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Cancer Registry-Based Real-World Evidence Confirms Efficacy of Treatments Comparable to KEYNOTE-189/-407 and Impower-133

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Background

- The KEYNOTE-189 (KN189), KEYNOTE-407 (KN407), and IMpower-133 (IP133) clinical trials established the standard-of-care treatment regimens for metastatic non-small-cell lung cancer (mNSCLC) and extensive-stage small-cell lung cancer (ED-SCLC).
- However, the generalizability of their results to broader clinical practice remains uncertain due to differences in patient populations between the highly controlled settings of RCTs and real-world clinical environments.
- This study evaluates the external validity of these treatment regimens by analyzing comparable real-world data from the Baden-Württemberg Cancer Registry (BWCR),Germany.

Methods

- We conducted a retrospective cohort analysis of patients aged 18 years and older, diagnosed 2011-2023 with mNSCLC or ED-SCLC, who received chemoimmunotherapy (CITx) or chemotherapy (CTx) protocols consistent with those in the RCTs.
- Patients were selected to match the baseline characteristics of those in the original phase III trials
  - **CITx arms**:
    - **A1**: non-squamous mNSCLC treated with platinum-based-CTx
    - **B1**: squamous mNSCLC treated with taxane-based-CTx
    - **C1**: ED-SCLC treated with platinum-based-CTx
  - CTx arms:
    - **A2:** non-squamous mNSCLC treated with pembrolizumab + platinum-based-CTx
    - **B2:** squamous mNSCLC treated with pembrolizumab + taxane-based-CTx
    - **C2:** ED-SCLC treated with atezolizumab + platinum-based-CTx
- The primary endpoint was overall survival (OS), assessed using Kaplan-Meier and Cox models, adjusted for age, sex and ECOG.

Table 1: Patient characteristics

Characteristic	emulated KN 189 overall	emulated KN 189 CTx	emulated KN 189 CITx	emulated KN 189 p-value	emulated KN 407 overall	emulated KN 407 CTx	emulated KN 407 CITx	emulated KN 407 p-value	emulated Impower 133 overall	emulated Impower 133 CTx	emulated Impower 133 CITx	emulated Impower 133 p-value
n	1214	432 (35.6)	782 (64.4)		291	87 (29.9)	204 (70.1)		848	436 (51.4)	412 (48.6)	
Age - mean (SD)	64.45 (9.29)	63.58 (9.52)	64.93 (9.14)	0.015	67.10 (8.95)	67.01 (9.93)	67.14 (8.52)	0.909	66.86 (8.75)	67.17 (8.82)	66.54 (8.68)	0.298
<65	594 (48.9)	218 (50.5)	376 (48.1)	0.463	117 (40.2)	36 (41.4)	81 (39.7)	0.892	327 (38.6)	162 (37.2)	165 (40.0)	0.427
65+	620 (51.1)	214 (49.5)	406 (51.9)		174 (59.8)	51 (58.6)	123 (60.3)		521 (61.4)	274 (62.8)	247 (60.0)	
Sex												
m	669 (55.1)	236 (54.6)	433 (55.4)	0.851	220 (75.6)	65 (74.7)	155 (76.0)	0.935	491 (57.9)	250 (57.3)	241 (58.5)	0.786
w	545 (44.9)	196 (45.4)	349 (44.6)		71 (24.4)	22 (25.3)	49 (24.0)		357 (42.1)	186 (42.7)	171 (41.5)	
Histology												
Adeno	1155 (95.1)	404 (93.5)	751 (96.0)	0.070								
Others NSCLC	59 (4.9)	28 (6.5)	31 (4.0)									
squamous					291	87 (29.9)	204 (70.1)					
ECOG												
0	414 (34.1)	133 (30.8)	281 (35.9)	0.081	100 (34.4)	30 (34.5)	70 (34.3)	1.000	296 (34.9)	135 (31.0)	161 (39.1)	0.016
1	194 (16.0)	66 (15.3)	128 (16.4)	0.678	191 (65.6)	57 (65.5)	134 (65.7)		552 (65.1)	301 (69.0)	251 (60.9)	
metastasis location												
BRA	414 (34.1)	133 (30.8)	281 (35.9)	0.081	48 (16.5)	20 (23.0)	28 (13.7)	0.076	246 (29.0)	124 (28.4)	122 (29.6)	0.764
HEP	194 (16.0)	66 (15.3)	128 (16.4)	0.678	65 (22.3)	25 (28.7)	40 (19.6)	0.119	391 (46.1)	189 (43.3)	202 (49.0)	0.112
Platinum CTx....												
Carboplatin	933 (76.9)	262 (60.6)	671 (85.8)	<0.001								
Cisplatin	281 (23.1)	170 (39.4)	111 (14.2)									
Taxane CTx....												
Paclitaxel					134(46.0)	49 (56.3)	85 (41.7)	<0.001				
Paclitaxel nab					157(54.0)	38 (43.7)	119 (58.3)					

Results

- A total of 2,353 patients were included (Fig. 1):
  - **Emulated KN189:** 782 patients in the A1 arm and 432 in the A2 arm.
  - **Emulated KN407:** 204 patients in the B1 arm and 87 in the B2 arm.
  - **Emulated IP133:** 412 patients in the C1 arm and 436 in the C2 arms
- The median age was 65 years, with 58% of patients being male.
- Multivariate Cox analysis identified age, and ECOG as significant prognostic factors.
- In line with the results from the original trials, we observed a plateau in OS across the CITx- groups:
  - In **non-squamous mNSCLC**, the 3-year OS was 28.2% for A1 with pembrolizumab plus CTx versus 16.3% for CTx only (A2). The benefit of adding pembrolizumab was consistent across all prespecified subgroups (Fig. 2A).
  - In **squamous mNSCLC**, the 3-year OS was 23.8% for B1 versus 13.3% for B2 (Fig. 2B).
  - For **ED-SCLC**, the 18-month OS was 23.8% for CITx vs. 13.6% for CTx only. The addition of atezolizumab showed benefit in all prespecified subgroup (Fig. 2C).
- These results closely mirror the results observed in the landmark RCTs.

Fig. 1: Consort Diagram
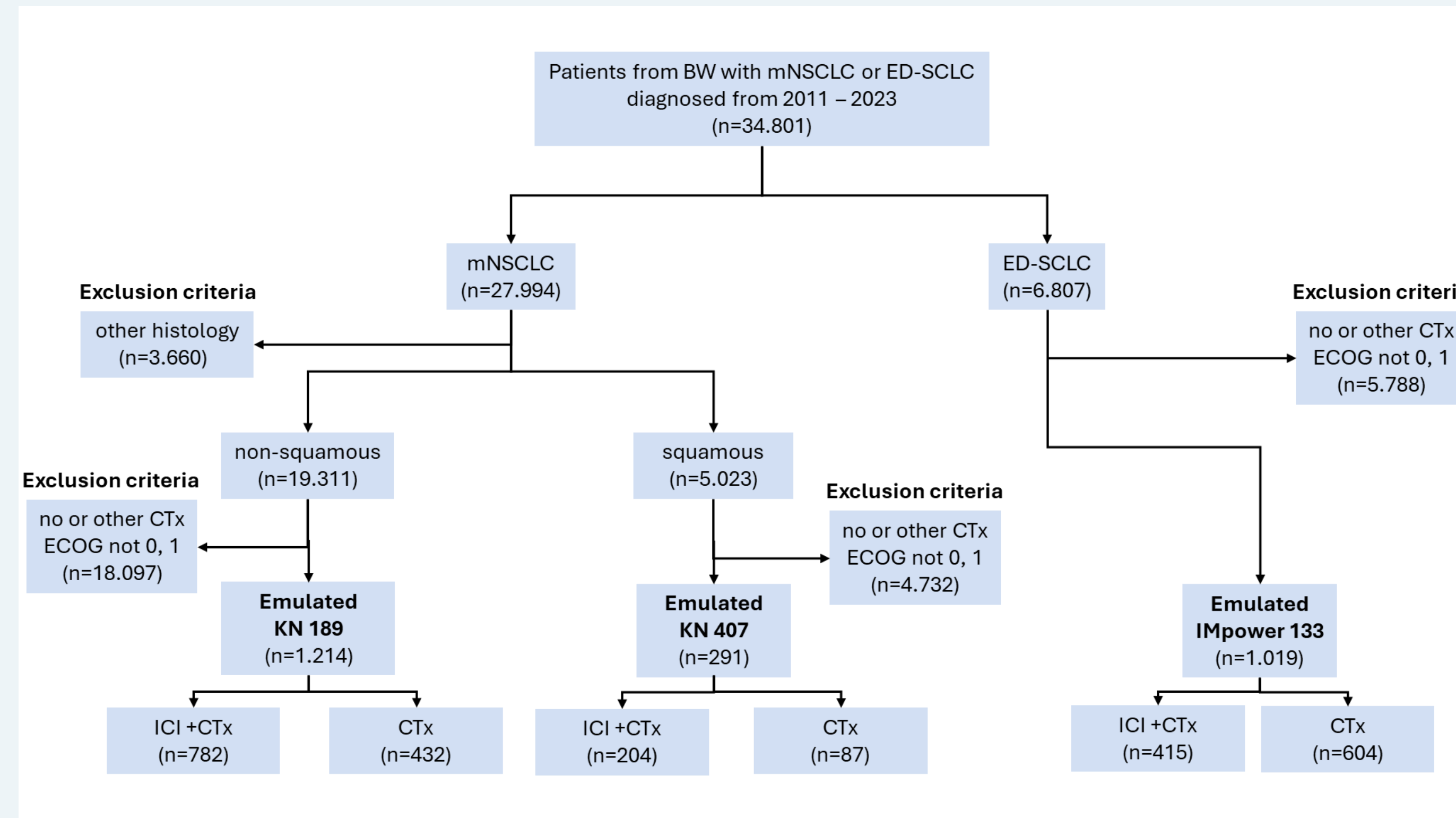
Conclusion

- Real-world data from the BWCR successfully replicated the outcomes of KEYNOTE-189, KEYNOTE-407, and Impower-133, confirming the external validity of these treatment principles.
- This highlights the potential of using real-world data from modern state-run cancer registries to bridge the gap between clinical trials and everyday oncology practice, offering valuable insights for clinicians in real-world treatment decisions.

Fig. 2: Overall Survival: Subgroup Analysis.

A. Emulated KEYNOTE 189

B. Emulated KEYNOTE-407

C. Emulated IMPOWER-133

Conflict of interest : No conflict of interest

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