800 CLINICOPATHOLOGICAL AND MOLECULAR PREDICTIVE FACTORS OF SURVIVAL IN NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH FIRST-LINE IMMUNOTHERAPY WITH OR WITHOUT CHEMOTHERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background The majority of advanced non-small cell lung cancer (NSCLC) patients derives modest benefit from immunotherapy (IO) alone. For some of them, adding chemotherapy (CT) may significantly improve the outcomes, but the reliability of PD-L1 expression as the only biomarker to identify patients that might need concomitant CT is unsatisfactory.[1,2]

Methods A systematic research of articles using PubMed/MEDLINE, and the Cochrane Database of Systematic Reviews and Central Register of Controlled Trials was performed, last updated April 11th, 2022. Abstract from main oncology congresses were also searched, including ASCO 2022. Eligible studies were randomized controlled clinical trials (RCT) investigating IO, alone or combined with CT, versus CT alone in previously untreated advanced NSCLC patients. The objective was to detect clinicopathological and molecular predictive factors of survival (progression-free survival and overall survival). Study characteristics and outcome estimates (hazard ratio and 95% CI) were extracted. Random-effects meta-analyses were performed to investigate IO alone versus CT, and IO plus CT versus CT. Random-effects meta-regression analyses were performed to provide a comparison of IO alone versus IO plus CT.

Results a total of 14367 patients with advanced NSCLC in 25 RCT was included (table 1).[3-48] Squamous histology, male gender, current/former smoker status, PD-L1 expression >=50%, and high TMB correlated with improved survival with IO alone compared to CT. Conversely, female gender, absence of smoking history, negative PD-L1 expression, and low TMB correlated with unsatisfactory outcomes with IO alone versus CT (figure 1), but not with IO plus CT versus CT (figure 2). IO plus CT improved survival versus IO alone in female patients [HR for PFS: 1.65, 95% CI, 1.25-2.18, p=0.0004; HR for OS: 1.31, 95% CI, 1.01-1.71, p=0.044], never smokers [HR for PFS: 3.59, 95% CI, 1.62-7.94, p=0.0016; HR for OS: 1.28, 95% CI, 0.95-1.72, p=0.10], in those having a PD-L1 expression >=1% [HR for PFS: 1.88, 95% CI, 1.55-2.28, p<0.0001; HR for OS: 1.28, 95% CI, 1.11-1.48, p=0.0007] or a low TMB [HR for PFS: 2.08, 95% CI, 1.61-2.70, p <0.0001; HR for OS: 1.43, 95% CI, 1.12-1.82, p=0.004], and in patients with central nervous system metastasis [HR for PFS: 1.51, 95% CI, 1.01-2.25, p=0.045; HR for OS: 1.32, 95% CI, 0.85-2.06, p=0.22] (figure 3).

Conclusions Certain clinicopathological and molecular features may add predictive value to PD-L1 expression in the selection of the most appropriate first-line treatment for advanced NSCLC patients.

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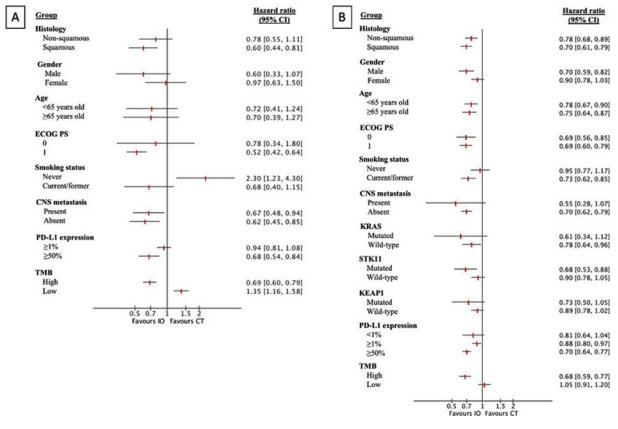
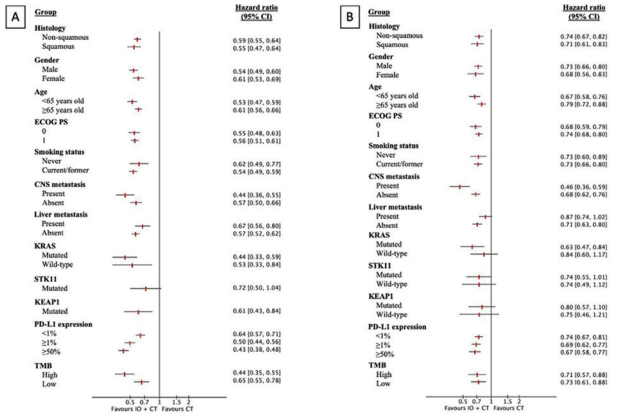
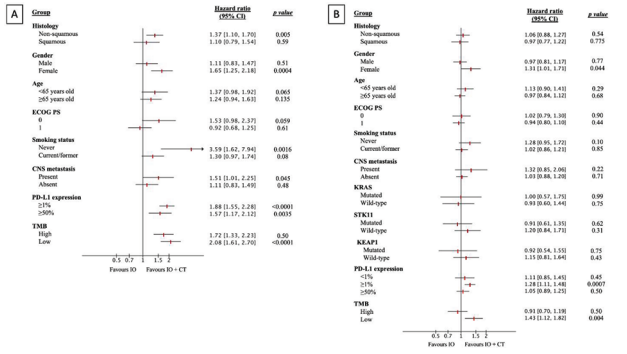


Abstract 800 Figure 1 IO versus CT
Graphical representation of the PFS (A) and OS (B) of patients treated with IO versus CT resulting from the meta-analysis in each group. PFS: progression-free survival; OS: overall survival; IO: immunotherapy; CT: chemotherapy; CNS: central nervous system; PD-L1: programmed death-ligand 1; ECOG PS: eastern cooperative group performance status; TMB: tumor mutation burden.



Abstract 800 Figure 2 IO plus CT versus CT
Graphical representation of the PFS (A) and OS (B) of patients treated with IO plus CT versus CT resulting from the meta-analysis in each group.
PFS: progression-free survival; OS: overall survival; IO: immunotherapy; CT: chemotherapy; CNS: central nervous system; PD-L1: programmed death-ligand 1; ECOG PS: eastern cooperative group performance status; TMB: tumor mutation burden.



Abstract 800 Figure 3. IO versus IO plus CT
Graphical representation of the PFS (A) and OS (B) of patients treated with IO versus IO plus CT resulting from the meta-regression analysis in each group.
PFS: progression-free survival; OS: overall survival; IO: immunotherapy; CT: chemotherapy; CNS: central nervous system; PD-L1: programmed death-ligand 1; ECOG PS: eastern cooperative group performance status; TMB: tumor mutation burden.

Abstract 800 Table 1. Included trials

Trial	Phase	Histology	No. intervention/ control	Arms of treatment
CameL-Sq	III	Squamous	193/196	Camrelizumab + carboplatin + paclitaxel vs carboplatin + paclitaxel
CheckMate 026	III	Squamous & non-squamous	211/212	Nivolumab vs Platinum-based CT
CheckMate 227	III	Squamous & non-squamous	Part 1a: 396/396/397 Part 1b: 187/177/186	Part 1a: nivolumab + ipilimumab vs nivolumab vs platinum-based CT Part 1b: nivolumab + ipilimumab vs nivolumab + platinum-based CT vs platinum-based CT
CheckMate 9LA	III	Squamous & non-squamous	361/358	Nivolumab + ipilimumab + platinum-based CT vs Platinum-based CT
CHOICE-01*	III	Squamous & non-squamous	309/156	Toripalimab + platinum-based CT vs Platinum-based CT
EMPOWER-Lung 1	III	Squamous & non-squamous	283/280	Cemiplimab vs Platinum-based CT
EMPOWER-Lung 3*	III	Squamous & non-squamous	312/154	Cemiplimab + platinum-based CT vs Platinum-based CT
GEMSTONE-302	III	Squamous & non-squamous	320/159	Sugemalimab + platinum-based CT vs Platinum-based CT
Keynote 021	II	Non-squamous	60/63	pembrolizumab + carboplatin + pemetrexed vs carboplatin + pemetrexed
Keynote 024	III	Squamous & non-squamous	154/151	Pembrolizumab vs platinum-based CT
Keynote 042	III	Squamous & non-squamous	637/637	Pembrolizumab vs platinum-based CT
Keynote 189	III	Non-squamous	410/206	pembrolizumab + cisplatin/carboplatin + pemetrexed vs cisplatin/carboplatin + pemetrexed
Keynote 407	III	Squamous	278/281	pembrolizumab + carboplatin + (nab)paclitaxel vs carboplatin + (nab)paclitaxel
IMpower 110	III	Squamous & non-squamous	277/277	Atezolizumab vs Platinum-based CT
IMpower 130	III	Non-squamous	483/240	atezolizumab + carboplatin + nab-paclitaxel vs carboplatin + nab-paclitaxel
IMpower 131	III	Squamous	343/340	atezolizumab + carboplatin + nab-paclitaxel vs carboplatin + nab-paclitaxel
IMpower 132	III	Non-squamous	292/286	atezolizumab + cisplatin or carboplatin + pemetrexed vs cisplatin or carboplatin + pemetrexed
IMpower 150	III	Non-squamous	400/400	atezolizumab + bevacizumab + carboplatin + paclitaxel vs bevacizumab + carboplatin + paclitaxel
MYSTIC	III	Squamous & non-squamous	163/163/162	Durvalumab vs Durvalumab + tremelimumab vs platinum-based CT
ORIENT-11	III	Non-squamous	266/131	Sintilimab + pemetrexed + cisplatin/carboplatin vs Pemetrexed + cisplatin/carboplatin
ORIENT-12	III	Squamous	179/178	Sintilimab + cisplatin/carboplatin + gemcitabine vs Cisplatin/carboplatin + gemcitabine
POSEIDON*	III	Squamous & non-squamous	637/336	Durvalumab + platinum-based CT vs Durvalumab + tremelimumab + platinum-based CT vs platinum-based CT
RATIONALE 304	III	Non-squamous	223/111	tislelizumab + pemetrexed + cisplatin/carboplatin vs Pemetrexed + cisplatin/carboplatin
RATIONALE 307	III	Squamous	120/119/121	Tislelizumab + carboplatin + paclitaxel vs Tislelizumab + carboplatin + nab-paclitaxel vs Carboplatin + nab-paclitaxel
TASUKI-52	III	Non-squamous	275/275	Nivolumab + carboplatin + paclitaxel + bevacizumab vs Carboplatin + paclitaxel + bevacizumab

Main characteristics of randomized controlled clinical trials selected for the meta-analysis.
ORR: Objective Response Rate; PFS: Progression-Free Survival; OS: Overall Survival.
*only published as conference abstract

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