Bonù, P. Borghetti, E. Roca, Triggiani, L. Bardoscia, F. Trevisan, S. Pedretti, S.Ciccarelli, N. Pasinetti, B. Bonetti, L. Pegurri, D. Greco, M. Buglione and S.M. Magrini

Spedali Civili di Brescia, Università degli studi di Brescia.

XXV Congresso A.I.R.O.
2 ottobre 2016 - **Rimini**

Stage IV NSCLC with a driver mutation:

TKI → **Impressive initial tumor response** → BUT → **Median PFS 8-13m**
Median OS 18-25m

- strategies beyond progression -

II LINE THERAPY

LOCAL TREATEMENT + CONTINUATION OF TKI

-Besse B, 2nd ESMO consensus conference on Lung Cancer, Ann Oncology 2014

-NCCN NSCLC Guidelines 2016

Indications for Locoregional treatments with continuation of TKI

- Synthomatic progression
- Brain metastasis
- Oligoprogression

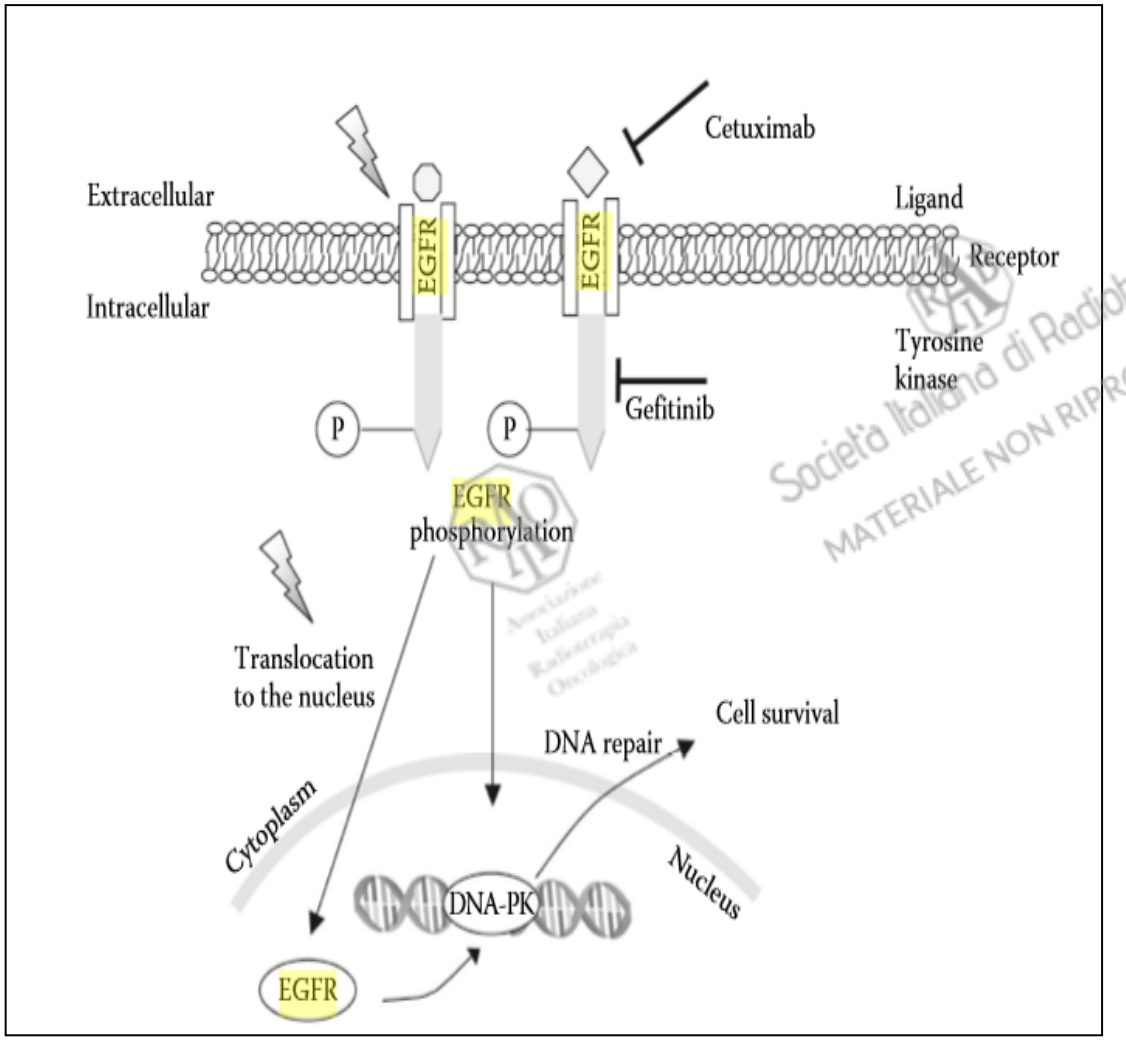
In **oligometastatic progression** most of the disease is controlled by the targeted therapy, except for a **small, limited number of drug-resistant tumor clones** (usually from **1 to 5 metastases** are accepted).

In patients with oligoprogression, it is possible to treat the metastatic lesion(s) with **local therapies,** which include **radiotherapy (whenever possible SBRT)**.

-Besse B, 2nd ESMO consensus conference on Lung Cancer, Ann Oncology 2014

-NCCN NSCLC Guidelines 2016

RATIONALE OF THE ASSOCIATION RT-TKI



- **POTENTIAL RADIOSENSITIZING EFFECT OF TKI**

Li, L., Wang, H., Yang, E. et al. Erlotinib attenuates homologous recombinational repair of chromosomal breaks in human breast cancer cells. Cancer Res 2008;68:9141–9146.

Chinnaiyan, P., Huang, S., Vallabhaneni, G. et al. Mechanisms of enhanced radiation response following epidermal growth factor receptor signaling inhibition by erlotinib (Tarceva). Cancer Res 2005;65:3328–3335.

Schmidt-Ullrich, R., Valerie, K., Fogleman, P., and Walters, J. Radiation-induced autophosphorylation of epidermal growth factor receptor in human malignant mammary and squamous epithelial cells. Radiat Res 1996;145:81–85.

MATERIALS AND METHODS

Retrospective series of 50 consecutive patients with stage IV NSCLC treated with Radiation therapy and Tirosine-Kinase inhibitors from 2010 to 2015 at Spedali Civili of Brescia

OBJECTIVES:

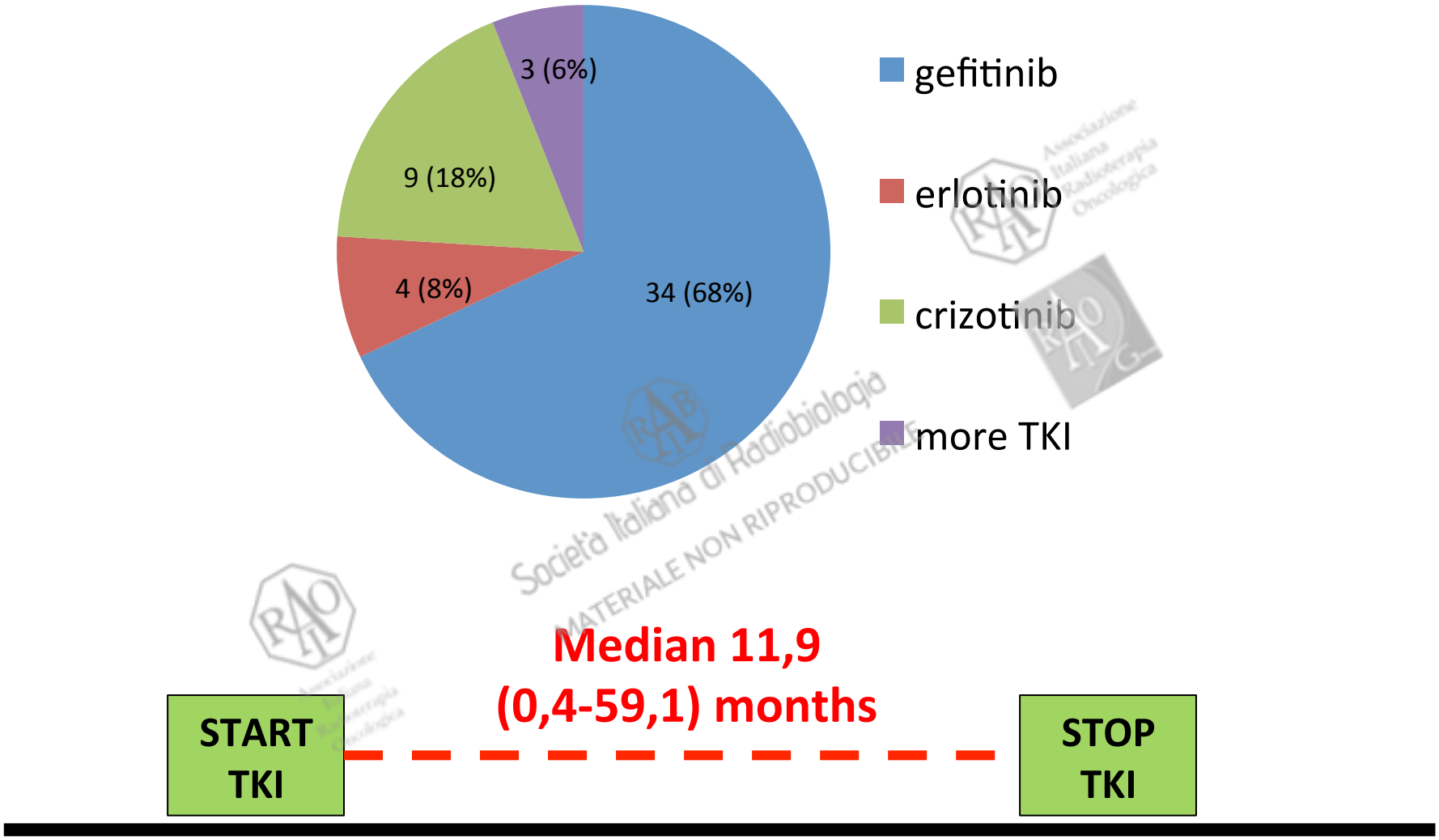
- ✓ *Overall Survival (OS)*
- ✓ *Clinical and therapeutic factors related to OS*
- ✓ *Toxicity*

Description of the series

	n. (%)
Age (median 65 yrs)	
≤ 65 yrs	26 (52)
> 65 yrs	24 (48)
Performance status	
0	16 (32)
1	29 (58)
2	5 (10)
Presentation at Rt	
≤ 4	11 (22)
> 4	39 (78)
Previous CHT	
0	27 (54)
1	15 (30)
2	8 (16)

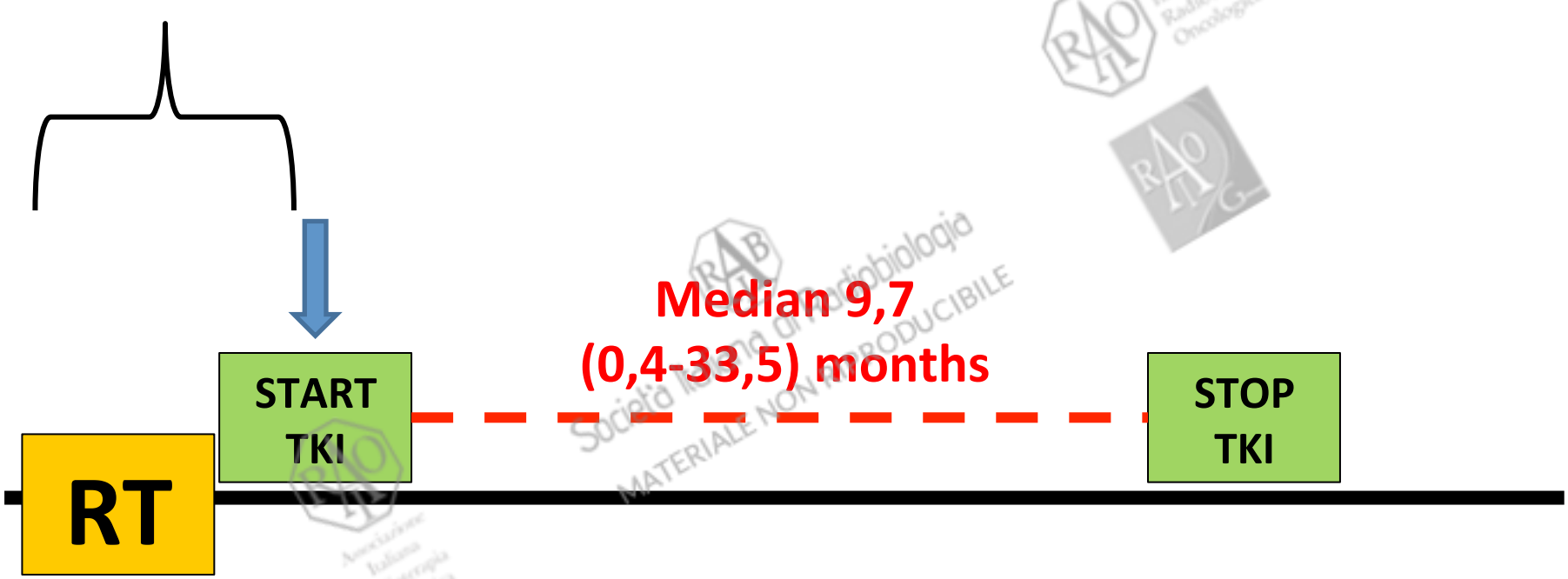
	n. (%)
RT schedule	
SRT	9 (18)
No SRT	41 (82)
RT target	
Brain	27 (54)
Bone	19 (38)
others	4 (8)
RT aim	
Symptomatic	28 (56)
Palliative	14 (28)
Ablative	8 (16)

50 patients 2010-2015

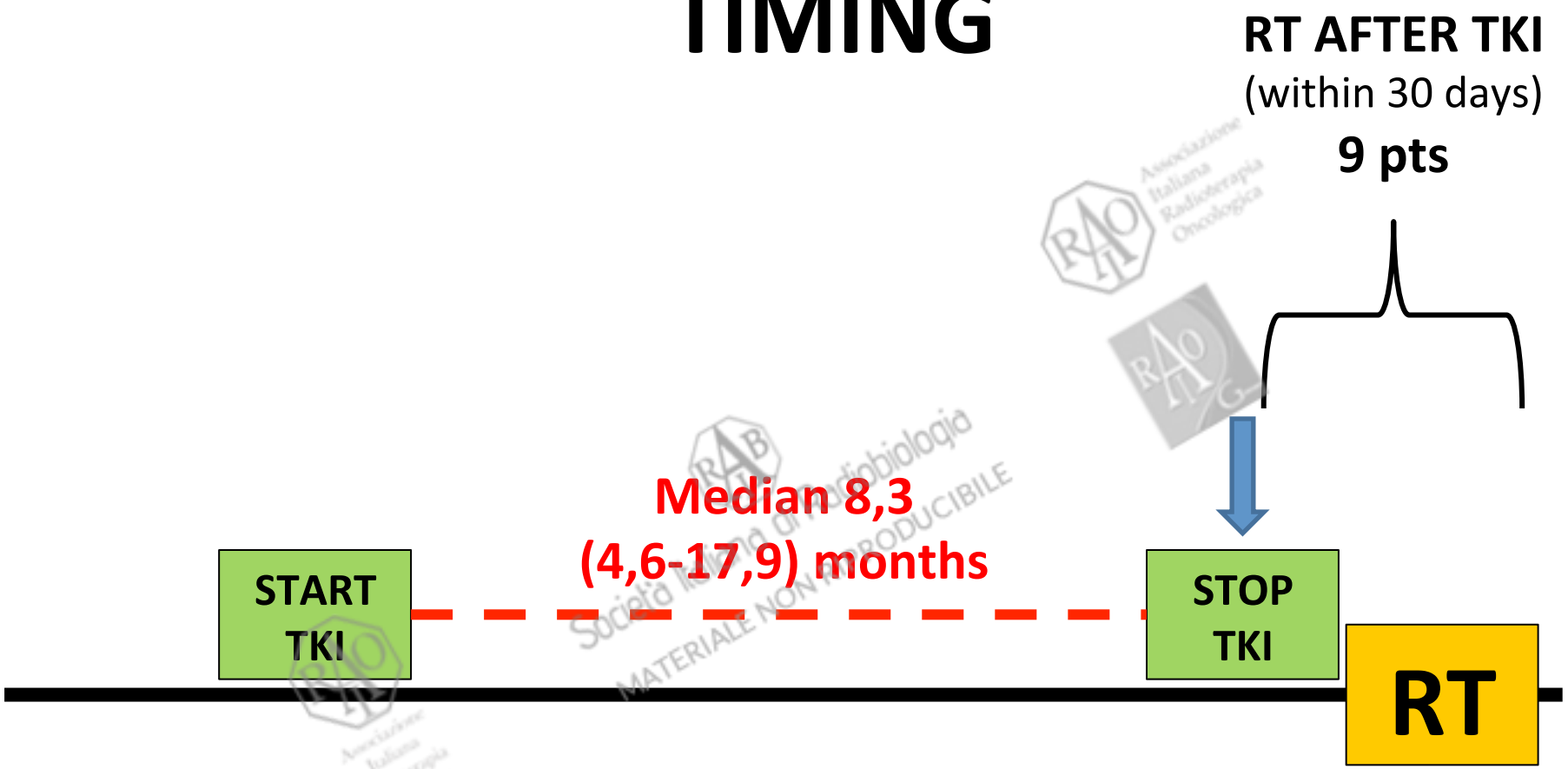


TIMING

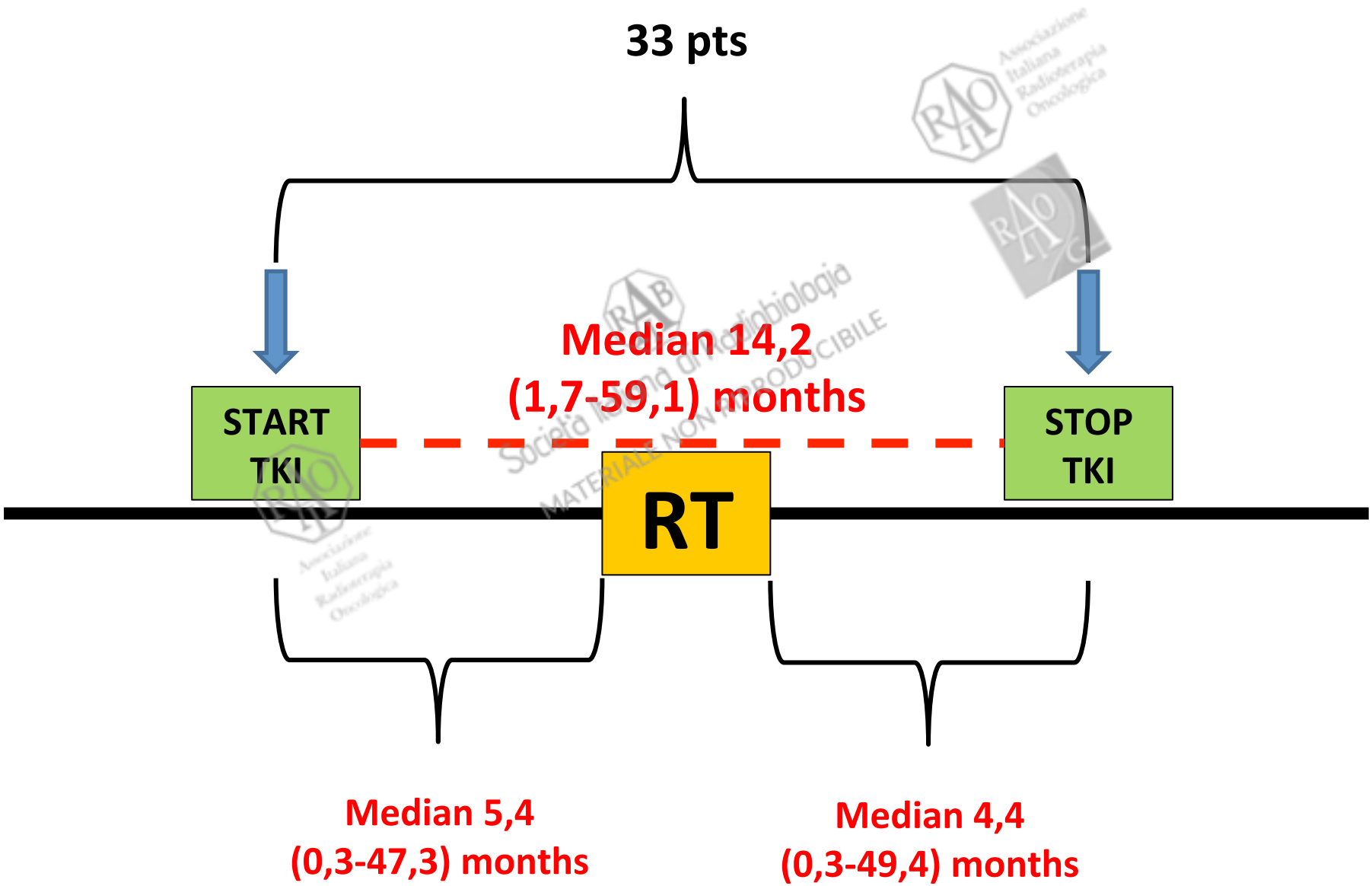
RT BEFORE TKI
(within 30 days)
8 pts



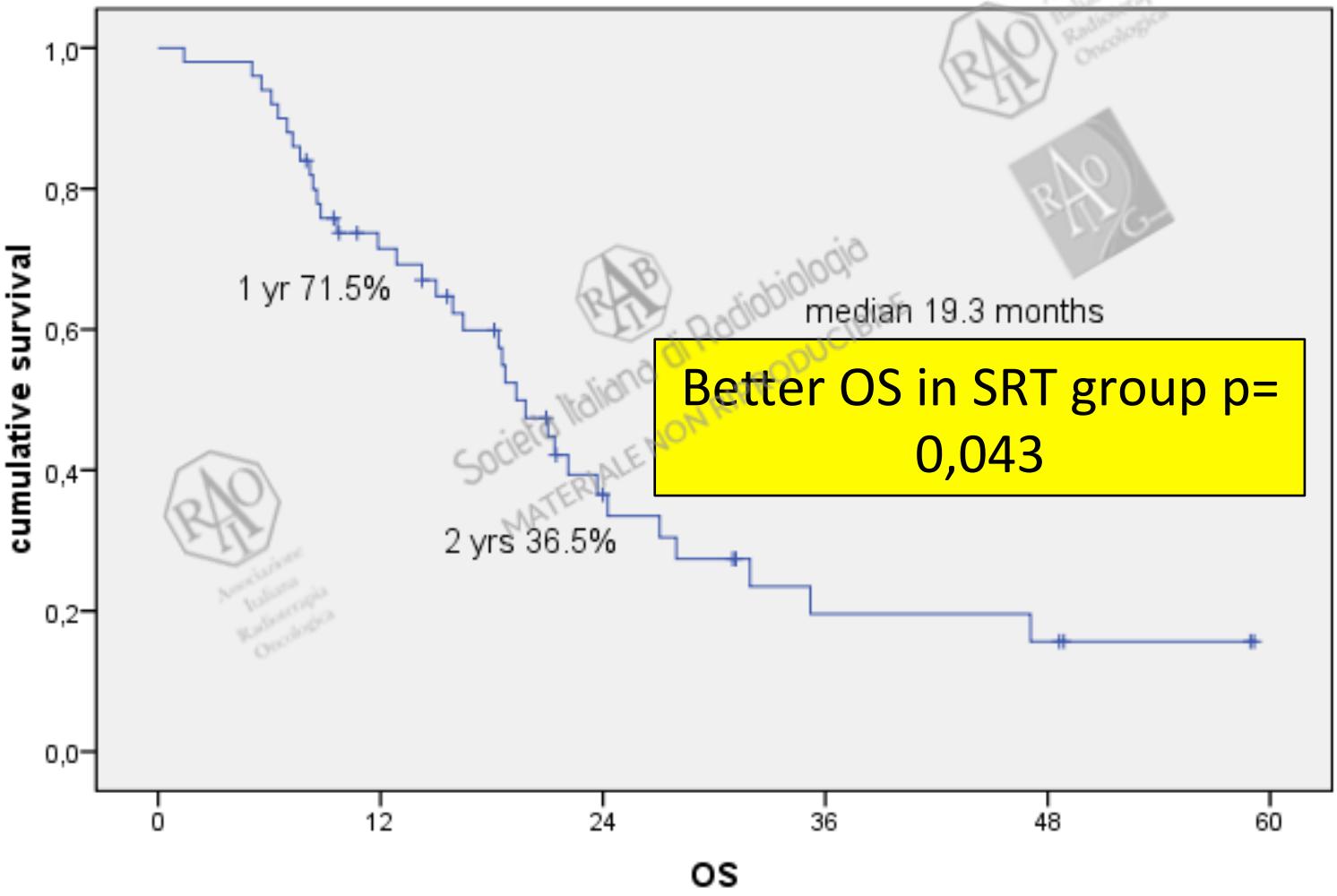
TIMING


RT AFTER TKI
(within 30 days)
9 pts
Median 8,3
(4,6-17,9) months
START TKI
STOP TKI
RT

CONCOMITANT RT-TKI



OS



Better OS in SRT group p= 0,043

TOXICITY RT-RELATED

Acute Toxicity	N°	%
none	36	72
Headache, confusion, worsening of other neurological signs/symptoms	7	14
Pain	3	6
Emesis	4	8

- ✓ **All Toxicities were G1-2**
- ✓ All the adverse events did not determined the suspension of RT
- ✓ No increasing of adverse events if compared to RT alone (Historical data)
- ✓ No dermatitis were observed

CONCLUSIONS

- Our series is larger than most of published experiences
- Results are convincing in term of:
  - **OS (comparable to data reported in TKI Pivotal studies)**
  - **Toxicity profile**
- RT (**ablative** and **also palliative-symptomatic**) at the time of progression is a treatment that could potentially **increase** the **duration** of the **systemic therapy**
- Better outcomes could be achieved with **stereotactic RT (selected patients)**
- RT combined with TKI is a promising approach in Stage IV NSCLC with a driver mutation but it needs **prospective studies**

Concomitant radiotherapy and TKI in EGFR-mutant or ALK positive metastatic non-small cell lung cancer.

M.L. Bonù, P. Borghetti, E. Roca, Triggiani, L. Bardoscia, F. Trevisan, S. Pedretti, S.Ciccarelli, N. Pasinetti, B. Bonetti, L. Pegurri, D. Greco, M. Buglione and S.M. Magrini

Spedali Civili di Brescia, Università degli studi di Brescia.

XXV Congresso A.I.R.O.
2 ottobre 2016 - **Rimini**