

NSCLC PD-L1 >1% - Nivolumab/Ipilimumab

Low Value Regimen Rationale

- Nivolumab+ipilimumab is considered a low value regimen for NSCLC when PD-L1 >1%
- Progression free survival (PFS) and Overall Survival (OS) are similar for nivolumab+ipilimumab (with or without chemotherapy) compared to other immunotherapy agents (with or without chemotherapy) in the initial treatment setting
- In the absence of head-to-head trials, a matching-adjusted indirect comparison demonstrated clinical benefit for immunotherapy (pembrolizumab)+chemotherapy compared to nivolumab+ipilimumab in patients with PD-L1 >1% across multiple endpoints
- The risk of financial toxicity is much greater with nivolumab+ipilimumab compared to other immunotherapy agents (annual cost of greater than \$300K for two IO agents).
- Nivolumab+ipilimumab displays clinical benefit and remains a treatment option for patients with PD-L1<1%

RECOMMENDED ALTERNATIVES

- Non-small cell lung cancer
 - Initial therapy, Non-squamous and Squamous (PD-L1 ≥50%)
 - Pembrolizumab (Keytruda)
- Initial therapy, Squamous (PD-L1 1-49%)
 - Carboplatin (Paraplatin) + Paclitaxel (Taxol) + Pembrolizumab (Keytruda)
- Initial therapy, Non-squamous (PD-L1 1-49%)
 - Carboplatin (Paraplatin) + Pemetrexed (Alimta, Pemfexy) + Pembrolizumab (Keytruda)

Data Summary

Study	Regimen	mOS PDL1 <1%	mOS PDL1 1-49%	mOS PDL 1 >50%	mPFS PDL1 <1%	mPFS PDL1 1-49%	mPFS PDL1 >50%	Comment
KEYNOTE -407	Pembrolizumab + carboplatin + paclitaxel or nab-paclitaxel	10.7% vs 13.1% 15 mo vs 11 mo	20.6% vs 7.6% 18 mo vs 13.1 mo	23.3% vs 8.3% 19.9 mo vs 11.5 mo	7.1 mo vs 6.7 mo	8.2 mo vs 6 mo	8.3 mo vs 4.2 mo	5 year follow up
KEYNOTE -189	Pembrolizumab + pemetrexed + cisplatin or carboplatin	9.6% vs 5.3% 17.2 mo vs 10.2 mo	19.8% vs 7.7% 21.8 mo vs 12.1 mo	29.6% vs 21.4% 27.7 mo vs 10.1 mo	6.2 mo vs 5.1 mo	9.4 mo vs 4.9 mo	11.3 mo vs 4.8 mo	5 year follow up (mPFS was null in control arm)
CHECKMATE 227	Nivolumab + Ipilimumab	19% vs 7% 17.4 mo vs 12.2 mo	24% vs 14% (Includes patients with PD-L1 >1% or more) 17.1 mo vs 14.9 mo		5.1 mo vs 4.7 mo	5.1 mo vs 5.6 mo (Includes patients with PD-L1 >1% or more)		5 year follow up
CHECKMATE 9LA	Nivolumab + Ipilimumab + chemotherapy	23% vs 13% 17.7 mo vs 9.8 mo	21% vs 16% (Includes patients with PD-L1 >1% or more) 15.8 mo vs 10.9 mo		12% vs 3%	12% vs 6% (Includes patients with PD- L1 >1% or more)		5 year follow up
IMPOWER 150	Atezolizumab + bevacizumab + carboplatin + paclitaxel	ACP: 14.8 mo vs 14.1 mo ABCP: 16.9 mo vs 14.1 mo	ACP: 24 mo vs 16 mo ABCP: 23 mo vs 16 mo	ACP: 26.3 mo vs 15 mo ABCP: 30 mo vs 15 mo	NR “similar to OS trends”			39.8 months (~3 year) follow up.
EMPOWER- Lung 3	Cemiplimab- rwlc + chemotherapy	12.8 mo vs 14.2 mo	23.2 mo vs 12 mo	23.5 mo vs 14.4 mo	6.2 mo vs 4.4 mo	8.2 mo vs 6.1 mo	10.8 mo vs5.5 mo	2 year follow up
POSEIDON	Trem + Durva + CT Durva + CT CT	T+D+CT: 14 mo (32.9%) D+CT: 13.3 mo (29.6%) CT: 11.7 mo (22%)			T+D+CT: 6.2 mo D+CT: 5.5 mo CT: 4.8 mo			OS reported as 24 month PFS reported as 12 month
Matching adjusted indirect comparison	Pemrbolizumab +chemo vs Nivolumab+ ipilimumab	Pembro+Chemo: 23.7 mo Nivo+ipi: 16.9 mo			Pembro+Chemo: 10.7 mo Nivo+ipi: 5 mo			Sub-group analyses in PD-L1 TPS ≥50% and 1–49% patients were consistent with results in the overall PD-L1 TPS ≥1% population

Immunotherapy Agent	Quarterly Cost	Annual Cost
Nivolumab + ipilimumab (nivolumab 360mg every 3 weeks + ipilimumab 1mg/kg every 6 weeks)	\$75,790	\$303,150
Pembrolizumab (200mg every 3 weeks)	\$47,000	\$188,100
Carboplatin + paclitaxel + pembrolizumab (4 cycles) fb pembrolizumab maintenance	\$47,350	\$188,400
Carboplatin + pemetrexed + pembrolizumab (4-6 cycles) fb pemetrexed + pembrolizumab maintenance	\$51,490	\$205,400
Atezolizumab (1200mg every 3 weeks)	\$42,600	\$170,250
Cemiplimab (350mg every 3 weeks)	\$40,420	\$161,700

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