# CLINICAL COMPARISON OF FIRST-LINE PLATIN CHEMOTHERAPY REGIMENS IN PATIENTS WITH ADVANCED NONSQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC) USING GERMAN REGISTRY DATA

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## BACKGROUND

- Lung cancer, one of the most common cancers worldwide, is a leading cause of mortality. Over 80% is comprised by non-small cell lung cancers (NSCLC) which can be subdivided in non-squamous and squamous cell carcinoma.[1]
- In 2016, it was estimated that there were 55,300 incident cases in Germany.[2]
- The majority of incident cases is observed in men, where it is the 2nd most prevalent malignant tumor and 3rd for women within German-speaking countries. The median age for disease onset is between 68 and 70 years of age.[3]
- Most patients are diagnosed in stages IIIB/IV where available therapy is mainly palliative.[4]

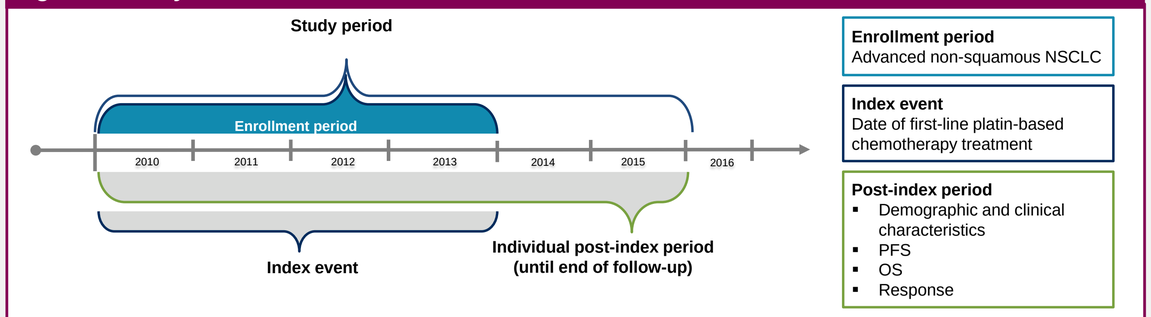
## OBJECTIVE

- The aim of the analysis was to describe the overall treatment landscape for advanced non-squamous NSCLC and to compare progression free survival (PFS) and overall survival (OS) of patients treated with the most prevalent platinum-based chemotherapy regimens.

## METHODS

- Data from the iOMEDICO prospective, multicenter Tumor Registry Lung Cancer (TLK) assessing oncological care in Germany was utilized.
- The study period spanned from February 2010 to the end of follow-up in the registry as shown in **Figure 1**.
- Inclusion criteria for the TLK were:
  - Histologically confirmed NSCLC or small cell lung cancer (SCLC)
  - Age ≥ 18 years of age on the index date, defined as the start of the first-line platinum based chemotherapy regimen
  - Systemic antineoplastic treatment
- For this analysis, non-squamous NSCLC patients staged IIIB/IV who received antineoplastic first-line treatment between February 1, 2010 and December 31, 2013 were identified. The date of initiation of the first-line therapy served as the index date. Other criteria for this analysis were:
  - No history of SCLC or squamous tumor
  - No evidence of other primary cancers
  - No evidence of participation in a clinical trial(s) during the study period
  - Informed consent within 6 weeks of start of first-line treatment (prospective documentation)
- Patients were assessed in terms of demographic characteristics including age and gender distribution, smoking status, body mass index, stage at diagnosis, and Eastern Cooperative Oncology Group (ECOG) performance status.
- OS is defined as the interval between start of first-line treatment and the date of death from any cause. Patients alive or lost to follow-up at data cut (January 31, 2016) were censored at last contact according to the Kaplan-Meier method. PFS was defined as the interval between start of first-line treatment and the date of progression or death. Patients without such an event before start of second-line treatment were censored at either the start of second-line treatment or at last contact.
- Patient and tumor characteristics, systemic therapies, PFS and OS of patients receiving one of the three most prevalent first-line platinum-based chemotherapies were descriptively compared using an unadjusted analysis, and an inverse probability of treatment weighting (IPTW) analysis adjusting for age, gender, tumor stage, ECOG performance status, and smoking status. Median PFS and OS were assessed using Kaplan-Meier analyses, and log rank test was used to compare these outcomes between the treatment groups.

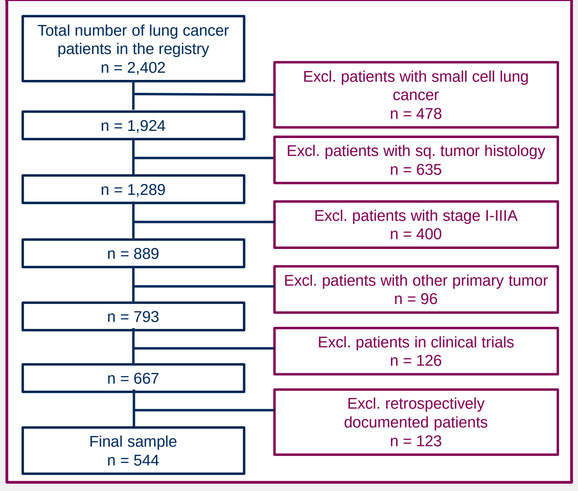
### Figure 1. Study Period




## RESULTS

- The TLK included 2,402 patients. Applying the study selection criteria resulted in a final sample of 544 patients (**Figure 2**).

### Figure 2. Patient Selection




First-line NSCLC Treatment Summary

- In the overall sample, the most prevalent chemotherapy treatments included combinations with carboplatin (n=223, 41.0%) or cisplatin (n=245, 45.0%). Aside from platin combination therapies, patients received mono chemotherapy (n=54, 9.9%), tyrosine-kinase inhibitors (n=29, 5.3%) and other (n=1, 0.2%). Eight (1.5%) of the identified patients switched their initial first-line treatment between carboplatin and cisplatin and are counted in both groups.
- In total, n=280 patients received either pemetrexed/platin (Pem/Plat, n=158), paclitaxel/platin (Pac/Plat, n=52) or vinorelbine/platin (Vin/Plat, n=70) and were included in the subsequent analyses.

Baseline Characteristics Before and After IPTW (Table 1)

- Pac/Plat patients were slightly older (65.94 vs. 63.60 years Pem/Plat, 63.48 years Vin/Plat), and more often male (90% vs. <66% in Pem/Plat, Vin/Plat).
- ECOG 0 was more prevalent in Pem/Plat patients (34% vs. 21% Pac/Plat, 17% Vin/Plat). Only 11% - 13% in each group presented with ECOG 2 or worse.
- The majority of patients (92% Pem/Plat, 79% Pac/Plat, 77% Vin/Plat) already presented with AJCC stage IV at diagnosis across all three treatment groups.
- After IPTW, patient counts were slightly reduced Pac/Plat (n=134), Pem/Plat (n=49) and Vin/Plat (n=63) due to missing data for performance status.
  - Balancing diagnostics after IPTW revealed some differences in the distribution of patient characteristics among the compared treatment groups.

### Table 1. Demographic and clinical characteristics

| | Unadjusted | | | | IPTW | | | |
|---|---|---|---|---|---|---|---|---|
| | Overall [a] n=544 | Pem/Plat n=158 | Pac/Plat n=52 | Vin/Plat n=70 | Overall [b] n=246 | Pem/Plat n=134 | Pac/Plat n=49 | Vin/Plat n=63 |
| **Age** | | | | | | | | |
| Mean | 64.57 | 63.60 | 65.94 | 63.48 | 64.79 | 64.57 | 64.77 | 65.04 |
| SD | 10.31 | 9.32 | 8.54 | 9.61 | | | | |
| 95%CI | | | | | 63.30 – 66.28 | 62.92 – 66.23 | 61.47 – 68.06 | 62.34 – 67.74 |
| Median | 64.79 | 62.89 | 66.91 | 62.59 | 64.04 | 63.67 | 66.18 | 63.89 |
| **Age (yrs. Groups)** | | | | | | | | |
| <40 | 0.7% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| 40-49 | 7.2% | 6.3% | 5.8% | 8.6% | 4.9% | 5.2% | 4.5% | 5.1% |
| 50-59 | 25.6% | 29.8% | 17.3% | 31.4% | 28.7% | 25.4% | 28.4% | 32.2% |
| 60-69 | 33.3% | 37.3% | 46.2% | 31.4% | 34.9% | 37.3% | 38.8% | 28.6% |
| 70-79 | 27.0% | 22.8% | 25.0% | 27.1% | 28.2% | 28.7% | 24.6% | 31.3% |
| 80+ | 6.3% | 3.8% | 5.8% | 1.4% | 3.3% | 3.4% | 3.7% | 2.8% |
| **Gender** | | | | | | | | |
| Female | 34.6% | 34.8% | 9.6% | 38.6% | 32.7% | 31.7% | 33.9% | 32.5% |
| Male | 65.4% | 65.2% | 90.4% | 61.4% | 67.3% | 68.3% | 66.1% | 67.5% |
| **Performance status** | | | | | | | | |
| ECOG 0 | 24.5% | 33.5% | 21.2% | 17.1% | 31.8% | 30.5% | 31.4% | 33.3% |
| ECOG 1 | 49.8% | 39.9% | 61.5% | 60.0% | 53.7% | 55.7% | 52.3% | 53.2% |
| ECOG 2 | 15.3% | 11.4% | 11.5% | 11.4% | 13.9% | 13.8% | 16.3% | 11.8% |
| ECOG 3 | 0.4% | 0.0% | 0.0% | 1.4% | 0.6% | 0.0% | 0.0% | 1.7% |
| ECOG 4+ | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.00% |
| Unknown | 10.1% | 15.2% | 5.8% | 10.0% | | | | |

### Table 1. Demographic and clinical characteristics (cont'd)

| | Unadjusted | | | | IPTW | | | |
|---|---|---|---|---|---|---|---|---|
| | Overall [a] n=544 | Pem/Plat n=158 | Pac/Plat n=52 | Vin/Plat n=70 | Overall [b] n=246 | Pem/Plat n=134 | Pac/Plat n=49 | Vin/Plat n=63 |
| **AJCC stage** | | | | | | | | |
| IIIB | 12.3% | 7.6% | 21.2% | 22.9% | 17.5% | 15.0% | 23.0% | 14.6% |
| IV | 87.7% | 92.4% | 78.8% | 77.1% | 82.5% | 85.0% | 77.0% | 85.4% |
| **Smoking status** | | | | | | | | |
| Yes | 74.8% | 81.0% | 82.7% | 77.1% | 78.4% | 80.2% | 78.3% | 76.6% |
| No | 12.0% | 10.1% | 3.9% | 10.0% | 9.9% | 8.6% | 11.9% | 9.1% |
| Unknown | 13.2% | 8.9% | 14.5% | 12.9% | 11.8% | 11.1% | 9.8% | 14.3% |
| **BMI** | | | | | | | | |
| Mean | 24.94 | 24.85 | 24.09 | 25.02 | 24.76 | 24.76 | 24.64 | 24.89 |
| SD | 4.36 | 4.34 | 4.48 | 4.28 | | | | |
| 95% CI | | | | | 24.11 - 25.41 | 24.03 - 25.49 | 23.19 - 26.09 | 23.70 - 26.08 |
| Median | 24.52 | 24.52 | 23.69 | 25.02 | 24.84 | 24.74 | 25.55 | 24.52 |
| Missing | 2.4% | 1.9% | 0.0% | 2.9% | | | | |
| **Metastases** | | | | | | | | |
| Yes | 99.1% | 100.0% | 100.0% | 98.6% | 100.0% | 100.0% | 100.0% | 100.0% |
| No | 0.9% | 0.0% | 0.0% | 1.4% | 0.0% | 0.0% | 0.0% | 0.0% |

Notation:
[a] Including therapies with other combinations than Pem/Plat, Pac/Plat, Vin/Plat.
[b] Excluding therapies with other combinations than Pem/Plat, Pac/Plat, Vin/Plat.

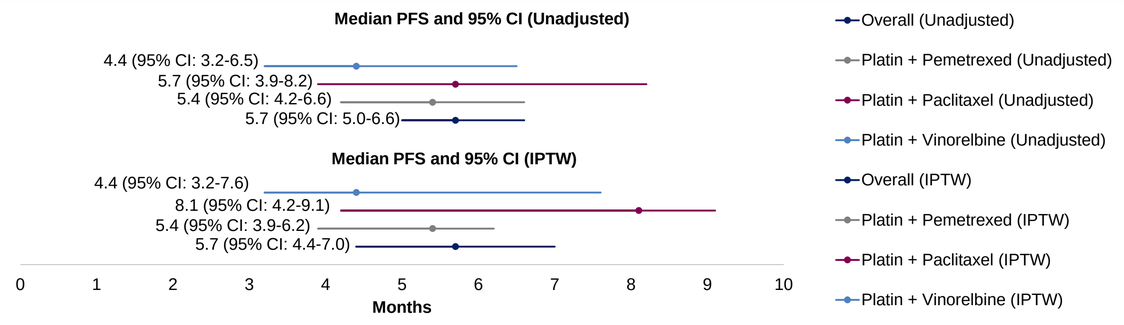
Unadjusted Outcomes

- In unadjusted analysis, 76.6%, 73.1%, and 77.1% of patients treated with Pem/Plat, Pac/Plat, and Vin/Plat, respectively, had progressed or died during follow-up. Also, 74.7%, 71.2%, and 67.1% of patients treated with Pem/Plat, Pac/Plat, and Vin/Plat, respectively, died.
- Median PFS and OS in months were comparable when Pem/Plat (5.4 [95% CI 4.2-6.6] and 11.3 [8.5-14.9]) was compared to Pac/Plat (5.7 [95% CI 3.9-8.2], P=0.290 and 11.5 [7.2-16.2], P=0.907) and Vin/Plat (4.4 [95% CI 3.2-6.5], P=0.155 and 10.8 [7.0-16.0], P=0.693) (**Figures 3 and 4**).

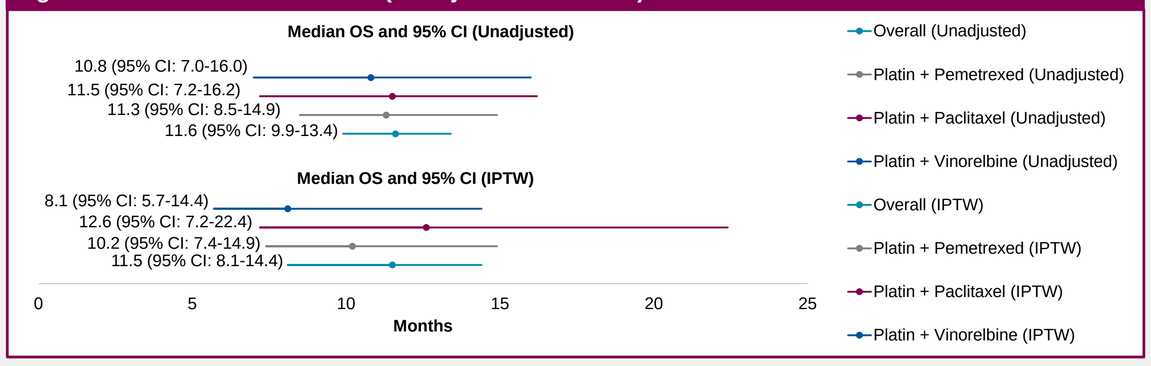
IPTW Adjusted Outcomes

- IPTW results differed slightly from unadjusted results; however showed no significant differences between the treatment groups.
- 78.4%, 71.4%, and 77.8% of patients treated with Pem/Plat, Pac/Plat, and Vin/Plat, respectively, had progressed or died during follow-up. Also, 75.4%, 69.4%, and 66.7% of patients treated with Pem/Plat, Pac/Plat, and Vin/Plat, respectively, died.
- Median PFS and OS were comparable when Pac/Plat (8.1 [95% CI 4.2-9.1] and 12.6 [7.2-22.4]) was compared to Pem/Plat (5.4 [95% CI 3.9-6.2], P=0.306 and 10.2 [7.4-14.9], P=0.198) and Vin/Plat (4.4 [95% CI 3.2-7.6], P=0.981 and 8.1 [5.7-14.4], P=0.649) (**Figures 3 and 4**).

### Figure 3. Median PFS and 95% CI (Unadjusted and IPTW)

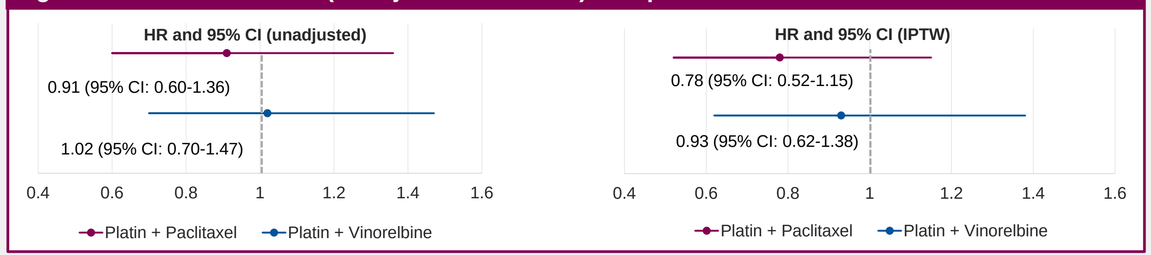



### Figure 4. Median OS and 95% CI (Unadjusted and IPTW)

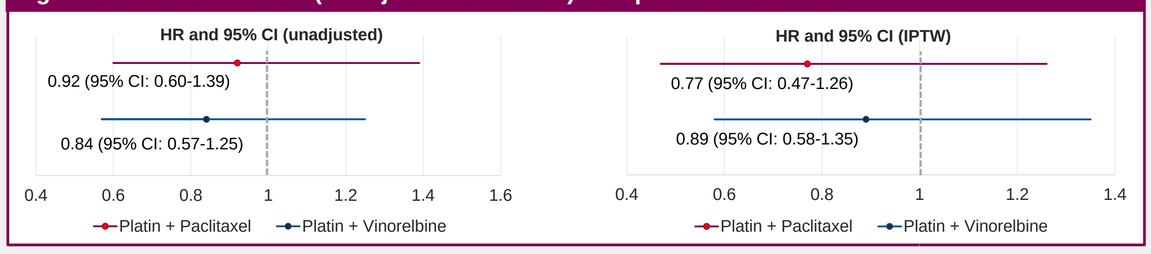



- The unadjusted and IPTW hazard ratios for PFS and OS with Pem/Plat as reference group are shown in **Figures 5 and 6**.

### Figure 5. Hazard Ratio PFS (Unadjusted and IPTW) Compared to Pem/Plat




### Figure 6. Hazard Ratio OS (Unadjusted and IPTW) Compared to Pem/Plat




## CONCLUSIONS

- Baseline comparisons of the treatment groups revealed differences in patient characteristics which could not be adequately balanced with the chosen method of IPTW. These differences suggest possible prescribing preferences for these regimens based on patient characteristics.
- No difference in PFS and OS was found between Pac/Plat, Pem/Plat, and Vin/Plat.
- Further research is warranted regarding imbalances between the respective groups and how to specify the balancing parameters.

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