

Use of adjuvant chemotherapy (CT) and radiotherapy (RT) in incompletely resected (R1) early stage Non-Small Cell Lung Cancer (NSCLC): a European survey conducted by the European Society for Medical Oncology (ESMO) Young Oncologists Committee.

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Background

Early stage NSCLC is potentially curable with radical surgery. Cisplatin-based adjuvant CT improves survival and is recommended in the ESMO guidelines for stage II-III completely resected NSCLC. There is limited evidence to guide the use of adjuvant CT and RT in incompletely resected (R1) early stage NSCLC.

Design and objective

A European survey of oncologists treating lung cancer was conducted to evaluate the use of adjuvant CT and RT for R1-resected NSCLC and to identify factors influencing treatment decisions. Demographics were collected and outcomes such as clinical stage, regimens, cycles planned, radiotherapy site, multidisciplinary management and discussion about inconclusive evidence with the patient were analyzed. Logistic regression model was used to detect statistical association and to estimate Odds Ratio; Cochrane-Armitage test was used to detect trend.

Results

| Country | N | % | Country | N | % |
|--------------------|-----|------|------------------------|---|-----|
| ITALY | 138 | 18.0 | SLOVENIA | 6 | 0.8 |
| UNITED KINGDOM | 71 | 9.2 | NORWAY | 5 | 0.7 |
| SPAIN | 60 | 7.8 | SWEDEN | 5 | 0.7 |
| FRANCE | 59 | 7.7 | ISRAEL | 5 | 0.7 |
| GERMANY | 58 | 7.6 | ALBANIA | 4 | 0.5 |
| TURKEY | 44 | 5.7 | CYPRUS | 4 | 0.5 |
| GREECE | 43 | 5.6 | SLOVAKIA | 4 | 0.5 |
| AUSTRIA | 38 | 4.9 | IRELAND | 4 | 0.5 |
| RUSSIAN FEDERATION | 25 | 3.3 | UKRAINE | 4 | 0.5 |
| BELGIUM | 25 | 3.3 | ESTONIA | 3 | 0.4 |
| ROMANIA | 24 | 3.1 | LATVIA | 3 | 0.4 |
| CZECH REPUBLIC | 16 | 2.1 | FINLAND | 3 | 0.4 |
| BULGARIA | 16 | 2.1 | BOSNIA AND HERZEGOVINA | 2 | 0.3 |
| PORTUGAL | 16 | 2.1 | BELARUS | 2 | 0.3 |
| HUNGARY | 14 | 1.8 | LUXEMBOURG | 2 | 0.3 |
| POLAND | 12 | 1.6 | LITHUANIA | 1 | 0.1 |
| DENMARK | 12 | 1.6 | ICELAND | 1 | 0.1 |
| SERBIA | 11 | 1.4 | CROATIA | 1 | 0.1 |
| NETHERLANDS | 9 | 1.2 | MACEDONIA | 1 | 0.1 |
| SWITZERLAND | 8 | 1.0 | MONTENEGRO | 1 | 0.1 |
| GEORGIA | 8 | 1.0 | | | |

Between January and April 2012, 768 surveys were collected from 41 European countries (Table 1). The majority (82.9%) of participants are medical oncologists, about a half are ESMO members and more than one-third are based in a University Hospital (Demographics are summarized in Table 2).

| Are you an ESMO Member? | N | % | Are you active in clinical research? | N | % |
|----------------------------|-----|------|--|-----|------|
| Yes | 378 | 49.3 | Yes | 623 | 81.4 |
| No | 388 | 50.7 | No | 142 | 18.6 |
| Missing data | 2 | 0.3 | Missing data | 3 | 0.4 |
| Gender | | | Which percentage of your patients has lung cancer? | | |
| Male | 458 | 59.8 | <25% | 257 | 33.6 |
| Female | 308 | 40.2 | 25-50% | 240 | 31.3 |
| Missing data | 2 | 0.3 | 51-75% | 121 | 15.8 |
| Type of Institution | | | 76-100% | 148 | 19.3 |
| University Hospital | 285 | 37.1 | Missing data | 2 | 0.3 |
| Cancer Center | | | How frequently do you consult ESMO Clinical Practice Guidelines? | | |
| | 228 | 29.3 | Once a week | 95 | 12.7 |
| General Hospital | 210 | 27.3 | Once a month | 203 | 27.2 |
| Private Center | 45 | 5.9 | Once every two months | 62 | 8.3 |
| Specialty | | | Occasionally | 318 | 42.6 |
| Medical Oncology | 637 | 82.9 | Never | 69 | 9.2 |
| Radiation Oncology | 131 | 17.1 | Missing data | 21 | 2.7 |
| Years practising specialty | | | | | |
| | N | % | | | |
| 0-5 | 200 | 26.1 | | | |
| 5<-10 | 184 | 24.0 | | | |
| 10<-15 | 133 | 17.3 | | | |
| >15 | 250 | 32.6 | | | |
| Missing data | 1 | 0.1 | | | |

Multiple choice was allowed for different questions on prescription of adjuvant CT (Table 3) and adjuvant RT (Table 4). Adjuvant CT is prescribed by 91.4% of participants with wide variation according to stage. Most commonly chosen regimens are: Cisplatin/Vinorelbine (81.2%) and Cisplatin/Carboplatin (42.9%). Notably 13% and 44% of respondents prescribe adjuvant chemo for stage IA and IB, respectively. Furthermore, carboplatin-based doublets are largely used and, despite no indication in this setting, pemetrexed-based doublets are chosen by 17-26% of participants.

| Do you prescribe chemotherapy? | N | % | Other regimens | N | % |
|--------------------------------|-----|------|---|-----|------|
| Yes | 702 | 91.4 | Cisplatin/Etoposide | 26 | 3.9 |
| No | 66 | 8.6 | Carboplatin/Etoposide | 5 | 0.7 |
| If YES, Stage | | | Bevacizumab, erlotinib, gefitinib, platinum doublet/bevacizumab, etoposide, carboplatin, Vinorelbine, oxaliplatin/ Vinorelbine, cisplatin/ Irinotecan/mitomycin | 18 | 2.7 |
| IA | 90 | 13.3 | Missing data | 540 | 84.8 |
| IB | 303 | 44.8 | No | 97 | 15.2 |
| IIA | 567 | 83.9 | Regimen | | |
| IIIB | 612 | 90.5 | Cisplatin/Vinorelbine | 547 | 81.2 |
| IIIA | 639 | 94.5 | Cisplatin/Carboplatin | 289 | 42.9 |
| Missing data | 26 | 3.7 | Missing data | 65 | 9.3 |
| Regimen | | | Number of cycles planned | | |
| Cisplatin/Docetaxel | 144 | 21.4 | Yes | 545 | 87.1 |
| Cisplatin/Paclitaxel | 95 | 14.1 | No | 81 | 12.9 |
| Cisplatin/Pemetrexed | 178 | 26.4 | Missing data | 76 | 10.8 |
| Carboplatin/Vinorelbine | 213 | 31.6 | Missing data | 17 | 2.7 |
| Carboplatin/Docetaxel | 180 | 26.7 | 3 cycles | 50 | 7.5 |
| Carboplatin/Paclitaxel | 209 | 31.0 | 4 cycles | 97 | 14.5 |
| Carboplatin/Pemetrexed | 116 | 17.2 | Missing data | 31 | 4.4 |
| Missing Data | 28 | 4.0 | Lack of conclusive evidence discussed with the patient | | |
| | | | Yes | 578 | 85.5 |
| | | | No | 98 | 14.5 |
| | | | Missing data | 26 | 3.7 |

Multidisciplinary discussion happens very frequently and lack of clinical evidence is discussed with the patient by 85% of physicians. About a half of respondents prescribe adjuvant RT and notably the majority (85%) suggest its use also for pN2 disease despite this is not recommended by ESMO guidelines neither for completely resected tumors. Univariate analysis showed that prescription of CT was associated with Medical Oncology specialty and ESMO membership (p<0.001 for both), activity in clinical research (p=0.002) and increased frequency of consultation of ESMO guidelines (p for trend <0.001). Prescription of RT was associated with Radiation Oncology specialty (p<0.001), years practicing specialty (p for trend = 0.001) and increased workload (p for trend = 0.027).

| Do you prescribe radiotherapy? | N | % | Radiotherapy for surgical bed | N | % |
|--------------------------------|-----|------|-------------------------------|-----|------|
| Yes | 359 | 48.3 | Yes | 289 | 84.8 |
| No | 384 | 51.7 | No | 52 | 15.2 |
| Missing data | 25 | 3.3 | Missing data | 18 | 5.0 |
| Regimen | | | Regimen | | |
| 50 Gy in 20 Fx | 64 | 23.4 | 50 Gy in 20 Fx | 65 | 24.1 |
| 54 Gy in 27-30 Fx | 81 | 29.6 | 54 Gy in 27-30 Fx | 92 | 34.1 |
| 60 Gy in 30 Fx | 125 | 45.6 | 60 Gy in 30 Fx | 95 | 35.2 |
| 52.5 Gy in 20 Fx | 10 | 3.6 | 52.5 Gy in 20 Fx | 6 | 2.2 |
| Missing data | 17 | 5.8 | Missing data | 19 | 6.6 |
| Other regimens | 40 | 14.6 | Other regimens | 52 | 19.3 |
| OVERALL | | | OVERALL | | |
| 55 Gy in 20 Fx | 10 | 3.6 | 50 Gy in 25 Fx | 13 | 4.8 |
| 66 Gy in 33 Fx | 8 | 2.9 | 66 Gy in 33 Fx | 4 | 1.5 |
| Other | 22 | 8.1 | Other | 35 | 13 |

Percentages are relative to respondents with not-missing data; Fx: Fractions

Conclusions

This European survey indicates that adjuvant CT and RT for incompletely resected (R1) NSCLC are commonly used in clinical practice despite limited clinical evidence. There is a high level of variability in the chemotherapy regimens prescribed and in the dose of radiotherapy delivered both to the surgical bed and for pN2 disease. Prospective clinical trials for R1-resected NSCLC are necessary to clarify optimal management.

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