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PD－1/PD－L1 抑制剂治疗晚期非小细胞肺癌有效性和安全性网状 Meta 分析*

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摘要：目的　系统评价程序性死亡受体－1/程序性死亡受体配体－1(PD－1/PD－L1)抑制剂单药或联合化学药物治疗(简称化疗)治疗晚期非小细胞肺癌(NSCLC)的有效性和安全性。**方法**　采用计算机检索中国知网(CNKI)、中国生物医学文献数据库(CBM)、万方(WanFang)、维普(VIP)及 PubMed，The Cochrane Library，Embase 数据库中自建库起至 2023 年 10 月有关 PD－1/PD－L1 抑制剂治疗晚期 NSCLC 的随机对照试验(RCT)。采用 Cochrane 5.3 偏倚风险评估工具评价纳入文献的质量，采用 R 4.3.1 软件 gemtc 程序包进行贝叶斯网状 Meta 分析。**结果**　共纳入 25 篇文献，涉及 11 660 例患者和 17 种干预措施。网状 Meta 分析结果显示，与单纯化疗相比，卡瑞利珠单抗联合化疗和帕博利珠单抗联合化疗能同时改善患者的总生存期(OS)、无进展生存期(PFS)和客观缓解率(ORR)，替雷利珠单抗联合化疗能同时改善患者的 PFS 和 ORR，替雷利珠单抗和信迪利单抗能显著改善患者的 ORR；替雷利珠单抗、纳武利尤单抗、阿维鲁单抗能显著降低 3 级及以上药品不良反应发生率。**结论**　与其他 PD－1/PD－L1 抑制剂相比，替雷利珠单抗单药或联合化疗治疗晚期 NSCLC 改善 OS，PFS，ORR 的疗效相当，但其安全性更好。

关键词：替雷利珠单抗；程序性死亡受体－1/程序性死亡受体配体－1 抑制剂；非小细胞肺癌；有效性；安全性；网状 Meta 分析

Efficacy and Safety of PD－1/PD－L1 Inhibitors in the Treatment of Advanced Non－Small Cell Lung Cancer：A Network Meta－Analysis

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Abstract: Objective　To systematically evaluate the efficacy and safety of programmed－death receptor－1/programmed－death receptor ligand－1 (PD－1/PD－L1) inhibitors as monotherapy or in combination with chemotherapy for advanced non－small cell lung cancer (NSCLC). **Methods**　Randomized controlled trials (RCTs) of PD－1/PD－L1 inhibitors in the treatment of advanced NSCLC in the CNKI, CBM, WanFang, VIP, PubMed, The Cochrane Library, and Embase databases from their inception to October 2023 were retrieved. The quality of the included stduies was evaluated by the Cochrane 5.3 bias risk assessment tool, and Bayesian network Meta－analysis was conducted by the gemtc package of the R 4.3.1 software. **Results**　A total of 25 studies were included, involving 11 660 patients and 17 intervention measures. The results of the network Meta－analysis showed that compared with chemotherapy alone, both the combination of camrelizumab with chemotherapy and the combination of pembrolizumab with chemotherapy could improve the overall survival (OS), progression－free survival (PFS), and objective response rate (ORR) of patients,

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[23] EVANS RW. Raynaud's Phenomenon Associated with Calcitonin Gene: Related Peptide Monoclonal Antibody Antagonists [J]. Headache, 2019, 59(8): 1360－1364.

[24] TERENGHI G, BUNKER CB, LIU YF, et al. Image analysis quantification of peptide: immunoreactive nerves in the skin of patients with Raynaud's phenomenon and systemic sclerosis[J]. J Pathol, 1991, 164(3): 245－252.

[25] 佘延芬，杨继军，张瑞娟，等. 加味青麟丸对高脂血症小鼠脂代谢及血浆内皮素－1 及降钙素基因相关肽含量的影响[J]. 时珍国医国药，2010，21(5)：1154－1155.

[26] IANNONE LF, DE CESARIS F, FERRARI A, et al. Effectiveness of anti－CGRP monoclonal antibodies on central symptoms of migraine[J]. Cephalalgia, 2022, 42(13): 1323－1330.

[27] WOODS RH. Alopecia signals associated with calcitonin gene－related peptide inhibitors in the treatment or prophylaxis of migraine: A pharmacovigilance study [J]. Pharmacotherapy, 2022, 42(10): 758－767.

[28] BEDRIN KO, DOUGHERTY C. Cephalgia Alopecia[J]. Curr Pain Headache Rep, 2020, 24(9): 46.

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the combination of tislelizumab with chemotherapy could significantly improve PFS and ORR of patients. Tislelizumab and sintilimab could significantly improve the ORR of patients. Tislelizumab, nivolumab, and avelumab could significantly reduce the incidence of grade ≥ 3 adverse drug reactions. **Conclusion** Compared with other PD - 1 / PD - L1 inhibitors, tislelizumab inhibitor monotherapy or combination chemotherapy has comparable efficacy in improving OS, PFS, and ORR in advanced NSCLC, but its safety is better.

Key words: tislelizumab; PD - 1 / PD - L1 inhibitors; advanced non - small cell lung cancer; efficacy; safety; network Meta - analysis

肺癌是我国发病率和死亡率最高的恶性肿瘤[1-2]。非小细胞肺癌（NSCLC）是肺癌的主要病理类型，约占肺癌的85%，一旦确诊多为晚期，预后差[3]。晚期NSCLC的治疗已由化学治疗（简称化疗）为主转变为靶向治疗、抗血管生成治疗及免疫治疗，特别是程序性死亡受体-1（PD-1）/程序性死亡受体配体-1（PD-L1）抑制剂等已被推荐用于晚期NSCLC的一线治疗，提高了患者的临床获益。替雷利珠单抗的Fc段经过基因工程改造，消除了抗体依赖的细胞吞噬作用，避免了由于T细胞数量减少而影响抗肿瘤疗效，不良反应发生率相对较低，抗肿瘤活性相对更强[4-5]。2021年，替雷利珠单抗在中国已获批联合化疗用于局部晚期或转移性NSCLC的一线治疗。但目前缺乏替雷利珠单抗与其他PD-1/PD-L1抑制剂“头对头”的临床试验，已发表的PD-1/PD-L1抑制剂治疗NSCLC的网状Meta分析较少涉及替雷利珠单抗[6-9]，或未涉及本研究中关注的结局指标，或已发表的网状Meta分析研究结果不一致[7,9]。另外，目前关于PD-1/PD-L1抑制剂治疗NSCLC的部分高质量随机对照试验（RCT）的研究数据未区分病理类型。在实际临床工作中，仍有部分NSCLC患者因各种原因未能明确病理类型。故本研究中采用网状Meta分析法比较了包含替雷利珠单抗在内的PD-1/PD-L1抑制剂治疗NSCLC的有效性和安全性，为临床合理用药提供参考。现报道如下。

1 资料与方法

1.1 纳入与排除标准

纳入标准：患者均经组织细胞学或病理学确诊为NSCLC，且无人表皮生长因子受体突变及间变性淋巴瘤激酶重排，性别、年龄不限；研究类型为RCT，语种不限；干预措施为试验组患者予PD-1/PD-L1抑制剂单药或联合化疗，对照组仅予化疗，具体方案不限；结局指标包括有效性[①总生存期（OS），②无进展生存期（PFS），③客观缓解率（ORR）]和安全性[④3级及以上药品不良反应（ADR）发生率（grade ≥ 3 ADR）]指标。

排除标准：未包含上述任一结局指标；数据未公开或无法获取原始数据；综述，系统评价，摘要，会议报告等；重复发表。

1.2 文献检索策略

采用计算机检索PubMed, Embase, The Cochrane Library及中国知网（CNKI）、万方（WanFang）、维普（VIP）、中国生物医学文献数据库（CBM）中自建库起至2023年10月的相关RCT。英文检索词为“tislelizumab”“pembrolizumab”“avelumab”“atezolizumab”“cemiplimab”“camrelizumab”“durvalumab”“nivolumab”“sintilimab”“sugemalimab”“PD-1 inhibitor”“PD-L1 inhibitor”“NSCLC”，中文检索词为“替雷利珠单抗”“帕博利珠单抗”“阿维鲁单抗”“阿替利珠单抗”“西米普利单抗”“卡瑞利珠单抗”“度伐利尤单抗”“纳武利尤单抗”“信迪利单抗”“舒格利单抗”“PD-1抑制剂”“PD-L1抑制剂”“非小细胞肺癌”。

1.3 文献筛选、数据提取与质量评价

由2位研究员独立筛选文献，若存在分歧，则由第三位研究员协助裁定。资料提取包括第一作者、发表年份、人口学基线特征、病理类型、干预措施、结局指标等。采用Cochrane 5.3风险偏倚评估工具评价纳入文献的质量，包括随机序列的产生、分配隐藏、对受试者和研究人员施盲、结局评估中的盲法、不全的结局数据、选择性报告、其他偏倚等。

1.4 统计学处理

采用R 4.3.1软件gemtc程序包进行贝叶斯网状Meta分析。OS及PFS以风险比（*HR*）及其95%Crl为效应量，ORR及grade ≥ 3 ADR以比值比（*OR*）及其95%Crl为效应量。绘制排序概率图，计算累积排序概率图下面积（SUCRA），评估某一药物成为最佳干预措施的概率。模型采用4条马尔可夫链进行初始值的设定，迭代次数设为10 000次，前100 000次用于退火，以消除初始值的影响，通过潜在尺度减少因子（PSRF）诊断模型收敛程度，PSRF值趋近于1提示模型收敛满意，否则继续增加迭代次数。参考误差信息准则（DIC）值选择随机或固定效应模型，一般认为DIC值越小越好。若2个模型间的差异值 < 5，则认为2个模型的拟合程度一致，采用固定效应模型分析；反之，采用随机效应模型分析。

2 结果

2.1 文献检索结果与纳入文献基本情况

共检索到6 473篇文献，经筛选，最终纳入25篇文献[10-34]，涉及患者11 660例，共17种干预措施。文献筛选流程见图1，纳入文献的基本信息见表1。

2.2 纳入文献质量评价

纳入的25项RCT中，6项RCT[14,21,26,30-31,33]被评

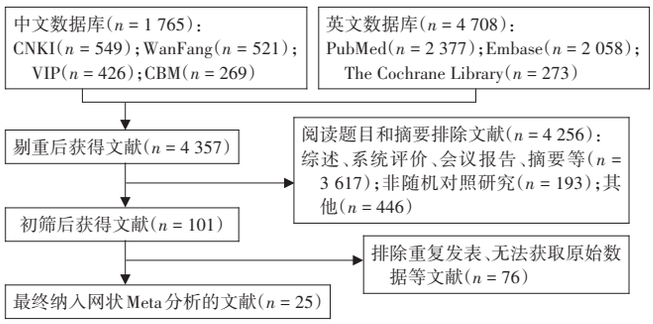


图1 文献筛选流程

Fig. 1 Flowchart of literature screening

为低偏倚风险;1项RCT被评为中偏倚风险[23];18项RCT[10-13,15-20,22,24-25,27-29,32,34]被评为高偏倚风险,主要问题为存在实施偏倚和检测偏倚。纳入文献偏倚风险分析结果见图2和图3。

2.3 网状 Meta 分析

2.3.1 网络证据关系

OS, PFS, ORR, grade ≥ 3 ADR 的网络证据关系见图4。因缺乏 PD-1/PD-L1 抑制剂间“头对头”的RCT,故4项结局指标的网络证据关系均未形成闭环,无法进行后续的局部一致性检验,故本研究中的网状Meta分析主要提供了PD-1/PD-L1抑制剂的间接比较证据。

2.3.2 有效性

OS:共23篇文献报道[10-24,26,28-34],涉及16种干预措施(见图4 A),改善OS的优劣排序见表2。因纳入研究不存在整体不一致,固定效应模型和随机效应模型的*DIC*值分别为46.13和43.03,差异值 < 5,故采用固

表1 纳入文献基本信息

Tab. 1 Basic information of included studies

第一作者及发表年份	病理类型	性别(男/女,例)		中位年龄(岁)		中位随访	干预措施		结局指标
		试验组	对照组	试验组	对照组	时间(个月)	试验组	对照组	
LANGER[10] 2016	nsq-NSCLC	22/38	26/37	62.50	63.20	10.60	帕博利珠单抗(Pem)+Che	Che[a]	①②③④
RECK[11] 2016	NSCLC	92/62	95/56	64.50	66.00	11.20	Pem	Che[a]	①②③④
CARBONE[12] 2017	NSCLC	184/87	148/122	63.00	65.00	13.50	纳武利尤单抗(Niv)	Che[a]	①②④
BARLESI[13] 2018	NSCLC	269/127	273/123	64.00	63.00	18.90	阿维鲁单抗(Ave)	Che[b]	①②③④
GANDHI[14] 2018	nsq-NSCLC	254/156	109/97	65.00	63.50	10.50	Pem+Che	Che[a]	①②③④
MOK[15] 2019	NSCLC	450/187	452/185	63.00	63.00	12.80	Pem	Che[a]	①②③④
WU[16] 2019	NSCLC	263/75	134/32	60.00	60.00	10.40	Niv	Che[b]	①②③④
PLANCHARD[17] 2020	NSCLC	42/20	48/16	63.50	62.00	11.70	度代利尤单抗(Dur)	Che[c]	①②③④
HERBST[18] 2020	NSCLC	196/81	193/84	64.00	65.00	13.40	阿替利珠单抗(Ate)	Che[a]	①②③④
RIZVI[19] 2020	NSCLC	113/50	106/56	64.00	64.50	30.20	Dur	Che[a]	①②③④
NISHIO[20] 2021	nsq-NSCLC	192/100	192/94	64.00	63.00	14.80	Ate+Che	Che[a]	①②③④
YANG[21] 2020	nsq-NSCLC	204/62	99/32	61.00	61.00	8.90	信迪利单抗(Sin)+Che	Che[a]	①②③④
SEZER[22] 2021	NSCLC	248/35	231/49	63.00	64.00	13.10	西米普利单抗(Cem)	Che[a]	①②③④
SUGAWARA[23] 2021	nsq-NSCLC	205/70	206/69	66.00	66.00	13.70	Niv+Che	Che[a]	①②③④
ZHOU[24] 2021	nsq-NSCLC	146/59	149/58	59.00	61.00	11.90	卡瑞利珠单抗(Cam)+Che	Che[a]	①②③④
WANG[25] 2021	sq-NSCLC	107/13	111/10	60.00	62.00	8.60	替雷利珠单抗(Tis)+Che	Che[a]	②③④
ZHOU[26] 2021	sq-NSCLC	163/16	164/14	64.00	62.00	12.90	Sin+Che	Che[a]	①②③④
LU[27] 2021	nsq-NSCLC	168/55	79/32	60.00	61.00	9.80	Tis+Che	Che[a]	②③④
SHI[28] 2022	sq-NSCLC	136/9	122/13	61.00	60.00	23.56	Sin	Che[b]	①②③④
PETERS[29] 2022	NSCLC	106/39	108/38	65.00	66.00	18.20	Ate	Che[a]	①②③④
GOGISHVILI[30] 2022	NSCLC	268/44	123/31	63.00	63.00	16.30	Cem+Che	Che[a]	①②③④
REN[31] 2022	sq-NSCLC	179/14	180/16	64.00	62.00	13.50	Cam+Che	Che[a]	①②③④
FORDE[32] 2022	NSCLC	128/51	127/52	64.00	65.00	21.00	Niv+Che	Che[a]	①③④
ZHOU[33] 2022	NSCLC	254/66	129/30	62.00	64.00	17.80	舒格利单抗(Sug)+Che	Che[a]	①②③④
ZHOU[34] 2023	NSCLC	416/119	206/64	61.00	61.00	16.00	Tis	Che[b]	①②③④

注:NSCLC为非小细胞肺癌,sq-NSCLC为鳞状非小细胞肺癌,nsq-NSCLC为非鳞状非小细胞肺癌。Che指单纯化学治疗,其中a,b,c分别指以铂制剂为基础,多西他赛,厄洛替尼、吉西他滨或长春瑞滨。

Note: NSCLC refers to non-small cell lung cancer, sq-NSCLC refers to squamous non-small cell lung cancer, and nsq-NSCLC refers to non squamous non-small cell lung cancer. Che refers to the chemotherapy monotherapy regimen, and the a, b, and c respectively refer to platinum preparations, docetaxel, and erlotinib / gemcitabine / vinorelbine as the basis.

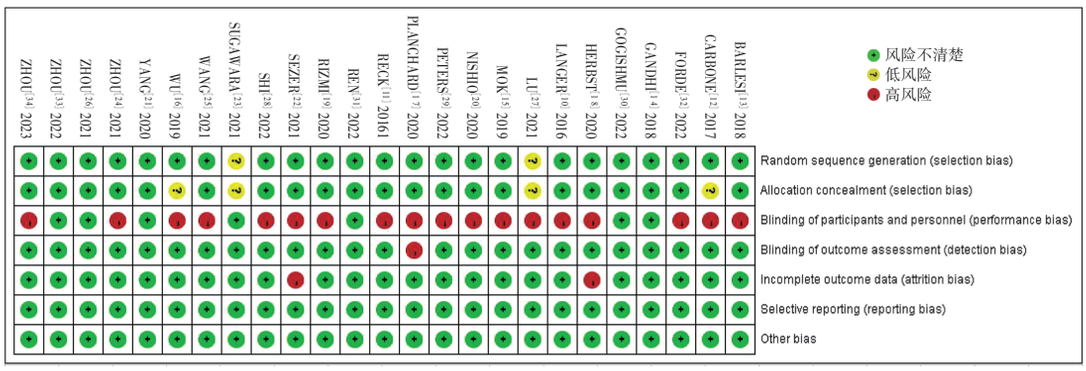


图 2　纳入随机对照试验的偏倚风险分析

Fig. 2　Bias risk for included RCTs

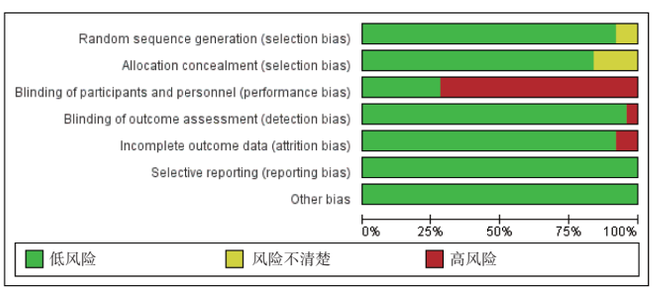
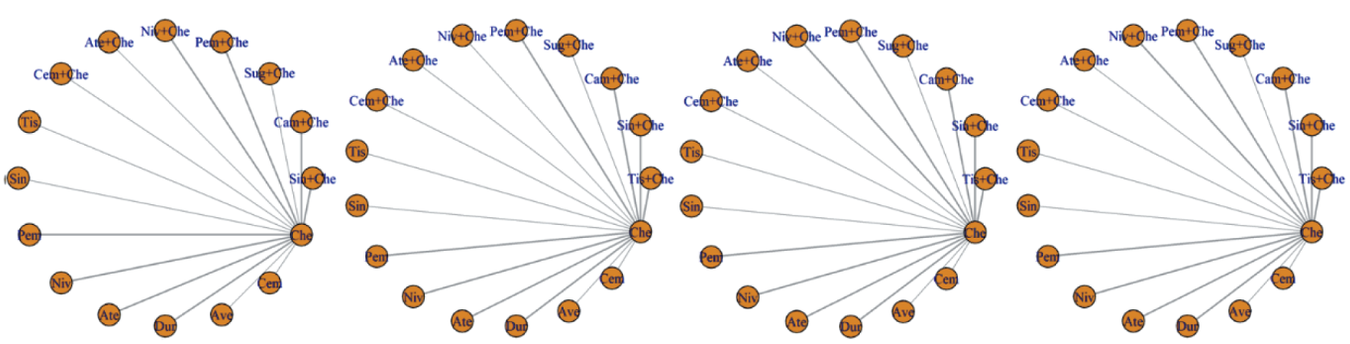


图 3　纳入随机对照试验偏倚风险项目所占比例

Fig. 3　Proportion of bias risk items of included RCTs

定效应模型评估各种干预措施的相对疗效。网状 Meta 分析结果显示，与单纯化疗（Che）比较，仅信迪利单抗联合化疗（Sin + Che）[*HR* = 0.59, 95%CrI（0.38, 0.92）]，卡瑞利珠单抗联合化疗（Cam + Che）[*HR* = 0.64, 95%CrI（0.44, 0.92）]，帕博利珠单抗联合化疗（Pem + Che）[*HR* = 0.60, 95%CrI（0.42, 0.91）]，西米普利单抗（Cem）[*HR* = 0.57, 95%CrI（0.33, 0.97）]4 种干预措施可显著延长 OS。详见图 5。

PFS：共 24 篇文献报道[10-31,33-34]，涉及 17 种干预措施（见图 4 B），改善 PFS 的优劣排序见表 2。因纳入研究不存在整体不一致，固定效应模型和随机效应模型分



A. OS　B. PFS　C. ORR　D. grade ≥ 3 ADR

图 4　4 项结局指标的网络证据关系

A. OS　B. PFS　C. ORR　D. grade ≥ 3 ADR

Fig. 4　Network evidence relationship of four outcome indicators

表 2　4 种结局指标中不同干预措施的 SUCRA 值排序

Tab. 2　Ranking of SUCRA values for different intervention measures among the four outcome indicators

结局指标		排序																
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
OS	SUCRA(%)	Cem	Sin + Che	Pem + Che	Cam + Che	Cem + Che	Tis	Sug + Che	Pem	Sin	Niv + Che	Dur	Ate	Ate + Che	Niv	Ave	Che	
	干预措施	78.35	76.18	75.05	68.71	66.04	64.59	61.78	50.82	50.36	46.45	33.51	32.32	31.51	28.69	26.33	9.31	
PFS	SUCRA(%)	Cam + Che	Sug + Che	Pem + Che	Sin + Che	Sin	Cem	Cem + Che	Niv + Che	Tis + Che	Ate + Che	Tis	Ate	Pem	Dur	Niv	Che	Ave
	干预措施	80.38	73.63	71.60	70.43	67.27	63.90	62.64	61.15	58.27	55.14	50.88	33.02	32.97	32.01	16.68	11.13	8.91
ORR	SUCRA(%)	Sin	Tis	Pem + Che	Cam + Che	Cem + Che	Sug + Che	Tis + Che	Cem	Sin + Che	Ate + Che	Niv + Che	Niv	Ave	Pem	Dur	Ate	Che
	干预措施	97.82	76.57	73.81	66.15	62.98	60.34	60.07	59.07	47.03	45.06	41.09	35.84	31.61	31.23	28.71	21.96	10.66
grade ≥ 3 ADR	SUCRA(%)	Tis	Ave	Niv	Dur	Cem	Sin + Che	Pem	Ate	Sin	Sug + Che	Niv + Che	Che	Pem + Che	Ate + Che	Tis + Che	Cam + Che	Cem + Che
	干预措施	87.33	84.66	79.85	72.45	68.44	67.73	64.43	62.14	56.94	34.69	34.23	32.83	24.11	20.60	20.55	20.06	18.96

Tis+Che	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1.14 (0.58, 2.24)	Sin+Che	0.92 (0.52, 1.64)	0.88 (0.44, 1.75)	0.98 (0.53, 1.72)	0.78 (0.42, 1.47)	0.69 (0.35, 1.32)	0.91 (0.46, 1.76)	0.89 (0.46, 1.70)	0.80 (0.40, 1.57)	0.80 (0.46, 1.44)	0.67 (0.39, 1.20)	0.70 (0.39, 1.23)	0.71 (0.40, 1.29)	0.65 (0.34, 1.25)	1.04 (0.51, 2.06)	0.59 (0.38, 0.92)
1.28 (0.65, 2.51)	1.13 (0.58, 2.17)	Cam+Che	0.96 (0.50, 1.81)	1.06 (0.61, 1.77)	0.84 (0.48, 1.51)	0.75 (0.4, 1.37)	0.99 (0.52, 1.84)	0.97 (0.52, 1.76)	0.87 (0.45, 1.62)	0.87 (0.53, 1.49)	0.73 (0.44, 1.24)	0.76 (0.44, 1.26)	0.76 (0.47, 1.32)	0.71 (0.38, 1.31)	1.13 (0.58, 2.13)	0.64 (0.44, 0.92)
1.21 (0.54, 2.72)	1.06 (0.48, 2.38)	0.94 (0.43, 2.1)	Sug+Che	1.11 (0.56, 2.10)	0.88 (0.45, 1.78)	0.78 (0.38, 1.6)	1.03 (0.50, 2.14)	1.02 (0.50, 2.07)	0.91 (0.43, 1.88)	0.91 (0.49, 1.76)	0.77 (0.41, 1.47)	0.79 (0.41, 1.51)	0.80 (0.43, 1.58)	0.75 (0.36, 1.53)	1.18 (0.55, 2.48)	0.67 (0.40, 1.13)
1.15 (0.58, 2.29)	1.02 (0.52, 1.98)	0.90 (0.46, 1.75)	0.96 (0.42, 2.11)	Pem+Che	0.79 (0.46, 1.49)	0.70 (0.38, 1.34)	0.93 (0.50, 1.78)	0.92 (0.50, 1.72)	0.82 (0.43, 1.58)	0.82 (0.50, 1.46)	0.69 (0.42, 1.21)	0.71 (0.42, 1.24)	0.72 (0.44, 1.30)	0.67 (0.37, 1.28)	1.06 (0.56, 2.09)	0.60 (0.42, 0.91)
1.04 (0.46, 2.37)	0.91 (0.41, 2.05)	0.81 (0.36, 1.81)	0.86 (0.34, 2.15)	0.90 (0.40, 2.04)	Niv+Che	0.89 (0.45, 1.66)	1.17 (0.59, 2.22)	1.15 (0.59, 2.14)	1.03 (0.51, 1.96)	1.03 (0.59, 1.81)	0.87 (0.49, 1.51)	0.90 (0.50, 1.54)	0.91 (0.52, 1.61)	0.85 (0.43, 1.58)	1.34 (0.66, 2.60)	0.76 (0.48, 1.15)
0.96 (0.43, 2.14)	0.85 (0.38, 1.87)	0.75 (0.34, 1.66)	0.80 (0.32, 1.96)	0.83 (0.38, 1.86)	0.93 (0.37, 2.33)	Ate+Che	1.33 (0.65, 2.68)	1.30 (0.65, 2.58)	1.16 (0.57, 2.36)	1.16 (0.65, 2.21)	0.99 (0.54, 1.84)	1.02 (0.55, 1.86)	1.02 (0.58, 1.97)	0.95 (0.48, 1.91)	1.51 (0.73, 3.11)	0.86 (0.53, 1.40)
1.05 (0.47, 2.36)	0.92 (0.42, 2.05)	0.82 (0.37, 1.82)	0.87 (0.35, 2.16)	0.91 (0.41, 2.04)	1.01 (0.40, 2.53)	1.09 (0.44, 2.71)	Cem+Che	0.98 (0.49, 2.00)	0.88 (0.43, 1.81)	0.87 (0.48, 1.68)	0.74 (0.41, 1.40)	0.77 (0.41, 1.43)	0.77 (0.43, 1.51)	0.72 (0.36, 1.46)	1.14 (0.54, 2.38)	0.65 (0.39, 1.08)
0.92 (0.41, 2.07)	0.81 (0.37, 1.78)	0.72 (0.33, 1.59)	0.76 (0.31, 1.89)	0.80 (0.36, 1.78)	0.89 (0.35, 2.21)	0.95 (0.39, 2.38)	0.88 (0.35, 2.17)	Tis	0.89 (0.44, 1.81)	0.89 (0.51, 1.68)	0.75 (0.42, 1.40)	0.78 (0.43, 1.42)	0.78 (0.44, 1.51)	0.73 (0.37, 1.45)	1.16 (0.56, 2.39)	0.66 (0.41, 1.06)
1.12 (0.49, 2.54)	0.98 (0.43, 2.22)	0.87 (0.39, 1.96)	0.92 (0.36, 2.33)	0.96 (0.42, 2.21)	1.08 (0.42, 2.72)	1.16 (0.46, 2.92)	1.06 (0.42, 2.70)	1.21 (0.48, 3.02)	Sin	1.00 (0.55, 1.94)	0.85 (0.46, 1.62)	0.87 (0.46, 1.65)	0.88 (0.49, 1.73)	0.82 (0.41, 1.69)	1.30 (0.62, 2.74)	0.74 (0.44, 1.25)
0.75 (0.39, 1.51)	0.66 (0.35, 1.31)	0.59 (0.31, 1.15)	0.62 (0.29, 1.40)	0.65 (0.34, 1.30)	0.72 (0.33, 1.65)	0.78 (0.36, 1.76)	0.71 (0.33, 1.62)	0.81 (0.38, 1.83)	0.67 (0.30, 1.56)	Pem	0.85 (0.50, 1.40)	0.87 (0.50, 1.43)	0.88 (0.53, 1.50)	0.82 (0.44, 1.47)	1.30 (0.66, 2.41)	0.74 (0.50, 1.04)
0.61 (0.31, 1.18)	0.53 (0.28, 1.02)	0.47 (0.25, 0.91)	0.50 (0.23, 1.10)	0.52 (0.27, 1.02)	0.58 (0.26, 1.31)	0.63 (0.29, 1.38)	0.57 (0.26, 1.27)	0.66 (0.30, 1.45)	0.54 (0.24, 1.22)	0.81 (0.41, 1.51)	Niv	1.03 (0.60, 1.70)	1.04 (0.63, 1.78)	0.97 (0.53, 1.76)	1.53 (0.79, 2.88)	0.87 (0.60, 1.24)
0.75 (0.39, 1.47)	0.66 (0.34, 1.27)	0.59 (0.30, 1.13)	0.62 (0.28, 1.36)	0.65 (0.33, 1.27)	0.73 (0.32, 1.62)	0.78 (0.35, 1.71)	0.72 (0.32, 1.58)	0.82 (0.37, 1.79)	0.67 (0.30, 1.52)	1.00 (0.51, 1.87)	1.24 (0.65, 2.36)	Ate	1.01 (0.62, 1.77)	0.94 (0.51, 1.74)	1.49 (0.78, 2.88)	0.85 (0.59, 1.23)
0.74 (0.36, 1.50)	0.65 (0.32, 1.29)	0.58 (0.29, 1.15)	0.61 (0.27, 1.39)	0.64 (0.32, 1.29)	0.71 (0.31, 1.64)	0.77 (0.34, 1.74)	0.70 (0.31, 1.60)	0.80 (0.35, 1.80)	0.66 (0.29, 1.53)	0.99 (0.48, 1.91)	1.22 (0.61, 2.41)	0.98 (0.50, 1.96)	Dur	0.93 (0.49, 1.66)	1.47 (0.75, 2.72)	0.84 (0.56, 1.17)
0.50 (0.22, 1.12)	0.44 (0.20, 0.97)	0.39 (0.18, 0.86)	0.41 (0.17, 1.02)	0.43 (0.19, 0.97)	0.48 (0.19, 1.20)	0.52 (0.21, 1.28)	0.48 (0.19, 1.18)	0.54 (0.22, 1.33)	0.45 (0.18, 1.13)	0.67 (0.29, 1.43)	0.83 (0.37, 1.80)	0.67 (0.30, 1.47)	0.68 (0.30, 1.53)	Ave	1.58 (0.77, 3.24)	0.90 (0.55, 1.46)
1.07 (0.47, 2.44)	0.94 (0.42, 2.1)	0.84 (0.38, 1.86)	0.89 (0.36, 2.22)	0.93 (0.42, 2.10)	1.03 (0.41, 2.62)	1.11 (0.45, 2.77)	1.02 (0.41, 2.58)	1.17 (0.47, 2.88)	0.96 (0.38, 2.45)	1.43 (0.62, 3.11)	1.77 (0.80, 3.94)	1.43 (0.65, 3.16)	1.45 (0.63, 3.32)	2.15 (0.86, 5.37)	Cem	0.57 (0.33, 0.97)
0.58 (0.35, 0.95)	0.51 (0.32, 0.82)	0.45 (0.29, 0.72)	0.48 (0.25, 0.91)	0.50 (0.31, 0.82)	0.56 (0.29, 1.08)	0.60 (0.32, 1.14)	0.55 (0.29, 1.05)	0.63 (0.33, 1.19)	0.52 (0.27, 1.01)	0.77 (0.47, 1.20)	0.96 (0.61, 1.51)	0.77 (0.49, 1.23)	0.78 (0.47, 1.30)	1.16 (0.62, 2.22)	0.54 (0.28, 1.04)	Che

注：右上角为OS，左下角为PFS。

图5 OS与PFS的网状Meta分析结果

Note: The upper right corner refers to OS, and the lower left corner refers to PFS.

Fig. 5 Network Meta - analysis of OS and PFS

Tis+Che	5.84 (0.78, 87.83)	0.99 (0.11, 8.37)	1.69 (0.12, 22.92)	1.16 (0.13, 9.89)	1.70 (0.19, 14.46)	0.91 (0.07, 12.43)	0.84 (0.06, 11.57)	17.52 (1.24, 245.26)	4.06 (0.29, 57.45)	5.26 (0.61, 45.37)	10.24 (1.17, 88.73)	4.84 (0.56, 41.91)	7.35 (0.82, 68.19)	14.79 (1.06, 204.28)	6.52 (0.47, 89.03)	1.66 (0.36, 7.61)
1.29 (0.36, 4.57)	Sin+Che	0.17 (0.01, 1.22)	0.29 (0.01, 3.22)	0.20 (0.01, 1.44)	0.29 (0.02, 2.09)	0.16 (0.01, 1.78)	0.14 (0.01, 1.64)	3.01 (0.12, 33.37)	0.70 (0.03, 7.96)	0.91 (0.06, 6.47)	1.75 (0.11, 12.67)	0.83 (0.06, 5.93)	1.25 (0.08, 9.54)	2.54 (0.11, 28.56)	1.12 (0.05, 12.45)	0.28 (0.03, 1.19)
0.88 (0.25, 3.15)	0.69 (0.19, 2.43)	Cam+Che	1.70 (0.13, 23.47)	1.18 (0.13, 10.08)	1.72 (0.20, 14.83)	0.93 (0.07, 12.72)	0.85 (0.06, 11.84)	17.71 (1.27, 244.85)	4.13 (0.29, 59.06)	5.34 (0.63, 47.00)	10.35 (1.23, 89.33)	4.91 (0.58, 42.52)	7.42 (0.88, 68.34)	14.91 (1.10, 211.30)	6.63 (0.49, 93.16)	1.67 (0.37, 7.79)
0.96 (0.21, 4.58)	0.75 (0.16, 3.51)	1.10 (0.24, 5.10)	Sug+Che	0.69 (0.05, 9.54)	1.01 (0.07, 14.06)	0.55 (0.03, 11.14)	0.50 (0.02, 10.20)	10.46 (0.49, 218.22)	2.44 (0.11, 50.11)	3.14 (0.23, 43.53)	6.08 (0.45, 82.93)	2.89 (0.21, 38.52)	4.35 (0.32, 65.54)	8.80 (0.43, 178.11)	3.89 (0.18, 78.60)	0.98 (0.12, 8.43)
0.73 (0.2, 2.71)	0.57 (0.16, 2.07)	0.83 (0.23, 3.04)	0.76 (0.16, 3.61)	Pem+Che	1.47 (0.17, 12.77)	0.79 (0.06, 11.18)	0.72 (0.05, 10.66)	15.07 (1.10, 214.81)	3.50 (0.24, 50.33)	4.56 (0.53, 40.50)	8.81 (1.02, 78.12)	4.17 (0.49, 36.54)	6.35 (0.74, 59.57)	12.70 (0.93, 181.26)	5.62 (0.42, 78.53)	1.43 (0.31, 6.73)
1.44 (0.41, 5.11)	1.12 (0.32, 3.91)	1.64 (0.47, 5.64)	1.49 (0.32, 6.83)	1.96 (0.54, 7.00)	Niv+Che	0.54 (0.04, 7.44)	0.50 (0.04, 6.98)	10.27 (0.75, 148.25)	2.40 (0.17, 33.69)	3.12 (0.37, 26.83)	5.98 (0.69, 51.49)	2.85 (0.34, 24.55)	4.29 (0.50, 39.53)	8.69 (0.62, 121.20)	3.86 (0.29, 52.20)	0.97 (0.21, 4.47)
1.34 (0.29, 6.24)	1.04 (0.22, 4.79)	1.52 (0.33, 6.90)	1.39 (0.24, 8.04)	1.83 (0.39, 8.34)	0.93 (0.20, 4.22)	Ate+Che	0.92 (0.04, 18.88)	19.12 (0.93, 397.03)	4.45 (0.20, 92.36)	5.75 (0.44, 76.59)	11.17 (0.82, 150.77)	5.29 (0.39, 71.42)	8.00 (0.57, 112.35)	16.03 (0.78, 336.95)	7.15 (0.36, 143.72)	1.81 (0.22, 15.09)
0.91 (0.19, 4.31)	0.70 (0.15, 3.36)	1.03 (0.22, 4.81)	0.94 (0.16, 5.58)	1.23 (0.26, 5.91)	0.63 (0.13, 2.90)	0.68 (0.12, 4.02)	Cem+Che	20.73 (1.01, 423.61)	4.84 (0.22, 102.44)	6.25 (0.45, 86.13)	12.15 (0.89, 169.12)	5.75 (0.40, 80.68)	8.71 (0.62, 128.64)	17.51 (0.83, 372.20)	7.81 (0.38, 155.46)	1.97 (0.23, 16.59)
0.64 (0.13, 3.08)	0.49 (0.10, 2.36)	0.72 (0.15, 3.43)	0.65 (0.11, 3.90)	0.86 (0.18, 4.20)	0.44 (0.09, 2.08)	0.47 (0.08, 2.81)	0.70 (0.11, 4.23)	Tis	0.23 (0.01, 5.04)	0.30 (0.02, 4.20)	0.59 (0.04, 8.09)	0.28 (0.02, 3.90)	0.42 (0.03, 6.21)	0.84 (0.04, 18.00)	0.37 (0.02, 7.65)	0.09 (0.01, 0.80)
0.14 (0.02, 1.94)	0.11 (0.01, 1.73)	0.16 (0.02, 1.04)	0.15 (0.02, 1.16)	0.19 (0.02, 1.28)	0.10 (0.01, 1.64)	0.11 (0.02, 1.67)	0.16 (0.02, 1.24)	0.23 (0.02, 1.83)	Sin	1.30 (0.09, 18.76)	2.51 (0.18, 36.43)	1.19 (0.08, 17.24)	1.80 (0.13, 27.51)	3.62 (0.17, 77.16)	1.60 (0.08, 33.70)	0.41 (0.05, 3.61)
1.74 (0.49, 6.1)	1.35 (0.38, 4.69)	1.98 (0.56, 6.80)	1.81 (0.38, 8.16)	2.38 (0.65, 8.27)	1.21 (0.35, 4.10)	1.31 (0.28, 5.80)	1.92 (0.41, 8.76)	2.75 (0.57, 12.86)	12.10 (1.85, 93.03)	Pem	1.93 (0.23, 16.23)	0.91 (0.11, 7.80)	1.39 (0.16, 12.72)	2.78 (0.21, 39.17)	1.24 (0.09, 16.98)	0.31 (0.07, 1.41)
1.61 (0.41, 5.59)	1.25 (0.32, 4.27)	1.83 (0.47, 6.21)	1.67 (0.33, 7.39)	2.20 (0.54, 7.71)	1.12 (0.29, 3.75)	1.20 (0.24, 5.28)	1.78 (0.35, 7.98)	2.54 (0.49, 11.69)	11.14 (1.62, 86.30)	0.93 (0.25, 3.18)	Niv	0.47 (0.05, 4.02)	0.72 (0.08, 6.44)	1.45 (0.10, 19.80)	0.64 (0.05, 8.64)	0.16 (0.04, 0.74)
2.12 (0.58, 7.56)	1.65 (0.46, 5.76)	2.41 (0.66, 8.47)	2.20 (0.46, 10.06)	2.90 (0.78, 10.35)	1.47 (0.41, 5.09)	1.59 (0.34, 7.10)	2.34 (0.49, 10.75)	3.36 (0.69, 15.85)	14.76 (2.30, 113.84)	1.22 (0.35, 4.32)	1.32 (0.38, 5.03)	Ate	1.52 (0.18, 13.57)	3.04 (0.22, 42.00)	1.35 (0.10, 18.56)	0.34 (0.07, 1.57)
1.86 (0.47, 6.67)	1.44 (0.37, 5.08)	2.10 (0.55, 7.42)	1.93 (0.38, 8.78)	2.53 (0.65, 9.05)	1.28 (0.34, 4.51)	1.39 (0.28, 6.32)	2.04 (0.41, 9.54)	2.92 (0.57, 14.02)	12.84 (1.89, 100.24)	1.06 (0.29, 3.77)	1.15 (0.31, 4.43)	0.87 (0.23, 3.16)	Dur	2.02 (0.14, 28.46)	0.89 (0.06, 12.08)	0.23 (0.05, 1.05)
1.78 (0.38, 8.38)	1.38 (0.29, 6.53)	2.02 (0.42, 9.45)	1.86 (0.31, 10.8)	2.44 (0.50, 11.54)	1.24 (0.26, 5.65)	1.34 (0.23, 7.75)	1.97 (0.33, 11.78)	2.82 (0.46, 17.09)	12.48 (1.58, 117.21)	1.02 (0.22, 4.86)	1.11 (0.25, 5.70)	0.84 (0.18, 4.01)	0.96 (0.20, 4.85)	Ave	0.44 (0.02, 9.10)	0.11 (0.01, 0.95)
0.99 (0.21, 4.72)	0.77 (0.17, 3.65)	1.12 (0.25, 5.28)	1.03 (0.17, 6.12)	1.35 (0.28, 6.45)	0.69 (0.15, 3.17)	0.74 (0.13, 4.33)	1.10 (0.18, 6.53)	1.57 (0.26, 9.36)	6.96 (0.88, 64.89)	0.57 (0.13, 2.70)	0.62 (0.14, 3.17)	0.54 (0.10, 2.23)	0.54 (0.11, 2.67)	0.56 (0.10, 3.29)	Cem	0.25 (0.03, 2.08)
2.50 (1.00, 6.28)	1.94 (0.79, 4.75)	2.83 (1.16, 6.93)	2.59 (0.74, 8.97)	3.41 (1.33, 8.53)	1.73 (0.72, 4.17)	1.87 (0.54, 6.37)	2.76 (0.78, 9.64)	3.94 (1.09, 14.33)	17.33 (3.41, 111.33)	1.43 (0.60, 3.52)	1.55 (0.65, 4.22)	1.18 (0.49, 2.94)	1.35 (0.55, 3.62)	1.40 (0.40, 4.96)	2.51 (0.72, 8.77)	Che

注：右上角为grade ≥ 3 ADR，左下角为ORR。

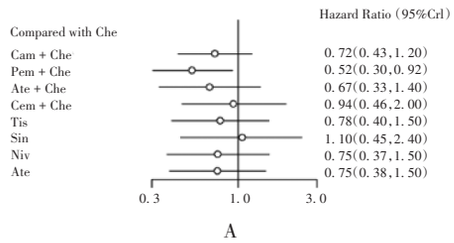
图6 ORR与grade ≥ 3 ADR的网状Meta分析结果

Note: The upper right corner refers to grade ≥ 3 ADR, and the lower left corner refers to ORR.

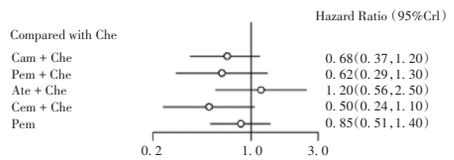
Fig. 6 Network Meta - analysis of ORR and grade ≥ 3 ADR

析的*DIC*值分别为68.20和46.13，差异值＞5，故采用随机效应模型评估各种干预措施的相对疗效。网状Meta分析结果显示，与Che比较，仅替雷利珠单抗联合化疗(Tis + Che)[*HR* = 0.58，95%Crl (0.35，0.95)]，Sin + Che [*HR* = 0.51，95%Crl (0.32，0.82)]，Cam + Che[*HR* = 0.45，95%Crl (0.29，0.72)]，舒格利单抗联合化疗(Sug + Che)[*HR* = 0.48，95%Crl (0.25，0.91)]，Pem + Che [*HR* = 0.50，95%Crl (0.31，0.82)]5种干预措施可显著延长PFS。详见图5。

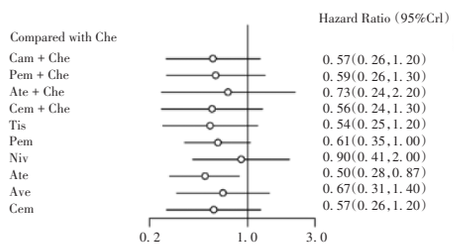
ORR：共24篇文献报道[10-11,13-34]，涉及17种干预措施(见图4 C)，改善ORR的优劣排序见表2。因纳入研究不存在整体不一致，固定效应模型和随机效应模型分析的*DIC*分别为121.26和99.50，差异值＞5，故采用随机效应模型评估各种干预措施的相对疗效。网状Meta分析结果显示，与Che比较，Tis + Che[*OR* = 2.50，95%Crl (1.00，6.28)]，Cam + Che[*OR* = 2.83，95%Crl (1.16，6.93)]，Pem + Che[*OR* = 3.41，95%Crl (1.33，8.53)]，Tis [*OR* = 3.94，95%Crl (1.09，14.33)]，Sin [*OR* = 17.33，95%Crl (3.41，111.33)]5种干预措施可显著提高ORR。详见图6。



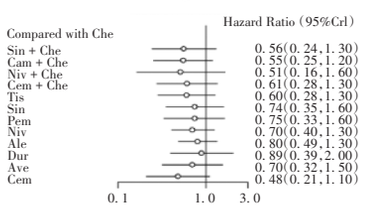
A



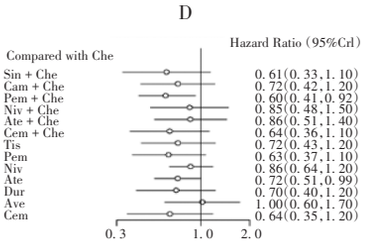
B



C



D



E

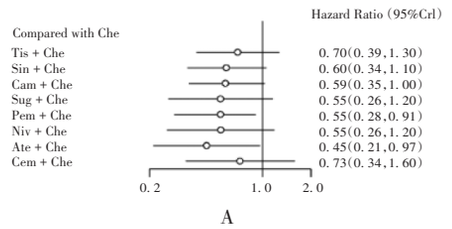
A. TPS < 1%　B. TPS = 1%～49%　C. TPS ≥ 50%
D. sq - NSCLC　E. nsq - NSCLC

图 7　OS 的亚组 Meta 分析森林图

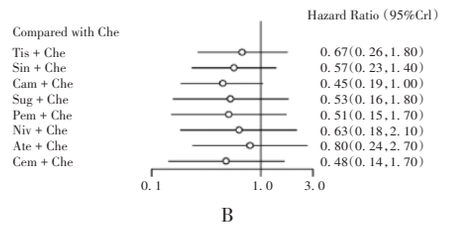
A. TPS < 1%　B. TPS = 1% - 49%　C. TPS ≥ 50%
D. sq - NSCLC　E. nsq - NSCLC

Fig. 7　Forest plot of subgroup Meta - analysis for OS

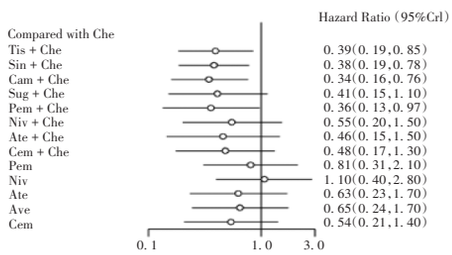
亚组分析：以 PD - L1 肿瘤细胞阳性比例分数（TPS，< %，1%～49%，≥ 50%）及病理类型［鳞状 NSCLC（sq - NSCLC）和非鳞状 NSCLC（nsq - NSCLC）］对 NSCLC 患者的 OS，PFS，ORR 进行亚组分析，结果见图 7 至图 9。可见，与 Che 比较，Tis + Che 仅在 PD - L1 TPS ≥ 50% 的患者中能显著延长 PFS，改善 sq - NSCLC 和 nsq - NSCLC 患者 OS，PFS，ORR 的疗效均相当；各 PD - 1 / PD - L1 抑制剂间无论单药还是联合化疗，改善 NSCLC 患者的 OS，PFS，ORR 的疗效均相当。



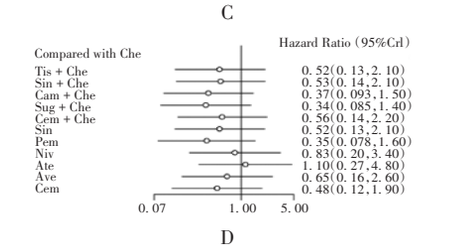
A



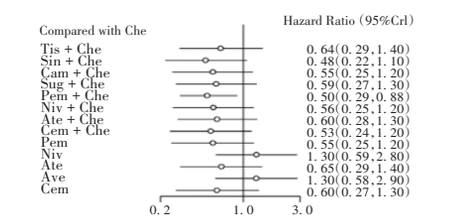
B



C



D



E

A. TPS < 1%　B. TPS = 1%～49%　C. TPS ≥ 50%
D. sq - NSCLC　E. nsq - NSCLC

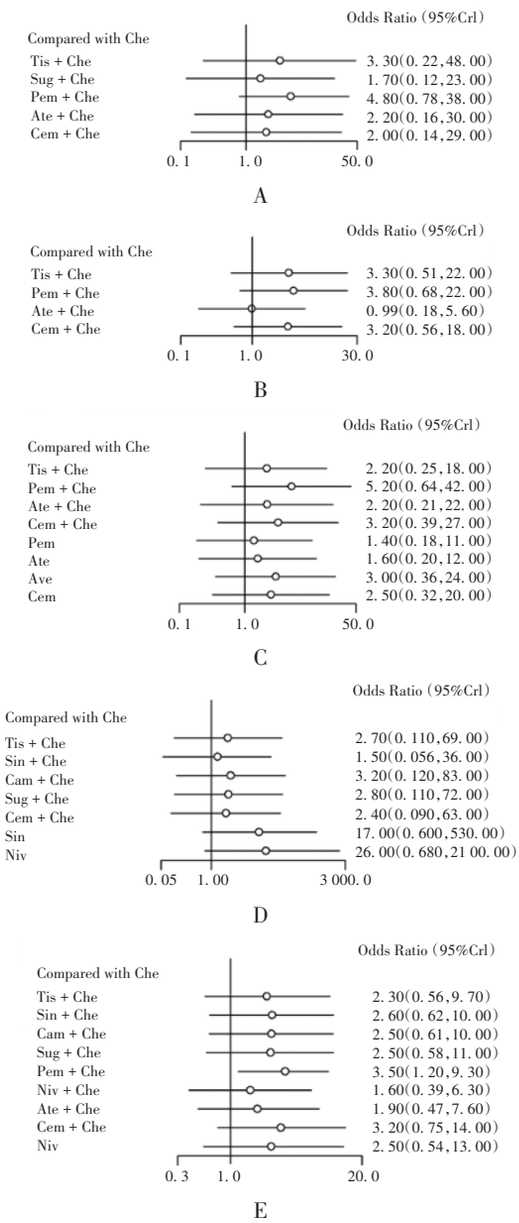
图 8　PFS 的亚组 Meta 分析森林图

A. TPS < 1%　B. TPS = 1% - 49%　C. TPS ≥ 50%
D. sq - NSCLC　E. nsq - NSCLC

Fig. 8　Forest plot of subgroup Meta - analysis for PFS

2.3.3　安全性

grade ≥ 3 ADR：共 25 篇文献报道了 grade ≥ 3 ADR[10-34]，涉及 17 种干预措施（见图 4 D），grade ≥ 3 ADR 发生风险的优劣排序见表 2。因纳入研究不存在整体不一致，固定效应模型和随机效应模型分析的 *DIC* 值分别为 90.95 和 91.97，差异值 < 5，故采用固定效应模型评估各种干预措施的安全性。网状 Meta 分析结果显示，与 Che 比较，仅 Tis［*OR* = 0.09，95%Crl（0.01，0.80）］，纳武利尤单抗（Niv）［*OR* = 0.16，95%Crl（0.04，0.74）］，阿维鲁单抗（Ave）［*OR* = 0.11，95%Crl

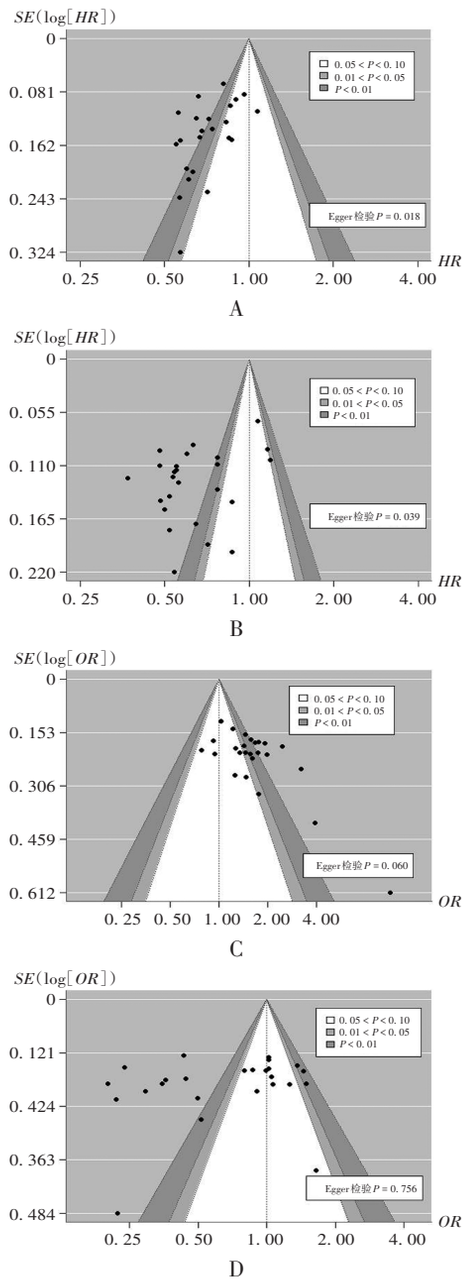


A. TPS < 1%　B. TPS = 1%～49%　C. TPS ≥ 50%
D. sq - NSCLC　E. nsq - NSCLC

图 9　ORR 的亚组 Meta 分析森林图

A. TPS < 1%　B. TPS = 1% - 49%　C. TPS ≥ 50%
D. sq - NSCLC　E. nsq - NSCLC

Fig. 9　Forest plot of subgroup Meta - analysis for ORR



A. OS　B. PFS　C. ORR　D. grade ≥ 3 ADR

图 10　4 种结局指标发表偏倚倒漏斗图

A. OS　B. PFS　C. ORR　D. grade ≥ 3 ADR

Fig. 10　Inverted funnel plot of publication bias for four outcome indicators

(0. 01, 0. 95)]3 种干预措施可显著降低 grade ≥ 3 ADR 的发生率。详见图 6。

2. 4　发表偏倚

OS 和 PFS 的倒漏斗图中散点分布不对称，Eggers 检验 *P* 值分别为 0. 018 和 0. 039，提示结果存在一定发表偏倚；2 个倒漏斗图中均存在分布于漏斗图底部的散点，且分布不对称，提示研究结果可能受小样本效应影响。详见图 10 A 和图 10 B。ORR 和 grade ≥ 3 ADR 的倒漏斗图中散点分布相当对称，Eggers 检验 *P* 值分别为 0. 060 和 0. 756，提示存在发表偏倚的可能性较小。详见图 10 C 和图 10 D。

3　讨论

本研究结果显示，PD - 1 / PD - L1 抑制剂联合化疗作为晚期或转移性 NSCLC 患者的一线治疗较单纯化疗能给患者带来更多显著的临床获益，其中 Cam + Che 和 Pem + Che 的临床疗效最显著。纳入的 8 种联合方案中，与 Che 相比，仅 Cam + Che 和 Pem + Che 2 种干预措施可同时改善 NSCLC 患者的 OS，PFS，ORR；Tis + Che 可同时改善患者的 PFS 和 ORR；Sug + Che 仅可改善患者的 PFS。纳入的 9 种单药方案中，与 Che 相比，仅 Tis 和

Sin可显著改善患者的ORR，改善患者OS和PFS的疗效相当（$P>0.05$）。亚组分析结果显示，与Che相比，Tis + Che仅在PD - L1 TPS ≥ 50%的患者中能显著延长PFS。虽在sq - NSCLC患者中，PD - 1 / PD - L1抑制剂与Che改善患者OS，PFS，ORR的疗效相当，但OS，PFS，ORR的绝对值提示PD - 1 / PD - L1抑制剂可能给sq - NSCLC患者带来临床获益。Tis + Che和Tis与其他PD - 1 / PD - L1抑制剂单药或联合化疗改善NSCLC患者OS，PFS，ORR的疗效相当（$P>0.05$）。安全性方面，PD - 1 / PD - L1抑制剂中安全性最高的为Tis单药治疗，PD - 1 / PD - L1抑制剂联合化疗较单药化疗的grade ≥ 3 ADR发生率更高。

本研究结果与HERBST等[9]的研究结果部分一致，均显示PD - 1 / PD - L1抑制剂可显著改善nsq - NSCLC患者的临床结局，对sq - NSCLC患者临床获益不显著。但HERBST等[9]的研究结果显示除上述联合方案外，Pem和Cem较Che也能显著改善PD - L1 TPS ≥ 50% NSCLC患者的OS，PFS，ORR，可能是由于本研究中多纳入RATIONALE303，RATIONALE307等研究，导致网状Meta分析结果存在部分差异。另外，高婧[7]的研究结果显示，Tis + Che和Pem + Che均能显著延长sq - NSCLC患者的PFS，且无论PD - L1 TPS评分如何，其均能显著延长sq - NSCLC患者的PFS。本研究结果与此不一致，可能是与纳入研究不同相关，由于本研究中关注的重点是替雷利珠单抗较其他PD - 1 / PD - L1抑制剂治疗NSCLC的有效性和安全性，故未纳入细胞毒性T淋巴细胞相关蛋白4（CTLA - 4）抑制剂的相关数据。而高婧[7]关注的是一线免疫治疗用于sq - NSCLC患者的疗效，除纳入PD - 1 / PD - L1抑制剂相关研究外，还纳入多项关于CTLA - 4抑制剂的研究。本研究结果显示，仅Tis，Niv，Ave的grade ≥ 3 ADR发生率显著低于Che（$P<0.05$），提示在PD - 1 / PD - L1抑制剂中这3种药物的安全性相对较高。另外，Tis的ADR发生率虽与Niv和Ave相当，但*OR*绝对值提示Tis的安全性可能更好。

本研究存在以下局限性：1）纳入研究有限，除干预措施Pem + Che有多项研究纳入外，其他干预措施仅1～2项研究，样本量少，可能引入偏倚，且本研究中倒漏斗图显示存在一定小样本效应。2）缺乏“头对头”试验。

综上所述，PD - 1 / PD - L1抑制剂联合化疗的有效率更高，但ADR发生率也更高。与其他PD - 1 / PD - L1抑制剂相比，替雷利珠单抗单药治疗或联合化疗改善NSCLC患者OS，PFS，ORR的疗效均相当，但其不受PD - L1 TPS评分影响，且安全性更好。

参考文献

[1] SIEGEL RL, MILLER KD, FUCHS HE, et al. Cancer Statistics, 2021[J]. CA Cancer J Clin, 2021, 71 (1): 7 - 33.
[2] SUNG H, FERLAY J, SIEGEL RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries[J]. CA Cancer J Clin, 2021, 71(3): 209 - 249.
[3] ROSELL R, KARACHALIOU N. Large - scale screening for somatic mutations in lung cancer[J]. Lancet, 2016, 387(10026): 1354 - 1356.
[4] DAHAN R, SEGA E, ENGELHARDT J, et al. FcγRs Modulate the Anti - tumor Activity of Antibodies Targeting the PD - 1 / PD - L1 Axis[J]. Cancer Cell, 2015, 28(3): 285 - 295.
[5] ZHANG T, SONG X, XU L, et al. The binding of an anti - PD - 1 antibody to FcγRI has a profound impact on its biological functions[J]. Cancer Immunol Immunother, 2018, 67(7): 1079 - 1090.
[6] 张珊珊. 免疫抑制剂治疗肺癌有效性与安全性的网状Meta分析[D]. 兰州：兰州大学，2021.
[7] 高　婧. 晚期鳞状非小细胞肺癌一线免疫治疗疗效与安全性评价[D]. 济南：山东大学，2021.
[8] 丁妲之，祝伟伟，杨　洋，等. 程序性死亡受体 - 1抑制剂安全性的网状Meta分析[J]. 中国药学杂志，2021，56(21)：1770 - 1779.
[9] HERBST R, JASSEM J, ABOGUNRIN S, et al. A Network Meta - Analysis of Cancer Immunotherapies Versus Chemotherapy for First - Line Treatment of Patients with Non - Small Cell Lung Cancer and High Programmed Death - Ligand 1 Expression[J]. Front Oncol, 2021, 11: 676732.
[10] LANGER CJ, GADGEEL SM, BORGHAEI H, et al. Carboplatin and pemetrexed with or without pembrolizumab for advanced, non - squamous non - small - cell lung cancer: a randomised, phase 2 cohort of the open - label KEYNOTE - 021 study[J]. The Lancet Oncology, 2016, 17(11): 1497 - 1508.
[11] RECK M, RODRÍGUEZ - ABREU D, ROBINSON AG, et al. Pembrolizumab versus chemotherapy for PD - L1 - positive non - small - cell lung cancer[J]. New England Journal of Medicine, 2016, 375(19): 1823 - 1833.
[12] CARBONE DP, RECK M, PAZ - ARES L, et al. First - line nivolumab in stage Ⅳ or recurrent non - small - cell lung cancer[J]. New England Journal of Medicine, 2017, 376(25): 2415 - 2426.
[13] BARLESI F, VANSTEENKISTE J, SPIGEL D, et al. Avelumab versus docetaxel in patients with platinum - treated advanced non - small - cell lung cancer (JAVELIN Lung 200): an open - label, randomised, phase 3 study[J]. The Lancet Oncology, 2018, 19(11): 1468 - 1479.
[14] GANDHI L, RODRÍGUEZ - ABREU D, GADGEEL S, et al. Pembrolizumab plus chemotherapy in metastatic non - small -

cell lung cancer[J]. New England Journal of Medicine, 2018, 378(22): 2078 - 2092.
[15] MOK TSK, WU YL, KUDABA I, et al. Pembrolizumab versus chemotherapy for previously untreated, PD - L1 - expressing, locally advanced or metastatic non - small - cell lung cancer (KEYNOTE - 042): a randomised, open - label, controlled, phase 3 trial[J]. The Lancet, 2019, 393(10183): 1819 - 1830.
[16] WU YL, LU S, CHENG Y, et al. Nivolumab versus docetaxel in a predominantly Chinese patient population with previously treated advanced NSCLC: CheckMate 078 randomized phase Ⅲ clinical trial[J]. Journal of Thoracic Oncology, 2019, 14(5): 867 - 875.
[17] PLANCHARD D, REINMUTH N, ORLOV S, et al. ARCTIC: durvalumab with or without tremelimumab as third - line or later treatment of metastatic non - small - cell lung cancer[J]. Annals of Oncology, 2020, 31(5): 609 - 618.
[18] HERBST RS, GIACCONE G, DE MARINIS F, et al. Atezolizumab for first - line treatment of PD - L1 - selected patients with NSCLC[J]. New England Journal of Medicine, 2020, 383(14): 1328 - 1339.
[19] RIZVI NA, CHO BC, REINMUTH N, et al. Durvalumab with or without tremelimumab vs standard chemotherapy in first - line treatment of metastatic non - small cell lung cancer: the MYSTIC phase 3 randomized clinical trial[J]. JAMA Oncology, 2020, 6(5): 661 - 674.
[20] NISHIO M, BARLESI F, WEST H, et al. Atezolizumab plus chemotherapy for first - line treatment of nonsquamous NSCLC: results from the randomized phase 3 IMpower132 trial[J]. Journal of Thoracic Oncology, 2021, 16(4): 653 - 664.
[21] YANG Y, WANG Z, FANG J, et al. Efficacy and safety of sintilimab plus pemetrexed and platinum as first - line treatment for locally advanced or metastatic nonsquamous NSCLC: a randomized, double - blind, phase 3 study (Oncology pRogram by InnovENT anti - PD - 1 - 11)[J]. Journal of Thoracic Oncology, 2020, 15(10): 1636 - 1646.
[22] SEZER A, KILICKAP S, GÜMÜŞ M, et al. Cemiplimab monotherapy for first - line treatment of advanced non - small - cell lung cancer with PD - L1 of at least 50%: a multicentre, open - label, global, phase 3, randomised, controlled trial[J]. The Lancet, 2021, 397(10274): 592 - 604.
[23] SUGAWARA S, LEE JS, KANG JH, et al. Nivolumab with carboplatin, paclitaxel, and bevacizumab for first - line treatment of advanced nonsquamous non - small - cell lung cancer[J]. Annals of Oncology, 2021, 32(9): 1137 - 1147.
[24] ZHOU C, CHEN G, HUANG Y, et al. Camrelizumab plus carboplatin and pemetrexed versus chemotherapy alone in chemotherapy - naive patients with advanced non - squamous non - small - cell lung cancer (CameL): a randomised, open - label, multicentre, phase 3 trial[J]. The Lancet Respiratory Medicine, 2021, 9(3): 305 - 314.
[25] WANG J, LU S, YU X, et al. Tislelizumab plus chemotherapy *vs* chemotherapy alone as first - line treatment for advanced squamous non - small - cell lung cancer: a phase 3 randomized clinical trial[J]. JAMA Oncology, 2021, 7(5): 709 - 717.
[26] ZHOU C, WU L, FAN Y, et al. Sintilimab plus platinum and gemcitabine as first - line treatment for advanced or metastatic squamous NSCLC: results from a randomized, double - blind, phase 3 trial (ORIENT - 12)[J]. Journal of Thoracic Oncology, 2021, 16(9): 1501 - 1511.
[27] LU S, WANG J, YU Y, et al. Tislelizumab plus chemotherapy as first - line treatment for locally advanced or metastatic nonsquamous NSCLC (RATIONALE 304): a randomized phase 3 trial[J]. Journal of Thoracic Oncology, 2021, 16(9): 1512 - 1522.
[28] SHI Y, WU L, YU X, et al. Sintilimab versus docetaxel as second-line treatment in advanced or metastatic squamous non-small-cell lung cancer: an open-label, randomized controlled phase 3 trial (ORIENT - 3)[J]. Cancer Communications, 2022, 42(12): 1314 - 1330.
[29] PETERS S, DZIADZIUSZKO R, MORABITO A, et al. Atezolizumab versus chemotherapy in advanced or metastatic NSCLC with high blood - based tumor mutational burden: primary analysis of BFAST cohort C randomized phase 3 trial[J]. Nature Medicine, 2022, 28(9): 1831 - 1839.
[30] GOGISHVILI M, MELKADZE T, MAKHARADZE T, et al. Cemiplimab plus chemotherapy versus chemotherapy alone in non - small cell lung cancer: a randomized, controlled, double - blind phase 3 trial[J]. Nature Medicine, 2022, 28(11): 2374 - 2380.
[31] REN S, CHEN J, XU X, et al. Camrelizumab plus carboplatin and paclitaxel as first - line treatment for advanced squamous NSCLC (CameL - Sq): a phase 3 trial[J]. Journal of Thoracic Oncology, 2022, 17(4): 544 - 557.
[32] FORDE PM, SPICER J, LU S, et al. Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer[J]. New England Journal of Medicine, 2022, 386(21): 1973 - 1985.
[33] ZHOU C, WANG Z, SUN Y, et al. Sugemalimab versus placebo, in combination with platinum - based chemotherapy, as first - line treatment of metastatic non - small - cell lung cancer (GEMSTONE - 302): interim and final analyses of a double - blind, randomised, phase 3 clinical trial[J]. The Lancet Oncology, 2022, 23(2): 220 - 233.
[34] ZHOU C, HUANG D, FAN Y, et al. Tislelizumab versus docetaxel in patients with previously treated advanced NSCLC (RATIONALE - 303): A phase 3, open - label, randomized controlled trial[J]. Journal of Thoracic Oncology, 2023, 18(1): 93 - 105.

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