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Metastatic spread and PD-L1 expression co-determine benefit from pembrolizumab in advanced non-squamous NSCLC

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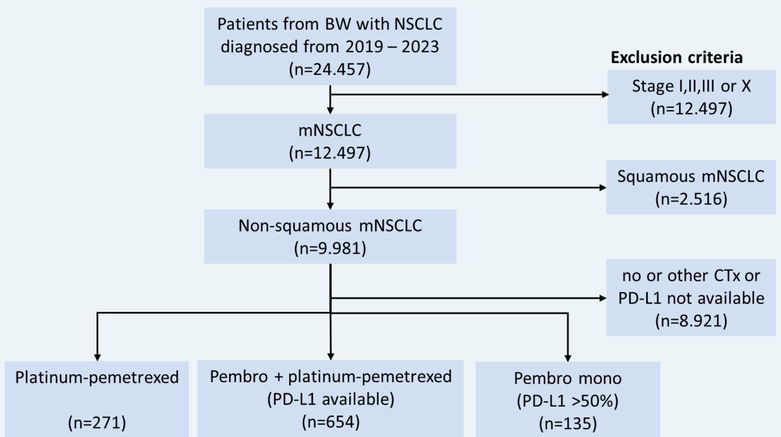
Background

- Pembrolizumab (pembro), either with chemotherapy (CTX) or as monotherapy for PD-L1 TPS ≥50%, is standard first-line treatment for metastatic non-squamous NSCLC (mnsqNSCLC)
- Real-world evidence from a state cancer registry includes all patients of the catchment area as required by law without the selection bias inherent in other cohorts
- **Aim:** To evaluate the impact of PD-L1 expression and metastatic stage (M1a-M1c) on the survival benefit of pembrolizumab-based first-line therapy compared with CTX in real-world mnsqNSCLC

Methods

- **Study type**: retrospective cancer registry study
- **Data source**: Baden-Wuerttemberg Cancer Registry (BWCR), Germany
- **Patients**: metastatic non-squamous NSCLC (diagnosed 2019-2023)
- **Treatment**: Platinum-pemetrexed, pembro monotherapy, or pembro combined with platinum-pemetrexed, with available PD-L1 status
- **Statistics**: Fisher's exact/chi-square test; Kaplan-Meier and Cox models
- **Endpoints**: Overall survival (OS), overall response (ORR) stratified by PD-L1 expression (<1%, 1-49%, ≥50%) and M-stage (M1a-M1c)
- **Parameter Adjustment:** propensity score weighting (PSW)

Fig. 1: Consort Diagram



Results

Baseline characteristics (Table 1):

- well balanced between treatment groups
- median age: 66.0 years, 57.9% males
- Pembro mono patients: median 4-5 years older

Conflict of interest : No conflict of interest

Table 1: Patient characteristics

Characteristic	overall	CTX	Pembro + CTX	Pembro mono
n	1060	271 (25.6)	654 (61.7)	135(12.7)
Age - median(IQR)	66.0[60.0, 73.0]	66.0 [59.0, 72.0]	65.0 [59.0, 72.0]	70.0 [63.0, 76.5]
Sex - no(%)				
m	614 (57.9)	157 (57.9)	375 (57.3)	82 (60.7)
w	446 (42.1)	114 (42.1)	279 (42.7)	53 (39.3)
cM - no(%)				
M1a	220 (20.8)	57 (21.0)	140 (21.4)	23 (17.0)
M1b	187 (17.6)	47 (17.3)	109 (16.7)	31 (23.0)
M1c	653 (61.6)	167 (61.6)	405 (61.9)	81 (60.0)
ECOG -no(%)				
0	262 (34.6)	50 (26.9)	182 (38.1)	30 (31.9)
1	369 (48.7)	96 (51.6)	226 (47.3)	47 (50.0)
2-4	127 (16.8)	40 (21.5)	70 (14.6)	17 (18.1)
metastasis location				
brain - no(%)	363 (34.2)	79 (29.2)	234 (35.8)	50 (37.0)
liver - no(%)	162 (15.3)	55 (20.3)	86 (13.1)	21 (15.6)

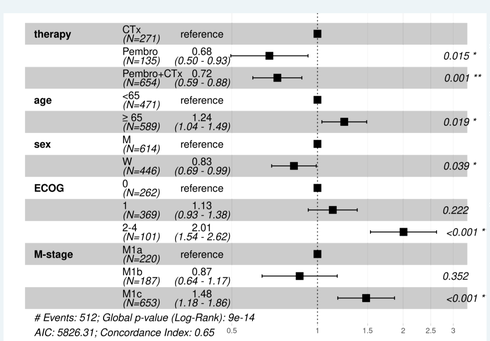
Table 2: Overall response

	Overall	M1ab: CTX	M1c: CTX	M1ab: Pembro	M1c: Pembro
cofactors					
n	756	69	104	233	350
objective response					
stable disease	107 (14.2)	16 (23.2)	13 (12.5)	32 (13.7)	46 (13.1)
overall response	293 (38.8)	20 (29.0)	24 (23.1)	102 (43.8)	147 (42.0)
progress	356 (47.1)	33 (47.8)	67 (64.4)	99 (42.5)	157 (44.9)

	Overall	CTX	PD-L1<1: Pembro	PD-L1 1-49: Pembro	PD-L1>50: Pembro
cofactors					
n	756	173	129	247	207
objective response					
stable disease	107 (14.2)	29 (16.8)	19 (14.7)	30 (12.1)	29 (14.0)
overall response	293 (38.8)	44 (25.4)	41 (31.8)	111 (44.9)	97 (46.9)
progress	356 (47.1)	100 (57.8)	69 (53.5)	106 (42.9)	81 (39.1)

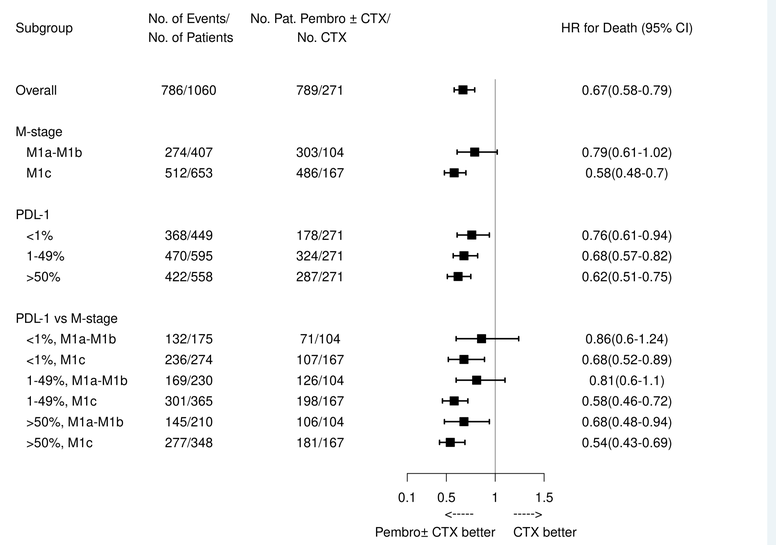
- **CTX**: lowest OR, especially in M1c(23%) with more frequent progression (64%)
- **Pembro ±CTX**:
  - improved ORR across subgroups and reduced progression
  - greatest benefit: in patients with M1c disease and PD-L1 ≥50%
- **Higher PD-L1** correlated with greater OR and low progression

Fig.2. OS: multivariate Cox model



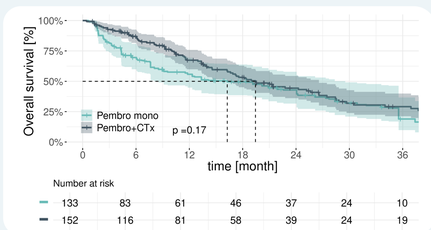
- median follow-up:
  - 37.6 months
- Pembrolizumab (±CTX) significantly improves survival vs CTX alone
- prognostic factors:
  - Higher age (≥ 65)
  - ECOG (2-4)
  - M-stage (M1c)

Fig 3. Impact of PD-L1 and M-stage on the survival benefit of Pembro



- **Overall:** Pembrolizumab (±CTX) associated with improved OS vs. CTX
- **PD-L1 ≥50%:** clear and strongest OS benefit (esp. M1c)
- **PD-L1 1–49%:** benefit mainly in M1c; limited in M1a/b
- **PD-L1 <1%**: benefit overall weak, but advantage in M1c subgroup
- **M-stage effect:** OS benefit most pronounced in M1c, regardless of PD-L1

Fig.4: OS: patients with PD-L1 ≥50%



- Pembro+CTX outperformed pembro mono in univariate OS-analysis (p=0.02)
- Patients with Pembro mono were ~5 years older
- after PSW adjustment, the OS difference lost significance (p=0.17)

Discussion and Conclusion

- Pembrolizumab improved response and survival compared with chemotherapy, with the strongest effect in M1c disease
- Benefit was most pronounced in patients with high PD-L1 (≥50%), but also evident in M1c even at low PD-L1 expression
- M-stage modifies treatment effect: extent of metastatic spread is as relevant as PD-L1 status
- Real-world registry data confirm trial evidence and highlight patient subgroups with limited benefit

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