Abstract: # Treatment Patterns and Outcomes in Stage III Non-small Cell Lung Cancer (NSCLC): Real-world Experience in Singapore From the KINDLE Study

Background
With 2.09 million new cases and 1.76 million deaths in 2018 globally, lung cancer remains the main contributor to cancer-related morbidity and mortality.1 With 2969 deaths in Singapore (2018), lung cancer was the deadliest cancer among the total Singapore resident population, accounting for 27.2% of all cancer deaths.1,2 NSCLC forms 85% of all lung cancer and one third of patients present at stage III. The wide heterogeneity of stage III poses numerous challenges for favourable management and is associated with poor prognosis, with 1-year, 3-year, and 5-year survival rates of 30.2%, 10.1% and 7.2%, respectively.3

We conducted a global real-world KINDLE study to understand the treatment patterns and clinical outcomes in patients with stage III NSCLC in the pre-immuno-oncology era, with Singapore as one of the sites.

Objectives
The objectives of the study were to characterize: Treatment patterns including type of treatment, duration of each treatment regimen and reason(s) for stopping/changing treatment • Treatment patterns according to TNM stage, pathology, whether surgically resectable (resectable tumour vs. unresectable tumours), EGFR mutation status and surgical or non-surgical treatment • Demographic and clinical characteristics • Clinical (ORR, DCR, if available) and survival estimates (OS and PFS).

Methods
KINDLE, an international, multi-centre, real-world study was conducted across 3 non-European and non-North American regions – Singapore was one of the sites.

Descriptive data were included and continuous data were described in a summary manner. The study cohort was N = 210 patients aged ≥18 years, diagnosed with primary stage III NSCLC between January 1, 2013 and December 31, 2017, and with at least 9 months of documented follow-up from the index date. Patients initially diagnosed at stage I (N=22) before progressing to stage III and those with concomitant cancers within 5 years of stage III NSCLC diagnosis (except non-metastatic non-melanoma skin cancer) were not included.

The data extracted included:
• Socio-demographic characteristics: age, gender, BMI, ethnicity, smoking status
• Clinical characteristics: TNM stage at diagnosis, pathology, EGFR mutation status, PD-L1 expression, ECOG performance score, co-morbidities
• Treatment modalities: type of systemic anti-cancer therapy, RT, agents, dose, duration, timing and setting (inpatient, outpatient, home); duration, timing and setting (inpatient, outpatient, home)
• Clinical outcomes (ORR, DCR, if available) and survival estimates (OS and PFS)
• Medical and surgical procedures
• Demographic and treatment patterns were summarised by descriptive statistics, and inferential statistics was used for correlation of PFS and OS with clinical and treatment characteristics.
• Median OS and PFS for Singapore cohort and by treatment patterns were calculated from the index date (date of the first diagnosis of stage III NSCLC), and reported with 95% CI.

Results
Key Patient Characteristics:
The median age (range) was 63 (35 to 86) years, with a male preponderance (72.4%). More than half of the patients (61.6%) had adenocarcinoma, a quarter (24.8%) of the patients had squamous cell carcinoma. 61.8% of patients had stage IIIA at presentation. 91.0% of the patients had an EOG performance score of 0 or 1 at diagnosis.

Key Treatment & Outcome Statistics:
In the global KINDLE cohort of n = 209 patients, the median OS and mPFS were 14.3 months (95% CI: 9.1 to 19.5) and 12.6 months (95% CI: 8.4 to 16.8), respectively. mPFS was longer in patients who had squamous cell carcinoma vs. adenocarcinoma (13.2 months vs. 11.6 months; p=0.0041) than those aged ≤65 years, while surgery as initial therapy was comparatively shorter than chemotherapy or RT (21.5 months vs. 17.2 to 47.5 months; p<0.0001). In patients with stage IIIB, CRT-based therapy (25.9 months [95% CI: 20.4 to 31.4]) was associated with better mOS than surgery-based therapy (4.1 months [95% CI: 0.0 to 8.0]; p=0.0049).

Conclusions
Similar to the global KINDLE study, this Singapore cohort demonstrates the heterogeneity in treatment modalities for stage III NSCLC. Poor OS with existing treatment options in Singapore in the pre-immuno-oncology era reiterates the unmet medical need for optimal management, and calls for improved access to newer innovative therapies and better quality of care.

Abbreviations
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References

Table 1: Socio-demographic and Baseline Characteristics of Stage III NSCLC Patients in Singapore

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age (years), median (range)</td>
<td>63 (35-86)</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>152 (72.4)</td>
</tr>
<tr>
<td>BMI (kg/m²), median (range)</td>
<td>22.5 (18-36)</td>
</tr>
<tr>
<td>Smoking history, n (%)</td>
<td>87 (41.4)</td>
</tr>
<tr>
<td>Ex smoker</td>
<td>51 (24.3)</td>
</tr>
<tr>
<td>Never-smoker</td>
<td>72 (35.3)</td>
</tr>
</tbody>
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Figure 1B: Summary of Treatment Modalities by AJCC Stage

Figure 3A: mPFS, Overall and by AJCC Stage (n=210)

Figure 4A: mPFS and mOS (months) as per Treatment Status by Stage

Figure 4B: mPFS and mOS (months) as per AJCC Stage

Key Treatment Characteristics & Survival Outcomes [presented as 95% CI]:
- Overall, most frequent treatment modality was CRT (31.2%) followed by RT (12.9%).
- mPFS was 26.3 months in stage IIIA (95% CI: 23.7 to 31.5) and was comparatively shorter than surgery (25.9 months [95% CI: 20.4 to 31.4]).
- mOS was 47.5 months in stage IIIA (95% CI: 36.2 to 58.8) vs. stage IIIB (3.9 months [95% CI: 2.6 to 5.5]; p<0.0001).
- In patients with stage IIIA, CRT and surgery (4.1 months [95% CI: 0.0 to 8.0]; p=0.0049).
- In patients with stage IIIB, CRT-based therapy (25.9 months [95% CI: 20.4 to 31.4]) was associated with better mOS than surgery-based therapy (4.1 months [95% CI: 0.0 to 8.0]; p=0.0049).

Acknowledgement


Figure 1A: Overall and by AJCC Stage (n=210)

Figure 3B: mOS (months), overall and by AJCC Stage (n=210)

Figure 4C: mPFS and mOS (months) as per AJCC Stage

Figure 4D: mPFS and mOS (months) as per Treatment Status by Stage

AACC: American Cancer Society; CRT: Concurrent Chemotherapy & RT; CT: Computed Tomography; CR: Complete response; DCR: Disease control rate; EGFR: Epidermal Growth Factor Receptor; Emission CT: Emission Computed Tomography; ECOG: Eastern Cooperative Oncology Group; ECT: Emission Computed Tomography; F: Female; G: Gender; H: Histology; IBC: Involved border control; ICR: Involved Cancer Ratio; L1: L1 expression; mPFS: Median Progression Free Survival; mOS: Median Overall Survival; mPFS: Median Progression Free Survival; mOS: Median Overall Survival; RT: Radiation Therapy; SCCRT: Surgery-based Chemotherapy & Radiotherapy; T1: T stage; T2: T stage; T3: T stage; T4: T stage; TSD: Toxicity profile; W: White; X: X ray; Y: Year.