

Figure 1: Predicted Death rates in the world population (EU) form 1970 to 2010; Lung cancer (green crosses); European cancer mortality predictors for the year 2014; MalvezziM, et al. Annals of Oncology : 25:1650-1656, 2014

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **n** | **Treatment** | **RR****%** | **p** | **PFS months** | **HR****p** | **OS months** | **HR****p** |
| **IPASS 9** | 437 | Geftinib/Carboplatin +Paclitaxel | 71.2/47.3 | 0.01 | 9.5/5.3 | 0.48(<0,001) | 21.6/21.9 | 0.99 |
| **WJTOG 10** | 177 | Geftinib/Cisplatin +Docetaxel | 62.1/32.2 | 0.01 | 9.2/6.3 | 0.49(0.001) | 30.9/NA | 1.64 |
| **NEJ 11** | 230 | Geftinib/Carboplatin +Paclitaxel | 73.7/30.7 | 0.01 | 10.8/5.4 | 0.30(0.001) | 30.5/23.6 | NA |
| **OPTIMAL 12** | 154 | Erlotinib/Carboplatin +Gemcitabin | 83/36 | 0.01 | 13.1/4.6 |  0.16(0.001) | 22.6/28.8 | 1.06 |
| **EURTAC 13** | 173 | Erlotinib/Platin doublet | 58/15 | 0.01 | 9.7/5.2 | 0.37(0.001) | 19.3/19.5 | 1.04 |
| **LUX-LUNG3 14** | 345 | Afatinib/Cisplatin +pemetrexed | 56/23 | 0.01 | 11.1/6.9 | 0.58(0.001) | NA | 1.12 |

Table 1: Results from studies with TKI’s in 1st line treatment of NSCLC

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EGFR mutations** |  | **RR****%** | **PFS** **months** | **OS** **months** |
| **Most common** | Del exon 9 | 74.0 | 8.5 | 19.6 |
| L858R exon 21 |
| **Less Frequent** | G719X exon18  | 53.3 | 8.1 | 16.4 |
| L861Q exon 21 | 60.0 | 6.0 | 15.2 |
| **Uncommon** | V769M | 20.0 | 1.6 | 11.1 |
| A871E |
| **EGFR wild-type** | 16.5 | 2.0 | 10.4 |

Table 2: Evaluation of outcome of TKI’s treatment according to EGFR mutations or EGFR wild-type 20,29.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **n** | **EGFR****Mutations** | **ORR****%** | **ORR in****EGFRT790M****%** | **ORR in non****EGFRT790M****%** |
| **AZD929126** | 232 | exon 19delL858RT790M | 53.0 | 64.0 | 22.0 |
| **CO-168627** | 72 | exon 19delL858RT790M | NA | 58.0 | NA |
| **HM6171328** | 83 | T790M | 21.7 | 29.2 | NA |

Table 3: Phase I clinical studies of third generation EGFR-TKI’s 26-28.

  Normal Cell

 Initial clone

 Lung Tumor at diagnosis

 Tumor after treatment

 Tumor at relapse

Figure 2: Lung Cancer Resistance: model showing how tumor may acquire stronger clones after first treatment, leading to predominant second sub-clones, demonstrating the tumor heterogeneity.