Transportability of RATIONALE-315 Trial Outcomes Assessing Perioperative Tislelizumab to the European Patient Population With Resectable Non-Small Cell Lung Cancer

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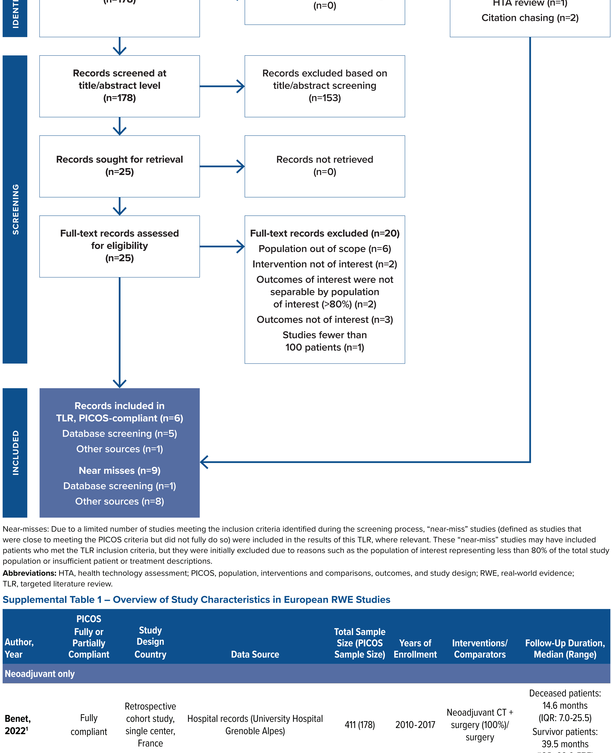
SUPPLEMENTARY METHODS

Search and Study Selection

- A de novo search was conducted in Embase/MEDLINE. Published systematic literature reviews, clinical trials registry databases, and health technology assessment documents were used as grey literature sources to identify key RWE and relevant RCTs to inform target European populations and potential EMs or predictive factors for clinical efficacy outcomes in the neoadjuvant/adjuvant/perioperative NSCLC setting
- Captured abstracts were screened to select those that adequately adhered to the population, interventions and comparisons, outcomes, and study design (PICOS) criteria
  - Shortlisted full texts were further screened based on the availability of patient characteristics identified as potential EMs (age, sex, ECOG PS, smoking status, disease stage, PD-L1, histology, lymph node station)

Supplemental Figure 1. Study Flow Diagram for the 3 TLRs (10 Studies Included in the RWE TLR) as of April 9, 2024



Near-misses: Due to a limited number of studies meeting the inclusion criteria identified during the screening process, "near-miss" studies (defined as studies that were close to meeting the PICOS criteria but did not fully do so) were included in the results of this TLR, where relevant. These "near-miss" studies may have included patients who met the TLR inclusion criteria, but they were initially excluded due to reasons such as the population of interest representing less than 80% of the total study population or insufficient patient or treatment descriptions.

Abbreviations: HTA, health technology assessment; PICOS, population, interventions and comparisons, outcomes, and study design; RWE, real-world evidence; TLR, targeted literature review.

Supplemental Table 1 – Overview of Study Characteristics in European RWE Studies

Author, Year	PICOS Fully or Partially Compliant	Study Design Country	Data Source	Total Sample Size (PICOS Sample Size)	Years of Enrollment	Interventions/ Comparators	Follow-Up Duration, Median (Range)
Neoadjuvant only							
Benet, 2022[1]	Fully compliant	Retrospective cohort study, single center, France	Hospital records (University Hospital Grenoble Alpes)	411 (178)	2010-2017	Neoadjuvant CT + surgery (100%)/ surgery	Deceased patients: 14.6 months (IQR: 7.0-25.5) Survivor patients: 39.5 months (IQR: 23.6-57.7)
Damhuis, 2024[2]	Fully compliant	Retrospective cohort study, multicenter, Netherlands	NCR - Netherlands Cancer Registry	1,295 (111)	2017-2021	Neoadjuvant CT + surgery (100%)/none	Deceased patients: 27 months (NR)
Joosten, 2020[3]	Fully compliant	Retrospective cohort study, multicenter, Netherlands	NCR - Netherlands Cancer Registry	9,591 (428)	2010-2016	Neoadjuvant therapy + surgery (100%)/none	Censored patients: 53 months (NR)
Adjuvant only							
Dalvi, 2023[4]	Fully compliant	Retrospective cohort study, multicenter, Denmark	Registry-based data. Danish registries: Danish Cancer Registry of mandatory cancer reporting; Danish Lung Cancer Registry of all lung cancers diagnosed in Denmark since 2000; Danish National Patient Registry; Danish National Pathology Registry; and the Civil Registration System, an administrative register.	391 (391)	2001-2012	Adjuvant CT[J]/none	NR
Cortinovis, 2023[5]	Partially compliant	Retrospective cohort study, multicenter, Italy	Administrative databases and pathological anatomy databases of three local health units	418 (NR)[A]	2015-2021	Adjuvant CT[J]/none	NR
Uldbjerg, 2023[6]	Partially compliant	Retrospective cohort study, single center, Denmark	Hospital electronic medical records	1,341 (1,040 with stage II or IIIA NSCLC)[E]	2010-2021	Surgery (51%) + adjuvant CT (46%)/ none	Overall population: 20 months (IQR: 9-43); Stage II: 24 months (IQR: 10-48); Stage IIIA: 12 months (IQR: 8-27)
Mixed settings							
Counago, 2019[7]	Fully compliant	Retrospective cohort study, multicenter, Spain	Hospital records (14 hospitals)	118 (118)	2005-2014	Neoadjuvant (CRT or CT) + surgery (53.8%) + perioperative (neoadjuvant [CRT or CT + adjuvant CT or RT or both]) (43.2%)/none	42.5 months (NR)
Sørensen, 2022[8]	Partially compliant	Retrospective cohort study, multicenter, Denmark	National registries (the National Patient Register and the Cause of Death Register) and Danish Cancer Registry	31,939 (5,068 with stage II, IIIA disease)[E]	2005-2016	Any initial treatment, including SACT, RT, and surgery (combined or alone)/ none	NR
Zens, 2022[9]	Partially compliant	Retrospective cohort study, single center, Switzerland	Hospital records	210 (96 [neoadjuvant cohort], 114 [surgical cohort])[B]	2000-2016	Neoadjuvant CRT + surgery (100%) + adjuvant therapy (26.1%)/surgery + adjuvant therapy (67.7%)	Up to 5 years (for survival outcomes)
Mixed settings with segregated data on neoadjuvant or perioperative/adjuvant only							
Baltus, 2023[10]	Partially compliant	Retrospective cohort study, multicenter, Germany	Population-based cancer registries	2,039 (Unclear)[C]	2016-2019	Adjuvant SACT + RT (22.2%)/neoadjuvant SACT (+ RT [21.1%]) or perioperative SACT + surgery (100% [assumed])	15.0 months (IQR: 6.0-29.1)

Colored rows: studies selected for statistical analysis.

[A]Information on neoadjuvant/adjuvant treatment not available. Information on *EGFR* mutations and *ALK* rearrangements not available. Detailed baseline characteristics not available (available: age, sex, Charleson Comorbidity index).

[B]Neoadjuvant cohort <100 patients. Stages I-IV (in the neoadjuvant cohort, 78% patients with stage II-III. Further breakdown in IIIA and IIIB not reported). Surgery group with adjuvant therapy <80%.

[C]Limited information on population details, for example, ECOG, *EGFR*, *ALK* characteristics were not reported, therefore N of patients completing PICOS is unclear. 1716 (84.2%) received adjuvant SACT ± RT; 323 (15.8%) received neoadjuvant SACT ± RT or perioperative SACT (of this population, 69 [21.4%] received perioperative SACT).

[D]Less than 80% of patients with stage II-IIIA, around 26% with ECOG 2+, and unclear how many of these underwent surgery.

[E]Less than 80% of patients with stage II-IIIA. 24% patients received surgery alone and only 24% received surgery associated with SACT or RT.

[J]Receipt of adjuvant chemotherapy was defined as surgery within the first 60 days of diagnosis of stage IB/II/IIIA NSCLC and initiation of chemotherapy within 120 days of diagnosis.

[K]Patients receiving chemotherapy during the 4-month period following the surgery date.

Abbreviations: CRT, chemoradiotherapy; CT, chemotherapy; IQR, interquartile range; NSCLC, non-small cell lung cancer; NR, not reported; RCT, randomised controlled trial; RT, radiotherapy; SACT, systemic anti-cancer therapy.

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