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


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

-NCCN NSCLC Guidelines 2016
Indications for Locoregional treatments with continuation of TKI

- Synthomatic progression
- Brain metastasis
- Oligoprogession

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

-NCCN NSCLC Guidelines 2016
RATIONALE OF THE ASSOCIATION
RT-TKI

- POTENTIAL RADIOSENSITIZING EFFECT OF TKI


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

<table>
<thead>
<tr>
<th>Description</th>
<th>n. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (median 65 yrs)</strong></td>
<td></td>
</tr>
<tr>
<td>( \leq 65 \text{ yrs} )</td>
<td>26 (52)</td>
</tr>
<tr>
<td>( &gt; 65 \text{ yrs} )</td>
<td>24 (48)</td>
</tr>
<tr>
<td><strong>Performance status</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>16 (32)</td>
</tr>
<tr>
<td>1</td>
<td>29 (58)</td>
</tr>
<tr>
<td>2</td>
<td>5 (10)</td>
</tr>
<tr>
<td><strong>Presentation at Rt</strong></td>
<td></td>
</tr>
<tr>
<td>( \leq 4 )</td>
<td>11 (22)</td>
</tr>
<tr>
<td>( &gt; 4 )</td>
<td>39 (78)</td>
</tr>
<tr>
<td><strong>Previous CHT</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>27 (54)</td>
</tr>
<tr>
<td>1</td>
<td>15 (30)</td>
</tr>
<tr>
<td>2</td>
<td>8 (16)</td>
</tr>
<tr>
<td><strong>RT schedule</strong></td>
<td></td>
</tr>
<tr>
<td>SRT</td>
<td>9 (18)</td>
</tr>
<tr>
<td>No SRT</td>
<td>41 (82)</td>
</tr>
<tr>
<td><strong>RT target</strong></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>27 (54)</td>
</tr>
<tr>
<td>Bone</td>
<td>19 (38)</td>
</tr>
<tr>
<td>others</td>
<td>4 (8)</td>
</tr>
<tr>
<td><strong>RT aim</strong></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>28 (56)</td>
</tr>
<tr>
<td>Palliative</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Ablative</td>
<td>8 (16)</td>
</tr>
</tbody>
</table>

**50 patients 2010-2015**
Median 11.9
(0.4-59.1) months

- START TKI
- STOP TKI
RT BEFORE TKI (within 30 days) 8 pts

START TKI

STOP TKI

Median 9.7 (0.4-33.5) months
RT AFTER TKI
(within 30 days)
9 pts

START TKI

STOP TKI

Median 8.3
(4.6-17.9) months

RT
CONCOMITANT RT-TKI

33 pts

START TKI

RT

STOP TKI

Median 14.2 (1.7-59.1) months

Median 5.4 (0.3-47.3) months

Median 4.4 (0.3-49.4) months
Better OS in SRT group $p=0.043$
# TOXICITY RT-RELATED

<table>
<thead>
<tr>
<th>Acute Toxicity</th>
<th>N°</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>36</td>
<td>72</td>
</tr>
<tr>
<td>Headache, confusion, worsening of other neurological signs/symptoms</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Pain</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Emesis</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

- 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
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